acetoxy-6α-methylprogesterone, m.p. 197–200°; λ_{max} 240 mμ (ε 15,400), 289 mμ (ε 2,140).[21]

Anal. Calcd. for $C_{24}H_{33}FO_4$: C, 71.26; H, 8.22. Found: C, 71.79; H, 8.18.

(21) A purer sample of this same material (identity established by mixed m.p.'s and infrared spectra) made by an alternate procedure (to be reported later) had the following physical constants: m.p. 198–200°, $[\alpha]_D$ +40.5°; λmax. 240 mμ (ε 15,700), 290 mμ (ε 525). Found: C, 71.35; H, 8.19. The molecular rotatory contribution of the 6-methyl group, $M_D(XX) - M_D(Xa) = -37°$, establishes its α-configuration.

Acknowledgment.—We wish to thank Dr. R. L. Elton of the Biological Research Division of G. D. Searle and Company for the pharmacological data reported herein. We are indebted to Dr. R. T. Dillon and the Analytical Division of the same company for the analytical and optical data reported.

CHICAGO 80, ILL.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, MASSACHUSETTS INSTITUTE OF TECHNOLOGY]

Terpenes. XI.[1] The Total Synthesis of Maaliol

BY R. B. BATES,[2] G. BÜCHI, TERUO MATSUURA[3] AND R. R. SHAFFER

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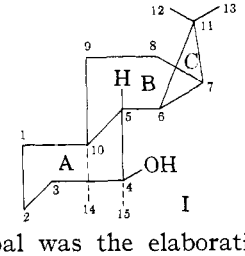
The recently proposed structure I for the tricyclic sesquiterpene alcohol maaliol has been confirmed by total synthesis. Addition of hydrobromic acid to (−)-epi-α-cyperone (IX) followed by dehydrobromination with potassium hydroxide produced the tricyclic key intermediate (XI). Wolff–Kishner reduction yielded a mixture of hydrocarbons which on oxidation with selenium dioxide gave some of the aldehyde XX. Reduction according to Wolff–Kishner followed by osmylation to the diol XXII, tosylation and hydride reduction yielded maaliol (I). A second synthesis was initiated by lithium–ammonia reduction of XI which gave an interesting array of products of which the alcohol XXV was transformed to maaliol (I) in the following manner: Acetylation followed by pyrolysis and osmium tetroxide oxidation produced, besides other products, the desired glycol XLVII. This synthesis was completed by oxidation to the acyloin and Wolff–Kishner reduction. The main synthetic paths are marked by heavy arrows.

We have recently proposed[1] structure I for the tricyclic sesquiterpene alcohol maaliol and now wish to report its synthesis.

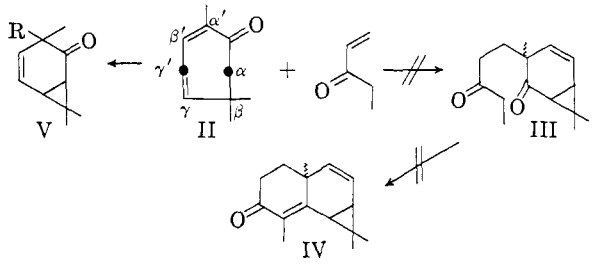


I

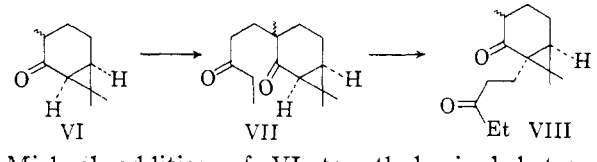
Our first goal was the elaboration of the unsaturated ketone XI for which we considered three approaches: (1) direct synthesis from the monocyclic precursor eucarvone; (2) introduction of ring A by Robinson–Mannich ring extension of the bicyclic carone; (3) ring closure of a suitable derivative of epi-α-cyperone to provide ring C. We initiated our investigations with a study of the Michael reaction of eucarvone (II) with ethyl vinyl ketone which we expected to yield the tricyclic ketone IV already containing the complete carbon skeleton of maaliol. This particular approach to the problem was patterned after the investigations of Corey and co-workers[4] who found that alkylation of eucarvone (II) leads to bicyclic (V) rather than monocyclic substitution products.

In practice the condensation of eucarvone (II) with ethyl vinyl ketone as well as with 1-chlorpentanone-3 yielded none of the desired products III and IV.

While the study of the synthesis of IV from the monocyclic eucarvone (II) was in progress we were



also investigating[5] the elaboration of its dihydroderivative XI from the bicyclic (−)-carone (VI).[6,7]



Michael addition of VI to ethyl vinyl ketone produced a bicyclic diketone (λ_{max}^{EtOH} 216 mμ, ε2790; $\nu_{max}^{CCl_4}$ 1721 (aliph. C=O), 1692 cm.$^{-1}$ (C=O conjugated with cyclopropane)) whose spectral properties are in excellent agreement with VII although the less likely alternative VIII is by no means excluded. Attempts to cyclize this diketone to a tricyclic unsaturated ketone led to recovered starting material. When efforts were made to effect cyclization at elevated temperatures, the diketone suffered retro-Michael cleavage and carone (VI) was the only isolable product.

We turn now to a discussion of the third approach which represents a convenient synthesis of the tricyclic ketone XI. It originated with (−)-epi-α-cyperone (IX) of known absolute configuration which is available in quantity by the elegant and reliable two-stage synthesis of Howe and Mc-

(1) Part X, G. Büchi, M. Schach v. Wittenau and D. M. White, THIS JOURNAL, **81**, 1968 (1959).

(2) National Institutes of Health postdoctoral fellow, 1957–1958.

(3) Visiting scientist from Osaka City University, Japan.

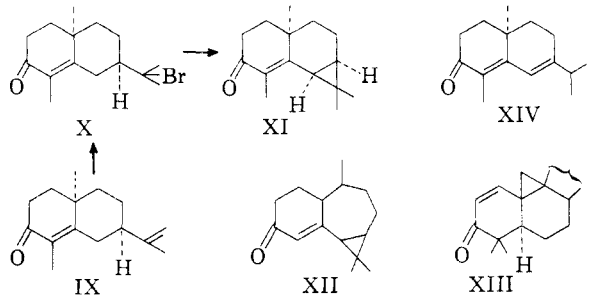
(4) E. J. Corey and H. J. Burke, THIS JOURNAL, **78**, 174 (1956); E. J. Corey, H. J. Burke and W. A. Remers, *ibid.*, **78**, 180 (1956).

(5) Richard R. Shaffer, B.Sc. Thesis, M. I. T., 1958.

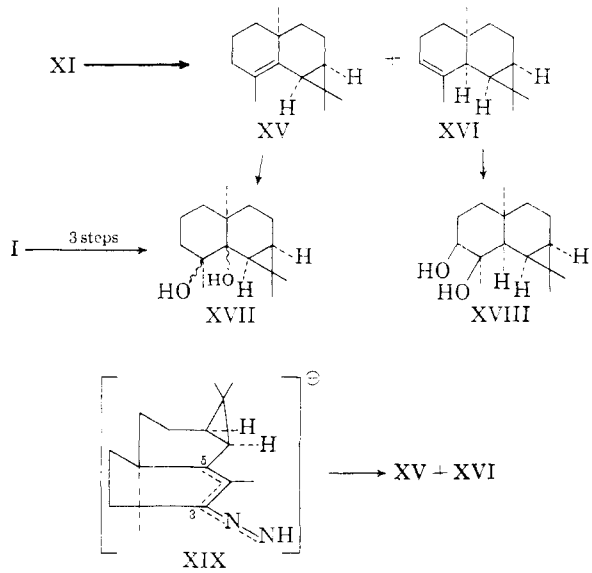
(6) G. Wagner, *Ber.*, **27**, 2270 (1894).

(7) A. v. Bayer, *ibid.*, **27**, 1919 (1894).

Quillin.[3] In analogy to the well-known synthesis of eucarvone from carvone, treatment of IX with hydrobromic acid in acetic acid solution produced a bromide (X) which was not further characterized. Dehydrobromination by treatment with hot potassium hydroxide in methanol gave XI, m.p. 68°, in 62% over-all yield. Contrary to carenone[9] which can revert easily to a monocyclic structure, XI is stable to basic reagents. The spectral properties of XI are of some interest. It had λ_{max}^{EtOH} 266 mμ, ε 13700, while its precursor IX had λ_{max}^{EtOH} 253 mμ.[8] The bathochromic shift of 13 mμ due to the conjugated cyclopropane ring compares favorably with that observed for the unsaturated ketone XII, λ_{max}^{EtOH} 254 mμ[10] (calculated ignoring cyclopropane conjugation 244 mμ), but less so with those for the ketone XIII, λ_{max}^{EtOH} 269 mμ[11] (cholest-1-en-3-one has λ_{max}^{EtOH} 230 mμ),[12] and 22-dihydroisosuprasterone-II[13] (λ_{max} 268 mμ; calcd. 244 mμ). The effect of the cyclopropane ring was also discernible in the spectrum of the 2,4-dinitrophenylhydrazone of XI which had λ_{max}^{EtOH} 400 mμ while the corresponding derivatives of α-cyperone[14] and (−)-β-cyperone (XIV)[14] have λ_{max}^{EtOH} 395 and 415 mμ, respectively.



Our first objective had thus been reached and it became necessary to remove the carbonyl group in XI. Wolff–Kishner reduction led to a mixture of olefins XV and XVI which could not be separated easily, but catalytic reduction over palladium revealed the presence of about 85% of the non-reducible tetrasubstituted olefin XV. Osmylation produced a mixture of two isomeric diols separable by chromatography. The major product was identical by melting point, mixed melting point, optical rotation and infrared spectrum with β-maalidiol (XVII) (configuration of glycol system not established) which we had previously encountered in our degradative work.[1] This correlation already demonstrated that the carbon skeleton of maaliol and both the relative and absolute configurations at C_6, C_7 and C_{10} are in fact as shown in I. The second diol was not identical with either of the diastereomeric *cis*-α-maalidiols and must therefore have been 5-iso-α-maalidiol (XVIII). The formation of two olefins in the Wolff–Kishner reduction can be attributed to



competitive irreversible discharge of the anion XIX by a proton at both C_3 and C_5.[15] For reasons to be discussed in the sequel, we believe XVI to be the thermodynamically more stable of the two diastereomeric $\Delta^{3,4}$-olefins. In these circumstances it became necessary to investigate the Wolff–Kishner reduction of the α,β-unsaturated aldehyde XX which should lead to γ-maaliene (XXI) with the A/B *trans* configuration because we had previously shown[1] that normaalione, also containing a trigonal center at C_4, was likewise more stable in that configuration. The desired aldehyde XX, λ_{max}^{EtOH} 227, 272 mμ, ε 5100, 9150,[16] was available by oxidation of crude XV with selenium dioxide[17] albeit in poor yield. Reduction led to a mixture of olefins XXI and XV which was directly oxidized to β-maalidiol (XVII) and γ-maalidiol (XXII) identical with samples obtained earlier by degradation of maaliol.[1] Consequently, proton addition from the C_5-β-side to the anion XXIV can indeed occur and this finding suggests strongly that the *cis*-decalin XVI was in fact the product of thermodynamic control. The Stuart–Briegleb model of XXI shows that osmium tetroxide should

(8) (a) R. Howe and F. J. McQuillin, *J. Chem. Soc.*, 2423 (1955); (b) 2670 (1956); (c) 1194 (1958).

(9) The mechanistic aspects of the carvone → eucarvone transformation have been discussed previously; A. Eschenmoser, Diss. E. T. H., Zürich, 1952, p. 28; E. E. v. Tamelen and G. T. Hildahl, THIS JOURNAL, **78**, 4405 (1956); E. E. v. Tamelen, J. McNary and F. A. Lornitzo, *ibid.*, **79**, 1231 (1957).

(10) M. Palmade and G. Ourisson, *Bull. soc. chim. France*, 886 (1958).

(11) D. S. Irvine, J. A. Henry and F. S. Spring, *J. Chem. Soc.*, 1316 (1955).

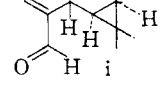
(12) A. Butenandt, L. Mamoli, H. Dannenberg, L.-W. Masch and J. Paland, *Ber.*, **72**, 1617 (1939).

(13) W. G. Dauben, I. Bell, T. W. Hutton, G. F. Laws, A. Rheiner, Jr., and H. Urscheler, THIS JOURNAL, **80**, 4116 (1958).

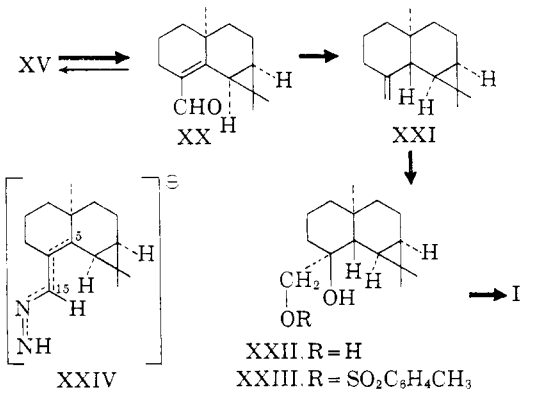
(14) D. H. R. Barton and E. J. Tarlton, *J. Chem. Soc.*, 3492 (1954).

(15) For pertinent literature concerning such reductions, see (a) W. Seibert, *Ber.*, **80**, 494 (1947); (b) R. Fischer, G. Lardelli and O. Jeger, *Helv. Chim. Acta*, **33**, 1335 (1950); (c) D. H. R. Barton, N. J. Holness and W. Klyne, *J. Chem. Soc.*, 2456 (1949); (d) R. B. Turner, R. Anliker, R. Helbling, J. Meier and H. Heusser, *Helv. Chim. Acta*, **38**, 411 (1955).

(16) The purity of this aldehyde cannot be guaranteed and it is conceivable that some i was present which should absorb in the neighborhood of 227 mμ. The wave length of the high intensity peak again appears to be influenced by the cyclopropane ring, because trisubstituted unsaturated aldehydes with one exocyclic double bond absorb at about 250 mμ.

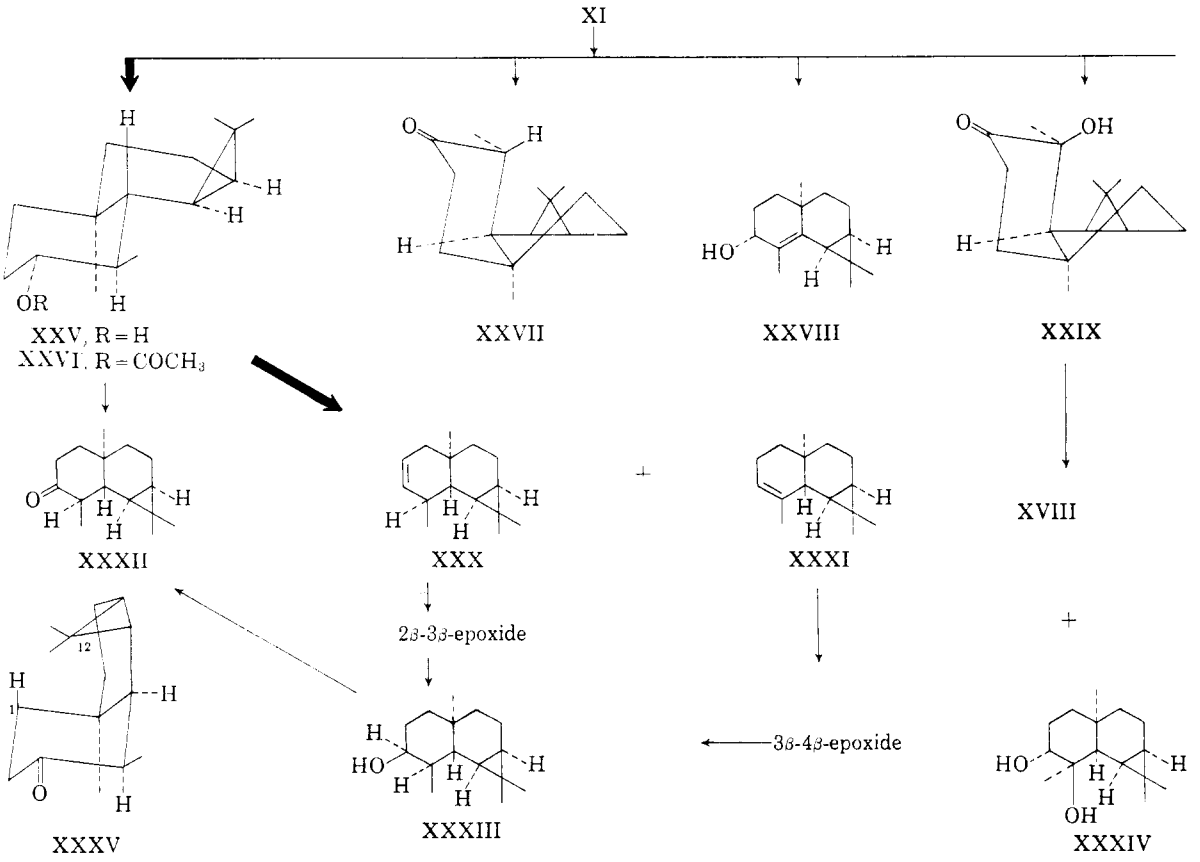


(17) *Cf.* the oxidations of ψ-taraxastene [G. Lardelli, H. K. Krüsi, O. Jeger and L. Ruzicka, *Helv. Chim. Acta*, **31**, 1815 (1948)] and of lupene-I [T. R. Ames, J. L. Beton, A. Bowers, T. G. Halsall and E. R. H. Jones, *J. Chem. Soc.*, 1905 (1954)].



attack from the β-side and we were confident that the tertiary hydroxyl group in XXII was equatorially oriented. γ-Maalidiol was subsequently converted to the monotosylate XXIII which upon hydride reduction yielded the desired maaliol (I) identical in melting point, mixed melting point, infrared spectrum and rotation with the natural product. Whether the final reduction was direct or passed through the intermediate epoxide is immaterial because both changes proceed with retention at C_4. Although the stereochemical arguments concerning the configurations at C_4 and C_5 seem reasonable, they are scarcely rigorous and we decided to prepare maaliol by a second route.

Reduction of the tricyclic ketone XI with lithium and ethanol in liquid ammonia[18] gave a mixture of substances from which we were able to isolate four in pure form. The major product was the desired saturated alcohol XXV. Its structure was assigned on the following basis: (a) Such reductions have been reported to give mainly the thermodynamically more stable epimer at the position β to the carbonyl group.[19] (b) The C–OH stretching vibration occurred at 1050 $cm.^{-1}$ while the corresponding acetate XXVI had a simple band at 1242 $cm.^{-1}$. Both properties are characteristic of equatorial alcohols.[20] (c) Oxidation of XXV with chromium trioxide yielded the ketone XXXII which was stable to hot alkali, and on base-catalyzed hydrogen–deuterium exchange 3 D atoms were introduced. The C_4-methyl thus had β-configuration which may suggest that the alcohol XXV also had this configuration at this center. The second product formed in the lithium–ammonia reduction was a saturated ketone which was not identical with XXXII and its stability to basic reagents furthermore suggested that it was not the C_4-epimer of XXXII either. On deuteration 3 H atoms were exchanged and structure XXVII is in agreement with these facts. The preferred conformation of this *cis*-decalin is that shown in XXVII rather than its competitor XXXV which is drastically destabilized by non-bonded interaction between C_1 and C_{12}. As a consequence the methyl group at C_4 probably has the α-configuration. The third substance was identified as the



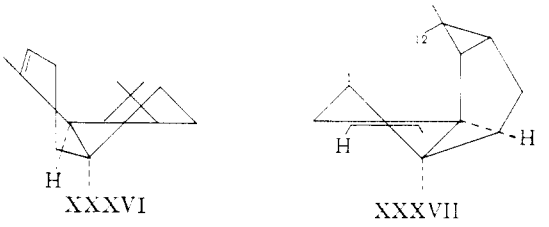
(18) A. L. Wilds and N. A. Nelson, THIS JOURNAL, **75**, 5360 (1953).

(19) D. H. R. Barton and C. H. Robinson, *J. Chem. Soc.*, 3045 (1954); C. Djerassi and G. H. Thomas, THIS JOURNAL, **79**, 3835 (1957).

(20) E. A. Braude and E. S. Waight in W. Klyne, "Progress in Stereochemistry," Vol. I, Butterworth, London, 1954, p. 166.

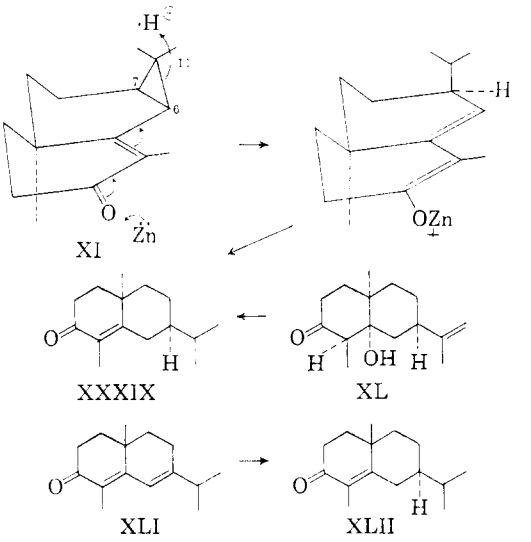
allylic alcohol XXVIII, λ_{210}^{EtOH} 8750 mμ (vinylcyclopropane) and the mode of formation tentatively suggests the presence of a pseudo-equatorial hydroxyl group. Incidentally, compound XXVIII was also available by reduction of the tricyclic ketone XI with lithium aluminum hydride. The fourth and last substance isolated from the lithium reduction had the unexpected composition $C_{15}H_{24}O_2$ and its infrared spectrum with bands at 3650 (free OH), 3521 (bonded OH) and 1709 cm.$^{-1}$ (C=O) was in agreement with an axial α-hydroxyketone structure.[26] Reduction with lithium aluminum hydride yielded 5-iso-α-maalidiol (XVIII) (34%) and the epimeric diol XXXIV (45%). The configuration of the hydroxyl group in the hydroxyketone XXIX could be deduced with some confidence from conformational considerations. If it is assumed that rings A and B exist preferentially in a chair and a pseudo-chair conformation, respectively, the conformer XXIX seems considerably more stable than its counterpart and consequently the hydroxyl group, known to be axial, has the C_4-β-OH configuration.

The preferential formation of the C_3-axial alcohol XXXIV on hydride reduction of the unhindered carbonyl function in XXIX can be attributed to intramolecular hydride transfer within the initially formed complex.[21] The configuration of 5-iso-α-maalidiol (XVIII), a substance which we had previously encountered, now follows but its formation on osmium tetroxide oxidation of 5-iso-α-maaliene (XVI) requires comment. A study of scale models of this olefin points strongly to the higher stability of XXXVI which is less crowded than its other conformer XXXVII, which is destabilized by non-bonded interaction between C_1 and C_{12}. Although the convex face[22] of XXXVI seems more accessible, the argument just presented indicates that the diol XVIII has the 3β-OH, 4β-OH configuration which, however, is thermodynamically more stable than XXXVIII assuming that a hydroxyl group is less space demanding than a methyl group.[23]



The lithium–ammonia reduction has thus yielded both *trans*- and *cis*-decalins,[24] but the mechanistic reasons for this are not clear.

The complexity of the lithium–ammonia reduction of the tricyclic ketone XI led us to investigate its reduction with zinc in hot acetic acid which proceeded smoothly to give an α,β-unsaturated ketone (λ_{max} 251 mμ, ε13300; $\nu_{max}^{CCl_4}$ 1667, 1613 cm.$^{-1}$ (cyclohexenone)) which was identical with XXXIX prepared by catalytic reduction of the aldol XL[8a] followed by base-catalyzed dehydration. The enantiomer of XXXIX had already been prepared by Howe and McQuillin[8b] by the same method. Reduction of XI with zinc, which involved cleavage of the cyclopropane ring, seems to be direct and a prior acid-catalyzed isomerization of XI to (−)-β-cyperone (XIV) is excluded because the starting material was not affected by hot acetic acid containing zinc acetate. Furthermore, partial reduction of (+)-β-cyperone (XLI) with zinc was reported[8b] to give the more stable α,β-unsaturated dihydroketone XLII with the isopropyl group in the $C_{7-\beta}$ configuration. A mechanistic interpretation of this interesting change involves approximately concerted nucleophilic attack on the carbonyl group by zinc and electrophilic attack on a σ-bond of the cyclopropane ring by a proton. Maximum overlap in the product-determining transition state demands the breaking of the $C_6 \rightarrow C_{11}$ rather than the C_6–C_7 bond. (*Cf.* XI → XXXIX.)



The second synthesis of maaliol was continued by pyrolysis of the acetate XXVI which yielded an equal mixture of the anticipated olefins XXX and XXXI. Epoxidation followed by reduction with lithium aluminum hydride led to only one isolable alcohol which was neither maaliol (I) nor the equatorial alcohol XXV. It was converted to the ketone XXXII by oxidation with chromium trioxide in pyridine and is therefore the axial alcohol XXXIII. Its formation can be rationalized if we assume that the mixture of epoxides consisted mainly of the 2β,3β-epoxide of XXX and the 3β,4β-epoxide of XXXI which according to the

(21) *Cf.* H. Henbest and B. Nicholls, *J. Chem. Soc.*, 221 (1959), and earlier papers.

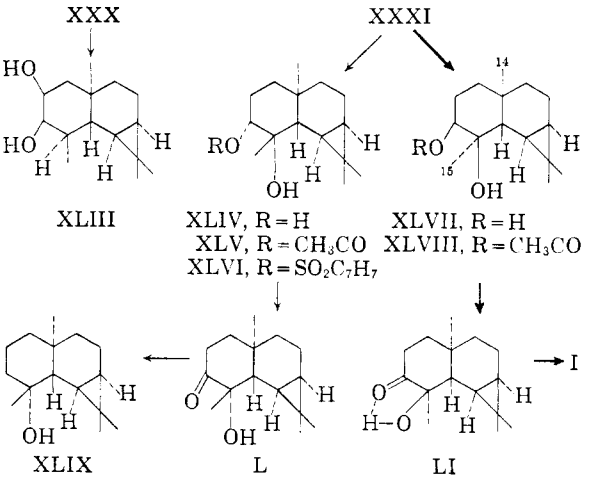
(22) For definition of the term, see R. B. Woodward, F. E. Bader, H. Bickel, A. J. Frey and R. W. Kierstead, *Tetrahedron*, **2**, 1 (1958).

(23) K. Biemann and J. Seibl, THIS JOURNAL, **81**, 3149 (1959); E. L. Eliel and C. A. Lukach, *ibid.*, **79**, 5986 (1957).

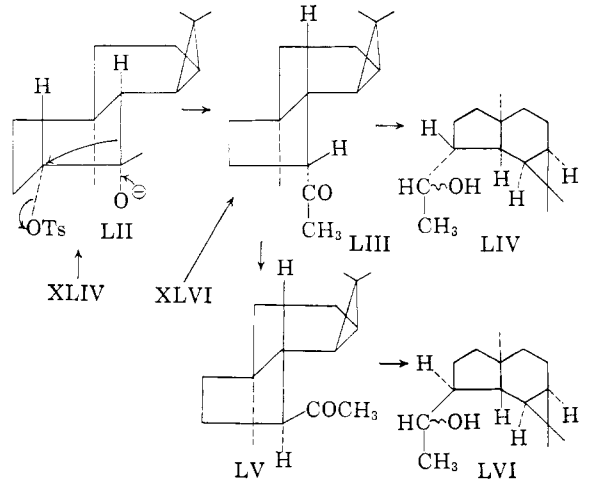
(24) *Cf.* the reduction of 10-methyl-$\Delta^{1(9)}$-octal-2-one; F. Sondheimer and D. Rosenthal, *ibid.*, **80**, 3995 (1958).

Fürst–Plattner rule would indeed both produce XXXIII on hydride reduction. Our hopes that hindrance to the approach of the nucleophilic reducing agent at C_4 would be sufficiently great to produce some maaliol (I) were thus not fulfilled.[25] Catalytic reduction of the mixture of epoxides also produced XXXIII as the sole isolable product.

We were thus compelled to effect the conversion of α-maaliene (XXXI) to maaliol by a different sequence. Oxidation of the olefin mixture XXX and XXXI with osmium tetroxide produced α-maalidiol (XLIV) and two new glycols. One of them was undoubtedly the disecondary diol XLIII to which we tentatively assigned the 2βOH, 3βOH configuration. Further oxidation of the second diol XLVII with chromium trioxide under carefully defined conditions gave an acyloin (LI) which exhibited infrared bands at 1715 (C=O) and a single peak at 3571 cm.$^{-1}$ (C=O. . . H–O–; intramolecular bonding). Oxidation of α-maalidiol (XLIV) under identical conditions yielded a second acyloin (L) which possessed infrared peaks at 1712 (C=O); 3650 (free OH) and 3546 cm.$^{-1}$ (intermolecular hydrogen bonded OH). The spectral characteristics of the two hydroxyketones demonstrate that LI has the hydroxyl group equatorially oriented while the epimer L contains an axial hydroxyl group.[26] The configurations of iso-α-maalidiol (XLVII) and α-maalidiol (XLIV) are thus established.[27] The appearance of two epimeric α-glycols in the osmium tetroxide oxidation of α-maaliene (XXXI) was not observed previously[1] and this transformation had to be reinvestigated. Dehydration of a larger quantity of natural maaliol (I) with acetic anhydride in boiling pyridine solution produced a mixture of liquid olefins which on reaction with osmium tetroxide followed by hydrolysis of the intermediary osmate esters did in fact yield XVII, XXII, α-maalidiol (XLIV) and iso-α-maalidiol (XLVII). The latter two glycols were isolated in a ratio of approximately 3:1 and used for the transformations to be described. Their monoacetates XLV and XLVIII had the anticipated spectral properties and were resistant to chromium trioxide in pyridine solution. The preferential formation of the epimer XLIV was again somewhat surprising because the molecular model of α-maaliene (XXXI) shows the β-face of the double bond to be more readily accessible. The resultant osmic ester of iso-α-maalidiol (XLVII) however is destabilized by C_{14}-methyl–C_{15}-methyl interaction and therefore the thermodynamically less stable epimer. This finding as well as the conversion of XVI to XVIII demonstrate that the configuration of a glycol, produced by osmium tetroxide oxidation of an olefin, cannot always be predicted simply by assuming attack of the electrophilic oxidizing agent from the less hindered side of the molecule. Our findings may suggest that the transition state actually has a geometry similar to that of the resulting osmate.[28]



We were now ready to effect the final transformation, which required the removal of the oxygen function at C_3, and decided to carry out exploratory work with the more readily available α-maalidiol (XLIV). On treatment with tosyl chloride it was smoothly converted to the monotosylate which, in analogy to the monoacetate XLV, was formulated as XLVI. We now hoped that hydrogenolysis of XLVI with lithium aluminum hydride would produce epi-maaliol (XLIX) but the product actually isolated, although an alcohol, was clearly different from epi-maaliol (XLIX), maaliol (I) and the two secondary alcohols XXV and XXXIII. It therefore seemed likely that the new alcohol had a different carbon skeleton and the molecular geometry of the monotosylate does indeed permit the rearrangement LII → LIII. Naturally, the initially formed methyl ketone was reduced to a mixture of the epimeric alcohols LIV. To test this hypothesis, the monotosylate XLVI was



treated with potassium *t*-butoxide and as anticipated the product formed was not an allylic alcohol but a ketone whose infrared spectrum with peaks

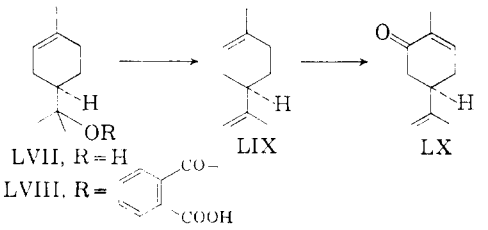
(25) The reduction of 5β,6β-epoxycholestane with lithium aluminum hydride gives 60% of the equatorial alcohol; A. S. Hallsworth and H. B. Henbest, *J. Chem. Soc.*, 4604 (1957).

(26) The infrared spectra of epimeric α-hydroxyketones were first interpreted by N. L. Wendler, D. Taub, S. Dobriner and D. Fukushima, THIS JOURNAL, **78**, 5027 (1956). An additional case was recently studied by A. R. H. Cole and G. T. A. Müller, *J. Chem. Soc.*, 1224 (1959).

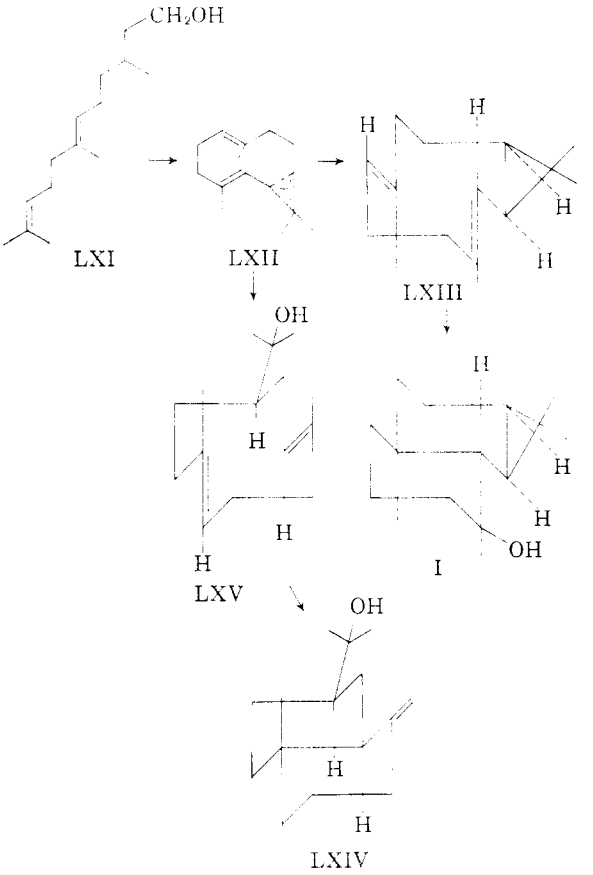
(27) The configurations at C_3 and C_4 of α-maalidiol, m.p. 129°, were incorrectly assigned in ref. 1, p. 1972.

(28) G. S. Hammond, THIS JOURNAL, **77**, 334 (1955).

at 1715 (C=O) and 1357 cm.$^{-1}$ (symmetrical CH_3 deformation of acetyl group) was in agreement with formula LV. Its reduction with lithium aluminum hydride yielded an alcohol which was different from LIV obtained by direct reduction of the monotosylate. Since the isomerization with potassium *t*-butoxide was carried out under conditions which should lead to equilibration of the initially formed ketone LIII to the more stable isomer LV, the final product of this sequence is undoubtedly LVI. It was not possible to prepare the tosylate of iso-α-maalidiol (XLVII) which has an axially oriented secondary hydroxyl group. We finally studied the removal of the carbonyl groups in the two acyloins L and LI by the method of Wolff–Kishner. Although we were aware of the fact that this procedure usually results in the formation of much olefin,[15c-d] we anticipated little competition from this elimination because our earlier studies indicated the highly strained nature of α-maaliene (XXXI) which would result from such eliminations. In the event, the major product formed in the reduction of L was epi-maaliol (XLIX) which we had encountered previously[1] and likewise LI was converted to maaliol (I). The synthetic product was identical by melting point, mixed melting point and infrared spectrum with natural material. It should now be remembered that our synthesis originated from L-(−)-carvone (LX), the main constituent of spearmint oil. To our knowledge, racemic carvone has never been resolved, but the levorotatory isomer has been synthesized from (+)-limonene (LIX).[29] Furthermore, (+)-limonene is available by base-catalyzed elimination of phthalic acid from (+)-α-terpineol hydrogen phthalate[30] (LVIII). Since racemic α-terpineol (*dl*-LVII) has been resolved,[30,31] prepared from its elements[32] and the enantiomers related to glyceraldehyde,[33] the stages outlined in this paper constitute a formal total synthesis of maaliol (I).



In conclusion, we must briefly consider a possible biogenesis of maaliol (I). It has been proposed that cyclic sesquiterpenes originate from the aliphatic farnesol (LXI)[34] which has been isolated from natural sources. We assume that all-*trans*-farnesol (LXI) cyclizes to the π-complex (LXII) in analogy to the postulated biogenetic transformation of nerol to Δ^3-carene.[34] This cationic intermediate can now stabilize itself in two different manners: (a) Loss of a proton results in a bicyclic structure which seems most stable in the conformation LXIII. Monocyclic cyclodecane derivatives have been previously proposed[34,35] as precursors for bicyclic sesquiterpenes and the absolute configuration at C_7 in LXIII is that experimentally ascertained for a number of eudalene - type sesquiterpenes. Transannular antiplanar addition[36] of the elements of water to LXIII gives maaliol (I). (b) The π-complex LXII can also be stabilized by addition of water which results in the monocyclic cyclodecane LXV which seems to be most stable in the conformation shown. An analogous con-



formation for the bicyclo[0.1.8]undecane structure, however, is destabilized by non-bonded interactions between three methyl groups all situated on the β-face of the molecule. Antiplanar cyclization within LXV proceeds to yield eudesmol (LXIV) which is probably a precursor of most other eudalene-type sesquiterpenes.

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(32) W. H. Perkin, Jr., *J. Chem. Soc.*, **85**, 654 (1904); K. Alder and W. Vogt, *Ann.*, **564**, 109 (1949).

(33) The stereochemical correlations of the monoterpenes were summarized by W. Hückel, *J. prakt. Chem.*, **157**, 225 (1941), and by K. Freudenberg and W. Lwowski, *Ann.*, **587**, 213 (1954).

(34) L. Ruzicka, A. Eschenmoser and H. Heusser, *Experientia*, **9**, 357 (1953).

(35) D. H. R. Barton and P. de Mayo, *J. Chem. Soc.*, 150 (1957).

(36) For theory and biogenetic implications, see A. Eschenmoser, L. Ruzicka, O. Jeger and D. Arigoni, *Helv. Chim. Acta*, **38**, 1890 (1955). For experimental verification, see P. A. Stadler, A. Nechvatal, A. J. Frey and A. Eschenmoser, *ibid.*, **40**, 1373 (1957).

for many friendly discussions. The mass spectra were kindly measured by Drs. K. Biemann and J. Seibl, M. I. T.

Experimental

Microanalyses by Dr. S. M. Nagy and associates, M. I. T. Melting points were taken on a Kofler hot-stage microscope and are corrected. All ultraviolet spectra were determined on a Cary recording spectrophotometer, model 11. Infrared spectra, unless otherwise indicated, were measured on a Perkin–Elmer Infracord with a sodium chloride prism. The listing of infrared bands include those which are relevant to structural arguments and other strong bands. For all chromatograms carried out on alumina, neutralized Alcoa alumina (grade F-20, 80-200 mesh) and Woelm neutral aluminum oxide were used. The former is designated as alumina A and the latter as B. The activity of the alumina was determined by the absorption of dyes according to the procedure of Brockmann.[37]

(−)-Epi-α-cyperone (IX).—(−)-Epi-α-cyperone was prepared according to the method of Howe and McQuillin[8]; b.p. 104–105° (0.15 mm.), $n^{26}D$ 1.5330, $[\alpha]^{25.3}D$ −180° (*c* 4.3, chloroform).

Tricyclic Ketone XI from (−)-Epi-α-cyperone (IX).—A solution of dry hydrogen bromide (26.0 g., 0.32 mole) in 70 ml. of glacial acetic acid was added slowly with stirring and ice-cooling to a solution of (−)-epi-α-cyperone (54.73 g., 0.25 mole) in 110 ml. of glacial acetic acid. After standing at room temperature for 15 min., the brown mixture was poured into ice-water and extracted with ether. The ether layer was washed with cold bicarbonate solution and then with water, dried over anhydrous magnesium sulfate and concentrated to about 100 ml. *in vacuo* below room temperature. The concentrated solution, which contained the hydrobromide X, was refluxed with potassium hydroxide (100 g.) in 1 l. of absolute methanol for 30 min. After removal of most of the solvent, the mixture was poured into ice-water and extracted with ether. The ether layer was washed with water, dried over anhydrous magnesium sulfate and evaporated. Recrystallization of the crystalline residue from petroleum ether (b.p. 30–60°) at −60° gave 34.18 g. (62.5%) of the tricyclic ketone XI as colorless prisms, m.p. 68–70°; infrared spectrum (CCl_4): 929, 962, 1020, 1059, 1094, 1116, 1202, 1230, 1294, 1311, 1319, 1355, 1377, 1422, 1447, 1464, 1613, 1667, 2907, 2976 cm.$^{-1}$; ultraviolet spectrum (EtOH): 266 mμ, ε 13700.

Anal. Calcd. for $C_{15}H_{22}O$: C, 82.51; H, 10.61. Found: C, 82.56; H, 9.88.

2,4-Dinitrophenylhydrazone of the Tricyclic Ketone XI.—The 2,4-dinitrophenylhydrazone was prepared with 2,4-dinitrophenylhydrazine in hydrochloric acid–ethanol in the usual manner. Recrystallization from ethyl acetate gave dark red plates, m.p. 234–235°; ultraviolet spectrum ($CHCl_3$): 400 mμ, ε 29500.

Anal. Calcd. for $C_{21}H_{26}N_4O_4$: C, 63.30; H, 6.58; N, 14.06. Found: C, 62.70; H, 6.80; N, 14.54.

Wolff–Kishner Reduction of the Tricyclic Ketone XI.—The ketone XI (4.35 g., 20 mmoles) was dissolved in a solution of potassium hydroxide (5.7 g.) and 6 ml. of 85% hydrazine hydrate in 45 ml. of triethylene glycol and the solution was gently boiled for 1 hr. Water and excess hydrazine were distilled until the temperature of the vapor reached 200°. After refluxing for 4 hr., the mixture was diluted with water and extracted with petroleum ether. The organic layer was washed with water, dried over anhydrous magnesium sulfate and evaporated to a yellow liquid which was dissolved in petroleum ether and passed through a column containing 150 g. of alumina A (activity I). Elution with petroleum ether gave 3.21 g. of colorless liquid. Distillation afforded a mixture of the olefins, XV and XVI, b.p. 82–83° (1.0 mm.), yield 63.5% (2.58 g.); infrared spectrum (pure liquid): 770, 809, 885, 955, 1136, 1229, 1370, 1449, 1664, 2725, 2857–2941 cm.$^{-1}$.

Anal. Calcd. for $C_{15}H_{24}$: C, 88.16; H, 11.84. Found: C, 88.58; H, 11.49.

Hydrogenation over 10% palladium-on-charcoal in ethanol showed that this olefin mixture contained 84% of β-maaliene (XV). In another run, which was carried out in diethylene glycol instead of triethylene glycol, the product contained 65% of β-maaliene.

(37) H. Brockmann and H. Schodder, *Ber.*, **74**, 73 (1941).

Osmium Tetroxide Oxidation of the Mixture of XV and XVI.—A solution of osmium tetroxide (0.5 g., 2.9 mmoles) in 1 ml. of pyridine was added to an ice-cooled solution of the olefin mixture (400 mg., 2 mmoles) in 1 ml. of pyridine and the mixture was allowed to stand at room temperature in the dark for 2 days. The mixture was refluxed with a mixture of mannitol (3.5 g.), potassium hydroxide (3.5 g.), water (10 ml.), benzene (10 ml.) and ethanol (30 ml.) for 4 hr. The solvent was evaporated *in vacuo* and the residue extracted with ether. The ether layer was washed with water, dried over anhydrous magnesium sulfate and evaporated. The crystalline residue (0.44 g.) was digested in 8 ml. of ice-cooled petroleum ether and filtered, whereupon 0.17 g. of 5-iso-α-maalidiol (XVIII) was obtained, which was recrystallized from benzene–petroleum ether as colorless fine needles, m.p. 131–131.5°. The mixed m.p. with α-maalidiol (XLIV) was depressed; infrared spectrum ($CHCl_3$) 823, 918, 927, 1022, 1034, 1054, 1116, 1372, 1453, 2950, 3497, 3610 cm.$^{-1}$.

Anal. Calcd. for $C_{15}H_{26}O_2$: C, 75.58; H, 10.99. Found: C, 75.50; H, 10.31.

The filtrate from 5-iso-α-maalidiol was chromatographed through a column containing 20 g. of alumina B (activity III). Elution with benzene yielded 0.141 g. of crystalline material, which was recrystallized from petroleum ether at −60°; colorless needles, m.p. 95–97°, pure and mixed with β-maalidiol (XVII) derived from maaliol; $[\alpha]D$ −34° (*c* 4.3, in $CHCl_3$), $[\alpha]D$ of authentic β-maalidiol, −32° (*c* 3.2, in $CHCl_3$). The infrared spectrum was identical with that of β-maalidiol.

Elution with benzene–ether (1:1) yielded an additional 0.033 g. of 5-iso-α-maalidiol.

Selenium Dioxide Oxidation of β-Maaliene (XV).—A solution of 3.58 g. (17.5 mmoles) of the olefin mixture XV, and XVI, in 30 ml. of ethanol was hydrogenated in the presence of 100 mg. of 30% palladium-on-charcoal at 25°. Hydrogen uptake (148 ml., 6.0 mmoles) ceased after 85 min. The catalyst was filtered off and the filtrate evaporated *in vacuo*. The residual liquid, which corresponded to 2.34 g. (11.5 mmoles) of β-maaliene, was refluxed with a solution of selenium dioxide (1.4 g.) in 30 ml. of dioxane and 1 ml. of water for 15 min. Then selenium dioxide (2.2 g.) was added and the mixture refluxed for 1 hr. Insoluble selenium was filtered off and the filtrate evaporated *in vacuo*. Petroleum ether and water were added and the petroleum ether layer was washed with water, dried over anhydrous magnesium sulfate and evaporated to a viscous liquid (2.20 g.), which was dissolved in 50 ml. of petroleum ether and chromatographed through a column containing 67 g. of alumina A (activity I). Elution with benzene yielded a yellow liquid (200 mg.), which was rechromatographed through a column containing 15 g. of alumina A (activity I). Elution with petroleum ether–benzene (9:1) and later with benzene yielded a yellow liquid. Distillation at 105–110° (bath temperature) (0.1 mm.) gave the aldehyde XX as a pale yellow liquid; yield 140 mg. (5.6%); infrared spectrum (CCl_4): 695, 831, 908, 928, 956, 1057, 1134, 1167, 1205, 1235, 1269, 1361, 1372, 1451, 1610, 1667, 2740, 2857, 2933 cm.$^{-1}$; ultraviolet spectrum (EtOH): 227 mμ, ε 5110; 272 mμ, ε 9150.

2,4-Dinitrophenylhydrazone of the Aldehyde XX.—The 2,4-dinitrophenylhydrazone was prepared as described for the preparation of the derivative of the tricyclic ketone XI. Recrystallization from ethanol gave orange-red needles, m.p. 162.5–163.0°; ultraviolet spectrum ($CHCl_3$): 392 mμ, ε 30100.

Anal. Calcd. for $C_{21}H_{26}N_4O_4$: C, 63.30; H, 6.58; N, 14.06. Found: C, 63.47; H, 6.80; N, 14.62.

Wolff–Kishner Reduction of the Aldehyde XX.—The crude aldehyde (135 mg.) was boiled gently with a solution of 0.6 ml. of 85% hydrazine hydrate in 15 ml. of diethylene glycol for 40 min. After water and excess hydrazine had been distilled, potassium hydroxide (0.15 g.) was added to the cooled solution, and the solution refluxed for 4 hr. The mixture was worked up as described for the Wolff–Kishner reduction of the tricyclic ketone XI. The residual liquid (126 mg.) was dissolved in 10 ml. of petroleum ether and passed through a column containing 3 g. of alumina B (activity I). Elution with petroleum ether yielded 80 mg. of a mixture of the olefins XXI, XV and XVI as a colorless liquid.

Osmium Tetroxide Oxidation of the Olefin Mixture XXI, XV and XVI.—The olefin mixture obtained above was dissolved in 1 ml. of pyridine and mixed with osmium tetroxide

(0.15 g.) in 1 ml. of pyridine under ice-cooling. After standing at room temperature in the dark overnight, the mixture was decomposed by refluxing with a mixture of mannitol (1 g.), potassium hydroxide (1 g.), water (2.5 ml.), benzene (2.5 ml.), ethanol (7.5 ml.) and treated as usual. The product was dissolved in 10 ml. of petroleum ether and chromatographed through a column containing 5 g. of alumina B (activity III). Elution with benzene yielded 29 mg. of colorless needles, m.p. 96–97°, pure and mixed with β-maalidiol. Elution with benzene–ether (4:1) yielded 4 mg. of fine needles, m.p. 128.5–130.5°, pure and mixed with 5-iso-α-maalidiol (XVIII). Elution with ether yielded 2 mg. of needles, m.p. 139–140°, pure and mixed with γ-maalidiol (XXII).

Monotosylate (XXIII) of γ-Maalidiol.—γ-Maalidiol (0.24 g., 1 mmole) was mixed with *p*-toluenesulfonyl chloride (0.21 g., 1.1 mmoles) in 5 ml. of dry pyridine, and the mixture allowed to stand at room temperature overnight. The pyridine was evaporated *in vacuo* and the residue taken up in ether and water. The ether layer was washed with water, dried over anhydrous magnesium sulfate and evaporated to a crystalline mass, which was recrystallized from cyclohexane as colorless plates, m.p. 131.5–132.0°, yield 0.29 g. (75%); infrared spectrum ($CHCl_3$): 815, 843, 893, 972, 1096, 1174, 1186, 1359, 1457, 1600, 1931(wk), 2959, 3663 cm.$^{-1}$.

Anal. Calcd. for $C_{22}H_{32}SO_4$: C, 67.31; H, 8.22. Found: C, 67.58; H, 8.29.

Lithium Aluminum Hydride Reduction of the Monotosylate XXIII [Maaliol (I)].—The monotosylate (150 mg.) and lithium aluminum hydride (200 mg.) were refluxed in 5 ml. of dry tetrahydrofuran for 4 hr. The solvent was evaporated *in vacuo*, and the residue suspended in ether and decomposed with ethyl acetate followed by the addition of diluted sodium hydroxide solution. The ether layer was washed with water, dried over anhydrous magnesium sulfate and evaporated. Recrystallization of the residue from petroleum ether gave nleedles, m.p. 103–104°, pure and mixed with natural maaliol, m.p. 103–104°. The infrared spectra of the two samples of I were superimposable, $[\alpha]^{25}D$ +15.1° (*c* 1.4, EtOH).

Dehydration of Maaliol with Acetic Anhydride and Pyridine.—A mixture of maaliol (9.60 g. 45 mmoles), 35 ml. of pyridine and 100 ml. of acetic anhydride was refluxed for 17 hr.[38] After the mixture had been evaporated to a small volume *in vacuo*, petroleum ether and water were added. The organic layer was washed with bicarbonate solution, then with water, dried over anhydrous magnesium sulfate and evaporated. The residue was dissolved in 100 ml. of petroleum ether and passed through a column containing 400 g. of alumina A (activity I). Elution with 400 ml. of petroleum ether yielded 8.18 g. (93%) of a mixture of α-, β- and γ-maalienes as a colorless liquid; infrared spectrum (pure liquid): 840, 861, 886, 965, 1136, 1372, 1459, 1645, 1779(wk), 2688(wk), 2755(wk), 2874–2976, 3115(wk) cm.$^{-1}$.

Osmium Tetroxide Oxidation of the Maalienes XXI, XV and XXXI.—The maaliene mixture (8.17 g., 39.5 mmoles), which was obtained from maaliol as described above, was dissolved in 20 ml. of pyridine. A solution of osmium tetroxide (10.0 g., 39 mmoles) in 15 ml. of pyridine was slowly added under ice-cooling to the solution of the maalienes. After standing at room temperature in the dark for 3 days, the mixture was refluxed with a mixture of mannitol (70 g.), potassium hydroxide (70 g.), 180 ml. of water, 180 ml. of benzene and 500 ml. of ethanol for 4 hr. The solution was treated as described for the oxidation of the olefin mixture XV and XVI. The crystalline residue was dissolved in 50 ml. of hot benzene, and the solution diluted with 50 ml. of petroleum ether and cooled in an ice-bath. γ-Maalidiol (XXII) (2.84 g.) which separated as fine needles was filtered off, m.p. 139–140°. The filtrate was evaporated to 6.34 g. of semi-crystalline material, which was dissolved in 100 ml. of benzene and chromatographed through a column containing 230 g. of alumina A (activity III). Elution with 400 ml. of benzene yielded a crystalline solid, which on recrystallization from petroleum ether gave β-maalidiol XVII, 1.42 g., m.p. 96–97°. Elution with 100 ml. of ether yielded 2.15 g. of a liquid. Further elution with ether yielded γ-maalidiol (1.33 g.). The liquid obtained from the first ether eluate was rechromatographed through a column containing 80 g. of alumina A (activity III). Elution with benzene yielded 0.16 g. of β-maalidiol. Elution with benzene–ether (4:1 and later 1:1) yielded a crystalline solid. Recrystallization from petroleum ether gave 0.53 g. of α-maalidiol (XLIV), m.p. 129–130°. The mother liquor of the recrystallization of α-maalidiol slowly separated prisms. Recrystallization from *n*-hexane gave 0.16 g. of iso-α-maalidiol (XLVII) as colorless prisms, m.p. 135–136°. Iso-α-maalidiol was recovered unchanged after standing with *p*-toluenesulfonyl chloride and pyridine at room temperature overnight; infrared spectrum (CCl_4): 693, 837, 867, 892, 928, 952, 981, 992, 1013, 1053, 1074, 1230, 1383, 1453, 2933, 3344, 3584 cm.$^{-1}$.

Anal. Calcd. for $C_{15}H_{26}O_2$: C, 75.58; H, 10.99. Found: C, 75.54; H, 11.01.

The total yield of maalidiols was 69.5% and the individual diols were isolated in the following proportion: α-, 8.3%; iso-α-, 2.5%; β-, 24.5%; γ-, 64.7%.

Lithium Aluminum Hydride Reduction of the Tricyclic Ketone XI to the Unsaturated Alcohol XXVIII.—A solution of the tricyclic ketone (400 mg.) in 7 ml. of ether was added to lithium aluminum hydride (100 mg.) in 8 ml. of ether, and the mixture refluxed for 2 hr. The mixture was decomposed by the addition of water and dilute hydrochloric acid. The ether layer was washed with bicarbonate solution, then with water, dried over anhydrous magnesium sulfate and evaporated. Recrystallization from petroleum ether gave 234 mg. (58%) of the unsaturated alcohol XXVIII as fine needles, m.p. 84.5–85.5°, which decomposed on standing at room temperature within a few days to form a liquid; infrared spectrum (CCl_4): 1007, 1025, 1374, 1451, 1653, 2595, 3425, 3690 cm.$^{-1}$.

Anal. Calcd. for $C_{15}H_{24}O$: C, 81.76; H, 10.98. Found: C, 81.16; H, 10.68.

Catalytic Hydrogenation of the Unsaturated Alcohol XXVIII.—The alcohol (96 mg.) was hydrogenated in 3 ml. of acetic acid in the presence of prereduced platinum oxide (50 mg.) at 27°. Two moles of hydrogen was absorbed within 20 min. and then an additional 0.78 mole of hydrogen was slowly absorbed in 3 hr. The catalyst was filtered and the filtrate evaporated *in vacuo*. Distillation of the residue gave 80 mg. of a saturated hydrocarbon as a colorless liquid, b.p. 75–80° (bath temperature) (0.1 mm.), which had no hydroxyl absorption band in infrared spectrum.

Zinc–Acetic Acid Reduction of the Tricyclic Ketone XI.—The tricyclic ketone (200 mg.) was refluxed with zinc powder (1 g.) in 10 ml. of acetic acid for 3.25 hr. Zinc powder (0.5 g.) was added and refluxing continued for an additional 90 min. Unreacted zinc was filtered off and the acetic acid evaporated *in vacuo*. Ether and water were then added and the ether layer washed with aqueous bicarbonate solution. After drying over anhydrous magnesium sulfate, the solvent was evaporated. Distillation of the residue gave 158 mg. of the ketone XXXIX as colorless liquid, b.p. 105–110° (bath temperature) (0.1 mm.); infrared spectrum (CCl_4): 1613, 1667 cm.$^{-1}$; ultraviolet spectrum (EtOH): 251 mμ, ε 13300.

2,4-Dinitrophenylhydrazone of the Ketone XXXIX.—The 2,4-dinitrophenylhydrazone was prepared in the usual manner. Two recrystallizations from ethyl acetate gave dark red crystals, m.p. 196–197°.

Preparation of the Ketone XXXIX from the Ketol XL.—The ketol XL (236 mg., 1 mmole), prepared according to the method of Howe and McQuillin,[8] was hydrogenated in the presence of 10% palladium–charcoal (20 mg.) in 5 ml. of ethanol at 26°. One mole (25.2 ml.) of hydrogen was taken up in 30 min. The catalyst was filtered and the solvent was evaporated. The saturated ketol was obtained as a colorless liquid (225 mg.). The infrared spectrum showed no bands due to a terminal methylene group.

The saturated ketol (120 mg.) was refluxed with 5 ml. of 10% ethanolic potassium hydroxide for 7 hr. The solvent was evaporated, the residue diluted with water and extracted with petroleum ether. The petroleum ether layer was dried and evaporated. Vacuum distillation of the residue gave a pale yellow liquid (160 mg.), b.p. 110–115° (bath temperature)/(0.1 mm.), $[\alpha]^{27}D$ −119° (*c* 3.8, $CHCl_3$), whose infrared spectrum was identical with that of the ketone XXXIX obtained from the tricyclic ketone XI by reduction with zinc and acetic acid.

The 2,4-dinitrophenylhydrazone was prepared as usual. Recrystallization from ethyl acetate gave dark red crystals, m.p. 195–197°, pure and mixed with the 2,4-dinitrophenyl-

(38) Y. R. Naves and P. Ardizio, *Ann. pharm. France*, **12**, 471 (1954).

hydrazone of the ketone XXXIX obtained from the tricyclic ketone XI.

Anal. Calcd. for $C_{21}H_{28}O_4N_4$: C, 62.98; H, 7.05. Found: C, 62.58; H, 6.80.

Lithium–Ammonia–Ethanol Reduction of the Tricyclic Ketone XI.—A solution of the tricyclic ketone (6.0 g., 27.5 mmoles) in 160 ml. of anhydrous ether and 200 ml. of absolute ethanol was added to 1 l. of liquid ammonia. Lithium wire (7.0 g., 1.05 atoms) was added under stirring and Dry Ice–acetone cooling to the mixture during a period of 5 min. After the blue color of the mixture had disappeared (10 min.), lithium wire (10.1 g., 1.5 g. atoms) was added and the mixture stirred for 4 hr. The Dry Ice–acetone bath was removed and the ammonia evaporated. The mixture was decomposed by the addition of ice-water and extracted with ether twice. The ether layer was washed with water, dried over anhydrous magnesium sulfate and evaporated. The residue was dissolved in 180 ml. of petroleum ether and chromatographed through a column containing 180 g. of alumina A (activity III). Elution with petroleum ether yielded a mixture of ketonic substances (1.66 g., see below). Elution with benzene and later with ether gave a mixture of crystalline alcoholic substances[39] (4.05 g.), which was hydrogenated in the presence of platinum oxide (300 mg.) in 30 ml. of 95% acetic acid. After the hydrogen uptake had ceased (456 ml. at 24°), the catalyst was filtered and the solvent evaporated. The residue was dissolved in 100 ml. of petroleum ether and chromatographed through a column containing 120 g. of alumina A (activity III). Elution with petroleum ether yielded a colorless liquid (1.51 g.) which consisted of a saturated hydrocarbon. Elution with benzene yielded a crystalline material. Recrystallization from petroleum ether at −60° gave 1.68 g. (27.5%) of the alcohol XXV as fine needles, m.p. 97–100°. An analytical sample was recrystallized from the same solvent, m.p. 99.5–100.5°; infrared spectrum (CCl_4): 997, 1016, 1036, 1050, 1374, 1458, 2941, 3425, 3676 cm.$^{-1}$.

Anal. Calcd. for $C_{15}H_{26}O$: C, 81.02; H, 11.79. Found: C, 80.65; H, 11.42.

The ketonic substances (5.55 g.) from several runs were combined and dissolved in 200 ml. of petroleum ether–benzene (4:1) and chromatographed through a column containing 200 g. of alumina A (activity I-II). Elution with petroleum ether–benzene 4:1 (400 ml.) and later with petroleum ether–benzene 1:1 (100 ml.) yielded a crystalline mass. Recrystallization from petroleum ether gave 1.00 g. of the ketone XXVII as colorless needles, m.p. 102–103°. The ketone XXVII was recovered unchanged after refluxing in 5% potassium hydroxide–ethanol for 1 hr.; infrared spectrum (CCl_4): 1013, 1049, 1121, 1140, 1167, 1325, 1355, 1376, 1456, 1715, 2595 cm.$^{-1}$.

Anal. Calcd. for $C_{15}H_{24}O$: C, 81.76; H, 10.98. Found: C, 81.68; H, 11.07.

Elution with 100 ml. of petroleum ether–benzene (1:1) and later with 300 ml. of benzene produced a yellow liquid. Distillation at 115–120° (bath temperature) (0.3 mm.) gave 0.66 g. of a pale yellow liquid, which crystallized on seeding with the tricyclic ketone XI, and its infrared spectrum was identical with that of an authentic sample. Further elution with 100 ml. of ether yielded a semicrystalline material. Recrystallization from *n*-hexane gave 0.38 g. of the ketol XXIX as colorless prisms, m.p. 101–103°; infrared spectrum (CCl_4): 853, 1003, 1073, 1121, 1214, 1372, 1449, 1709, 2941, 3521, 3650 cm.$^{-1}$.

Anal. Calcd. for $C_{15}H_{24}O_2$: C, 76.22; H, 10.24. Found: C, 76.15; H, 10.30.

Deuterium Exchange of the Ketone XXVII.—Potassium (10 mg.) was dissolved in a mixture of 0.5 ml. of deuterium oxide and 1.5 ml. of deuterioethanol. The mixture was refluxed with the ketone (50 mg.) for 10 min. and evaporated *in vacuo*. Two additional exchanges were carried out by the following procedure: 1.5 ml. of deuterioethanol and 0.5 ml. of deuterium oxide were added, the mixture was refluxed for 10 min. and the solvent was evaporated *in vacuo*. The final residue was diluted with deuterium oxide (5 ml.) and extracted with petroleum ether. The organic layer was dried over anhydrous magnesium sulfate and evaporated. Recrystallization of the residue from petroleum ether gave colorless needles, m.p. 102.5–103.5°. Its mass spectrum showed the presence of 73% trideuterioketone and 27% of dideuterioketone.

Lithium Aluminum Hydride Reduction of the Ketol XXIX.—The ketol (50 mg.) was refluxed with lithium aluminum hydride (40 mg.) in 4 ml. of absolute ether for 2 hr. After treatment as described for the preparation of the unsaturated alcohol XXVIII, the crystalline residue was dissolved in 2 ml. of benzene and chromatographed through a column containing 1.5 g. of alumina B (activity III). Elution with benzene and later with benzene–ether (49:1) yielded 17 mg. (34%) of crystals. Recrystallization from *n*-hexane gave fine needles, m.p. 130.5–131.5°, pure and mixed with 5-iso-α-maalidiol (XVIII). Elution with benzene–ether (9:1) and later with ether yielded 22 mg. (44%) of crystals. Recrystallization from *n*-hexane gave the glycol XXXIV as fine needles, m.p. 112–114°; infrared spectrum ($CHCl_3$): 915, 1050, 1072, 1372, 1445, 2933, 3472, 3650 cm.$^{-1}$.

Acetate XXVI of the Alcohol XXV.—The alcohol (0.656 g., 2.96 mmoles) was allowed to stand in a mixture of 1 ml. of acetic anhydride and 5 ml. of pyridine at room temperature overnight. The mixture was poured into ice-water and extracted with ether. The ether layer was washed with water, dried over anhydrous magnesium sulfate and evaporated. Distillation of the residue gave the acetate XXVI as a colorless liquid, b.p. 95–100° (bath temperature) (0.05 mm.); infrared spectrum (CCl_4): 972, 983, 1002, 1032, 1049, 1242, 1376, 1458, 1739, 2976 cm.$^{-1}$. In several runs yields of 91–98% were obtained.

Anal. Calcd. for $C_{17}H_{28}O_2$: C, 77.23; H, 10.67. Found: C, 76.98; H, 10.56.

Pyrolysis of the Acetate XXVI to a Mixture of Olefins XXX and XXXI.—A mixture of the acetate (1.21 g., 4.6 mmoles) and 0.5 ml. of cyclohexane was passed through a Pyrex tube containing Pyrex glass helixes heated to 470° in a slow stream of nitrogen. The pyrolyzed product was taken up in ether and the ether solution washed successively with water, bicarbonate solution, water, dried over anhydrous magnesium sulfate and evaporated to a yellow liquid, which was dissolved in petroleum ether and passed through a column containing 30 g. of alumina A (activity I). Elution with petroleum ether yielded 0.70 g. (74%) of the olefin mixture XXX and XXXI as a pale yellow liquid, b.p. 110° (bath temperature) (0.1 mm.); infrared spectrum (pure liquid): 680, 696, 742, 783, 804, 840, 887, 900, 958, 991, 1020, 1062, 1130, 1222, 1374, 1449, 1613(wk), 1656(wk), 2755(wk), 2882–2959 cm.$^{-1}$.

Osmium Tetroxide Oxidation of the Olefin Mixture XXX and XXXI.—A solution of osmium tetroxide (2.0 g., 7.9 mmoles) in 10 ml. of pyridine was added to an ice-cooled solution of the olefin mixture (1.444 g., 7.1 mmoles) in 5 ml. of pyridine. The solution was treated as described for the oxidation of the maalienes. The product (1.65 g.) was dissolved in 50 ml. of petroleum ether and chromatographed through a column containing 100 g. of alumina A (activity III). Elution with benzene–ether (9:1 and later 4:1) yielded 0.73 g. of crystals. Recrystallization from *n*-hexane gave 0.24 g. (14%) of fine needles, m.p. 128.5–129.5°, pure and mixed with α-maalidiol (XLIV). An infrared spectrum was identical with that of α-maalidiol. The mother liquor was evaporated to dryness and the residue dissolved in ether. During a slow evaporation of the ether solution prisms deposited which were recrystallized from cyclohexane as prisms (0.08 g., 5%), m.p. 135–136°, pure and mixed with iso-α-maalidiol (XLVII). The infrared spectrum was identical with that of an authentic sample. Elution with benzene–ether and later with ether yielded 0.57 g. of crystals, which on recrystallization from *n*-hexane gave the glycol XLIII (0.37 g., 22%) as needles, m.p. 105.5–106.5°; infrared spectrum (CCl_4): 887, 935, 954, 1000, 1052, 1374, 1460, 2950, 3534 cm.$^{-1}$.

Anal. Calcd. for $C_{15}H_{26}O_2$: C, 75.58; H, 10.99. Found: C, 75.18; H, 10.95.

Epoxidation of the Mixture of Olefins XXX and XXXI and Reduction of the Epoxides.—A solution of the olefin mixture (0.35 g., 1.7 mmoles) in 8 ml. of chloroform was added to a freshly prepared solution of perbenzoic acid (284 mg., 2 mmoles) in 3.7 ml. of chloroform. After the mixture had

(39) This fraction consisted of the alcohol XXV, the unsaturated alcohol XXVIII and possibly other alcohols. On chromium trioxide–pyridine oxidation, this fraction gave the tricyclic ketone XI, the ketone XXXII, m.p. 98–99°, and a mixture of ketones which could not be separated into individual components.

been allowed to stand at room temperature in the dark for 3 days, an additional amount of perbenzoic acid (154 mg., 1.1 mmoles) in 2 ml. of chloroform was added and the mixture allowed to stand for 1 day. The solution was washed with bicarbonate, and with water, dried over anhydrous magnesium sulfate and evaporated. The residual liquid was dissolved in 10 ml. of anhydrous ether and the solution added dropwise to a suspension of lithium aluminum hydride (80 mg., 1.9 mmoles) in 15 ml. of ether. The suspension was refluxed for 1.5 hr. After the usual treatment, there was obtained a colorless liquid, which was dissolved in 20 ml. of petroleum ether and chromatographed through a column containing 15 g. of alumina B (activity III). Elution with petroleum ether yielded 0.12 g. of colorless liquid, which was probably a mixture of unreacted olefins and epoxides. Elution with petroleum ether–benzene (49:1–4:1) yielded 0.17 g. (45%) of crystals. Recrystallization from petroleum ether gave the alcohol, XXXIII as prisms, m.p. 114.0–115.5°; infrared spectrum (CCl_4): 901, 968, 981, 1025, 1066, 1372, 1451, 2924, 3663 cm.$^{-1}$.

Anal. Calcd. for $C_{15}H_{26}O$: C, 81.02; H, 11.79. Found: C, 81.03; H, 11.85.

The alcohol XXXIII, m.p. 114.0–115.5°, was also obtained by catalytic hydrogenation (platinum oxide in acetic acid) of the epoxides obtainable from the olefin mixture XXX and XXXI.

Oxidation of the Alcohol XXXIII to the Ketone XXXII.—A solution of the alcohol (70 mg.) in 1.5 ml. of pyridine was mixed with chromium trioxide–pyridine complex, which was prepared from chromium trioxide (200 mg.) and 2 ml. of pyridine. After standing for 24 hr. at room temperature, the mixture was poured into water and extracted with ether. The ether layer was washed successively with water, dilute hydrochloric acid, water, dried over anhydrous magnesium sulfate and evaporated. Recrystallization of the crystalline residue from petroleum ether gave the ketone XXXII as needles, m.p. 98–99°; infrared spectrum (CCl_4): 1000, 1009, 1019, 1053, 1119, 1181, 1241, 1377, 1425(wk), 1451, 1712, 2809, 2941 cm.$^{-1}$.

Anal. Calcd. for $C_{15}H_{24}O$: C, 81.76; H, 10.98. Found: C, 81.36; H, 11.09.

The ketone XXXII was recovered unchanged after refluxing in 5% potassium hydroxide–ethanol for 1 hr.

Deuterium Exchange of the Ketone XXXII.—The ketone (50 mg.) was treated as described above for XXVII. Recrystallization of the product from petroleum ether gave colorless needles, m.p. 97–99°. Its mass spectrum showed the presence of 92% of trideuterioketone and 8% of dideuterioketone.

Oxidation of the Alcohol XXV to the Ketone XXXII.—The alcohol (70 mg.) was oxidized as described above. Recrystallization gave colorless needles, m.p. 98–99°, pure and mixed with the ketone XXXII.

Monoacetate XLV of α-Maalidiol (XLIV).—A mixture of α-maalidiol (200 mg., 0.84 mmole), 0.5 ml. of acetic anhydride and 2 ml. of pyridine was allowed to stand at room temperature overnight. The mixture was poured into ice-water and extracted with ether. The ether layer was washed successively with water, dilute hydrochloric acid and water, dried over anhydrous magnesium sulfate and evaporated. Recrystallization of the residue from petroleum ether gave 170 mg. (72%) of the acetate as fine needles, m.p. 77–78°; infrared spectrum (CCl_4): 702, 879, 908, 939, 978, 1020, 1031, 1117, 1172, 1182, 1235, 1370, 1453, 1742, 2950, 3676 cm.$^{-1}$.

Anal. Calcd. for $C_{17}H_{28}O_3$: C, 72.81; H, 10.07. Found: C, 72.82; H, 10.17.

Pyrolysis of the Monoacetate XLV.—The acetate (97 mg.) was heated to 310–320° in a small glass tube for 30 min. The product after distillation *in vacuo* was recrystallized from petroleum ether to give fine needles (40 mg., 49%), m.p. 93–97°. Further recrystallization gave crystals, m.p. 96–98°, pure and mixed with the ketone XXXII, m.p. 98–99°. The infrared spectrum was identical with that of an authentic sample of XXXII.

Monoacetate XLVIII of Iso-α-maalidiol (XLVII).—Iso-α-maalidiol (70 mg., 0.3 mmole) was treated with 0.3 ml. of acetic anhydride and 1 ml. of pyridine as described for the preparation of the monoacetate of α-maalidiol. Recrystallization from *n*-hexane gave 58 mg. (70%) of the acetate XLVIII as colorless needles, m.p. 141.0–141.5°; infrared spectrum (CCl_4): 1018, 1034, 1058, 1073, 1172, 1235, 1379, 1453, 1745, 2959, 3676 cm.$^{-1}$.

Anal. Calcd. for $C_{17}H_{28}O_3$: C, 72.81; H, 10.07. Found: C, 72.45; H, 9.94.

Pyrolysis of the Monoacetate XLVIII.—The acetate (55 mg.) was pyrolyzed as described for the pyrolysis of XLV. Chromatographic separation of the products gave at least four substances: an olefin [infrared spectrum (CCl_4): 887, 1600(wk) cm.$^{-1}$], an acetate [infrared spectrum (CCl_4): 1235, 1736 cm.$^{-1}$], a ketone [infrared spectrum (CCl_4): 1715 cm.$^{-1}$] and an unsaturated alcohol [infrared spectrum (CCl_4): 674, 900, 1639, 1808(wk), 3472, 3636 cm.$^{-1}$].

Oxidation of α-Maalidiol (XLIV) to the Ketol L.—A solution of α-maalidiol (300 mg., 1.25 mmoles) in 10 ml. of pyridine was added to the ice-cooled chromium trioxide–pyridine complex prepared from chromium trioxide (500 mg.) and 10 ml. of pyridine. After standing in the ice-bath for 1 week, the mixture was worked up as described for the preparation of the ketone XXXII. The product (0.33 g.) was dissolved in 10 ml. of petroleum ether and chromatographed through a column containing 10 g. of alumina A (activity III). Elution with benzene yielded crystals. Recrystallization from petroleum ether at −60° gave 70 mg. (24%) of the ketol L as fine needles, m.p. 108–110°. An analytical sample was recrystallized from the same solvent, m.p. 109.5–110.0°; infrared spectrum (CCl_4): 880, 940, 997, 1016, 1027, 1094, 1109, 1115, 1142, 1182, 1372, 1422(wk), 1445, 1460, 1712, 2941, 3546, 3650 cm.$^{-1}$.

Anal. Calcd. for $C_{15}H_{24}O_2$: C, 76.22; H, 10.24. Found: C, 76.07; H, 10.16.

Wolff–Kishner Reduction of the Ketol L to Epi-maaliol (XLIX).—A mixture of the ketol (45 mg.), 0.15 ml. of 85% hydrazine hydrate, potassium hydroxide (0.13 g.) and 6.5 ml. of triethylene glycol was heated to about 175° for 4 hr. Water and excess hydrazine were distilled until the pot temperature was 185°. After refluxing for 2 hr., the mixture was poured into water and extracted with petroleum ether. The distillate was also extracted with petroleum ether and the combined organic layer washed with water, dried over anhydrous magnesium sulfate and evaporated. The residual liquid was dissolved in 2 ml. of petroleum ether and chromatographed through a column containing 1.2 g. of alumina B (activity III). Elution with petroleum ether yielded 14 mg. of a liquid. Elution with petroleum ether–benzene (9:1) yielded 11 mg. of a semi-crystalline solid. The infrared spectrum was identical with that of epi-maaliol (XLIX) and recrystallization from petroleum ether gave colorless needles, m.p. 58.0–59.5°, pure and mixed with epi-maaliol.

Oxidation of Iso-α-maalidiol (XLVII) to the Ketol LI.—Iso-α-maalidiol (52 mg.) was oxidized during 15 hr. at 0° with chromium trioxide–pyridine complex which was prepared from chromium trioxide (50 mg.) and 2 ml. of pyridine. The mixture was worked up as usual and the product chromatographed through a column containing 1.5 g. of alumina B (activity III). Elution with petroleum ether–benzene (1:1) and later with benzene yielded 13 mg. (25%) of the ketol LI as a viscous liquid which was used for the reduction without further purification; infrared spectrum (CCl_4): 1065, 1120, 1170, 1261, 1383, 1453, 1715, 2890, 2941, 3571 cm.$^{-1}$.

Wolff–Kishner Reduction of the Ketol LI to Maaliol (I).—The ketone (18 mg.) was reduced with 0.1 ml. of 85% hydrazine hydrate, potassium hydroxide (0.1 g.) and 3 ml. of triethylene glycol as described for the preparation of epi-maaliol. The product was chromatographed through a column containing 1 g. of alumina B (activity III). Elution with petroleum ether yielded 5 mg. of a liquid. Elution with petroleum ether–benzene (4:1) yielded 3 mg. of a crystalline solid. The infrared spectrum was identical with that of maaliol (I). Recrystallization from petroleum ether gave colorless needles, m.p. 99–102°, which showed no depression on admixture with maaliol, m.p. 103–104°.

Monotosylate (XLVI) of α-Maalidiol.—α-Maalidiol (40 mg., 0.17 mmole) was allowed to stand with *p*-toluenesulfonyl chloride (38 mg., 0.2 mmole) in 1 ml. of pyridine at room temperature overnight. The mixture was evaporated to dryness *in vacuo*, and the residue stirred with bicarbonate solution and extracted with ether. The ether layer was dried over anhydrous magnesium sulfate and evaporated. Recrystallization from petroleum ether gave the monotosylate as long plates, m.p. 141–142°; infrared spectrum (CCl_4):

675, 708, 849, 873, 903, 917, 954, 1099, 1122, 1176, 1188, 1372, 1456, 1603(wk), 1748(wk), 2933, 3650 cm.$^{-1}$.

Anal. Calcd. for $C_{22}H_{32}SO_3$: C, 67.31; H, 8.22. Found: C, 67.08; H, 8.19.

On standing, the mother liquor separated colorless plates, m.p. 135–136°, which were dimorphic with the above material. The crystals, m.p. 135–136°, changed to the crystals, m.p. 141–142°, when seeded with the latter in the recrystallization.

Lithium Aluminum Hydride Reduction of the Tosylate XLVI.—The monotosylate (77 mg.) and lithium aluminum hydride (110 mg.) were refluxed in 3 ml. of anhydrous tetrahydrofuran for 5 hr. The mixture was worked up as usual and the product (39 mg.) chromatographed through a column containing 1.5 g. of alumina B (activity III). Elution with petroleum ether yielded 18 mg. of the alcohol LIV as prisms, m.p. 79–80°, which were not reducible over platinum oxide in ethanol solution; infrared spectrum (CCl_4): 907, 957, 1044, 1103, 1261, 1379, 1464, 2950, 3484, 3650 cm.$^{-1}$.

Elution with petroleum ether–benzene (9:1 and later 4:1) yielded 7 mg. of colorless needles, m.p. 69–71° (sintering at 60°); infrared spectrum (CCl_4): 900, 954, 1007, 1131, 1379, 1460, 2959, 3521, 3676 cm.$^{-1}$.

Elution with ether yielded 6 mg. of colorless needles, m.p. 127–129°, pure and mixed with α-maalidiol (XLIV).

Reaction of Monotosylate XLVI with Potassium *t*-Butoxide.—The monotosylate (58 mg., 0.15 mmole) was refluxed in a solution of potassium (60 mg., 1.5 mmoles) in 2.6 ml. of anhydrous *t*-butyl alcohol for 1 hr. The mixture was evaporated *in vacuo*, and the residue worked up by the conventional procedure. The residue was chromatographed through a column containing 1 g. of alumina B (activity II). Elution with petroleum ether yielded 20 mg. of the ketone LV as a liquid; infrared spectrum (CCl_4): 1040, 1139, 1166, 1183, 1357, 1377, 1427(wk), 1464, 1715, 2959 cm.$^{-1}$.

Anal. Calcd. for $C_{15}H_{24}O$: C, 81.76; H, 10.98. Found: C, 81.51; H, 11.13.

Lithium Aluminum Hydride Reduction of the Ketone LV to the Alcohol LVI.—The ketone (20 mg.) and lithium aluminum hydride (20 mg.) were refluxed in 1 ml. of anhydrous tetrahydrofuran for 4 hr. The mixture was worked up as usual. The alcohol(s) LVI was obtained as a liquid (16 mg.); infrared spectrum (CCl_4): 860, 878, 903, 926, 953, 996, 1022, 1047, 1078, 1107, 1136, 1252, 1374, 1464, 2959 3546, 3690 cm.$^{-1}$.

CAMBRIDGE, MASS.

[CONTRIBUTION FROM THE POLYCHEMICALS DEPARTMENT, E. I. DU PONT DE NEMOURS & CO., INC.]

Polynorbornene by Coördination Polymerization[1]

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Norbornene has been polymerized to high molecular weight polymers using catalysts derived from lithium aluminum tetraalkyls and titanium tetrachloride. Structural studies on these polymers have shown that a major portion of the polymer chain consists of cyclopentane rings linked in a *cis*-1,3-fashion with *trans*-CH=CH groups. This polymerization has occurred by an unusual ring opening reaction having high stereospecificity.

Introduction

The finding in these laboratories[2–6] of catalysts, designated coördination catalysts, which afforded the facile polymerization of ethylene and other olefins has also provided a means for effecting the polymerization of norbornene (bicyclo[2,2,1]-2-heptene), a monomer which heretofore had not been polymerized by any catalytic method. In general, active catalysts have been prepared from a variety of organometallics with derivatives of Groups IVB to VIB of the Periodic Table. Similar systems have also been disclosed by Ziegler.[7]

This new method of polymerization is being designated as "coördination polymerization"[1–7] as a means of emphasizing and distinguishing its important features from the well-known free radical, cationic and anionic methods. We consider coordination polymerization to involve successive steps of coördination and activation of the monomer at a fixed site on a transition element derivative in a reduced state, followed by a rearrangement (usually with a high degree of stereospecificity) and propagation. The rearrangement and propagation frees the catalyst site for further coördination and activation of monomer. It is believed that the rearrangement step involves a minimum of charge separation and neither carbonium ions nor carbanions in the usual sense are involved.

It is believed that the reaction is more closely related to an SNi type rearrangement rather than an SN2 type displacement. Another important feature of coördination catalysis is found in the stereospecific nature of this polymerization leading to polymer with a high degree of order not likely with other means of polymerization. Other workers in this field of olefin polymerization[8] have also reported on the exceptional regularity found in polymer chains derived from the polymerization of α-olefins using these catalysts.

Discussion

For the work reported here, we have used a catalyst system derived from lithium aluminum tetraheptyl and titanium tetrachloride. At least two kinds of polynorbornene polymers can be made using catalysts derived from these components. Use of less than a molar equivalent of lithium aluminum tetraheptyl for each mole of titanium tetrachloride leads to a rigid, brittle polynorbornene (type A). When a 100% excess of lithium aluminum tetraheptyl over titanium

(1) Presented at the 130th National Meeting, Am. Chem. Soc., Atlantic City, N. J., September 18, 1956.

(2) E. I. du Pont de Nemours & Co., British Patent 682,420 (November 12, 1952).

(3) A. W. Anderson and N. G. Merckling, U. S. Patent 2,721,198 (October 18, 1955).

(4) A. W. Anderson, *et al.*, French Patent 1,134,740 (December 3, 1956).

(5) E. I. du Pont de Nemours & Co., British Patent 776,326 (September 25, 1957).

(6) A. W. Anderson, *et al.*, U. S. Patent 2,905,645 (September 22, 1959) (Application August 16, 1954).

(7) K. Ziegler, *et al.*, *Angew. Chem.*, **67**, 426 (1955); **67**, 541 (1955); Belgian Patent 533,362 (May 16, 1955) (see Ger. application of November 17, 1953, December 15, 1953, and December 23, 1953).

(8) G. Natta, *J. Polymer Sci.*, **16**, 143 (1955); *Makromol. Chem.*, **16**, 77, 213 (1955); *Angew. Chem.*, **68**, 393 (1956).