Total synthesis of amphilectane-type diterpenoids: (±)-8,15-diisocyano-11(20)-amphilectene

EDWARD PIERS,[1] MONTSE LLINAS-BRUNET, AND RENATA M. OBALLA
Department of Chemistry, University of British Columbia, 2036 Main Mall, University Campus, Vancouver, BC V6T 1Z1, Canada

Received April 6, 1993

EDWARD PIERS, MONTSE LLINAS-BRUNET, and RENATA M. OBALLA. Can. J. Chem. **71**, 1484 (1993).

A total synthesis of the structurally novel, antimicrobial diterpenoid (±)-8,15-diisocyano-11(20)-amphilectene (**2**) is described. Alkylation of 2-methoxycarbonyl-3-methylcyclohexanone (**13**) with (*E*)-1-(*tert*-butyldimethylsiloxy)-6-iodo-3-(trimethylstannyl)-2-hexene (**14**) provided, stereoselectively, the functionalized keto ester **15**, which was converted efficiently into the diene **17**. Diels–Alder reaction of **17** with acrolein, followed by base-catalyzed equilibration of the resultant product mixture, gave the aldehydes **19** (58%) and **20** (29%). Allylic oxidation of the alkene **24** (derived from **19**) afforded the enone **25**. Reduction (Na, NH_3, *t*-BuOH) of **25** gave **28**, which was converted, via a sequence of eight synthetic steps, into the diacid **45**. Efficient transformation of the carboxyl functions of **45** into isonitrile groups completed the synthesis of (±)-**2**.

EDWARD PIERS, MONTSE LLINAS-BRUNET et RENATA M. OBALLA. Can. J. Chem. **71**, 1484 (1993).

On décrit une synthèse totale du diterpéne antimicrobien, (±)-8,15-diisocyanoamphilect-11(20)-ène (**2**) qui est structuralement nouveau. L'alkylation de la 2-méthoxycarbonyl-3-méthylcyclohexanone (**13**) avec le (*E*)-1-(*tert*-butyldiméthylsiloxy)-6-iodo-3-(triméthylstannyl)hex-2-ène (**14**) permet d'accéder stéréosélectivement au cétoester fonctionnalisé **15**, que l'on transforme efficacement en un diène **17**. La réaction de Diels–Alder du composé **17** avec l'acroléine, suivie de l'équilibration catalysée par une base du mélange de produits résultant, donne les aldéhydes **19** (58%) et **20** (29%). L'oxydation allylique de l'alcène **24** (dérivé du composé **19**) fournit l'énone **25**. La réduction (par Na, NH_3, *t*-BuOH) du composé **25** conduit au composé **28** qui, par une synthèse à huit étapes, donne le diacide **45**. La transformation efficace des fonctions carboxyles du composé **45** en groupes isonitriles complète la synthèse du composé (±)-**2**.

[Traduit par la rédaction]

Introduction

The small family of amphilectane-type diterpenoids share the structurally interesting tricyclic carbon skeleton **1** (1–3). One member of this group of marine natural products, (−)-8,15-diisocyano-11(20)-amphilectene, was isolated from *Hymeniacidon amphilecta*, a sponge of the Order Halichondrida collected at Glover Reef, Belize (1). This substance, which was shown by X-ray diffraction analysis to possess the constitution and relative configuration shown in formula **2** (1), exhibits antibiotic activity against *Staphyloccocus aureus, Bacillus subtilis*, and *Candida albicans*.

Recently, we have reported, inter alia, the efficient preparation of the dienes **3**–**5** (4, 5) and have studied in some detail the Diels–Alder reactions of these substrates with a variety of dienophiles (6). For the present work, the cycloaddition reaction of the diene **4** with methyl acrylate (eq. [1]) is particularly pertinent. This process produced, in high yield (87%), a mixture of products **6**, **7**, and **10** (~3:1:2, respectively). With regards to the possibility of using this chemistry to effect a total synthesis of **2**, the completely regioselective nature of the transformation was gratifying. Thus, substances structurally related to **6** and **7** (e.g., **8** and **9**) should serve as suitable intermediates for the synthesis of **2**. In this regard, it has been shown (6) that, upon treatment with sodium methoxide in methanol, compound **6** epimerizes to give primarily the "desired" isomer **7**. By analogy, equilibration of **8** and **9** should produce predominately **9**. Similarly, although the relative configuration at C* in **9** is "incorrect" for the synthesis of **2**, it should be possible to make the necessary stereochemical adjustment at some (later) stage of the synthesis.

Unfortunately, the face-selectivity of the Diels–Alder reaction of **4** with methyl acrylate is mediocre (**6** + **7**:**10** ≈ 2:1). Furthermore, it would appear to be rather difficult to make efficient use of an intermediate structurally related to **10** (e.g., **11**) for the synthesis of **2**. Nevertheless, the overall efficiency of the reactions involved (synthesis of dienes such as **4** (5), Diels–Alder reactions of **4** (6)) encouraged us to attempt a total synthesis of (±)-**2** via a route that makes use of this chemistry. We report herein the details of this study (7).

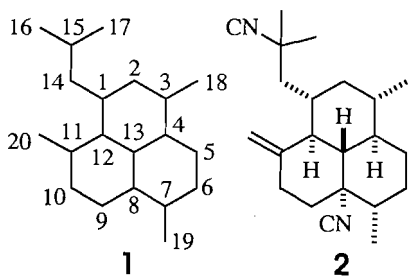
Results and discussion

(a) Preparation of the tricyclic enone 25 (Scheme 1)

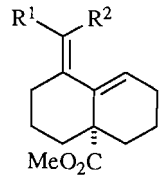
The synthesis of (±)-**2** began with methyl 2-methyl-6-oxocyclohexanecarboxylate (**13**) (see Scheme 1). This substance had been prepared previously in our laboratory (8) by reaction of methyl 6-oxo-1-cyclohexenecarboxylate (**12**) (9) with lithium methyl(phenylthio)cuprate (10). However, we found subsequently that this conversion is generally more efficient and less capricious if lithium methyl(cyano)cuprate (11) is used in place of the (phenylthio)cuprate. Thus, treatment of **12** with Me(CN)CuLi in tetrahydrofuran (THF)–Et_2O at −78°C gave **13** in 86% yield.

Alkylation of **13** with (*E*)-1-(*tert*-butyldimethylsiloxy)-6-iodo-3-(trimethylstannyl)-2-hexene (**14**) (5) was attempted under a variety of conditions. Use of potassium or sodium hydride as base and THF or 1,2-dimethoxyethane as solvent produced good yields (70–75%) of alkylated material. However, the product invariably consisted of a mixture of the desired C-alkylation product **15** and the corresponding O-alkylation substance (~3–4:1, respectively). Eventually, it was found that alkylation of the potassium enolate of **13** with **14** in refluxing toluene gave the required keto ester **15**, accompanied by only traces of the O-alkylation product. The isolated yield of **15** was 66% (~70% based on recovered **14**).

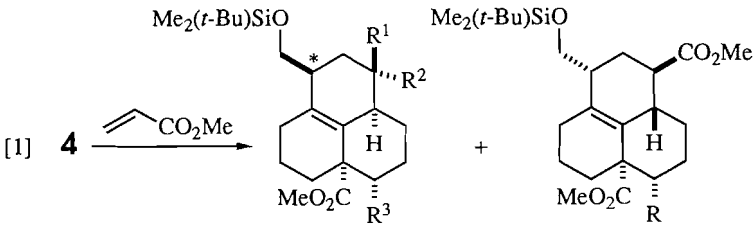
[1]Author to whom correspondence may be addressed.



1 **2**



3 $R^1 = R^2 = H$
4 $R^1 = CH_2OSi(t\text{-}Bu)Me_2$, $R^2 = H$
5 $R^1 = H$, $R^2 = CH_2OSi(t\text{-}Bu)Me_2$



6 $R^1 = CO_2Me$, $R^2 = R^3 = H$
7 $R^1 = R^3 = H$, $R^2 = CO_2Me$
8 $R^1 = CO_2Me$, $R^2 = H$, $R^3 = Me$
9 $R^1 = H$, $R^2 = CO_2Me$, $R^3 = Me$

10 R = H
11 R = Me

For steric reasons, alkylation at C-1 of the enolate anion of **13** would be expected to occur from the face of the enolate opposite to the adjacent secondary methyl group. Thus, the relative configuration of the alkylation product **15** could be assigned with confidence.

Sequential treatment of the intermediate **15** with lithium diisopropylamide (LDA) and *N*-phenyltrifluoromethanesulfonimide (12) in THF gave a solution of the enol trifluoromethanesulfonate (triflate) **16**. Although the latter substance could be isolated and subsequently cyclized in a separate step, the overall conversion of **15** into the required diene **17** could be achieved more conveniently and more efficiently by use of a one-pot protocol (5). Thus, direct treatment of the reaction mixture containing **16** with ~0.06–0.07 equivalents of tetrakis(triphenylphosphine)palladium(0), followed by a period of reflux and an appropriate work-up procedure, provided the diene **17** in 86% overall yield from **15**.

The tricyclic carbon skeleton necessary for the synthesis of the amphilectene **2** was to be derived from the diene **17** via a Diels–Alder reaction. In this connection, the earlier work (6) on the cycloaddition reaction of the diene **4** with methyl acrylate served as an informative prelude to the present study. However, since the reaction of **4** with methyl acrylate is quite sluggish (6), we chose, in the current work, to use the more reactive dienophile acrolein.

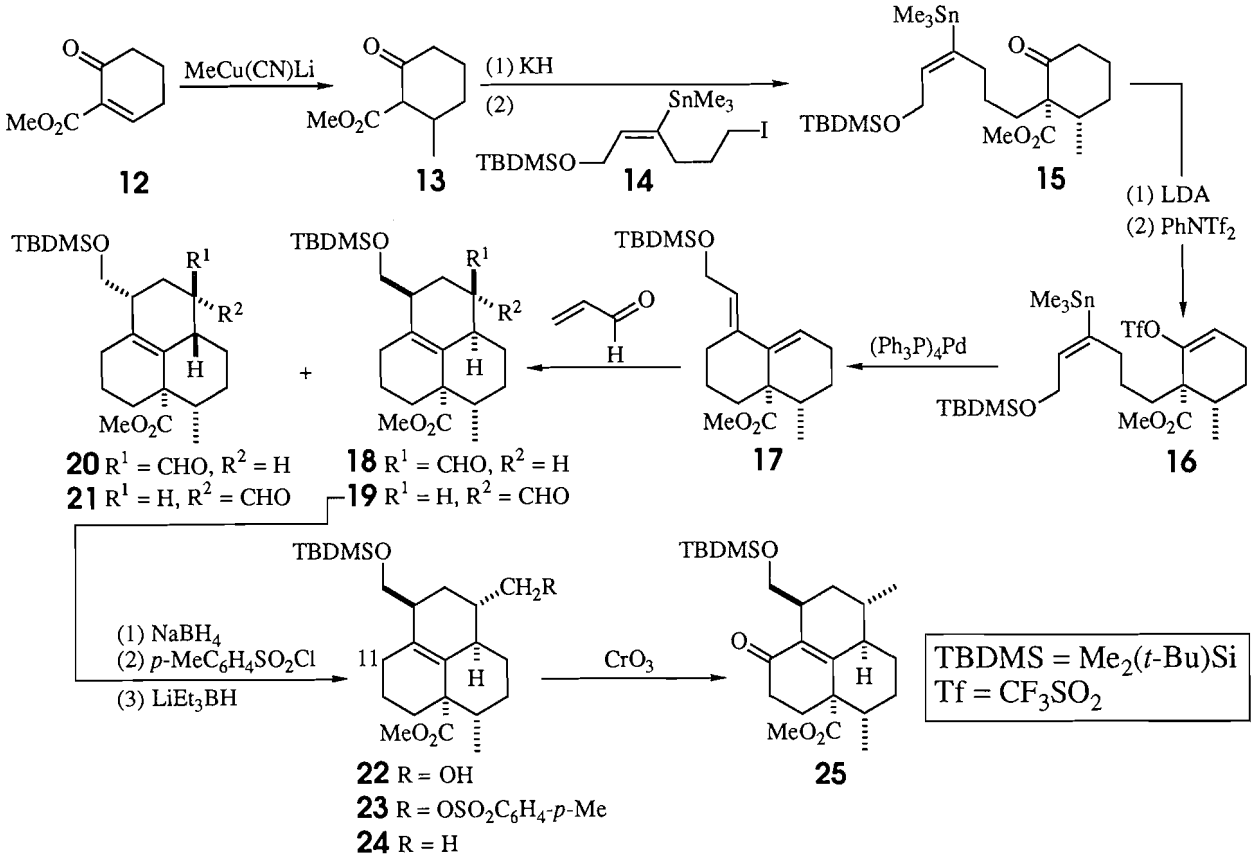
Treatment of the diene **17** with an excess of acrolein in refluxing benzene gave a high yield of four Diels–Alder adducts. The composition (~62:8:28:2) of this mixture was determined by ^1H nmr spectroscopy, involving integration of the aldehydic proton signals at δ 9.79, 9.62, 9.65, and 9.87, respectively. On the basis of the earlier work (6) (vide supra), the four cycloaddition products were assigned structures **18–21**, respectively. Compounds **18** and **19** are the result of attack of the dienophile on the face of the diene opposite to the angular CO_2Me function (*endo* and *exo* transition states, respectively), while substances **20** and **21** are derived from approach of acrolein to the bottom face of **17** (*syn* to the CO_2Me group) via *exo* and *endo* transition states, respectively. Thus, as expected (6), the face-selectivity (~7:3 in favor of top-side attack of the dienophile) of the cycloaddition reaction is modest and, although an *endo* transition state is favored in the approach of acrolein to the top face of **17**, bottom-side attack takes place predominately via an *exo* orientation of the dienophile.

Flash chromatography of the mixture on silica gel (13) gave a mixture of **19–21** (~4:14:1) (33%) and pure **18** (53%). In compound **18**, the CHO group has a pseudoaxial orientation on the cyclohexene ring and is in a 1,3-diaxial-type relationship with the $CH_2OSi(t\text{-}Bu)Me_2$ function. Consequently, one would expect that equilibration of **18** and **19** would favor the latter epimer. Indeed, treatment of **18** with sodium methoxide in methanol produced **19** in 92% yield. In the ^1H nmr spectrum of **19**, the coupling constants associated with the proton α to the CHO function show clearly that this hydrogen is pseudoaxially oriented (see experimental).

Molecular models indicate that equilibration of the epimers **20** (pseudoequatorial CHO) and **21** (pseudoaxial CHO) should favor the former isomer. Evidence for this expectation was acquired from the observation that treatment of a mixture of **19–21** (4:14:1, see above) with sodium methoxide in methanol provided cleanly an oil that consisted only of substances **19** and **20**.

Of the four aldehydes **18–21**, intermediate **19** was required for the synthesis of (±)-**2**. To optimize the acquisition of **19** from the diene **17**, the crude product derived from the reaction of **17** with acrolein was immediately subjected to equilibration with sodium methoxide in methanol. As expected (vide supra), this protocol produced cleanly and efficiently a mixture that consisted only of the aldehydes **19** and **20**. Fortunately, separation of these substances by flash chromatography (13) was readily accomplished and, by this means, **19** and **20** were obtained in isolated yields of 58 and 29%, respectively.

Reductive conversion of the formyl function in **19** into a methyl group was accomplished efficiently by known meth-



SCHEME 1

ods. Reduction of **19** with sodium borohydride in methanol, followed by treatment of the resultant alcohol **22** with *p*-toluenesulfonyl chloride in dichloromethane containing 4-*N*,*N*-dimethylaminopyridine (DMAP), provided the *p*-toluenesulfonate **23** (87% from **19**). Reaction of **23** with lithium triethylborohydride in THF (14) afforded the tricyclic olefinic ester **24** (90%).

At this stage of our envisaged synthesis of (±)-**2**, a carbonyl function had to be introduced at C-11 (amphilectane numbering) of the intermediate **24**. Not only would this function subsequently serve as a precursor for the required exocyclic methylene group, but, in theory, it would also provide a "handle" for effecting the necessary, stereochemically controlled, reduction of the olefinic double bond in **24**. In the event, treatment of **24** with chromium trioxide-3,5-dimethylpryazole complex (15) in dichloromethane afforded the α,β-unsaturated ketone **25** in 77% yield.

(b) Conversion of the enone 25 into the ketone 28

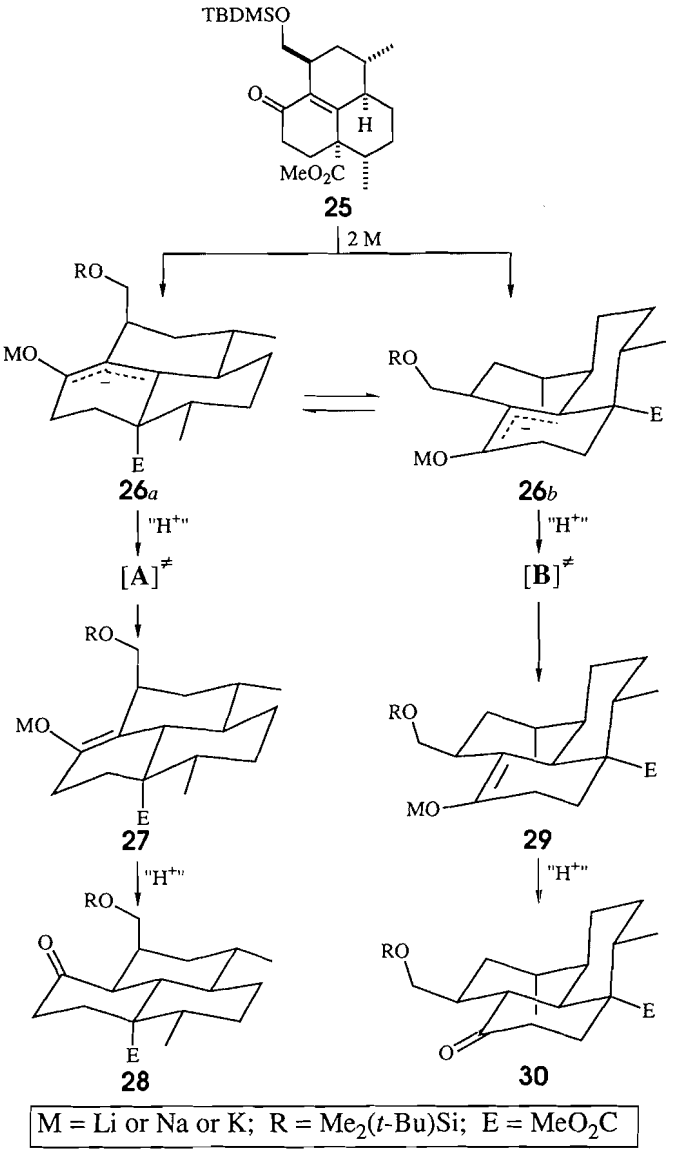
A successful, chemoselective reduction of the enone **25** with an alkali metal in ammonia (16) could, in theory, produce either or both of the intermediate enolate anions **27** and **29** (see Scheme 2). Protonation of these species during work-up would give the ketones **28** (the desired product) and (or) **30**, respectively. The question as to which pathway should be preferred may be addressed on the basis of proposals originally set forth by Robinson (17) (see also ref. 18).

Transfer of the two electrons to the enone system of **25** would afford (16) an anionic intermediate that can adopt two "reasonable" conformations, **26***a* and **26***b*. It has been proposed (17) that the allylic anion portion of intermediates such as these should be planar. Furthermore, protonation of **26***a* would be expected (17) to take place face-selectively to provide, via transition state **A**, the enolate **27**, in which the three rings are produced directly in chair (or half-chair) conformations. Similarly, selective protonation (17) of the allylic anion of **26***b* from the bottom face of the molecule would give **29**, which, again, has the three six-membered rings in stable conformations.

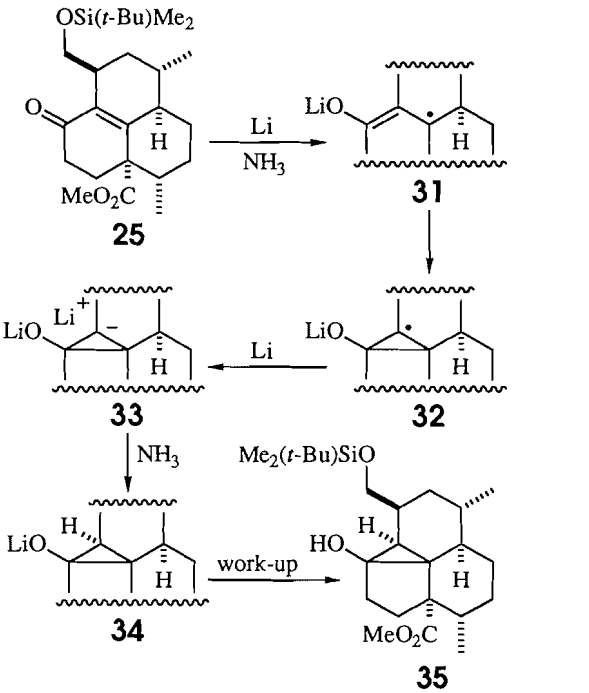
It has been convincingly argued (17) that the transition states for protonation of intermediates such as **26** have, in terms of molecular shape, a significant amount of reactant-like character. Consequently, the relative stability of the transition states **A** and **B** should be related to the relative stability of **26***a* and **26***b*. Of the latter two conformers, it appears that **26***b* is, due to the presence of more angle and torsional strain and, perhaps more importantly, due to a notable steric repulsion between the $ROCH_2$ and MO moieties, considerably less stable than **26***a*. On this basis, one would predict that transition state **A** would be preferred to transition state **B** and that, therefore, the predominant product derived from dissolving metal reduction of **25** should be substance **28**.

Top-face protonation of **26***a* via **A** is sterically hindered by the pseudoaxial CH_2OR function. However, protonation of **26***b*, via **B**, is impeded by the pseudoaxial methyl group and by the fact that the proton must be delivered in an orientation *gauche* to the angular CO_2Me group. Thus, in terms of ease of approach of a proton source, transition state **A** is, again, preferred.

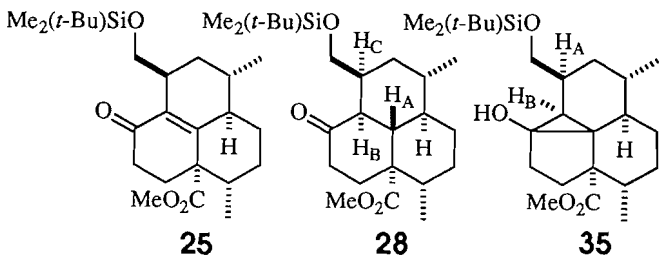
In practice, finding a suitable procedure for successful alkali metal – ammonia reduction of **25** was not straightforward. Treatment of **25** with an excess (~15 equiv.) of lith-



SCHEME 2



SCHEME 3

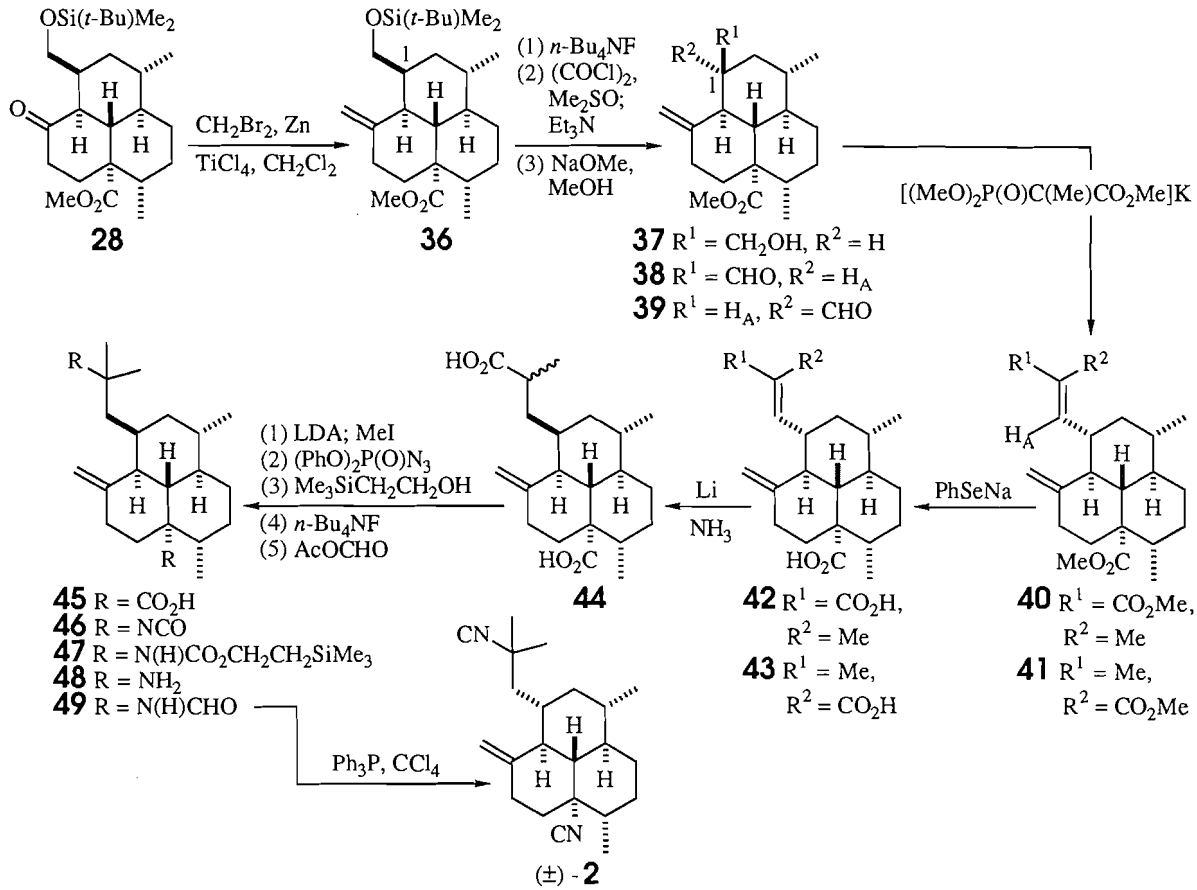


ium in ammonia – diethyl ether gave cleanly one product. The ir spectrum of this (quite unstable) material showed absorptions due to ester (1719 cm^{-1}) and hydroxyl (3240 cm^{-1}) groups. In the ^1H nmr spectrum, a singlet due to the OH function (D_2O exchange) appeared at δ 5.01. Although signals due to the $CH_2OSi(t\text{-Bu})Me_2$ protons were present, no resonance for a CHOH hydrogen was observed. On the other hand, a high-field one-proton signal (δ 1.02, d, J = 8 Hz) was present and, on this basis, it was tentatively concluded that the product possesses the cyclopropanol structure shown in **35**. Further evidence for this conclusion was derived from a ^1H nmr decoupling experiment. Thus, irradiation at δ 2.44 (m, unequivocally assigned to proton H_A in **35**) caused the doublet at δ 1.02 (H_B) to collapse to a singlet. The configuration of the stereogenic center bearing H_B is (provisionally) assigned on the basis of the size of J_{AB} (8 Hz). Molecular models indicate that a *trans* relationship between H_A and H_B would have resulted in a much weaker coupling between these hydrogens.

Mechanistically, it may be proposed that conversion of the enone **25** into **35** proceeds via a pathway summarized in Scheme 3. Transfer of an electron to **25** would produce the radical anion **31**. Cyclization of **31** to give the isomeric radical anion **32**, followed by a second electron transfer, would provide the anionic intermediate **33**. Protonation of **33** with ammonia to give the alkoxide **34** and a subsequent work-up would afford the tetracyclic product **35**.

Reaction of the enone with excess lithium in NH_3–Et_2O in the presence of *tert*-butyl alcohol (2 equiv.) gave better results. However, the desired product **28** was accompanied by varying amounts of the cyclopropanol **35** and, at times, by the starting material **25**. The capricious nature of this reaction was discouraging. On the other hand, when **25** was treated with excess lithium in the presence of *t*-BuOH and *N*,*N*,*N*′,*N*′-tetramethylethylenediamine (TMEDA), the starting material was consumed and the cyclopropanol **35** was not produced. However, the desired ketone **28** was accompanied by products resulting from reduction of the ester function.

Replacement of lithium with other alkali metals was investigated. The results obtained from reaction (NH_3, Et_2O, 2 equiv. of *t*-BuOH) of **25** with 10–15 equivalents of potassium metal also proved to be variable. Gratifyingly, these conditions did not produce any of the cyclopropanol **35**. However, although some experiments gave good yields of **28**, others produced mixtures of the desired product and the



SCHEME 4

starting material **25**. Since the latter substances are inseparable by chromatography on silica gel, this method for effecting an efficient conversion of **25** into **28** also proved to be unsatisfactory.

The best, most consistent results were obtained from use of sodium metal. Treatment of **25** with sodium (15 equiv.) and *t*-BuOH (2 equiv.) in NH_3–Et_2O consistently gave excellent yields of the required tricyclic ketone **28**.

The ^1H nmr spectrum of the reduction product provided strong evidence for the conclusion that this substance possesses the (expected) relative configuration shown in **28**. Explicitly, the signal due to the proton H_A (δ 1.56) is a doublet of doublets (J = 13, 11 Hz), while the hydrogen H_B gives rise to a dd (J = 13, 4 Hz) at δ 2.32. The observed coupling constants (J_{AB} = 13 Hz, J_{BC} = 4 Hz) are consistent with the stereostructure **28**, but are incompatible with the alternative possibility **30** (see Scheme 2 for conformational representations).

(c) Conversion of the ketone 28 into the (±)-8,15-diisocyano-11(20)-amphilectene (2) (Scheme 4)

Attempted conversion of the carbonyl group of **28** into an exocyclic methylene group by treatment of this material with methylenetriphenylphosphorane under a variety of conditions gave back only starting material. Presumably, competition between the reagent acting as a base (enolate anion formation) and a nucleophile favors the former process. Similarly, starting material was obtained from treatment of **28** with $Ph_3P{=}CHLi$ (19). On the other hand, reaction of **28** with a reagent derived from dibromomethane, zinc dust, and titanium tetrachloride (20) afforded the required alkene **36** in very good yield (Scheme 4).

For a successful synthesis of (±)-**2** from **36**, the configuration at C-1 (amphilectane numbering) of the latter substance had to be inverted. Since the $CH_2OSi(t\text{-}Bu)Me_2$ group on this stereogenic center is axially oriented, the required epimerization was envisaged to be effected via an appropriate, thermodynamically driven, equilibration process. In the event, cleavage of the silyl ether function of **36** with tetra-*n*-butylammonium fluoride in THF, followed by oxidation (21) of the resultant alcohol **37**, provided the aldehyde **38** (83% from **36**). As expected, treatment of **38** with sodium methoxide in MeOH provided cleanly and efficiently (95%) the epimeric substance **39**.

Decoupling experiments in ^1H nmr spectroscopy verified that the formyl groups in compounds **38** and **39** are axially and equatorially oriented, respectively. In the spectrum of **38**, irradiation at δ 9.92 (CHO signal) changed the resonance (multiplet, δ 2.88) due to H_A (see Scheme 4) to a quartet (overlapped ddd), with a coupling constant of 3 Hz. On the other hand, irradiation at δ 9.45 in the spectrum of **39** modified the signal (δ 2.50) due to H_A to a ddd (J = 10, 10, 4 Hz). Thus, it is evident that the H_A protons in **38** and **39** are equatorial and axial, respectively.

Reaction of the aldehyde **39** with the potassium salt of trimethyl 2-phosphonopropionate in the presence of 18-crown-6 (22) provided, in excellent yield, a mixture of the geometrically isomeric α,β-unsaturated esters **40** and **41** in a ratio of ~4:1, respectively. The configurations of the en-

oate double bonds in these substances, which were readily separated by flash chromatography (13) on silica gel, were determined by ^{1}H nmr spectroscopy. The olefinic enoate proton H_A in **40**, being *cis* to the CO_2Me function, should resonate at lower field than the corresponding hydrogen in **41** (H_A *trans* to the CO_2Me group). In the ^{1}H nmr spectra of the minor and major products, H_A gives rise to signals at δ 5.73 (broad doublet, J = 10 Hz) and 6.56 (broad doublet, J = 9 Hz), respectively. Thus, it was clear that the major enoate product possesses the *E* configuration.

Attempts to effect efficient, chemoselective reduction of the enoate carbon–carbon double bond of **40** proved to be fruitless. Consequently, the required reduction was carried out on the corresponding diacid **42**. Treatment of **40** with PhSeNa in refluxing THF–hexamethylphosphoramide (HMPA) (23) for 78 h[2] gave **42** in 88% yield. Reaction of the latter substance with lithium in ammonia–THF (24) gave, in excellent yield, the diacid **44**, which consisted of a mixture of epimers in a ratio of approximately 4:1. The major isomer could be obtained in pure form by flash chromatography (13) of the mixture on silica gel.[3]

An alkylation reaction was employed to introduce the last carbon atom necessary to complete the synthesis. Treatment of **44** (mixture of epimers) with an excess of LDA in THF, followed by reaction of the resultant trianion with methyl iodide, gave the required diacid **45**.

Completion of the total synthesis of (±)-**2** required the degradation of the carboxyl groups of **45** to isonitrile functions. These synthetic operations were carried out conveniently and efficiently as follows.

Treatment of **45** with diphenyl phosphorazidate and triethylamine (25) in toluene at 80°C, followed by reaction of the resultant diisocyanate **46** (ir: 2170 cm^{-1}) with 2-(trimethylsilyl)ethanol (26) in the presence of triethylamine in the same solvent (100°C), produced the dicarbamate **47** (colorless oil, ir: 1731 cm^{-1}). Acquisition of the diamine **48** was accomplished by reaction of **47** with tetra-*n*-butylammonium fluoride in warm THF (26). Treatment of **48** with acetic formic anhydride in diethyl ether (27) gave the diformamide **49**, which, as expected, consisted of a mixture of rotamers associated with the amide functions.

The final step for the synthesis of the amphilectene **2** required the overall dehydration of the two formamide functions present in **49**. Although a number of methods for the transformation of formamides into isonitriles are known, we found that the protocol developed by Appel et al. (28) is, at least in the present case, particularly effective. Thus, treatment of **49** with triphenylphosphine – carbon tetrachloride in the presence of triethylamine (28) afforded crystalline (±)-8,15-diisocyano-11(20)-amphilectene (**2**) (41% from the diacid **45**). Racemic **2** (mp 84–86°C) exhibited ^{1}H and ^{13}C nmr spectra identical with those derived from natural (−)-**2**.[4]

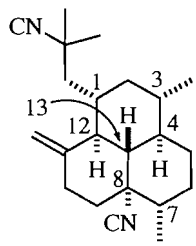
[2]With shorter reaction times, it is possible to effect the chemoselective cleavage of the α,β-unsaturated ester function.

[3]Treatment of the α,β-unsaturated ester **41** with PhSeNa in refluxing THF–HMPA (23) provided the diacid **43**, which, like **42**, could be cleanly reduced (Li, NH_3–THF (24)) to **44**. Alternatively, a mixture of **40** and **41** could be converted efficiently, via the corresponding mixture of diacids **42** and **43**, into the diacid **44**.

[4]We are very grateful to Dr. D.J. Faulkner for a sample of natural (−)-**2**.

Conclusion

The structure of the antimicrobial diterpenoid (−)-8,15-diisocyano-11(20)-amphilectene (**2**) contains seven contiguous stereogenic centers. In the work reported above, which culminated in the first recorded total synthesis of (±)-**2**, the relative configurations at carbons 4, 7, 8, 12, and 13 (amphilectane numbering) were established under conditions of kinetic control. The reactions involved consisted of an alkylation of the keto ester **13** with the iodide **14** (centers 7 and 8), a key Diels–Alder reaction of the diene **17** with acrolein (center 4), and a reduction (Na, NH_3, *t*-BuOH) of the enone **25** (centers 12 and 13). On the other hand, the correct relative stereochemical orientations at carbons 3 and 1, the two remaining stereogenic centers, were secured by thermodynamically controlled epimerizations of the aldehydes **18** and **38**, respectively. Starting from the keto ester **13**, the synthesis of (±)-**2** involved approximately 20 synthetic operations and was accomplished in an overall yield of about 1.5%.



2

Experimental

General information

Distillation temperatures, which refer to short-path (Kugelrohr) distillations, and melting points are uncorrected. Proton nuclear magnetic resonance (^{1}H nmr) spectra were recorded on $CDCl_3$ solutions, unless otherwise noted. Signal positions (δ values) were measured relative to the resonances of Me_4Si (internal standard) or $CHCl_3$ (δ 7.25). Carbon nuclear magnetic resonance (^{13}C nmr) spectra were taken on $CDCl_3$ solutions (unless otherwise noted) and signal positions are given relative to the signal for $CDCl_3$ (δ 77.0). Flash chromatography (13) was carried out with 230–400 mesh silica gel (E. Merck). Thin-layer chromatography (tlc) was carried out with commercial aluminum-backed silica gel plates. Gas–liquid chromatography (glc) was performed on instruments equipped with 25 m × 0.21 mm fused silica columns coated with cross-linked SE-54. Reagents and solvents were purified and dried using standard methods. Aqueous NH_4Cl–NH_4OH (pH 8) refers to a solution prepared by addition of ~50 mL of aqueous NH_4OH (30%) to ~950 mL of saturated aqueous NH_4Cl.

Note: Unless otherwise noted, all reactions were carried out under an atmosphere of dry argon in flame- or oven-dried glassware.

Note: All compounds for which high-resolution mass measurements are given exhibited one spot on tlc analyses and produced clean ^{1}H nmr spectra.

Methyl 2-methyl-6-oxocyclohexanecarboxylate (13)

To a cold (−78°C) stirred solution of lithium methyl(cyano)cuprate (11) (28.3 mmol) in dry THF–Et_2O (10:1, 220 mL) was added a solution of methyl 6-oxo-1-cyclohexenecarboxylate (**12**) (9) (3.36 g, 21.8 mmol) in 10 mL of dry THF. The clear yellow solution was stirred at −78°C for 2 h. Aqueous NH_4Cl–NH_4OH (pH 8) (250 mL) and Et_2O (125 mL) were added and the mixture was allowed to warm to room temperature. The mixture was opened to the atmosphere and was stirred vigorously until the aqueous layer was deep blue. The phases were separated and the aqueous layer was extracted three times with Et_2O. The combined organic extracts were washed sequentially with saturated aqueous NH_4Cl and

brine, dried ($MgSO_4$), and concentrated. Distillation (80–90°C/0.1 Torr (1 Torr = 133.3 Pa)) of the residual oil gave 3.19 g (86%) of compound **13**, the spectral data of which agreed with those obtained previously (8).

*Methyl (±)-[1α, 1(*E*), 2α]-1[6-[[(1,1-dimethylethyl)-dimethylsilyl]oxy]-4-(trimethylstannyl)-4-hexenyl]-2-methyl-6-oxocyclohexanecarboxylate (**15**)*

To a stirred suspension of KH (9.8 mmol) in dry toluene (80 mL) at room temperature was added, dropwise, a solution of the keto ester **13** (1.66 g, 9.8 mmol) in dry toluene (10 mL). After the mixture had been stirred for 30 min, a solution of (*E*)-1-(*tert*-butyldimethylsiloxy)-6-iodo-3-(trimethylstannyl)-2-hexene (**14**) (5) (4.44 g, 8.8 mmol) in dry toluene (10 mL) was added and the reaction mixture was refluxed for 48 h. The mixture was cooled to 0°C and aqueous NH_4Cl–NH_4OH (pH 8) (~50 mL) was added. The phases were separated and the aqueous phase was washed with brine, dried ($MgSO_4$), and concentrated. Flash chromatography of the residual material on silica gel (600 g, 98:2 and 94:6 petroleum ether – Et_2O) gave 250 mg of the iodide **14** and 3.18 g (66%; 70% based on recovered **14**) of the keto ester **15**. The latter material, a colorless oil, exhibited ir (neat): 1743, 1715, 1088, 836 cm^{-1}; ^1H nmr (400 MHz) δ: 0.06 (s, 6H), 0.11 (s, 9H, $^2J_{Sn-H}$ = 54 Hz), 0.90 (s, 9H), 1.11 (d, 3H, J = 7 Hz), 1.11–1.20 (m, 2H), 1.22–1.32 (m, 1H), 1.57–1.87 (m, 4H), 1.90–2.02 (m, 2H), 2.24 (m, 2H), 2.39 (br d, 1H, J = 15 Hz), 2.63 (ddd, 1H, J = 15, 13.5, 6.5 Hz), 3.65 (s, 3H), 4.27 (d, 2H, J = 5.5 Hz, $^4J_{Sn-H}$ = 17 Hz), 5.65 (t, 1H, J = 5.5 Hz, $^3J_{Sn-H}$ = 79 Hz). Exact Mass calcd. for $C_{23}H_{43}O_4{}^{120}Sn$ (M^+ − Me): 531.1952; found: 531.1957.

*Methyl (±)-1(1*E*, 4aα, 5α)-1-[2-[[(1,1-dimethylethyl)-dimethylsilyl]oxy]ethylidene]-1,3,4,5,6,7-hexahydro-5-methyl-4a(2*H*)-naphthalenecarboxylate (**17**)*

To a cold (−48°C), stirred solution of LDA (5.14 mmol) in dry THF (50 mL) was added a solution of the keto ester **15** (2.55 g, 4.67 mmol) in dry THF (10 mL). After the solution had been stirred at −48°C for 1 h, *N*-phenyltrifluoromethanesulfonimide (2.84 g, 7.93 mmol) was added as a solid. The yellow solution was warmed to room temperature and was stirred at this temperature for 30 min. Analysis of the reaction mixture by tlc showed that all of the starting material **15** had been converted into the enol trifluoromethanesulfonate **16**. Solid $(Ph_3P)_4Pd$ (0.37 g, 0.32 mmol) was added and the resulting solution was refluxed overnight. The solution was cooled to room temperature and the solvent was removed under reduced pressure. The remaining crude material was filtered through a short column of silica gel (100 g, elution with 1:1 petroleum ether – Et_2O). Concentration of the eluate gave a yellowish oil, which was subjected to flash chromatography (500 g silica gel, 96:4 petroleum ether – Et_2O). Concentration of the appropriate fractions, followed by removal of last traces of solvent (vacuum pump), gave 1.46 g (86%) of the diene **17**, a colorless oil that displayed ir (neat): 1728, 1655, 837, 776 cm^{-1}; ^1H nmr (400 MHz) δ: 0.02 (s, 6H), 0.87 (s, 9H), 1.13 (ddd, 1H, J = 13, 13, 4 Hz), 1.42–1.63 (m, 4H), 1.71–1.82 (m, 2H), 2.15 (m, 2H), 2.52 (br d, 1H, J = 15 Hz), 2.64 (br d, 1H, J = 13 Hz), 3.64 (s, 3H), 4.18, 4.22 (ddd, ddd, 1H, 1H, J = 13, 7, 1 Hz in each case), 5.42 (ddd, 1H, J = 7, 1.5, 1.5 Hz), 5.73 (br t, 1H, J = 7 Hz). In decoupling experiments, irradiation at δ 1.13 caused collapse of the signal at 2.64 to a br s, while irradiation at δ 2.64 converted the signal at 1.13 into a dd (J = 13, 4 Hz). Exact Mass calcd. for $C_{21}H_{36}O_3Si$: 364.2434; found: 364.2428.

*Diels–Alder reaction of the diene **17** with acrolein. Isolation of methyl (±)-(3α, 3aα, 7β, 9β, 9aα)-7-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]methyl]-9-formyl-2,3,5,6,7,8,9,9a-octahydro-3-methyl-1*H*-phenalene-3a(4*H*)-carboxylate (**18**)*

A stirred solution of the diene **17** (73 mg, 0.20 mmol) and acrolein (0.5 mL, 7.48 mmol) in dry benzene was refluxed for 20 h. After the mixture had been cooled to room temperature, the volatile material was removed under reduced pressure and the crude residual oil was subjected to flash chromatography (50 g silica gel, 9:1 petroleum ether – Et_2O). The initial fractions produced 28 mg (33%) of a mixture of three aldehydes. Analysis of this mixture by ^1H nmr spectroscopy (integration of the *CH*O signals, δ 9.62, 9.65, 9.87) showed that the three substances were present in a ratio of ~4:14:1. These Diels–Alder adducts were assigned structures **19**, **20**, and **21**, respectively. The later fractions from the flash chromatography provided 45 mg (53%) of the aldehyde **18**, a colorless oil that showed ir (neat): 2852, 1724, 837, 775 cm^{-1}; ^1H nmr (400 MHz) δ: 0.05 (s, 6H), 0.89 (s, 9H), 1.09 (d, 3H, J = 7 Hz), 1.19 (ddd, 1H, J = 13, 13, 3 Hz), 1.25–1.40 (m, 2H), 1.49–1.71 (m, 6H), 1.86–2.07 (m, 3H), 2.2 (m, 1H), 2.33 (br d, 1H, J = 13 Hz), 2.60 (ddd, 1H, J = 13, 5, 2 Hz), 2.82 (br d, 1H, J = 13 Hz), 3.67 (s, 3H), 3.66 (m, 2H), 9.79 (s, 1H). Exact Mass calcd. for $C_{24}H_{40}O_4Si$: 420.2695; found: 420.2695.

*Epimerization of the aldehyde **18**. Preparation of methyl (±)-(3α, 3aα, 7β, 9α, 9aα)-7-[[[(1,1-dimethylethyl)-dimethylsilyl]oxy]-methyl]-9-formyl-2,3,5,6,7,8,9,9a-octahydro-3-methyl-1*H*-phenalene-3a(4*H*)-carboxylate (**19**)*

A solution of the aldehyde **18** (42 mg, 0.115 mmol) in 3 mL of 0.1 M sodium methoxide in dry methanol was stirred at room temperature for 1 h. Water (10 mL) was added and the mixture was extracted with pentane. The combined extracts were washed with water, dried ($MgSO_4$), and concentrated. Flash chromatography (15 g silica gel, 9:1 petroleum ether – Et_2O) of the residual material gave 40 mg (92%) of the aldehyde **19**, a colorless oil that displayed ir (neat): 2858, 1724, 838, 776 cm^{-1}; ^1H nmr (400 MHz) δ: 0.06 (s, 6H), 0.90 (s, 9H), 1.02 (d, 3H, J = 7 Hz), 1.09 (m, 1H), 1.23 (ddd, 1H, J = 13, 13, 3 Hz), 1.34–1.37 (m, 6H), 1.80–1.90 (m, 2H), 1.98 (ddd, 1H, J = 13, 4, 4 Hz), 2.19 (m, 2H), 2.27 (dddd, 1H, J = 11, 8, 3.5, 2.5 Hz), 2.46 (br d, 1H, J = 13 Hz), 2.83 (br s, 1H), 3.50 (dd, 1H, J = 10, 8 Hz), 3.67 (s, 3H), 3.68 (dd, 1H, J = 10, 4 Hz), 9.62 (d, 1H, J = 2.5 Hz). In a decoupling experiment, irradiation at δ 9.62 changed the signal at 2.27 to a ddd (J = 11, 8, 3.5 Hz). Anal. calcd. for $C_{24}H_{40}O_4Si$: C 68.53, H 9.58; found: C 68.78, H 9.59. Exact Mass calcd.: 420.2695; found: 420.2693.

*Diels–Alder reaction of the diene **17** with acrolein. Equilibration of the crude product mixture. Isolation of the aldehydes **19** and methyl (±)-(3α, 3aα, 7α, 9β, 9aβ)-7-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]methyl]-9-formyl-2,3,5,6,7,8,9,9a-octahydro-3-methyl-1*H*-phenalene-3a(4*H*)-carboxylate (**20**)*

A stirred solution of the diene **17** (233 mg, 0.64 mmol) and acrolein (1.2 mL, 18 mmol) in dry benzene (20 mL) was refluxed for 20 h. The mixture was cooled and concentrated under reduced pressure. The crude material was passed through a small column of silica gel (10 g, 1:1 petroleum ether – Et_2O). Concentration of the eluate gave a mixture of aldehydes. This material was dissolved in a 0.1 M solution of sodium methoxide in dry methanol (10 mL) and the solution was stirred at room temperature for 1 h. Water (20 mL) was added and the mixture was extracted three times with pentane. The combined organic extracts were washed with water, dried ($MgSO_4$), and concentrated. Flash chromatography (90 g silica gel, 9:1 petroleum ether – Et_2O) of the residual material gave 158 mg (58%) of the aldehyde **19** (spectra identical with those obtained previously, vide supra) and 77 mg (29%) of the aldehyde **20**. The latter substance, a colorless oil, displayed ir (neat): 2707, 1724 (br), 838, 777 cm^{-1}; ^1H nmr (400 MHz) δ: 0.06 (s, 6H), 0.91 (s, 9H), 1.03 (d, 3H, J = 7 Hz), 1.15–1.25 (m, 2H), 1.36–1.97 (m, 8H), 2.08–2.22 (m, 3H), 2.31–2.36 (m, 2H), 2.55 (m, 1H), 3.43 (dd, 1H, J = 10, 10 Hz), 3.64 (s, 3H), 3.72 (dd, 1H, J = 10, 4 Hz), 9.65 (d, 1H, J = 3.5 Hz). Exact Mass calcd. for $C_{24}H_{40}O_4Si$: 420.2695; found: 420.2700.

*Methyl (±)-(3α, 3aα, 7β, 9α, 9aα)-7-[[[(1,1-dimethylethyl)-dimethylsilyl]oxy]methyl]-2,3,5,6,7,8,9,9a-octahydro-9-(hydroxymethyl)-3-methyl-1*H*-phenalene-3a(4*H*)-carboxylate (**22**)*

To a cold (0°C), stirred solution of the aldehyde **19** (722 mg, 1.72 mmol) in methanol (60 mL) was added solid sodium boro-

hydride (79 mg, 2.08 mmol) and the mixture was stirred for 1 h. Saturated aqueous NH_4Cl (40 mL) was added and the mixture was extracted with dichloromethane. The combined extracts were washed with brine, dried ($MgSO_4$), and concentrated to give 687 mg (95%) of the alcohol **22**, a colorless oil that showed ir (neat): 3406 (br), 1723, 837, 776 cm^{-1}; ^1H nmr (400 MHz) δ: 0.04 (s, 6H), 0.90 (s, 9H), 1.04 (d, 3H, J = 7 Hz), 1.27 (m, 2H), 1.34–1.67 (m, 10H), 1.90 (m, 2H), 2.15 (m, 2H), 2.36 (br d, 1H, J = 13 Hz), 3.50 (dd, 1H, J = 10, 7 Hz), 3.55 (dd, 1H, J = 10, 7 Hz), 3.64 (s, 3H), 3.65 (m, 2H). Anal. calcd. for $C_{24}H_{42}O_4Si$: C 68.20, H 10.01; found: C 68.13, H 10.10. Exact Mass calcd.: 422.2852; found: 422.2846.

*Methyl (±)-(3α, 3aα, 7β, 9α, 9aα)-7-[[[(1,1-dimethylethyl)-dimethylsilyl]oxy]methyl]-2,3,5,6,7,8,9,9a-octahydro-3-methyl-9-[[[(4-methylphenyl)sulfonyl]oxy]methyl]-1H-phenalene-3a(4H)-carboxylate (**23**)*

A solution of the alcohol **22** (678 mg, 1.61 mmol), *p*-toluenesulfonyl chloride (614 mg, 3.22 mmol), and 4-*N*,*N*-dimethylaminopyridine (492 mg, 4.03 mmol) in dry dichloromethane (20 mL) was stirred at room temperature overnight. Water (30 mL) and diethyl ether (40 mL) were added and the phases were separated. The aqueous layer was washed with diethyl ether. The combined organic phases were washed with brine, dried ($MgSO_4$), and concentrated. Flash chromatography (80 g silica gel, 4:1 petroleum ether – Et_2O) of the crude material gave 851 mg (92%) of the *p*-toluenesulfonate **23**, a colorless oil that displayed ir (neat): 1723, 1178, 837, 776 cm^{-1}; ^1H nmr (400 MHz) δ: 0.02 (s, 6H), 0.87 (s, 9H), 1.01 (d, 3H, J = 6 Hz), 1.09–1.50 (m, 5H), 1.60 (m, 2H), 1.68–1.85 (m, 4H), 2.00–2.15 (m, 4H), 2.35 (br d, 1H, J = 12 Hz), 2.44 (s, 3H), 3.43 (dd, 1H, J = 10, 7.5 Hz), 3.58 (dd, 1H, J = 10, 4 Hz), 3.62 (s, 3H), 3.91 (dd, 1H, J = 9.5, 7.5 Hz), 4.03 (dd, 1H, J = 9.5, 5 Hz), 7.34, 7.78 (d, d, 2H each, J = 8 Hz in each case). Exact Mass calcd. for $C_{24}H_{40}O_3Si$ (M^+ – $MeC_6H_4SO_3H$): 404.2747; found: 404.2757.

*Methyl (±)-(3α, 3aα, 7β, 9α, 9aα)-7-[[[(1,1-dimethylethyl)-dimethylsilyl]oxy]methyl]-3,9-dimethyl-1H-phenalene-3a(4H)-carboxylate (**24**)*

To a cold (0°C) solution of the *p*-toluenesulfonate **23** (1.242 g, 2.16 mmol) in dry THF (25 mL) was added a solution of lithium triethylborohydride in THF (5.4 mmol). The solution was warmed to room temperature, was stirred for 3 h, and was recooled to 0°C. Aqueous sodium hydroxide (3 N, 8 mL) and aqueous hydrogen peroxide (30%, 8 mL) were added slowly and the mixture was stirred at 0°C for 40 min. Water (25 mL) was added and the mixture was extracted thoroughly with pentane. The combined organic extracts were washed with brine, dried ($MgSO_4$), and concentrated. Flash chromatography (500 g silica gel, 95:5 petroleum ether – Et_2O) of the residual material gave 785 mg (90%) of the ester **24**, a colorless oil that showed ir (neat): 1725, 837, 775 cm^{-1}; ^1H nmr (400 MHz) δ: 0.06 (s, 6H), 0.91 (s, 9H), 0.93 (d, 3H, J = 6 Hz), 1.01 (d, 3H, J = 6 Hz), 1.25 (m, 2H), 1.26–1.70 (m, 7H), 1.76 (ddd, 1H, J = 13, 4, 4 Hz), 1.85 (br d, 1H, J = 16 Hz), 1.95 (m, 2H), 2.05 (m, 1H), 2.19 (m, 1H), 2.41 (br d, 1H, J = 13 Hz), 3.45 (dd, 1H, J = 10, 9.5 Hz), 3.64 (s, 3H), 3.66 (dd, 1H, J = 10, 5 Hz). Anal. calcd. for $C_{24}H_{42}O_3Si$: C 70.88, H 10.41; found: C 71.00, H 10.50. Exact Mass calcd.: 406.2903; found: 406.2895.

*Methyl (±)-(3aα, 4α, 6aα, 7α, 9β)-9-[[[(1,1-dimethylethyl)-dimethylsilyl]oxy]methyl]-2,3,5,6,6a,7,8,9-octahydro-4,7-dimethyl-1-oxo-1H-phenalene-3a(4H)-carboxylate (**25**)*

To a cold (−20°C), stirred suspension of chromium trioxide (2.25 g, 22.5 mmol) in dry dichloromethane (25 mL) was added, in one portion, 3,5-dimethylpyrazole (2.18 g, 22.5 mmol). The mixture was stirred at −20°C for approximately 30 min. A solution of the alkene **24** (365 mg, 0.899 mmol) in dry dichloromethane (10 mL) was added; the mixture was warmed to 0°C and then was stirred for 1.5 h. Dry diethyl ether (30 mL) was added and the mixture was filtered through a column of Florisil (elution with dry diethyl ether). The eluate was concentrated and the residual material was subjected to flash chromatography (80 g silica gel, 9:1 petroleum ether – Et_2O). Concentration of the appropriate fractions gave 291 mg (77%) of the enone **25**, a crystalline solid, mp 53–54°C, that exhibited ir (KBr): 1725, 1672, 1596, 836, 776 cm^{-1}; ^1H nmr (400 MHz) δ: 0.03 (s, 3H), 0.06 (s, 3H), 0.89 (s, 9H), 1.02 (d, 3H, J = 6 Hz), 1.04 (d, 3H, J = 6 Hz), 1.08 (m, 1H), 1.14 (ddd, 1H, J = 13, 13, 5 Hz), 1.58 (m, 4H), 1.68 (ddd, 1H, J = 14, 14, 5 Hz), 1.97 (ddd, 1H, J = 13, 4, 2 Hz), 2.24 (m, 2H), 2.44 (ddd, 1H, J = 18, 5, 3 Hz), 2.50 (ddd, 1H, J = 18, 14, 5 Hz), 2.69 (ddd, 1H, J = 13, 5, 3 Hz), 2.98 (m, 1H), 3.32 (dd, 1H, J = 9.5, 9.5 Hz), 3.62 (dd, 1H, J = 9.5, 4 Hz), 3.70 (s, 3H). Anal. calcd. for $C_{24}H_{40}O_4Si$: C 68.53, H 9.58; found: C 68.66, H 9.69. Exact Mass calcd.: 420.2696; found: 420.2702.

*Methyl (±)-(3aα, 4α, 6aα, 7α, 9α, 9aα, 9bβ)-9-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]-methyl]decahydro-4,7-dimethyl-1-oxo-1H-phenalene-3a(4H)-carboxylate (**28**)*

A solution of the enone **25** (35 mg, 0.083 mmol) and *tert*-butyl alcohol (17 μL, 0.18 mmol) in dry diethyl ether (0.8 mL) was added via cannulation to a stirred solution of sodium (29 mg, 1.26 mmol) in ammonia (3 mL, freshly distilled from sodium). The mixture was refluxed for 40 min. Isoprene was added dropwise until the blue color of the solution disappeared. Saturated aqueous NH_4Cl (10 mL) and diethyl ether (5 mL) were added. While the mixture was stirred for 4 h, it was warmed occasionally with a water bath (~40–45°C) until the ammonia was distilled. During this time, diethyl ether was added occasionally to the mixture. The phases were separated and the aqueous phase was extracted with diethyl ether (2 × 10 mL). The combined organic extracts were washed with water, dried ($MgSO_4$), and concentrated. Flash chromatography of the crude material on silica gel (20 g, 9:1 petroleum ether – Et_2O) afforded 30 mg (86%) of the ketone **26**, a white solid (mp 79–81°C, from pentane) that exhibited ir (KBr): 1724, 1707, 836, 776 cm^{-1}; ^1H nmr (400 MHz) δ: 0.03 (s, 3H), 0.05 (s, 3H), 0.89 (s, 9H), 0.90 (d, 3H, J = 6 Hz), 0.95 (d, 3H, J = 6 Hz), 0.79–1.00 (m, 1H), 1.12 (ddd, 1H, J = 13.5, 13.5, 3.5 Hz), 1.28 (m, 1H), 1.32–1.47 (m, 3H), 1.52 (m, 1H), 1.56 (dd, 1H, J = 13, 11 Hz), 1.74 (dddd, 1H, J = 11, 11, 11, 3 Hz), 1.88 (ddd, 1H, J = 13.5, 3, 3 Hz), 2.08 (dddd, 1H, J = 13, 3, 3, 3 Hz), 2.32 (dd, 1H, J = 13, 4 Hz), 2.35–2.50 (m, 2H), 2.53 (m, 1H), 2.62 (ddd, 1H, J = 13.5, 8, 3.5 Hz), 3.60 (dd, 1H, J = 10, 10 Hz), 3.65 (dd, 1H, J = 10, 5.5 Hz), 3.68 (s, 3H). In decoupling experiments, irradiation at δ 1.12 simplified the m at 2.53 and collapsed the signal at 1.88 to a br s; irradiation at δ 1.88 sharpened the m at 2.53 and changed the resonance at 1.12 to a dd (J = 13.5, 3.5 Hz); irradiation at δ 2.32 simplified the m at 2.53 and changed the dd at 1.56 to a d (J = 11 Hz). Exact Mass calcd. for $C_{23}H_{39}O_4Si$ (M^+ – Me): 407.2618; found: 407.2610.

*Methyl (±)-(3aα, 4α, 6aα, 7α, 9β, 9aα, 9bβ)-9-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]-methyl]decahydro-4,7-dimethyl-1-methylene-1H-phenalene-3a(4H)-carboxylate (**36**)*

To a stirred solution of the ketone **28** (51 mg, 0.05 mmol) in dry dichloromethane (3 mL) was added, in small portions over a period of about 30 min, a THF slurry of a reagent prepared from CH_2Br_2, Zn dust, and $TiCl_4$ as described by Lombardo (20). After about 1 mL of the reagent solution had been added, analysis of an aliquot of the reaction mixture by glc showed that the reaction was complete. The mixture was diluted with Et_2O (15 mL) and saturated aqueous sodium bicarbonate (10 mL) was added. The mixture was stirred vigorously until a clear organic phase was obtained. The phases were separated and the aqueous layer was washed with Et_2O. The combined organic solutions were washed (brine), dried ($MgSO_4$), and concentrated. Flash chromatography (10 g silica gel, 95:5 petroleum ether – Et_2O) of the residue gave 40 mg (79%) of the alkene **36**, a white solid (mp 46–48°C) that displayed ir (KBr): 1726, 1636, 1095, 840, 788 cm^{-1}; ^1H nmr (400 MHz) δ: 0.02 (s, 6H), 0.88 (d, 3H, J = 6 Hz), 0.89 (s, 9H), 0.90 (d, 3H, J = 6 Hz),

1.06 (dd, 1H, J = 12.5, 11 Hz), 1.09–1.60 (diffuse m, 8H), 1.79 (dddd, 1H, J = 11, 11, 11, 3.5 Hz), 1.98 (ddd, 1H, J = 13, 3, 3 Hz), 2.02 (dddd, 1H, J = 13, 3.5, 3.5, 3.5 Hz), 2.11–2.29 (m, 3H), 2.42 (br d, 1H, J = 12 Hz), 2.52 (ddd, 1H, J = 13, 6, 6 Hz), 3.60 (dd, 1H, J = 10, 10 Hz), 3.63 (s, 3H), 3.76 (dd, 1H, J = 10, 3.5 Hz), 4.75 (br s, 1H), 4.81 (dd, 1H, J = 1.5, 1.5 Hz). Exact Mass calcd. for $C_{25}H_{44}O_3Si$: 420.3060; found: 420.3058.

*Methyl (±)-(3aα, 4α, 6aα, 7α, 9β, 9aα, 9bβ)-decahydro-9-(hydroxymethyl)-4,7-dimethyl-1-methylene-1*H*-phenalene-3a(4*H*)-carboxylate (**37**)*

A solution of compound **36** (40 mg, 0.095 mmol) in 3 mL of dry THF was added to 0.3 mL of a 1 M solution of n-Bu_4NF in THF and the resultant mixture was stirred at room temperature for 4 h. Water (5 mL) and Et_2O (5 mL) were added, the phases were separated, and the aqueous layer was washed with Et_2O. The combined organic solutions were washed (brine), dried ($MgSO_4$), and concentrated. Flash chromatography (10 g silica gel, 3:2 petroleum ether – Et_2O) of the residue gave 28 mg (96%) of the alcohol **37**, a white solid (mp 60–62°C) that showed ir (KBr): 3348, 1724, 1636 cm^{-1}; ^1H nmr (400 MHz) δ: 0.89 (d, 3H, J = 6 Hz), 0.92 (d, 3H, J = 6 Hz), 1.06 (dd, 1H, J = 12.5, 11 Hz), 1.12 (ddd, 1H, J = 13, 9, 7 Hz), 1.22–1.40 (m, 5H), 1.48 (dddd, 1H, J = 13, 3.5, 3.5, 3.5 Hz), 1.81 (dddd, 1H, J = 10, 10, 10, 4 Hz), 1.93 (dd, 1H, J = 10, 3 Hz), 2.03 (dddd, 1H, J = 13, 3.5, 3.5, 3.5 Hz), 2.21 (m, 3H), 2.48 (br d, 1H, J = 13 Hz), 2.53 (ddd, 1H, J = 13.5, 6, 6 Hz), 3.64 (s, 3H), 3.65 (dd, 1H, J = 10, 10 Hz), 3.87 (dd, 1H, J = 10, 4 Hz), 4.77, 4.84 (s, s, 1H each). Exact Mass calcd. for $C_{19}H_{30}O_3$: 306.2195; found: 306.2195.

*Methyl (±)-(3aα, 4α, 6aα, 7α, 9β, 9aα, 9bβ)-9-formyldecahydro-4,7-dimethyl-1-methylene-1*H*-phenalene-3a(4*H*)-carboxylate (**38**)*

To a cold (−78°C), stirred solution of dimethyl sulfoxide (9.3 μL, 0.131 mmol) in dry CH_2Cl_2 (2 mL) was added oxalyl chloride (10 μL, 0.117 mmol) and the solution was stirred at −78°C for 15 min. A solution of alcohol **37** (20 mg, 0.065 mmol) in dry CH_2Cl_2 (0.8 mL) was added, stirring was continued for 20 min, Et_3N (45 μL, 0.325 mmol) was added, stirring was continued (−78°C) for 5 min, and then the mixture was allowed to warm to room temperature. Water (5 mL) and Et_2O (10 mL) were added, the phases were separated, and the aqueous layer was washed with Et_2O. The combined organic extracts were washed (brine), dried ($MgSO_4$), and concentrated. Flash chromatography (6 g silica gel, 94:6 petroleum ether – Et_2O) of the remaining material gave 17.3 mg (87%) of the aldehyde **38**, a white solid (mp 68–70°C) that exhibited ir (KBr): 2857, 1720, 1638 cm^{-1}; ^1H nmr (400 MHz), δ: 0.89 (d, 3H, J = 6 Hz), 0.91 (m, 1H), 0.96 (d, 3H, J = 6 Hz), 1.03 (m, 1H), 1.15 (ddd, 1H, J = 13, 13, 4 Hz), 1.18–1.32 (m, 2H), 1.38–1.58 (m, 4H), 2.03 (m, 3H), 2.15 (br dd, 1H, J = 15, 13 Hz), 2.38 (ddd, 1H, J = 15, 4, 4 Hz), 2.53 (ddd, 1H, J = 13, 4, 4 Hz), 2.60 (dd, 1H, J = 12, 3 Hz), 2.88 (m, 1H), 3.69 (s, 3H), 4.42, 4.85 (br s, br s, 1H each), 9.92 (d, 1H, J = 2 Hz). In decoupling experiments, irradiation at δ 2.15 changed the ddd at 1.15 to a dd (J = 13, 4 Hz), sharpened the ddd at 2.38 to a broad, unresolved signal, altered the ddd at 2.53 to a dd (J = 13, 4 Hz), and changed the broad singlets at 4.42 and 4.85 to sharp doublets (J = 2 Hz in each case); irradiation at δ 2.38 changed the signals at 1.15, 2.15, and 2.53 to a dd (J = 13, 13 Hz), a broad d (J = 13 Hz), and a dd (J = 13, 4 Hz), respectively; irradiation at δ 2.88 simplified the multiplets at 1.38–1.58 and 2.03, sharpened the dd at 2.60 to a d (J = 12 Hz), and converted the d at 9.92 to a s; irradiation at δ 9.92 caused the m at 2.88 to collapse to a ddd (J = 3, 3, 3 Hz). Exact Mass calcd. for $C_{19}H_{28}O_3$: 304.2038; found: 304.2035.

*Methyl (±)-(3aα, 4α, 6aα, 7α, 9α, 9aα, 9bβ)-9-formyldecahydro-4,7-dimethyl-1-methylene-1*H*-phenalene-3a(4*H*)-carboxylate (**39**)*

A solution of the aldehyde **38** (17 mg, 0.056 mmol) in 1.5 mL of dry 0.1 M sodium methoxide in methanol was stirred at room temperature for 1 h. Water (5 mL) was added and the mixture was extracted thoroughly with pentane. The combined organic extracts were washed (brine), dried ($MgSO_4$) and concentrated. Flash chromatography (5 g silica gel, 93:7 petroleum ether – Et_2O) of the residual material gave 16 mg (95%) of the aldehyde **39**, a white solid (mp 65–67°C) that showed ir (KBr): 2853, 1723, 1645 cm^{-1}; ^1H nmr (400 MHz) δ: 0.85 (dddd, 1H, J = 13, 13, 13, 4 Hz), 0.94 (d, 3H, J = 6 Hz), 0.95 (m, 1H), 0.96 (d, 3H, J = 6 Hz), 1.05 (m, 1H), 1.09 (ddd, 1H, J = 13, 13, 4 Hz), 1.14 (ddd, 1H, J = 12, 12, 12 Hz), 1.26 (ddd, 1H, J = 13, 13, 4 Hz), 1.37 (m, 1H), 1.52 (dddd, 1H, J = 13, 4, 4, 4 Hz), 1.67 (ddd, 1H, J = 13, 4, 4 Hz), 2.04 (m, 2H), 2.12 (ddd, 1H, J = 14, 14, 3.5 Hz), 2.29 (ddd, 1H, J = 14, 3.5, 3.5 Hz), 2.45 (dd, 1H, J = 10, 10 Hz), 2.50 (dddd, 1H, J = 10, 10, 4, 4 Hz), 2.64 (ddd, 1H, J = 13, 3.5, 3.5 Hz), 3.73 (s, 3H), 4.45, 4.75 (s, s, 1H each), 9.45 (d, 1H, J = 4 Hz). In a decoupling experiment, irradiation at δ 9.45 changed the dddd at 2.50 to a ddd (J = 10, 10, 4 Hz). Exact Mass calcd. for $C_{19}H_{28}O_3$: 304.2038; found: 304.2035.

*Methyl (±)-(3aα, 4α, 6aα, 7α, 9α(*E*), 9aα, 9bβ)-decahydro-9-(3-methoxy-2-methyl-3-oxo-1-propenyl)-4,7-dimethyl-1-methylene-1*H*-phenalene-3a(4*H*)-carboxylate (**40**) and the geometric isomer **41***

A 35% dispersion of KH in mineral oil (~23 mg) was washed three times with dry THF (3 mL) and the remaining KH (~8 mg, 0.2 mmol) was covered with 4 mL of dry THF. To this stirred suspension (0°C) was added trimethyl 2-phosphonopropionate (35 μL, 0.2 mmol) and 18-crown-6 (~1 mmol, recrystallized from MeCN) and the mixture was stirred at room temperature for 20 min. A solution of the aldehyde **39** (40 mg, 0.132 mmol) in dry THF (1.5 mL) was added and the mixture was stirred at room temperature for 3.5 h. Water (10 mL) and Et_2O (15 mL) were added and the phases were separated. The aqueous layer was extracted twice with Et_2O. The combined extracts were washed (brine), dried ($MgSO_4$), and concentrated. Flash chromatography (15 g silica gel, 94:6 pentane–Et_2O) of the residual material gave 9.5 mg (19%) of the Z ester **41** (the first product to be eluted) and 38 mg (77%) of the E ester **40**.

The ester **41**, a white solid with mp 100–103°C, exhibited ir (KBr): 1718, 1648, 1212, 1151, 1110 cm^{-1}; ^1H nmr (400 MHz) δ: 0.83 (dddd, 1H, J = 13, 13, 13, 4 Hz), 0.89 (d, 3H, J = 6 Hz), 0.90 (d, 3H, J = 6 Hz), 0.93 (dd, 1H, J = 11, 11 Hz), 1.03 (m, 2H), 1.23 (dddd, 1H, J = 13, 13, 13, 4 Hz), 1.35 (m, 1H), 1.48 (dddd, 1H, J = 14, 14, 14, 4 Hz), 1.59 (m, 2H), 1.85 (d, 3H, J = 1 Hz), 1.90–2.10 (m, 4H), 2.23 (ddd, 1H, J = 14, 3.5, 3.5 Hz), 2.62 (ddd, 1H, J = 13, 3.5, 3.5 Hz), 3.32 (dddd, 1H, J = 10, 10, 10, 4 Hz), 3.70 (s, 3H), 3.75 (s, 3H), 4.56 (s, 1H), 4.68 (d, 1H, J = 1 Hz), 5.73 (br d, 1H, J = 10 Hz). Exact Mass calcd. for $C_{23}H_{34}O_4$: 374.2456; found: 374.2454.

The ester **40**, a white solid with mp 106–108°C, displayed ir (KBr): 1718, 1642, 1277, 1224, 1157 cm^{-1}; ^1H nmr (400 MHz) δ: 0.85 (dddd, 1H, J = 13, 13, 13, 4 Hz), 0.91 (d, 6H, J = 6 Hz), 0.95 (dd, 1H, J = 11, 11 Hz), 1.06 (m, 3H), 1.26 (ddd, 1H, J = 13, 13, 3 Hz), 1.36 (m, 1H), 1.48 (m, 2H), 1.89 (s, 3H), 2.06 (m, 4H), 2.23 (ddd, 1H, J = 14, 4, 4 Hz), 2.53 (dddd, 1H, J = 11, 11, 9, 4 Hz), 2.63 (ddd, 1H, J = 13, 3.5, 3.5 Hz), 3.70 (s, 3H), 3.71 (s, 3H), 4.35 (s, 1H), 4.67 (s, 1H), 6.56 (d, 1H, J = 9 Hz). Exact Mass calcd. for $C_{23}H_{34}O_4$: 374.2456; found: 374.2462.

*(±)-[(3aα, 4α, 6aα, 7α, 9α(*E*), 9aα, 9bβ]-9-(2-Carboxy-1-propenyl)-decahydro-4,7-dimethyl-1-methylene-1*H*-phenalene-3a(4*H*)-carboxylic acid (**42**)*

To a stirred suspension of oil-free NaH (75 mg, 3.1 mmol) in dry THF (1 mL) were added benzeneselenol (0.33 mL, 3.1 mmol) and dry HMPA (1.11 mL, 6.4 mmol). The deep red solution was treated with a solution of the diester **40** (48 mg, 0.128 mmol) in dry THF (1 mL) and the mixture was refluxed for 78 h. The solution was allowed to cool to room temperature and was concentrated under reduced pressure. The residual material was treated with water (4 mL), and the basic mixture was washed with pentane

(5 mL). The aqueous phase was acidified with 10% hydrochloric acid and the mixture was extracted with Et_2O (3 × 5 mL). The combined extracts were washed (brine), dried ($MgSO_4$), and concentrated. Flash chromatography of the residue (15 g silica gel, Et_2O) produced 39 mg (88%) of the diacid **42**, a white solid (mp 273–275°C) that exhibited ir (KBr): 1687, 1665, 1648 cm^{-1}; ^1H nmr (400 MHz) δ: 0.90 (m, 1H), 0.91 (d, 3H, J = 6 Hz), 0.99 (d, 3H, J = 6 Hz), 1.00–1.15 (m, 3H), 1.32 (m, 1H), 1.39 (m, 2H), 1.52 (m, 2H), 1.87 (s, 3H), 2.05 (m, 3H), 2.22 (m, 2H), 2.60 (m, 2H), 4.40 (s, 1H), 4.68 (s, 1H), 6.54 (br d, 1H, J = 9 Hz). Exact Mass calcd. for $C_{21}H_{30}O_4$: 346.2144; found: 346.2152.

*Preparation of the dicarboxylic acid **44***

To a stirred solution of lithium metal (4.5 mg) in dry ammonia (3 mL, freshly distilled from sodium metal) was added, via cannulation, a solution of the diacid **42** (20 mg, 0.058 mmol) in dry THF (1 mL) and the mixture was refluxed for 30 min. Solid ammonium chloride was added in small portions until the blue color was discharged. Diethyl ethyl (4 mL) was added, the mixture was warmed gently to distill the ammonia, and the residual mixture was acidified with 6 N hydrochloric acid. The mixture was extracted with Et_2O (3 × 5 mL). The combined extracts were washed (brine), dried ($MgSO_4$), and concentrated. Flash chromatography (10 g silica gel, 55:45 pentane–Et_2O) gave 10 mg (50%) of **44** as a single isomer (white solid, mp 248–250°C) and 8 mg (40%) of **44** as a mixture of two epimers (ratio ~1.5:1, by ^1H nmr spectroscopy). The single isomer exhibited ir (KBr): 1702, 1644 cm^{-1}; ^1H nmr (400 MHz, acetone-d_6) δ: 0.75 (m, 1H), 0.80–0.92 (m, 5H), 0.94 (d, 3H, J = 6 Hz), 1.04 (ddd, 1H, J = 13, 13, 5 Hz), 1.10 (d, 3H, J = 6 Hz), 1.30–1.40 (m, 2H), 1.46 (m, 1H), 1.59 (m, 1H), 1.71 (m, 1H), 1.77 (m, 1H), 1.97 (m, 3H), 2.12–2.30 (m, 4H), 2.64 (m, 2H), 4.74 (s, 1H), 4.79 (s, 1H). Exact Mass calcd. for $C_{21}H_{32}O_4$: 348.2295; found: 348.2300.

*(±)-(1α, 3α, 3aα, 6α, 6aα, 9aα, 9bβ)-6a-Carboxydecahydro-α,α,3,6-tetramethyl-9-methylene-1H-phenalene-1-propanoic acid (**45**)*

To a cold (0°C), stirred solution of LDA (1.0 mmol) in dry THF (1.5 mL) was added a solution of the diacid **44** (35 mg, 0.1 mmol, mixture of epimers) in dry THF (2 mL). The mixture was allowed to warm to room temperature and was stirred for 2.5 h. Methyl iodide (~0.5 mL, passed through a small, dry basic alumina column) was added and the mixture was stirred at room temperature for 1 h. The solution was acidified with 10% hydrochloric acid and the mixture was extracted with Et_2O (3 × 5 mL). The combined extracts were washed (brine), dried ($MgSO_4$), and concentrated. Flash chromatography (5 g silica gel, 1:1 pentane–Et_2O) gave 20 mg (55%) of the diacid **45**, a white solid (mp 245–247°C) that showed ir (KBr): 1705 cm^{-1}; ^1H nmr (400 MHz, acetone-d_6) δ: 0.79–0.92 (m, 5H), 0.93 (d, 3H, J = 6 Hz), 1.01–1.12 (m, 2H), 1.15 (s, 3H), 1.18 (s, 3H), 1.30–1.50 (m, 5H), 1.60 (m, 1H), 1.78–2.00 (m, 5H), 2.12–2.32 (m, 2H), 2.65 (ddd, 1H, J = 12, 4, 4, 4 Hz), 4.69 (s, 1H), 4.79 (s, 1H). Exact Mass calcd. for $C_{22}H_{34}O_4$: 362.2457; found: 362.2463.

*(±)-(1α, 3α, 3aα, 6α, 6aα, 9aα, 9bβ)-Dodecahydro-6a-isocyano-1-(2-isocyano-2-methylpropyl)-3,6-dimethyl-9-methylene-1H-phenalene [(±)-8,15-diisocyano-11(20)-amphilectene (**2**)]*

To a stirred solution of the diacid **45** (19 mg, 0.052 mmol) in dry toluene (0.4 mL) were added dry Et_3N (38 μL, 0.273 mmol) and diphenyl phosphorazidate (38 μL, 0.186 mmol) and the mixture was heated to 80°C. Evolution of nitrogen began immediately. After a period of 2 h, the ir spectrum of the material obtained from a small sample of the mixture showed an absorption at 2170 cm^{-1} (-N=C=O, compound **46**). No carbonyl absorption was present. Dry 2-(trimethylsilyl)ethanol (0.15 mL, 1.06 mmol) and dry Et_3N (76 μL, 0.546 mmol) were added and the mixture was heated at 100°C for 60 h. During this time, after periods of 20 h and 40 h, additional amounts of $Me_3SiCH_2CH_2OH$ (0.15 mL) and Et_3N (76 μL) were added. The reaction mixture was cooled, diluted with Et_2O, and passed through a small column of silica gel (2 g, elution with Et_2O). The eluate was concentrated and the residue was subjected to flash chromatography (15 g silica gel, 9:1 pentane–Et_2O) to provide 16 mg (52%) of the dicarbamate **47**, a colorless oil that exhibited ir (neat): 3448, 3371, 1731, 1645, 1505 cm^{-1}; ^1H nmr (400 MHz) δ: 0.04 (s, 9H), 0.06 (s, 6H), 0.64–0.86 (m, 3H), 0.87 (d, 3H, J = 6 Hz), 0.93 (d, 3H, J = 6 Hz), 0.90–1.10 (m, 7H), 1.22–1.32 (m, 2H), 1.31 (s, 3H), 1.34 (s, 3H), 1.42 (m, 1H), 1.68–2.10 (m, 7H), 2.21 (br ddd, 1H, J = 13, 3.5, 3.5 Hz), 3.52 (br d, 1H, J = 13 Hz), 4.10 (m, 4H), 4.43 (s, 1H), 4.50 (s, 1H), 4.55 (s, 1H), 4.80 (s, 1H).

To a stirred solution of the dicarbamate (16 mg, 0.027 mmol) in dry THF (0.6 mL) was added a solution of tetra-*n*-butylammonium fluoride in THF (0.21 mL) and the mixture was heated at 50°C for 2 h. The mixture was cooled and concentrated. The residue was treated with pentane (3 mL) and aqueous NH_4Cl–NH_4OH (2 mL, 1.6 mL of saturated aqueous NH_4Cl diluted with 0.4 mL of concentrated aqueous NH_4OH) and the mixture was stirred rapidly for 15 min. The phases were separated and the aqueous layer was washed with pentane (2 × 2 mL). The combined organic extracts were concentrated to provide the crude diamine **48** (~9 mg) as a pale yellow oil. This material was dissolved in dry Et_2O (0.5 mL) containing 30 μL (0.23 mmol) of acetic formic anhydride and the solution was stirred at room temperature for 2 h. Water (2 mL) and Et_2O (3 mL) were added and the phases were separated. The aqueous layer was extracted with Et_2O (2 × 2 mL) and the combined extracts were washed (brine), dried ($MgSO_4$), and concentrated to give the diformamide **49** (~10 mg) as a white solid. The ^1H nmr spectrum of this material showed that it was a mixture of *cis* and *trans* isomers with respect to the formamide functions. A solution of this material in dry CH_2Cl_2 (0.5 mL) was treated with Ph_3P (22.5 mg, 0.086 mmol), dry CCl_4 (8 μL, 0.08 mmol) and dry Et_3N (30 μL, 0.18 mmol) and the mixture was heated at 55°C for 6.5 h. The mixture was concentrated and the solid residue was extracted (triturated) with 1:1 pentane–Et_2O. The combined organic extracts were concentrated and the residue was subjected to flash chromatography (2 g silica gel, 93:7 pentane–Et_2O) to afford 7 mg (41% from the diacid **45**) of (±)-8,15-diisocyano-11(20)-amphilectene (**2**), a crystalline solid (mp 84–86°C) that displayed ir (KBr): 2127, 1647 cm^{-1}; ^1H nmr (400 MHz) δ: 0.78–0.94 (m, 2H), 0.92 (d, 3H, J = 6 Hz), 1.00 (d, 3H, J = 6 Hz), 1.02–1.15 (m, 2H), 1.20–1.50 (m, 4H), 1.45 (t, 3H, J = 2 Hz), 1.47 (t, 3H, J = 2 Hz), 1.54 (m, 2H), 1.85 (dd, 1H, J = 11, 11 Hz), 1.93–2.04 (m, 2H), 2.09 (dd, 1H, J = 15, 2 Hz), 2.23–2.36 (m, 4H), 4.68 (s, 1H), 4.87 (s, 1H); ^{13}C nmr (75.3 MHz, C_6D_6) δ: 15.9, 19.9, 30.0, 30.2, 30.5, 31.5, 33.5, 33.9, 35.6, 39.7, 40.9, 41.2, 42.9, 45.7, 46.3, 55.5, 56.5 (t, J = 4 Hz), 66.9 (t, J = 4 Hz), 106.6, 150.0, 158.1 (t, J = 4 Hz), 159.9 (t, J = 4 Hz). Exact Mass calcd. for $C_{22}H_{32}N_2$: 324.2565; found: 324.2556.

Acknowledgements

We thank the Natural Sciences and Engineering Research Council of Canada for financial support and for an Undergraduate Student Research Award (to R.M.O.). We are grateful to Dr. Miguel Romero for carrying out model studies related to the conversion of the diacid **45** into (±)-**2**.

1. S.J. Wratten, D.J. Faulkner, K. Hirotsu, and J. Clardy. Tetrahedron Lett. 4345 (1978).
2. R. Kazlauskas, P.T. Murphy, R.J. Wells, and J.F. Blount. Tetrahedron Lett. **21**, 315 (1980).
3. T.F. Molinski, D.J. Faulkner, G.D. Van Duyne, and J. Clardy. J. Org. Chem. **52**, 3334 (1987).
4. E. Piers, R.W. Friesen, and B.A. Keay. Tetrahedron, **47**, 4555 (1991).
5. E. Piers, R.W. Friesen, and S.J. Rettig. Can. J. Chem. **70**, 1385 (1992).
6. E. Piers and R.W. Friesen. Can. J. Chem. **65**, 1681 (1987);

E. Piers, R.W. Friesen, P. Kao, S.J. Rettig, and J. Trotter. Can J. Chem. **71**, 1463 (1993).
7. E. Piers and M. Llinas-Brunet. J. Org. Chem. **54**, 1483 (1989).
8. E. Piers and H.L.A. Tse. Tetrahedron Lett. **25**, 3155 (1984).
9. H.J. Reich, J.M. Renga, and I.L. Reich. J. Am. Chem. Soc. **97**, 5434 (1975).
10. G.H. Posner, C.E. Whitten, and J.J. Sterling. J. Am. Chem. Soc. **95**, 7788 (1973).
11. J.-P. Gorlier, L. Hamon, J. Levisalles, and J. Wagnon. J. Chem. Soc. Chem. Commun. **88** (1973); L. Hamon and J. Levisalles. J. Organomet. Chem. **251**, 133 (1983).
12. J.E. McMurry and W.J. Scott. Tetrahedron Lett. **24**, 979 (1983).
13. W.C. Still, M. Kahn, and A. Mitra. J. Org. Chem. **43**, 2923 (1978).
14. S. Krishnamurthy and H.C. Brown. J. Org. Chem. **41**, 3064 (1976).
15. W.G. Salmond, M.A. Barta, and J.L. Havens. J. Org. Chem. **43**, 2057 (1978).
16. D. Caine. Org. React. **23**, 1 (1976).
17. M.J.T. Robinson. Tetrahedron, **21**, 2475 (1965).
18. E. Piers, W.M. Phillips-Johnson, and C. Berger. Can. J. Chem. **53**, 1291 (1975).
19. E.J. Corey, J. Kang, and K. Kyler. Tetrahedron Lett. **26**, 555 (1985).
20. L. Lombardo. Tetrahedron Lett. **23**, 4293 (1982).
21. K. Omura and D. Swern. Tetrahedron, **34**, 1651 (1978).
22. W.C. Still and C. Gennari. Tetrahedron Lett. **24**, 4405 (1983).
23. D. Liotta, U. Sunay, H. Santiesteban, and W. Markiewicz. J. Org. Chem. **46**, 2605 (1981).
24. J.E. Shaw and K.K. Knutson. J. Org. Chem. **36**, 1151 (1971).
25. T. Shioiri, K. Ninomiya, and S. Yamada. J. Am. Chem. Soc. **94**, 6203 (1972).
26. T.L. Capson and C.D. Poulter. Tetrahedron Lett. **25**, 3515 (1984).
27. C.W. Huffman. J. Org. Chem. **23**, 727 (1958).
28. R. Appel, R. Kleinstuck, and K.-D. Ziehn. Angew. Chem. Int. Ed. Engl. **10**, 132 (1971).