(36) M. R. Johnson and B. Rickborn, *J. Org. Chem.*, **35**, 1041 (1970).
(37) K. Bowden, I. M. Heilbron, E. R. H. Jones, and B. C. L. Weedon, *J. Chem. Soc.*, 39 (1946).
(38) H. C. Brown and R. F. McFarlin, *J. Am. Chem. Soc.*, **80**, 5372 (1958); cf. S. G. Levine and N. H. Eudy, *J. Org. Chem.*, **35**, 549 (1970), and ref 31.
(39) Without results of the $LiAlH_4$ reductions of **17** and **18**, formation of a ketal which must be either trans-syn-cis or trans-anti-cis from an enedione which must be either trans-syn-cis or trans-anti-trans would not suffice to define the configuration of the compounds as trans-syn-cis, because it is possible to suggest mechanisms by which a trans-anti-trans enedione might have led to a trans-anti-cis ketal during synthesis of either **20** or **22** from **6g**.
(40) A mixture of 2.675 g of CrO_3 and 2.30 mL of concentrated H_2SO_4 diluted to 10.0 mL with water; cf. C. Djerassi, R. R. Engle, and A. Bowers, *J. Org. Chem.*, **21**, 1547 (1956).
(41) It is probable that material loss during this purification resulted largely from the unsuspected volatility of the product.

Diterpenoid Total Synthesis, an A → B → C Approach. 10. Bicyclic Intermediates for Resin Acids and Alkaloids[1a-d]

Walter L. Meyer,* Thomas E. Goodwin,[1e] R. John Hoff,[1f] and Carl W. Sigel[1g]

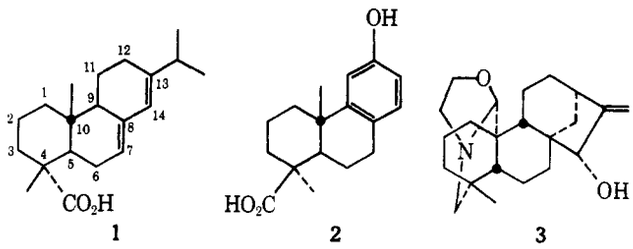
Department of Chemistry, University of Arkansas, Fayetteville, Arkansas 72701

Received December 22, 1976

Synthesis of 4α-carbomethoxy-4β,10-dimethyl-*trans*-7-decalone (**4**),[2] 4β-carbethoxy-10-cyano-4α-methyl-*trans*-7-decalone (**15**), and several derivatives of 4β,10-iminobismethyl-4α-methyl-*trans*-7-decalone (**6a**) is described. Compounds **4** and **15** are of interest as intermediates for synthesis of the abietic–pimaric and the podocarpic families of diterpenoid resin acids, respectively, and **6** is a similar intermediate for diterpenoid alkaloid synthesis. Alkylation of diethyl methylmalonate with δ-bromovaleronitrile affords cyano diester **7** which is cyclized to 2-carbethoxy-2-methyl-6-cyanocyclohexanone (**8**) by KO*t*-Bu. Ethoxide-catalyzed reaction of **8** with methyl vinyl ketone gives a 45:55 mixture of octalones **13** and **14** which can be hydrogenated either selectively to produce a mixture of the 4β-carbethoxydecalone **15** and 4α-carbethoxyoctalone **14** or exhaustively to afford a mixture of the two trans decalones **15** and **16**. Several chemical procedures for separating **15** from **14** or from **16** are described. Decalone **4** is produced from **16** either by ketalization, $LiAlH_4$ reduction to imino alcohol **23**, Huang-Minlon reduction, ketal hydrolysis, Jones oxidation, and esterification, or by $LiAlH_4$ reduction to the imino diol (which exists as amino ether tautomer **24**), Huang-Minlon reduction, Jones oxidation, and esterification. Concentrated H_2SO_4 converts **15** to the 4β,10-dicarboximido decalone **21** which by $LiAlH_4$ reduction, diacetylation, methanolysis of the *O*-acetate, and Jones oxidation gives the *N*-acetyl derivative of **6a**. Alternatively the *N*-mesyl derivative of **6a** is obtained by ketalization of **21**, $LiAlH_4$ reduction, mesylation, and ketal hydrolysis, and by omitting the mesylation step **6a** itself is available. Reduction of the ketal of **21** by sodium bis(2-methoxyethoxy)aluminohydride selectively removes oxygen from the C-4 substituent, giving lactam **32** which is hydrolyzed to keto lactam **33**.

In earlier papers we have described a new approach to synthesis of perhydrophenanthrene diterpenoids,[3] and have partially illustrated its versatility by total syntheses of ferruginol,[4] carnosic acid,[5] and related natural products. The general synthetic plan incorporates two major stages. The first of these involves construction of a *trans*-7-decalone[2] which carries appropriate substituents at C-4 and C-10 so that it can easily become the A/B ring system of the target molecule. The second deals with attachment of the C ring with its substituents and functional groups.

Two important classes of diterpenoids which must be included in any such general synthetic framework are the resin acids and the alkaloids, typified by abietic acid (**1**), podocarpic acid (**2**), and veatchine (**3**). Extension of our general sequence into these areas therefore requires preparation of a series of 7-decalones containing as 4 and 10 substituents either the groups which are usually present in those families of natural products or groups which can be readily transformed into the natural substituents. Three general functionality patterns of these three extraannular carbons are most common, viz., the 4α substituent may be the only one which is in an oxidation level higher than methyl (e.g., **1**), the 4β substituent may be that which is oxidized (e.g., **2**), or the 4β and 10 substituents may both be functionalized, as when they are joined by nitrogen in the characteristic E ring of the diterpenoid alkaloids. Consequently, the most directly related A/B ring intermediates for our purposes might be the epimeric carbomethoxydecalones **4** and **5** and the tricyclic amino derivative **6**. In this paper we describe a convenient synthesis of these or related decalones belonging to each of the three series.



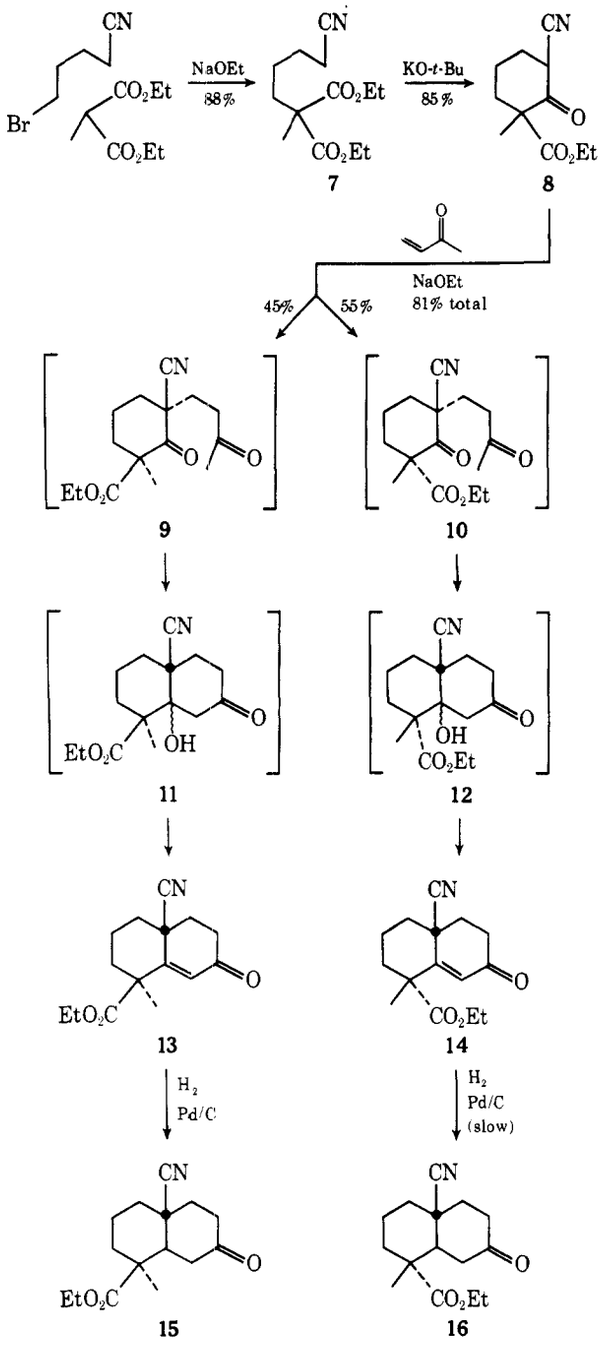
1 **2** **3**

4 **5**

6a, R = H
b, R = Ac
c, R = Ms

A very direct approach to carbomethoxydecalones **4** and/or **5** might seem to lie in Michael–Robinson annulation of 2-carbomethoxy-2,6-dimethylcyclohexanone followed by reduction. However, that Michael reaction is unsatisfactory,[6] as is often the case when the appropriate α hydrogen of a ketonic addend is not activated by a second electron-withdrawing group. Furthermore, even if that reaction were improved as a route to **4** and **5**, an independent synthesis of **6** would be required. We felt that it would be more desirable to use common intermediates as much as possible in both alkaloid and resin acid synthesis, and thus sought a single primary route which would later branch to afford all three key structures. Inasmuch as a 10-cyano group is a potentially useful synthon for both the 10-methyl of **4** and **5** and the 10-aminomethyl of **6**, the epimeric 4-carbethoxy-10-cyano-4-methyl-

Scheme I



trans-7-decalones **15** and **16** seemed ideally suited to be intermediates in such a plan, and they were chosen as initial synthetic objectives (Scheme I). This use of the cyano group also proves to have other beneficial consequences.

Alkylation of diethyl methylmalonate with δ-bromovaleronitrile affords cyano diester **7** (88%), which upon exposure to potassium *tert*-butoxide in toluene cyclizes to the trisubstituted cyclohexanone **8** (85%). The latter was obtained as a single diastereomeric racemate, although the available evidence does not identify which it is. This point is not pertinent to its synthetic utility, however, because the configurational integrity of this intermediate is destroyed during the next reaction wherein ketone **8** is subjected to Michael–Robinson annulation with methyl vinyl ketone. At this stage the cyano unit plays in important part in addition to its role as a future methyl or aminomethyl group, for it serves as the crucial second activator of the α hydrogen. Accordingly, when this reaction is carried to completion the yield of octalones **13** and **14** is good (81%). They are formed in a 45:55 ratio.

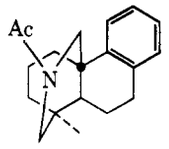
The lack of stereoselectivity during reaction of methyl vinyl ketone with the enolate of cyano ketone **8** is hardly surprising. The incoming ketobutyl group experiences a developing 1,3 syn-axial interaction either with carbethoxyl, leading to **10**, or with methyl, leading to **9**, but these should be little different at the relatively early point the transition state is reached.[7] However, in this instance the absence of stereoselectivity is not synthetically disadvantageous if one is interested in construction of both the abietic and podocarpic families of resin acids or the abietic family of acids and the terpenoid alkaloids, for it allows the same preparative route to afford satisfactory amounts of intermediates appropriate for all of these syntheses. Although a convenient method for direct separation of the two octalones has not been found, several indirect techniques are available, as described later.

If the Michael–aldol reaction is interrupted at an earlier point, the predominant products are octalone **14** and one C-5 diastereomer of intermediate ketol **11**. The latter can be easily isolated, and its subsequent dehydration by reexposure to base provides a convenient source of the pure 4β-carbethoxyoctalone **13**. Small amounts of octalone **13** and perhaps Michael adducts **9** and/or **10** are also present in the Michael–aldol product mixture at this intermediate stage, but ketol **12** appears to be absent. Thus the striking difference in rates of formation of octalones **13** and **14** seems to result primarily from an appreciable difference in the rates of dehydration of ketols **11** and **12**.

Like the corresponding 2,2-dimethyl-6-cyanocyclohexanone derivative,[3] intermediate diketones **9** and **10** cyclize under conditions to which the analogous 2,2-dimethyl-6-carbethoxycyclohexanone adduct is stable.[8] This supports the suggestion that cyclization is facilitated when the developing angular group is cyano, presumably either for the steric reasons discussed earlier[3] or because the electrophilicity of the ketonic carbon is significantly increased by the greater inductive effect of cyano compared to carbethoxy as an α substituent, or a combination of both factors.

Tentative assignment of relative configurations to the 4β-carbethoxy and 4α-carbethoxy series of intermediates was based on their spectroscopic properties. The most striking differences between spectra of the two octalones **13** and **14** are in the chemical shifts of their vinyl protons and C-4 methyl groups (τ 3.76 and 8.57, respectively, for one isomer and τ 4.12 and 8.37 for the other) and the multiplicity of their OCH_2 proton resonances (the AB part of an ABC_3 system for one isomer and the simple quartet from isochronous protons for the other). Each of these differences can be interpreted in stereochemical terms. First, the equatorial carbethoxy group of isomer **14** would probably prefer a conformation in which its carbonyl eclipses either the C-3–C-4 bond or the C-4–methyl bond rather than the C-4–C-5 bond, in order to avoid nonbonded interaction with H-6; particularly with the carbonyl and methyl eclipsed H-6 should be magnetically shielded by the ester compared to its environment when the carbethoxy group is axial. Second, the axial 4β-methyl of isomer **14** should be deshielded by the angular nitrile compared to the 4α-methyl of its epimer. Finally, the most reasonable explanation for anisochronicity of the two *O*-methylene protons in one but not the other of the enones is that the relative population of various conformers of the axial carbethoxy group in **13** is strongly affected by its syn-axial interaction with the angular nitrile, just as an angular ester is perturbed by an axial C-4 methyl.[9] All three inferences imply that the enone with the upfield H-6 resonance, the downfield 4-methyl resonance, and the isochronous OCH_2 protons is **14**. Because each octalone affords only *one* decalone upon hydrogenation, the trans ring fusion configuration was tentatively ascribed to decalones **15** and **16** based on the principle of catalyst approach to the less hindered face of the olefin.

Subsequent conversion of decalone **16** to dehydroabietic acid by a sequence which perturbs neither the C-4 nor the C-5 configuration[1b] confirms these structures for **13, 14, and 16.** Accuracy of the 5α configurational assignment to decalone **15** is demonstrated by its transformation to the tetracyclic amide **17**[10] which has been related to abietic acid, podocarpic acid,



17

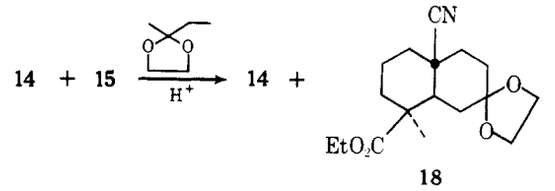
and veatchine[11] and therefore must have the trans A/B fusion.

Several chemical procedures for separating intermediates in the 4β-carbethoxy series (**13, 15,** etc.) from those in the 4α-carbethoxy series (**14, 16,** etc.) have been devised. They fall into two general classes. One set owes its success to the remarkable differential reactivity of the two octalones toward catalytic hydrogenation. The other group is fundamentally dependent upon the proximity of the two A-ring functional groups in **13, 15,** and their progeny. Which of the techniques is most expedient in a particular instance will be determined by the specific objectives of that investigation.

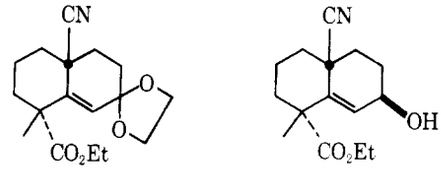
The mixture of octalones **13** and **14** can be hydrogenated over palladium on carbon to produce a similarly inseparable mixture of decalones **15** and **16.** However, the 4α-carbethoxyoctalone is reduced much more slowly than its 4β-carbethoxy epimer, so slowly that with some samples of catalyst it has not been possible to completely reduce all of octalone **14** in the mixture within a reasonable length of time. In fact, the rates of these two reductions are so different that it is possible to completely saturate the olefinic bond of the 4β-carbethoxy derivative **13** before any significant reduction of its isomer **14** has taken place. Inasmuch as the mole fraction of **13** in a given octalone mixture can be readily determined by integration of the two vinyl proton resonances, it is a simple matter to interrupt reduction after absorption of the correct amount of hydrogen for saturation of just that substance, so as to quantitatively produce a mixture of 4α-carbethoxyoctalone **14** and 4β-carbethoxydecalone **15.** We ascribe the slow reduction of octalone **14** to a steric effect of the equatorial C-4 ester. The β face of both isomers is seriously congested by the angular nitrile and the axial C-4 substituent, so the only route for catalyst approach and reduction is α. Unlike any part of an equatorial methyl, the ethoxyl group of the equatorial ester can significantly project into space on the α side of the ring, and we believe that this retards α face absorption on the catalyst sufficiently to produce the difference in hydrogenation rates.

Availability of this selective reduction turns the problem of separating a 4α- from a 4β-carbethoxy compound into that of separating a conjugated enone (**14**) from a saturated ketone (**15**). Although physical methods again failed, chemical differentiation is now less difficult. For example, hydrolysis of nonconjugated hydrazone derivatives is usually significantly faster than that of their conjugated counterparts. Thus decalone **15** and octalone **14** can be separated either by formation and stepwise selective cleavage of their *p*-carboxyphenylhydrazones[12] or by selective reaction with Girard's Reagent T.[13] In the latter separation the Girard derivative of the decalone would be expected to form faster than that of the octalone, so the fact that the decalone itself is isolated together with the octalone derivative suggests that selective hydrolysis of the saturated derivative occurs during the isolation process. Of these two techniques the Girard separation is preferable not only because the yield of octalone is a little higher, but also because the *p*-carboxyphenylhydrazone method sometimes leads to emulsions which are difficult to extract quantitatively.

A third separation procedure is based on selective transketalization of the octalone:decalone mixture (**14:15**) using an amount of 2-methyl-2-ethyl-1,3-dioxolane[14] sufficient to ketalize only the latter. We have no evidence to indicate whether these reaction conditions lead to kinetic or thermodynamic control of products, and formation of saturated ketal **18** to the complete exclusion of olefinic ketal **19** would be in accord with either factor. The resulting mixture of ketal **18** and enone **14** can be separated chromatographically, but it is simpler to first reduce it with sodium borohydride to a mixture of ketal **18** and octalol **20,** which differ from



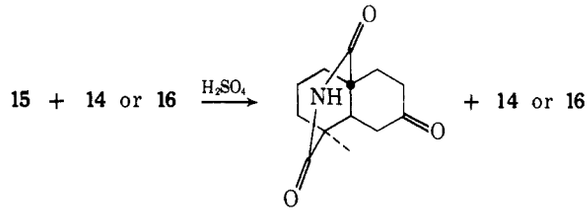
18



19 **20**

one another even more in chromatographic mobility than do **14** and **18.** Assignment of the 7β-hydroxy configuration to octalol **20** follows from the 2-Hz coupling of its 6- and 7-protons[5,15] and analogy with the steric course of reduction of 10-carbethoxy-4,4-dimethyl-Δ^8-7-octalone.[5]

One of the reasons that the angular nitrile was selected for incorporation into these intermediates was the expectation that in a 4β ester such as **15** the proximity of the cyano and carbethoxy groups would allow facile construction of the potential E ring of the diterpenoid alkaloids. Exposure of the mixture of 4α- and 4β-carbethoxydecalones **15** and **16** to concentrated sulfuric acid indeed brings about such a cyclization of the former to produce imide **21.** Furthermore, it is



21

possible to conduct this reaction under conditions which leave most of the epimeric decalone **16** unaltered. Inasmuch as the imide can be separated from the decalone by alkaline extraction, this process provides both a separation technique and a synthetic step toward the diterpenoid alkaloids. It is reasonably efficient, providing 70% of the available α-carbethoxydecalone **16** for resin acid synthesis and 85% of the available β-carbethoxy isomer as the imide. Octalone **14** is also stable to the conditions for imide formation, so sulfuric acid treatment of the mixture of decalone **15** and octalone **14** from selective hydrogenation of the octalones is an equally useful procedure for separation of the 4α and 4β functional series of compounds.

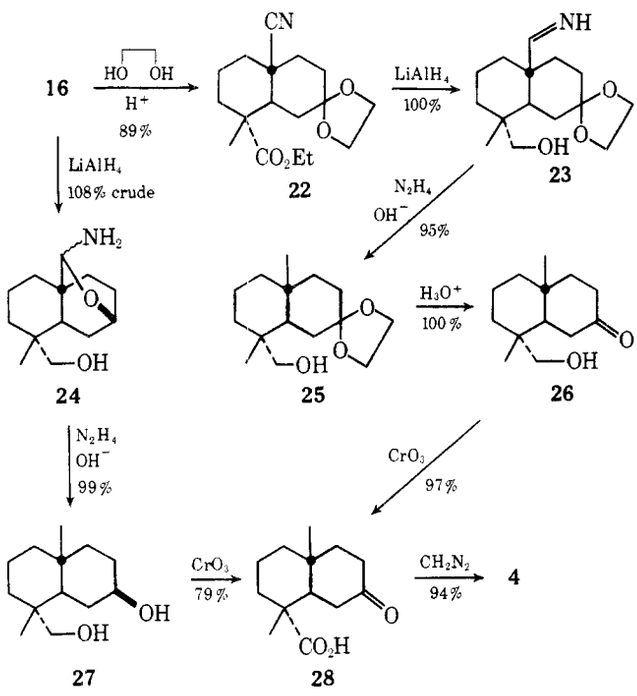
The precise sequence of steps in conversion of cyano ester **15** to imide **21** has not been examined, but from the fact that octalone **14** and decalone **16** survive it seems apparent that the β-carbethoxy group participates in and thereby facilitates nucleophilic addition to the cyano group. This might be

through action of one of the ester oxygens as an intramolecular nucleophile which attacks the carbon of a protonated nitrile or it might be by action of the carbonyl carbon as an electrophile which is attacked by the nitrogen of an appropriate angular species, i.e., the initial intermediates might be either oxygen bridged (derivatives of an imino anhydride) or nitrogen bridged.[16]

These techniques make readily available the 4α-carbethoxydecalone **16** or octalone **14** together with either the 4β-carbethoxydecalone **15** or imide **21**, depending on the particular separation method which is selected in a given instance. Although all of these compounds are suitably constituted for direct attachment of ring C by the general sequence which has been described,[3-5] under some circumstances it may be preferable to first convert them to intermediates which more closely resemble the A and B rings of a particular polycyclic synthetic target. Such transformations have thus far been explored with decalone **16** and imide **21**.

Conversion of the 4α-carbethoxydecalone **16** to an intermediate more closely related to the abietic and pimaric families of resin acids involves transformation of its cyano group to methyl. This can be accomplished either with or without protection of the keto group (Scheme II). Ketalization fol-

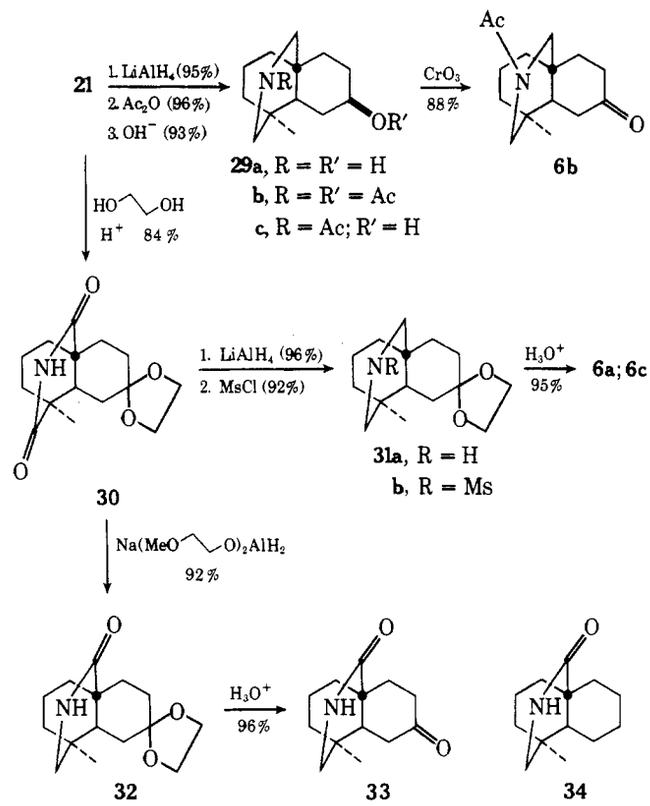
Scheme II



lowed by lithium aluminum hydride reduction of both the ester and nitrile units quantitatively affords hydroxy imine **23**, without overreduction to the angular aminomethyl substance even in the presence of a 5 molar equiv excess of the hydride reagent.[17] Use of limited amounts of lithium aluminum hydride brings about reduction of the ester rather than the nitrile, so retention of the former in order to avoid the necessity of its later regeneration is precluded with this reductant. The imino group is resistant to the usual conditions for alkaline hydrolysis,[17] no doubt for steric reasons, but it does undergo direct Huang-Minlon reduction to methyl.[4,18] Removal of the ketal and Jones oxidation[19] then afford keto acid **28**. Alternatively, reduction of cyano keto ester **16** by lithium aluminum hydride without prior protection of the keto group converts both oxygen functions to the alcohols but still carries the nitrile only to the imino level of oxidation. Resonance with a chemical shift characteristic of a proton of the type O–CH–N rather than CH=N indicates that the product exists as the amino ether tautomer **24**, which allows assignment of the β configuration to the 7 hydroxyl. It may well be that the presence of an analogous cyclic form during the hydride reduction prevents further reduction at the angular carbon. Again the availability of a potential aldehyde group is sufficient for successful Huang-Minlon reduction, which affords diol **27**. Jones oxidation leads to the same keto acid (**28**). The two routes are nearly comparable in overall efficiency (82 and 79% overall from decalone **16**).

Reduction of the imide ring of **21** so as to create alternative intermediates for diterpenoid alkaloid synthesis has also been examined both with and without protection of the keto group (Scheme III). Lithium aluminum hydride reduction of imido

Scheme III



ketone **21** is slow, but when carried to completion amino alcohol **29a** is the sole product. Diacetylation, selective alkaline methanolysis of the ester, and Jones oxidation produce amido ketone **6b**. The β configuration of the C-7 oxygen function in this group of intermediates is inferred from the breadth of the H-7 resonance of **29b** ($W_{1/2}$ ca. 20 Hz). Although this series of reactions leads to the desired structural result in good yield (85% overall from **21** to **6b**), these intermediates are not completely desirable for synthetic manipulation. With the exception of hydroxy amide **29c** and keto amide **6b** they are difficult to crystallize, and even the latter remelts when it is carefully purified and then freed of solvent. The *N*-acetyl group has two favored conformations, of course, and as with other *N,N*-dialkylamides these are of about equal energy so the substances consist of mixtures of the two structures, which may account for the crystallization difficulties. This also makes the use of NMR spectroscopy awkward for examination of reaction mixtures and products, for in solution at room temperature these conformers interconvert at a moderate rate on the NMR time scale and the 4-CH_3 resonances appear either as doublets or broadened singlets which only become sharp time-averaged singlets at elevated temperatures.[20]

Lithium aluminum hydride reduction of imido ketal **30** is much faster than that of its ketonic parent, and subsequent

hydrolysis produces amino ketone **6a**. Primarily owing to the mutual reactivity of the two functional groups in this substance it is preferable to protect the nitrogen before liberating the ketone, and for this purpose the methanesulfonyl group is superior to the acetyl group because the derivatives are readily crystalline. Accordingly keto mesylate **6c** is available in 72% overall yield by the sequence **21** → **30** → **31a** → **31b** → **6c**.

A final type of synthetic intermediate which might be favorable under appropriate circumstances is one in which the nitrogenous ring is present as a lactam, for in a substance such as **33** not only is the nitrogen protected in a relatively nonbasic and nonnucleophilic form but also the carbons α to the nitrogen are differentiated for later synthetic manipulation. Reduction of imido ketal **30** with sodium bis(2-methoxyethoxy)aluminohydride[21] is highly regioselective, producing a single lactam in 92% yield. Formulation of this product and the keto lactam produced from it by hydrolysis as compounds in which the lactam carbonyl is attached to C-10 (**32** and **33**) is based on the chemical shifts of their C-4 methyl groups. Pelletier and Oeltmann have tabulated this property of a large number of diterpenoid alkaloid derivatives, and have shown that in those systems the chemical shift is related to the environment of rings A and E but is not significantly influenced by the functional nature of rings C and D.[22] The 4-methyl chemical shifts of our free amino derivatives **29a** and **31a** (τ 9.30–9.32) and *N*-acetyl compounds **6b**, **29b**, and **29c** (τ 9.14–9.18) correlate well with the ranges found in the alkaloid series (τ 9.27–9.28 and 9.12–9.18, respectively),[22] which indicates that the absence of rings C and D is no deterrent to use of the Pelletier–Oeltmann correlations and that the nature of the C-7 function is of little consequence. The diterpenoid C-4 lactams have 4-methyl resonances in the τ 8.83–8.88 range, and our imides **21** and **30** are similar (τ 8.82), substantially deshielded by the adjacent anisotropic carbonyl. A C-10 carbonyl is too distant to have much more effect on the 4-methyl than does an *N*-acetyl group, shifts of τ 9.05 being found in the alkaloid series and τ 9.12 for the decalin derivative **34**.[23] Lactams **32** and **33** have *C*-methyl resonances at τ 9.08, a value which corresponds to the model systems only if the carbonyl is attached to C-10. The carbonyls of imide **30** are almost symmetrically situated with respect to ring A and C-6, and C-9 bears the same steric relation to the C-10 substituent as the methyl does to that at C-4. Thus the regioselectivity of this reduction seems to result primarily from the additional crowding which the 8-axial hydrogen produces in the transition state for reaction at the angular carbonyl.

Use of these intermediates in resin acid and alkaloid synthesis will be described in future papers of this series.

Experimental Section

General procedures and techniques were the same as described earlier.[4] Unless otherwise specified, HCl, NaOH, KOH, $NaHCO_3$, K_2CO_3, and Na_2CO_3 solutions were aqueous. Brine refers to saturated aqueous NaCl. General procedures for isolation of reaction products are abbreviated as follows: (A) the specified organic solution was washed with the indicated sequence of aqueous solutions followed by water or brine and dried ($MgSO_4$ or Na_2SO_4 unless otherwise specified), and solvent was removed either in vacuo or by evaporation on the steam bath under a stream of dry N_2; (B) the indicated aqueous mixture was thoroughly extracted with the specified organic solvent followed by the steps in procedure A; (C) the reaction mixture was added to water or brine followed sequentially by the steps in procedures B and A. When no temperature is specified, the reaction was conducted at room temperature, ca. 23 °C. Mass spectral data were obtained at 80 eV unless otherwise indicated, and are expressed in the form *m/e* (percent base peak intensity). ^{1}H NMR spectra are reported for $CDCl_3$ solutions and IR spectra for $CHCl_3$ solutions unless otherwise indicated. Melting points (open capillary tubes) are corrected for stem exposure.

Diethyl α-(4-Cyanobutyl)-α-methylmalonate (7). A stirred solution of NaOEt from 27 g (1.17 g-atoms) of Na in 50 mL of absolute EtOH and 4 L of dry PhH under N_2 was treated with 185 g of commercial diethyl methylmalonate (94% pure by GLC, 1.00 mol), EtOH was removed by distillation, and 1 L of dry PhH was added. The mixture was heated to reflux and after 10 min 181 g (1.12 mol) of δ-bromovaleronitrile (bp 108–110 °C, 10 mm) in 1 L of dry PhH was added dropwise over 30 min. After 36 h at reflux and 24 h at ca. 23 °C PhH was distilled until ca. 2 L remained. The cooled mixture was treated with 30 mL of glacial HOAc and washed with brine which was reextracted with ether. Isolation A followed by distillation afforded 223 g (88%) of **7** as a colorless liquid: bp 150–165 °C (2.5 mm); IR 2247, 1725 cm^{-1}; ^{1}H NMR τ 5.83 (q, J = 8 Hz, 4 H), 8.61 (s, 3 H), 8.77 (t, J = 8 Hz, 6 H); mass spectrum *m/e* 85 (69), 83 (100), 47 (23) (no molecular ion).

Anal. Calcd for $C_{13}H_{21}NO_4$: C, 61.52; H, 8.29; N, 5.49. Found: C, 61.49; H, 8.32; N, 5.81.

2-Carbethoxy-6-cyano-2-methylcyclohexanone (8). Under N_2 18 g (0.46 g-atom) of K was dissolved in 250 mL of *t*-BuOH and 2 L of PhMe, excess *t*-BuOH was distilled, 2 L of PhMe was added, the mixture was heated to reflux, and 95 g (0.37 mol) of **7** (bp 150–165 °C, 2.5 mm) in 150 mL of PhMe was added dropwise during 1 h with EtOH being distilled as it formed. After 8 h at reflux with periodic distillation of EtOH the mixture was concentrated to ca. 500 mL by distillation in vacuo, cooled, and treated with 30 mL of glacial HOAc. Isolation C (Et_2O) and distillation afforded 66 g (85%) of **8** as a colorless oil which slowly solidified and could be recrystallized from hexane as colorless prisms: mp 50–51 °C; bp 140–150 °C (1.0–1.25 mm); UV max (95% EtOH) 230 nm (ϵ 2900); IR 2250, 1728 cm^{-1}; ^{1}H NMR τ 5.77 (q, J = 7 Hz, 2 H), 8.67 (s, 3 H), 8.72 (t, J = 7 Hz, 3 H); mass spectrum *m/e* 209 (1), 137 (11), 58 (37), 56 (20), 43 (100).

Anal. Calcd for $C_{11}H_{15}NO_3$: C, 63.14; H, 7.23; N, 6.70. Found: C, 63.79; H, 7.41; N, 6.62.

4β-Carbethoxy-10-cyano-4α-methyl-Δ^5-7-octalone (13) and 4α-Carbethoxy-10-cyano-4β-methyl-Δ^5-7-octalone (14). A solution of 50.9 g (0.24 mol) of **8** (bp 140–150 °C, 1.0–1.25 mm) in 450 mL of PhH was added to a stirred solution of 1.2 g (0.052 g-atom) of Na in 500 mL of absolute EtOH under N_2 and 15 min later 35 g (0.50 mol) of 3-buten-2-one in 60 mL of absolute EtOH and 60 mL of PhH was added over 30 min. After 24 h the mixture was diluted with brine, neutralized with concentrated HCl, and processed by isolation B (Et_2O) to afford 68 g of an oil. Distillation provided 51 g (81%) of **13** and **14** in a 9:11 ratio (integration of the respective =CH resonances) as a brown oil: bp 170–220 °C (2–5 mm); ^{1}H NMR spectrum identical with a summation of those of pure **13** and **14**.

4β-Carbethoxy-10-cyano-5ξ-hydroxy-4α-methyl-7-decalone (11). Reaction of 2.0 g (9.5 mmol) of **8** (bp 160–170 °C, 2.5 mm) in 15 mL of PhH with NaOEt from 10 mg (0.43 mg-atom) of Na in 15 mL of EtOH and then 1.4 g (20 mmol) of 3-buten-2-one in 3 mL of EtOH and 7 mL of PhH, as described above, was quenched with brine after 6 h. Isolation B (PhH) afforded a semisolid which was chromatographed over 30 g of Florisil. Elution with PhH–cyclohexane and PhH afforded oily mixtures containing primarily **13** and **14**, the latter preponderant, and perhaps small amounts of **9** and **10** (^{1}H NMR identification). The 75% Et_2O–25% PhH fractions provided 0.60 g (23%) of **11** as a colorless, crystalline solid which was not purified further: mp 165–180 °C; IR 3510, 2247, 1715 cm^{-1}; ^{1}H NMR τ 5.79 (q, J = 7 Hz, 2 H), 6.77 (s, 1 H, removed by D_2O), 8.69 (t, J = 7 Hz, 3 H), 8.77 (s, 3 H). The ^{1}H NMR spectrum gave no indication of the presence of more than one isomeric ketol.

4β-Carbethoxy-10-cyano-4α-methyl-Δ^5-7-octalone (13). A solution of 350 mg (1.25 mmol) of **11**, mp 165–180 °C, in 10 mL of absolute EtOH and 10 mL of PhH containing 15 mg (0.65 mg-atom) of dissolved Na was stirred for 42 h, poured into 100 mL of brine, and neutralized with 1 N HCl. Isolation B (Et_2O) afforded 280 mg (86%) of a yellowish oil which solidified. Recrystallization from pentane provided **13** as white prisms: mp 69–71 °C; UV max (95% EtOH) 231 nm (ϵ 11 500); IR 2227, 1728, 1677, 1618 cm^{-1}; ^{1}H NMR τ 3.76 (s, 1 H), 5.74 and 5.86 (m,[24] 2 H), 8.57 (s, 3 H), 8.75 (t, J = 7 Hz, 3 H).

Anal. Calcd for $C_{18}H_{19}NO_3$: C, 68.94; H, 7.33; N, 5.36. Found: C, 68.88; H, 7.37; N, 5.52.

4β-Carbethoxy-10-cyano-4α-methyl-5α-7-decalone (15) and 4α-Carbethoxy-10-cyano-4β-methyl-5α-7-decalone (16). A 10.4-g (39.8 mmol) mixture of **13** and **14** (bp 170–210 °C, 2–4 mm; 45% **13** from integration of the =CH resonances) in 170 mL of 95% EtOH was hydrogenated at 1 atm over 500 mg of 30% Pd/C until the theoretical amount of H_2 was absorbed (28 h; 150 mg of additional catalyst was added after 70% H_2 absorption). Filtration and distillation of EtOH in vacuo left 10.5 g (100%) of a mixture of **15** and **16** as a colorless oil with a ^{1}H NMR spectrum which was identical with a summation of those of pure **15** and **16** and contained no =CH resonance or extra

C-CH_3 resonances.[25]

4β-Carbethoxy-10-cyano-4α-methyl-5α-7-decalone (15) and 4α-Carbethoxy-10-cyano-4β-methyl-Δ⁵-7-octalone (14). A. p-Carboxyphenylhydrazone Separation. Two grams (7.66 mmol) of the mixture of **13** and **14** (bp 170–220 °C, 2–5 mm; 45% **13** from ^1H NMR integration) in 45 mL of 95% EtOH was hydrogenated at 1 atm over 300 mg of 30% Pd/C. Reaction was interrupted after 3.5 mmol of H_2 was absorbed. Filtration and evaporation in vacuo left 2.05 g (102%) of a mixture with a ^1H NMR spectrum devoid of resonances characteristic of **13** and containing all resonances characteristic of **14** and **15**.

The separation procedure follows that of Anchel and Schoenheimer.[12] A solution of 5.1 g (19 mmol) of an analogous mixture of **14** and **15** and 4.5 g (30 mmol) of *p*-hydrazinobenzoic acid in 130 mL of 95% EtOH was refluxed for 12 h, cooled, diluted with 300 mL of 4% K_2CO_3, and extracted with Et_2O which was washed with 4% K_2CO_3. The Et_2O fraction contained only a few milligrams of yellow oil which was discarded. The K_2CO_3 solutions were acidified to Congo red with concentrated HCl, and isolation B (Et_2O) afforded 10.8 g of a mixture of *p*-carboxyphenylhydrazones. This was refluxed for 6 h in 150 mL of 95% EtOH containing 16.7 mL of 37% aqueous CH_2O, cooled, and diluted with 300 mL of 4% K_2CO_3. Isolation B (Et_2O) provided 2 g of a yellowish residue which was filtered in PhH through a Florisil column to afford 1.8 g of **15** as a clear oil which slowly crystallized (78% based on available **13**). Recrystallization from hexane yielded **15** as colorless prisms, mp 68–75 °C, and repeated recrystallization raised the melting point to 91–92 °C: IR 2230, 1715 cm^{-1}; ^1H NMR τ 5.80 (q, J = 7 Hz, 2 H), 8.68 (t, J = 7 Hz, 3 H), 8.78 (s, 3 H); mass spectrum *m/e* 263 (17), 236 (21), 207 (10), 190 (24), 189 (20), 163 (25), 162 (23), 79 (31), 55 (100).

Anal. Calcd for $C_{15}H_{21}NO_3$: C, 68.41; H, 8.04; N, 5.32. Found: C, 68.45; H, 8.06; N, 5.46.

Acidification of the K_2CO_3 solution to Congo red with concentrated HCl, isolation with Et_2O, and evaporation provided the residual hydrazone which was stirred and refluxed for 20 min in 150 mL of 2:1 HOAc–H_2O containing 3 mL of 50% aqueous pyruvic acid. Solid K_2CO_3 was added to bring the pH to 9, and isolation B (Et_2O; K_2CO_3 washing) left 1.79 g (64%) of the original **14** as an oil which was filtered in PhH through a Florisil column. Recrystallization of the 1.6 g (57%) of **14** from pentane afforded colorless prisms: mp 59–60 °C; UV max (95% EtOH) 228 nm (ϵ 13 500); IR 2227, 1727, 1680, 1612 cm^{-1}; ^1H NMR τ 4.12 (s, 1 H), 5.80 (q, J = 7 Hz, 2 H), 8.37 (s, 3 H), 8.72 (t, J = 7 Hz, 3 H); mass spectrum *m/e* 261 (0.4), 91 (21), 77 (20), 41 (33), 39 (34), 29 (100).

Anal. Calcd for $C_{15}H_{19}NO_3$: C, 68.94; H, 7.33; N, 5.36. Found: C, 68.85; H, 7.28; N, 5.37.

B. Girard Reagent T Separation. The procedure is patterned after work of Wheeler and Rosado-Lojo.[13] A solution of 591 mg of the 55:45 **14**:**15** mixture (325 mg, 1.25 mmol, of **14** and 2.66 mg, 1.01 mmol, of **15** as determined by ^1H NMR prior to hydrogenation) and 380 mg (2.27 mmol) of trimethylaminoacetohydrazide chloride [Girard's Reagent T, mp 184–185 °C (lit.[26] 185 °C)] in a 52-mL aliquot of a mixture of 1.2 g of glacial HOAc and 100 mL of MeOH was stirred under N_2 for 24.5 h and diluted with 75 mL of 2:1 water–brine. Isolation B (Et_2O; H_2O and $NaHCO_3$ wash) afforded 305 mg of crude **15** which was filtered in PhH through a column of 1 g of Florisil to provide 207 mg (78%) of pure **15** as a colorless oil which crystallized from cold hexanes: mp 87–88 °C; ^1H NMR identical with that described above.

The aqueous fraction was concentrated to ca. 60 mL in vacuo, treated with 57 mL of glacial HOAc and a solution of 229 mg of 99% pyruvic acid in 4.6 mL of water, and refluxed for 35 min. Isolation C ($CHCl_3$; H_2O and $NaHCO_3$ wash) left 252 mg (78%) of **14** as a colorless oil which crystallized from cold hexanes: mp 59–60 °C; IR and ^1H NMR identical with those described above.

4α-Carbethoxy-10-Cyano-4β-methyl-5α-7-decalone (16). Hydrogenation of crude **14** (mp 51–59 °C) was conducted as described for the enone mixture to afford crude **16** as a colorless solid in 92% yield. Recrystallization from hexane gave pure **16** as colorless prisms: mp 85–87 °C; IR 2232, 1720 cm^{-1}; ^1H NMR τ 5.87 (q, J = 7 Hz, 2 H), 8.59 (s, 3 H), 8.76 (t, J = 7 Hz, 3 H); mass spectrum *m/e* 263 (31), 236 (15), 207 (29), 190 (68), 189 (100), 163 (29), 162 (19), 79 (20), 55 (89).

Anal. Calcd for $C_{15}H_{21}NO_3$: C, 68.41; H, 8.04; N, 5.32. Found: C, 68.39; H, 7.93; N, 5.35.

4β-Carbethoxy-10-cyano-7,7-ethylenedioxy-4α-methyl-5α-decalin (18) and 4α-Carbethoxy-10-cyano-4β-methyl-Δ⁵-7-octalone (14). The procedure follows one of Dauben et al.[14] A solution of 200 mg of the 50:50 mixture of **14** and **15** from selective hydrogenation of a **13**:**14** mixture as described (100 mg, 0.380 mmol, of **15** and 100 mg, 0.383 mmol, of **14**), 44 mg (0.38 mmol) of 2-ethyl-2-methyl-1,3-dioxolane, bp 111–112 °C,[14] and 2 mg of TsOH in 50 mL of PhH was refluxed under N_2 for 4 h, cooled, diluted with 10 mL of PhH and 1 drop of pyridine, and added to 10 mL of 2 N KOH. Isolation B (Et_2O and $CHCl_3$) afforded 211 mg (97%) of a colorless oil with a ^1H NMR spectrum which contained only the resonances of pure **14** (above) and pure **18** (below). There was no τ 4.65 resonance characteristic of **19**.

4β-Carbethoxy-10-cyano-7,7-ethylenedioxy-4α-methyl-5α-decalin (18). The procedure follows one by Nagata.[17] A mixture of 1.580 g (6.01 mmol) of **15** (mp 68–75 °C), 20 mg of TsOH, 2 mL of $(CH_2OH)_2$, and 40 mL of PhH was refluxed for 9 h with azeotropic removal of water in a Dean-Stark trap, cooled, treated with 9 drops of pyridine, and poured into 60 mL of 2 N KOH. Isolation B (Et_2O) afforded 1.705 g (92%) of solid, mp 98–110 °C, fractional sublimation of which (120 °C, 0.25 mm) provided 1.580 g (86%) of **18**, mp 109–115 °C. Recrystallization from hexane gave pure 18 as colorless prisms: mp 116.5–118 °C; IR 2223, 1713 cm^{-1}; ^1H NMR τ 5.84 (q, J = 7 Hz, 2 H), 6.06 (m, 4 H), 8.71 (t, J = 7 Hz, 3 H), 8.79 (s, 3 H).

Anal. Calcd for $C_{17}H_{25}NO_4$: C, 66.42; H, 8.20; N, 4.56. Found: C, 66.56; H, 8.20; N, 4.75.

4α-Carbethoxy-10-cyano-7,7-ethylenedioxy-4β-methyl-Δ⁵-octalin (19). A mixture of 200 mg (0.766 mmol) of **14**, 20 mg of TsOH, 1.0 mL of $(CH_2OH)_2$, and 25 mL of PhH was refluxed for 60 h under a Dean-Stark trap, cooled, and added to 200 mL of 2 N KOH. Isolation B (Et_2O and $CHCl_3$) afforded 286 mg of colorless oil which solidified and was filtered in hexane through a 1 × 20 cm column of Florisil to provide 230 mg (98%) of **19** as a colorless solid which was not further purified: ^1H NMR τ 4.65 (s, 1 H), 5.82 (q, J = 7 Hz, 2 H), 6.10 (m, $W_{1/2}$ = 6 Hz, 4 H), 8.40 (s, 3 H), 8.72 (t, J = 7 Hz, 3 H).

4β-Carbethoxy-10-cyano-7,7-ethylenedioxy-4α-methyl-5α-decalin (18) and 4α-Carbethoxy-10-cyano-4β-methyl-Δ⁵-7β-octalol (20). An ice-cold solution of the crude mixture of **14** and **18** from selective ketalization (211 mg) in 50 mL of absolute EtOH was treated with 46 mg (1.2 mmol) of $NaBH_4$ and stirred under N_2 for 1 h. Isolation C ($CHCl_3$ and Et_2O) left 197 mg (93%) of a colorless solid with a ^1H NMR spectrum containing only resonances of **18** and **20**. Chromatography on 1 × 33 cm of Woelm grade I neutral Al_2O_3 afforded in 1:1 Et_2O–hexane fractions 68 mg of **18** (58% based on the original **14**:**15** mixture) with a ^1H NMR spectrum identical with that of the analytical sample (above).

Elution with MeOH afforded 92 mg of **20** (91% based on the original **14**:**15** mixture) as a colorless oil: ^1H NMR τ 4.50 (d, J = 2.0 Hz, 1 H), 5.80 (q, J = 7 Hz, 2 H), 8.40 (s, 3 H), 8.70 (t, J = 7 Hz, 3 H).

The same reduction procedure gave **20** in 95% yield from pure **14**.

4α-Carbethoxy-10-cyano-4β-methyl-5α-7-decalone (16) and 4,10-Dicarboximido-4α-methyl-5α-7-decalone (21). A 32-g (0.122 mol) mixture of crude **15** and **16** (from exhaustive hydrogenation of a 45:55 mixture of **13** and **14**) in a flask containing a large stirring bar and a thermometer was cooled to 15 °C in ice, 140 mL of 96% H_2SO_4 was added in one portion (exothermic reaction), and the mixture was cooled to 30 °C, stirred for 15 min, poured over 600 g of ice, and extracted with $CHCl_3$. The $CHCl_3$ was extracted with 25% NaOH and then subjected to isolation A to afford 17 g (97% based on **14** in the mixture which was hydrogenated) of **16** as a yellowish oil which solidified. One recrystallization from hexane afforded 12.2 g (69%) of **16**, mp 79–86 °C, spectrally identical with the analytical sample (above). A second recrystallization sharpened the melting point to 87–88 °C.

The 25% NaOH extract was acidified to pH 2 with concentrated HCl. Isolation B ($CHCl_3$) gave 11 g (85% based on **13** in the mixture which was hydrogenated) of **21** as a tan solid, mp 130–155 °C. Recrystallization from cyclohexane–EtOAc provided pure **21** as colorless prisms: mp 167–168 °C; IR 3355, 1710 cm^{-1}; ^1H NMR τ 0.64 (broad s, 1 H), 8.82 (s, 3 H); mass spectrum *m/e* 235 (27), 207 (63), 164 (34), 93 (36), 91 (35), 79 (54), 77 (41), 55 (86), 41 (100).

Anal. Calcd for $C_{13}H_{17}NO_3$: C, 66.36; H, 7.28; N, 5.95. Found: C, 66.11; H, 7.04; N, 6.22.

4β-Carbethoxy-10-carboxamido-4α-methyl-5α-7-decalone. A solution of 160 mg (0.608 mmol) of **15** in 15 mL of commercial 96% H_2SO_4[16] was stirred at 50 °C under N_2 for 1 h, cooled to 10 °C, and treated slowly with 5 mL of water. Isolation B ($CHCl_3$ and Et_2O) left 110 mg (64%) of the amido ester i[16] as a tan oil which was not further purified: IR 3400, 1724, 1670 cm^{-1}; ^1H NMR τ 2.90 (broad s, 1 H), 3.80 (broad s, 1 H), 5.89 (q, J = 7 Hz, 2 H), 8.78 (t, J = 7 Hz, 3 H), 8.82 (s, 3 H).

4,10-Dicarboximido-4α-methyl-5α-7-decalone (21). The procedure was adapted from one of van Tamelen and Baran.[27] A solution of 110 mg (0.391 mmol) of crude amido ester i[16] and the NaOEt from 10 mg (0.43 g-atom) of Na in 2 mL of absolute EtOH was refluxed

under N_2 for 4 h, cooled, acidified to pH 4 with glacial HOAc, and taken to dryness in vacuo. Dissolution of the residue in $CHCl_3$ and isolation A gave 70 mg (76%) of **21** as a yellowish oil which crystallized upon trituration with Et_2O: IR and ^1H NMR spectra identical with those described above.

4α-Carbethoxy-10-cyano-4β-methyl-Δ⁵-7-octalone (14) and 4β,10-Dicarboximido-4α-methyl-5α-7-decalone (21). A 925-mg mixture of **14** and **15** (from selective hydrogenation of a 53:47 mixture of **14** and **13**; 490 mg, 1.88 mmol, of **14** and 435 mg, 1.65 mmol, of **15**) was chilled in ice for 1 h, treated with 5 mL of concentrated H_2SO_4, stirred for 50 min with the ice bath being removed after 15 min, and poured over ice. Isolation as described for the **16–21** mixture afforded 384 mg (78% based on that available in the **13–14** mixture which was hydrogenated) of **14** as a yellowish oil which was purified by filtration through a short Florisil column and crystallization from pentane as colorless prisms, mp 59–60 °C. From the alkaline fraction there was obtained 418 mg (108%) of crude solid **21** which could be purified as described above.

4α-Carbethoxy-10-cyano-7,7-ethylenedioxy-4β-methyl-5α-decalin (22). The procedure follows one by Nagata.[17] A mixture of 9.46 g (0.0360 mol) of **16** (mp 79–86 °C), 90 mg of TsOH, 13 mL of $(CH_2OH)_2$, and 200 mL of PhH was refluxed with azeotropic removal of water in a Dean-Stark trap for 11 h, treated with 1 mL of pyridine, and poured into 300 mL of 2 N KOH. Isolation B (Et_2O) afforded 10.5 g (95%) of yellowish residue which solidified and was sublimed (115 °C, 0.25 mm) to provide 9.8 g (89%) of **22** as colorless needles, mp 78–83 °C. Recrystallization from pentane and resublimation produced an analytical sample: mp 81–82 °C; IR 2230, 1717 cm^{-1}; ^1H NMR τ 5.83 and 5.91 (m,[24] 2 H), 6.10 (s, 4 H), 8.65 (s, 3 H), 8.75 (t, J = 7 Hz, 3 H); mass spectrum m/e 307 (0.7), 99 (100), 86 (67), 55 (18).

Anal. Calcd for $C_{17}H_{25}NO_4$: C, 66.42; H, 8.20; N, 4.56. Found: C, 66.74; H, 8.35; N, 4.60.

7,7-Ethylenedioxy-10-formimidoyl-4α-hydroxymethyl-4β-methyl-5α-decalin (23). The procedure was adapted from one by Nagata.[17] Powdered $LiAlH_4$ (1.33 g, 0.035 mol) was suspended in 200 mL of dry tetrahydrofuran (THF) by stirring for 1 h, and this mixture was added dropwise over 1 h to a stirred solution of 2.00 g (0.0065 mol) of **22** (mp 75–80 °C) in 50 mL of dry THF at 0 °C under N_2. After 1 h at 0 °C and 7 h at ca. 23 °C the mixture was cooled to 10 °C and poured into 250 mL of ice-cold saturated potassium sodium tartrate solution. Isolation B ($CHCl_3$) left 1.74 g (100%) of **23** as a colorless oil which was not purified further: IR 3610, 1625 cm^{-1}; ^1H NMR τ 1.47 (broad s, 1 H), ca. 4.28 (very broad s, 1 H), 6.07 (s, 4 H), 6.64 and 6.87 (AB, J = 11 Hz, 2 H), 8.17 (s, 1 H), 9.29 (s, 3 H).

4β,10-Dimethyl-7,7-ethylenedioxy-4α-hydroxymethyl-5α-decalin (25). A procedure of Nagata[17] was modified. A stirred solution of 3.5 g of KOH and 1.74 g (0.0065 mol) of crude **23** in 80 mL of redistilled triethylene glycol under N_2 was heated for 5 min at 70 °C, a mixture of 11.5 mL of 95% N_2H_4 and 2 mL of water was added, and the mixture was heated at 70 °C for 90 min, at 130 °C for 3 h, and at 225–230 °C for 3 h, with distillate being collected in a Dean-Stark trap. The mixture was poured onto 100 g of ice, and isolation B ($CHCl_3$) afforded 1.56 g (95%) of crystalline **25**, mp 93–96 °C. Recrystallization from hexane provided pure **25** as colorless needles: mp 101–102 °C; IR 3620, 3430 cm^{-1} (br); ^1H NMR τ 6.08 (s, 4 H), 6.68 and 6.95 (AB, J = 11 Hz, 2 H), 7.32 (s, 1 H), 9.02 (s, 3 H), 9.27 (s, 3 H); mass spectrum m/e 254 (0.2), 99 (100), 86 (48), 67 (39), 55 (98).

Anal. Calcd for $C_{15}H_{26}O_3$: C, 70.83; H, 10.30. Found: C, 70.64; H, 10.13.

4β,10-Dimethyl-4α-hydroxymethyl-5α-7-decalone (26). The procedure follows one of Magerlein and Levin.[28] A solution of 3 drops of concentrated H_2SO_4, 3 mL of water, and 480 mg (1.90 mmol) of **25** (mp 93–96 °C) in 30 mL of Me_2CO was stirred at reflux under N_2 for 2 h, and Me_2CO was distilled in vacuo. Isolation C (Et_2O; 5% $NaHCO_3$ wash) left 395 mg (100%) of solid **26**, mp 51–55 °C. Recrystallization from hexane afforded pure **26** as colorless prisms: mp 63–64 °C; IR 3618, 3425 (br), 1700 cm^{-1}; ^1H NMR τ 6.58 (s, 1 H), 6.72 and 7.00 (AB, J = 11 Hz, 2 H), 8.86 (s, 3 H), 9.23 (s, 3 H); mass spectrum m/e 210 (3), 121 (21), 109 (37), 97 (49), 95 (39), 81 (59), 69 (85), 67 (52), 55 (98), 41 (100).

Anal. Calcd for $C_{13}H_{22}O_2$: C, 74.24; H, 10.54. Found: C, 74.27; H, 10.56.

10-Formimidoyl-4α-hydroxymethyl-4β-methyl-5α-7β-decalol Amino Ether Tautomer (24). Reduction of 5.00 g (0.0190 mol) of **16** (mp 76–83 °C) in 110 mL of THF by 3.0 g (0.079 mol) of $LiAlH_4$ in 500 mL of THF was conducted as described for reduction of **22**, with 400 mL of potassium sodium tartrate being used during isolation. Crude **24** was obtained as 4.62 g (108%) of a colorless oil which was used directly: IR 3610, 3380 cm^{-1} (br); ^1H NMR τ 5.12 (s, 1 H), 6.12 (broad m, $W_{1/2}$ = 7 Hz, 1 H), 6.75 and 6.90 (AB, J = 10 Hz, 2 H), 7.04 (broad s, 3 H), 9.07 (s, 3 H).

4β,10-Dimethyl-4α-hydroxymethyl-5α-7β-decalol (27). Huang-Minlon reduction of 3.00 g (13.3 mmol) of crude **24** was conducted as described for **23**, using 8 g of KOH in 160 mL of triethylene glycol and 22 mL of 95% N_2H_4 mixed with 4 mL of water to produce 2.8 g (99%) of crude solid **27**, mp 139–146 °C. Fractional sublimation followed by recrystallization from CH_2Cl_2–hexane afforded pure **27** as colorless needles: mp 150–151 °C; IR (KBr) 3315 cm^{-1}; ^1H NMR (as the bistrifluoroacetate in CF_3CO_2H) τ 5.07 (m, $W_{1/2}$ = ca. 20 Hz, 1 H), 5.78 and 6.00 (AB, J = 11 Hz, 2 H), 8.89 (s, 3 H), 9.03 (s, 3 H).

Anal. Calcd for $C_{13}H_{24}O_2$: C, 73.53; H, 11.39. Found: C, 73.44; H, 11.23.

4β,10-Dimethyl-4α-carboxy-5α-7-decalone (28). A. Oxidation of Ketol 26. The procedure was adapted from one by Djerassi et al.[29] A solution of 648 mg (3.09 mmol) of **26** (mp 52–55 °C) in 100 ml of Me_2CO (distilled from $KMnO_4$ and flushed with N_2) at 10 °C was treated with 2.0 mL (5.4 mmol of CrO_3) of Jones reagent[19] (2.675 g of CrO_3 dissolved in 2.3 mL of concentrated H_2SO_4 and diluted to 10.0 mL with water) in one portion. After 2 h, during which the mixture was warmed to ca. 23 °C, it was diluted with water and extracted with $CHCl_3$ which was extracted with 5% $NaHCO_3$. Acidification to pH 3 with dilute HCl and isolation B ($CHCl_3$) provided 670 mg (97%) of **28**, mp 126–129 °C. Recrystallization from cyclohexane gave pure **28** as colorless microcrystals: mp 130–131 °C; IR 1702 cm^{-1}; ^1H NMR τ −1.80 (s, 1 H), 8.82 (s, 3 H), 8.84 (s, 3 H); mass spectrum m/e 224 (13), 178 (38), 163 (22), 123 (100), 110 (60), 109 (56), 95 (48), 81 (40), 55 (42).

Anal. Calcd for $C_{13}H_{20}O_3$: C, 69.61; H, 8.99. Found: C, 69.58; H, 9.16.

B. Oxidation of Diol 27. Oxidation of 1.70 g (8.00 mmol) of **27** in 150 mL of Me_2CO with 6.00 mL (16.0 mmol of CrO_3) of Jones reagent by the procedure used for oxidation of **26** produced 1.41 g (79%) of crude **28** as a yellowish oil which solidified and had a ^1H NMR spectrum identical with that of pure **28**.

4α-Carbomethoxy-4β,10-dimethyl-5α-7-decalone (4). A solution of 1.2 g (5.4 mmol) of **28** (mp 126–129 °C) in 50 mL of Et_2O at 0 °C was treated with 150 mL of Et_2O containing the CH_2N_2 from 2.5 g (24 mmol) of *N*-methyl-*N*-nitrosourea.[30] After 2 h at 0 °C excess CH_2N_2 was destroyed with glacial HOAc, and isolation A (5% $NaHCO_3$ wash) provided 1.33 g (104%) of crude **4**. Recrystallization from pentane afforded 1.24 g (94%) of **4**, mp 80–84 °C, and further recrystallization produced an analytical sample as colorless needles: mp 84–85.5 °C; IR 1718 cm^{-1}; ^1H NMR τ 6.37 (s, 3 H), 8.82 (s, 3 H), 8.85 (s, 3 H); mass spectrum m/e 238 (9), 178 (97), 123 (59), 109 (50), 95 (54), 81 (59), 69 (63), 67 (60), 55 (96), 41 (100).

Anal. Calcd for $C_{14}H_{22}O_3$: C, 70.55; H, 9.31. Found: C, 70.73; H, 9.25.

4β,10-Iminobismethyl-4α-methyl-5α-7β-decalol (29a). The procedure follows one of Tahara and Hirao.[31] A mixture of 1.50 g (6.38 mmol) of **21** (mp 150–155 °C) and 6.0 g (0.16 mol) of $LiAlH_4$ in 160 mL of dry dioxane and 15 mL of Et_2O was stirred at reflux under N_2 for 7 days, cooled to 10 °C, and poured slowly into 500 mL of ice-cold saturated potassium sodium tartrate. Isolation B (Et_2O and $CHCl_3$) provided 1.270 g (95%) of **29a** as a tan semisolid which was used without further purification: IR 3590, 3300 cm^{-1} (broad); ^1H NMR τ 9.30 (s, 3 H). This material is probably the monohydrate, because it shows ^1H resonance from two extra protons (integration) as a broad peak of variable chemical shift which disappears upon addition of D_2O.

7β-Acetoxy-4β,10-acetyliminobismethyl-4α-methyl-5α-decalin (29b). A procedure of Regan and Hayes was used.[32] A solution of 2.477 g (11.8 mmol) of crude **29a** and 12 mL of Ac_2O in 26 mL of dry pyridine was stirred for 5.5 h. Isolation C (Et_2O and $CHCl_3$; 2 N HCl and 5% $NaHCO_3$ wash) gave 3.328 g (96%) of **29b** as a yellow gum which could not be induced to crystallize even after molecular distillation: IR 1725, 1625 cm^{-1}; ^1H NMR τ 5.30 (m, $W_{1/2}$ = ca. 20 Hz, 1 H), 7.92 (s, 3 H), 7.98 (s, 3 H), 9.15 (s) and 9.17 (s) (total 3 H).

4β,10-Acetyliminobismethyl-4α-methyl-5α-7β-decalol (29c). A procedure of Regan and Hayes was used.[32] A refluxing solution of 3.028 g (10.3 mmol) of crude **29b** in 100 mL of MeOH under N_2 was treated with 10 mL of 10% NaOH, held at reflux for 5 min, and cooled to ca. 23 °C over 55 min. Isolation C ($CHCl_3$) gave 2.400 g (93%) of solid **29c**, mp 155–156 °C, which was recrystallized from EtOAc to produce an analytical sample: mp 181–182 °C; IR 3540, 3335 (br), 1622 cm^{-1}; ^1H NMR τ 7.92 (s, 3 H), 9.14 (s) and 9.16 (s) (total 3 H).

Anal. Calcd for $C_{15}H_{25}NO_2$: C, 71.67; H, 10.03; N, 5.57. Found: C, 71.69; H, 9.96; N, 5.57.

4β,10-Acetyliminobismethyl-4α-methyl-5α-7-decalone (6b). Oxidation of 2.400 g (9.56 mmol) of crude **29c** (mp 155–160 °C) in 100

mL of Me_2CO was conducted as described for preparation of **28**, using 2.90 mL of Jones reagent[19] (7.75 mmol of CrO_3) and a reaction time of 6 min at 10–15 °C. The mixture was poured into 1.3 L of 5% $NaHCO_3$, and isolation B ($CHCl_3$) afforded 2.400 g (100%) of crude **6b** as a yellow oil. Distillation gave 2.10 g (88%) of **6b** as a colorless oil: bp 190–200 °C (bath temperature, 0.25 mm); IR 1625, 1708 cm^{-1}; ^1H NMR τ 7.88 (s, 3 H), 9.16 (s) and 9.18 (s) (total 3 H); mass spectrum *m/e* 249 (100), 206 (54), 178 (20), 164 (31), 107 (19), 91 (24), 79 (27), 55 (29). Crystallization occurred slowly from cyclohexane–EtOAc to provide colorless prisms, mp 71–74 °C, which liquefy upon drying at 0.25 mm and ca. 23 °C. The analytical sample was a semisolid from three such recrystallizations.

Anal. Calcd for $C_{15}H_{23}NO_2$: C, 72.25; H, 9.30; N, 5.62. Found: C, 71.73; H, 9.15; N, 5.94.

4β,10-Dicarboximido-7,7-ethylenedioxy-4α-methyl-5α-decalin (30). Ketalization of 3.00 g (12.8 mmol) of **21** was conducted as described for preparation of **22**, using 3.0 mL of $(CH_2OH)_2$ and 20 mg of TsOH in 150 mL of PhH, a reaction time of 18 h, quenching with 1 mL of pyridine, and isolation B ($CHCl_3$) from 5% $NaHCO_3$ rather than KOH to afford 3.075 g (86%) of crude solid **30**. Recrystallization from CH_2Cl_2–pentane produced 2.976 g (84%) of pure **30** as colorless needles: mp 185–189 °C; IR 3367, 1725, 1700 cm^{-1}; ^1H NMR τ 1.15 (broad s, 1 H), 6.08 (s, 4 H), 8.82 (s, 3 H); mass spectrum *m/e* 279 (37), 99 (100), 86 (36).

Anal. Calcd for $C_{15}H_{21}NO_4$: C, 64.49; H, 7.58; N, 5.01. Found: C, 64.57; H, 7.55; N, 4.98.

7,7-Ethylenedioxy-4β,10-iminobismethyl-4α-methyl-5α-decalin (31a). A procedure of Nagata et al. was followed.[33] A solution of 0.513 g (13.5 mmol) of $LiAlH_4$[34] and 0.750 g (2.69 mmol) of **30** (mp 186–188 °C) in 50 mL of diglyme (filtered through grade I basic Al_2O_3 and distilled from $LiAlH_4$) was stirred at 120 °C under N_2 for 6 h, 0.513 g (13.5 mmol) of $LiAlH_4$ was added, and stirring at 120 °C was continued for 6 h. The cooled mixture was added slowly to 250 mL of ice-cold potassium sodium tartrate, and isolation B ($CHCl_3$) gave 0.647 g (96%) of **31a**, mp 89–93 °C. Recrystallization from hexane and sublimation gave pure **31a** as colorless prisms: mp 92.5–93.5 °C; IR 3370 cm^{-1}; ^1H NMR τ 6.07 (s, 4 H), 9.32 (s, 3 H); mass spectrum *m/e* 251 (35), 220 (14), 207 (92), 206 (100), 99 (30), 86 (44).

Anal. Calcd for $C_{15}H_{25}NO_2$: C, 71.71; H, 9.96; N, 5.58. Found: C, 71.87; H, 10.10; N, 5.66.

7,7-Ethylenedioxy-4β,10-methanesulfonyliminobismethyl-4α-methyl-5α-decalin (31b). The procedure follows one by Nagata et al.[33] A cold (−5 °C) solution of 375 mg (1.49 mmol) of **31a** (mp 89–93 °C) in 5 mL of dry pyridine was treated with 0.60 mL (0.91 g, 7.9 mmol) of MsCl, stirred, and brought to ca. 23 °C over 12 h, and treated with ice. Isolation C ($CHCl_3$) gave 466 mg (95%) of semisolid which was filtered in $CHCl_3$ through 2 × 22 cm of Florisil to provide 451 mg (92%) of **31b**, mp 160–163 °C. Recrystallization from CH_2Cl_2–pentane provided pure **31b** as colorless needles: mp 165.5–166 °C; IR 1335, 1153 cm^{-1}; ^1H NMR τ 6.08 (s, 4 H), 7.27 (s, 3 H), 9.18 (s, 3 H); mass spectrum *m/e* 329 (3), 328 (10), 251 (74), 250 (100), 206 (53), 99 (87), 67 (24), 55 (25).

Anal. Calcd for $C_{16}H_{27}NO_4S$: C, 58.36; H, 8.21; N, 4.26; S, 9.72. Found: C, 58.24; H, 8.34; N, 4.36; S, 9.76.

4β,10-Methanesulfonyliminobismethyl-4α-methyl-5α-7-decalone (6c). A solution of 640 mg (1.94 mmol) of crude **31b** (mp 169–176 °C) and 2 mL of concentrated H_2SO_4 in 60 mL of MeOH and 7 mL of water was refluxed under N_2 for 13 h, concentrated in vacuo to ca. 10 mL, and poured into 5% $NaHCO_3$. Isolation B ($CHCl_3$) gave 585 mg (106%) of solid, mp 179–187 °C, and chromatography on 6 g of Florisil (1 × 20 cm; elution with hexane, 1:1 hexane–Et_2O, $CHCl_3$) provided 523 mg (95%) of **6c**, mp 182–185 °C. Recrystallization from CH_2Cl_2–hexane produced pure **6c** as colorless prisms: mp 183.5–184.5 °C; IR 1705, 1335, 1152 cm^{-1}; ^1H NMR τ 7.21 (s, 3 H), 9.17 (s, 3 H); mass spectrum *m/e* 285 (9), 206 (100), 55 (11).

Anal. Calcd for $C_{14}H_{23}NO_3S$: C, 58.95; H, 8.07; N, 4.91; S, 11.23. Found: C, 58.77; H, 7.92; N, 4.80; S, 11.18.

4β-Aminomethyl-10-carboxy-7,7-ethylenedioxy-4α-methyl-5α-decalin Lactam (32). A procedure of Cerny et al. was modified.[21] A solution of 500 mg (1.79 mmol) of crude **30** (mp 176–184 °C) in 20 mL of PhH was added over 10 min to a refluxing solution of 1.540 g (8.56 mmol) of bis(2-methoxyethoxy)aluminohydride (2.200 g of a 70% solution in PhH; Aldrich "Red-Al") in 20 mL of PhH. After 1 h at reflux the mixture was cooled and acidified with concentrated HCl, and water was added to just dissolve the white precipitate. Isolation B ($CHCl_3$) gave 445 mg (94%) of a clear oil which crystallized, mp 190–201 °C. Sublimation (153 °C, 0.30–0.35 mm) afforded 438 mg (92%) of **32** as an analytically pure mixture of two crystal forms, mp 194–195 and 197–198 °C. Recrystallization from CH_2Cl_2—pentane produced pure **32** as colorless needles: mp 197–198 °C; IR 3390, 1650 cm^{-1}; ^1H NMR τ 3.55 (broad s, 1 H), 6.03 (s, 4 H), 6.87 (m, $W_{1/2}$ = 7 Hz, 2 H), 9.08 (s, 3 H); mass spectrum *m/e* 265 (3), 264 (18), 193 (10), 99 (100), 86 (25), 55 (11).

Anal. Calcd for $C_{15}H_{23}NO_3$: C, 67.89; H, 8.74; N, 5.28. Found: C, 67.97; H, 8.63; N, 5.35.

4β-Aminomethyl-10-carboxy-4α-methyl-5α-7-decalone Lactam (33). Hydrolysis of **32** was conducted as described for preparation of **6c**, using 350 mg (1.32 mmol) of **32** (mp 197–199 °C) and 6 drops of concentrated H_2SO_4 in 25 mL of MeOH and 3 mL of water for 16 h. The crude product, 296 mg (101%; mp 155–161 °C), was recrystallized from CH_2Cl_2–*n*-hexane to afford 280 mg (96%) of pure **33** as colorless prisms, mp 156–159 °C. Sublimation gave the analytical sample: mp 158.5–160.5 °C; IR 3405, 1710, 1655 cm^{-1}; ^1H NMR τ 3.21 (broad s, 1 H), 6.78 (m, $W_{1/2}$ = 5 Hz, 2 H), 9.08 (s, 3 H); mass spectrum *m/e* 221 (15), 220 (100), 193 (52), 178 (55), 150 (58).

Anal. Calcd for $C_{13}H_{19}NO_2$: C, 70.55; H, 8.69; N, 6.33. Found: C, 70.83; H, 8.71; N, 6.28.

Acknowledgment. We are grateful to Ms. Nancy Calton, National Science Foundation Undergraduate Research Participant, 1971, for collection and interpretation of much of the mass spectrometric data reported in the Experimental Section, and to the Laboratory for Organic Chemistry, Swiss Federal Institute of Technology (ETH), Zurich, for making their facilities available to W.L.M. during the period when much of this and the accompanying paper was written.

Registry No.—**4**, 16981-49-0; **6b**, 62461-28-3; **6c**, 62461-29-4; **7**, 16981-42-3; **8**, 16981-43-4; **11**, 62461-30-7; **13**, 62461-31-8; **14**, 62461-32-9; **15**, 16981-46-7; **16**, 16981-47-8; **18**, 62461-33-0; **19**, 62461-34-1; **20**, 62461-35-2; **21**, 16981-48-9; **22**, 62504-21-6; **23**, 62461-36-3; **24**, 62461-37-4; **25**, 62461-38-5; **26**, 62461-39-6; **27**, 62461-40-9; **28**, 62461-41-0; **29a**, 62461-42-1; **29b**, 62461-43-2; **29c**, 62461-44-3; **30**, 62461-45-4; **31a**, 62461-46-5; **31b**, 62461-47-6; **32**, 62461-48-7; **33**, 62461-49-8; i, 62461-50-1; diethyl methylmalonate, 609-08-5; δ-bromovaleronitrile, 5414-21-1; 3-buten-2-one, 24512-07-0; *p*-hydrazinobenzoic acid, 619-67-0; trimethylaminoacetohydrazide chloride, 123-46-6; 2-ethyl-2-methyl-1,3-dioxolane, 126-39-6; MsCl, 124-63-0.

References and Notes

(1) (a) Part 9: W. L. Meyer, R. A. Manning, P. G. Schroeder, and D. C. Shew, *J. Org. Chem.*, preceding paper in this issue. (b) Preliminary communication: W. L. Meyer and C. W. Sigel, *Tetrahedron Lett.*, 2485 (1967). (c) Abstracted in part from Ph.D. Dissertations of T.E.G., R.J.H., and C.W.S., University of Arkansas, 1974 and 1972, and Indiana University, 1967, respectively. (d) Supported in part by Research Grants AM-4215 and AM-10123 from the National Institute of Arthritis and Metabolic Diseases and by the University of Arkansas Research Reserve Fund; the UV, 90-MHz NMR, and mass spectrometers were obtained with partial support of National Science Foundation Grants GP-8286, GP-18291, and GP-6978, respectively. (e) National Science Foundation Trainee, 1969–1970 and 1971–1972; National Aeronautics and Space Administration Trainee, 1970–1971; Phillips Petroleum Co. Fellow, 1972–1973. (f) Eastman Kodak Research Fellow, 1969–1970. (g) National Institutes of Health Predoctoral Fellow, 1965–1967.

(2) For convenience all bicyclic and tricyclic compounds in this paper will be numbered by the steroid–terpenoid convention as in **1** and **4**, with the *gem*-disubstituted ring of decalins being ring A. The configurational notations α and β denote a trans or cis relationship to the C-10 angular group, respectively. All synthetic substances were prepared only in racemic form, although the prefix (±) is omitted and only one enantiomer is depicted in structural formulas.

(3) W. L. Meyer, R. W. Huffman, and P. G. Schroeder, *Tetrahedron*, **24**, 5959 (1968).

(4) W. L. Meyer, G. B. Clemans, and R. A. Manning, *J. Org. Chem.*, **40**, 3686 (1975).

(5) W. L. Meyer, R. A. Manning, E. Schindler, R. S. Schroeder, and D. C. Shew, *J. Org. Chem.*, **41**, 1005 (1976).

(6) T. A. Spencer, M. A. Schwartz, and K. B. Sharpless, *J. Org. Chem.*, **29**, 782 (1964).

(7) Cf. H. O. House, "Modern Synthetic Reactions", 2nd ed., W. A. Benjamin, New York, N.Y., 1972.

(8) W. L. Meyer and A. S. Levinson, *J. Org. Chem.*, **28**, 2184 (1963).

(9) W. L. Meyer, D. L. Davis, L. Foster, A. S. Levinson, V. L. Sawin, D. C. Shew, and R. F. Weddleton, *J. Am. Chem. Soc.*, **87**, 1573 (1965).

(10) C. W. Sigel, unpublished research.

(11) A. Tahara, K. Hirao, and Y. Hamazuki, *Chem. Ind. (London)*, 850 (1965); A. Tahara and K. Hirao, *Tetrahedron Lett.*, 1453 (1966).

(12) M. Anchel and R. Schoenheimer, *J. Biol. Chem.*, **114**, 539 (1936).

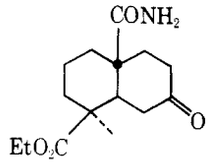
(13) O. H. Wheeler and O. Rosado-Lojo, *Tetrahedron*, **18**, 477 (1962); O. H. Wheeler, *Chem. Rev.*, **62**, 205 (1962).

(14) H. J. Dauben, Jr., B. Loken, and H. J. Ringold, *J. Am. Chem. Soc.*, **76**, 1359 (1954).

(15) E. W. Garbisch, Jr., *J. Am. Chem. Soc.*, **86**, 5561 (1964).

(16) On one occasion amido ester **i** rather than imide **21** was obtained from

treatment of decalone **15** with H_2SO_4. Reaction of this amide with NaOEt produces the imide. The water content of commercial "concentrated" H_2SO_4 was not routinely examined in these reactions, and it is quite possible that such a result was due to a variation in the water concentration.



i

(17) W. Nagata, *Tetrahedron*, **13**, 287 (1961).
(18) W. S. Johnson, J. A. Marshall, J. F. W. Keana, R. W. Franck, D. G. Martin, and V. J. Bauer, *Tetrahedron, Suppl.*, **No. 8**, 541 (1966).
(19) K. Bowden, I. M. Heilbron, E. R. H. Jones, and B. C. L. Weedon, *J. Chem. Soc.*, 39 (1946).
(20) The CH_3CO resonances of **6b**, **29b**, and **29c** do not show significant broadening at room temperature.
(21) M. Cerny, J. Malek, M. Capka, and V. Chvalovsky, *Collect. Czech. Chem. Commun.*, **34**, 1023 (1969), and earlier papers.
(22) S. W. Pelletier and T. N. Oeltmann, *Tetrahedron*, **24**, 2019 (1968).
(23) W. L. Meyer and A. S. Levinson, *J. Org. Chem.*, **28**, 2859 (1963).
(24) This ethoxyl resonance shows distinct ABC_3 character with $J_{AB} = J_{AC} = 7$ Hz, but was not precisely analyzed; these chemical shifts are only estimated visually, ±0.02 ppm, cf. ref 9.
(25) On some occasions absorption of the theoretical amount of H_2 could not be induced within a reasonable time even with a much higher catalyst:enone ratio. The product then contained up to 10% of **14** in addition to **15** and **16**.
(26) L. F. Fieser and M. Fieser, "Reagents for Organic Synthesis", Vol. I, Wiley, New York, N.Y., 1967, p 410.
(27) E. E. van Tamelen and J. S. Baran, *J. Am. Chem. Soc.*, **80**, 4659 (1958).
(28) B. J. Magerlein and R. H. Levin, *J. Am. Chem. Soc.*, **77**, 1904 (1955).
(29) C. Djerassi, R. R. Engle, and A. Bowers, *J. Org. Chem.*, **21**, 1547 (1956).
(30) F. Arndt in "Organic Syntheses", Collect. Vol. II, Wiley, New York, N.Y., 1943, p 165.
(31) A. Tahara, K. Hirao, and Y. Hamazaki, *Chem. Pharm. Bull.*, **15**, 1785 (1967).
(32) B. M. Regan and F. N. Hayes, *J. Am. Chem. Soc.*, **78**, 639 (1956).
(33) W. Nagata, T. Sugasawa, M. Narisada, T. Wakabayashi, and Y. Hayase, *J. Am. Chem. Soc.*, **89**, 1483 (1967).
(34) If the $LiAlH_4$ is not of high quality, reduction is incomplete and **31a** is accompanied by large amounts of other reduction products.

Diterpenoid Total Synthesis, an A → B → C Approach. 11. C-Ring Deoxy Aromatic Systems. Total Synthesis of Methyl (±)-Dehydroabietate[1]

Walter L. Meyer* and Carl W. Sigel[1e]

Department of Chemistry, University of Arkansas, Fayetteville, Arkansas 72701

Received December 28, 1976

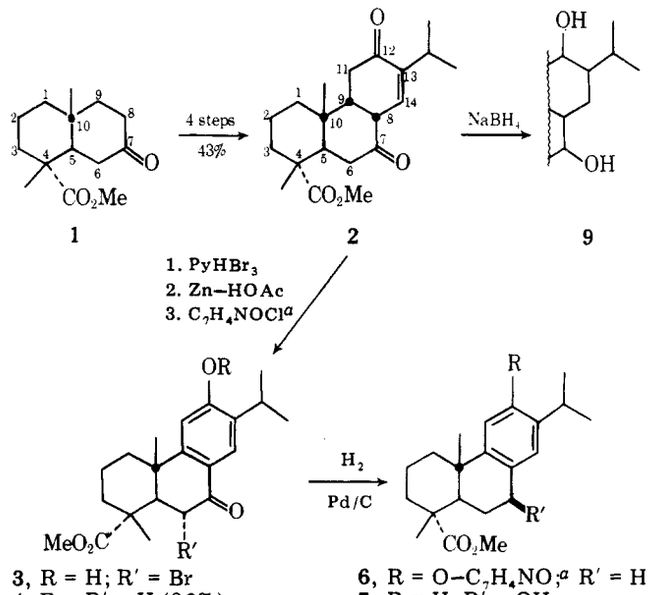
Condensation of 4α-carbomethoxy-4β,10-dimethyl-*trans*-7-decalone (1)[2] with ethyl formate followed by DDQ dehydrogenation produces the corresponding 8-formyl-Δ^8-7-octalone, which is converted to trans-syn-cis tricyclic enedione **2** by sequential Michael addition of *tert*-butyl isovalerylacetate and treatment of the adduct with acid. Reaction of **2** with pyridine hydrobromide perbromide affords 7-keto-12-phenol **4** and its 6α-bromo derivative, and the latter is transformed to **4** by zinc–acetic acid. Hydrogenolysis of the 12-(2′-benzoxazolyloxy) derivative of **4** leads to methyl (±)-dehydroabietate.

Total syntheses which have been fully described in previous parts of this series have all involved target diterpenoids which bear one or more hydroxyl groups on ring C. However, the general synthetic plan can also be adapted for preparation of C-aromatic terpenoids devoid of C-ring oxygen functions, as illustrated here in a total synthesis of methyl dehydroabietate (**8**, Scheme I).

Conversion of the carbomethoxydimethyldecalone **1**[1a] to enedione **2** is completely analogous to the annulation sequence which was used in synthesis of ferruginol[3] and carnosic acid[4] (see Scheme I of accompanying part 9[5]), although in this system the yield was not quite as high (43% overall) and the intermediates and enedione were all noncrystalline. Surprisingly, enedione **2** is much less stable than most of the corresponding compounds we have examined, and it must be used within a few hours of its preparation. As initially isolated, however, it appears spectrally (^1H NMR, IR) to be free of contaminants and to correspond to the $\Delta^{13,14}$ trans-syn-cis structure shown.[5]

The initial plan for aromatization of ring C with ejection of the C-7 and C-12 oxygens envisioned reduction of enedione **2** to a 13-ene-7,12-diol followed by bisdehydration and rearrangement of the 7,8 unsaturation. However, sodium borohydride reduction produces saturated diol **9** (probably as a mixture of diastereomers) rather than the enediol, a reaction which has subsequently been found typical of such enediones.[5] Alternate reductants were not investigated as a route to the enediol. Instead, attention was turned to reversal of the deoxygenation–aromatization sequence.

Scheme I



3, R = H; R′ = Br
4, R = R′ = H (82%)
5, R = C_7H_4NO;[a] R′ = H (88%)
6, R = O–C_7H_4NO;[a] R′ = H
7, R = H; R′ = OH
8, R = R′ = H (80%)

[a] C_7H_4NO = 2-benzoxazolyl.

Aromatization of enedione **6** by pyridine hydrobromide perbromide is more complex than the corresponding reaction in the ferruginol or carnosol series.[3,4] In those instances, where