# Experiments Directed toward the Total Synthesis of Terpenes. XVIII. The Convergent, Stereoselective Total Synthesis of the Unsymmetrical Pentacyclic Triterpene Alnusenone[1]

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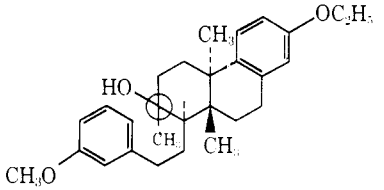
**Abstract:** A convergent synthetic scheme is outlined for the synthesis of the pentacyclic trans-anti-cis diether **13** and the isomer trans-anti-trans diether **2**. A key stage in this process is the aluminum alkyl catalyzed conjugate addition of hydrogen cyanide to the enone **6** which serves as a common precursor to both pentacyclic isomers. The structure and stereochemistry of the two isomer diethers **13** and **2** were determined by single crystal X-ray structural analysis. Subsequent transformations of the diether **2** allowed the completion of the total synthesis of the pentacyclic triterpene alnusenone in its racemic form.

Previous reports[4] in this series have delineated a plan for the total synthesis of *dl*-alnusenone (**3**)-type pentacyclic triterpenes in which the diether **2** was envisaged as the key synthetic intermediate. Evidence[5] from a model study on tetracyclic analogs suggested that the stereochemical outcome of the Friedel–Crafts cyclialkylation reaction of the tricyclic diether **1** would be predominantly the generation of the desired trans-fused system **2**. In order to implement these latter findings for the alnusenone synthesis itself, construction of the intermediate phenanthrene derivative **1** (or a functionally similar equivalent[5]) was of foremost concern. The efficient and stereoselective convergent scheme (Chart I) developed for this purpose has as its central feature the utilization of the elegant Nagata procedure[6] for the hydrocyanation of $\alpha,\beta$-unsaturated ketones in the formation of the previously troublesome[4,7] trans-fused C/D ring system with its two angular methyl groups.

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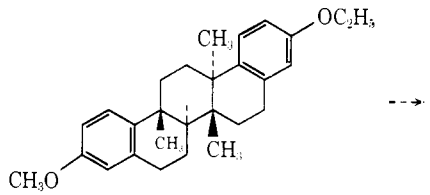


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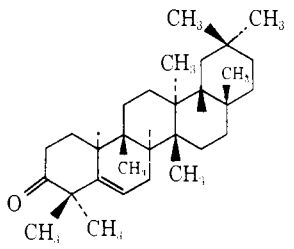


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The starting point for this investigation was the tricyclic enone **6**, which was conveniently prepared from the known[8] vinyl ketone **4** and the $\beta$-tetralone derivative **5** in the manner similar to that previously described[4] for the dimethoxylated analog. The use here of the methoxy, ethoxy derivative **6** foreshadows the eventually necessary differentiation of the two aromatic rings in the diether **2**. The hydrocyanation of this enone **6** was first carried out with the preformed diethylaluminum cyanide reagent[6c] in benzene solution (Table I). This process resulted in the nearly quantitative conversion of the enone **6** to three saturated cyano ketones. Two of these products were shown to be epimers about the C-1[9] side chain adjacent to the

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(2) Postdoctoral Fellow (5F02A135418) of the National Institute of Allergy and Infectious Diseases, 1968–1970.

(3) Trainee of the Public Health Service, National Institute of General Medical Sciences.

(4) R. E. Ireland, D. A. Evans, D. Glover, G. M. Rubottom, and H. Young, *J. Org. Chem.*, **34**, 3717 (1969).

(5) R. E. Ireland, S. W. Baldwin, and S. C. Welch, *J. Amer. Chem. Soc.*, **94**, 2056 (1972).

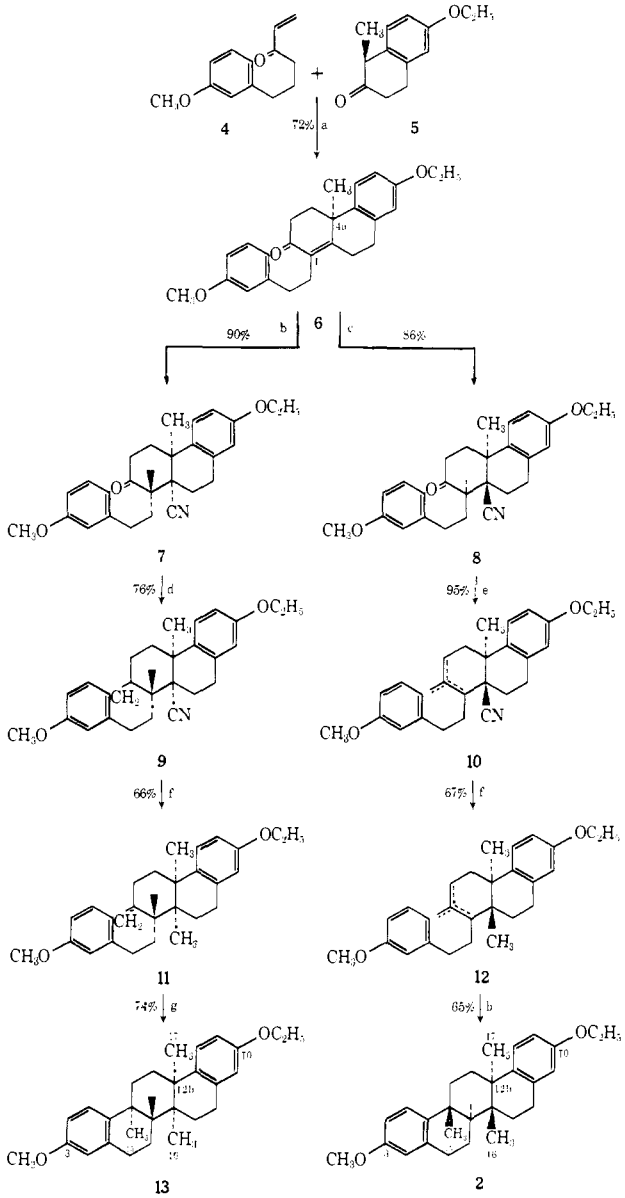
(6) (a) W. Nagata, M. Yoshioka, and S. Hirai, *J. Amer. Chem. Soc.*, **94**, 4635 (1972); W. Nagata, M. Yoshioka, and M. Murakami, *ibid.*, **94**, 4654 (1972); (b) W. Nagata, M. Yoshioka, and T. Terasawa, *ibid.*, **94**, 4672 (1972); (c) W. Nagata and M. Yoshioka, *Org. Syn.*, **52**, 90 (1972); (d) *ibid.*, **52**, 100 (1972).

(7) For other methods, see R. E. Ireland, M. I. Dawson, J. Bordner, and R. E. Dickerson, *J. Amer. Chem. Soc.*, **92**, 2568 (1970); R. E. Ireland, D. R. Marshall, and J. W. Tilley, *ibid.*, **92**, 4754 (1970).

(8) G. H. Douglas, J. M. H. Graves, D. Hartley, G. A. Hughes, B. J. McLoughlin, J. Siddall, and H. Smith, *J. Chem. Soc.*, 5072 (1963).

(9) The structural formulas containing one or more asymmetric carbon atoms depict one enantiomer but refer to racemic compounds throughout. In the text the (±) prefix will be omitted and intermediates are to be assumed to be racemic. In this discussion, phenanthrene nomenclature and numbering will be used to describe tricyclic compounds, and each racemate is arbitrarily represented by that enantiomer that has the C-4a methyl group in the $\alpha$ configuration. The pentacyclic compounds will be described by the picene nomenclature and numbering [A. M. Patterson, L. T. Capell, and D. F. Walker, "The Ring Index," 2nd ed, American Chemical Society, Washington, D. C., 1960, No. 6384], and each racemate is arbitrarily represented by that enantiomer that has the C-12b methyl group in the $\alpha$ configuration. In discussions where naturally occurring triterpenes are involved, the nomenclature and numbering suggested by S. Allard and G. Ourisson [*Tetrahedron*, **1**, 277 (1957)] will be used as necessary.

**Chart I.** Synthesis of Octahydropicenes **13** and **2**[a]



[a] a, aqueous KOH, $CH_3OH$; b, $(C_2H_5)_2AlCN$, $C_6H_6$; KO-*t*-Bu, *t*-BuOH, $C_6H_6$; c, $(C_2H_5)_3Al$, HCN, THF (recycle *cis*-cyano ketone by dehydrocyanation with base); d, $(C_6H_5)_3P{=}CH_2$, $C_6H_6$; e, $CH_3MgI$; $SOCl_2$, pyridine; f, $(i\text{-Bu})_2AlH$, $C_6H_6$; $N_2H_4\cdot 2HCl$, $N_2H_4\cdot H_2O$, TEG, KOH; g, PPA, 60°, 1.5 hr; h, $p\text{-}CH_3C_6H_4SO_3H$, $C_6H_6$.

ketone function through base-catalyzed epimerization of one isomer to the other. While Nagata has shown[6b] that hydrocyanation under these conditions results in the preponderant formation of the thermodynamically more stable cyano ketone isomer, it was not readily apparent in this system whether this represented the *cis*-**7** or the *trans*-**8** stereoisomer. Convincing evidence on which to base the stereochemical assignments of the two base stable isomers was not readily available from their rather complex infrared and nmr spectra. Hence the predominant isomer, formed in 90% yield, was used to investigate the further transformations necessary for the formation of a pentacyclic structure. This latter stage seemed a more propitious one for detailed structural analysis.

The cyano ketone was therefore converted (Chart I) into the corresponding cyano olefin with methylenetriphenylphorane for the twofold purpose of protection of the C-2[9] functionality during reduction of the cyano group and introduction of the potential C-12b[9] angular methyl group. Conversion of the cyano to the methyl group was accomplished through first hydride reduction to the aldimine and then application of the Nagata modification[10] of the Wolff–Kishner reduction. The resulting dimethyl olefin was readily converted to the desired pentacyclic system on mild treatment with poly(phosphoric acid). The stereochemical outcome of these useful and efficient transformations that can generate the desired pentacyclic structure in an overall 26% yield from β-tetralone **5** was settled by single crystal X-ray structural analysis of the diether **13** (Figure 1).

Since this product was shown to be the undesired trans-anti-cis stereoisomer **13**, the tricyclic precursors must then be *cis*-dimethyl olefin **11**, the *cis*-cyano olefin **9**, and the *cis*-cyano ketone **7**. The stereochemistry about the saturated ring fusion of these intermediates is a direct result of the hydrocyanation reaction, and the formation of these cis-fused systems under thermodynamically controlled conditions[6b] $[(C_2H_5)_2AlCN/C_6H_6]$ implies the greater stability of the cis-fused enolate over the corresponding trans isomer. This result would be difficult to predict *a priori* for such a system in which the two fused cycloalkane rings each contain two carbon atoms.

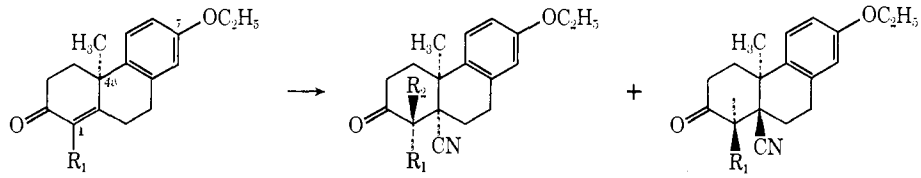
It is interesting to note that the trans-anti-cis diether **13** must arise from the anti-cis cation I (or its equivalent) and that the stereochemical outcome of the cyclization will be governed by the axial C-10a[9] methyl group, as previously described.[5] The virtually exclusive formation of this pentacyclic isomer precludes cyclization through alternate tertiary cations possible as a result of conformational mobility of the cis-fused tricyclic system and/or isomerization of the C-1[9] side chain under the acidic reaction conditions. Thus, cyclization through the other conformationally favorable syn-cis cation II would result[5] in the formation of the unobserved trans-syn-cis pentacyclic system. Reaction through cations that resemble either of the flipped conformations related to I or II in which the C-1[9] side chain must occupy an axial orientation is precluded by the lack of any evidence for the cis-anti-cis or cis-syn-cis products, respectively, that should result.

It seems reasonable also to propose that the dimethyl olefin precursor to the intermediate cation I has the anti-cis structure **11** and exists in a closely similar conformation. Were this dimethyl olefin better represented by the syn-cis structure **14**, related to cation II, it would be necessary to propose that acid-catalyzed isomerization of the system to the anti-cis-cation I and then cyclization was so much faster than direct cyclization through the syn-cis cation II that *none* of the trans-syn-cis pentacyclic was observed from the latter mode of reaction. This situation seems unlikely, since there is no apparent reason why the isomerization of the syn-cis cation II should be preferred before *any* trans-syn-cis pentacyclic products are formed through cyclization of this cation.

An interesting consequence of this analysis is that the structure and conformation of the reactive species during cyclization, and probably also for the dimethyl olefin **11**, that appears to be favored is the one (I) in which the aryl group of the tricyclic portion of the

(10) W. Nagata and H. Itazaki, *Chem. Ind.* (*London*), 1194 (1964).

Table I. Hydrogenation of Tricyclic Enones



| Enone | Reagent | Product ratio cis:trans | Products (% isolated yield) Cis (%) | Trans (%) |
|---|---|---|---|---|
| A,[a] $R_1$ = H | $Et_2AlCN$–$C_6H_6$, 1 hr | 2:1 | $R_1, R_2$ = H (57) | $R_1, R_2$ = H (27) |
| | $Et_3Al$–HCN–THF, 19 hr | 0.7:1 | $R_1, R_2$ = H (27) | $R_1, R_2$ = H (41) |
| B, $R_1$ = $CH_3$ | $Et_2AlCN$–$C_6H_6$, 1 hr | | $R_1$ = $CH_3$, $R_2$ = H (48)<br>$R_1$ = H, $R_2$ = $CH_2$ (27) | None observed |
| | $Et_3Al$–HCN–THF, 19 hr | 0.5:1 | $R_1$ = $CH_3$, $R_2$ = H (15)<br>$R_1$ = H, $R_2$ = $CH_3$ (10) | $R_1$ = $CH_3$ (50) |
| | $Et_2AlCN$–$C_6H_6$, 2 hr | 15:1 | $R_1$ = H, $R_2$ = *m*-$CH_3OC_6H_4(CH_2)_2$– (35)<br>$R_1$ = *m*-$CH_3OC_6H_4(CH_2)_2$–, $R_2$ = H (58) | $R_1$ = *m*-$CH_3OC_6H_4(CH_2)_2$– (6) |
| 6, $R_1$ = *m*-$CH_3OC_6H_4(CH_2)_2$– | $Et_3Al$–HCN–THF, 22 hr | 0.2:1 | $R_1$ = H, $R_2$ = *m*-$CH_3OC_6H_4(CH_2)_2$– (4)<br>$R_1$ = *m*-$CH_3OC_6H_4(CH_2)_2$–, $R_2$ = H (11) | $R_1$ = *m*-$CH_3OC_6H_4(CH_2)_2$– (72) |

[a] As the C-7 $OCH_3$ ether.

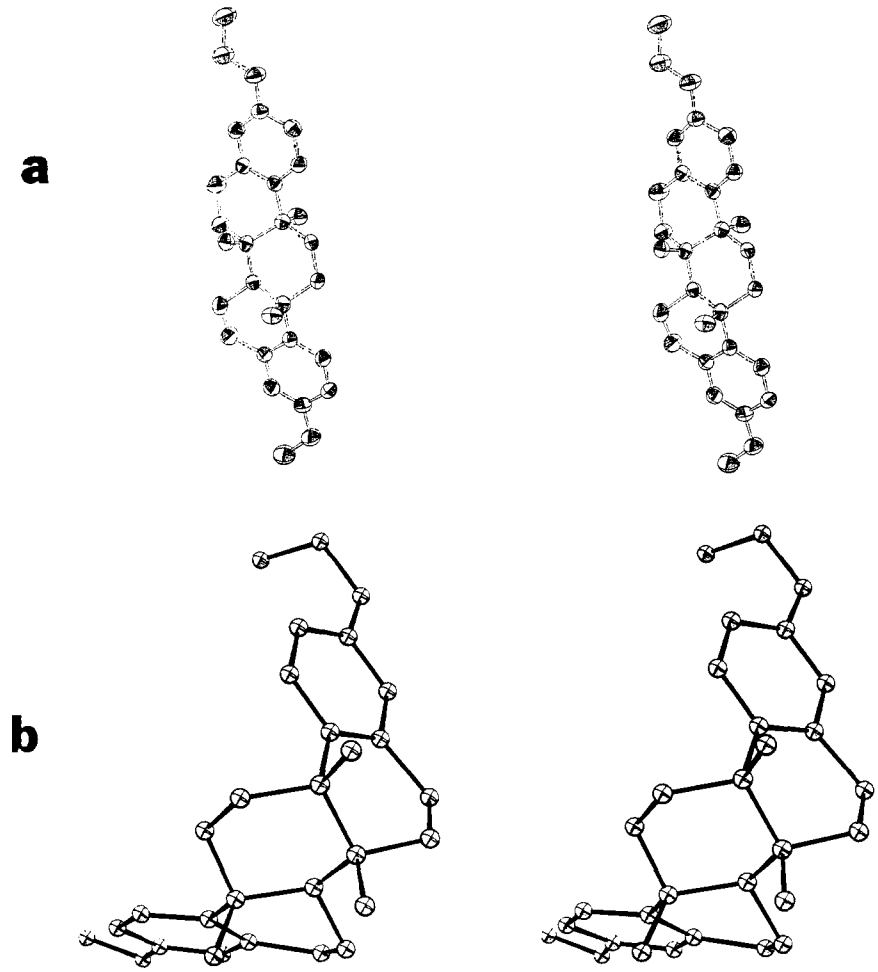
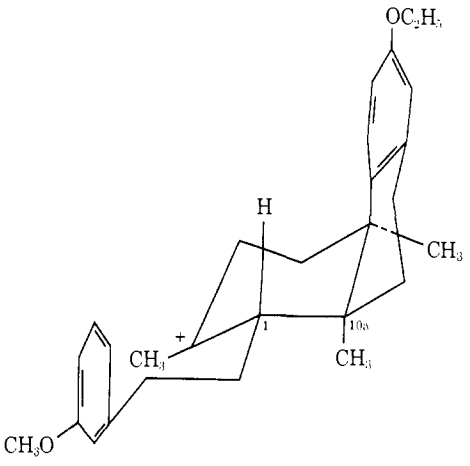



Figure 1. Stereoplots of the molecules: (a) trans-anti-cis diether **13**, (b) trans-anti-trans diether **2**.

molecule occupies an axial conformation. Since *both* angular positions are substituted by methyl groups, the principal difference between the structures represented by the conformations I and II is the orientation of the aryl portion of the tricyclic system. The preference for an axial aryl conformation probably reflects a significant difference in steric bulk between the trigonal aryl carbons and the tetrahedral methyl group.[11] It

(11) See, for instance, R. E. Ireland, P. S. Grand, R. E. Dickerson, J. Bordner, and D. Rydjeski, *J. Org. Chem.*, **35**, 570 (1970); B. L. Shapiro, M. J. Gattuso, N. F. Hepfinger, R. L. Shone, and W. L. White, *Tetrahedron Lett.*, 219 (1971).



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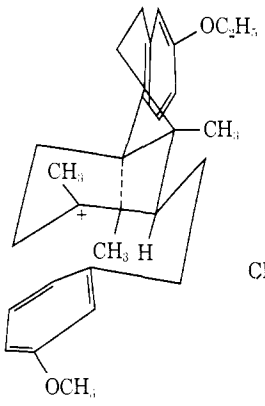

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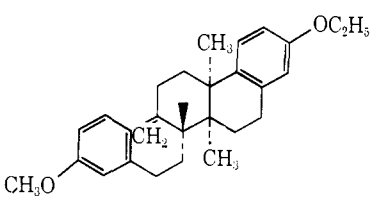

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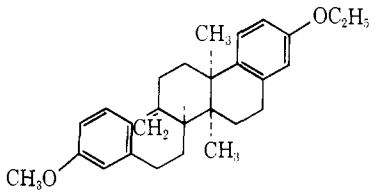

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seems reasonable then to propose that this preference will be manifest in the precursors of the dimethyl olefin **11** and that the cyano olefin **9** and the base stable cyano ketone **7** are best represented by structures with conformations similar to I. This same preference for a system in which the aryl group rather than the methyl group occupies the axial conformation may account for the formation of the *cis*-cyano ketone **7** during the thermodynamically controlled hydrocyanation reaction.

In view of the unfavorable stereochemical outcome that attended the thermodynamically controlled hydrocyanation conditions[6b,c] ($Et_2AlCN$–$C_6H_6$), we turned our attention to the kinetically controlled conditions[6b,d] ($Et_3Al$–HCN–THF) with the hope of increasing the proportion of trans-fused material formed. Model studies (Table I) on related tricyclic systems A and B proved quite promising when in each case a significant increase in the trans-fused isomer was observed when the kinetically controlled conditions were used. Confident determinations of the proportions of the isomers formed in these reactions at the crude product stage is a result of the spectral assignments made possible by the X-ray structure determination of the trans-anti-cis diether **13**. This allowed firm correlation between known stereochemistry and the nmr spectra of the two pentacyclic diethers **13** and **2**, as well as their respective precursors.

The result (Table I) of kinetically controlled hydrocyanation[6b,d] of the enone **6** was particularly gratifying and represents the most dramatic variation in stereochemical outcome between the two methods yet reported.[6a] From a practical synthetic standpoint the yield of the desired trans-fused cyano ketone **8** could be increased even more (Chart I) by recycling any *cis*-cyano ketone **7** formed through base elimination of hydrogen cyanide and rehydrocyanation of the resulting enone **6**.

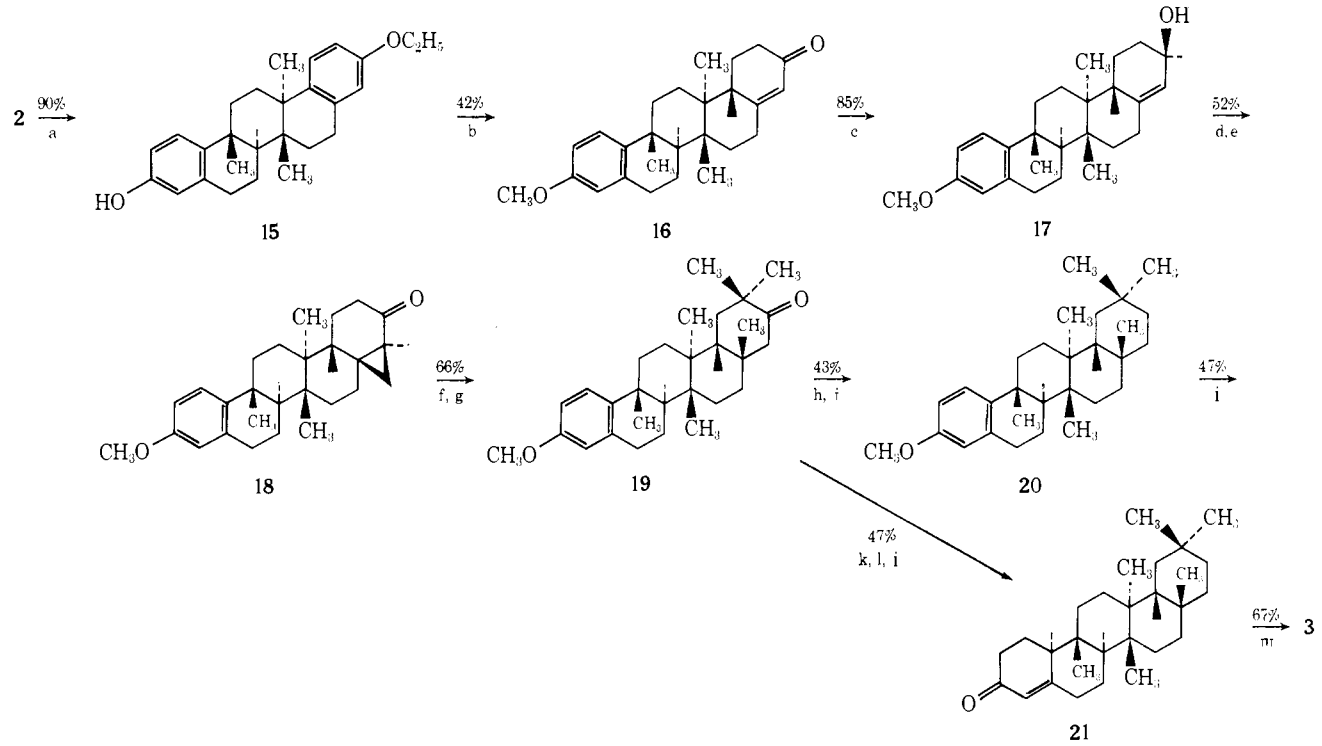
Interestingly, the *trans*-cyano ketone **8** did not react with methylenetriphenylphosphorane and was quantitatively recovered unchanged. Several different conditions were tried to effect this olefination with the same results or simply dehydrocyanation. The problem was overcome when it was found that methylmagnesium bromide added to the ketone group efficiently and selectively, and that the elimination of water from the resulting cyano alcohol led in high overall yield to the mixture of cyano olefins **10**. Since each component of the olefin mixture could be expected[5] to generate the same C-2[9] cation on protonation, this result was equally as satisfactory as the Wittig olefination to the exocyclic methylene would have been. Further conversion of this cyano olefin mixture **10** through the dimethyl olefin mixture **12** and thence to the long sought trans-anti-trans pentacyclic diether **2** was accomplished in a manner (Chart I) similar to that used in the trans-anti-cis series. Again, an efficient synthetic scheme was realized, and the key intermediate diether **2** was available from β-tetralone **5** in 25% overall yield. Single crystal X-ray structure analysis of the diether **2** confirmed the structure and stereochemistry inferred.[12]

Stereoscopic views of the diethers **2** and **13** are shown in Figure 1. In the trans-anti-cis diether **13**, the B and D rings exist in half-boat conformations while the same rings have half-chair conformations in the trans-anti- while the same rings have half-chair conformations in the trans-anti-trans diether **2**. Ring C is a chair in both compounds. The methyl–methyl repulsions in the trans-anti-cis diether **13** cause the molecule to be severely bent; thus, the dihedral angle between the planes of the terminal aromatic rings is 72° in diether **13** but only 6° in the trans-anti-trans isomer **2**. Methyl groups C(17) and C(16) are closely trans in this latter diether **2** (torsion angle = −168.2°), but deviate from cis in the trans-anti-cis isomer **13** by approximately 45°. Indeed, C(17) in this diether **13** is very nearly trans to the ring atoms C(14) and C(6a). Because the methyl hydrogens on C(17) and C(16) are so close in the trans-anti-cis diether **13**, they are seen to be staggered with respect to each other. However, the methyl hydrogens on carbons C(15) and C(16) are not staggered in the trans-anti-cis diether **13**, but these methyl hydrogens are staggered in the trans-anti-trans isomer **2**.

Both methoxy groupings are approximately coplanar with the adjacent benzene rings, but they are twisted in opposite directions in the two compounds. The terminal carbon atom C(19) of the ethoxy group is coplanar with the benzene ring in the trans-anti-trans di-

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

**Chart II.** Conversion of Diether **2** to *dl*-Alnusenone (**3**)[a]




[a] a, $LiPPh_2$, THF; b, Li, $NH_3$, glyme; evap. $NH_3$, add $CH_3I$; c, $LiAl(O\text{-}t\text{-}Bu)_3H$, THF–$C_6H_6$; d, $CH_2I_2$, Zn(Cu), DME–$Et_2O$; e, $CrO_3 2Py$, $CH_2Cl_2$; f, KO-*t*-Bu, THF, $CH_3I$; g, Li, $NH_3$, THF; $NH_4Cl$; h, $N_2H_4$, $N_2H_4 \cdot 2HCl$, TEG; i, KO-*t*-Bu, $C_6H_5CH_3$; 10% Pd–C, EtOH, $H_2$; j, Li, $NH_3$, THF–EtOH; $H_3O^+$; k, $LiAlH_4$, THF–$Et_2O$; l, *n*-BuLi, DME; HMPA–$NEt_3$, $ClPO(NMe_2)_2$; m, KO-*t*-Bu, *t*-BuOH, $CH_3I$.

ether **2**, but rotated out of plane in the trans-anti-cis isomer **13**.

The conversion of the long-sought trans-anti-trans diether **2** to *dl*-alnusenone (**3**) requires the differentiation of the two aromatic A and E rings before their reduction to saturated systems. This situation was anticipated when the present scheme was devised, and it was planned to carry out the first Birch reduction on an alkoxyphenol (Chart II). In this manner the ring bearing the alkoxy group could be expected to reduce to the desired dihydroaromatic system, while the hydroxy containing aromatic ring was unaffected[13] by virtue of the higher reduction potential of the derived phenoxide. In order to set the stage for this Birch reduction, it was necessary to incorporate the capability of selective ether cleavage into the diether **2**. Initial attempts[14] to do this through utilization of the benzyl group for the protection of one of the two phenolic systems were very discouraging. As molecular size grew through the early stages of the synthesis, the materials became more and more insoluble in common organic solvents, and intermediates appeared sensitive to light induced air oxidation of the benzyloxy grouping. To avoid these problems and still retain the potential if selective ether cleavage, the elegant and efficient method of Mann[15] was studied. Preliminary investigations[14] showed that use of the slightly modified procedure described herein provided consistent, high yields of selective methoxy group cleavage in the presence of ethoxy aromatic systems, even when a fourfold excess of the lithium diphenylphosphide reagent was present. These results allowed the replacement of the large and sensitive benzyl blocking group with the simple ethyl group. The resulting diether **2** still retained the required potential for differentiation of the aromatic A and E rings. Thus, application of this ether cleavage procedure to the trans-anti-trans diether **2** was quite satisfying (Chart I) and the ethoxyphenol **15** became readily available.

Birch reduction of the ethoxyphenyl **15** was as selective as expected, and after remethylation of the A ring phenoxide ion and then acid cleavage of the dihydroaromatic E ring, the pentacyclic enone **16** was obtained. Extensive experimentation was undertaken in order to increase the yield of this reduction–remethylation step, but no significant improvement was realized. The principal factor that appears to be responsible for both erratic results and low yields is the low solubility of the pentacyclic phenoxide in the ammonia–cosolvent reaction medium. There was no relief from this situation when ethylamine or various other cosolvents were employed.

Having established the desired partial reduction of the pentacyclic diether **2** our attention was turned to the transformation of the cyclohexenone E ring to the necessary methyl substituted, cis-fused D/E ring system. It was rapidly ascertained that the addition of lithium dimethyl cuprate[16] to this enone system was of no synthetic value. The only result observed on treatment of the enone **16** with this reagent was the decon-

(13) For another example of such selectivity during the Birch reduction, see J. Fried and N. A. Abraham, *Tetrahedron Lett.*, 3505 (1965); J. Fried, N. A. Abraham, and T. S. Santhanakrisknan, *J. Amer. Chem. Soc.*, **89**, 1044 (1967).

(14) J. Bolen, unpublished work in these laboratories.

(15) F. G. Mann and M. J. Pragnell, *Chem. Ind. (London)*, 1386 (1964).

(16) J. A. Marshall, W. I. Fanta, and H. Roebke, *J. Org. Chem.*, **31**, 1016 (1966).

jugation of the double bond, probably through enolation and then $\alpha$ protonation on work-up. The apparent reason for this disappointing observation is the axial, angular methyl group at C-12b[9] which hinders reaction on either face of the enone molecule.

An effective reaction sequence was then developed which utilized the equatorial C-10[9] hydroxyl function of the alcohol **17** to direct Simmons–Smith methylenation[17] in the desired $\beta$-stereochemical sense. The cyclopropyl group in the ketone **18** that results from oxidation of the intermediate cyclopropyl alcohol serves not only as the latent angular C-8a[9] methyl group but also to reduce the likelihood of enolization of the C-10 carbonyl toward the C-9 position. Thus direct methylation of the ketone **18** under standard conditions proved a very efficient means for the introduction of the C-11 geminal dimethyl groups. Reduction[18] of the intermediate methylated cyclopropyl ketone with lithium in ammonia–tetrahydrofuran produced the ketone **19** with the substitution and stereochemistry required of the D/E ring system.

The ketone **19** proved very stubborn toward reduction under even vigorous Wolff–Kishner conditions. Even after much experimentation and modification of these reduction conditions, the pentacyclic ether **20** could only be obtained in 32% yield by this procedure.

A more efficient method for the removal of the apparently hindered carbonyl group in the ketone **20** was found through the lithiumethylamine reduction of the TMPDA derivative,[19] prepared by phosphorodiamidation of the alcohol mixture obtained by hydride reduction. This sequence, while still not ideal, resulted in both the reductive removal of the TMPDA grouping and the reduction of the aromatic A ring. On aqueous acid hydrolysis of the intermediate dihydroaromatic system the $\alpha,\beta$-unsaturated ketone **21** was obtained in 47% overall yield. The conclusion of this synthetic scheme was foreshadowed in earlier work[20] in these laboratories on the total synthesis of *dl*-rimuene. The A ring substitution and functionality pattern of this diterpenoid hydrocarbon is similar to that of *dl*-alnusenone (**3**), and the methods developed in that investigation were found to be applicable as well to the present system. Thus Birch reduction of the aromatic A ring and then methylation of the resulting enone **21** provided the first samples of the racemic pentacyclic triterpene **3**. This material was judged to be identical with a sample of the naturally derived substance which was kindly provided by Professor Robert Stevenson through comparison of their nmr and solution ir spectra and mobility on thin-layer and vapor phase chromatography.

The demonstration of the viability of this synthetic scheme for the synthesis of pentacyclic systems of the alnusenone type provides the basis for schemes directed toward the synthesis of the slightly more complex triterpene friedelin, and the investigation of backbone rearrangements of pentacyclic derivatives that might lead to the amyrin classes of triterpenoids. These objectives are actively being sought.

(17) H. E. Simmons and R. D. Smith, *J. Amer. Chem. Soc.*, **80**, 5323 (1958); **81**, 4256 (1959).
(18) W. G. Dauben and E. J. Deviny, *J. Org. Chem.*, **31**, 3794 (1966).
(19) R. E. Ireland, D. C. Muchmore, and U. Hengartner, *J. Amer. Chem. Soc.*, **94**, 5098 (1972).
(20) R. E. Ireland and L. N. Mander, *J. Org. Chem.*, **32**, 689 (1967).

## Experimental Section[21]

**6-Ethoxy-1-methyl-3,4-dihydronaphthalene.** Methylmagnesium iodide was prepared by the slow addition of 40.6 ml (0.65 mol) of methyl iodide in 14.8 g (0.61 g-atom) of magnesium in 640 ml of anhydrous ether under dry nitrogen. After completion of the addition the solution was allowed to stir at room temperature for 30 min, and then 53.4 g (0.281 mol) of 6-ethoxy-1-tetralone in 225 ml of dry benzene was added dropwise with stirring. The resulting gray solution was allowed to stir at room temperature for 1 hr, and then the reaction mixture was poured into ice and aqueous ammonium chloride solution. The aqueous layer was separated and extracted with ether (3 × 500 ml). The combined organic layers were washed with 5% aqueous hydrochloric acid (50 ml) and saturated aqueous sodium chloride solution (3 × 500 ml), dried ($Na_2SO_4$), and concentrated at reduced pressure to give an orange liquid. Distillation gave 48.3 g (91%) of 6-ethoxy-1-methyl-3,4-dihydronaphthalene as a colorless liquid, bp 85–92° (0.15 mm). The analytical sample was prepared by distillation: bp 76.0–76.5° (0.10 mm); ir (film) 3020, 1605, 1565, 1495 (ArH), 1640 (>C=C<) and 1245, 1035 $cm^{-1}$ (EtOAr); nmr ($CDCl_3$) $\delta$ 6.44–7.13 (m, 3, ArH), 5.46–5.73 (m, 1, vinylic H), 3.91 (q, 2, $J$ = 7 Hz, $OCH_2CH_3$), 1.94 (d, 3, $J$ = 1.5 Hz, $CH_3C$=CH), and 1.32 (t, 3, $J$ = 7 Hz, $OCH_2CH_3$).

*Anal.* Calcd for $C_{13}H_{16}O$: C, 82.94; H, 8.57. Found: C, 82.86; H, 8.54.

**6-Ethoxy-1-methyl-2-tetralone (5).** An ethereal solution of 735 ml (0.274 mol, 0.373 *M* solution) of freshly prepared and standardized monoperphthalic acid was added to a stirred solution of 48.3 g (0.256 mol) of 6-ethoxy-1-methyl-3,4-dihydronaphthalene in 400 ml of anhydrous ether at 5° (internal temperature) with stirring under nitrogen. The addition was performed at such a rate as to maintain an internal temperature of 5 ± 1°. After the addition, the mixture was allowed to stir at 5° for 3 hr, then 340 ml of 40% aqueous sulfuric acid was added, and the resulting pink two-phase mixture was allowed to stir at room temperature under nitrogen for 40 hr.

The pink mixture was separated, and the lower layer was extracted with ether (5 × 250 ml). The combined organic solutions were washed with saturated aqueous sodium bicarbonate solution (4 × 100 ml) and saturated aqueous sodium chloride solution (4 × 100 ml), dried ($Na_2SO_4$), and concentrated at reduced pressure to give an orange liquid. Distillation gave 40.9 g (76%) of 6-ethoxy-1-methyl-2-tetralone (**5**) as a colorless liquid which crystallized in the refrigerator, bp 123–130° (0.25 mm); mp 30–31°. The analytical sample was prepared by distillation: bp 106.5–108° (0.22 mm); ir (film) 3020, 1610, 1575, 1495 (aromatic), 1710 (C=O), and 1255, 1035 $cm^{-1}$ (EtOAr); nmr ($CDCl_3$) $\delta$ 6.51–7.19 (m, 3, aromatic), 3.94 (q, 2, $J$ = 7 Hz, $OCH_2CH_3$), 3.37 (q, 1, $J$ = 7 Hz, $CH_3CHC$=O), 1.38 (d, 3, $J$ = 7 Hz, $CH_3CHC$=O), and 1.34 (t, 3 $J$ = 7 Hz, $OCH_2CH_3$).

*Anal.* Calcd for $C_{13}H_{16}O_2$: C, 76.44; H, 7.90. Found: C, 76.45; H, 7.91.

**7-Ethoxy-1-(2′-*m*-methoxyphenylethyl)-4a$\alpha$-methyl-3,4,4a,9,10-pentahydro-2(3*H*)-phenanthrone (6).** A solution of potassium hydroxide (3.96 g, 59.9 mmol) in distilled water (5.0 ml) and methanol (50 ml) was added slowly to a stirred solution of 6-ethoxy-1-methyl-2-tetralone (**5**) (10.6 g, 51.9 mmol) in methanol (90 ml) at 0° (ice bath) under nitrogen. The faintly yellow solution was allowed to stir at 0° (ice bath) for 30 min, then cooled to −15° (ice–methanol bath) and 10.5 g (51.5 mmol) of 6-(*m*-methoxyphenyl)-1-hexen-3-one (**4**) in 70 ml of methanol was added dropwise over a period of 15 min. The cooling bath was removed, and the reaction mixture was allowed to stir at room temperature for 16 hr.

The resulting orange solution was heated under reflux for 4 hr while the reaction was monitored by glpc using 6 ft × 1/8 in. stainless steel column packed with 4% SE-30 on Diatoport S 60–80 mesh. After cooling to room temperature the reaction mixture was poured into a mixture of water (300 ml) and benzene (300 ml). The mixture was acidified with 5% aqueous hydrochloric

(21) All melting and boiling points are uncorrected. Infrared (ir) spectra were measured with a Perkin-Elmer Model 237 B spectrometer and unless otherwise specified nuclear magnetic resonance (nmr) spectra were measured with a Varian Associates Model A60A or T60. All gas chromatographic analyses (glpc) were carried out on an F&M Model 810 gas chromatograph. Anhydrous solvents were dried immediately prior to use. Ether, benzene, tetrahydrofuran, and dimethoxyethane were distilled from lithium aluminum hydride; *tert*-butyl alcohol was distilled from calcium hydride. All microanalyses were performed by Spang Microanalytical Laboratory, Ann Arbor, Mich.

acid, and the aqueous layer was separated and extracted with benzene (4 × 300 ml). The combined organic solutions were washed with saturated aqueous sodium bicarbonate solution (150 ml) and saturated aqueous sodium chloride solution (3 × 150 ml), dried ($MgSO_4$) and concentrated at reduced pressure to give 19.6 g of an orange liquid. The product was purified by column chromatography over Woelm neutral alumina (1970 g, activity II) using a 6-cm diameter column. The crude product was placed on the column (packed in 5% ether–petroleum ether, bp 30–60°) with benzene (3 × 15 ml). The column was eluted as follows: 2 l. of 5% ether–petroleum ether, bp 30–60°; 6 l. of 10% ether–petroleum ether, of 30–60°; 4 l. of 15% ether–petroleum ether, bp 30–60°; 4 l. of 20% ether–petroleum ether, bp 30–60°; 9 l. of 30% ether–petroleum ether, bp 30–60°; and 50 × 500-ml fractions were collected. Fractions 33–50 were combined and gave 14.5 g (72%) of 7-ethoxy-1-(2′-*m*-methoxyphenylethyl)-4α-methyl-3,4,4a,9,10-pentahydro-2(3*H*)-phenanthrone (**6**) as a pale yellow liquid. The analytical sample was prepared by bulb-to-bulb distillation to give a colorless liquid: bp 193–195° (0.01 mm, external temperature); ir (film) 1665 (C=O), 1615, 1610, 1605, 1585, 1500, 1490 (aromatic), 1040, 2830 $cm^{-1}$ (ArOR); nmr ($CDCl_3$) δ 6.40–7.23 (m, 7, aromatic), 3.94 (q, 2, $J$ = 7 Hz, $OCH_2CH_3$), 3.69 (s, 3, $OCH_3$), 1.45 (s, 3, $\equiv CCH_3$), and 1.35 (2/3 of a t, 3, $J$ = 7 Hz, $OCH_2CH_3$).

*Anal.* Calcd for $C_{26}H_{30}O_3$: C, 79.97; H, 7.74. Found: C, 80.11; H, 7.82.

**Hydrocyanation of Enone 6 with Diethylaluminum Cyanide. A. Initial Product Mixture.** The enone **6** (3.68 g, 9.44 mmol) was dissolved in 50 ml of anhydrous benzene and stirred under dry nitrogen at room temperature while a solution of diethylaluminum cyanide[6c] in benzene (57.0 ml of a 0.591 $M$ solution, 44.4 mmol) was added over a period of 5 min. The resulting orange solution was allowed to stir at room temperature for 2 hr, then poured into ice-cold 5% aqueous sodium hydroxide solution (200 ml) and extracted with chloroform (8 × 100 ml). The combined organic extracts were washed with 10% aqueous sodium hydroxide solution (100 ml) and water (3 × 200 ml), dried ($Na_2SO_4$), and concentrated at reduced pressure to give 4.15 g of a pale yellow foam. The product was purified by column chromatography over 400 g of silica gel. The crude product was placed on the column (packed with 50% ether–petroleum ether, bp 30–60°) with benzene (3 × 3 ml). The column was eluted very slowly with 50% ether–petroleum ether, bp 30–60°, and 30 × 100-ml fractions were collected. Three compounds were obtained.

(1) ***cis*-Cyano ketone 7:** 2.28 g (58%); mp 135–140°. The analytical sample was prepared by recrystallization from ether–dichloromethane to give the pure *cis*-cyano ketone **7** as white crystals: mp 142–143°; ir ($CHCl_3$) 2230 (CN), 1720 (C=O), 1605, 1595, 1585, 1500 (aromatic), 1380, 1390 ($CH_3$), and 1040 $cm^{-1}$ (ArOR); nmr ($CDCl_3$) δ 6.30–7.26 (m, 7, aromatic), 3.95 (q, 2, $J$ = 7 Hz, $OCH_2CH_3$), 3.63 (s, 3, $OCH_3$), 1.38 (s, 3, $\equiv CCH_3$), and 1.38 (t, 3, $J$ = 7 Hz, $OCH_2CH_3$, coincident with the angular methyl group absorption).

*Anal.* Calcd for $C_{27}H_{31}O_3N$: C, 77.67; H, 7.48; N, 3.35. Found: C, 77.68; H, 7.56; N, 3.27.

(2) **1-*epi*-*cis*-Cyano ketone:** 1.35 g (35%); mp 106.5–108°. The analytical sample was prepared by recrystallization from ether–dichloromethane: mp 111.5–112.5°; ir ($CHCl_3$) 2220 (CN), 1720 (C=O), 1605, 1595, 1585, 1500 (aromatic), 1385 ($CH_3$), and 1040 $cm^{-1}$ (ArOR); nmr ($CDCl_3$) δ 6.42–7.31 (m, 7, aromatic), 3.93 (3/4 of a q, 2, $J$ = 7 Hz, $OCH_2CH_3$), 3.74 (s, 3, $OCH_3$), 1.84 (s, 3, $-CH_3$), 1.34 (t, 3, $J$ = 7 Hz, $OCH_2CH_3$).

*Anal.* Calcd for $C_{27}H_{31}O_3N$: C, 77.67; H, 7.48; N, 3.35. Found: C, 77.57; H, 7.46; N, 3.31.

(3) ***trans*-Cyano ketone 8:** 0.231 g (6%); mp 128.7–129.9°. The analytical sample was prepared by recrystallization from ether–dichloromethane: mp 131.7–132.7°; ir ($CHCl_3$) 2225 (CN, the extinction coefficient is significantly smaller than the above cis isomers), 1720 (C=O), 1605, 1595, 1585, 1500 (aromatic), 1380, 1390 ($CH_3$), and 1040 $cm^{-1}$ (ArOH); nmr ($CDCl_3$) δ 6.44–7.30 (m, 7, aromatic), 3.92 (3/4 of a q, 2, $J$ = 7 Hz, $OCH_3CH_3$), 3.72 (s, 3, $OCH_3$), 1.34 (t, 3, $J$ = 7 Hz, $OCH_2CH_3$), and 1.31 (s, 3, $\equiv CCH_3$).

*Anal.* Calcd for $C_{27}H_{31}O_3N$: C, 77.67; H, 7.48; N, 3.35. Found: C, 77.70; H, 7.48; N, 3.29.

**B. Optimized Conditions for the Formation of *cis*-Cyano Ketone 7.** The enone **6** (0.603 g, 1.54 mmol) was dissolved in 5 ml of anhydrous benzene and stirred under dry nitrogen at room temperature while a solution of diethylaluminum cyanide[6c] in benzene (5.0 ml of a 1.63 $M$ solution, 8.15 mmol) was added dropwise. The resulting orange solution was allowed to stir at room temperature for 2 hr, then poured into ice-cold 5% aqueous sodium hydroxide solution (20 ml) and extracted with chloroform (5 × 20 ml). The combined chloroform extracts were washed with 5% aqueous sodium hydroxide solution (10 ml) and water (3 × 10 ml), dried ($Na_2SO$), and concentrated at reduced pressure to give 0.640 g of the crude cyano ketones. This crude product was dissolved in 10 ml of anhydrous benzene and 5 ml of dry *tert*-butyl alcohol. The solution was stirred under dry nitrogen and 15 mg of potassium *tert*-butoxide was added. The resulting nitrogen and potassium *tert*-butoxide (0.015 g) was added. The resulting orange solution was allowed to stir at room temperature for 2 hr, and then poured into water (20 ml). The aqueous layer was separated and extracted with benzene (5 × 10 ml). The combined organic extracts were washed with water (5 × 25 ml) and saturated aqueous sodium chloride solution (25 ml), dried ($Na_2SO_4$), and concentrated at reduced pressure to give a pale yellow crystalline product. Recrystallization from ether–dichloromethane–hexane gave 0.581 g (90%) of *cis*-cyano ketone **7**, mp 138–140°. The nmr ($CDCl_3$) was identical with that of the *cis*-cyano ketone **7** isolated above.

**10aα-Cyano-7-ethoxy-1α-(2′-*m*-methoxyphenylethyl)-4aα-methyl-2-methylene-1β,3,4,4a,9,10,10a-heptahydrophenanthrene (9).** A slurry of triphenylmethylphosphonium bromide (0.401 g, 1.12 mmol) in anhydrous ether (20 ml) was stirred at 0° (ice bath) while a solution of phenyllithium (0.78 ml of a 2.0 $M$ solution in 70:30 benzene–ether, 1.56 mmol) was added. The resulting clear yellow solution was allowed to stir at 0° (ice bath) for 15 min, and then a solution of the *cis*-cyano ketone **6** (0.210 g, 0.503 mmol) in dry benzene–ether (9 ml: 4 ml, respectively) was added over a period of 10 min. The yellow slurry was allowed to stir at room temperature for 22 hr.

The crude mixture was taken up in methanol (25 ml) and water (25 ml), and the aqueous layer was separated and extracted with ether (3 × 25 ml). The combined organic solutions were washed with water (3 × 20 ml) and saturated aqueous sodium chloride solution (20 ml), dried ($Na_2SO_4$), and concentrated at reduced pressure to give 0.413 g of semicrystalline yellow liquid. Preparative thin-layer chromatography on silica gel in 40% ether–petroleum ether, bp 30–60°, gave 0.158 g (76%) of the methylene *cis*-cyano ketone **9** as a pale yellow liquid ($R_f$ 0.51) after a single development. The analytical sample was prepared by drying the chromatographed liquid at 60° and 0.05 mm for 72 hr; ir ($CHCl_3$) 2225 (CN), 1645, 900 (=$CH_2$), 1605, 1585, 1495 (aromatic), 1390, 1380 ($CH_3$), and 1040 $cm^{-1}$ (ArOR); nmr ($CDCl_3$) δ 6.34–7.30 (m, 7, aromatic), 4.98 (broad d, 2, $J$ = 9.5 Hz, =$CH_2$), 3.96 (q, 2, $J$ = 7 Hz, $OCH_2CH_3$), 3.64 (s, 3, $OCH_3$), 1.36 (t, 3, $J$ = 7 Hz, $OCH_2CH_3$), and 1.34 (s, 3, $\equiv CCH_3$).

*Anal.* Calcd for $C_{28}H_{33}O_2N$: C, 80.93; H, 8.00; N, 3.37. Found: C, 81.04; H, 8.00; N, 3.39.

**4aα,10aα-Dimethyl-7-ethoxy-1α-(2′-*m*-methoxyphenylethyl)-2-methylene-1β,3,4,4a,9,10,10a-heptahydrophenanthrene (11).** A solution of 146 mg (0.35 mmol) of the methylene cyano ketone **9** in 10 ml of anhydrous benzene was stirred under dry nitrogen at room temperature while a solution of diisobutylaluminum hydride in benzene (1.15 ml of a 0.34 $M$ solution, 0.388 mmol) was added dropwise. The resulting clear solution was allowed to stir under nitrogen at room temperature for 16 hr.

An additional 0.20 ml (0.068 mmol) of a 0.34 $M$ solution of diisobutylaluminum hydride in benzene was added and stirring was continued for 2 more hr. The reaction mixture was then poured into a mixture of 10% aqueous sodium hydroxide solution (10 ml) and ice (20 g). The aqueous layer was separated and extracted with ether (4 × 20 ml). The combined organic extracts were washed with water (3 × 20 ml) and saturated aqueous sodium chloride solution (20 ml), dried ($Na_2SO_4$), and concentrated at reduced pressure to give 0.150 g of a pale yellow liquid, the infrared spectrum ($CHCl_3$) of which showed no band due to the cyano group and a band at 1630 $cm^{-1}$ due to the imine function.

The crude imine was dissolved in triethylene glycol (10 ml) and 1.0 ml (~17.5 mmol) of hydrazine hydrate and 255 mg (1.43 mmol) of hydrazine dihydrochloride were added. This colorless solution was allowed to stir at 130–135° (internal temperature) under nitrogen for 3 hr and then cooled to <100°. Potassium hydroxide pellets (1.59 g, 24.0 mmol) were added in portions, and the temperature was then raised to 155–160° (internal temperature) while the low boiling material was removed in a stream of nitrogen over a period of 60 min. The reaction vessel was then sealed under nitrogen, and the temperature was maintained at 155–160° (internal) with stirring for 6 hr. After cooling the mixture was taken up in water (50 ml) and extracted with ether (5 × 20 ml). The combined ethereal extracts were washed with water (10 × 20 ml) and saturated

aqueous sodium chloride solution (20 ml), dried ($Na_2SO_4$), and concentrated at reduced pressure to give 0.126 g of a colorless liquid. Preparative thin-layer chromatography on silica gel in 10% ether–petroleum ether, bp 30–60°, gave 0.093 g (66%) of the dimethyl olefin **11** as a pale yellow liquid ($R_f$ 0.36) after a single development. The analytical sample was prepared by drying the chromatographed liquid at 60° and 0.05 mm for 72 hr: ir ($CHCl_3$) 3075, 885 (=$CH_2$), 1610, 1605, 1585, 1495 (aromatic), 1390, 1380, 1370 ($CH_3$), and 1040 $cm^{-1}$ (ArOR); nmr ($CDCl_3$) $\delta$ 6.34–7.33 (m, 7, aromatic), 4.76 (broad d, 2, $J \simeq 16$ Hz, =$CH_2$), 4.01 (q, 2, $J$ = 7 Hz, $OCH_2CH_3$), 3.69 (s, 3, $OCH_3$), 1.39 (t, 3, $J$ = 7 Hz, $OCH_2CH_3$), 1.06 (s, 3, ≡$CCH_3$), and 0.79 (s, 3, ≡$CCH_3$).

*Anal.* Calcd for $C_{23}H_{36}O_2$: C, 83.12; H, 8.97. Found: C, 83.09; H, 9.05.

**10-Ethoxy-3-methoxy-6bα,2bα,14aα-trimethyl-5,6,6aβ,6b,7,8,12b,-13,14,14a-decahydropicene (13).** Freshly prepared poly(phosphoric acid) (12 ml) was added to 93 mg (0.23 mmol) of the dimethyl olefin **11** at room temperature with mechaninal stirring. The solution was allowed to stir at 60° (bath temperature) under nitrogen for 1.5 hr. After cooling to room temperature the resulting pale yellow slurry was poured into ice (100 g) and extracted with ether (5 × 20 ml). The combined ethereal extracts were washed with saturated aqueous sodium bicarbonate solution (3 × 10 ml) and saturated aqueous sodium chloride solution (3 × 10 ml), dried ($Na_2SO_4$), and concentrated at reduced pressure to give 0.089 g of pale yellow liquid. Double elution preparative thin-layer chromatography on silica gel in 5% ether–petroleum ether, bp 30–60°, gave 0.069 g (74%) of pentacyclic diether **13** ($R_f$ 0.34) as white crystals, mp 148–150°. The analytical sample was prepared by recrystallization of a sample from ether–hexane and gave the pentacyclic diether **13** as white crystalline needles: mp 151–152°; ir ($CHCl_3$) 1610, 1580, 1495 (aromatic), 1390, 1385, 1375, ($CH_3$), 1040, 1035 $cm^{-1}$ (ArOR); nmr ($CDCl_3$) $\delta$ 6.37–7.34 (m, 6, aromatic), 3.92 (q, 2, $J$ = 7 Hz, $OCH_2CH_3$), 3.67 (s, 3, $OCH_3$), 1.31 (t, 3, $J$ = 7 Hz, $OCH_2CH_3$), 1.21 (s, 3, ≡$CCH_3$), 1.11 (s, 3, ≡$CCH_3$), and 1.00 (s, 3, ≡$CCH_3$).

*Anal.* Calcd for $C_{28}H_{36}O_2$: C, 83.12; H, 8.97. Found: C, 83.35; H, 9 12.

**Hydrocyanation of Tricyclic Enone A. I. With Triethylaluminum–Hydrogen Cyanide.** To 6.0 ml (4.18 mmol) of a 0.696 *M* solution of triethylaluminum in dry tetrahydrofuran under a nitrogen atmosphere at 0° was added 0.54 ml (3.14 mmol) of a 5.81 *M* solution of hydrogen cyanide in dry benzene.[6d] Immediately to this clear solution was added a solution of 2.46 mg (1.02 mmol) of the tricyclic enone A in 9 ml of dry tetrahydrofuran, and the resulting yellow solution was allowed to warm to room temperature with stirring. After stirring at room temperature for 19 hr, the reaction mixture was poured at 25 ml of chilled 5% aqueous sodium hydroxide solution, and the aqueous mixture was extracted with four 25-ml portions of ether. The combined ethereal extracts were washed with water (5 × 25 ml) and saturated aqueous sodium chloride solution (25 ml) and then dried ($Na_2SO_4$). Evaporation of this extract at reduced pressure gave 254 mg (93%) of a pale yellow semicrystalline solid: nmr ($CDCl_3$) $\delta$ 1.34 and 1.54 [2 × s (ratio 65:35) 3, ≡$CCH_3$], 3.75 (s, 3, $OCH_3$), and 6.56–7.41 (m, 3, ArH).

Quadruple elution preparative thin-layer chromatography of this crude product on a 20 × 20 × 0.2 cm silica gel plate in 40% ether–petroleum ether, bp 30–60°, gave

| | $R_f$ | mp, °C | Amount, mg (yield, %) |
|---|---|---|---|
| *trans*-cyano ketone | 0.30 | 165–166 | 111 (41) |
| *cis*-cyano ketone | 0.56 | 85–86.5 | 74 (27) |

The analytical sample of the *trans*-cyano ketone, obtained after three crystallizations from ether–methylene chloride, melted at 170–171°: ir ($CHCl_3$) 2225 (CN), 1720 (>C=O), 1610, 1575, and 1500 (ArH), 1380 (≡$CCH_3$), 1040, 1030 $cm^{-1}$ ($ArOCH_3$); nmr ($CDCl_3$) $\delta$ 1.35 (s, 3, ≡$CCH_3$), 3.76 (s, 3, $ArOCH_3$), and 6.65–7.34 (m, 3, ArH).

*Anal.* Calcd for $C_{17}H_{19}O_2N$: C, 75.81; H, 7.11; N, 5.20. Found: C, 75.64; H, 7.31; N, 5.10.

The analytical sample of the *cis*-cyano ketone, obtained after one crystallization from ether–hexane, melted at 86–87°: ir ($CHCl_3$) 2225 (CN), 1720 (>C=O), 1610, 1575, and 1500 (ArH), 1380 (≡$CCH_3$), 1030 $cm^{-1}$ ($ArOCH_3$); nmr ($CDCl_3$) $\delta$ 1.56 (s, 3, ≡$CCH_3$), 3.76 (s, 3, $ArOCH_3$), and 6.65–7.14 (m, 3, ArH).

*Anal.* Calcd for $C_{17}H_{19}O_2N$: C, 75.81; H, 7.11; N, 5.20. Found: C, 75.89; H, 7.10; N, 5.13.

**II. With Diethylaluminum Cyanide in Benzene.** To a solution of 294 mg (1.28 mmol) of the tricyclic enone A in 10 ml of dry benzene under a nitrogen atmosphere at room temperature was added with stirring 2.0 ml (3.4 mmol) of a 1.7 *M* solution of diethylaluminum cyanide[6c] in dry benzene, and the resulting solution was allowed to stir for 1 hr. The reaction mixture was worked up as described above and evaporation of the solvent at reduced pressure afforded 328 mg (100%) of a pale yellow oil: nmr ($CDCl_3$) $\delta$ 1.34 and 1.54 (2 × s (ratio 30:70), 3, ≡$CCH_3$), 3.76 (s, 3, $ArOCH_3$), and 6.56–7.34 (m, 3, ArH).

Quadruple elution preparative thin-layer chromatography of this crude product on a 20 × 40 × 0.2 cm silica gel plate in 50% ether–petroleum ether, bp 30–60°, gave

| | $R_f$ | mp, °C | Amount, mg (yield, %) |
|---|---|---|---|
| *trans*-cyano ketone | 0.30 | 163–164 | 88 (27) |
| *cis*-cyano ketone | 0.56 | 86–87 | 169 (52) |

**Hydrocyanation of Tricyclic Enone B. I. With Triethylaluminum–Hydrogen Cyanide.** In a manner similar to that described above for the hydrocyanation of the tricyclic enone A, 220 mg (0.815 mmol) of the tricyclic enone B in 8 ml of dry tetrahydrofuran was added under a nitrogen atmosphere at 0° to a solution prepared from 6.2 ml (3.26 mmol) of a 0.525 *M* solution of triethylaluminum in dry tetrahydrofuran and 0.42 ml (2.45 mmol) of a 5.81 *M* solution of hydrogen cyanide in dry benzene.[6d] After the reaction mixture was stirred for 1 hr at 0° and 19 hr at room temperature, the solution was treated as before and afforded 240 mg (99%) of a pale yellow oil. This oil, the nmr of which was too complex for accurate estimation of the isomer ratio, was separated by triple elution preparative thin-layer chromatography on a 20 × 20 × 0.2 cm silica gel plate in 60% ether–petroleum ether, bp 30–60°.

| | $R_f$ | mp, °C | Amount, mg (yield, %) |
|---|---|---|---|
| *trans*-cyano ketone | 0.46 | 155.5–157 | 120 (50) |
| *cis*-cyano ketone a | 0.65 | 131–132 | 25 (10) |
| *cis*-cyano ketone b | 0.75 | Oil | 36 (15) |

The analytical sample of the *trans*-cyano ketone, obtained after two crystallizations from ether–hexane–methylene chloride, melted at 157–158°: ir ($CHCl_3$) 2225 (CN), 1720 (>C=O), 1610, 1575, 1500 (ArH), 1395, 1385 (≡$CCH_3$), and 1045 $cm^{-1}$ ($ArOC_2H_5$); nmr ($CDCl_3$), 1.41 (s, 3, ≡$CCH_3$), 4.00 (q, 2, $J$ = 7 Hz, $ArOCH_2CH_3$), and 6.56–7.30 (m, 3, ArH).

*Anal.* Calcd for $C_{19}H_{23}O_2N$: C, 76.74; H, 7.80; N, 4.71. Found: C, 76.56; H, 7.66; N, 4.81.

The *cis*-cyano ketone a on treatment with a solution of potassium *tert*-butoxide in *tert*-butyl alcohol was converted into a product with the identical nmr and ir spectra of the *cis*-cyano ketone b. The analytical sample of the *cis*-cyano ketone a, obtained after two crystallizations from hexane–ether, melted at 137–138°: ir ($CHCl_3$) 2220 (CN), 1720 (>C=O), 1610, 1575, 1500 (ArH), 1385 ($CH_3$), and 1045 $cm^{-1}$ ($ArOC_2H_5$); nmr ($CDCl_3$) $\delta$ 1.25 (d, 3, $J$ = 7 Hz, C-1 $CH_3$), 1.36 (t, 3, $J$ = 7 Hz, $ArOCH_2CH_3$), 1.94 (s, 3, ≡$CCH_3$), 3.98 (q, 2, $J$ = 7 Hz, $ArOCH_2CH_3$), and 6.50–7.44 (m, 3, ArH).

*Anal.* Calcd for $C_{19}H_{23}O_2N$: C, 76.74; H, 7.80; N, 4.71. Found: C, 76.85; H, 7.77; N, 4.62.

The analytical sample of the *cis*-cyano ketone b was obtained as an oil after rechromatography of a sample on silica gel and drying at 60° and 0.05 mm: ir ($CHCl_3$) 2220 (CN), 1720 (>C=O), 1610, 1575, 1500 (ArH), 1390, 1380 ($CH_3$), and 1040 $cm^{-1}$ ($ArOC_2H_5$); nmr ($CDCl_3$) $\delta$ 1.24 (d, 3, $J$ = 7 Hz, C-1 $CH_3$), 1.41 (t, 3, $J$ = 7 Hz, $ArOCH_2CH_3$), 1.47 (s, 3, ≡$CCH_3$), 4.04 (q, 2.0, $J$ = 7 Hz, $ArOCH_2CH_3$), and 6.59–7.47 (m, 3, ArH).

*Anal.* Calcd for $C_{19}H_{23}O_2N$: C, 76.74; H, 7.80; N, 4.71. Found: C, 76.73; H, 7.83; N, 4.63.

**II. With Diethylaluminum Cyanide in Benzene.** In a manner similar to that described above for the hydrocyanation of the tricyclic enone A, a solution of 306 mg (1.13 mmol) of the tricyclic enone B in 10 ml of dry benzene under a nitrogen atmosphere at room temperature was treated with 2.0 ml (3.4 mmol) of a 1.7 *M* solution of diethylaluminum cyanide[6c] in dry benzene, and the resulting yellow solution was allowed to stir for 1 hr. The reaction mixture was worked up as before, and there was obtained 339 mg (100%) of a white foam. Triple elution preparative thin-layer

chromatography of this material on a 20 × 20 × 0.2 cm silica gel plate in 50% ether–petroleum ether, bp 30–60°, gave

| | $R_f$ | mp, °C | Amount, mg (yield, %) |
|---|---|---|---|
| *cis*-cyano ketone a | 0.40 | 131–132 | 90 (27) |
| *cis*-cyano ketone b | 0.75 | Oil | 164 (48) |

None of the *trans*-cyano ketone was observed.

**Hydrocyanation of the Enone 6 with Triethylaluminum–Hydrogen Cyanide. A. Initial Product Mixture.** A solution of hydrogen cyanide in benzene (0.90 ml of a 5.81 *M* HCN–benzene solution, 5.24 mmol) was added with stirring to a solution of triethylaluminum in anhydrous tetrahydrofuran (10.0 ml of a 0.696 *M* $Et_3Al$–THF solution, 0.696 mmol) under nitrogen at 0°.[6d] The enone **6** (903 mg, 2.31 mmol) dissolved in 9 ml of dry tetrahydrofuran was then added immediately. The cooling bath was removed after 60 min, and the yellow solution was allowed to stir under nitrogen for 21 hr. The orange reaction mixture was poured into ice-cold 5% aqueous sodium hydroxide solution (25 ml) and extracted with ether (4 × 25 ml). The combined organic extracts were washed with water (5 × 25 ml) and saturated aqueous sodium chloride solution (25 ml), dried ($Na_2SO_4$), and concentrated at reduced pressure to give 0.920 g of a pale yellow foam. Triple elution preparative thin-layer chromatography on silica gel in 40% ether–petroleum ether, bp 30–60°, gave

| | $R_f$ | mp, °C | Amount, mg (yield, %) |
|---|---|---|---|
| *cis*-cyano ketone **7** | 0.45 | 140.5–142.5 | 110 (11) |
| 1-*epic*-*cis*-cyano ketone | 0.34 | 108–110 | 40 (4) |
| *trans*-cyano ketone **8** | 0.15 | 129–130 | 693 (72) |

**B. Optimized Conditions for the Formation of the *trans*-Cyano Ketone.** Triethylaluminum (12.8 g, 0.112 mmol) was added dropwise with stirring to 150 ml of anhydrous tetrahydrofuran at 0° (ice bath) under nitrogen.[6d] A benzene solution of hydrogen cyanide (8.95 ml of a 9.44 *M* HCN–benzene solution, 84.3 mmol) was then added dropwise over a period of 30 min while the bath temperature was maintained at 0°. To this reagent solution was added a solution of 12.6 g (32.3 mmol) of the enone in 125 ml of anhydrous tetrahydrofuran. The resulting yellow solution was allowed to stir at 0° (ice bath) for 2 hr, and then at room temperature for 24 hr. The reaction mixture was poured into ice-cold 5% aqueous sodium hydroxide solution (1 l.) and extracted with ether (5 × 500 ml). The combined ethereal extracts were washed with water (3 × 500 ml) and saturated aqueous sodium chloride solution (2 × 100 ml), dried ($Na_2SO_4$), and concentrated at reduced pressure to give 13.3 g of pale yellow crystals. The mass was dissolved in 1:3 dichloromethane–ether (300 ml) and hexane (100 ml) was added. The solution was concentrated under reflux to approximately 100 ml, cooled, seeded with pure *trans*-cyano ketone **8**, and then placed in the refrigerator overnight. The pale yellow crystalline *trans*-cyano ketone **8** (10.2 g, mp 129–131°, 76%) was collected by filtration.

The residue from the mother liquors (3.52 g, ~8.43 mmol) was dissolved in 50 ml of dry benzene and 20 ml of anhydrous dimethyl sulfoxide. To this stirred solution at room temperature under nitrogen was added 2.25 g (20 mmol) of potassium *tert*-butoxide. The resulting brown-black mixture was allowed to stir for 24 hr, and then poured into water–ether (50 ml:50 ml). The organic layer was separated and washed with water (10 × 50 ml) and saturated aqueous sodium chloride solution (50 ml), dried ($Na_2SO_4$), and concentrated at reduced pressure to give 2.86 g (87%) of the enone **6** as pale yellow crystals. This material was recycled as above using triethylaluminum (4.78 g, 41.7 mmol)–hydrogen cyanide (3.3 ml of a 0.44 *M* solution of HCN benzene, 31 mmol) in anhydrous tetrahydrofuran (50 ml) to give an additional 1.33 g (10%) of the *trans*-cyano ketone **8**, mp 128–130°. The total yield of *trans*-cyano ketone **8** was 11.5 g (86%).

**10aβ-Cyano-2,4aα-dimethyl-7-ethoxy-2-hydroxy-1β-(2′-*m*-methoxyphenylethyl)-1,2,3,4,4a,9,10,10a-octahydrophenanthrene.** Methylmagnesium iodide was prepared from magnesium (6.61 g, 0.273 g-atom) and methyl iodide (16.9 ml, 0.273 mol) in 400 ml of anhydrous ether under nitrogen. This solution was cooled to 0° (ice bath), and the 10.8 g (25.9 mmol) of the *trans*-cyano ketone **8** in 150 ml of 2:1 dry benzene–ether was added. The resulting mixture was allowed to stir at 0° (ice bath) for 30 min, and then poured into ice-cold saturated aqueous ammonium chloride solution (600 ml) with stirring. This mixture was extracted with 3:1 ether–benzene (5 × 100 ml), and the combined organic extracts were washed with water (4 × 100), saturated aqueous sodium chloride solution (100 ml), dried ($Na_2SO_4$), and concentrated at reduced pressure to give 11.0 g (98%) of cyano alcohol as a pale yellow foam. The analytical sample was prepared by double elution preparative thin-layer chromatography on silica gel in 70% ether–petroleum ether, bp 30–60°. The pure cyano alcohol ($R_f$ 0.30) was obtained as a white foam which was dried at 25° and 0.01 mm for 4 days: ir ($CHCl_3$) 3600 (sharp, OH), 3500 (broad, OH), 1610, 1595, 1585, 1500 (aromatic), 1390, 1380 ($CH_3$), and 1040 $cm^{-1}$ (ArOR); nmr ($CDCl_3$) δ 6.56–7.50 (m, 7, aromatic), 3.98 (3/4 of a q, 2, $J$ = 7 Hz, $OCH_2CH_3$) 3.76 (s, 3, $OCH_3$), 1.35 (t, 3, $J$ = 7 Hz, $OCH_2CH_3$), 1.16 (s, 3, $\equiv CCH_3$).

*Anal.* Calcd for $C_{28}H_{35}O_3N$: C, 77.56; H, 8.14; N, 3.23. Found: C, 77.64; H, 8.26; N, 3.16.

**Cyano Olefin Mixture 10.** A solution of 281 mg (0.65 mmol) of the above cyano alcohol in 10 ml of anhydrous pyridine was stirred at 0° (ice bath) under nitrogen while 0.30 ml (~4.2 mmol) of thionyl chloride was added dropwise. The pale yellow reaction mixture was allowed to stir at 0° (ice bath) for 60 min, warmed to room temperature for 30 min, and then poured into ether (100 ml). The ethereal solution was washed with ice–water (25 ml), saturated aqueous sodium bicarbonate solution (25 ml), water (4 × 25 ml), and saturated aqueous sodium chloride solution (25 ml), dried ($Na_2SO_4$), and concentrated at reduced pressure to give 0.277 g of a colorless liquid. On single elution preparative thin-layer chromatography on silica gel in 40% ether–petroleum ether, bp 30–60°, this material gave 0.264 g (98%) of a mixture of the cyano olefins **10** as a colorless liquid. The analytical sample was prepared by drying this chromatographed product at 60° and 0.01 mm for 72 hr: ir ($CHCl_3$) 2220 (CN), 1605, 1585, 1500 (aromatic), 1390, 1275 ($CH_3$), and 1040 $cm^{-1}$ (ArOR); nmr ($CDCl_3$) δ 6.52–7.52 (m, 7, aromatic), 4.93–5.80 (m, 0.9, vinyl), 3.98 (3/4 of a q, 2, $J$ = 7 Hz, $OCH_2CH_3$), 13.78 (s, 3, $OCH_3$), 1.68 (s, ~3, vinyl, $CH_3$), 1.35 (t, 3, $J$ = Hz, $OCH_2CH_3$), and 1.09 (s, 3, $\equiv CCH_3$), nmr is indicative of a mixture of olefins.

*Anal.* Calcd for $C_{28}H_{33}O_2N$: C, 80.93; H, 8.00; N, 3.37. Found: C, 81.08; H, 7.97; N, 3.32.

**Dimethyl Olefin Mixture 12.**[10] To a solution of 10.0 g (23.9 mmol) of cyano olefin mixture **10** (mp 105–110°) in 300 ml of dry benzene, 6.2 ml (34.7 mmol, 1.46 equiv) of diisobutylaluminum hydride was added under argon. The pale yellow solution was stirred for 4.5 hr, and then poured into 500 ml of cold 10% aqueous sodium hydroxide solution. This mixture was extracted with 5 × 100 ml of ether, and the combined ether extracts were washed with 2 × 100 ml of 10% aqueous sodium hydroxide, 2 × 100 ml of 10% aqueous hydrochloric acid, 100 ml of 10% aqueous sodium hydroxide, and 2 × 100 ml of brine and dried ($Na_2SO_4$). Concentration of the ethereal extracts at reduced pressure gave 10.1 g of the crude imine as a white solid: ir ($CHCl_3$) 2220 (CN) very weak, 1650 (C=N), and 1610, 1575 $cm^{-1}$ (arom); nmr ($CDCl_3$) δ 0.97 and 1.13 (15:85) (s, $\equiv CCH_3$), 1.37 (t, $J$ = 7 Hz, 3, $CH_3CH_2$), 1.80 (s, 3, vinylic $CH_3$), 3.80 (s, 3, $OCH_3$), 4.0 (q, $J$ = 7 Hz, 2, $CH_3CH_2$) 5.6–6.2 (m, 0.36 H, vinylic H), 6.7–7.3 (m, 3, arom), and 7.76 (m, 0.8 H, CH=NH).

The crude imine was dissolved with heating in 300 ml of triethylene glycol and 39.5 ml of hydrazine hydrate (0.81 mol) and 11.8 g of hydrazine dihydrochloride (0.112 mol) were added. The mixture was stirred under argon at 135–140° (internal temperature) for 4.5 hr, and then cooled to 120–130° while 75.5 g (1.34 mol) of potassium hydroxide pellets was added. The temperature of the reaction mixture was again raised to 140–150° with concomitant distillation of volatile materials under a stream of argon (43 ml of distillate was collected). The argon flow was then decreased, and the reaction mixture was kept under an argon atmosphere at 140–150° for a total of 7 hr. The reaction mixture was then cooled to room temperature, and the solid white cake was dissolved in 1.5 l. of water. This aqueous solution was extracted with 4 × 500 ml of ether, and the combined extracts were washed with 6 × 250 ml of water and 2 × 150 ml of brine and dried ($MgSO_4$). Removal of the solvent at reduced pressure gave 9.8 g of a white solid, which was chromatographed on 800 g of Merck silica gel. After the first column volume, a 2-l. portion of 15% ether in petroleum ether, bp 30–60°, eluted 6.55 g of the methyl olefins, white plates, mp 108–109.5° (67% yield): ir ($CHCl_3$) 1610 and 1575 $cm^{-1}$ (arom); nmr ($CDCl_3$) δ 0.55, 0.71, 0.85, 1.07, 1.10, 1.20 (s, $\equiv CCH_3$, in olefin mixture), 1.37 (t, $J$ = 7 Hz, 3, $OCH_2CH_3$), 1.68 (s, vinylic $CH_3$) 3.82 (s, 3, $OCH_3$), 4.03 (q, $J$ = 7 Hz, 2, $-OCH_2CH_3-$), 5.0–5.8 (m, 0.8 H, vinylic H), and 6.6–7.4 (m, 3, arom).

*Anal.* Calcd for $C_{28}H_{36}O_2$: C, 83.12; H, 8.97. Found: C, 83.15; H, 8.87.

**10-Ethoxy-3-methoxy-6bβ,12bα,14aβ-trimethyl-5,6,6aα,6b,7,8,-12b,13,14,14a-decahydropicene (2). A. *p*-Toluenesulfonic Acid Catalyzed Reaction.** A solution of 4.16 g (10.4 mmol) of the dimethyl olefin mixture **12** (mp 85–100°, prepared by a procedure similar to that described above but having a different double bond isomer distribution) and 1.69 g (8.9 mmol) of *p*-toluenesulfonic acid monohydrate in 100 ml of dry toluene was stirred under reflux under an argon atmosphere for 5 hr. An additional 0.5-g portion (2.6 mmol) of *p*-toluenesulfonic acid monohydrate was then added, and heating was continued for an additional 5 hr. The course of the reaction was followed by glpc at 270° on a 6-ft 4% SE-30 on Chromosorb W with 50 ml/mm flow rate, and after this period the reaction mixture no longer showed any change. This mixture consisted of three components with retention times of 3.9 (16%), 4.9 (10%), and 5.9 min (74%). The orange solution was poured into 600 ml of ether and then washed with two 50-ml portions of water, saturated aqueous sodium bicarbonate solution, water, and brine, and dried ($Na_2SO_4$). Removal of the solvent at reduced pressure afforded 4.3 g of a yellow-orange oil. Crystallization of this material from dichloromethane–ether–hexane afforded the desired pentacyclic diether **2** in two crops: 2.37 g of off-white prisms, mp 140–141° [glpc as above showed one main component at retention time 5.9 min (98.5%)] and 0.16 g of off-white prisms, mp 139–142° [glpc as above retention time 5.9 min (96.5%)]. Preparative tlc (Merck silica gel, two 20 × 40 cm plates, 10% ether–petroleum ether, bp 30–60°) of the 1.3 g of mother liquors afforded 1.0 g of a colorless oil ($R_f$ 0.35–0.7), which on crystallization from the aforementioned solvent mixture gave an additional 0.13 g of the pentacyclic diether **2**, mp 138–141°. These crops were combined and afforded 2.66 g (64%), mp 139–141° [glpc as above retention time 5.9 min (97%)]. The analytical sample was prepared by recrystallization from ether–dichloromethane to give white crystals: mp 152–153; ir ($CHCl_3$) 1605, 1575, 1495 $cm^{-1}$ (intensities characteristic of a 3,4-disubstituted anisole), 1385, 1380 $cm^{-1}$ ($CH_3$), and 1035 $cm^{-1}$ (ArOR); nmr ($CDCl_3$), δ 6.40–7.30 (m, 6, aromatic), 3.95 (q, 2, $J$ = 7 Hz, $OCH_2CH_3$), 3.71 (s, 3, $OCH_3$), 1.35 (t, 3, $J$ = 7 Hz, $OCH_2CH_3$), 1.17 (s, 3, $\equiv CCH_3$), 1.07 (s, 3, $\equiv CCH_3$), and 0.62 (s, 3, $\equiv CCH_3$).

*Anal.* Calcd for $C_{28}H_{36}O_2$: C, 83.12; H, 8.97. Found: C, 83.06, H, 9.04.

Two careful crystallizations (dichloromethane–ether–hexane) of the mother liquors from the preparative plate sample afforded 62 mg of 10-ethoxy-3-methoxy-6bβ,12bα,14aα-trimethyl-5,6,6aα,7,8,-12b,13,14,14a-decahydropicene as fluffy white needles, mp 159–161°, glpc as above, retention time 4.9 min (99%) at 270° and 1.4 min (99%) at 300°; ir ($CHCl_3$) 1605 and 1575 $cm^{-1}$ (arom): nmr ($CCl_4$) δ 0.10 (s, 3, $\equiv CCH_3$), 1.17 (s, 6, $\equiv CCH_3$), 1.30 (t, $J$ = 7 Hz, 3, $OCH_2CH_3$), 2.70–3.0 (m, 4, $CH_2Ph$), 3.67 (s, 3, $OCH_3$), 3.87 (q, $J$ = 7 Hz, 2, $OCH_2CH_3$), and 6.3–7.3 (m, 6, aromatic).

*Anal.* Calcd for $C_{28}H_{36}O_2$: C, 83.12; H, 8.97. Found: C, 83.19; H, 8.90.

Retreatment of 7 mg of this B/C cis pentacyclic diether with 14 mg of *p*-toluenesulfonic acid in 5 ml of refluxing toluene for 7 hr effected no useful change in recovered B/C cis material and led to decomposition.

**B. Cyclization with Trifluoroacetic Acid.** A solution of 4.5 g (11.1 mmol) of the dimethyl olefin mixture **12** in 70 ml of trifluoroacetic acid was heated at reflux temperature under argon for 1 hr. After cooling to room temperature the dark brown solution was poured into 700 ml of benzene and washed with 2 × 100 ml of water and 10% aqueous sodium hydroxide, and water, and 2 × 75 ml of brine. The aqueous fractions were back extracted with 200 ml of benzene, which, in turn was washed with 50-ml portions of water, 10% aqueous sodium hydroxide, water, and brine. The combined benzene extracts were dried ($MgSO_4$) and concentrated at reduced pressure to afford 4.5 g of a yellow foam. Similar cyclizations were performed with 10 g and 7.3 g of the dimethyl olefin mixture **12** in 140 and 110 ml of the acid, respectively, and the products were combined and crystallized from dichloromethane-ether–hexane. In this manner there was obtained 12.4 g of the pentacyclic diether **2** as pale yellow prisms, mp 137–141° (57%).

**10-Ethoxy-3-hydroxy-6bβ,12bα,14aβ-trimethyl-5,6-6aα,6b,7,8,-12b,13,14,14a-decahydropicene (15).** To a solution of 5.4 g (13.4 mmol) of the pentacyclic diether **2** (mp 137–141°) and 9.3 ml (9.7 mmol) of a 1.04 *M* solution of diphenylphosphine in benzene dissolved in 40 ml of tetrahydrofuran was added 25 ml of the deep red solution resulting from reaction of 10 g (19 mmol) of triphenylphosphine with 1.4 g (0.2 g-atom) of lithium in 50 ml of dry tetrahydrofuran for 3 hr. The resulting bright red solution was heated at reflux under argon for 3 hr. Another 9.3-ml (9.7 mmol) portion of a 1.04 *M* solution of diphenylphosphine in benzene and 25 ml of the phenyllithium–lithium diphenylphosphide solution were added and heating under reflux was continued for 7 hr. After cooling to room temperature, the red solution was poured into 200 ml of aqueous hydrochloric acid solution and extracted with five 100-ml portions of chloroform. The chloroform extracts were washed with 100 ml of water, six 100-ml portions of fresh 10% aqueous hydrogen peroxide, three 100-ml portions of water, and two 50-ml portions of brine, and dried ($Na_2SO_4$). Removal of the solvent at reduced pressure afforded 14.4 g of a yellow oil which was chromatographed on 800 g of silica gel. Elution with 5 l. of 50% ether–petroleum ether, bp 30–60° (250-ml fractions), gave first 0.18 g of starting diether **2** (7%), then 4.8 g (91%) of the phenol **15**. This latter material was recrystallized from dichloromethane–ether–dioxane and afforded 4.5 g, mp 189–191°, and 0.15 g, mp 186–190°. The cruder material was submitted to preparative thin-layer chromatography in 50% ether–petroleum ether, bp 30–60°, and gave 100 mg, mp 189–191°, after recrystallization. The total yield of the pure phenol **15** was 4.75 g (90%). The analytical sample, obtained after a further crystallization of this material from the same solvent mixture, melted at 189.5–191°: ir ($CHCl_3$) 3610 (OH), 1610, and 1585 $cm^{-1}$ (arom); nmr ($CDCl_3$) δ 0.80, 1.09, 1.16 (s, 3 each $\equiv C-CH_3$), 1.4 (t, 3, $J$ = 7 Hz, $OCH_2CH_3$), 2.7–3.1 (m, 4, $CH_2Ph$), 4.00 (q, 2, $J$ = 7 Hz, $OCH_2CH_3$), 4.56 (s, 1, OH), and 6.46–7.15 (m, 6, arom).

*Anal.* Calcd for $C_{27}H_{34}O_2$: C, 83.03; H, 8.77. Found: C, 83.26; H, 8.66.

**3-Methoxy-6bβ,12bα,14aβ-trimethyl-5,6,6aα,6b,7,8,12,12aβ,12b,-13,14,14a-dodecahydro-10(11*H*)-picenone (16).** Into a solution of 1.0 g (2.56 mmol) of the phenol (mp 189–191°) in 450 ml of dry glyme was distilled 900 ml of dry ammonia. A 0.5-cm piece (2.7 mg-atom) of lithium wire was then added with rapid stirring to generate the phenoxide. After 5 min the blue color had faded; to the resulting clear, colorless solution was added an 11-cm piece (57.4 mg-atom) of lithium wire cut in small pieces. The blue solution was stirred for 15 min before 12 ml (0.26 mol) of absolute ethanol was added over a 10–15-min period. After the blue color had disappeared (30–45 min) another 11-cm portion of lithium wire was added, followed by another 11-cm piece when the color again faded (about 1.5 hr). After the solution had remained blue for a total of 3 hr, the excess lithium was destroyed by the addition of 10 ml of methanol. The ammonia was removed under a stream of argon by heating the flask with a hot air gun, followed by evaporation at reduced pressure. The resulting white paste was diluted with 300 ml of dimethoxyethane, and then 130 ml (2.1 mol) of methyl iodide was added. This mixture was stirred under argon for 14 hr, and then diluted with 1500 ml of water and extracted with five 200-ml portions of ether. The combined ether extracts were washed with three 100-ml portions of water and two 100-ml portions of brine and dried ($Na_2SO_4$). Removal of the solvent at reduced pressure gave 1.05 g of an off-white oily solid, which was hydrolyzed by heating under reflux with 80 ml of 5 *N* aqueous hydrochloric acid in 30 ml of benzene and 150 ml of ethanol for 0.5 hr. After cooling to room temperature, the pale yellow solution was poured into 200 ml of 50% brine and extracted with five 100-ml portions of ether. The combined extracts were washed with 100-ml portions of water, saturated aqueous sodium bicarbonate, water, and two 50-ml portions of brine and dried ($MgSO_4$). Removal of the solvent at reduced pressure afforded 1.0 g of an off-white oil which was chromatographed on 100 g of silica gel. Elution with 50% ether–petroleum ether, bp 30–60°, first afforded 0.53 g of an oil which appeared by glpc, ir, and nmr to be a mixture of over reduced hydrocarbon and methylated phenol.

The main fraction amounted to 0.43 g of crystalline material eluted with ether. These white crystals were recrystallized from dichloromethane–ether and gave 0.34 g (mp 201–204.5°) and 0.67 g (mp 198–201°) of α,β-unsaturated ketone, a 42% yield (51% conversion): ir ($CHCl_3$) 1660 (C=O), 1610, 1575 (1500 and 1465 (arom), 1385 ($\equiv CCH_3$), 1030 ($ArOCH_3$), and 870 $cm^{-1}$ (C=C); nmr ($CDCl_3$) δ 0.80, 1.13, 1.20 (s, 3 each, $\equiv CCH_3$), 2.9 (m, 2, $CH_2Ph$), 3.76 (s, 3, $OCH_3$), 5.92 (m, 1, C=CH), and 6.5–7.4 (m, 3, aromatic).

*Anal.* Calcd for $C_{26}H_{34}O_2$: C, 82.49; H, 9.05. Found: C, 82.39; H, 9.08.

**10β-Hydroxy-3-methoxy-6bβ,12bα,14aβ-trimethyl-5,6,6aα,6b,7,-8,10,11,12,12aβ,12b,13,14,14a-tetradecahydropicene (17).** A solution of 2.35 g (5.8 mmol) of the enone **16** in 22 ml of benzene and 90 ml of tetrahydrofuran was added dropwise under argon over a 10-min period to a stirred solution of 5.6 g (22 mmol) of lithium aluminum tri-*tert*-butoxyhydride in 100 ml of tetrahydrofuran.

After heating under reflux for 4.5 hr, the solution was cooled in an ice bath while 9.9 ml of 10% aqueous sodium hydroxide (28 mmol) was added dropwise. This white mixture was stirred at room temperature overnight and then filtered through a Celite pad, which was then washed with 400 ml of tetrahydrofuran and 200 ml of 50% ether–chloroform. The 3.4 g of residue obtained after removal of the solvent at reduced pressure was dissolved in 200 ml of 50% ether–chloroform and 6 g of silica gel was added. The suspension was stirred for a few minutes and filtered (200 ml of ether–chloroform wash). Removal of the solvent at reduced pressure gave 2.75 g of a white solid, which was adsorbed on 300 g of Merck silica gel (and eluted) with 50% ether–chloroform. Elution with 1.2 l. of this solvent mixture afforded 2.37 g of the alcohol **17**, mp 90–97°, which afforded 2.01 g (85%) of pure material, mp 97.5–101°, after preparative thin-layer chromatography in 50% ether–chloroform and then crystallization of main fraction from dichloromethane. The analytical sample, obtained after two further crystallizations from dichloromethane–ether, melted at 99–101°: ir ($CHCl_3$) 3600, 3450 (OH), 1660 (C=C) and 1610, 1575 $cm^{-1}$ (arom); nmr ($CDCl_3$) $\delta$ 0.76, 1.03, 1.17 (s, 3 each, $\equiv CCH_3$), 2.8 (m, 2, $CH_2Ph$), 3.75 (s, 3, $OCH_3$), 4.1 (m, 1, C*H*OH), 5.45 (m, 1, C=CH), and 6.5–7.1 (m, 3, aromatic).

*Anal.* Calcd for $C_{26}H_{36}O_2$: C, 82.06; H, 9.53. Found: C, 81.95; H, 9.35.

**10$\beta$-Hydroxy-8a$\beta$,9$\beta$-methano-3-methoxy-6b$\beta$,12b$\alpha$,14a$\beta$-trimethyl-5,6,6a$\alpha$,6b,7,8,8a,9,10,11,12,12a$\beta$,12b,13,14,14a-hexadecahydropicene.** To 300 mg (0.79 mmol) of the allylic alcohol in 7 ml of dimethoxyethane was added 43 ml of an ethereal solution of the Simmons–Smith reagent prepared in 50 ml of ether from a mixture of 3.5 ml (43.4 mmol) of methylene iodide and 8.0 g of the zinc–copper couple. This mixture was allowed to stir under reflux for 1.25 hr, cooled to room temperature, poured into 175 ml of 10% aqueous sodium hydroxide solution, and extracted with four 100-ml portions of ether. The combined ether extracts were washed with three 20-ml portions of brine, swirled with anhydrous magnesium sulfate, and quickly concentrated at reduced pressure and room temperature. In this manner, 0.5 g of a semisolid was obtained and then chromatographed on 100 g of Woelm activity III alumina. Petroleum ether, bp 30–60°, eluted methylene iodide, and the six column volumes of ether eluted first 35 mg of side products and then 160 mg (mp 219–222°, 51%) of the desired cyclopropyl alcohol, as a white solid. The analytical sample, prepared after two crystallizations from dichloromethane–ether, was obtained as plates, vacuum mp 223–225°: ir ($CHCl_3$), 3450, 3600 (OH), 3050 (cyclopropyl), 1575, 1610 (aromatic), and 1030, 1020 $cm^{-1}$ ($ArOCH_3$); nmr ($CDCl_3$) $\delta$ 0.3–0.8 (m, cyclopropyl H), 0.98, 1.17, 1.20 (s, 3 each, $\equiv CCH_3$), 2.65–3.1 (m, 2, $CH_2Ph$), 3.77 (s, 3, $OCH_3$), 3.9–4.55 (m, 1, CHO), and 6.5–7.3 (m, 3, aromatic).

*Anal.* Calcd for $C_{27}H_{38}O_2$: C, 82.18; H, 9.71. Found: C, 82.20; H, 9.68.

**8a$\beta$,9$\beta$-Methano-3-methoxy-6b$\beta$,12b$\alpha$,14a$\beta$-trimethyl-5,6,6a$\alpha$,6b,7,8,8a,9,12,12a$\beta$,12b,13,14,14a-tetradecahydro-10(11*H*)picenone (18).** To 3.7 ml (46 mmol) of pyridine in 76.5 ml of dichloromethane was added 2.28 g (23 mmol) of chromic anhydride, and the deep brown solution was allowed to stir under argon for 15 min. Then 910 mg (2.3 mmol) of the above cyclopropyl alcohol in 38 ml of dichloromethane was added, and the mixture was allowed to stir 15 min before it was filtered through 100 g of Woelm activity III alumina with the aid of 1 l. of dichloromethane. Removal of the solvent at reduced pressure gave 850 mg (95%) of cyclopropyl ketone, mp 200–206°. The analytical sample, prepared after two recrystallizations of a portion of this material from dichloromethane–ether, was obtained as plates: mp 207–210°; ir ($CHCl_3$) 1670 (C=O), 1610, and 1575 $cm^{-1}$ (aromatic); nmr ($CDCl_3$) 0.6–1.0 (m, cyclopropyl H), 1.00, 1.13, and 1.20 (s, 3 each, $\equiv CCH_3$), 2.9 (m, 2, $CH_2Ph$), 3.73 (s, 3, $OCH_3$), and 6.5–7.3 (m, 3, aromatic).

*Anal.* Calcd for $C_{27}H_{36}O_2$: C, 82.61; H, 9.24. Found: C, 82.57; H, 9.23.

**8a$\beta$,9$\beta$-Methano-3-methoxy-6b$\beta$,11,11,12b$\alpha$,14a$\beta$-pentamethyl-5,6,6a$\alpha$,6b,7,8,8a,9,12,12a$\beta$,12b,13,14,14a-tetradecahydro-10(11*H*)-picenone.** To a stirred solution of 0.83 g (2.12 mmol) of the cyclopropyl ketone **18** in 240 ml of tetrahydrofuran was added 4.7 g (4.2 mmol) of potassium *tert*-butoxide. The orange solution was allowed to stir under argon for 15 min before 2.73 ml (44.3 mmol) of methyl iodide was added. The off-white slurry was allowed to stir at room temperature for 20 hr, and then another 0.55 ml (8.8 mmol) of methyl iodide was added, and stirring was continued for an additional hour. The mixture was poured into 480 ml of water and extracted with eight 200-ml portions of ether. The extracts were washed with two 150-ml portions of water and 100 ml of brine, and dried ($MgSO_4$). Removal of the solvent at reduced pressure gave 0.86 g of a white solid which was chromatographed on 100 g of Merck silica gel. Elution with 100 ml of 30% ether–petroleum ether, bp 30–60°, gave an oily mixture (0.12 g) first. The dimethylated product (0.67 g) was eluted with 400 ml of the same solvent mixture. Trituration of this material with ether gave 0.60 g (67%) of a white microcrystalline solid: mp 173–175°; ir ($CHCl_3$) 1675 (C=O), 1610, and 1575 $cm^{-1}$ (aromatic); nmr ($CDCl_3$) $\delta$ 1.03, 1.08, 1.17, 1.20, 1.27 (s, 3, each $\equiv CCH_3$), 2.8 (m, 2, $CH_2Ph$), 3.7 (s, 3, $OCH_3$), and 6.5–7.3 (m, 3, aromatic H).

*Anal.* Calcd for $C_{29}H_{40}O_2$: C, 82.81; H, 9.59. Found: C, 82.93; H, 9.57.

**6b$\beta$,8a$\beta$,11,11,12b$\alpha$,14a$\beta$-Hexamethyl-3-methoxy-5,6,6a$\alpha$,6b,7,8,8a,9,12,12a$\beta$,12b,13,14,14a-tetradecahydro-10(11*H*)-picenone (19).** To 0.58 g (1.38 mmol) of the above cyclopropyl ketone in 140 ml of tetrahydrofuran 340 ml of dry ammonia was added by distillation. Lithium wire (74 mg, 10.6 mg-atom) was then added during the course of 1 hr so as to maintain a blue color in the stirred solution. Excess sodium benzoate (0.3 g) was added until the blue color was dispelled and then 0.77 g (15 mmol) of ammonium chloride was carefully added. The ammonia was removed under a stream of argon, and the white residue was diluted with 360 ml of water and extracted with 4 × 200 ml of ether. The combined extracts were washed with 3 × 50 ml of 10% aqueous sodium hydroxide solution and 2 × 50 ml each of water and brine and dried ($MgSO_4$). Removal of the solvent at reduced pressure gave 0.58 g (100%) of the methylated ketone **19** as a white solid, mp 175–179°. The analytical sample prepared after two recrystallizations of a portion of this material from dichloromethane–ether was obtained as white prisms: mp 186–189°; ir ($CHCl_3$) 1705 (C=O) and 1610, 1675 $cm^{-1}$ (arom); nmr ($CDCl_3$) $\delta$ 1.06 (b s, 2 × 3, $\equiv CCH_3$), 1.16 (b s, 4 × 3, $\equiv CCH_3$), 3.73 (s, 3, $OCH_3$), and 6.5–7.3 (m, 3, arom).

*Anal.* Calcd for $C_{29}H_{42}O_2$: C, 82.41; H, 10.01. Found: C, 82.34; H, 9.94.

**The Hydrazone of 6b$\beta$,8a$\beta$,11,11,12b$\alpha$,14a$\beta$-Hexamethyl-3-methoxy-5,6,6a$\alpha$,6b,7,8,8a,9,12,12a$\beta$,12b,13,14,14a-tetradecahydro-10-(11*H*)-picenone.** A mixture of 95 mg (2.25 mol) of the hexamethyl ketone **19**, 1.82 ml (35.2 mmol) of hydrazine hydrate (99–100%), and 384 mg (3.66 mmol) of hydrazine dihydrochloride in 14 ml of triethylene glycol was stirred at 130–135° (oil bath temperature) under argon for 20 hr. After 5 hr, solution was complete. The solution was cooled to room temperature, diluted with 70 ml of water, and then extracted with 6 × 50 ml of ether. The combined extracts were washed with 7 × 20 ml of water and 2 × 20 ml of brine, and dried ($MgSO_4$). Removal of the solvent at reduced pressure gave 92 mg (94% yield) of the hydrazone as a white solid, mp 172–175°, which was used without further purification in the following experiment. The analytical sample, prepared after crystallization of a portion of this material from dichloromethane, was obtained as a white, microcrystalline solid: mp 174–177°; ir ($CHCl_3$) 3400 ($NH_2$), 1650 (C=N), and 1610, 1575 $cm^{-1}$ (aromatic); nmr ($CDCl_3$) $\delta$ 1.05, 1.28 (s, 3 each, $\equiv CCH_3$), 1.17, 1.20 (s, 6, each, $\equiv CCH_3$), 2.93 (m, 2, $CH_2Ph$), 3.75 (s, 3, $OCH_3$), and 6.6–7.4 (m, 3, aromatic).

*Anal.* Calcd for $C_{29}H_{43}O_1N_2$: C, 79.67; H, 10.16; N, 6.14. Found: C, 79.21; H, 9.92; N, 6.22.

**6b$\beta$,8a$\beta$,11,11,12b$\alpha$,14a$\beta$-Hexamethyl-3-methoxy-5,6,6a$\alpha$,6b,7,8,8a,9,10,11,12,12a$\beta$,12b,13,14,14a-hexadecahydropicene (20).** A mixture of 105 mg (0.24 mmol) of crude hydrazone above and 1.25 g (11.2 mmol) of potassium *tert*-butoxide in 25 ml of dry toluene was heated under reflux with stirring under an argon atmosphere for 6 hr. The mixture was then cooled to room temperature, diluted with 100 ml of 50% brine, and extracted with six 50-ml portions of ether. The combined extracts were washed with two 20-ml portions of water and brine and dried ($MgSO_4$). Removal of the solvent at reduced pressure gave 98 mg of an oil which was chromatographed on 7 g of silica gel. Elution with 30 ml of 10% ether–petroleum ether, bp 30–60°, afforded 27 mg (29%) of a mixture of the hydrocarbon **20** and an olefin as an oily solid: nmr ($CDCl_3$) $\delta$ 0.97, 1.00, 1.08, 1.12, 1.20, 1.28 (s, 3 each, $\equiv CCH_3$), 3.76 (s, 3, $OCH_3$), 5.38 (d, 0.55, $J$ = 3 Hz, vinylic H), 6.6–7.4 (m, 3, aromatic).

Continued elution with 50 ml of ether gave 27 mg (29% recovery) of the ketone **19**, the ir and nmr spectra of which were the same as those described above. This ketone was allowed to react with 1.82 ml of hydrazine hydrate and 384 mg of hydrazine dihydrochloride in 14 ml of triethylene glycol as reported above and gave 24 mg of crude hydrazone.

Continued elution with 50 ml of 10% methanol–chloroform afforded 38 mg of unreacted hydrazone. This material was combined with the hydrazone above (61 mg, 0.14 mmol), dissolved in 20

ml of dry toluene, and 0.85 g (7.6 mmol) of potassium *tert*-butoxide was added; this mixture was heated under reflux for 6 hr. Work-up and chromatography as described afforded an additional 22 mg (38%) of hydrocarbon–olefin mixture. The total yield was 49 mg (53%).

A 70:30 mixture of 83 mg of hydrocarbon and olefin (obtained from this and an earlier experiment) and 20 mg of 10% palladium on charcoal in 50 ml of ethanol was stirred under hydrogen for 72 hr. The catalyst was then removed by filtration of the suspension through a Celite pad with the aid of 200 ml of acetone. Concentration of the filtrate at reduced pressure gave 80.6 mg of an oily solid which was chromatographed on 7 g of silica gel. Elution with 50 ml of ether and trituration of the solid obtained in ether gave 68 mg (83%) of the hydrocarbon **20**, plates, mp 150–158°; this represents an overall yield of 43%. The analytical sample, prepared after crystallization of a portion of this material from ether–hexane, was obtained as needles: mp 159–163°; ir ($CHCl_3$) 1610 and 1575 $cm^{-1}$ (aromatic); nmr ($CDCl_3$) $\delta$ 0.97, 1.00, 1.03, 1.13, 1.20, and 1.23 (s, 3 each, $\equiv CCH_3$), 2.95 (m, 2, $CH_2Ph$), 3.69 (s, 3, $OCH_3$), and 6.5–7.2 (m, 3, aromatic H).

*Anal.* Calcd for $C_{29}H_{44}O$: C, 85.23; H, 10.85. Found: C, 85.04; H, 10.91.

**6b$\beta$,8a$\beta$,11,11,12b$\alpha$,14a$\beta$-Hexamethyl-1,5,6,6a$\alpha$,7,8,8a,9,10,11,-12,12a$\beta$,12b,13,14,14a,14b$\alpha$-octadecahydro-3(2*H*)-picenone (21). A. From Reduction of the Hydrocarbon 20.** Into a solution of 44 mg (0.11 mmol) of the pentacyclic hydrocarbon **20** in 35 ml of dry tetrahydrofuran was distilled 70 ml of dry ammonia. Lithium wire (37 mg, 5.3 mg-atom) was added, and the deep blue solution was allowed to stir at reflux temperature under argon for 20 min before 0.3 ml (5.1 mmol) of ethanol was added. After 1 hr another 0.3-ml portion of ethanol was added, and stirring was continued for 0.75 hr before the blue color faded. After the ammonia was removed by evaporation under a stream of argon, the residue was treated with 50 ml of water and extracted with 5 × 50 ml of ether. The combined extracts were washed with 2 × 20 ml of water and 20 ml of brine, and dried ($MgSO_4$). Removal of the solvent at reduced pressure gave an oil which was dissolved in a mixture of 6 ml of benzene and 30 ml of ethanol. A mixture of 9 ml of water and 7 ml of concentrated hydrochloric acid was then added, and the resulting solution was heated under reflux in an argon atmosphere for 30 min. After the mixture was cooled to room temperature, it was diluted with 20 ml of brine, and extracted with 5 × 50 ml of ether. The combined extracts were washed with 10 ml of saturated aqueous sodium bicarbonate solution, 10 ml of water and 2 × 10 ml of brine, and dried ($MgSO_4$). Removal of the solvent at reduced pressure gave 50 mg of a yellowish semisolid. Chromatography of this material on 7 g of Merck silica gel afforded 19.6 mg (69% yield), mp 181–185°, of crude enone **21** on elution with 50 ml of ether. Analytically pure material (20.2 mg, mp 184–187°, 47%) was obtained after two crystallizations of this material from ether: ir ($CHCl_3$) 1660 (C=O) and 1620 $cm^{-1}$ (C=C); nmr ($CDCl_3$) $\delta$ 0.87, 1.00, 1.03, 1.23 (s, 3, each, $\equiv CCH_3$), 1.12 (s, 6, $CH_3$), and 5.9 (m, 1, C=CH); uv (EtOH) 242 nm ($\epsilon$ 15,100) (calcd, 239 nm).

*Anal.* Calcd for $C_{28}H_{44}O$: C, 84.79; H, 11.18. Found: C, 84.57; H, 11.06.

**B. From Reduction of the Phosphorodiamidate of the Alcohol Mixture Derived from the Ketone 19.** To a stirred suspension of 29 mg (0.76 mmol) of lithium aluminum hydride in 6 ml of dry ether under an argon atmosphere at 0° was added a solution of 77 mg (0.182 mmol) of the ketone **19** in 6 ml of dry tetrahydrofuran over a 5-min period. After the mixture was brought to room temperature and stirred for 1 hr, 0.15 ml of water and then excess magnesium sulfate were added and stirring was continued for 1.5 hr. The suspension was then filtered, and the filter cake was washed with 300 ml of dichloromethane. Evaporation of the solvents from the filtrate at reduced pressure afforded 77 mg of a mixture of the corresponding alcohols as a colorless solid: mp 178–182°; ir ($CHCl_3$) 3630, 3460 (OH), 1610, 1575 $cm^{-1}$ (aromatic); nmr ($CDCl_3$) $\delta$ 0.97, 1.07, 1.10, 1.15, 1.20, 1.45 (s, 3 each, $\equiv CCH_3$), 2.9 (m, 2, $CH_2Ar$), 3.75 (s, 3, $OCH_3$), 3.8 (m, 1, CHOH), and 6.6–7.3 (m, 3, ArH).

To a solution of this alcohol mixture (77 mg, 0.18 mmol) and 1 mg of 1,10-phenanthroline indicator in 4 ml of dimethoxyethane, 0.3 ml (0.81 mmol) of a 2.7 *M* solution of *n*-butyllithium in hexane was added, and the mixture was allowed to stir at room temperature under argon for 5 min. This red solution was then treated subsequently with 0.8 ml of triethylamine, 0.4 ml of hexamethylphosphoramide, and 0.8 ml (4.0 mmol) of *N,N,N',N'*-tetramethyldiamidophosphorochloridate and stirring was continued for an additional 30 min. The resulting yellow solution was diluted with 150 ml of ether, washed with two 50-ml portions of water and 50 ml of saturated aqueous sodium chloride solution, and then dried ($Na_2SO_4$). Evaporation of the solvents at reduced pressure afford the TMPDA derivative (105 mg) as a yellow semicrystalline solid. This material was not further purified but used directly in the reduction below.

Into a solution of the crude TMPA derivative above (105 mg, ~0.18 mmol) in 32 ml of tetrahydrofuran was distilled 70 ml of dry ammonia and then 74 mg (10.6 mg-atom) of lithium wire was added in small pieces. The blue solution was allowed to stir for 25 min before 0.6 ml of dry ethanol was added over a 5-min period. After 1 hr the blue color faded, and an additional 74 mg (10.6 mmol) of lithium was added. After the blue reaction mixture had stirred for an additional 2 hr, the color was dispelled by the addition of 5 ml of dry ethanol, and the ammonia was removed in a stream of dry argon. The resulting white residue was partitioned between 60 ml of 20% aqueous ammonium sulfate solution and 150 ml of ether. The ethereal layer was separated, and the aqueous layer was extracted with four 60-ml portions of ether. The combined ethereal solutions were washed with 60 ml of water and 60 ml of saturated brine and then dried ($Na_2SO_4$).

The yellow, semicrystalline solid (136 mg) that remained after evaporation of this ethereal solution at reduced pressure was dissolved in 2 ml of benzene and 12 ml of 95% ethyl alcohol. This solution was then treated with 8 ml of 5 *N* hydrochloric acid, and the mixture was heated under reflux in an argon atmosphere for 1 hr. The cooled reaction mixture was then diluted with 100 ml of water and extracted with four 100-ml portions of ether. The combined ethereal extracts were washed with 100 ml of saturated aqueous sodium bicarbonate solution and 100 ml of saturated brine and then dried ($Na_2SO_4$). Removal of the solvent at reduced pressure afforded 69 mg of a yellow solid which was chromatographed on 50 g of Merck silica gel. Elution with 500 ml of 50% ether–petroleum ether, bp 30–60°, afforded 34 mg (47% overall yield) of the enone **21**, mp 183–186°, which was identical with a sample of material prepared by method A above.

***dl*-Alnusenone (3).** To 32.2 mg (0.076 mmol) of enone **21** in 3 ml of dry *tert*-butyl alcohol was added 0.52 ml (0.26 mmol) of a 0.50 *M* solution of potassium *tert*-butoxide in *tert*-butyl alcohol. This solution was allowed to stir for 5 min, and then 0.053 ml (121 mg, 0.85 mmol) of methyl iodide was added. The mixture was allowed to stir at room temperature for 1 hr, and then was diluted with 100 ml of ether. This ethereal solution was washed with two 10-ml portions of water and saturated brine, and then dried ($MgSO_4$). Removal of the solvent at reduced pressure gave 38.8 mg of a yellow oil, which after three crystallizations from ether afforded 7.7 mg of *dl*-alnusenone (**3**), mp 163–165°. The 24.2 mg of mother liquors was chromatographed on 7 g of silica gel. *dl*-Alnusenone (**3**) (14.1 mg, mp 163–165°) was eluted first with 50 ml of 35% ether–petroleum ether, bp 30–60°. The total yield was 21.8 mg (67%), mp 163–165°, as colorless prisms. In another experiment a similar yield of *dl*-alnusenone (**3**) as plates was obtained which melted at 199–203°.

Several recrystallizations of the prismatic material, mp 163–165°, from ether seeded with the plate material, mp 199–203°, gave white plates, mp 203.5–205°. The melting point of a mixture of material melting at 163–165° and that melting at 199–203° was 199-204°. Two further recrystallizations of this higher melting material from ether gave the analytically pure racemic triterpene: mp 208–208.5°; ir ($CHCl_3$) 3020 (vinyl H), 1700 (>C=O), and 1655 $cm^{-1}$ (>C=C<); nmr (220 MHz) ($CDCl_3$) $\delta$ 0.82 (3 H), 0.96 (3 H), 1.00 (3 H), 1.03 (3 H), 1.10 (3 H), 1.17 (3 H), 1.23 (3 H), 1.24 (3 H), (s, $\equiv CCH_3$), and 5.71 (m, 1, C-6 H); glpc (0.125 in. × 6 ft 10% W-98 on Chromosorb W at 300° with 50 ml/min flow) retention time 6.5 min; tlc (silica gel, 10% ether–petroleum ether, bp 30–60°), $R_f$ 0.41.

*Anal.* Calcd for $C_{30}H_{48}O$: C, 84.84; H, 11.39. Found: C, 84.83; H, 11.40.

The same above parameters were observed for an authentic sample of *dl*-alnusenone kindly supplied by Professor Stevenson (Brandeis Univ.).

**X-Ray Analysis of the Pentacyclic Diethers 13 and 2.** Precession photographs of the needle-like crystals of diether **13** indicated the monoclinic space group $P2_1/c$. The cell dimensions were established by NaCl calibrated precession photographs. Weissenberg photographs of the needle-like crystals of diether **2** indicated the orthorhombic space group *Pbca*. Accurate unit-cell dimensions were obtained by a least-squares fit to $2\theta$ values measured on a diffractometer. The crystal data are summarized in Table II.

Intensity data to a resolution of 1 Å (max $\sin\theta/\lambda = 0.5$) were

**Table II.** Crystal Data

| Molecule | Trans-anti-cis diether **13** | Trans-anti-trans diether **2** |
|---|---|---|
| Formula | $C_{28}H_{36}O_2$ | $C_{28}H_{36}O_2$ |
| Formula wt | 404.6 | 404.6 |
| Space group | $P2_1/c$ | $Pbca$ |
| Systematic absences | $h0l, l = 2n + 1$<br>$0k0, k = 2n + 1$ | $0kl, k = 2n + 1$<br>$h0l, l = 2n + 1$<br>$hk0, h = 2n + 1$ |
| $a$ | 9.709 (2) Å | 11.823 (1) Å |
| $b$ | 30.231 (6) Å | 7.094 (2) Å |
| $c$ | 7.522 (1) Å | 54.973 (5) Å |
| $\beta$ | 91.75 (8)° | |
| $Z$ | 4 | 8 |
| $F_{000}$ | 880 | 1760 |
| $\lambda$ | Cu K$\alpha$ 1.5418 Å | Fe K$\alpha$ 1.9373 Å |
| $D_c$ | 1.218 g cm$^{-3}$ | 1.165 g cm$^{-3}$ |
| $D_m$ | 1.26 g cm$^{-3}$ | 1.14 g cm$^{-3}$ |
| $\mu$ | 5.8 cm$^{-1}$ | 10.7 cm$^{-1}$ |
| $V$ | 2207 Å$^3$ | 4611 Å$^3$ |
| Diffractometer background time | 10 sec | 30 sec |
| Diffractometer scan rate | 2°/min | 2°/min |
| No. of reflections | 2393 | 2387 |
| Nonzero reflections | 2246 | 2260 |
| Final $R$ index[a] | 0.069 | 0.092 |
| Standard deviations in C, O bond lengths | 0.01 Å | 0.007 Å |
| Standard deviations in C, O bond angles | 0.5° | 0.4° |

[a] $R = \Sigma||F_o| - |F_c||/\Sigma|F_o|$.

collected on a Datex automated General Electric diffractometer using $\theta$–$2\theta$ scanning (except near the $c^*$ axis for the diether **2**, where $\omega$ scans were necessary to separate neighboring reflections). A single check reflection (041) was monitored every 30 reflections for the diether **13**, and two check reflections were monitored every 40 reflections for the diether **2**. The crystals showed no sign of decomposition in the course of the data collection.

Each reflection was assigned a variance $\sigma^2(I)$ based on counting statistics plus an empirical term $(0.02s)^2$, where $s$ is the scan count. Values of $F_o^2$ and $\sigma(F_o^2)$ were derived from the net intensities by application of Lorentz and polarization factors. Any reflection for which the net value of $|F_o|^2$ was less than or equal to zero was assigned an intensity and a weight of zero. The data were scaled by Wilson's[22] method, and values of $|E|$ and $|F|$ calculated.

**Determination and Refinement of the Diether 13 Structure.** A trial structure was derived by direct methods. A set of phases was obtained by iterative application of Sayre's equation[23] using Long's program.[24] Input to the program consisted of 317 reflections with normalized structure factors, $|E|$, greater than or equal to 1.5. A starting set of seven signs was used to phase the remaining reflections. Of these seven, three were used to define the origin ($\bar{1}71$, +3.48; $\bar{1}184$, −3.52; $\bar{1}21$, + 2.49); the remaining four (315, $\bar{5}124$, $\bar{3}81$, 230) were assigned all possible combinations of signs. Among the 16 solutions, the set of signs with the highest consistency, other than a trivial solution with complete consistency, was used in the preparation of an $E$ map. This map clearly revealed the entire trial structure.

Full-matrix least-squares refinement of coordinates, anisotropic temperature factors, and scale factor reduced the $R$ index to 0.134. A difference Fourier map indicated no misplaced or missing major atoms and was used to locate the hydrogen atoms. The addition of the hydrogen to the structure factor calculation (hydrogen parameters not refined) and added refinement including secondary extinction factor[25] in the list of parameters reduced the $R$ index to its final value of 0.069.

**Determination and Refinement of the Diether 2 Structure.** This structure was also solved by direct methods.[23,24] Three reflections (1336, 3240, and 551) having $E > 4.0$ were assigned positive signs to specify the origin. Two additional reflections (3340 and 463) were allowed to have the values + or − giving four sets of solutions. The correct solution was the one with the highest consistency (0.88). An $E$ map based on the 137 $E$'s $> 2.0$ clearly indicated a picene system. A structure factor calculation followed by a difference map showed the location of the remaining heavy atoms. The hydrogen atoms were located on subsequent difference maps, and were included in the structure factors in idealized positions (0.95 Å from the carbon atoms), but not refined. The hydrogen atoms were assigned isotropic temperature factors with $B = 5.0$ for those of the methyl groups and $B = 4.0$ for the remainder. Full-matrix least-squares refinement of coordinates and anisotropic temperature factors of the heavy atoms, a scale factor, and a secondary extinction factor[25] produced a final $R$ of 0.092.

**Supplementary Materials Available.** Structure factor tables and the final parameters and their standard deviations for the structural analyses of both the trans-anti-trans diether **2** and its trans-anti-cis isomer **13** are listed in Tables III–VIII which will appear following these pages in the microfilm edition of this volume of the journal. Photocopies of the supplementary material from this paper only or microfiche (105 × 148 mm, 20× reduction, negatives) containing all of the supplementary material for the papers in this issue may be obtained from the Journals Department, American Chemical Society, 1155 16th St., N.W., Washington, D. C. 20036. Remit check or money order for $3.00 for photocopy or $2.00 for microfiche, referring to code number JACS-73-7829.

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