Experiments Directed toward the Total Synthesis of Terpenes. X. A Stereoselective Scheme for Diterpenoid Resin Acid Synthesis[1,2]

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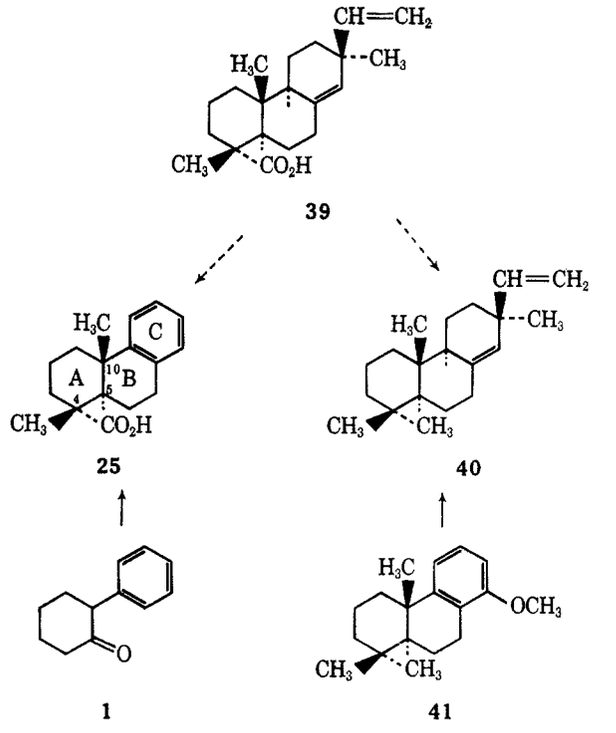
A stereoselective scheme for the conversion of 2-phenylcyclohexanone **1** to (±)-desisopropyldehydroabietic acid **25** in 10% over-all yield *via* 4β,9β-dimethyl-4α-phenyl-*trans*-decalone-6 **11** is described. Application of this procedure to 2-*p*-isopropylphenylcyclohexanone **30** leads to an 18% over-all yield of (±)-dehydroabietic acid **37**. Modification of the scheme allows for the synthesis of both (±)-4,5-isodesisopropyldehydroabietic acid **29** and (±)-4,5-isodehydroabietic acid **38**.

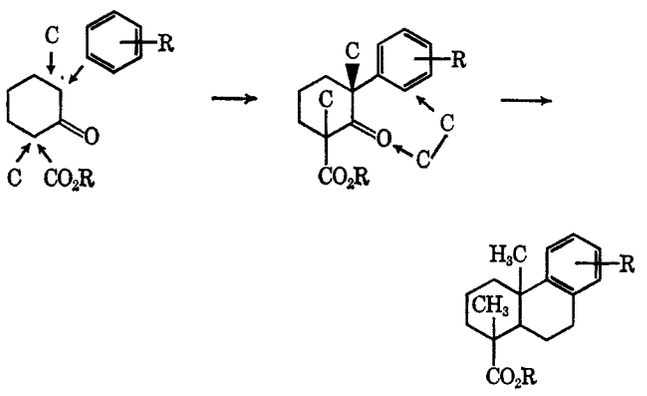
In an earlier paper in this series[5] we alluded to the design of a synthetic scheme for the construction of the diterpenoid resin acids. This plan called for the dissection of the pimaric acid molecule **39** so as to separate the synthetic problems it presented. Each of these portions embodied different structural features for which a synthetic sequence must be devised before the acid itself could be constructed. Our previous work[5] in this field described the modification of the tricyclic aromatic ether **41** so as to establish the requisite ring C substitution pattern of pimaric acid **39** that is contained in pimaradiene **40**. The present report delineates a sequence whereby 2-phenylcyclohexanone **1** can be transformed into (±)-desisopropyldehydroabietic acid **25**. The latter acid serves as a convenient model for schemes designed to construct the A/B ring system of the resin acids as well as a potential intermediate in a projected pimaric acid **39** synthesis itself. After the introduction of an oxygen function in the aromatic ring C of the acid **25**, the procedures used in the pimaradiene **40** synthesis could be applied to complete the resin acid synthesis. Thus, not only are the synthetically difficult structural features of the A/B ring system of pimaric acid **39** brought into sharp focus by the "aromatization" of ring C, but also the acid **25** is a useful synthetic stepping stone if it can be made available in large quantities (see Scheme I). The "economy" of this situation is particularly attractive.

In the recent past, much work[6] has been expended by others in an effort to synthesize resin acids. In particular, the successes in this endeavor recorded by Stork and Schulenberg,[7] Mahapatra and Dodson,[8] Wenkert and co-workers,[9] Spencer and co-workers,[10] and Dutta and co-workers[11] are of significant importance. Like ourselves, all of these workers addressed their syntheses to the structural problem of introducing the quaternary carbon at C_4 and the stereochemical problem presented by the *cis*-C_4,C_{10}-dimethyl system.

SCHEME I



Our approach to the solution of these problems is similar to the A → C → B route chosen earlier by Bachmann and Wick[12] in their effort to synthesize (±)-dehydroabietic acid **37**. The guidelines of this



(1) A preliminary report containing a portion of this work appeared in *J. Org. Chem.*, **27**, 703 (1962).

(2) Partial support for this work by the Research Corporation and the National Science Foundation (Grant NSF 19841) is gratefully acknowledged.

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(4) Stauffer Chemical Company Fellow, 1961–1962; University Fellow, 1962–1963.

(5) R. E. Ireland and P. W. Schiess, *J. Org. Chem.*, **28**, 6 (1963).

(6) For a review of this effort, see N. A. J. Rogers and J. A. Barltrop, *Quart. Rev.*, **16**, 117 (1962).

(7) G. Stork and J. W. Schulenberg, *J. Am. Chem. Soc.*, **84**, 284 (1962).

(8) S. N. Mahapatra and R. M. Dodson, *Chem. Ind.* (London), 253 (1963).

(9) E. Wenkert, A. Afonso, J. Bredenberg, C. Kaneko, and A. Tahara, *J. Am. Chem. Soc.*, **86**, 2038 (1964).

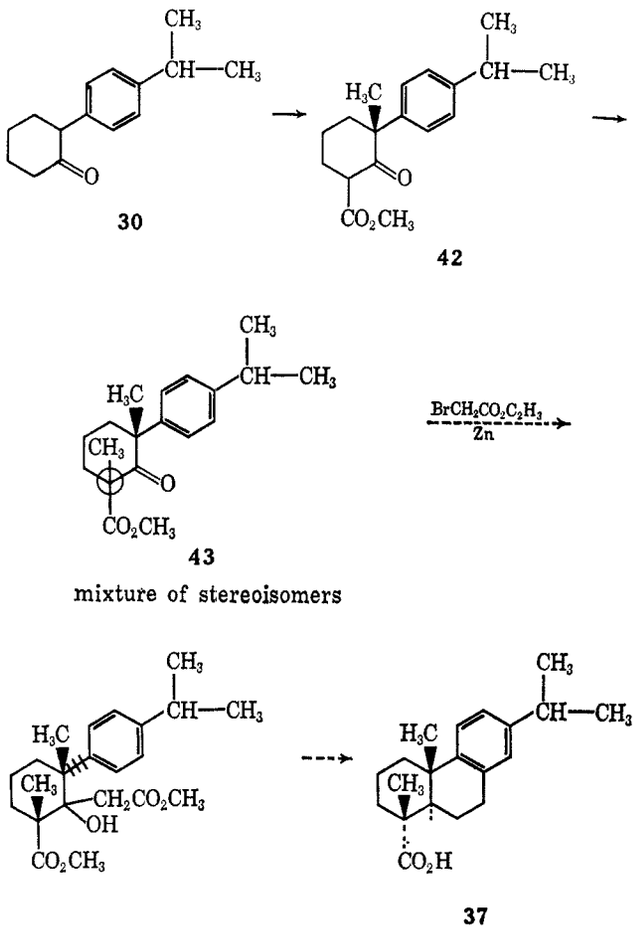
(10) T. A. Spencer, T. D. Weaver, M. A. Schwartz, W. J. Greco, Jr., and J. L. Smith, *Chem. Ind.* (London), 577 (1964); T. A. Spencer, T. D. Weaver, and W. J. Greco, Jr., *J. Org. Chem.*, **30**, 3333 (1965).

(11) C. T. Mathew, G. Sen Gupta, and P. C. Dutta, *Proc. Chem. Soc.*, 336 (1964); C. T. Mathew, G. C. Banerjee, and P. C. Dutta, *J. Org. Chem.*, **30**, 2754 (1965).

(12) (a) W. E. Bachmann, G. I. Fugimoto, and L. B. Wick, *J. Am. Chem. Soc.*, **72**, 1995 (1950); (b) W. E. Bachmann and L. B. Wick, *ibid.*, **72**, 2000 (1950).

plan are the construction of an appropriately substituted phenylcyclohexanone, and then the addition of the remaining two carbon atoms to form ring B. In the Bachmann scheme[12] this approach took the following form (see Scheme II).

SCHEME II



30 42 43

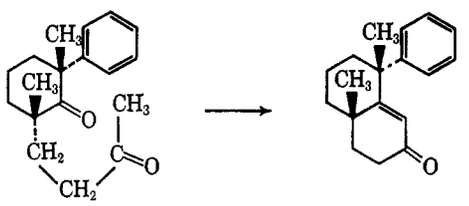
mixture of stereoisomers

37

This particular series, which proved to be unproductive, suffers from two serious drawbacks. First, the methylation of the β-keto ester **42** results in the formation of both possible stereoisomers. While one isomer crystallized and was used in further experiments, there appeared to be no way to control the stereochemical outcome of this reaction so as to obtain only one of the two isomers. However, the more serious drawback is the severe steric crowding about the keto group of the keto ester **42**. So congested is this functional group that condensation of the keto ester **43** with the Reformatsky reagent fails completely. The bulk of the organometallic reagent, the intermolecularity of this reaction, and the steric shield about the keto group all combined to contribute to the demise of the synthesis at this stage.

In order to render this A → C → B approach successful, we must first devise a system in which the ketone function is more susceptible to attack. Such a system might be that schematically represented below in formula **8**. Here we envisage attack of the highly hindered, tetrasubstituted ketone by the enolate anion in an *intra*molecular reaction. The smaller steric requirements of the potassium enolate and the *intra*molecularity of the reaction would appear to provide a solution to the introduction of carbon residue in place of the ketone. Adoption of this plan places the unsaturated ketone **10** in a key position in the synthetic scheme, and the aldol-type condensation envisaged for its generation is the core of the approach.

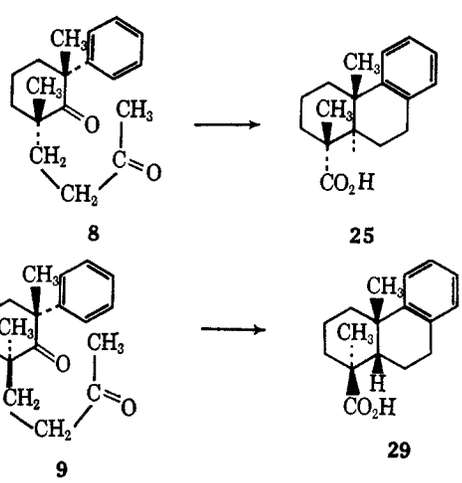
With this sequence as the heart of the synthetic plan, we have divided the scheme into two parts: the first concerned with the synthesis of the diketone **8** and the second, with the conversion of the unsaturated



8 10

ketone **10** to the desired (±)-desisopropyldehydroabietic acid **25**. Embodied in the first phase are the principal stereochemical aspects of the synthesis, while the stress on the latter conversion is the design of an efficient reaction scheme for the modification of the unsaturated ketone **10**. Our first consideration will be for the construction of the diketone **8**.

The problems associated with the synthesis of the diketone **8** are not so much structural as stereochemical. Of the two possible racemates that could arise, only isomer **8** will lead to the desired tricyclic acid **25**. The isomer **9** in which the methyl groups are *trans* oriented will lead to the isomeric tricyclic acid **29** which is epimeric with the desired acid **25** at both C_4 and C_5. By virtue of the sequence of reactions chosen to accomplish this over-all transformation (*vide infra*)



8 25

9 29

the configuration of the hydrogen at C_5 is directly linked to the configuration of the methyl and carboxyl groups at C_4. The latter stereochemical result is, in turn, determined by the configuration of the methyl and 3-oxobutyl groups at C_6 in the cyclohexanone derivatives **8**. Therefore, the ultimate stereochemical fate of the synthesis is determined at this relatively early stage.

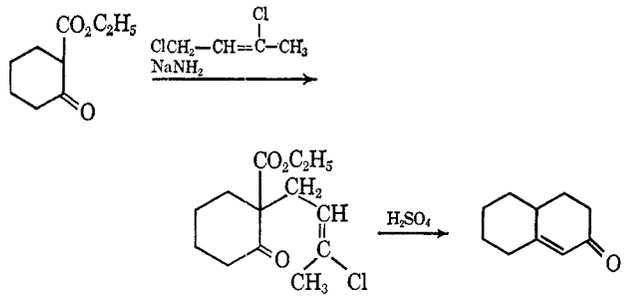
The most logical synthetic approach to the gross structure represented by the diketone **8** is from 2-phenylcyclohexanone **1** *via* 2-methyl-2-phenylcyclohexanone **2**. The activation of the 2 position of 2-phenylcyclohexanone **1** by both the carbonyl group and the phenyl group makes the introduction of the

first methyl group at this position particularly attractive.

The choice of 2-methyl-2-phenylcyclohexanone **2** as an intermediate leaves open the question of which alkyl residue is to be added to the 6 position first. In principle, either the 3-oxobutyl or the methyl group may be attached first, and at the outset of this work, there seemed to be no compelling reason to expect any stereochemical advantage from either sequence. The sequence that first introduced the methyl group, and then the 3-oxobutyl residue appeared more efficient and was investigated first.

The problem of introducing only one methyl group on the C_6 methylene of 2-methyl-2-phenylcyclohexanone **2** was overcome by utilization of the *n*-butylthiomethylene grouping[13] as a source of the desired monomethyl substituent. This grouping could also serve as a blocking group in order to prevent any polymethylation of the starting 2-phenylcyclohexanone **1** and was therefore introduced in the first stage. Condensation of 2-phenylcyclohexanone **1** with ethyl formate, and then treatment of the resulting hydroxymethylene derivative with *n*-butyl mercaptan led to the formation of the *n*-butylthiomethylene ketone **3**, as reported previously.[13] This ketone **3** was readily methylated with methyl iodide in the presence of potassium *t*-butoxide; the crude product was desulfurized with Raney nickel in alcohol solution. In this fashion an 86% yield of 2,6-dimethyl-2-phenylcyclohexanone **5** was realized (see Chart I).

Condensation of this ketone **5** with methyl vinyl ketone in a Michael-type reaction proved unrewarding and numerous attempts led only to polymeric tars. In an effort to provide a more irreversible reaction scheme for the addition of the desired 3-oxobutyl group, we turned to the alkylation of the ketone **5** with 1,3-dichloro-2-butene. The choice of this reagent was predicated on the examples provided by Prelog and co-workers[14] whereby alkylation of the 2-carbethoxycyclohexanone proceeded well and subsequent sulfuric acid hydrolysis led to loss of the activating carbethoxyl group as well as aldol-type cyclization.

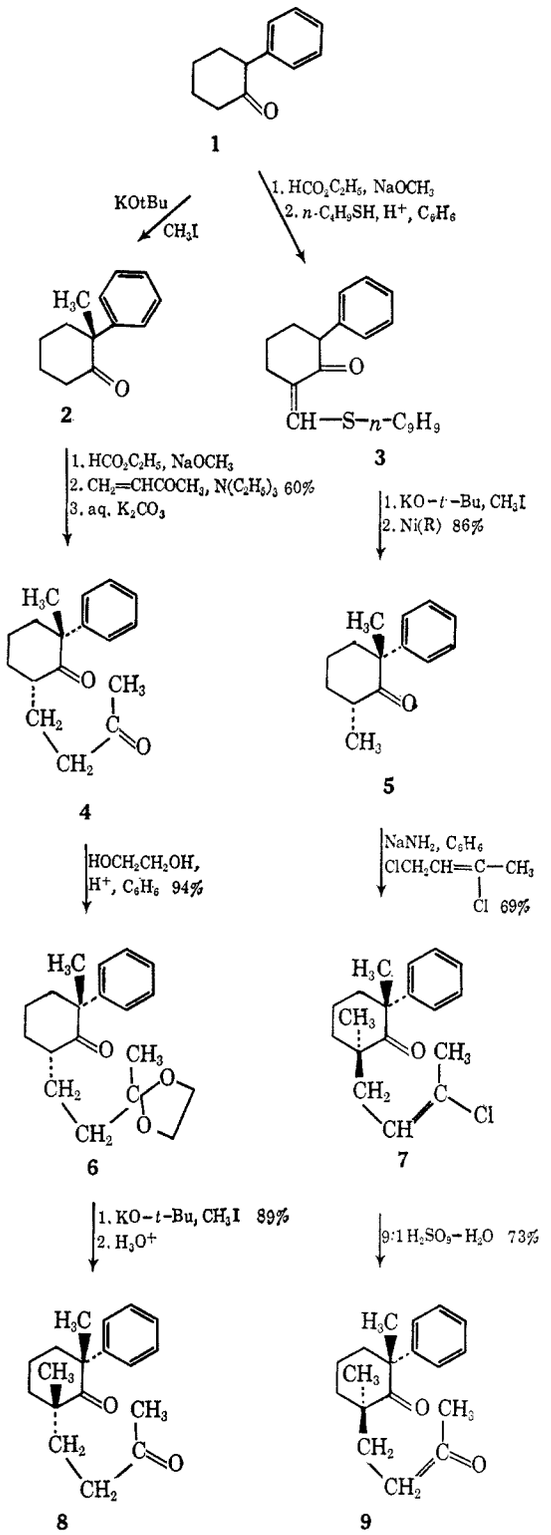


In this way the over-all result is the same as that expected by the use of methyl vinyl ketone but does not depend on conjugate addition to the α,β-unsaturated ketone system to effect addition of the 3-oxobutyl side chain.

When this sequence was applied to 2,6-dimethyl-2-phenylcyclohexanone **5**, the tetrasubstituted ketone **7** resulted in 69% yield. While this ketone **7** was a liquid, it behaved as a stereochemically homogeneous material on gas–liquid and thin layer chromatography, and showed no indication of heterogeneity by infrared spectroscopy. No stereoisomer of this chloro ketone **7** could be isolated from the alkylation reaction mixture. A 92% material balance was realized, and the reaction product always consisted of the chloro ketone **7** and recovered cyclohexanone **5**. This result indicates a very high degree of stereoselectivity during the alkylation reaction.

CHART I

THE SYNTHESIS OF THE EPIMERIC 2,6-DIMETHYL-2-(3-OXOBUTYL)-6-PHENYLCYCLOHEXANONES **8** AND **9**



(13) R. E. Ireland and J. A. Marshall, *J. Org. Chem.*, **27**, 1615 (1962).
(14) M. Prelog and M. Zimmermann, *Helv. Chim. Acta*, **32**, 2360 (1949).

Hydrolysis of the vinyl chloride **7** was effected in 9:1 sulfuric acid–water, but aldol-type cyclization did not take place under these acidic conditions. Thus, contrary to the example provided by Prelog and co-workers[14] only the diketone **9** resulted from this acid hydrolysis in 73% yield. Again the high degree of steric hindrance about the ring carbonyl can be held responsible for this lack of reaction. The steric congestion about this ring carbonyl is also evident from the position of absorption of the grouping in the infrared. The side-chain ketone absorbs at 5.85 μ, while the ring carbonyl absorption is shifted to 5.92 μ and is easily resolvable from that of the unhindered ketone.

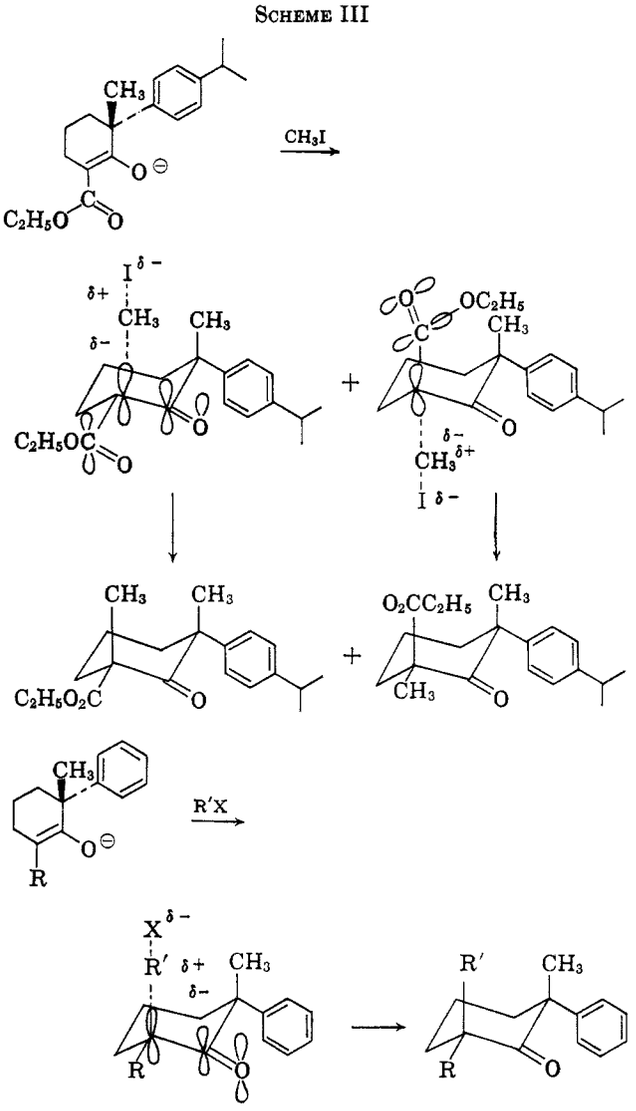
The stereoselectivity of the alkylation of 2,6-dimethyl-2-phenylcyclohexanone **5** is in contrast to the result of the methylation of the β-keto ester **42** observed by Bachmann and Wick,[12] and suggests that in the former case (*vide infra*) reversing the order of addition of the carbon residues at the 6 position might result in the equally stereoselective production of the isomeric diketone **8**. This was indeed found to be the case, for by appropriately modifying the synthetic scheme, the isomeric diketone **8** became readily available.

For this sequence the *n*-butylthiomethylene blocking group served no purpose, and therefore 2-phenylcyclohexanone **1** was methylated[15] directly in the 2 position with methyl iodide in the presence of potassium *t*-butoxide. The problem of adding the four-carbon side chain to the 6 position of this ketone **2** was solved by use of methyl vinyl ketone. In order to prevent polycondensation and to activate the 6 position, the hydroxymethylene derivative of 2-methyl-2-phenylcyclohexanone **2** was prepared. The resulting β-dicarbonyl system readily condensed with 1 equiv of methyl vinyl ketone in the presence of triethylamine and mild treatment with aqueous carbonate easily effected removal of the activating formyl group. In this fashion the ketone **2** was converted to the diketone **4** in 60% over-all yield.

Selective methylation of the 6 position of the ring requires that the side-chain carbonyl group be blocked. The steric congestion about the ring ketone worked to our advantage in this instance, for selective ketalization of the side-chain ketone was readily accomplished with no interference from the ring carbonyl. The monoketal **6** that resulted in 94% yield was then methylated with methyl iodide in the presence of potassium *t*-butoxide. The product from this methylation was not purified but immediately treated with aqueous mineral acid to remove the ketal; the diketone **8** was isolated and purified. This diketone **8** was available in 89% yield from the monoketal **6** by this procedure and again consisted of only one of the two possible stereoisomerides. In this instance the diketone **8** was a crystalline solid and a careful search of the mother liquors gave no indication of an appreciable quantity of the isomeric diketone **9**. Thus both alkylation reactions appear to be highly stereoselective, and in each case the new alkyl residue, regardless of size, is introduced *cis* to the C_2 methyl group.

These results are in striking contrast to the observations Bachmann and Wick[12b] made in connection with the methylation of the β-keto ester **42**.[16] It appears

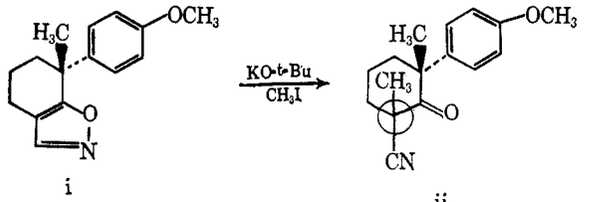
SCHEME III



that there is more stereoelectronic control of the alkylation of the ketones **5** and **6** (see Scheme III). In each case, the sole product observed is that in which the newly introduced alkyl residue has taken up an axial position in the more favorable conformation of the phenylcyclohexanone ring system.[17] The stereoelectronic factor seems to outweigh any steric effects during the alkylation,[18] for the bulk of the alkyl residue does not seem to change the stereochemical outcome.

(15) M. S. Newman and M. D. Farbman, *J. Am. Chem. Soc.*, **66**, 1550 (1944).

(16) Similar results were obtained in this laboratory (K. Toki, unpublished observations) when the isoxazole i was cleaved and methylated *in situ* with potassium *t*-butoxide and methyl iodide. In this case, a crystalline epimer of the nitrile ii resulted in 37% yield and there remained an oily, noncrystalline residue (48% by weight) which was methylated β-ketonitrile ii (negative ferric chloride test; insoluble in 20% aqueous sodium hydroxide). This material afforded an additional 7% yield of the crystalline epimer on chromatography on Florisil, but the remainder of the material resisted crystallization and was not further purified.



i ii

(17) W. S. Johnson, *Chem. Ind.* (London), 167 (1956).

(18) Compare H. O. House, "Modern Synthetic Reactions," W. A. Benjamin, Inc., New York, N. Y., 1965, p 202.

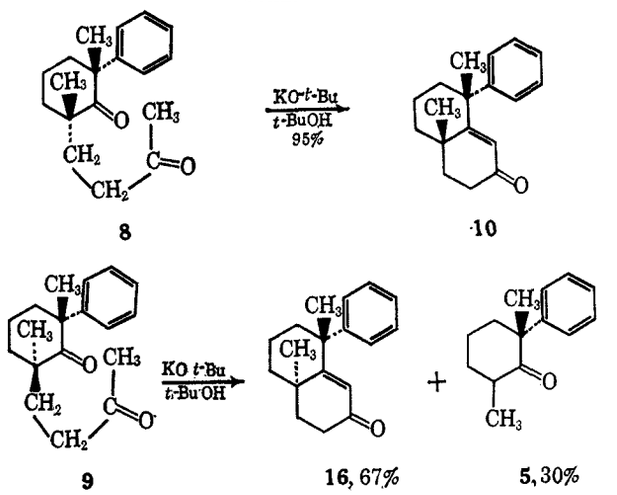
It is therefore tempting to conclude that during the transition from enolate to product, the lower energy reaction pathway is that which maintains the maximum orbital overlap between the carbonyl π system and the negative charge on the α carbon. In the ketones **5** and **6** the population of that conformation wherein the phenyl group is more equatorially oriented is probably very great. Therefore, the maintenance of overlap between the orbitals of the carbanion and the carbonyl group dictates the formation of only one product and is more important to determining the lower energy pathway than steric considerations in the enolate. In cases where the conformation of the enolate is not nearly as fixed, this stereoelectronic requirement may be satisfied in more than one conformation, and then other considerations will become more important in determining product stereochemistry.

Such is the situation in the methylation of the β-keto ester **42**. Here, due to the delocalization of charge through the carbomethoxyl group, it is possible to provide stabilization for the anion through orbital overlap with the carbomethoxyl carbonyl as well as the ketone group. In this fashion the stereoelectronic requirements of the reaction pathway will be less restrictive than the situation where the anion system is solely endocyclic. The alkyl residue can approach the β-keto ester enolate in an equatorial manner and not prevent stabilization by the carbomethoxyl group. In a case such as this, factors other than stereoelectronic ones will be more important in determining the stereochemical outcome, and where no compelling restrictions are placed on one pathway or the other—such as in the case of the β-keto ester **42** —a mixture of products will result.[12]

The high degree of stereoselectivity observed in the production of the diketones **8** and **9** removes the first of the two objections to the A → C → B route to (±)-dehydroabietic acid **25** as pursued by Bachmann and Wick.[12] In the case of the diketone **8** a 45% over-all yield was realized, while the diketone **9** was obtained in 43% over-all yield. Having solved this initial phase of the project satisfactorily, we turned our attention to the second part of the project, namely, the conversion of the isomeric diketones **8** and **9** to the isomeric tricyclic acids **25** and **29** *via* the octalones **10** and **16**.

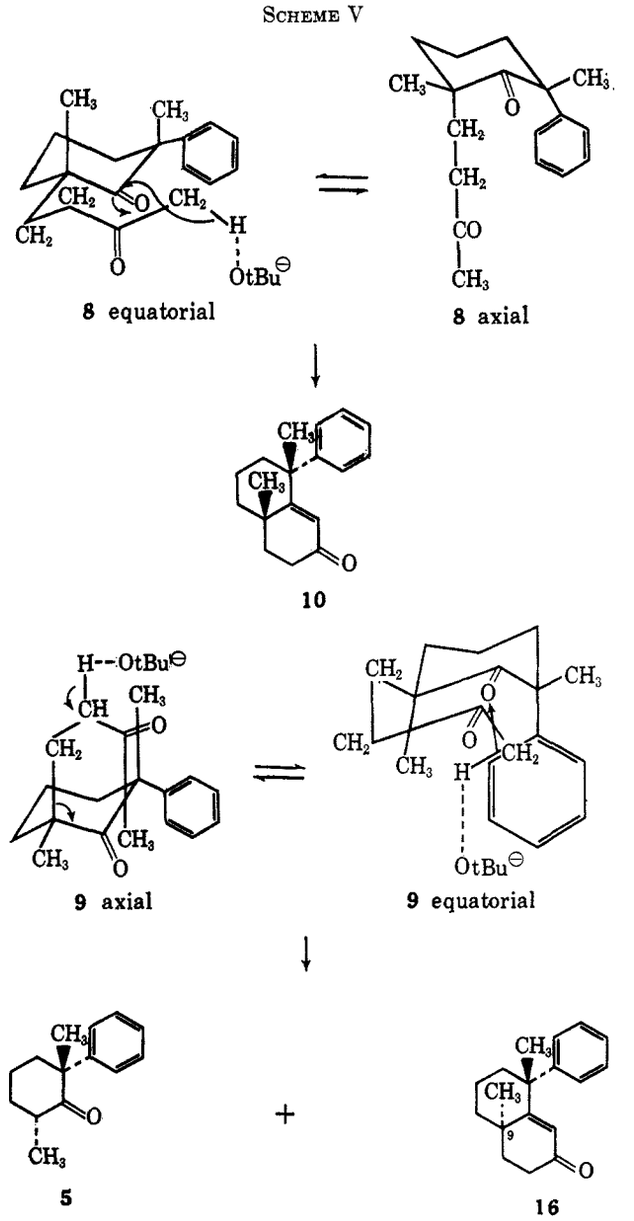
The observation that during the hydrolysis of the vinyl chloride **7** with concentrated sulfuric acid, no aldol-type condensation took place led us to discard acid catalysis for this reaction. The cyclization could, however, be effected through the agency of basic catalysis. While the two isomeric diketones **8** and **9** behaved similarly when treated with potassium *t*-butoxide in *t*-butyl alcohol and generated the desired octalones **10** and **16**, there was a significant difference in the yields of product in each case (see Scheme IV). The diketone **8** led exclusively to the cyclic product in very high yields, while under the same conditions the diketone **9** was only partially converted to cyclic material. In the latter case, a significant portion of the diketone **9** was cleaved to the monoketone **5**. This interesting result can be interpreted in terms of the conformations through which each diketone may react and provides further insight into their stereochemical configuration.

SCHEME IV



For the diketone **8** by far the more favorable conformation will be that in which the two larger groups are both equatorial. This form is pictured as **8** equatorial in Scheme V. In this conformation only one

SCHEME V



reaction pathway is open to the molecule, namely, aldol-type cyclization, as shown. Cleavage of the molecule by a reverse Michael-type reaction is stereoelectronically unfavorable, as the equatorially oriented side chain precludes stabilization of the transition state by overlap of the developing carbanion with the carbonyl π system. Therefore, the only observed transformation is that resulting from cyclization.

In the case of the diketone **19** the decision between the available chair conformations is less clear cut, and we might expect that each conformation **9** axial and **9** equatorial would be significantly populated. While the diketone **9** may undergo aldol-type cyclization in either conformation, in conformation **9** axial the side chain is oriented such that a reverse Michael reaction is favorable. Thus, if the side-chain carbonyl is enolized toward the methylene in conformation **9** axial rather than simply being reprotonated as in the isomeric diketone **8**, the molecule can cleave and generate the 2,6-dimethyl-2-phenylcyclohexanone **5** enolate. The axially oriented side-chain–ring bond is stereoelectronically ideally situated for maximum stabilization of the reverse Michael-type reaction pathway through delocalization of the developing negative charge through the ring carbonyl π system.

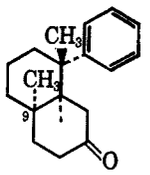
This difference in the behavior of these two isomers lends support to the stereochemical assignments made on the basis of axial alkylation. While not sufficient evidence for a firm stereochemical conclusion, the consistency of the two arguments is satisfying. It is also worth mentioning that the observed cleavage of the diketone **9** offers a possible explanation for the failure of the initial attempts to homoannelate the ketone **5** with methyl vinyl ketone. If one assumes that this conjugate addition behaves stereochemically as the foregoing alkylation reactions, the conformation of this initially formed methylene enolate would be represented by conformer **9** axial, wherein the side chain is axial to the ring. It is this very conformation that is probably responsible for the reverse Michael-type reaction. The success of the homoannelation reaction would then depend very heavily on a favorable equilibrium between the enolate of the ketone **5** and the adduct enolate **9** axial and/or a rapid protonation of the adduct enolate. It is unreasonable on both steric and electrostatic grounds to expect the answers to either of these points to favor the adduct, and hence no appreciable condensation would be observed.

The success of this intramolecular aldol-type cyclization overcomes the second and most crucial drawback to the originally conceived A → C → B route to the resin acids. We now have all of the necessary carbon–carbon bonds formed about the potential A ring. It remains to introduce the last center of asymmetry at C_{10} of the octalones **10**, and then cleave the ketone-containing ring so as to generate the necessary diacid prior to formation of the tricyclic ring system.

The steric congestion about the newly formed double bond of the octalones **10** is still a specter on the horizon, since catalytic hydrogenation will be particularly susceptible to this steric hindrance. Indeed, when the octalone **16** was hydrogenated over palladium on carbon in acetic acid solution, the uptake of hydrogen was slow, and the product was an oily mixture that contained a large proportion of unsaturated alcohol.

No concerted effort was made, however, to overcome the problems that faced catalytic hydrogenation of these octalones **10**, for chemical reduction of the enone system appeared better on two counts. Metal–ammonia reduction of the conjugated ketone system should not be susceptible to complication by the steric congestion about the C_{10} carbon. Probably even more significant is to recognize that in order to obtain the desired stereoisomer of the tricyclic acid—the *trans*-fused isomer **25**—it is necessary to reduce the enone system of the octalone **10** to generate a *trans*-fused β-decalone **11**. While it is probably reasonable to expect catalytic hydrogenation of the octalone **10** to produce principally the desired β-decalone **11** due to the greater hindrance to the β face of the molecule, it is a more firm assumption that a metal–ammonia will establish the desired *trans* fusion.[19,20] Thus, the structure of the octalone **10** would seem to dictate the use of the chemical reduction conditions on both steric and stereochemical grounds.

The situation is different with respect to the octalone **16**. This material is already epimeric at C_9 with the precursors to the natural resin acid series. In order to obtain a tricyclic acid that is only epimeric at this carbon, it would be necessary to reduce the enone system of the octalone **16** so as to form a *cis*-fused β-decalone **44**. The only possibility that such a trans-



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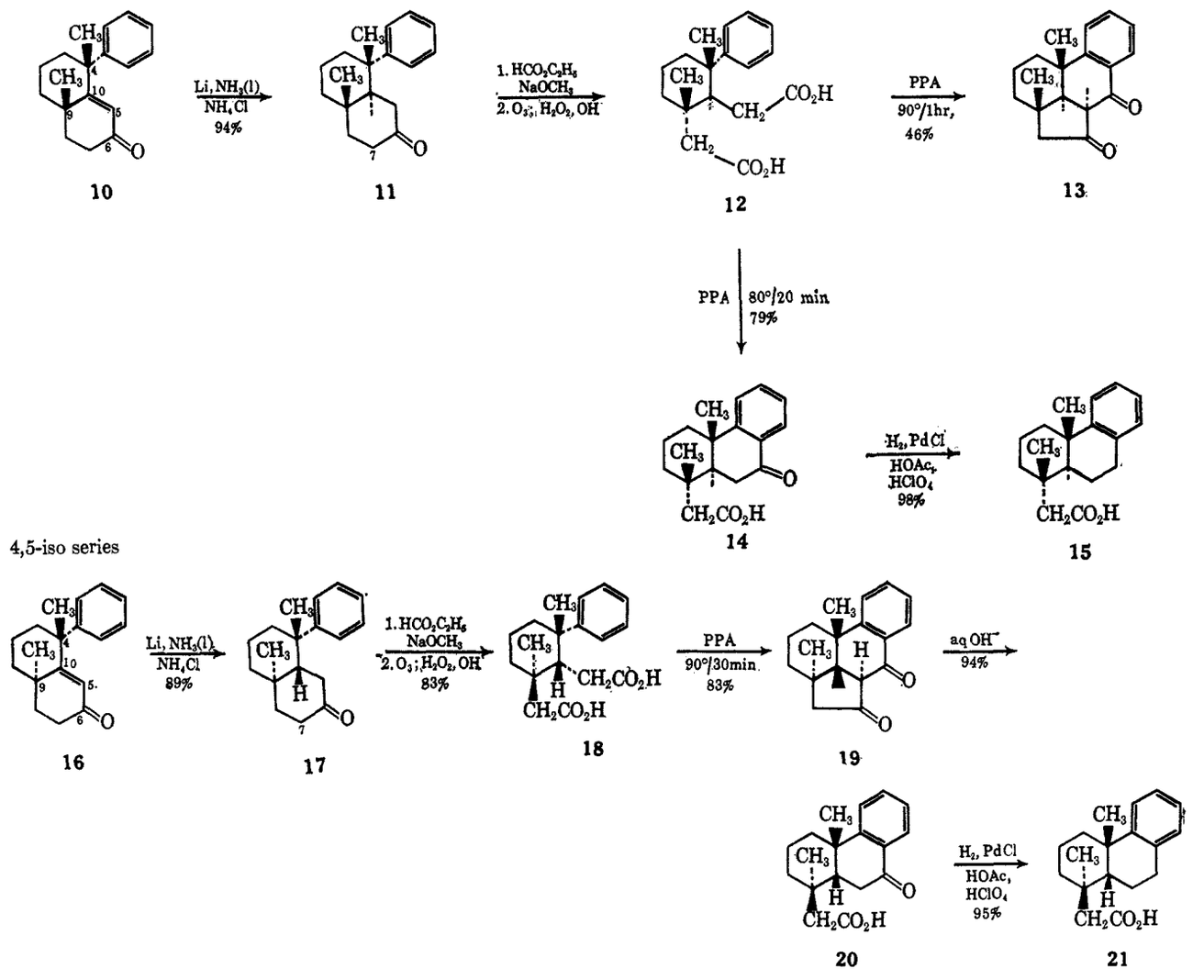
formation could be accomplished is through catalytic hydrogenation, and as mentioned above this was not a preparative method. Therefore again chemical reduction offers the more satisfactory solution to the structural transformation of the octalone **16** to an isomeric tricyclic acid **29**. The attending formation of a *trans*-fused β-decalone **17** must be expected, and hence the ultimate formation of the tricyclic acid **29**, which is epimeric to the natural series at both C_4 and C_5.

When each of the individual octalones **10** and **16** was reduced with lithium in liquid ammonia, there resulted quite satisfactory yields of the corresponding β-decalones **11** and **17**. In each case these ketones were considered to possess *trans*-fused bicyclic ring systems by virtue of their mode of formation. It was shown that the ketones **11** and **17** were brominated with bromine in acetic acid in the 7 position.[21] By analogy with the behavior of steroidal C_3 ketones,[22] this evidence supports the proposed *trans* fusion, for the *cis*-fused β-decalone might be expected to brominate in the 5 position. Such evidence is indicative of the desired *trans* fusion, but certainly not sufficient, as the 5-posi-

(19) G. Stork and S. D. Darling, *J. Am. Chem. Soc.*, **86**, 1761 (1964).
(20) M. J. T. Robinson, *Tetrahedron*, **21**, 2475 (1965).
(21) D. Crispin, F. F. Giarrisso, and R. E. Ireland, *J. Org. Chem.*, in press.
(22) L. F. Fieser and X. A. Dominquez, *J. Am. Chem. Soc.*, **75**, 1704 (1953).

CHART II

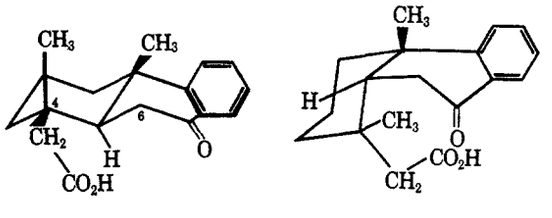
CONVERSION OF $\Delta^{5(10)}$-OCTALONES 10 AND 16 TO (±)-HOMODESISOPROPYLDEHYDROABIETIC ACIDS 15 AND 21



tion is exceedingly hindered and may not be brominated at any appreciable rate. (See Chart III.)

Cleavage of each β-decalone **11** and **17** between the C_4 and C_7 was readily accomplished by ozonization of the derived 7-hydroxymethylene-β-decalones. In each series the corresponding diacetic acid derivatives **12** and **18** were obtained in good yield. Polyphosphoric acid catalyzed cyclization of these isomeric diacids **12** and **18**, however, followed different courses. In each case the result of cyclization is explicable on the basis of the stereochemistry of the individual diacid involved.

In the natural series the diacid **12** cyclizes with polyphosphoric acid to the keto acid **14** as the sole product. Even after prolonged polyphosphoric acid treatment of the diacid **12**, only a meager yield of tetracyclic diketone **13**, resulting from acylation of the tetralone by the C_4 acetic acid residue, could be isolated. In contrast to this behavior, the isomeric diacid **18** led[23] solely to the diketone **19** with no trace of keto acid **20** present. Even when the polyphosphoric acid cyclization of the diacid **18** was interrupted after only partial completion, the only products isolable were recovered diacid **18** and diketone **19**. Apparently in the 4,5-iso series the keto acid is further acylated at a rate even greater than the benzene ring is initially attacked. A possible rationale for this behavior is embodied in the conformational representations of the two keto acids involved.



14 20

The keto acid **14** in which the A and B rings are *trans* locked has available only one conformation. In this form the C_4 acetic acid residue is equatorial to ring A and thus would have to attack ring B at position 6 in an equatorial rather than the stereoelectronically more favorable axial fashion. The keto acid **20** in which rings A and B are *cis* locked is more

(23) Similar results in another system were observed by W. Herz and G. Caple [*J. Am. Chem. Soc.*, **84**, 3517 (1962)].

flexible, and in one of the available conformations, the C_4 acetic acid residue is oriented so as to be able to attack the 6 position in an axial manner. This process will be stereoelectronically quite favorable, and hence further intramolecular acylation of the keto acid **20** takes place readily. Again, it is possible to explain quite diverse behavior of stereoisomers in this sequence on the basis of the spacial dispositions of the carbon residues.

In both the natural and the 4,5-iso series the completion of the transformations to the corresponding homotricyclic acids **15** and **21** was readily accomplished as indicated in Chart VII. The natural keto acid **14** required only catalytic hydrogenolysis of the C_7 ketone, while the 4,5-iso keto acid **20** first had to be prepared by basic cleavage[24] of the diketone **19**. In each case the reactions proceeded well and made available sufficient quantities of the homotricyclic acids **15** and **21** for conversion to their lower homologs.

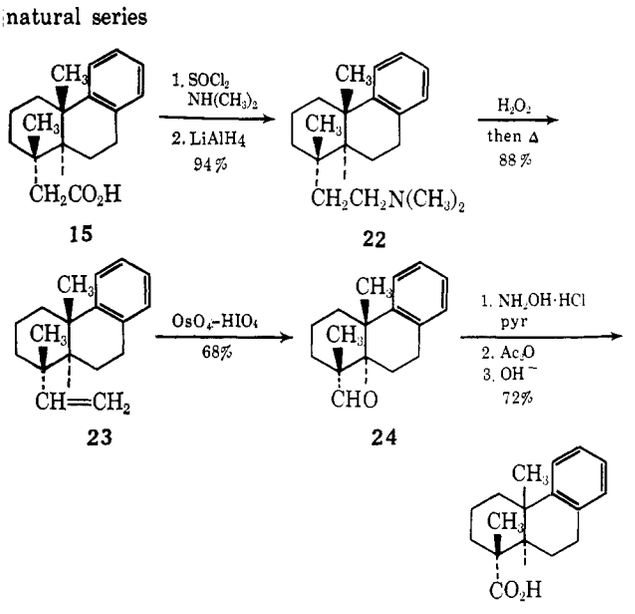
One of the important aspects of this synthetic scheme is the over-all yield of the keto acid **14**, for it is this compound that is envisaged as an intermediate for the preparation of ring C functionalized tricyclic acids. There are eight steps involved in the conversion of 2-phenylcyclohexanone **1** to the natural keto acid **14**, and the highly stereoselective route provides for the generation of this key intermediate in 26% over-all yield. The over-all yield in the natural series is significantly higher than that for the same transformation in the 4,5-iso series (16% over-all) where more side reactions are prevalent.

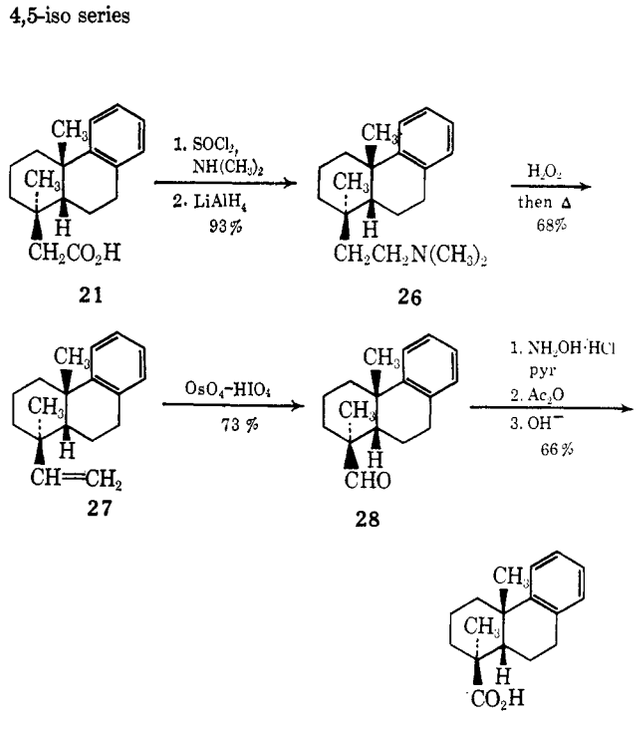
As satisfactory as the synthesis of the keto acid **14** is for the general plan for resin acids synthesis, there remains one thorny synthetic obstacle to be overcome before the scheme is complete. A method must be devised for the degradation of the C_4 acetic acid residue to the lower homolog. A similar problem was faced by Stork and Schulenberg[7] in their synthesis of (±)-dehydroabietic acid **37**, and they chose to employ the Barbier–Wieland degradation. The classical concept of this sequence suffers from one serious drawback: the chromic acid oxidation of the intermediate diphenylethylene derivative also causes extensive oxidation in ring B of the tricyclic nucleus. While it is possible to reduce the ketonic oxidation products, and thereby generate the desired tricyclic acid, the over-all yield of the process is not attractive, and the number of rough manipulations is high. It seemed attractive, then, to devise a less vigorous route whereby the extra carbon could be removed from the C_4 acetic acid side. The results of this phase of the endeavor are outlined in Chart III and offer an alternative to the Barbier–Wieland degradation that is not only efficient but also mild enough to avoid the over-oxidation of the molecule.

The degradative sequence outlined is very similar to the Barbier–Wieland process but takes advantage of the great susceptibility to oxidation of the vinyl group over the diphenylethylene system. The conversion of the acids **15** and **21** to the C_4 vinyl derivatives **23** and **27** was efficiently accomplished through the

CHART III

DEGRADATION OF DESISOPROPYLDEHYDROABIETIC ACID HOMOLOGS **15** AND **21**





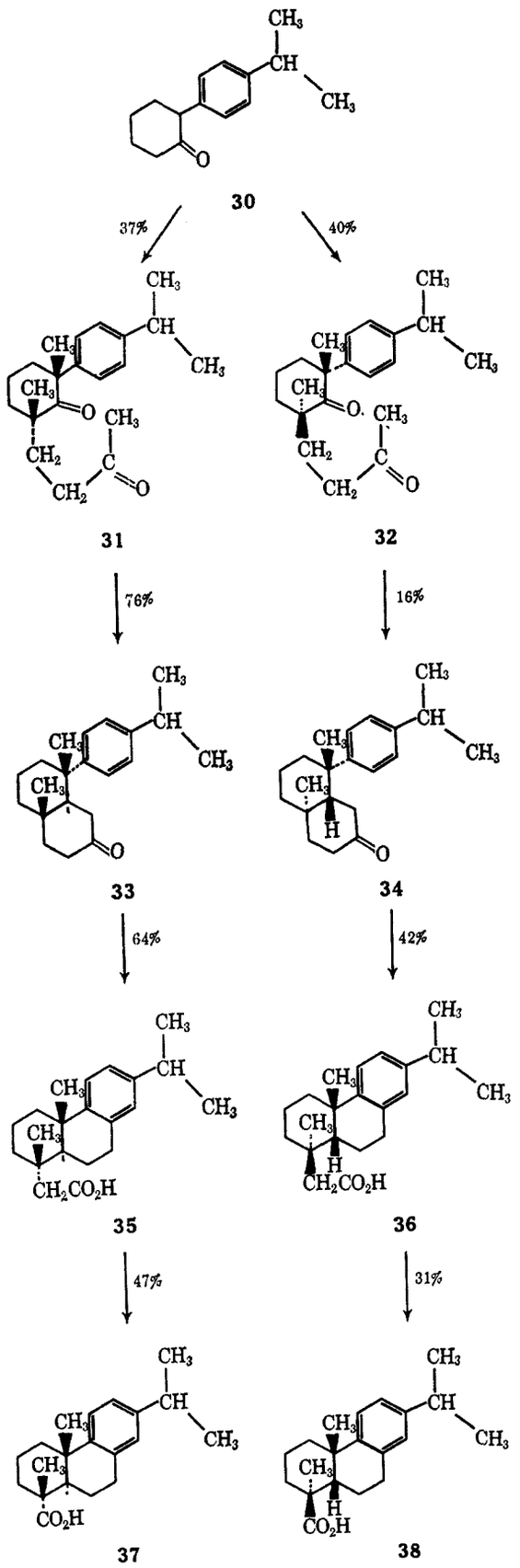
tertiary amines **22** and **26**. Direct oxidation of these olefins **23** and **27** to the corresponding acids was found to be impractical, for again overoxidation of the molecule was observed. However, when the more indirect route through the aldehydes **24** and **28** was followed, quite satisfactory yields of the two desired tricyclic acids **25** and **29** were obtained. Comparison of the melting points of these acids[9,25a] and their methyl

(24) C. R. Hauser, F. W. Swamer, and B. I. Ringler, *J. Am. Chem. Soc.*, **70**, 4023 (1948). By way of substantiating the above stereochemical argument, it is interesting to note that the diketone **13** in the natural series could *not* be cleaved by this or even more vigorous base treatment. Only salt formation was observed.

(25) (a) U. R. Ghatak, D. K. Datta, and S. C. Ray, *ibid.*, **82**, 1728 (1960); (b) J. A. Barltrop and A. C. Day, *Tetrahedron*, **14**, 310 (1961).

CHART IV

THE SYNTHESIS OF (±)-DEHYDROABIETIC ACID **37** AND 4,5-ISODEHYDROABIETIC ACID **38**



esters[9,25b] with those recorded by Ghatak and co-workers indicated that each compound had the assigned structure and stereochemistry.

The synthesis in each case was highly stereoselective, and the preparation of the natural isomer proceeded in quite satisfactory over-all yield. While no direct physical comparison with the synthetic specimens prepared by others was undertaken, the internal consistency and stereorationality of the sequences leaves little doubt as to the authenticity of the end products. The obvious choices for further effort were the naturally occurring resin acids themselves. The first of these to be accomplished was (±)-dehydroabietic acid **37**.

The (±)-dehydroabietic acid **37** sequence differs from the deisopropyl series above only in the choice of starting ketone. Thus, for this work we used 2-(*p*-isopropylphenyl)cyclohexanone **30**[12] in place of the 2-phenylcyclohexanone **1** used earlier. The results are outlined schematically in Chart IV together with the observed yields. Again it was found that the route to the natural (±)-dehydroabietic acid **37** afforded a much better over-all yield than that leading to the 4,5-isodehydroabietic acid **38**. A direct physical comparison of our synthetic (±)-dehydroabietic acid **37** and its methyl ester with their naturally derived counterparts[26] by infrared and proton magnetic resonance spectroscopy substantiated the identity of the synthetic material and corroborated the stereochemical conclusions mentioned above concerning the two synthetic sequences. It was possible through this route to prepare a sufficient quantity of (±)-dehydroabietic acid **37** to allow for its reduction to (±)-abietic acid by Professor A. W. Burgstahler.[27] Thus the combination of these efforts affords the first total synthesis of (±)-abietic acid as well.

Experimental Section[28]

I. Desisopropyldehydroabietic Acids. A. Natural Series. 6β-Methyl-2α-(3-ketobutyl)-6α-phenylcyclohexanone (4).—A modification of the procedure of Woodward and co-workers[29] was used. A solution of 19.6 g (0.09 mole) of the 6-hydroxymethylene-2-methyl-2-phenylcyclohexanone[30] and 12.7 g (0.18 mole) of freshly distilled methyl vinyl ketone in 250 ml of methanol was treated with 8 ml of triethylamine and allowed to stand in a nitrogen atmosphere for 48 hr at room temperature. Then most of the methanol was removed at reduced pressure, and the residue was diluted with water and extracted with ether. The resulting ether extract was washed successively with water, 10% aqueous hydrochloric acid, water, 5% aqueous sodium hydroxide, water, saturated salt solution, and dried over anhydrous sodium sulfate. After removal of the ether at reduced pressure, the residue was dissolved in 250 ml of methanol. This solution was treated with 50 ml of 10% aqueous potassium

(26) We are indebted to Professor W. Meyer of the University of Arkansas for a generous supply of natural dehydroabietic acid.

(27) A. W. Burgstahler and L. R. Worden, *J. Am. Chem. Soc.*, **86**, 96 (1964).

(28) Unless otherwise specified, the term "petroleum ether" refers to reagent grade material boiling in the range 30–60°. Melting points were determined on a Kofler hot stage and are corrected for stem exposure. Analyses were performed by Spang Microanalytical Laboratory, Ann Arbor, Mich. Infrared spectra that are recorded in microns were measured on a Perkin-Elmer Infracord Model 137 and those recorded in reciprocal centimeters were measured on a Perkin-Elmer Model 237 spectrometer. Strong bonds are marked s; all others reported are of moderated intensity unless otherwise designated. Ultraviolet spectra were determined on a Cary recording spectrophotometer (Model 11 MS). Florisil refers to the product of the Floridin Co., Tallahassee, Fla., 60–100 mesh.

(29) R. B. Woodward, F. Sondheimer, D. Taub, K. Hensler, and W. M. Metamore, *J. Am. Chem. Soc.*, **74**, 4223 (1952).

(30) Prepared from 2-methyl-2-phenylcyclohexanone[15] and ethyl formate in the standard manner.[13]

carbonate and allowed to stand overnight at room temperature. After dilution with water, the product was isolated by ether extraction. The ethereal solution was washed with water and saturated salt solution and then dried over anhydrous sodium sulfate. Removal of the solvent at reduced pressure and distillation of the residue afforded 14.15 g (61%) of the diketone **4**, bp 109–112° (0.04 mm). This material crystallized on standing, and on crystallization from petroleum ether (60–75°) there resulted 13.6 g (60%), mp 59–61°. The analytical sample was obtained after two further crystallizations from the same solvent and melted at 60.5–61.5°.

Anal. Calcd for $C_{17}H_{22}O_2$: C, 79.03; H, 8.58. Found: C, 79.17; H, 8.44.

Infrared showed $\lambda_{max}^{HCCl_3}$ 5.85 (s) (>C=O), 6.26 and 6.35 μ (phenyl).

6β-Methyl-2α-(3,3-ethylenedioxybutyl)-6α-phenylcyclohexanone (6).—A solution of 61.6 g (0.24 mole) of the diketone **4** and 14.55 ml (16.20 g, 0.26 mole) of ethylene glycol in 900 ml of dry benzene containing 200 mg of *p*-toluenesulfonic acid was maintained at reflux for 5 hr under a Dean–Stark water separator filled with Drierite. The solution was cooled, diluted with ether, washed successively with 10% aqueous potassium bicarbonate, water, saturated salt solution, and then dried over anhydrous sodium sulfate. Removal of the solvent at reduced pressure and distillation of the residue afforded 66.9 g (94%) of the monoketal **6**, bp 135–136° (0.01 mm), as a colorless, viscous liquid. Redistillation of a portion of this material afforded the analytical sample as a center cut with the same boiling range.

Anal. Calcd for $C_{19}H_{26}O_3$: C, 75.46; H, 8.67. Found: C, 75.57; H, 8.64.

Infrared showed λ_{max}^{film} 5.85 (s) (>C=O), 6.22 and 6.30 (weak) (phenyl), 9.2 (C–O–C of ketal), 13.0 and 14.2 μ (monosubstituted phenyl).

2β,6β-Dimethyl-2α-(3 ketobutyl)-6α-phenylcyclohexanone 8.—To a suspension of 100 g (0.90 mole) of potassium *t*-butoxide in 1500 ml of dry benzene in a nitrogen atmosphere was added with stirring at room temperature a solution of 66.9 g (0.22 mole) of the monoketal **6** in 100 ml of dry benzene. After the reaction mixture had stirred for 5 min, it was cooled in an ice–water bath for 3 min and then 68.5 ml (156 g, 1.1 moles) of methyl iodide was added all at once. The reaction mixture was then allowed to stir overnight as the cooling bath came to room temperature. An additional 30 ml of methyl iodide was then added, and the reaction mixture was stirred and maintained at reflux for 3 hr. The mixture was cooled, water was added, and the organic layer was separated and diluted with ether. The ethereal layer was washed with water, saturated salt solution, and then dried over anhydrous sodium sulfate. After removal of the solvents at reduced pressure, the residue was dissolved in 550 ml of acetone. This solution was treated with 100 ml of 3 *N* hydrochloric acid and allowed to stand for 3–4 hr at room temperature. The acetone was then removed at reduced pressure, and the solid diketone **8** was isolated by ether extraction. The ethereal solution was washed with water, 10% aqueous potassium bicarbonate, water, saturated salt solution, and then dried over anhydrous sodium sulfate. Removal of the ether at reduced pressure and crystallization of the residue from petroleum ether (60–75°) afforded 53.2 g (89%) of the diketone **8** in two crops of 52.1 g, mp 91–92° and 2.0 g, mp 90–91.5°. The analytical sample, obtained after two further crystallizations of a sample of this material from petroleum ether (60–75°), melted at 91–92°.

Anal. Calcd for $C_{18}H_{24}O_2$: C, 79.37; H, 8.88. Found: C, 79.40; H, 8.87.

Infrared showed $\lambda_{max}^{HCCl_3}$ 5.85 (s) (unhindered >C=O), 5.92 (s) (hindered >C=O), 6.26 and 6.35 μ (phenyl).

4β,9β-Dimethyl-4α-phenyl-Δ$^{5(10)}$-octalone-6 (10).—To a solution of 8.4 g (0.075 mole) of potassium *t*-butoxide in 150 ml of *t*-butyl alcohol was added a solution of 13.6 g (0.05 mole) of the diketone **8** in 60 ml of dry benzene, and the reaction mixture was allowed to stand overnight at room temperature in a nitrogen atmosphere. The wine-red solution was then diluted with 100 ml of 3 *N* hydrochloric acid and most of the *t*-butyl alcohol was removed at reduced pressure. The crude, crystalline product was isolated by ether extraction, and the residue which remained after removal of the ether at reduced pressure was evaporatively distilled at 155° (0.04 mm). Crystallization of the solid distillate from petroleum ether (60–75°) afforded 12.1 g (95%) of the octalone **10** in two crops of 10.8 g, mp 117.0–117.5°, and 1.3 g, mp 116.5–117.5°. The analytical sample was obtained after one further crystallization of a sample of this material from petroleum ether (60–75°) and melted at 117.0–117.5°.

Anal. Calcd for $C_{18}H_{22}O$: C, 84.99; H, 8.72. Found: C, 85.02; H, 8.74.

Infrared showed $\lambda_{max}^{HCCl_3}$ 6.0 (s) (unsaturated >C=O), 6.26 μ (s) (phenyl).

Ultraviolet showed λ_{max}^{MeOH} 248 mμ (8700). The melting range of a mixture of this octalone **10**, mp 117.0–117.5°, and the octalone **16**, mp 100–101°, was 80–90°.

4β,9β-Dimethyl-4α-phenyl-*trans*-decalone-6 (11).—In the same manner as described for the reduction of the octalone **16**, 7.62 g (0.03 mole) of the octalone **10** was reduced with 0.7 g (0.10 g-atom) of lithium in 600 ml of liquid ammonia and 300 ml of ether. After a similar work-up, the crude product was crystallized from methanol and afforded 7.2 g (94%) of the decalone **11**, mp 105–107°. The analytical sample, obtained after two further crystallizations from methanol, melted at 106–107°.

Anal. Calcd for $C_{18}H_{24}O$: C, 84.32; H, 9.44. Found: C, 84.29; H, 9.53.

Infrared showed $\lambda_{max}^{HCCl_3}$ 5.85 (s) (saturated >C=O), 6.26 and 6.35 μ (phenyl).

1β,3β-Dimethyl-3α-phenylcyclohexane-1α,2β-diacetic Acid (12).—In the same manner as described below for the preparation of the diacid **18**, 2.825 g (11.0 mmoles) of the decalone **11** was hydroxymethylated in 200 ml of dry benzene with 3.0 g (55.6 mmoles) of sodium methoxide and 8.0 ml (7.4 g, 100 mmoles) of ethyl formate. A solution of the crude hydroxymethylene derivative in 65 ml of ethyl acetate was then treated at −70° with a stream of ozonized oxygen (0.1 mole/hour) for 20 min; the ethyl acetate was removed at reduced pressure and 35°, and the residue, oxidized in 50 ml of 5% aqueous sodium hydroxide, was oxidized by the addition of two 15-ml portions of 30% hydrogen peroxide. The resulting crude diacid **12** was crystallized from ether–petroleum ether and afforded 2.413 g (73%) of material melting at 172–174°. The analytical sample was obtained by two further crystallizations of a portion of this material from acetone–petroleum ether (60–75°) and melted at 173–174°, with preliminary softening at 168°.

Anal. Calcd for $C_{18}H_{24}O_4$: C, 71.03; H, 7.95. Found: C, 70.96; H, 8.01.

Cyclization of the Diacid 12. (a) Formation of the Diketone 13.—In the same fashion as described below for the preparation of the diketone **19**, a mixture of 1.30 g (4.28 mmoles) of the diacid **12** and 10 ml of polyphosphoric acid was heated under a nitrogen atmosphere on the steam bath for 1 hr. When the crude neutral product that resulted was crystallized from ethyl acetate–petroleum ether (60–75°), there was obtained 525 mg (46%) of the diketone **13**, mp 190–993°. The analytical sample was obtained after one further crystallization from acetone and melted at 191.5–193.5°.

Anal. Calcd for $C_{18}H_{20}O_2$: C, 80.56; H, 7.51. Found: C, 80.25; H, 7.37.

Infrared showed $\lambda_{max}^{HCCl_3}$ 5.68 (s) (five-ring >C=O), 5.92 (s) (conjugated six-ring >C=O), 6.25 μ (s) (conjugated phenyl).

The diketone **13** formed a stable, slightly soluble salt when treated with 1% aqueous alcoholic sodium hydroxide, 5% aqueous sodium hydroxide in ethylene glycol, and 10% aqueous alcoholic ammonium hydroxide.

(b) Formation of (±)-7-Ketodesisopropylhomodehydroabietic Acid (14).—When a mixture of 1.73 g (5.37 mmoles) of the diacid **12** and 100 ml of polyphosphoric acid was heated under nitrogen in an oil bath at 78–80° for 20 min, none of the diketone **13** was obtained after the same work-up as described above. The acid fraction, isolated by neutralization of the 10% aqueous potassium carbonate washes of the original ethereal extracts, was taken up in ether, and the resulting ethereal solution was washed with water and saturated salt solution, and then dried over anhydrous sodium sulfate. Removal of the ether at reduced pressure and crystallization of the residue from benzene–petroleum ether (60–75°) afforded 1.212 g (79%) of the keto acid **14**, mp 155-157°. The analytical sample was obtained by one further crystallization of a sample of this material from 50% benzene–petroleum ether (60–75°) and melted at 156.5–158°.

Anal. Calcd for $C_{18}H_{22}O_3$: C, 75.49; H, 7.75. Found: C, 75.24; H, 7.73.

Infrared showed $\lambda_{max}^{HCCl_3}$ 5.85 (s) (COOH), 5.94 (s) (conjugated >CO) and 6.25 μ (s) (conjugated phenyl); λ_{max}^{film} 13.0 and 13.75 μ (*ortho*-disubstituted phenyl).

(±)-Desisopropylhomodehydroabietic Acid (15).—When 1.21 g (4.3 mmoles) of the keto acid **14** was hydrogenated over 0.3 g of 10% palladium on carbon in 30 ml of glacial acetic acid containing 0.2 ml of 70% aqueous perchloric acid in the same manner as described below for the keto acid **20**, there resulted 1.14 g (98%) of the acid **15**, mp 145–147°, after evaporative distillation at 150° (0.01 mm). The analytical sample was obtained by crystallization of a sample of this material from benzene–petroleum ether and melted at 146–147°.

Anal. Calcd for $C_{18}H_{24}O_2$: C, 79.37; H, 8.88. Found: C, 79.46; H, 8.96.

Infrared showed $\lambda_{max}^{HCCl_3}$ 5.83 (s) (*C*OOH), 5.94 (s) (conjugated six-ring >C=O), 6.25 μ (s) (conjugated phenyl).

(±)-N,N-Dimethyldesisopropylhomodehydroabietamide.—In the same fashion as described below for the preparation of the amide in the 4,5-iso series, 1.083 g (4.0 mmoles) of the acid **15** was converted to its acid chloride with 40 ml of thionyl chloride and thence to the amide (colorless oil evaporatively distilled at 160° at 0.01 mm; 96% over-all) with excess dimethylamine in benzene. The analytical sample was obtained by a further evaporative distillation at 165 ° (0.01 mm).

Anal. Calcd for $C_{20}H_{29}NO$: C, 80.22; H, 9.76; N, 4.68. Found: C, 80.58; H, 9.83; N, 4.43.

Infrared showed λ_{max}^{film} 6.10 (s) [–*C*ON$(CH_3)_2$], 13.1 and 13.8 μ (*ortho*-disubstituted phenyl).

(±)-N,N-Dimethyldesisopropylhomodehydroabietanylamine (22).—Reduction of 1.140 g (3.82 mmoles) of the amide was carried out exactly as described below for the preparation of the amine **26**. When the crude product, isolated after evaporation of the ether, was evaporatively distilled at 120° (0.01 mm), there resulted 1.050 g (98%) of the amine **22**, as a colorless, mobile oil. A sample of this material was used for combustion analysis without further purification.

Anal. Calcd for $C_{20}H_{31}N$: C, 84.15; H, 10.95; N, 4.91. Found: C, 84.14; H, 10.98; N, 4.97.

Infrared showed λ_{max}^{film} 3.50 [–N$(CH_3)_2$], 6.22 and 6.35 (weak) (phenyl); 13.1 and 13.8 μ (*ortho*-disubstituted phenyl).

Amine Oxide Pyrolysis.[31]—The procedure employed was the same as that used to prepare the olefin **27**. Thus, when 622 mg (2.18 mmoles) of the amine **22** was treated with 1.5 ml of 30% aqueous hydrogen peroxide, and the resulting amine oxide was pyrolyzed at 150–160° (0.02 mm), there resulted 460 mg (88%) of the olefin **26** as a colorless, mobile oil after chromatography over 10 g of alumina oxide and evaporative distillation at 95° (0.01 mm). A portion of this material was used for combustion analysis without further purification.

Anal. Calcd for $C_{18}H_{24}$: C, 89.94; H, 10.06. Found: C, 89.75; H, 10.14.

Infrared showed λ_{max}^{film} 3.18 (vinyl H), 5.45 (weak), 6.10, 10.0, and 11.0 (–CH=CH_2 grouping), 6.25 and 6.35 (weak) (phenyl), 13.10 and 13.85 μ (*ortho*-disubstituted phenyl).

(±)-Desisopropyldehydroabietanal (24).—In the same manner as described for the preparation of the 4,5-iso olefin **28**, 636 mg (2.66 mmoles) of the olefin **23** was oxidized with 50 mg of osmium tetroxide and 2.044 g (8.96 mmoles) of paraperiodic acid in 70 ml of dioxane, 7 ml of glacial acetic acid, and 14 ml of water. After the reaction mixture had stirred for 18 hr at room temperature, it was worked up as before, and the residue (537 mg), obtained after final evaporation of the solvents, was chromatographed on 40 g of Florisil. Elution with 500 ml of 5% ether–petroleum ether afforded 440 mg (68%) of the crystalline, low-melting aldehyde **24**. It was found more convenient to treat this material as a liquid, and the analytical sample was obtained by evaporative distillation at 60° (0.05 mm).

Anal. Calcd for $C_{17}H_{22}O$: C, 84.25; H, 9.15. Found: C, 84.24; H, 9.48.

Infrared showed λ_{max}^{film} 2696 (–C*H*O), 1729 (s) (aldehyde >C=O), 1600 and 1575 (weak) (phenyl), 755 and 730 cm^{-1} (*ortho*-disubstituted phenyl).

(±)-Desisopropyldehydroabietonitrile.—This material was obtained in the same fashion as was the corresponding 4,5-iso series nitrile. Thus the crude oxime, obtained by heating for 2 hr a solution of 152 mg (0.62 mmole) of the aldehyde **24** in 3 ml of pyridine and 5 ml of ethanol with 200 mg (2.88 mmoles) of hydroxylamine hydrochloride and then evaporating of the solvents, was heated under nitrogen for 5 hr with 5 ml of acetic anhydride. Evaporation of the acetic anhydride on a steam bath under a stream of nitrogen and crystallization of the residue from petroleum ether afforded 139 mg (93%) of the desired nitrile, mp 126–127°. The analytical sample, obtained after two further crystallizations from the same solvent and finally sublimation at 70° and 0.05 mm, melted at 127–127.5°.

Anal. Calcd for $C_{17}H_{21}N$: C, 85.30; H, 8.85; N, 5.85. Found: C, 85.36; H, 8.79; N, 5.90.

Infrared showed $\nu_{max}^{HCCl_3}$ 2230 (–C≡N), 1600 and 1575 cm^{-1} (weak) (phenyl).

(±)-Desisopropyldehydroabietic Acid (25).—When a solution of 96 mg (0.4 mmole) of the above nitrile in 10 ml of diethylene glycol containing 2 g of powdered potassium hydroxide was heated under reflux in a nitrogen atmosphere fo 6 hr, a portion of the nitrile sublimed and was trapped in the condenser. The reaction mixture was cooled and diluted with water; the condenser washed with ether. The ethereal layer was separated, washed with water, and dried over anhydrous sodium sulfate. Removal of the ether at reduced pressure afforded 22 mg (23%) of recovered nitrile (identified by infrared and mixture melting point with authentic material).

Acidification of the aqueous layer from the hydrolysis, afforded a solid acid which was extracted with ether. This ethereal layer was washed with water, saturated salt solution and dried over anhydrous sodium sulfate. Removal of the ether at reduced pressure afforded 81 mg of crude, crystalline acid. While crystallization of this material could be effected from acetone–petroleum ether (81 mg afforded 42 mg, mp 173–174°, of large off-colored prisms), a better method of purification was sublimation at 160° and 0.008 mm, whereby from the total crude material (recrystallized sample combined with residues from the mother liquor) afforded 80 mg (77%) of the acid **25**, mp 174.5–175° (lit.[9,25a] 174–175°, 171–173°). A sample of this material was used for combustion analysis.

Anal. Calcd for $C_{17}H_{22}O_2$: C, 79.03; H, 8.59. Found: C, 79.15; H, 8.77.

Infrared showed $\nu_{max}^{HCCl_3}$ 1700 (s) (–*C*OOH), 1600 and 1575 cm^{-1} (weak) (phenyl).

The **methyl ester**, obtained by the action of ethereal diazomethane on the acid **25**, melted at 112.0–112.5° (lit.[9,25b] 110–112°, 115°) after two crystallizations from methanol.

Anal. Calcd for $C_{18}H_{24}O_2$: C, 79.37; H, 8.88. Found: C, 79.28; H, 8.88.

Infrared showed $\nu_{max}^{HCCl_3}$ 1730 (s) (–*C*OOCH_3), 1600 and 1575 cm^{-1} (weak) (phenyl).

B. 4,5-Iso Series 2,6-Dimethyl-6-phenylcyclohexanone (5).—To a solution of 60.0 g (1.53 g-atoms) of potassium in 1400 ml of dry *t*-butyl alcohol in a nitrogen atmosphere was added 101.0 g (0.38 mole) of 2-*n*-butylthiomethylene-6-phenylcyclohexanone[13] in 200 ml of dry benzene. After the red-orange solution was stirred for 5 min at room temperature, the reaction mixture was cooled in an ice–water bath and 105.0 ml (240.0 g, 1.66 moles) of methyl iodide was added all at once. The mixture was stirred overnight at room temperature, and then most of the solvent was removed by distillation at reduced pressure while the vessel was warmed on the steam bath. The residue was treated with water, and the organic material was extracted with ether. The ethereal solution was washed successively with water, 5% aqueous sodium hydroxide, water, and saturated salt solution, and then dried over anhydrous sodium sulfate. After removal of the desiccant and evaporation of the solvent, the crude product, amounting to 115 g, was split into two equal portions. Each portion was individually dissolved in 1300 ml of ethanol, and each solution was treated with 40 teaspoons of W-2 Raney nickel, and stirred and heated under reflux for 15 hr. After the catalyst was removed by filtration and most of the ethanol was evaporated at reduced pressure, the two batches were combined and dissolved in ether. The ethereal solution was washed three times with water, once with saturated salt solution, and dried over anhydrous sodium sulfate. After removal of the drying agent and evaporation of the ether at reduced pressure, the residue was distilled and afforded 66.0 g (86%) of 2,6-dimethyl-6-phenylcyclohexanone, bp 85–89° (0.15 mm).

The analytical sample, obtained by redistillation of a portion, boiled at 74–74.5° (0.05 mm).

Anal. Calcd for $C_{14}H_{18}O$: C, 83.12; H, 8.97. Found: C, 82.91; H, 8.92.

Infrared showed λ_{max}^{film} 5.85 (s) (saturated >C=O), 6.25 and 6.33 (weak) (phenyl), 13.10 and 14.30 μ (monosubstituted phenyl).

(31) Following the procedure of K. W. Bently, J. C. Ball, and J. P. Ruige, *J. Chem. Soc.*, 1963 (1958).

2α,6β-Dimethyl-2β-(3-chloro-2-butenyl)-6α-phenylcyclohexanone (7).—To a suspension of sodium amide in 800 ml of dry ether in a nitrogen atmosphere (prepared by adding 5.0 g (0.22 g-atom) of sodium to *ca.* 200 ml of liquid ammonia containing a trace of ferric nitrate, replacing the ammonia with ether and placing the resulting suspension under nitrogen) was added 38.4 g (0.19 mole) of 2,6-dimethyl-6-phenylcyclohexanone **5** and the reaction mixture was heated and stirred under reflux for 6 hr. The system was then arranged for distillation, still maintaining a nitrogen atmosphere, and the ether was replaced by 800 ml of dry benzene. When the vapor temperature reached 78°, the system was cooled sufficiently to allow its change to a reflux apparatus, and then 32.3 g (0.26 mole) of freshly distilled 1,3-dichlorobutene was added all at once. This mixture was stirred and heated under reflux in a nitrogen atmosphere overnight (*ca.* 10 hr), and then cooled and treated with 250 ml of water. The benzene layer was separated, diluted with 300 ml of ether, and the resulting organic solution was washed successively with water, saturated salt solution, and dried over anhydrous sodium sulfate. After evaporation of the solvent at reduced pressure, and distillation of the residue in high vacuum, there was obtained 9.66 g of recovered 2,6-dimethyl-6-phenylcyclohexanone, bp 75–76° (0.05 mm), and 38.0 g (69% yield or 92% conversion based on the ketone **5** consumed) of the chloroketone **7**, bp 112–114° (0.05 mm). The analytical sample was obtained by redistillation of a portion of this material and boiled at 118° (0.06 mm).

Anal. Calcd for $C_{18}H_{23}ClO$: C, 74.34; H, 7.97; Cl, 12.19. Found: C, 74.18; H, 7.91; Cl, 12.04.

Infrared showed λ_{max}^{film} 5.91 μ (s) (α,α,α′,α′-tetrasubstituted >C=O), 6.02 (–C=C–Cl), 6.25 and 6.35 (weak) (phenyl), 13.10 and 14.30 μ (monosubstituted phenyl).

2α,6β-Dimethyl-2β-(3-oxobutyl)-6α-phenylcyclohexanone (9).—The hydrolysis of the vinyl chloride was accomplished by stirring a solution of 33.3 g (0.114 mole) of the chloro ketone **7** in 300 ml of 9:1 concentrated sulfuric acid–water for a 1.5-hr period at 0° and then for an additional 1.5 hr at room temperature. During this time the copious volumes of gaseous hydrogen chloride initially liberated subsided appreciably. The reaction mixture was poured onto ice, the slush diluted with water, and the oily organic material was extracted with ether. The ethereal solution was washed successively with water, saturated aqueous sodium bicarbonate, water, saturated salt solution, and dried over anhydrous sodium sulfate. Removal of the ether at reduced pressure and distillation of the residue under high vacuum afforded 22.71 g (73%) of the diketone **9**, bp 123–124° (0.03 mm). The analytical sample, obtained by redistillation of a portion of this material, boiled at 110° (0.015 mm).

Anal. Calcd for $C_{18}H_{24}O_2$: C, 79.37; H, 8.88. Found: C, 79.66; H, 9.12.

Infrared showed λ_{max}^{film} 5.85 (s) ($-CH_2COCH_3$), 5.92 (s) (α,α,α′,α′-tetrasubstituted >C=O), 6.28 and 6.35 (weak) (phenyl), 13.10 and 14.25 μ (monosubstituted phenyl).

4β,9α-Dimethyl-4α-phenyl-Δ$^{5(10)}$-octalone-6 (16).—To a solution of 2.0 g (0.052 g-atom) of potassium in 100 ml of dry *t*-butyl alcohol in a nitrogen atmosphere was added with stirring 4.0 g (0.0147 mole) of the diketone **9** in 8 ml of dry benzene, and then the mixture was stirred overnight (*ca.* 10 hr) at room temperature. The resulting red reaction mixture was treated with 100 ml of 10% aqueous acetic acid, and then most of the *t*-butyl alcohol was removed by distillation at reduced pressure. The suspended red oil that resulted was extracted with ether, and the ethereal solution was successively washed with water, saturated aqueous sodium bicarbonate, water, saturated salt solution, dried over anhydrous sodium sulfate, and evaporated at reduced pressure. The residual red oil was chromatographed on 200 g of basic alumina (Merck). After an initial wash with 3 l. of 10% benzene–petroleum ether, 0.90 g (30%) of 2,6-dimethyl-6-phenylcyclohexanone (identified by compraison of the infrared spectrum with that of authentic material) was eluted with 3 l. of 25% benzene–petroleum ether. Further elution with 2 l. of 50% benzene–petroleum ether and then 3 l. 75% benzene–petroleum ether afforded 2.38 g (64%) of slightly yellow, crystalline octalone **16**, mp 98–100°. Recrystallization of this material from petroleum ether and then sublimation at 100° (0.001 mm) afforded 1.55 g (41%) colorless, sugar-like crystals of the analytically pure octalone, mp 100–101°.

Anal. Calcd for $C_{18}H_{22}O$: C, 84.99; H, 8.72. Found: C, 84.88; H, 8.83.

Infrared showed λ_{max}^{film} 6.0 (s) (conjugated >C=O), 6.25 (phenyl), 13.05 and 14.25 μ (monosubstituted phenyl).

Ultraviolet showed $\lambda_{max}^{95\%\ EtOH}$ 242 mμ (15000).

The **2,4-dinitrophenylhydrazone** was obtained in quantitative yield from 24.5 mg (0.096 mmole) of the octalone **16** with 20.5 mg (0.104 mmole) of 2,4-dinitrophenylhydrazine in 1.5 ml of glacial acetic acid and melted at 222.5–224° when introduced at 180°. Recrystallization of this sample from chloroform–ethanol did not alter the melting point.

Anal. Calcd for $C_{24}H_{26}N_4O_4$: C, 66.36; H, 6.03; N, 12.90. Found: C, 66.25; H, 6.00; N, 12.85.

4β,9α-Dimethyl-4α-phenyl-*trans*-decalone-6 (17).—To a solution of 1.4 g (0.2 g-atom) of lithium in *ca.* 200 ml of distilled, liquid ammonia was rapidly added a solution of 2.70 g (0.0106 mole) of the octalone **16** in 75 ml of dry ether, and then the reaction mixture was stirred for 1 hr. After the excess lithium was destroyed by the addition of excess ammonium chloride, the ammonia was evaporated, and the residue was partitioned between ether and water. The ethereal layer was separated, washed with water and saturated salt solution, dried over anhydrous sodium sulfate, and evaporated at reduced pressure. The residue was crystallized from petroleum ether and afforded 2.20 g (81%) of the decalone **17**, mp 89–91°. When the mother liquors from this crystallization were chromatographed on 20 g of basic alumina (Merck), there was eluted a further portion of the decalone **17** with 750 ml of 30% benzene–petroleum ether. Crystallization of this material from petroleum ether gave 0.227 g (8%) of pure decalone that also melted at 89–91°. Hence, there was obtained a total of 2.427 g (89%) of decalone **17**, mp 89–91°. The analytical sample, obtained by sublimation at 90° (0.001 mm) and crystallization from petroleum ether, melted at 92–93° with preliminary softening at 89.5°.

Anal. Calcd for $C_{18}H_{24}O$: C, 84.32; H, 9.44. Found: C, 84.43; H, 9.37.

Infrared showed λ_{max}^{film} 5.85 (s) (saturated >C=O), 6.25 and 6.33 (weak) (phenyl), 13.05 and 14.15 μ (monosubstituted phenyl).

The **2,4-dinitrophenylhydrazone** was obtained in quantitative yield from 102 mg (0.4 mole) of analytically pure decalone **17** with 85 mg (0.43 mole) of 2,4-dinitrophenylhydrazine in 3 ml of glacial acetic acid and melted at 212.5–213° when introduced at 160°. Recrystallization of this sample from chloroform–ethanol did not alter the melting point.

Anal. Calcd for $C_{24}H_{28}N_4O_4$: C, 66.04; H, 6.47; N, 12.84. Found: C, 66.10; H, 6.38; N, 12.90.

1α,3β-Dimethyl-3α-phenylcyclohexane-1β,2α-diacetic Acid (18).—To an ice-cooled, stirred suspension of 1.5 g (27.8 mmoles) of sodium methoxide in 100 ml of dry benzene contained in a nitrogen atmosphere was added dropwise a solution of 1.56 g (6.1 mmoles) of the decalone **17** and 4.0 ml (3.7 g, 50 mmoles) of purified ethyl formate in 10 ml of dry benzene, and then the reaction mixture was allowed to come to room temperature while stirring was continued overnight. To the resulting yellow orange paste was added 50 ml of water, and the organic layer was separated and extracted twice with two 20-ml portions of 5% aqueous sodium hydroxide. The combined aqueous layers were cooled by the addition of ice, made acid to congo red paper, and rapidly extracted with ether. The resulting ethereal solution was washed with water, saturated salt solution, dried over anhydrous sodium sulfate, and evaporated to dryness at reduced pressure. The crude hydroxymethylene derivative that remained was not further purified but dissolved in 50 ml of ethyl acetate. This solution was cooled to −70°, and treated with a stream of ozonized oxygen (0.1 mole/hr) for 8.5 min. After removal of the ethyl acetate at reduced pressure and 35°, the residue was heated on the steam bath with 50 ml of 5% aqueous sodium hydroxide and 10 ml of 30% hydrogen peroxide for 15 min. After this time an additional 5 ml of 30% hydrogen peroxide was added, and heating was continued for 20 min. The reaction mixture was cooled, made acid to congo red paper, and extracted with ether. The resulting ethereal extract was washed with water, saturated salt solution, and dried over anhydrous sodium sulfate. After removal of the ether at reduced pressure and crystallization of the residue from ethyl acetate–petroleum ether, there was obtained 1.54 g (83%) of the diacid **18**, mp 210–217°. The analytical sample, obtained after two further crystallizations from the same solvent pair, melted at 216–218°.

Anal. Calcd for $C_{18}H_{24}O_4$: C, 71.03; H, 7.95. Found: C, 71.05; H, 8.07.

Cyclization of Diacid 18.—A mixture of 1.23 g (4.05 mmoles) of the well-pulverized diacid **18** and 90 ml of polyphosphoric acid was stirred and heated on the steam bath for 0.5 hr in a nitrogen atmosphere. Ice was then added to the cooled reaction mixture; the resulting slush was diluted and extracted with ether. The ethereal solution was washed successively with water, 10% aqueous potassium bicarbonate, water, and saturated salt solution, and then dried over anhydrous sodium sulfate. Removal of the ether at reduced pressure and crystallization of the residue from methanol afforded 900 mg (83%) of the diketone **19**, mp 153–155°. This material gave a black-green color with 1% alcoholic ferric chloride solution and a yellow precipitate with 2,4-dinitrophenylhydrazine test reagent. The analytical sample, obtained after two further crystallizations from ethyl acetate–petroleum ether, melted at 154–155.5°.

Anal. Calcd for $C_{16}H_{20}O_2$: C, 80.56; H, 7.51. Found: C, 80.55; H, 7.64.

Infrared showed $\lambda_{max}^{HCCl_3}$ 5.72 (s) (five-ring >C=O), 5.99 (s) (conjugated six-ring >C=O), and 6.26 μ (s) (conjugate phenyl).

Shorter reaction times than 0.5 hr produced a mixture of the dione **19** and the starting diacid **18** with no sign (infrared) of the presence of the keto acid **20**.

(±)-7-Keto-4,5-isodesisopropylhomodehydroabietic Acid (20).—A solution of 956 mg (3.56 mmoles) of the diketone **19** and 1.4 ml (3.92 mmoles) of 10% aqueous sodium hyroxide in 12.6 ml of methanol was heated under reflux in a nitrogen atmosphere for 1.5 hr. The reaction mixture was cooled, diluted with water, and extracted twice with ether. The aqueous layer was warmed to expel dissolved ether, made acid to congo red paper, and the precipitated acid was isolated by ether extraction. The ethereal solution was washed with water, saturated salt solution, and dried over anhydrous sodium sulfate. After removal of the ether at reduced pressure and crystallization of the residue from ethyl acetate–petroleum ether, there was obtained 947 mg (94%) of the keto acid **20**, mp 158–160°. The analytical sample was obtained after another crystallization from the same solvent pair and melted at 159–160.5°. This material gave a wine-red precipitate when treated with 2,4-dinitrophenylhydrazine test reagent.

Anal. Calcd for $C_{18}H_{22}O_3$: C, 75.49; H, 7.75. Found: C, 75.44; H, 7.86.

Infrared showed $\lambda_{max}^{HCCl_3}$ 5.83 (s) (-*C*OOH), 5.96 (s) (conjugated >C=O), and 6.25 μ (s) (conjugate phenyl).

(±)-4,5-Isodesisopropylhomodehydroabietic Acid (21).—To a suspension of 0.1 g of 10% palladium on carbon in 5 ml of glacial acetic acid was added a solution of 210 mg (0.74 mmole) of the keto acid **20** and 0.1 ml of 70% aqueous perchloric acid in 15 ml of glacial acetic acid, and the mixture was stirred in a hydrogen atmosphere for 20 min. During this period 39 ml of hydrogen was absorbed. The catalyst was removed by filtration and washed with benzene, and the filtrate was diluted with water and extracted with ether. The resulting ethereal solution was washed with water, saturated salt solution and dried over anhydrous sodium sulfate. Removal of the ether at reduced pressure and crystallization of the solid residue from petroleum ether (60–75°) afforded 192 mg (95%) of the acid **21**, mp 140–141°. The analytical sample, obtained after one further crystallization from the same solvent, also melted at 140–141°.

Anal. Calcd for $C_{18}H_{24}O_2$: C, 79.37; H, 8.88. Found: C, 79.23; H, 8.65.

Infrared showed $\lambda_{max}^{HCCl_3}$ 5.88 (s) (-*C*OOH), 6.26 and 6.35 μ (weak) (phenyl).

(±)-N,N-Dimethyl-4,5-isodesisopropylhomodehydroabietamide.—A solution of 660 mg (2.42 mmoles) of the acid **21** in 20 ml of thionyl chloride was heated under reflux on the steam bath for 1 hr. The excess thionyl chloride was then removed at reduced pressure, and the residue was freed of the last traces of the reagent by dissolution in 100 ml of benzene and removal of 50 ml of the solvent by distillation. The resulting solution was treated with excess dimethylamine and then diluted with ether, and the ethereal solution was successively washed with water, 10% hydrochloric acid, water, saturated salt solution, and dried over anhydrous sodium sulfate. Removal of the ether and crystallization of the residue from petroleum ether afforded 687 mg (95%) of the amide, mp 65–66°. The analytical sample, obtained after one further crystallization from petroleum ether, also melted at 65–66°.

Anal. Calcd for $C_{20}H_{29}NO$: C, 80.22; H, 9.76; N, 4.68. Found: C, 80.21; H, 9.66; N, 4.66.

Infrared showed $\nu_{max}^{HCCl_3}$ 1626 (s) (-*C*ONMe$_2$), 1600 and 1580 cm^{-1} (weak) (phenyl).

(±)-N,N-Dimethyl-4,5-isodesisopropylhomodehydroabietanylamine (26).—A solution of 632 mg (2.12 mmoles) of the amide in 15 ml of ether was added to a slurry of 250 mg of lithium aluminum hydride in 10 ml of ether and the reaction mixture was stirred for 0.5 hr at room temperature. The excess hydride was destroyed by adding 0.5 ml of water and then 0.4 ml of 10% aqueous sodium hydroxide, and the resulting salts were removed by filtration. The ethereal filtrate was evaporated at reduced pressure and the clear, colorless residue was evaporatively distilled at 115° (0.025 mm). In this manner there was obtained 594 mg (98%) of the amine **26** which crystallized on storing in the refrigerator under nitrogen and melted at 51.5–52.5°. This material was not purified further for analysis.

Anal. Calcd for $C_{20}H_{31}N$: C, 84.15; H, 10.95; N, 4.91. Found: C, 84.33; H, 11.00; N, 493.

Infrared showed ν_{max}^{film} 2760 and 2815 [-N(*C*H$_3$)$_2$], 1600 and 1580 (weak) (phenyl), 760 and 725 cm^{-1} (*ortho*-disubstituted phenyl).

Amine Oxide Pyrolysis.[31]—A mixture of 571 mg (2.0 mmoles) of the amine **26** and 1.5 ml of 30% hydrogen peroxide was heated under reflux on the steam bath until the amine had completely dissolved (*ca.* 15 min). The water and excess hydrogen peroxide were removed by flash distillation at reduced pressure, and the residual amine oxide was pyrolyzed at 150° and 0.025 mm. The pyrolysate was dissolved in ether and the resulting solution was washed successively with water, 10% hydrochloric acid, water, saturated salt solution, and dried over anhydrous sodium sulfate. Removal of the ether and evaporative distillation of the residue at 90° (0.025 mm) afforded 324 g (68%) of the olefin **27** as a mobile, colorless oil. This material was not purified further for analysis.

Anal. Calcd for $C_{18}H_{24}$: C, 89.94; H, 10.06. Found: C, 89.77; H, 9.92.

Infrared showed ν_{max}^{film} 3075 and 3055 (vinyl H), 1820 (weak), 1630, 1000, and 910 (-CH=CH$_2$ grouping), 1600 and 1575 (weak) (phenyl), 755 and 725 cm^{-1} (*ortho*-disubstituted phenyl).

(±)-4,5-Isodesisopropyldehydroabietanal (28).—A solution of 300 mg (1.25 mmoles) of the olefin **27** in a mixture of 27 ml of dioxane, 5 ml of water, and 3 ml of glacial acetic acid was treated with 50 mg of osmium tetroxide and 975 mg of *p*-periodic acid. After the reaction mixture had been stirred 20 hr at room temperature, 50 ml of water was added, and the precipitated aldehyde was extracted with ether. The ethereal extract was washed successively with water, 5% aqueous sodium hydroxide, water, saturated salt solution, and dried over anhydrous sodium sulfate. Removal of the ether at reduced pressure afforded 250 mg of crude, crystalline aldehyde **28** which was purified by chromatography on 60 g of Florisil. The aldehyde **28**, mp 58–60°, was eluted with 750 ml of 50% benzene–petroleum ether and amounted to 220 mg (73%). The analytical sample was prepared by one further crystallization from petroleum ether and finally sublimation at 53° (0.015 mm), and melted at 59–60°.

Anal. Calcd for $C_{17}H_{22}O$: C, 84.25; H, 9.15. Found: C, 84.14; H, 9.13.

Infrared showed ν_{max}^{film} 2695 (-C*H*O), 1720 (s) (aldehyde >C=O), 1600 and 1575 (weak) (phenyl), 760 and 725 cm^{-1} (*ortho*-disubstituted phenyl).

(±)-4,5-Isodesisopropyldehydroabietonitrile.—A solution of 188 mg (0.775 mmole) of the aldehyde **28** in 2 ml of pyridine and 2 ml of ethanol was treated with 300 mg (4.3 mmoles) of hydroxylamine hydrochloride, and the mixture was heated under reflux on the steam bath in a nitrogen atmosphere for 2 hr. Then most of the solvents were evaporated in a stream of nitrogen, the residue was partitioned between water and ether. The ethereal solution was separated and washed successively with water, 2% aqueous sulfuric acid, water, saturated salt solution, and dried over anhydrous sodium sulfate. After removal of the ether at reduced pressure, the crude, crystalline oxime was dissolved in 10 ml of acetic anhydride and heated under reflux in a nitrogen atmosphere for 5 hr. Then most of the acetic anhydride was removed at reduced pressure, and the crystalline residue was chromatographed on 10 g of Florisil. The nitrile, eluted with 750 ml of 50% benzene–petroleum ether, was crystallized from petroleum ether and amounted to 150 mg (81%). This material melted at 115–116° and further crystallization did not change this range.

Anal. Calcd for $C_{17}H_{21}N$: C, 85.30; H, 8.85; N, 5.85. Found: C, 85.34; H, 8.70; N, 5.86.

Infrared showed $\nu_{max}^{HCCl_3}$ 2230 (-C≡N), 1600 and 1576 cm^{-1} (weak) (phenyl).

(±)-4,5-Isodesisopropyldehydroabietic Acid (29).—A mixture of 100 mg (0.42 mmole) of the above nitrile and 2 g of potassium hydroxide in 10 ml of diethylene glycol was maintained at reflux in a nitrogen atmosphere for 20 hr, cooled, diluted with water, and extracted with ether. The aqueous layer was made acid to congo red paper, and the precipitated acid was isolated by ether extraction. The ethereal solution was washed with water, saturated salt solution, and dried over anhydrous sodium sulfate. The crude acid, obtained after removal of the ether at reduced pressure, was chromatographed on 10 g of silica gel. The acid **29** [88 mg (81%), mp 210–211° (lit.[23a] mp 206–207° uncorr)] was obtained after elution with 750 ml of benzene and crystallization of the residues from acetone.

Anal. Calcd for $C_{17}H_{22}O_2$: C, 79.03; H, 8.59. Found: C, 79.15; H, 8.56.

Infrared showed $\nu_{max}^{HCCl_3}$ 1695 (s) (-*C*OOH), 1600 and 1575 cm^{-1} (weak) (phenyl).

The **methyl ester**, obtained by the action of ethereal diazomethane on the acid **29**, melted at 80–81° (lit.[25a] 85–86° uncorr) after two crystallizations from methanol.

Anal. Calcd for $C_{18}H_{24}O_2$: C, 79.37; H, 8.88. Found: C, 79.46; H, 8.97.

Infrared showed ν_{max}^{film} 1730 (s) (-*C*OOCH$_3$), 1600 and 1575 (weak) (phenyl), 760 and 730 cm^{-1} (*ortho*-disubstituted phenyl).

II. Dehydroabietic Acids. A. Natural Series. 2α-(*p*-Isopropylphenyl)-6α-(3-ketobutyl)-2β-methylcyclohexanone.—A solution of 83.1 g (0.362 mole) of 2-(*p*-isopropylphenyl)-2-methylcyclohexanone[12] **30** in 134 g (1.81 moles) of ethyl formate was added to a cooled slurry of 97.6 g (1.81 moles) of sodium methoxide in 1.2 l. of benzene, and the experiment was carried out in the standard manner.[13] After work-up and distillation of the crude acidic product, there was obtained 70.1 g (75%), bp 115–116° (0.03 mm), of the desired hydroxymethylene ketone.

A solution of 28.31 g (0.11 mole) of the above hydroxymethylene ketone, 15.4 g (0.22 mole) of methyl vinyl ketone, and 8 ml of triethylamine, in 300 ml of methanol, was allowed to stand for 48 hr. The methanol was removed at reduced pressure, benzene was added, and the resulting solution was washed with 1 *N* hydrochloric acid, water, saturated sodium bicarbonate, water, and saturated salt solution, and dried over anhydrous sodium sulfate. The crude product obtained by filtration and removal of solvent was then dissolved in a solution of 100 ml of aqueous 20% potassium carbonate and 400 ml of methanol and allowed to stand overnight at room temperature. The methanol was removed at reduced pressure, and the residue was extracted with ether which was washed with 1 *N* hydrochloric acid, water, and saturated salt solution, and dried over anhydrous sodium sulfate. After filtration and removal of solvent, distillation of the residue afforded 28.74 g (88%) of oily diketone, bp 155–160° (0.07 mm). This material solidified on standing, and after crystallization from petroleum ether, there was obtained 22.9 g (70%) of crystalline diketone, mp 51–52°. Recrystallization of a small sample afforded the analytical sample with the same melting point.

Anal. Calcd for $C_{20}H_{28}O_2$: C, 79.95; H, 9.40. Found: C, 79.99; H, 9.43.

Infrared showed λ_{max}^{film} 5.84 μ (s) (saturated >C=O).

6α-(3,3-Ethylenedioxybutyl)-2α-(*p*-isopropylphenyl)-2β-methylcyclohexanone.—A solution of 5 g (16.7 mmoles) of the above diketone, 1.08 g (17.3 mmoles) of ethylene glycol, and 25 mg of *p*-toluenesulfonic acid in 50 ml of benzene was heated under reflux for 12 hr under a Dean–Stark water separator. The solution was cooled and washed with 10% sodium bicarbonate and water; the solvent was removed at reduced pressure. On chromatography of the crude product on 200 g of alumina, there was eluted 4.65 g (81%) of oily ketal with 2 l. of 1:1 benzene–petroleum ether. A small sample was evaporatively distilled at 145° (0.02 mm) for analysis.

Anal. Calcd for $C_{22}H_{32}O_3$: C, 76.70; H, 9.36. Found: C, 76.84; H, 9.52.

2β,6β-Dimethyl-2α-(*p*-isopropylphenyl)-6α-(3-ketobutyl)cyclohexanone (31).—In a nitrogen atmosphere a solution 4.44 g (12.9 mmoles) of the above ketal in 25 ml of benzene was added to a water-cooled suspension of 5.84 g (52 mmoles) of potassium *t*-butyl alcoholate in 75 ml of benzene. After stirring for 10 min, the reaction mixture was cooled in an ice bath and treated with 9.25 g (65 mmoles) of iodomethane. After stirring overnight at room temperature, the reaction mixture was decomposed by addition of water. The benzene layer was separated and washed with water, and the benzene was removed at reduced pressure. The crude methylated ketal was dissolved in 50 ml of acetone and 10 ml of 10% hydrochloric acid, and the solution was allowed to stand for 1 hr. The ether extract was washed with water and saturated salt solution, and dried over anhydrous sodium sulfate. After filtration and removal of solvent, crystallization of the crude product from petroleum ether afforded 3.22 g (80%) of solid, white methylated diketone **31**, mp 54–55°. A small sample was recrystallized twice from petroleum ether to obtain the analytical sample with unchanged melting point.

Anal. Calcd for $C_{21}H_{30}O_2$: C, 80.21; H, 9.62. Found: C, 80.33; H, 9.71.

Infrared showed $\bar{\nu}_{max}^{CHCl_3}$ 1710 (s) (saturated >C=O), 1695 cm^{-1} (s) (α,α,α′,α′-tetrasubstituted >C=O).

8β,10β-Dimethyl-8α-(*p*-isopropylphenyl)-Δ^{1,9}-octalone-2.—Cyclization of 27 g (86 mmoles) of diketone **31** in 150 ml of benzene with 16.8 g (0.43 mole) of potassium dissolved in 1 l. of dry *t*-butyl alcohol was effected by the procedure described below for the preparation of octalone in the 4,5-iso series. The crude product obtained on work-up was crystallized from petroleum ether and afforded 22.6 g (89%) of solid, white octalone, mp 70–72°. Two recrystallizations of a small sample from petroleum ether afforded the analytical sample, mp 72–73°.

Anal. Calcd for $C_{21}H_{28}O$: C, 85.08; H, 9.52. Found: C, 85.20; H, 9.65.

Infrared showed λ_{max}^{film} 6.0 μ (s) (α,β-unsaturated >C=O).

Ultraviolet showed λ_{max}^{EtOH} 243 mμ (ε 10,200).

8β,10β-Dimethyl-8α-(*p*-isopropylphenyl)-*trans*-decalone-2 (33).—The reduction of 1 g (3.37 mmoles) of the above octalone in 200 ml of ether with 97 mg (14 g-atoms) of lithium wire dissolved in 250 ml of liquid ammonia was carried out according to the procedure described below for the preparation of the decalone **34**. Crystallization of the crude product from methanol afforded 0.85 g (85%) of solid, white decalone **33**, mp 110–112°. The yields for other runs of this reaction were comparable where the product was crystallized, although the crude decalone was frequently used without further purification. Recrystallization of a small sample of the above solid afforded the analytical sample, mp 111–112.5°.

Anal. Calcd for $C_{21}H_{30}O$: C, 84.51; H, 10.13. Found: C, 84.57; H, 10.32.

Infrared showed $\lambda_{max}^{CHCl_3}$ 5.88 μ (s) (saturated >C=O).

2β-Carboxymethyl-1β,3β-dimethyl-3α-(*p*-isopropylphenyl)cyclohexylacetic Acid.—A solution of 3.86 g (13 mmoles) of decalone **33** in 4.81 g (65 mmoles) of ethyl formate was added to a cooled slurry of 3.51 g (65 mmoles) of sodium methoxide in 100 ml of benzene, and the experiment was effected in the standard fashion.[13] The crude hydroxymethylene decalone (3.77 g, 11.54 mmoles) in 200 ml of ethyl acetate was treated with 35 mmoles of ozone at −70°. After removal of solvent, the residue was treated with 150 ml of 5% sodium hydroxide and 85 ml of 30% hydrogen peroxide (in 45-8 and 40-ml portions, respectively). The crude product was crystallized from ether–petroleum ether (60–75°) and gave 3.45 g (86%, based on decalone) of solid, white diacid, mp 189–191°. Two recrystallizations of a small sample from the same solvent pair afforded the analytical sample, mp 191–192°.

Anal. Calcd for $C_{21}H_{30}O_4$: C, 72.77; H, 8.89. Found: C, 72.80; H, 8.73.

Infrared showed $\bar{\nu}_{max}^{CHCl_3}$ 2500–3500 (broad), 1710 cm^{-1} (carboxyl >C=O).

(±)-7-Ketohomodehydroabietic Acid.—A mixture of 2.78 g (8.04 mmoles) of the above diacid and 100 ml of polyphosphoric acid was heated at 80° for 20 min with vigorous stirring under a nitrogen atmosphere. While still warm the reaction mixture was poured into ice–water and extracted with ether. The ethereal extract was washed with water and extracted with 5% sodium bicarbonate. Acidification of the bicarbonate extracts with concentrated hydrochloric acid afforded the crude acid which was extracted with ether. The ethereal solution was washed with water and saturated salt solution, and dried over anhydrous sodium sulfate. After filtration and removal of solvent, the tricyclic keto acid was obtained as a glass which solidified on trituration with methanol. After crystallization from the same solvent, there was obtained 1.97 g (75%) of solid, white, crystalline keto acid, mp 182–184°. Recrystallization of a small sample from methanol afforded the analytical sample, mp 184–185°.

Anal. Calcd for $C_{21}H_{30}O_3$: C, 76.61; H, 8.69. Found: C, 76.79; H, 8.59.

Infrared showed $\lambda_{max}^{CHCl_3}$ 5.85 (s) (carboxyl >C=O), 5.96 μ (s) (benzylic >C=O).

The original ethereal layer, after extraction with bicarbonate, was washed with water and saturated salt solution, and dried over anhydrous sodium sulfate. Upon filtration and removal of solvent, there was obtained 125 mg of a neutral material which gave a strong violet color when a small amount in ethanol was treated with 3% ethanolic ferric chloride. Crystallization of this material from ethanol afforded a white, crystalline solid, mp 187–188°, whose properties indicate it to be 5,6-diketo-3aβ,10bβ-dimethyl-8-isopropyl-1,2,3,3a,3bα,5aβ,6,10b-octahydrophenanthrene. A small sample was recrystallized from ethanol to afford the analytical sample with unchanged melting point.

Anal. Calcd for $C_{21}H_{26}O_2$: C, 81.25; H, 8.44. Found: C, 81.15; H, 8.54.

Infrared showed $\bar{\nu}_{max}^{CHCl_3}$ 1750 (s) (pentanone >C=O), 1675 cm^{-1} (benzylic >C=O).

(±)-Homodehydroabietic Acid (35).—A solution of 3.20 g (9.74 mmoles) of the above keto acid and 0.5 ml of 70% aqueous perchloric acid in 160 ml of glacial acetic acid, in which was suspended 0.5 g of 10% palladium on carbon, was stirred in a hydrogen atmosphere for 2 hr, during which time the theoretical amount of hydrogen, 470 ml, was absorbed. After filtration and removal of the solvent, the crude product was crystallized from methylcyclohexane, and there was obtained 3.02 g (99%) of solid, white acid, mp 172–174°. Recrystallization of a small sample from the same solvent afforded the analytical sample, mp 173–174° (lit.[7] mp 173–174°).

Anal. Calcd for $C_{21}H_{30}O_2$: C, 80.21; H, 9.62. Found: C, 80.30; H, 9.71.

Infrared showed $\lambda_{max}^{CHCl_3}$ 5.86 μ (s) (carboxyl >C=O).

(±)-N,N-Dimethylhomodehydroabietamide.—In accordance with the procedure described below for preparation of the amide in the 4,5-iso series, 3.00 g (9.54 mmoles) of (±)-homodehydroabietic acid **35** was converted to the acid chloride with 100 ml of freshly distilled thionyl chloride, and thence to the amide with excess dimethylamine in benzene solution. After work-up and crystallization of the crude product from petroleum ether (60–75°), there was obtained 3.06 g (94%), mp 78–79°, of white, crystalline amide. Recrystallization of a small sample from the same solvent afforded the analytical sample, with unchanged melting point.

Anal. Calcd for $C_{23}H_{35}NO$: C, 80.88; H, 10.33; N, 4.10. Found: C, 80.70; H, 10.16; N, 4.20.

Infrared showed $\lambda_{max}^{CHCl_3}$ 6.1 μ (s) (amide >C=O).

(±)-N,N-Dimethylhomodehydroabietanylamine.—A solution of 277 mg (0.813 mmole) of the above amide in 20 ml of anhydrous ether was added dropwise to a well-stirred slurry of 75 mg (1.93 mmoles) of lithium aluminum hydride in 20 ml of ether. After the reaction mixture had stirred for 1 hr at room temperature, there was cautiously added 0.15 ml of water and then 0.125 ml of 10% sodium hydroxide. The resulting slurry was stirred for 1 hr in an ice bath. The solution was filtered, and the precipitate was washed with ether. Removal of ether afforded the crude amine as a colorless oil, the infrared spectrum of which had no amide carbonyl absorption. Evaporative distillation of this crude product at 135–140° (0.02 mm) afforded 263 mg (99%) of amine as a colorless oil. A small sample was redistilled at 135° (0.02 mm) for analysis.

Anal. Calcd for $C_{23}H_{37}N$: C, 84.34; H, 11.39; N, 4.28. Found: C, 84.06; H, 11.28; N, 4.46.

Infrared showed λ_{max}^{film} 3.48, 3.56 μ [$-N(CH_3)_2$].

A small sample of the amine in ethanol was treated with a saturated solution of picric acid in ethanol. The precipitate was filtered and crystallization from ethanol afforded the yellow picrate, mp 158–159° and 190–191°.

Anal. Calcd for $C_{29}H_{40}N_4O_7$: C, 62.57; H, 7.24; N, 10.07. Found: C, 62.74; H, 7.11; N, 10.19.

(±)-1β,4aβ-Dimethyl-1α-ethenyl-7-isopropyl-1,2,3,4,4a,9,10,-10aα-octahydrophenanthrene.—The olefin was prepared from 2.85 g (8.71 mmoles) of the above amine by first conversion to the amine oxide with 30% hydrogen peroxide and then pyrolysis of the crude product at 160–180° (0.05 mm), as described below for the preparation of the olefin in the 4,5-iso series. On chromatography of the crude pyrolysate on 100 g of alumina, 2.29 g (93%) of liquid olefin was eluted with 400 ml of petroleum ether. A small sample of the olefin was evaporatively distilled at 115° (0.02 mm) for analysis.

Anal. Calcd for $C_{21}H_{30}$: C, 89.29; H, 10.71. Found: C, 89.00; H, 10.57.

Infrared showed ν_{max}^{film} 1630, 1000, 910 cm^{-1} ($-CH=CH_2$).

(±)-Dehydroabietanal.—This aldehyde was obtained from 200 mg (0.708 mmole) of the above olefin, 15 mg of osmium tetroxide, and 650 mg of powdered *p*-periodic acid in 20 ml of dioxane, 2 ml of glacial acetic acid, and 4 ml of water according to the procedure described below for the preparation of aldehyde in the 4,5-iso series. When the crude solid obtained on work-up was chromatographed on 10 g of Florisil, 142 mg (71%), mp 105–107°, of colorless, crystalline aldehyde was eluted with 100 ml of 10% benzene in petroleum ether. Crystallization of a small sample from petroleum ether (60–75°) afforded the analytical sample, mp 106–108°.

Anal. Calcd for $C_{20}H_{28}O$: C, 84.45; H, 9.02. Found: C, 84.22; H, 9.88.

Infrared showed $\bar{\nu}_{max}^{CHCl_3}$ 2700 (weak) (aldehyde hydrogen), 1725 cm^{-1} (s) (aldehyde >C=O).

(±)-Dehydroabietonitrile.—The crude oxime prepared from 818 mg (2.88 mmoles) of the above aldehyde and 800 mg of hydroxylamine hydrochloride in 20 ml each of pyridine and absolute ethanol was dehydrated with 15 ml of acetic anhydride, as described below for the corresponding preparation of nitrile in the 4,5-iso series. When the crude nitrile was chromatographed on 48 g of Florisil, 519 mg (86%) of crystalline nitrile, mp 92–93°, was eluted with 400 ml of 25% benzene in petroleum ether. The analytical sample was obtained as a white, crystalline solid, mp 92.5–93°, by crystallization of a small amount of this material from petroleum ether (60–75°).

Anal. Calcd for $C_{20}H_{27}N$: C, 85.35; H, 9.67; N, 4.98. Found: C, 85.19; H, 9.71; N, 5.01.

Infrared showed $\nu_{max}^{CHCl_3}$ 2235 cm^{-1} (–C≡N).

(±)-Dehydroabietic Acid (37).—A solution of 94 mg (0.334 mmole) of the above nitrile and 2 g of potassium hydroxide in 10 ml of diethylene glycol was stirred at 200° for 7 hr under a nitrogen atmosphere. The cooled reaction mixture was diluted with water and extracted with ether, which was back-extracted with 5% sodium hydroxide. The combined aqueous layers were acidified with excess hydrochloric acid and extracted with ether. The ethereal extract was washed with water and saturated salt solution, and dried over anhydrous sodium sulfate. The residue that was obtained after filtration and removal of solvent was chromatographed on 7 g of acid-washed silica gel, and the acid was eluted with 100 ml of 1:1 benzene–petroleum ether. In this manner there was obtained 88 mg (88%) of colorless, crystalline acid **37**, mp 178–180°. On sublimation of a small sample of this material at 140° (0.01 mm), (±)-dehydroabietic acid (**37**), mp 178.5–180° (lit.[7] 179.5–180.5°), was obtained as a white solid. The infrared spectrum of this material was indistinguishable from that of the natural material.

Anal. Calcd for $C_{20}H_{28}O_2$: C, 79.95; H, 9.39. Found: C, 79.89; H, 9.40.

Methyl (±)-Dehydroabietate.—The ester was prepared from 50 mg of the acid **37** and excess ethereal diazomethane. The crude ester obtained from work-up was eluted from 5 g of Florisil with 50 ml of 25% benzene in petroleum ether. After crystallization from methanol, there was obtained 35 mg of the ester as long, feathery needles, mp 74.5–75° (lit.[7] 71.5–73°) The infrared spectrum of this material was indistinguishable from that of methyl ester of the natural acid.

Anal. Calcd for $C_{21}H_{30}O_2$: C, 80.21; H, 9.61. Found: C, 80.05; H, 9.70.

B. 4,5-Iso Series. 6-*n*-Butylthiomethylene-2-(*p*-isopropylphenyl)cyclohexanone.—A solution of 50.7 g (0.208 mole) of the 6-hydroxymethylene-2-methyl-2-(*p*-isopropylphenyl)cyclohexanone,[32] 19.8 g (0.22 mole) of 1-butanethiol, and 25 mg of *p*-toluenesulfonic acid in 300 ml of benzene was heated at reflux under a Dean–Stark water separator in a nitrogen atmosphere for 12 hr. The cooled reaction mixture was poured into 100 ml of 1% sodium hydroxide, and the organic layer was separated and washed with 5% sodium hydroxide, water, and saturated salt solution, and the solvent was removed at reduced pressure. After distillation of the residue, there was obtained 46.9 g (71%) of yellow oil, bp 195–196° (0.1 mm). A small sample was evaporatively distilled at 160° (0.05 mm) for analysis.

Anal. Calcd for $C_{16}H_{20}OS$: C, 75.89; H, 8.92; S, 10.13. Found: C, 75.86; H, 8.96; S, 10.24.

(32) Prepared from 2-methyl-2-(*p*-isopropylphenyl)cyclohexanone[12] and ethyl formate in the standard manner.[13]

2,6-Dimethyl-2-(*p*-isopropylphenyl)cyclohexanone.—A solution of 23.4 g (0.6 mole) of potassium in 600 ml of dry *t*-butyl alcohol was treated with 44.6 g (0.141 mole) of the above *n*-butylthiomethylene derivative in a nitrogen atmosphere. The resulting mixture was stirred for 15 min, cooled in an ice bath, and then treated all at once with 85.3 g (0.6 mole) of iodomethane. After heating at reflux for 3 hr, water was added and the *t*-butyl alcohol was removed at reduced pressure. The residual aqueous liquor was extracted with ether and the ethereal solution was washed with water, 5% sodium hydroxide, water, and saturated salt solution, and dried over anhydrous sodium sulfate. The product obtained after filtration and removal of solvent was dissolved in 1 l. of ethanol. This solution was treated with 31 measuring teaspoons of W-2 Raney nickel and heated at reflux overnight under a nitrogen atmosphere. The catalyst was filtered and washed with ethanol, and then the ethanol was removed at reduced pressure. On distillation of the residue there was obtained 31.5 g (92%) of the 2,6 dimethyl ketone, bp 95–98° (0.02 mm). A small sample was evaporatively distilled at 85° (0.01 mm) for analysis.

Anal. Calcd for $C_{17}H_{24}O$: C, 83.55; H, 9.90. Found: C, 83.57; H, 10.04.

Infrared showed λ_{max}^{film} 5.85 μ (s) (saturated >C=O).

6β-(3-Chloro-2-butenyl)-2β,6α-dimethyl-2α-(*p*-isopropylphenyl)-cyclohexanone.—A suspension of 11.7 g (0.3 mole) of a commercial sodium amide in 1 l. of benzene was treated with 64.4 g (0.236 mole) of the above 2,6-dimethyl ketone **37** and the resulting solution was heated at reflux for 6 hr until the evolution of ammonia ceased. The cooled reaction mixture was treated with 37.6 g (0.3 mole) of freshly distilled 1,3-dichlorobutene, and the solution was heated at reflux overnight under a nitrogen atmosphere. The reaction mixture was treated with water, and the organic layer was separated and washed with water and saturated salt solution. After removal of solvent and distillation, there was obtained 10.4 g, bp 90–125° (0.02 mm), of a mixture of starting material and product, and then 69.1 g (78%), bp 135–145° (0.02 mm), of the desired chloro ketone. A small sample was evaporatively distilled twice at 130° (0.02 mm) for analysis. There seemed to be some decomposition on heating and the analytical data obtained were variable.

Anal. Calcd for $C_{21}H_{29}ClO$: C, 75.76; H, 8.78; Cl, 10.65. Found: C, 75.20; H, 8.59; Cl, 10.77.

Infrared showed λ_{max}^{film} 5.92 (s) (saturated >C=O), 6.00 μ (-CH=CCl-).

2β,6α-Dimethyl-2α-(*p*-isopropylphenyl)-6β-(3-ketobutyl)cyclohexanone (32).—An ice-cold solution of 9 ml of water in 81 ml of concentrated sulfuric acid was treated with 13.55 g (40.7 mmoles) of the above chloro ketone, and the mixture was stirred occasionally at 0° for 3 hr. The reaction mixture was allowed to warm to room temperature over a period of 90 min, poured into ice–water, and extracted with ether; the ethereal extracts were washed with water, aqueous saturated sodium bicarbonate, and saturated salt solution, and dried over anhydrous sodium sulfate. Filtration and removal of solvent left a crude, oily product which on chromatography on 400 g of alumina and elution with 4 l. of 1:1 benzene–petroleum ether afforded 10.2 g (80%) of oily diketone **32**. A small sample was evaporatively distilled at 125° (0.01 mm) for analysis.

Anal. Calcd. for $C_{21}H_{30}O_2$: C, 80.21; H, 9.62. Found: C, 80.26; H, 9.67.

Infrared showed λ_{max}^{film} 5.85 (s) (saturated >C=O), 5.92 μ (s) ($\alpha,\alpha,\alpha',\alpha'$-tetrasubstituted >C=O).

8β,10α-Dimethyl-8α-(*p*-isopropylphenyl)-$\Delta^{1,9}$-octalone-2.—A solution of 10.2 g (32.4 mmoles) of diketone **32** in 25 ml of benzene was added to a solution of 3.91 g (0.1 mole) of potassium in 125 ml of dry *t*-butyl alcohol, and the reaction mixture was allowed to stir overnight at room temperature under a nitrogen atmosphere. The reaction mixture was then treated with 1 *N* hydrochloric acid, and most of the *t*-butyl alcohol was removed at reduced pressure. The residual aqueous suspension was extracted with ether, and the ethereal solution was washed with water and saturated salt solution, and dried over anhydrous sodium sulfate. Filtration and removal of solvent afforded an oily crude product from which there was obtained, after chromatography on 400 g of alumina and elution with 2.5 l of 1:1 benzene–petroleum ether, 4.14 g of the oily octalone. Trituration of this oil with petroleum ether in a Dry Ice–acetone bath afforded a solid. After two crystallizations of this solid from petroleum ether in a Dry Ice–acetone bath, there was obtained 2.64 g (24%) of solid white octalone, mp 61–62°. A small sample was recrystallized under the same conditions to afford the analytical sample, with unchanged melting point.

Anal. Calcd for $C_{21}H_{28}O$: C, 85.08; H, 9.52. Found: C, 84.96; H, 9.51.

Infrared showed λ_{max}^{film} 6.0 μ (s) (α,β-unsaturated >C=O).

Ultraviolet showed λ_{max}^{EtOH} 242 mμ (ϵ 14,500).

8β,10α-Dimethyl-8α-(*p*-isopropylphenyl)-*trans*-decalone-2 (34).—After 385 mg (55 g-atoms) of lithium wire had been allowed to dissolve in *ca.* 1 l. of liquid ammonia, a solution of 4.03 g (13.6 mmoles) of the above octalone in 500 ml of ether was added dropwise; the reaction mixture was stirred for 2 hr. Solid ammonium chloride was then added to discharge the blue color, and the ammonia was allowed to evaporate. The resulting solid white residue was taken up in water and extracted with ether. The ethereal solution was washed with water and saturated salt solution, and dried over anhydrous sodium sulfate. After filtration and removal of solvent, crystallization of the crude product from petroleum ether afforded 2.66 g (66%) of the solid, white decalone **34** mp 63–65°. The analytical sample, which was obtained by recrystallization of a small sample of the decalone from ethanol–water, had a melting point of 65–66°.

Anal. Calcd for $C_{21}H_{30}O$: C, 84.51; H, 10.13. Found: C, 84.62; H, 10.02.

Infrared showed λ_{max}^{film} 5.84 μ (s) (saturated >C=O).

2α-Carboxymethyl-1α,3β-dimethyl-3α-(*p*-isopropylphenyl)cyclohexylacetic Acid.—A solution of 3.73 g (11.4 moles) of the crude hydroxymethylene derivative of the decalone **34** (prepared in the standard manner[13] from the decalone **34** and ethyl formate) in 200 ml of ethyl acetate was treated with 34 mmoles of ozone at −70°. The ethyl acetate was removed at reduced pressure and room temperature, and the crude ozonide was treated with 150 ml of 5% sodium hydroxide and 45 ml of 30% hydrogen peroxide, and the mixture was heated on a steam bath for 30 min. Another 40 ml of 30% hydrogen peroxide was then added, and the solution was heated for another 30 min. The solution was cooled, washed with ether, and then acidified with concentrated hydrochloric acid. The aqueous suspension was extracted with ether, and the ethereal extracts were washed with water and saturated salt solution, and dried over anhydrous sodium sulfate. After filtration and removal of solvent, the crude diacid, 3.68 g, was obtained as a glass. A small sample was evaporatively distilled at 170° (0.01 mm) for analysis.

Anal. Calcd for $C_{21}H_{30}O_4$: C, 72.77; H, 8.89. Found: C, 72.59; H, 8.70.

Infrared showed $\bar{\nu}_{max}^{CHCl_3}$ 1705 cm^{-1} (s) (carboxyl >C=O).

5,6-Diketo-3aα,10bβ-dimethyl-3-isopropyl-1,2,3,3a,3bβ,5aβ,6,-10b-octahydroacephenanthrene.—A solution of 2.73 g (7.88 mmoles) of the above crude diacid in 50 ml of polyphosphoric acid was stirred at 100° for 30 min under a nitrogen atmosphere. The warm reaction mixture was poured into ice–water, and the resulting slush was extracted with ether. The ethereal extract was washed with water, 5% aqueous sodium bicarbonate, water, and saturated salt solution, and dried over anhydrous sodium sulfate. After filtration and removal of solvent, there was obtained 2.03 g of crude product which on crystallization from ether afforded 1.11 g of the desired dione. The mother liquors, on evaporative distillation at 165° (0.01 mm), yielded another 0.52 g of the dione. Hence, a total of 1.63 g (61%, based on decalone), mp 123–125°, was obtained. The analytical sample was obtained as colorless plates, mp 124.5–125.5°, after two recrystallizations of a small sample from ether.

Anal. Calcd for $C_{21}H_{26}O_2$: C, 81.25; H, 8.44. Found: C, 81.34; H, 8.54.

Infrared showed $\bar{\nu}_{max}^{CHCl_3}$ 1750 (s) (pentanone >C=O), 1670 cm^{-1} (benzylic >C=O).

(±)-7-Keto-4,5-isohomodehydroabietic Acid.—A solution of 1.11 g (3.58 mmoles) of the above diketone in 1.63 ml of 10% aqueous sodium hydroxide and 14.7 ml of ethanol was heated at reflux in a nitrogen atmosphere for 90 min. The cooled reaction mixture was poured into water; the aqueous solution was washed twice with ether, acidified with excess concentrated hydrochloric acid, and then extracted with ether. The resulting ethereal solution was washed with water and saturated salt solution, and dried over anhydrous sodium sulfate. After filtration and removal of solvent, the crude product was sublimed at 150° (0.02 mm) and afforded 0.61 g of solid keto acid. When the residue from the sublimation was chromatographed on 5 g of acid-washed silica gel, an additional 0.35 g of keto acid was eluted with 400 ml of 4% ether in benzene. When these two portions of the keto acid were combined and crystallized from ethyl acetate–petroleum

ether (60–75°), there was obtained 0.89 g (76%), mp 155–157°, of white, crystalline keto acid. The analytical sample, mp 155–158°, was obtained by sublimation of a small amount of the crystallized keto acid at 150° (0.01 mm).

Anal. Calcd for $C_{21}H_{28}O_3$: C, 76.61; H, 8.69. Found: C, 76.66; H, 8.59.

Infrared showed $\nu_{max}^{CHCl_3}$ 1700 (s) (carboxyl >C=O), 1670 cm^{-1} (s) (benzylic >C=O).

(±)-4,5-Isohomodehydroabietic Acid (36).—A suspension of 0.2 g of 10% palladium on carbon in 5 ml of glacial acetic acid was equilibrated with hydrogen for 5 min. A solution of 0.897 g (2.73 mmoles) of above keto acid in 50 ml of glacial acetic acid was added followed by 0.2 ml of 70% aqueous perchloric acid, and the resulting solution was stirred for 2 hr, during which time the theoretical amount of hydrogen, 130 ml, was absorbed. The catalyst was filtered and washed with benzene. Ether was added, and the resulting solution was washed six times with water, then with saturated salt solution, and the solvent was removed. After crystallization of the crude product from ethyl acetate–petroleum ether (60–75°) mixture, there was obtained 0.790 g (92%) of the acid **36** mp 164.5–165°. The analytical sample, prepared by sublimation of a small sample of crystallized acid **36** at 155° (0.01 mm), had a melting point of 167–169°.

Anal. Calcd for $C_{21}H_{30}O_2$: C, 80.21; H, 9.62. Found: C, 80.32; H, 9.71.

Infrared showed $\nu_{max}^{CHCl_3}$ 1700 cm^{-1} (s) (carboxyl >C=O).

(±)-N,N-Dimethyl-4,5-isohomodehydroabietamide.—A solution of 753 mg (2.39 mmoles) of acid **36** in 50 ml of freshly distilled thionyl chloride was heated at reflux for 1 hr and then the thionyl chloride was removed at reduced pressure. After the residue had been azeotropically distilled with two 25-ml portions of benzene, the crude acid chloride was taken up in 25 ml of benzene, and this solution was treated with dimethylamine until the reaction mixture became cold from the condensing amine. After stirring for 30 min more at room temperature, water was added, and the separated aqueous layer was extracted twice with ether. The combined organic layers were washed with water, 10% hydrochloric acid, water, 5% potassium carbonate, water, and saturated salt solution; the solvent was removed at reduced pressure. On chromatography of the crude product on 80 g of Florisil, the oily amide, 799 mg (98%), was eluted with 700 ml of 5% ether in benzene. A small sample was evaporatively distilled at 140° (0.01 mm) for analysis.

Anal. Calcd for $C_{23}H_{35}NO$: C, 80.80; H, 10.33; N, 4.10. Found: C, 81.00; H, 10.40; N, 41.4.

Infrared showed ν_{max}^{film} 1625 cm^{-1} (s) (amide >C=O).

(±)-N,N-Dimethyl-4,5-isohomodehydroabietanylamine.— A solution of 753 mg (2.21 mmoles) of the above amide in 30 ml of anhydrous ether was added dropwise to a well-stirred slurry of 171 mg (4.5 mmoles) of lithium aluminum hydride in 20 ml of ether. After the reaction mixture had stirred for 1 hr at room temperature, there was cautiously added 0.35 ml of water and then 0.30 ml of 10% aqueous sodium hydroxide. The resulting slurry was stirred for 1 hr in an ice bath; the solution was filtered; and the precipitate was washed with ether. Removal of the ether afforded the crude product which was evaporatively distilled at 125° (0.01 mm) to give 692 mg (96%) of colorless, oily amine. A small sample, on redistillation at 125° (0.01 mm), afforded the analytical sample.

Anal. Calcd for $C_{23}H_{37}N$: C, 84.37; H, 11.39; N, 4.28. Found: C, 84.60; H, 11.48; N, 4.14.

Infrared showed ν_{max}^{film} 2760, 2810 cm^{-1} [$-N(CH_3)_2$].

(±)-1α,4aβ-Dimethyl-1β-ethenyl-7-isopropyl-1,2,3,4,4a,9,10,-10aβ-octahydrophenanthrene.—A mixture of 630 mg (1.92 mmoles) of the above amine and 0.5 ml of 30% aqueous hydrogen peroxide was heated on a steam bath for 30 min during which time the solution became homogeneous. The excess hydrogen peroxide was removed at reduced pressure, and the crude amine oxide was pyrolyzed at 160–180° (0.05 mm). The pyrolysate was chromatographed on 20 g of alumina and 362 mg (67%) of liquid olefin was eluted with 100 ml of petroleum ether. A small sample of the olefin was evaporatively distilled at 110° (0.01 mm) for analysis.

Anal. Calcd for $C_{21}H_{30}$: C, 89.29; H, 10.71. Found: C, 89.11; H, 10.80.

Infrared showed ν_{max}^{film} 1630, 1000, 910 cm^{-1} ($-CH=CH_2$).

(±)-4,5-Isodehydroabietanal.—A solution of 241 mg (0.853 mmole) of the above olefin in 20 ml of dioxane, 2 ml of glacial acetic acid, and 4 ml of water was treated with 15 mg of solid oxmium tetroxide, and the resulting solution was allowed to stir for 15 min, during which time it became dark brown. There was then added in small portions over a period of 15 min 776 mg (3.42 mmoles) of powdered *p*-periodic acid. After stirring overnight, the reaction mixture was diluted with ether, and the ethereal solution was washed with water, 5% sodium hydroxide, water, and saturated salt solution, and dried over anhydrous sodium sulfate. Filtration and removal of solvent afforded 205 mg of crude solid aldehyde. Crystallization of a small sample from petroleum ether (60–75°) followed by sublimation at 85° (0.01 mm) afforded the analytical sample, mp 93–94°.

Anal. Calcd for $C_{20}H_{28}O$: C, 84.45; H, 9.92. Found: C, 84.24; H, 10.13.

Infrared showed $\nu_{max}^{CHCl_3}$ 2700 (weak) (aldehyde hydrogen), 1720 cm^{-1} (s) (>C=O).

(±)-4,5-Isodehydroabietonitrile.—A solution of 196 mg (0.688 mmole) of the above crude aldehyde and 250 mg of hydroxylamine hydrochloride in 6 ml of pyridine and 6 ml of ethanol was heated at reflux under nitrogen for 2 hr. The ethanol and pyridine were removed at reduced pressure, and the residue was taken up in ether. The ethereal solution was washed with water, cold 2% sulfuric acid, water, and saturated salt solution, and dried over anhydrous sodium sulfate. The crude oxime that was obtained after filtration and removal of solvent was dissolved in 20 ml of acetic anhydride, and the mixture was heated at reflux for 3 hr under a nitrogen atmosphere. The acetic anhydride was blown off with a stream of nitrogen, and the residual crude nitrile was chromatographed on 16 g of Florisil, whereupon 146 mg (65%, based on olefin) of solid, white nitrile, mp 128–129°, was eluted with 200 ml of 25% benzene in petroleum ether. The analytical sample, mp 129.5–130°, was obtained by crystallization of a small sample from petroleum ether (60–75°).

Anal. Calcd for $C_{20}H_{27}N$: C, 85.35; H, 9.67; N, 4.98. Found: C, 85.50; H, 9.78; N, 5.04.

Infrared showed $\nu_{max}^{CHCl_3}$ 2230 cm^{-1} (weak) (-C=N).

(±)-4,5-Isodehydroabietic Acid (38).—A solution of 125 mg (0.444 mmole) of the above nitrile and 2 g of potassium hydroxide in 10 ml of diethylene glycol was stirred at 198° for 7 hr under a nitrogen atmosphere. The cooled reaction mixture was diluted with water and extracted with ether, which was back extracted with 5% sodium hydroxide. The combined aqueous layers were acidified with excess concentrated hydrochloric acid and extracted with ether. The ethereal solution was washed with water and saturated salt solution, and dried over anhydrous sodium sulfate. The residue that was obtained upon filtration and removal of solvent was chromatographed on 10 g of acid-washed silica gel. There was eluted 101 mg (76%), mp 168–170°, of solid, white acid **38** with 100 ml of benzene. The analytical sample, a white, crystalline solid, mp 169–170°, was obtained by sublimation at 150° (0.05 mm) of a small sample of this chromatographed acid. The melting point of a mixture of this acid and (±)-dehydroabietic acid was depressed to 130–167°.

Anal. Calcd for $C_{20}H_{28}O_2$: C, 79.95; H, 9.39. Found: C, 79.76; H, 9.42.

Infrared showed $\nu_{max}^{CHCl_3}$ 1695 cm^{-1} (s) (carboxyl >C=O).

Methyl (±)-4,5-Isodehydroabietate.—An ethereal solution of 40 mg of acid **38** was treated with excess ethereal diazomethane, and then washed with dilute sodium bicarbonate, water, and saturated salt solution, and dried over anhydrous sodium sulfate. The crude ester was crystallized from methanol to give 30 mg of white, crystalline ester, mp 84.5–86°. Sublimation of this material at 75° (0.01 mm) afforded the analytical sample, with unchanged melting point.

Anal. Calcd for $C_{21}H_{30}O_2$: C, 80.21; H, 9.62. Found: C, 80.34; H, 9.73.

Infrared showed ν_{max}^{film} 1730 cm^{-1} (s) (ester >C=O).