Aqueous Sodium Hydroxide. To the liner of a stainless steel autoclave was added 3.6 g (16.6 mmol) of **2** and 125 mL of H_2O containing 3.4 g (83 mmol) of NaOH. The mixture was stirred under nitrogen for 5 h at approximately 300 °C. The autoclave was cooled to room temperature and vented, and the reaction products were removed by pipet. The autoclave liner and stirrer were rinsed with three 50-mL portions of $CHCl_3$. The aqueous alkaline reaction mixture was neutralized (pH 7) with 2 N HCl and extracted three times with 50-mL portions of $CHCl_3$ rinse from above. The $CHCl_3$ extracts were combined, dried (Na_2SO_4 and decolorizing carbon), and filtered. After removal of solvent from the dried solution, 2.82 g (100 mol %) of nearly colorless, crystalline **5** was isolated, mp 54–56 °C (lit.[21] mp 57–58 °C). The infrared spectrum of the product (KBr disk) was identical with that of authentic **5** and a mixture melting point of the product with an authentic specimen of **5** was not depressed. Recrystallization of the product from petroleum ether gave 2.75 g of product, mp 56–57 °C.

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Registry No.—1, 132-65-0; **2**, 1016-05-3; **5**, 90-43-7.

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Diterpenoid Total Synthesis, an A → B → C Approach. 9. Structure and Stereochemistry of Tricyclic Intermediates[1]

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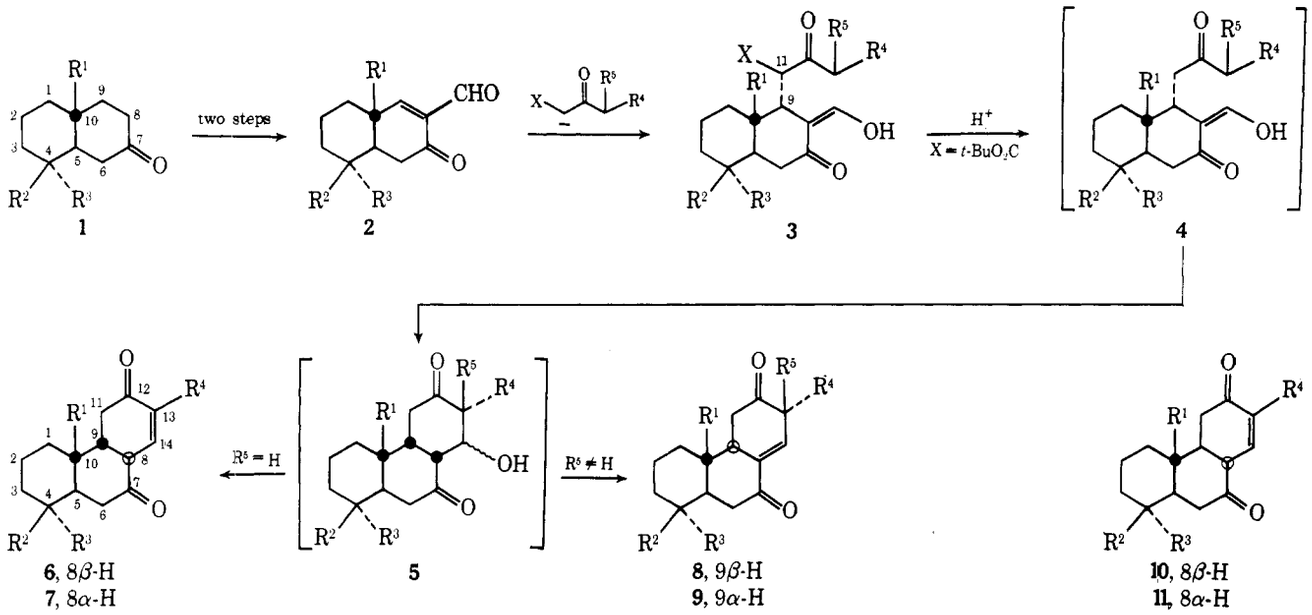
Michael addition of the sodium enolate of a *tert*-butyl β-keto ester to a 4,4,10-trisubstituted 8-formyl-Δ^8-7-octalone (**2**)[2] was shown earlier to afford adducts of general structure **3** which upon exposure to acid undergo *tert*-butyl ester cleavage, decarboxylation, and cyclodehydration to produce tricyclic enediones **6** or **8**. Spectroscopic evidence, primarily ^1H NMR, is presented to demonstrate that the double bond in these enediones is normally in the 13,14 position (**6**) rather than the 8,14 position (**8**) when C-13 carries fewer than two substituents, and that the relative configuration of the carbon skeleton is trans-syn-cis in **6** and by inference trans-syn in **8**. Intramolecular ketals **20** and **22**, in which the C-10–C-9–C-8 configuration can only be anti-cis or syn-cis, were synthesized from enedione **6g** by routes which do not alter the configuration at these sites. Relation of ketal **20** to saturated diketone **17**, which must be either trans-anti-trans or trans-syn-cis because it does not epimerize in base, confirms the trans-syn-cis configuration of these substances. Stereoselectivity in the Michael addition producing adducts **3** therefore leads exclusively to the 9α orientation of the β-keto ester side chain. In cases where more than one stereoisomeric adduct **3** is formed, it is shown that the configurational difference is only at C-11.

In previous publications we have described a new synthetic approach to the elaboration of a variety of perhydrophenanthrenoid diterpenoids,[3] and have partially illustrated its generality and versatility in total syntheses of racemic sugiol,[4,5] ferruginol,[4,5] nimbiol,[5] dehydroabietic acid,[6] carnosic acid,[1a,7,8] carnosol,[1a,8] and hinokiol.[9] A central stage in this sequence comes with addition of ring C to an A/B precursor in the form of a suitably substituted *trans*-7-decalone (**1**).[2] The decalone is condensed with ethyl formate and the resulting 8-hydroxymethylene derivative is dehydrogenated with 2,3-dichloro-5,6-dicyanobenzoquinone (DDQ) to produce an 8-formyl-Δ^8-7-octalone (**2**, Scheme I). Owing to its double conjugation this olefin is highly receptive to nucleophilic attack,[3] and reaction with the enolate of a suitably activated ketone affords an adduct of general structure **3** in which R^4 and in some cases also R^5 represent potential C-13 substitu-

Scheme I



1–11	R¹	R²	R³	R⁴	R⁵	Ref
a	Me	Me	Me	Me	H	4
b	Me	Me	Me	*i*-Pr	H	4
c	CO_2Et	Me	Me	*i*-Pr	H	1a
d	Me	Me	CO_2Me	*i*-Pr	H	5
e	CN	Me	Me	H	H ($\Delta^{5,6}$)	2
f	CO_2Et	Me	Me	H	H	1a
g	Me	Me	Me	H	H	1b
h	CN	CO_2Et	Me	H	H	11a
i	CH_2——NAc——CH_2		Me	H	H	11a
j	CH_2——NMs——CH_2		Me	H	H	11b
k	Me	Me	CO_2Me	Me	Me	11c,d
m	Me	Me	CO_2Me	Ph	Me	11c
n	Me	Me	CO_2Me	Me	Ph	11c
o	Me	Me	CO_2Me	*o*-$MeOC_6H_4$	Me	11c

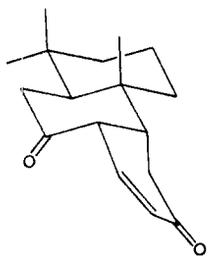
ents of the particular terpenoid at issue. In most of our early work *tert*-butyl β-keto esters were used as nucleophilic addends,[1a,3-7,9] so that the adducts **3** (X = *t*-BuO_2C) could be treated briefly with acid to induce sequential[1a] *tert*-butyl ester cleavage, decarboxylation, and aldol cyclodehydration to form tricyclic enediones, presumably through usually unisolated 14-hydroxy 7,12-diketones such as **5**.[3,10] Previous publications have presented preliminary evidence on the basis of which certain of the 13-mono- or unsubstituted enediones were tentatively assigned the 13,14 double bond location and the trans-syn-cis relative configuration (**6**) in preference to other possibilities (**7–11**), and adducts **3** were formulated with the 9β-H configuration shown, both epimers at C-11 often being produced. Here we describe substantiation of these assignments by means of detailed information which has been collected from several series of related intermediates.

A number of these enediones (**6a–f**) have already been reported,[1a,3-7] and several others (**6g–j, 8k–o**) have also been obtained in our laboratories.[1b,11] Preparation of most of these additional substances by the general path outlined in Scheme I will be described in publications dealing with their synthetic use. However, because enedione **6g** plays a central role in the structure investigations presently under discussion, details of its synthesis are included here. The reactions **2a** → **3g** → **6g** proceed normally,[1a,5] the only noteworthy feature being that in this series the Michael addition in benzene affords a single diastereomer of adduct **3g**, whereas in dimethyl sulfoxide a different C-11 diastereomer is the sole product (of which more below). Acid-catalyzed cyclization of either adduct leads to the same enedione.[12]

Location of the C-Ring Double Bond in Enediones 6. In most instances ^1H NMR spectroscopy has provided the only unequivocal evidence concerning location of the C-ring olefin in those enediones which are not disubstituted at C-13 so that a priori they can be unsaturated at either 13,14 or 8,14 (**6–11a–j**).[13-15] The $\Delta^{13,14}$ assignment is immediately apparent from spectra of the 13-unsubstituted compounds **6e–j** and the 13-methyl derivative **6a**. The former all show resonance from two C-ring vinyl protons, and the 13-methyl of the latter is allylic in chemical shift (τ 8.20) and spin coupled to both the vinyl proton and the 8 proton by ca. 1 Hz, as expected for the allylic and homoallylic arrangements.[17,18a] Evidence that the 13-isopropyl enediones **6b–d** are also $\Delta^{13,14}$ substances is less obvious, but can be found in their C=CCHC=O resonances, which appear as broad triplets near τ 6.3.[19] This proton is spin coupled by about 6 Hz to the vinyl proton (confirmed in the case of **6c** by spin decoupling and by deuterium exchange of H-8) and to one other vicinal proton, which would be H-9 if the structure were $\Delta^{13,14}$ or the isopropyl methine (H-18) if it were $\Delta^{8,14}$. The chemical shift of H-18 in enedione **6c** can be located at τ 7.13 by spin decoupling it from the two isopropyl methyls,[21] and the same irradiation removes 1-Hz allylic splitting from the vinyl proton resonance but does *not* simplify the C=CCH=O triplet; changes in the latter pattern are induced by irradiation near τ 7.37. Therefore the isopropyl methine proton and the proton vicinal to C=CCHC=O are different, as in structure **6** but not **8**. These spin-decoupling experiments were conducted only with enedione **6c**. However, the basic spectral properties of all three 13-isopropyl derivatives **6b–d** are very similar, and they closely resemble those

of **6a** and **6e–j** but differ significantly from those of the $\Delta^{8,14}$ compounds **8k–o**,[14] so it seems clear that all of **6a–j** are analogously constituted. It is the $\Delta^{13,14}$ structure which commonly results from these reactions in the absence of two substituents at C-13.

Enediones **6a–j** have all been prepared by acid-catalyzed cyclization, and since they are vinylogous β-diketones these acidic conditions should certainly establish equilibrium between the 13,14 and 8,14 unsaturated structures. Thus the 13,14 location is thermodynamically preferred for the unsaturation. This appears to result primarily from conformational effects in the tricyclic ring system. The trans fusion of rings A and B[22] and the 9β-H (syn) A/C configuration which these substances prove to possess both limit the conformations available to ring B. Within these constraints, location of unsaturation at 8,14 allows ring B to adopt only a conformation on the twist–boat pseudorotational cycle[23] somewhere between a boat with C-7 and C-10 as the prow and stern and a boat with C-5 and C-8 as the prow and stern or a conformation with carbons 6–10 all nearly coplanar. Only in the last of these can the enone system be coplanar, and this would come at the expense of eclipsing the 9–10 bond. In fact, all of these conformations involve some torsional strain at an sp^3–sp^3 carbon–carbon bond, either 9–10 or 5–6 or both.[24] On the other hand, the trans-syn-cis $\Delta^{13,14}$-12-enone structure allows both enone coplanarity and a B-ring chair conformation (**12**).



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Spectroscopic Investigation of the 8,9 Configuration. The second structural question concerning all of the enediones is that of their relative configuration at C-9, and in the case of compounds **6a–j** also at C-8. This, too, was initially explored by ^{1}H NMR spectroscopy. From Dreiding models of the four possible $\Delta^{13,14}$-7,12-diketone structures (**6, 7, 10, 11**) there appear to be 11 reasonable conformations which represent significant minima in valence angle bending strain with respect to small conformational distortions.[25] Spin-coupling relationships among the B- and C-ring protons in each of these were estimated by measuring dihedral angles in the models and applying the Garbisch expressions[17] for couplings involving vinylic protons ($J_{8,14}$ and $J_{8,13}$) and those of Abraham and Holker[26] for the sp^3–sp^3 types. The only pertinent resonances of the enediones which are clearly distinguishable at 60 MHz are those of H-13, H-14, and usually H-8, but in the 220-MHz spectrum of **6c** all of the B- and C-ring proton resonances can be identified and their spin couplings analyzed.[27] Comparison of the coupling constants derived from these data with the calculated values for all seven vicinal and allylic couplings in rings B and C shows that for only two of the hypothetical conformers are all of the predicted couplings in acceptable agreement with experiment (Table I). These are the trans-syn-cis B-ring chair (**12**) and a trans-anti-cis B-ring boat with C-5 and C-8 as the prow and stern. For each of the other structures at least two, and in most cases three or four, of the expected couplings diverge sufficiently from the observed values to allow the structure to be discounted.[14] Although 220-MHz data which reveal so many conformationally dependent couplings were obtained only for **6c**, extension of this configurational conclusion to all of enediones **6a–j** is justified by their general spectral similarity and particularly because at least one or two of the diagnostic couplings are usually visible even at 60 MHz. However, a decision between the trans-syn-cis structures and their trans-anti-cis isomers must be based on other grounds.

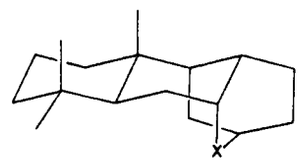
Table I. Calculated and Observed Coupling Constants for Enedione Structures

Protons	J, Hz Obsd[a]	Calcd for **12**	Calcd for t-a-c[b]
5,6α	4.5	4.1	3.1
5,6β	14.0	14.2	14.3
6α,6β	−14.3	*d*	*d*
8,14	6.0	5.9	5.9
8,13	|<1.0|	0.6	0.6
8,9	5.8	3.1	3.1
9,11α	15.1	14.3	3.1[c]
9,11β	3.7	3.1	14.3[c]
11α,11β	−16.5	*d*	*d*

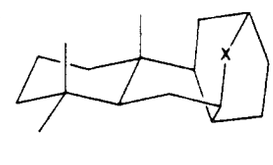
[a] All except $J_{8,13}$ are for **6c** from 220-MHz spectra; $J_{8,13}$ is for **6e–j** from 60-MHz spectra; all in $CDCl_3$ solution. [b] Trans-anti-cis conformer with B-ring boat (C-5 and C-8 at prow and stern). [c] Observed resonance assignments to H-11α and H-11β would be reversed if this were the structure. [d] See ref 29.

Acid-catalyzed equilibration of the double bond between the 8,14 and 13,14 sites during preparation of the enediones (above) should provide them with the more stable configuration at C-8 as well as the more stable location of the unsaturation. A trans-anti-cis compound, particularly one with the B-ring boat which would be required by the NMR data, should therefore have been converted to its trans-anti-trans epimer[28] and should not correspond to an enedione isolated after C-8 equilibration. On the other hand, the trans-syn-cis conformer which is in accord with the NMR data (**12**) should be energetically favored over its trans-syn-trans diastereomer, which would have ring B as a boat with serious eclipsing at the C-9–C-10 bond. Accordingly, the trans-syn-cis configuration is the only one which satisfies both the NMR evidence and energetic analysis, and thus it became the tentative assignment for which unequivocal support was sought.[29]

Chemical Confirmation of Configuration. If enediones **6a–j** are trans-syn-cis compounds, positions 7 and 12 of an appropriate derivative can be bridged by one atom (X) as in structure **13**. Analogous bridging is structurally feasible if the carbon skeleton is trans-anti-cis (**14**), but not if it is trans-anti-trans or trans-syn-trans. Consequently, a 7,12 bridged substance of this type must have the hydrogens at C-7, C-8, C-9, and C-12 either all β (**13**) or all α (**14**), and determination



13



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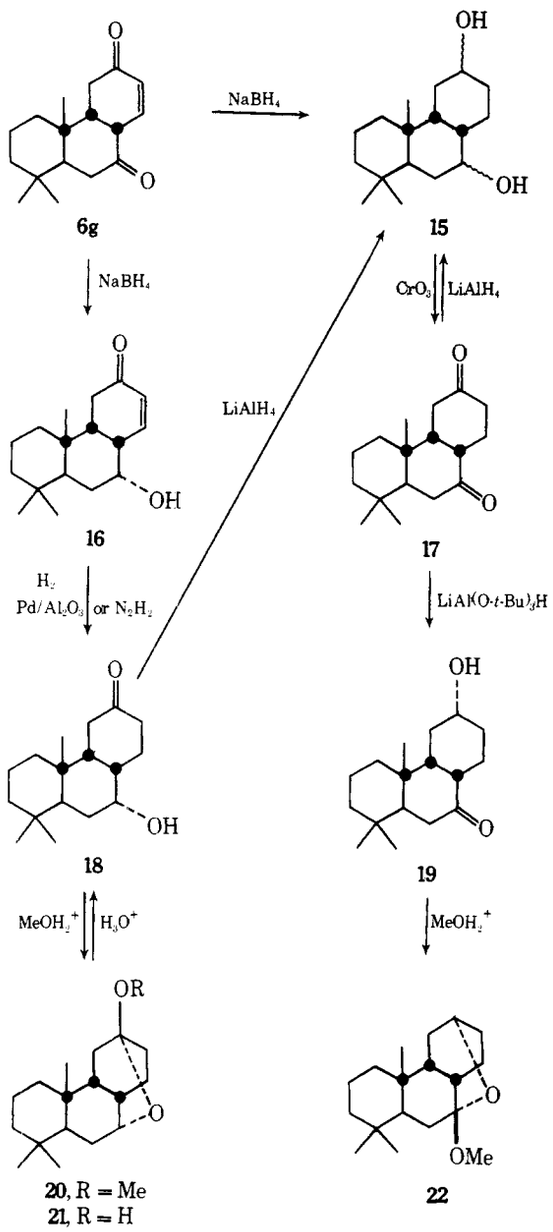
of its configuration at only one of these four centers will suffice to define its structure completely. Internal ketals **20** and **22** represent such bridged compounds, and their preparation from enedione **6g** was therefore undertaken (Scheme II).

Treatment of enedione **6g** with sodium borohydride under very mild conditions[30a,31] affords a monohydroxy compound containing a conjugated enone (IR and UV) with two vinyl protons (^{1}H NMR), so it is clear that this reduction occurs regioselectively at the nonconjugated carbonyl group. It is also highly stereoselective, producing at least 88% of the 7α-hy-

Scheme II



droxy enone **16**. The C-7 configurational assignment was initially based on the 6-Hz width of the CHOH resonance, because only a 7β proton can be gauche to all three 6 and 8 protons (irrespective of the skeletal configuration). It is ultimately confirmed by conversion of the hydroxy enone to syn-cis ketal **20**.[32] The steric course of the reduction is undoubtedly influenced primarily by the hindrance which a syn-cis ring C presents to approach of a reagent on the α face of C-7 (cf. **12**).

The olefinic bond in hydroxy enone **16** is hydrogenated smoothly over 5% palladium on alumina. Diimide reduction[33] also leads to ketol **18**,[34] but curiously enough in this instance the predominant isolated product appears to be the cyclic hemiketal tautomer **21** (weak C=O absorption) which slowly isomerizes to the ketol form. Exposure of this ketol–hemiketal mixture to *p*-toluenesulfonic acid in benzene–methanol affords a substance which can be assigned the constitution of ketal **20** on the basis of its composition ($C_{18}H_{30}O_2$), the presence of one methoxyl (^{1}H NMR) but no hydroxyl or carbonyl (IR), and its derivation from ketol **18** for which the 7-hydroxy-12-keto structure is synthetically unambiguous.

Sodium borohydride reduction of enedione **6g** under conventional conditions brings about saturation of the olefinic bond as well as the two carbonyl groups,[30a,36] with predominant formation of two diastereomers of diol **15**. Jones oxidation[37] of the mixture affords a single diketone (**17**). We anticipated that reduction of this diketone by 1 equiv of the very bulky and selective reagent lithium tri(*tert*-butoxy)aluminohydride[38] would occur preferentially at the less hindered carbonyl group, which would be that at C-12 if the trans-syn-cis configuration were correct. The reaction should also be stereoselective, favoring formation of the 12α alcohol **19** which corresponds both to reduction from the less hindered face of the ketone and to formation of an equatorial hydroxyl group.[30c] Exposure of the crude product of this reduction (**19**) to *p*-toluenesulfonic acid in methanol affords a second intramolecular ketal. Inasmuch as none of the reactions leading from enedione **6g** to either ketal should perturb the C-9 configuration, both ketals must have the same backbone geometry, so they must be constitutional isomers rather than stereoisomers. Therefore, since the first ketal unambiguously has the 12-methoxy structure **20**, this new ketal is the 7-methoxy derivative **22** and *tert*-butoxyaluminohydride reduction of diketone **17** follows the projected course. The absence of detectable amounts of ketal **20** from this second ketalization suggests that the reduction is highly regioselective. Whether recovery of an appreciable amount of hydroxy ketone from the ketalization experiment is a consequence of the presence of the 12β-hydroxy 7-ketone in the reduction product or only of the slowness of the 12α-hydroxy 7-ketone **19** to ketalize under these conditions was not determined.

Assignment of the trans-syn-cis configuration to ketals **20** and **22** and their progenitors rests on the following evidence. A diol of mp 200 °C (**15**) is the major product from lithium aluminum hydride reduction of ketol **18**. During this reduction and also during conversion of this ketol to ketal **20** and hydrolysis of the latter to regenerate **18** no mechanism is available for alteration of configuration at any chiral center, so ketol **18** and the 200 °C diol must be either trans-anti-cis or trans-syn-cis like the ketals. Diketone **17** is not epimerized by base. Therefore it must correspond to the thermodynamically preferred configuration at C-8 and be either trans-anti-trans or trans-syn-cis.[28] Reduction of the diketone by lithium aluminum hydride produces a mixture of diols **15** in which the same 200 °C isomer is predominant. Inasmuch as this reaction occurs in the absence of a proton source it cannot involve prior epimerization at C-8,[30b] so the 200 °C diol and the diketone must have the same relative configuration of the ring system. Accordingly, by its formation from ketol **18** the 200 °C diol is required to be either trans-syn-cis or trans-anti-cis and as derived from diketone **17** it must be either trans-syn-cis or trans-anti-trans. Only the trans-syn-cis configuration is compatible with both sets of data, so this structure must be assigned to the diol and also to compounds **17**–**22** in Scheme II. The same evidence substantiates the 9,10 syn relationship in both enedione **6g** and hydroxy enone **16** and the 7α hydroxyl orientation in the latter, because configurations at these sites cannot change during any of the reactions under discussion. From this foundation the 8,9 cis configuration can be extended to the enedione as a consequence of its C-8 configurational mobility and necessary correspondence to the thermodynamically preferred arrangement at that center[39] and to the hydroxy enone as a consequence of the 6-Hz width of its H-7β resonance.

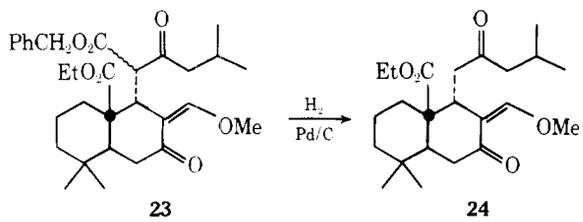
Stereochemistry of Adducts 3. With the structure of enedione **6g** unambiguously settled and those of the other enediones clearly assignable as $\Delta^{13,14}$ trans-syn-cis (**6a–j**) or $\Delta^{8,14}$ trans-syn (**8k–o**) on the basis of spectroscopic similarity and/or synthetic analogy, we can turn to certain stereochemical aspects of the reactions by which they are produced from α-formyl enones **2**. The configuration at C-9 is estab-

lished during Michael addition of the β-keto ester enolate to the aldehyde (2 → 3). With some systems only one adduct is produced in this reaction, and in other instances two diastereomeric adducts are formed as indicated either by their actual isolation or by the presence of appropriate resonances from two isomers in NMR spectra of the crude product. In all cases, however, acid-catalyzed cyclization with loss of the *tert*-butoxycarbonyl group leads only to enediones with the trans-syn configuration, usually in very good yield, even when a mixture of diastereomers of **3** is the reactant or when different pure adducts are individually cyclized. Both stereoisomers of the adduct must therefore give rise to the same enedione. Accordingly, in all of the adducts the 9–11 bond is α as it is in the enediones, for even if equilibration at C-9 were mechanistically possible under the cyclization conditions (which it should not be) an initial 9β (equatorial) side chain should not epimerize to the less stable 9α configuration and then cyclize with the rates of both steps being so great that the product from direct cyclization of the 9β epimer would be undetectable.

Further evidence that isomerism of adducts **3** involves differences only at C-11 is provided by their facile interconvertibility. As conventionally prepared by addition of the sodium enolate of *tert*-butyl acetoacetate to aldehyde **2c** in benzene followed by protonation with glacial acetic acid, adduct **3f** is obtained as a 3:1 mixture of isomers.[1a] However, this ratio depends on the solvent[1a] and also on the proton donor used to quench the reaction; for example, the ratio from reaction in benzene is 1:1 after protonation with pivalic acid and 2:3 with hydrochloric acid. Furthermore, exposure of a 2:1 mixture to benzoic acid in carbon tetrachloride leads to slow equilibration of the two isomers, with a static 1:1 ratio (determined by ^{1}H NMR) being produced after 15 h. If these two substances were C-9 epimers their interconversion would involve a retro-Michael reaction, and while their ratio could well depend upon the length of their exposure to base prior to protonation, it should not depend upon the manner of protonation. Nor should such equilibration be acid catalyzed, and it certainly should not give rise to a 50:50 mixture of a 9α and a 9β substituted adduct, but to exclusively the 9β isomer. On the other hand, all of these properties are consistent with stereoisomerism at C-11.

Base-catalyzed interconversion of the two adducts **3f** occurs relatively rapidly on treatment with a catalytic amount of sodium hydride in benzene, the 2:1 mixture being converted to a 1:4 mixture in 10 min. Longer exposure to these conditions induces a retro-Michael reaction with regeneration of aldehyde **2c** followed by unknown subsequent reactions which consume the reactants without producing 9β adducts or any other recognizable substances. Analogous base-catalyzed reversal of the Michael reaction by which adducts **3** are formed has also been observed during isolation of the adducts by extraction into aqueous alkali.[1a]

Finally, conversion of adducts such as **3** to hydroxymethylene enol ethers has been described.[1a] Like the adducts these enol ethers are often obtained as mixtures of two diastereomers.[1a] Hydrogenolysis of a mixture of the two diastereomers of enol ether **23**,[1a] the 11-carbobenzoxy analogue of the



23 **24**

enol ether of **3c**, is accompanied by decarboxylation to afford a single racemate of diketone **24**. If the stereoisomerism had been at any point except C-11 (e.g., at C-9 or the enol ether double bond) two diastereomeric products would have resulted. All of the foregoing observations are in accord with adduct mixtures which are diastereomeric only at C-11 and not at C-9.

It is thus apparent that Michael addition to form adducts **3** is kinetically controlled, and occurs rapidly and preferentially from the α face of the unsaturated aldehyde. From a mechanistic viewpoint this is not surprising, for that direction of addition is both sterically and stereoelectronically favored (less hindrance to approach and axial bond formation through a chairlike transition state). From a synthetic viewpoint it is important that reaction time be minimized, for the reaction is reversible, and slower undesirable processes are apparently thermodynamically favored under the basic conditions of the addition. Indeed, we have found that in several instances no more than 5 min is necessary to maximize adduct formation in dimethyl sulfoxide, and that in this solvent protonation by glacial acetic acid frequently affords a different C-11 stereoisomer than is preponderant when benzene has been used. There is no evidence, however, that under the usual conditions for this addition it is possible to bring about a mating of the formyl enone **2** and a β-keto ester enolate to produce an adduct with the constitution of **3** but under thermodynamic control so the C-9 side chain has the β orientation.

The acid-catalyzed deesterification–decarboxylation–cyclization sequence (3 → [4] → [5] → **6** or **8**) is stereochemically unexceptional. No change in the C-9 configuration occurs on passing from adduct to enedione. The olefinic bond is normally located 13,14 if this is possible, but when 13,13 disubstitution blocks that possibility the sequence still proceeds, with formation of a $\Delta^{8,14}$-enedione.

Experimental Section

General procedures and techniques were the same as described earlier.[5] Spin-decoupled 60-MHz ^{1}H NMR spectra were obtained with a Varian V-6058A spin decoupler and an A-60 spectrometer; 90-MHz spectra were obtained on a Bruker HFX-90 spectrometer. Mass spectral data is expressed in the form *m/e* (percent base peak intensity). GLC was conducted as described[5] using columns of 10% silicone gum SE-30 on Chromosorb W (2 ft × 0.25 in., designated A, or 6 ft × 0.25 in., designated B) or 1.5% Carbowax (6 ft × 0.125 in., designated C), at the indicated temperature. Melting points (open capillary tubes) are corrected for stem exposure. Unless otherwise specified, NaOH, $NaHCO_3$, and HOAc solutions were aqueous. Brine refers to saturated aqueous NaCl.

4,4,10-Trimethyl-8-hydroxymethylene-9α-(1′-*tert*-butoxycarbonyl-2′-oxopropyl)-5α-decalone-7 (3g, X = CO_2-*t*-Bu). Reaction of 3.8 g (0.024 mol) of *tert*-butyl acetoacetate and 384 mg of NaH (0.012 mol, as 662 mg of a 58% mineral oil dispersion) in 100 mL of Me_2SO for 20 min (time critical) formed the Na enolate,[1a] and 1.75 g (7.95 mmol) of crude **2a**[5] was added. After 5 min the mixture was treated with 6 mL of glacial HOAc and quickly partitioned between $CHCl_3$ and water. Extraction ($CHCl_3$), washing (H_2O), drying, and evaporation left a product which appeared (^{1}H NMR) to be a single adduct. It was purified by repeated washing with pentane to afford 2.1 g (70%) of **3g** (X = CO_2-*t*-Bu) as white platelets: mp 147–148.5 °C; ^{1}H NMR ($CDCl_3$) τ −4.58 (s, broad, 1 H), 1.58 (s, 1 H), 6.32 (d, *J* = 5 Hz, 1 H), 6.87 (d, *J* = 5 Hz, 1 H), 7.77 (s, 3 H), 8.63 (s, 9 H), 9.02 (s, 3 H), 9.08 (s, 6 H). Fractional sublimation (125 °C, 0.005 mm) afforded an analytical sample, mp 150–151 °C.

Anal. Calcd for $C_{22}H_{34}O_5$: C, 69.79; H, 9.06. Found: C, 69.41; H, 8.79.

When this reaction was conducted in PhH using equimolar quantities of *tert*-butyl acetoacetate and NaH for 10 min to form the enolate, a 3:2 molar ratio of *tert*-butyl acetoacetate to **2a**, a 20-min reaction time, and isolation by extraction into 1% NaOH followed by acidification with glacial HOAc and extraction with $CHCl_3$, a different stereoisomer of **3g** was isolated in 61% yield, with no indication of the presence of the first isomer (^{1}H NMR). Recrystallization from pentane afforded this isomer as white prisms: mp 113–116 °C; IR (CCl_4) 1730, 1705, 1640, 1590 cm^{-1}; ^{1}H NMR (CCl_4) τ −4.42 (s, broad, 1 H), 1.67 (s, 1 H), 6.47 (d, *J* = 5 Hz, 1 H), 6.93 (d, *J* = 5 Hz, 1 H), 7.85 (s, 3 H), 8.67 (s, 9 H), 9.00 (s, 3 H), 9.07 (s, 6 H).

5α,8β,9β-Podocarp-13-ene-7,12-dione (6g). A mixture of 400 mg of powdered $CaCl_2$ (dried at 120 °C for 2 h) and 247 mg (0.650 mmol) of **3g** (X = CO_2-*t*-Bu), mp 146–147.5 °C, in 55 mL of dry PhH was treated with 200 mg of $TsOH \cdot H_2O$ (dried at 0.05 mm for 2 h). Ca. 5 mL of solvent was distilled to remove traces of water and the mixture was held at reflux for 30 min (yellow color develops, changing to orange; time critical). Filtration, dilution with $CHCl_3$, washing with brine, and evaporation afforded 153 mg (90%) of **6g** as moist, yellowish crystals which were spectrally indistinguishable from the analytical sample. Repeated washing with ether (considerable material loss) produced white crystals, mp 159–162 °C dec. Recrystallization from EtOAc afforded an analytical sample as white needles: mp 152–158 °C; IR ($CHCl_3$) 1712, 1683, 1623 cm^{-1}; UV max (95% EtOH) 219 nm (ε 7400), 347 (1700); (base) 237 nm (ε 4100), 258 (4900); ^1H NMR ($CDCl_3$) τ 2.95 (dd, *J* = 10 and 6 Hz, 1 H), 3.85 (d, *J* = 10 Hz, 1 H), 6.35 (broad t, *J* = 5 Hz, 1 H), 8.67 (s, 3 H), 9.08 (s, 3 H), 9.12 (s, 3 H).

Anal. Calcd for $C_{17}H_{24}O_2$: C, 78.42; H, 9.29. Found: C, 78.60; H, 9.44.

5α,8β,9β-Podocarpane-7,12-diol (15). A. $NaBH_4$ Reduction of Enedione 6g. A stirred solution of 200 mg (0.77 mmol) of crude **6g** (no contamination evident by ^1H NMR) in 50 mL of absolute EtOH was treated at 0 °C with 100 mg (2.6 mmol) of $NaBH_4$. After 5 min the mixture was brought to ca. 23 °C for 1 h, poured into brine, and extracted with $CHCl_3$ which was washed (H_2O), dried, and evaporated to afford 200 mg (100%) of a yellowish solid which consisted of a 4:64:4:28 mixture (GLC C, 192 °C) presumed to be the four stereoisomeric diols **15.** Washing with ether afforded the predominant isomer as white crystals: mp 194–196 °C; ^1H NMR and IR spectra identical with those of the analytical sample from method B; mass spectrum *m/e* 266 (4), 248 (40), 230 (37), 69 (100). A small (<1%) peak at *m/e* 11 indicated slight contamination by a boron compound, presumably a borate ester.

B. $LiAlH_4$ Reduction of Diketone 17. A solution of 72 mg (0.27 mmol) of **17** (>96% pure by GLC A, 210 °C) in 15 mL of ether was added to 100 mg (2.6 mmol) of $LiAlH_4$ in 10 mL of ether at 0 °C, brought to ca. 23 °C, and after 3 h treated with 10 mL of ice-cold saturated potassium sodium tartrate solution. The product was extracted into $CHCl_3$ which was washed (H_2O), dried, and evaporated to afford 68 mg of (93%) of **22** as a pale yellow solid which consisted of a 2:54:2:42 mixture of four compounds (GLC C, 190 °C). Recrystallization from $CHCl_3$ yielded 10 mg of the predominant diol **15** as matted white needles: mp 199–200 °C; IR (KBr) 3350 cm^{-1}; ^1H NMR ($CDCl_3$) τ 5.8–6.7 (broad m, 2 H), 8.98 (s, 3 H), 9.13 (s, 3 H), 9.17 (s, 3 H).

Anal. Calcd for $C_{17}H_{30}O_2$: C, 76.64; H, 11.35. Found: C, 76.37; H, 11.10.

C. Reduction of 7α-Hydroxy 12-Ketone 18. A 36-mg (0.14 mmol) sample of crude **18** (from hydrolysis of **20**) was reduced with 50 mg (1.3 mmol) of $LiAlH_4$ in 13 mL of ether as described in method B above. The crude product amounted to 35 mg (96%) of a white solid which was a 6:94 mixture of two diols **15** (GLC C, 192 °C). Recrystallization from $CHCl_3$ afforded the major isomer as white microcrystals: mp 197–198 °C; IR and ^1H NMR indistinguishable from those of the pure diol obtained by method B; mmp 198–199 °C.

5α,8β,9β-Podocarpane-7,12-dione (17). A stirred solution of 250 mg (0.94 mmol) of crude **15** (4:64:4:28 mixture from $NaBH_4$ reduction of **6g**) in 45 mL of Me_2CO (dried over K_2CO_3 and redistilled over $KMnO_4$) at 10–15 °C was rapidly treated with 0.52 mL (0.0014 mol) of Jones reagent.[37,40] After 10 min it was diluted with water. Extraction (ether and $CHCl_3$), washing (10% HOAc, 1% NaOH, and water), drying, and evaporation afforded 170 mg (70%) of **17** as moist, yellowish crystals (>96% pure by GLC A, 210 °C). Fractional linear sublimation (ca. 120 °C, 0.005 mm) afforded an analytical sample as white needles: mp 142–143 °C; IR ($CHCl_3$) 1710 cm^{-1}; ^1H NMR ($CDCl_3$) τ 8.66 (s, 3 H), 9.08 (s, 3 H), 9.10 (s, 3 H).

Anal. Calcd for $C_{17}H_{26}O_2$: C, 77.82; H, 9.99. Found: C, 77.75; H, 9.96.

A solution of 58 mg (0.22 mmol) of **17** (98% pure by GLC C, 192 °C) and 48 mg (0.89 mmol) of NaOMe in 10 mL of absolute MeOH was refluxed for 2.5 h, diluted with brine, and acidified with 10 drops of concentrated HCl. The product, isolated by extraction, amounted to 50 mg of yellowish semisolid which was indistinguishable from the starting diketone by IR, ^1H NMR, and GLC C.

12α-Hydroxy-5α,8β,9β-podocarpan-7-one (19). A solution of 150 mg (0.59 mmol) of lithium tri-*tert*-butoxyaluminohydride and 140 mg (0.53 mmol) of **17** (>96% pure by GLC A, 210 °C) in 15 mL of tetrahydrofuran (THF) was stirred at 0 °C for 10 min, diluted with 15 mL of ice water, acidified with 8 drops of glacial HOAc, and diluted with water. Extraction ($CHCl_3$), washing (5% $NaHCO_3$ and H_2O), drying, and evaporation afforded 80 mg (57%) of **19** as a yellow glass: IR ($CHCl_3$) 3600, 3435, 1705 cm^{-1}; ^1H NMR ($CDCl_3$) τ 6.1–6.7 (m, broad, 1 H), 8.73 (s, 3 H), 9.12 (broad s, 6 H).

7β-Methoxy-7α,12α-epoxy-5α,8β,9β-podocarpane (22). A solution of 80 mg (0.30 mmol) of crude **19,** 15 mg of TsOH, 1 mL of absolute MeOH, and 10 mL of PhH was refluxed for 5 h, cooled, and partitioned between $CHCl_3$ and 5% $NaHCO_3$. Extraction (ether), washing (H_2O), drying, and evaporation afforded 66 mg of yellowish crystals with spectra similar to those of **19.** Treatment of this product with ca. 300 mg of Drierite and 20 mg of TsOH in 10 mL of absolute MeOH at reflux for 24 h, with isolation as before, afforded 53 mg of a yellow oil which spectrally appeared to be a mixture of **19** and **22.** The 5% ether–95% pentane fractions from chromatography over Al_2O_3 afforded 22 mg (26%) of analytically pure **22** as volatile, white needles: mp 74–75 °C; IR ($CHCl_3$) 1470, 1255 (w), 1102, 991 cm^{-1}; ^1H NMR ($CDCl_3$) τ 6.06 (m, 1 H), 6.70 (s, 3 H), 8.98 (s, 3 H), 9.10 (s, 3 H), 9.17 (s, 3 H); mass spectrum *m/e* 278 (6), 247 (12), 140 (100).

Anal. Calcd for $C_{18}H_{30}O_2$: C, 77.65; H, 10.86. Found: C, 77.45; H, 10.67.

Further elution with ether afforded 30 mg of **19** as a yellow oil (spectral identification).

7α-Hydroxy-5α,8β,9β-podocarp-13-en-12-one (16). A solution of 26.0 mg (0.69 mmol) of $NaBH_4$ in 10 mL of absolute EtOH was added dropwise to a stirred solution of 153 mg (0.59 mmol) of **6g,** mp 159–162 °C dec, in 16 mL of absolute EtOH at −15 °C. The mixture was held at −15 °C for 20 min, removed from the cold bath, and after 5 min added to 150 mL of brine. Extraction (ether and $CHCl_3$), washing (dilute HOAc and water), drying, and evaporation afforded 153 mg (100%) of **16** as yellow crystals comprised of 88% of one component and 12% of a variety of other substances (GLC C, 190 °C). Recrystallization from ether afforded white platelets: mp 188–189 °C; IR ($CHCl_3$) 3600, 3460, 1700 (sh), 1670 cm^{-1}; UV max (95% EtOH) 228 nm (ε 9300); ^1H NMR ($CDCl_3$) τ 3.08 (dd, *J* = 10 and 6 Hz, 1 H), 3.80 (d, *J* = 10 Hz, 1 H), 5.85 (m, $W_{1/2}$ = 6 Hz, 1 H), 8.92 (s, 3 H), 9.08 (s, 3 H), 9.13 (s, 3 H); mass spectrum *m/e* 262 (2), 94 (100).

7α-Hydroxy-5α,8β,9β-podocarpan-12-one (18). A. Diimide Reduction of Hydroxy Enone 16. This procedure is based on one by Garbisch et al.[33] A solution of 148 mg (0.858 mmol) of $C_6H_5SO_2NHNH_2$ (Aldrich, mp 103.5–104.5 °C), 75 mg (0.28 mmol) of **16,** and 90 mg (0.89 mmol) of Et_3N in 1.2 mL of diglyme was sealed in an 8 × 20 cm tube and heated at 80 °C for 42 h. The contents of two such tubes were diluted with 150 mL of brine and extracted with $CHCl_3$ which was washed with 2% NaOH and water, dried, and evaporated. Dissolution in ether left 10 mg of insoluble material. Evaporation afforded 130 mg (86%) of yellow, semicrystalline material which appeared to be a mixture of **18** and its hemiketal tautomer **21,** the latter preponderant: IR ($CHCl_3$) 3600, 3490, 1700 cm^{-1} (w); ^1H NMR ($CDCl_3$) τ 5.87 (m, $W_{1/2}$ = 12 Hz, 1 H), 8.98 (s, 3 H), 9.13 (s, 3 H), 9.17 (s, 3 H). This material was used directly for preparation of **20.** Shortly after isolation GLC C (192 °C) showed a peak of 38% intensity corresponding to that of **18** from method B below. This component increased to 61% intensity and the 1700-cm^{-1} IR absorption increased substantially in the spectrum of a sample which remained in $CHCl_3$ for 1 day.

B. Catalytic Hydrogenation of Hydroxy Enone 16. Hydrogenation of **16** (120 mg, 0.45 mmol) over 15 mg of 5% Pd/Al_2O_3 in 4 mL of absolute EtOH at ca. 23 °C and 1 atm afforded 100 mg (85%) of **18** as a light yellow semisolid: IR ($CHCl_3$) 3600, 3450 (br), 1700, 1011 cm^{-1}; ^1H NMR ($CDCl_3$) τ 5.75 (m, $W_{1/2}$ = 6 Hz, 1 H), 8.95 (s, 3 H), 9.12 (s, 3 H), 9.17 (s, 3 H). GLC C (190 °C) showed 92% of one component which was identical by retention times and mixed sample GLC analysis with the major component in the 1-day chromatogram of the diimide reduction product.

C. Hydrolysis of Ketal 20. A solution of 40 mg (0.14 mmol) of chromatographed **20,** a colorless oil, and 10 mL of TsOH in 10 mL of THF and 10 mL of water was refluxed for 2 h, cooled, diluted with 20 mL of cold 2.5% $NaHCO_3$, and extracted with $CHCl_3$ which was washed with water, dried, and evaporated to afford **18** as 36 mg (98%) of a white oil: IR (film) 3460, 1710 cm^{-1}; ^1H NMR ($CDCl_3$) τ 5.75 (m, $W_{1/2}$ = 7 Hz, 1 H), 8.97 (s, 3 H), 9.12 (s, 3 H), 9.16 (s, 3 H). Precise spectral comparisons were hindered owing to difficulty in removing the last traces of THF without loss of **18** by volatilization, but within this limitation IR and ^1H NMR spectra compared well with those of the product from hydrogenation of **16.**

12β-Methoxy-7α,12α-epoxy-5α,8β,9β-podocarpane (20). A solution of 61 mg (0.23 mmol) of crude **21** and 50 mg (0.26 mmol) of TsOH in 7 mL of absolute MeOH and 4 mL of PhH containing some $MgSO_4$ was refluxed for 18 h, cooled, and partitioned between $CHCl_3$ and 5% $NaHCO_3$ which was extracted with $CHCl_3$, washed with water, dried, and evaporated to afford 56 mg (87%) of **20** as an orange semisolid with IR and ^1H NMR spectra nearly identical with those of the

purified product. Chromatography on Al_2O_3 and elution with 5% ether in pentane afforded 16 mg (25%)[41] of **20** as a colorless oil: IR ($CHCl_3$) 1460, 1262, 1098, 1008 cm^{-1}; ^1H NMR ($CDCl_3$) τ 5.78 (m, $W_{1/2}$ = 7 Hz, 1 H), 6.65 (s, 3 H), 9.02 (s, 3 H), 9.12 (s, 3 H), 9.17 (s, 3 H); mass spectrum *m/e* 278 (100), 263 (41), 246 (38). GLC B, programmed from 175 to 200 °C, showed this material to be homogeneous.

10-Carbethoxy-4,4-dimethyl-8-methoxymethylene-9α-(2'-oxo-4'-methylpentyl)-5α-decalone-7 (24). A mixture of 60 mg (ca. 0.1 mmol) of **23** (a 3:2 mixture of isomers as an oil, contaminated with ca. 25% of the dimethyl acetal of **2c**[1a]), 1 drop of pyridine, and 10 mg of 30% Pd/C in 20 mL of EtOAc was hydrogenated at 1 atm and ca. 23 °C for 20 min and filtered with Celite, and the catalyst was thoroughly washed with EtOAc. Concentration in vacuo provided 42 mg (85%) of colorless oil which crystallized from petroleum ether. Recrystallization from petroleum ether–ethyl acetate afforded pure **24** as white needles: IR ($CHCl_3$) 1715, 1675, 1590 cm^{-1}; ^1H NMR ($CDCl_3$) τ 2.83 (d, J = 1 Hz, 1 H), 5.92 (q, J = 7 Hz, 2 H), 6.25 (s, 3 H), 8.80 (t, J = 7 Hz, 3 H), 9.10 (d, J = 7 Hz, 6 H), 9.12 (s, 3 H), 9.22 (s, 3 H). The intended analytical sample decomposed before a melting point or analysis was obtained, but the ^1H NMR spectrum showed no evidence of contamination or of the presence of more than one isomer.

Registry No.—**2a,** 56666-27-4; **3g** isomer a, 62461-79-4; **3g** isomer b, 62461-80-7; **6a,** 62461-81-8; **6b,** 56781-34-1; **6c,** 57636-84-7; **6d,** 62475-60-9; **6e,** 62461-82-9; **6f,** 62461-83-0; **6g,** 62504-26-1; **6h,** 62461-84-1; **6i,** 62461-85-2; **6j,** 62461-86-3; **8k,** 62461-87-4; **8m,** 62461-88-5; **8n,** 62461-89-6; **8o,** 62461-90-9; **15** isomer a, 62461-91-0; **15** isomer b, 62532-42-7; **15** isomer c, 62532-43-8; **15** isomer d, 62532-44-9; **16,** 62461-92-1; **17,** 62461-93-2; **18,** 62461-94-3; **19,** 62461-95-4; **20,** 62461-96-5; **21,** 62461-97-6; **22,** 62461-98-7; **23** isomer a, 57594-03-3; **23** isomer b, 57594-04-4; **24,** 62461-99-8; *tert*-butyl acetoacetate, 1694-31-1.

Supplementary Material Available. An appendix containing a table of pertinent NMR parameters for all 14 enediones (**6a–j** and **8k–o**), a table of the calculated dihedral angles and coupling constants for all 11 of the enedione conformations which were subjected to Karplus analysis, a figure showing 220-MHz spectra of **6c** which were analyzed, and a description of the details of analysis of the spectra of **6c** and the comparison of its coupling constants with the calculated ones (6 pages). Ordering information is given on any current masthead page.

References and Notes

(1) (a) Part 8: W. L. Meyer, R. A. Manning, E. Schindler, R. S. Schroder, and D. C. Shew, *J. Org. Chem.*, **41,** 1005 (1976). (b) Abstracted in part from Ph.D. Dissertations of R.A.M. and D.C.S. and the M.S. Thesis of P.G.S., University of Arkansas, 1971, 1969, and 1968, respectively. (c) Supported in part by Research Grant AM-10123 from the National Institute for 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. (d) Presented in part at the Midwest Regional Meeting of the American Chemical Society, Kansas City, Mo., Oct 21, 1969.

(2) For convenience all bicyclic and tricyclic derivatives in this paper will be numbered by the steroid–terpenoid convention as in **1** and **6,** with the *gem*-disubstituted ring of decalins being ring A. C-18 is the carbon of R^4 which is attached to C-13. The configurational notations α and β denote a trans or cis relation 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.

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

(4) W. L. Meyer, G. B. Clemans, and R. W. Huffman, *Tetrahedron Lett.,* 4255 (1966).

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

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(7) W. L. Meyer and E. Schindler, *Tetrahedron Lett.,* 4261 (1966).

(8) D. C. Shew and W. L. Meyer, *Tetrahedron Lett.,* 2963 (1968).

(9) A. W. McCollum, Ph.D. Dissertation, University of Arkansas, 1970.

(10) Corresponding hydroxy diketones have been isolated in an analogous bicyclic system.[11c]

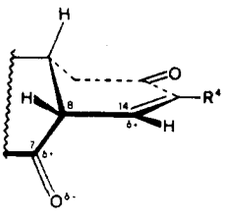
(11) Ph.D. Dissertations of (a) C. W. Sigel, Indiana University, 1967 (**6h, 6l**); (b) R. J. Hoff, University of Arkansas, 1972 (**6j**); (c) T. E. Goodwin, University of Arkansas, 1974 (**8k–o**); (d) Unpublished research of R. R. Frame (**8k**).

(12) We have usually conducted such cyclizations in glacial HOAc, with TsOH concentrations ranging from 0.001 to 0.02 M and molar ratios of TsOH:adduct between 0.03 and 0.4. However, in the particular case of **3g,** cyclization in benzene with a much higher acid:adduct ratio, as described in the Experimental Section, improved the yield substantially. This has not always been true with other adducts, and in general one must optimize concentrations, reaction time, and perhaps solvent for each individual adduct to be cyclized.

(13) ^1H NMR spectra of the enediones clearly exclude the possibility that the C-ring double bond migrates to 8,9 or 9,11 under the acidic cyclization conditions.[14]

(14) See paragraph at end of paper regarding supplementary material.

(15) Little weight can be placed on UV data for deduction of these structures, because enediones **6** (but not **8**) do not absorb in accord with the Woodward rules[16] (231 ± 1 nm observed for **6a–d** and 215 ± 4 nm for **6g–h**). It seems unlikely that these hypsochromic shifts of 6–16 nm result from nonplanarity of the enone system, which might be induced by the steric constraints of the trans-syn-cis backbone, because no such distortion is evident either from models or from the B- and C-ring proton spin couplings and because absorption of **16** is normal. The C-7 carbonyl group, C-8, and C-14 all lie nearly in a plane which is perpendicular to that of the enone system, so the 7-C=O dipole is well out of the enone plane and nearly coplanar with the C-14 p orbital (cf. I). This particular geometry may lead to a significant electrostatic interaction between the isolated C=O dipole and the β-carbon end of the enone's π and π^* orbitals which is reflected in the abnormal π–π^* transition.



I

(16) A. I. Scott, "Interpretation of the Ultraviolet Spectra of Natural Products", Macmillan, New York, N.Y., 1964, pp 57–58.

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

(18) Cf. L. M. Jackman and S. Sternhell, "Application of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry", 2nd ed, Pergamon Press, Oxford, 1969: (a) pp 316–328; (b) pp 281–294; (c) p 270; (d) pp 273–275.

(19) The broadening of this resonance is due to virtual coupling[20] of H-8 through H-9 to the 11-protons and to long-range coupling of H-8 and H-18 (ca. 1 Hz).

(20) J. I. Musher and E. J. Corey, *Tetrahedron,* **18,** 791 (1962).

(21) The isopropyl methine resonance is partially obscured by other resonances at 60 MHz, which made its location by double resonance preferable to inspection. It is clearly visible at 220 MHz, and shows the septet structure and allylic chemical shift which are required for **6c** but incompatible with **8c.**

(22) For substantiation of the trans A/B relative configuration in all of these compounds cf. ref 5, 6, and 11a and references cited therein.

(23) Cf. N. L. Allinger, J. Allinger, and M. A. DaRooge, *J. Am. Chem. Soc.,* **86,** 4061 (1964).

(24) Ring C in all of these $\Delta^{8,14}$ conformations also approaches a boat form, but not one which contains sp^3–sp^3 torsional strain, so this probably does not make a serious contribution to the destabilization of **8** relative to **6.**

(25) These are conformations to which the model will naturally return after moderate torsional distortion, in order to minimize mechanical bending strain. The models do not take torsional strain into account, of course, so actual minimum energy conformations of the molecule may well differ somewhat from the forms of these models, particularly with respect to their dihedral angles. We feel that errors from this source have been adequately taken into account in estimating the acceptable ranges for agreement between calculated and experimental coupling constants.[14]

(26) R. J. Abraham and J. S. E. Holker, *J. Chem. Soc.,* 806 (1963).

(27) The 220-MHz spectra were provided by Professor Norman Bhacca of Louisiana State University, to whom we are grateful.

(28) Cf. W. S. Johnson, *Experientia,* **7,** 315 (1951); *J. Am. Chem. Soc.,* **75,** 1498 (1953).

(29) The relative magnitudes of $J_{6\alpha,6\beta}$ and $J_{11\alpha,11\beta}$ also favors trans-syn-cis conformer **12.** Consideration of the geometric relationship between the carbonyl π orbital and the α-methylene protons predicts that for **12** $J_{11\alpha,11\beta}$ should be ca. 2 Hz more negative than $J_{8\alpha,8\beta}$, as observed, whereas for the trans-anti-cis structure $J_{8\alpha,8\beta}$ should be more negative than $J_{11\alpha,11\beta}$ by about 2 Hz; cf. ref 18d.

(30) Cf. H. O. House, "Modern Synthetic Reactions", 2nd ed, W. A. Benjamin, Menlo Park, Calif., 1972: (a) pp 89–96 and references cited therein; (b) pp 54–55 and references cited therein; (c) pp 59–65 and references cited therin.

(31) J. N. Gardner, B. A. Anderson, and E. P. Oliveto, *J. Org. Chem.,* **34,** 107 (1969).

(32) If this 6-Hz resonance were accepted as unequivocal evidence for the α-orientation of the 7-hydroxyl in **16,** conversion of **16** to an intramolecular ketal would establish 9,10-syn structures for these compounds without requiring further evidence for the configuration of the ketal. To form an intramolecular ketal a 9,10-anti substance would require a 7β hydroxyl group.

(33) E. W. Garbisch, Jr., S. M. Schilderout, D. B. Patterson, and D. M. Sprecher, *J. Am. Chem. Soc.,* **87,** 2932 (1965).

(34) Reports that conjugated enones are reduced very inefficiently by diimide[33,35] suggest that processes other than direct reduction of **16** should not be disregarded for this reaction. Alternative possibilities include (a) preliminary base-catalyzed (Et_3N) isomerization of **16** to its $\Delta^{8,14}$ isomer and reduction of the latter, and (b) preliminary tautomerization of **16** to an intramolecular hemiketal which undergoes reduction. By either path diimide could attack an unconjugated olefin. However, not all conjugated enones resist diimide; cf. R. Tschesche, M. Baumgarth, and P. Welzel, *Tetrahedron,* **24,** 5169 (1968), and particularly A. R. Stein, *Can. J. Chem.,* **43,** 1508 (1965).

(35) E. E. van Tamelen, M. Davis, and M. F. Deem, *Chem. Commun.,* 71 (1965); J. J. Looker, *J. Org. Chem.,* **32,** 472 (1967).

(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]

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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.

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-