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Synthetic study of hetisine-type aconite alkaloids. Part 2: Preparation of hexacyclic compound lacking the C-ring of the hetisan skeleton

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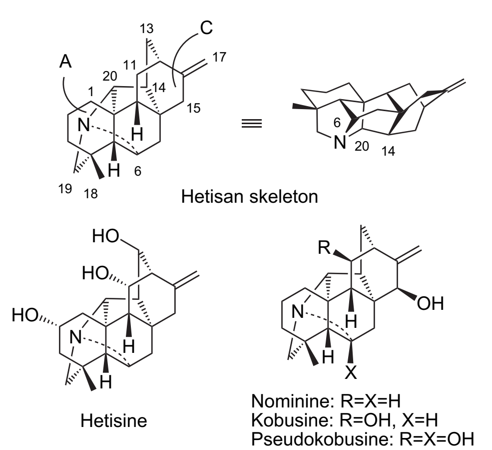
Abstract—A hexacyclic compound **1**, having almost the full hetisine-type aconite alkaloid framework lacking only the C-ring with an *exo*-methylene group, was synthesized from the intermediate **3** reported in the preceding paper. The synthesis involved the following key reactions the crucial conversion of **3** to **4**, a stereoselective hydrocyanation reaction to obtain **5** from **4**, and construction of the azabicyclic ring system (**5**→**1**).

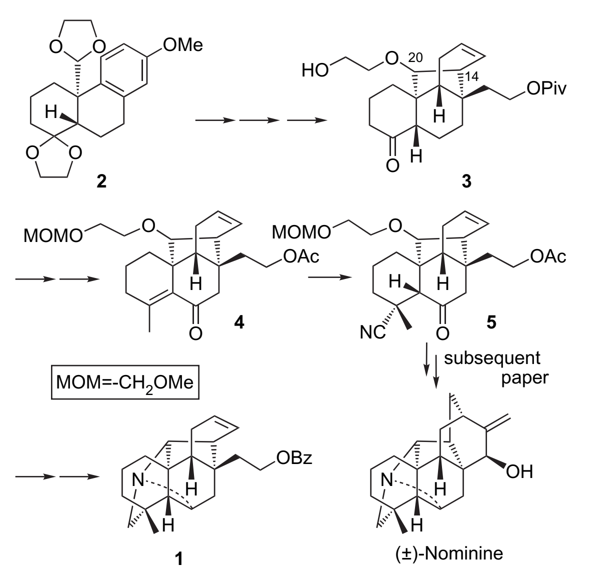
1. Introduction

Over 400 aconite alkaloids have been isolated so far from *Aconitum*, *Delphinium*, *Consolida*, *Thalictrum*, and *Spiraea*. They are generally classified into five skeletons, i.e., atidane, veatchane, cycloveatchane, aconitane, and hetisan (Scheme 1).[1,2] Extensive synthetic investigations over the last 40 years have led to total syntheses of the first four.[3] However, attempts to synthesize hetisine-type aconite alkaloids had met with no success until we recently reported the total synthesis of (±)-nominine.[4] Five synthetic investigations leading toward the total synthesis of this class of aconite alkaloids have been reported so far.[5–9]

It was several years ago that we set out to synthesize hetisine-type aconite alkaloids by applying our palladium-catalyzed intramolecular α-arylation of aliphatic ketone, formyl, and nitro groups.[10] Our synthetic strategy was based on early formation of the N–C6 and C14–C20 bonds, which are characteristic of the hetisan skeleton.[3] We first reported the preparation of the hexacyclic compound **1** lacking the C-ring of the hetisan skeleton by way of the intermediates **2–5** (Scheme 2).[11] Further synthetic efforts culminated in a total synthesis of (±)-nominine.[4] We described in the preceding paper the preparation of the intermediates, such as **3**, with the C14–C20 bond. In this paper (Part 2), we



Scheme 1. Representative hetisine-type alkaloids.



Scheme 2. Outline of the preparation of **1**.

Keywords: Aconite; Alkaloid; Hetisan; Hydrocyanation; Azabicyclic ring.
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present full details of the synthesis of **1** from the intermediate **3**.[3] In the final paper (Part 3), we will deal with the total synthesis of (±)-nominine diverging from the intermediate **5**. These three papers describe in detail the first total synthesis of a hetisine-type aconite alkaloid.

2. Results and discussion

2.1. Seeking a route from the acetal–ene reaction product

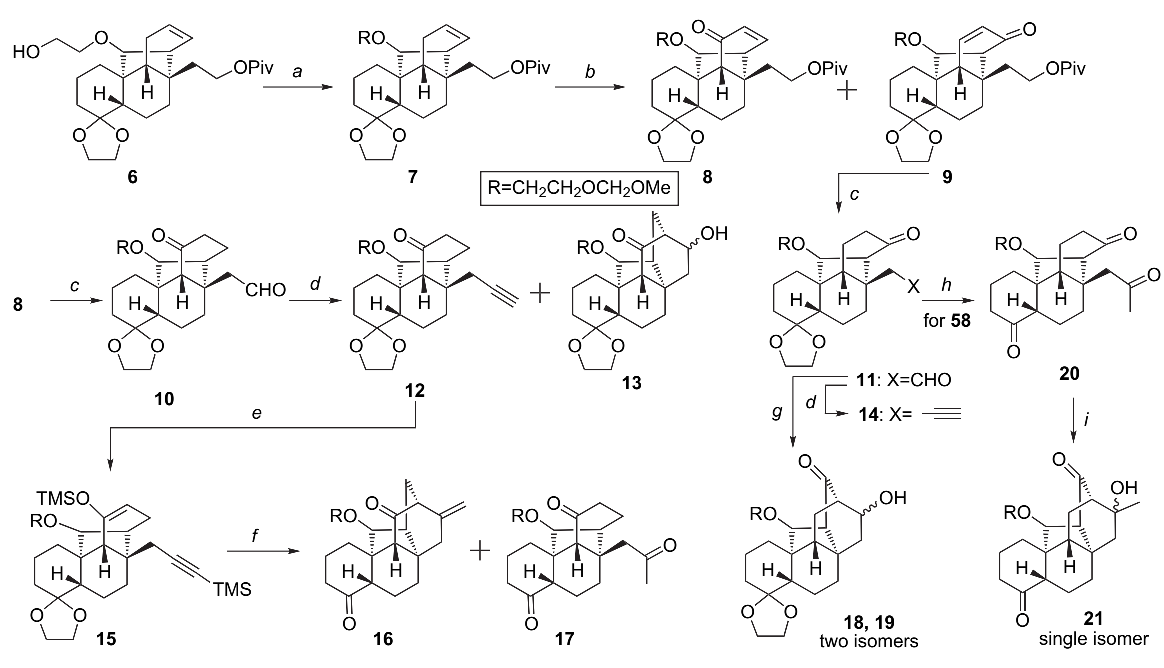
2.1.1. Seeking a method for the C-ring formation. As described in the preceding paper,[3] we planned to form the azabicyclic ring in the final stage of the synthesis, due to its strong basicity. Consequently, for further transformation from the acetal–ene reaction product (e.g., **3**) toward the hetisan skeleton, we considered the following three routes: (1) functionalization of C11, aiming at formation of the C-ring, as well as the synthesis of the alkaloids having a C11 hydroxy group, such as kobusine; (2) elaboration of the C8 side-chain for the C-ring formation; and (3) dehydration to form the $\Delta_{5,6}$ enone for construction of the pyrrolidine ring. After several trials on route (1), we found that chromium trioxide (CrO_3)-3,5-dimethylpyrazole functioned successfully in the oxidation of C11 and C13.[3] Therefore, we examined C-ring formation based on route (1) followed by route (2), starting from compound **6** prepared in the preceding paper (Scheme 3).

After protection of hydroxy group of **6** as methoxymethyl (MOM) ether as usual, the product **7** was oxidized as before[3] with CrO_3 and 3,5-dimethylpyrazole to obtain **8** (43%) and **9** (37%). In order to apply route (2), compound **8** was transformed to the keto-aldehyde **10** via three sequential operations: (i) hydrogenation on palladium (Pd), (ii) methanolysis with potassium carbonate (K_2CO_3), and (iii) oxidation with pyridinium chlorochromate (PCC) supported on alumina (20 wt % PCC–Al_2O_3).[12] The same treatment of **9** provided **11** without difficulty. The additional carbon corresponding to C17 of the hetisan skeleton was introduced at this stage as an alkyne carbon. Thus, dimethyl (1-diazo-2-oxopropyl)phosphonate[13] was allowed to react in the presence of K_2CO_3 with **10** and **11** to afford **12** and **14**, respectively, in high yields. A small quantity of the aldol product **13** was also isolated from **10**.

The carbomercuration and aldol reactions were examined for the C-ring formation from **11** and **12**. Although treatment of the silyl enol ether **15** derived from **12** with mercuric chloride ($HgCl_2$) and 1,1,1,3,3,3-hexamethyldisilazane (HMDS) according to the literature[14] gave no cyclized product, stirring of **15** with mercuric triflate–*N*,*N*,*N*′,*N*′-tetramethylurea complex [$Hg(OTf)_2(TMU)_2$][15] and then with HCl–H_2O secured the desired **16** in 50% yield along with the triketone **17** in 12% yield.

The aldol reaction was also applicable for the C-ring formation. On treatment of **11** with K_2CO_3 in boiling MeOH, two isomeric aldol products **18** and **19** were obtained in 56% and 31% yields, respectively. A similar aldol reaction of **20** with LDA, prepared from **14** with the above $Hg(OTf)_2(TMU)_2$, provided a single isomer **21** in 46% yield together with the recovery of **20** (21%). The stereochemistry of **18**, **19**, and **21** remains unclear.

2.1.2. Dehydrogenative oxidation of 22, 32, and 3 to form the $\Delta_{5,6}$ enone and attempted introduction of a nitrogen function at C6. The hetisan skeleton possesses a nitrogen function at C6 and a pyrrolidine ring, built onto the



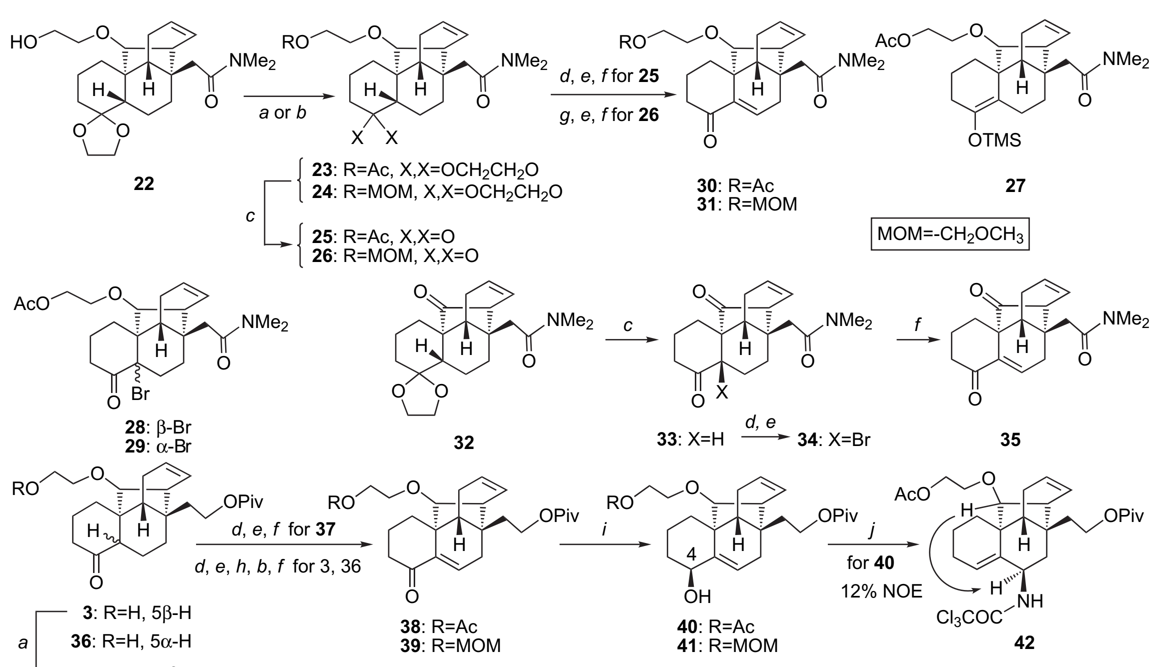
Scheme 3. Seeking a method for the C-ring formation. Reagents and conditions: (a) MOMCl, *i*-Pr_2NEt, CH_2Cl_2, **7** 98%; (b) CrO_3, 3,5-dimethylpyrazole, **8** 43%, **9** 37%; (c) (i) H_2 (1 atm), Pd–C, MeOH; (ii) K_2CO_3, MeOH; (iii) 20% PCC–Al_2O_3, CH_2Cl_2, **10** (i) 95%, (ii) 98%, (iii) 85%; **11** (i) 97%, (ii) 95%, (iii) 90%; (d) dimethyl(1-diazo-2-oxopropyl)phosphonate, K_2CO_3, MeOH, **12** 83%, **13** 7%, **14** 98%; (e) LDA, TMSCl, THF; (f) $Hg(OTf)_2(TMU)_2$, CH_3CN–CH_2Cl_2; then 5% HCl–H_2O, **16** 50% from **12**, **17** 12% from **12**; (g) K_2CO_3, MeOH, **18** 56%, **19** 31%; (h) $Hg(OTf)_2(TMU)_2$, CH_3CN–CH_2Cl_2–H_2O, **20** 80%; (i) LDA, THF, **21** 46%, recovery of **20** 21%.

azabicyclic ring system, is present involving C4, C5, and C6. The N–C6 bond is characteristic of the hetisan skeleton and its early formation accords with our fundamental synthetic strategy. We therefore tried to introduce the $\Delta_{5,6}$ olefin from **22**, **32**, and **3**, which were prepared in the preceding paper[3] (Scheme 4).

The primary alcohol of **22** was protected as an acetate or a MOM ether to obtain **23** and **24**, respectively. These compounds were deprotected with *p*-toluenesulfonic acid (*p*-TsOH) in acetone to yield ketones **25** and **26**, respectively. Acetate **25** was then treated with iodotrimethylsilane (TMSI) and HMDS to afford the thermodynamic enolate **27** selectively.[16] The enolate was allowed to react with *N*-bromosuccinimide (NBS) to acquire the 5-bromo derivatives **28** and **29**. These were separately led to the desired enone **30** by treatment with 1,8-diazabicyclo[5,4,0]undecene-7 (DBU) in benzene. The overall yield of **30** from **25** was improved to 62% without separation at the stage of bromides **28** and **29**. On the other hand, as the MOM group of **26** cannot tolerate the above conditions with TMSI, enolization of **26** was carried out with bromomagnesium diisopropylamide[17] to afford the silyl enol ether corresponding to **27**. This product could be transformed to **31** as above, but in only 27% overall yield from **26**. The four sequential reactions employed for the transformation of **23** to **30** was applied to compound **32** to furnish the keto-enone derivative **35**, though the overall yield was not so good, and only the β-isomer **34** was isolated as the intermediary bromide.

As mentioned above, the best overall yield of enone from the corresponding ketone was obtained in the acetyl series (**25**→**30**), as compared with the MOM (**26**→**31**) or ketone series (**33**→**35**). So, compound **3** was led to **38** by way of **37** in the same manner as above in good yield. But we considered that a MOM group would be preferable as the protecting group for the primary alcohol, rather than acyl groups such as acetyl, because (i) the previously reported ene reaction proceeded in better yield for **3** than for **22**,[3] (ii) discretionary removal of the protecting groups of the two primary alcohol of **3** would be easier in the MOM series than in the acetyl series, as compound **3** bears another acyl function, the pivaloyl group, and (iii) furthermore, the acetyl protecting group would be cleaved during prospective introduction of the C18-methyl group as a carbanion. We therefore devised a suitable reaction sequence to get **39** containing the MOM ether. Thus, after treatment with TMSI, HMDS, and then NBS, the resulting products (mixture of α- and β-bromo derivatives) were stirred briefly with dilute HCl–H_2O to cleave the trimethylsilyl (TMS) group from the 2-(trimethylsilyloxy)ethyl group. The MOM group was introduced at this point, and the resulting mixture was led to the desired enone **39** in a good overall yield of 57% after DBU treatment. In the same manner, **39** was also obtained from the cis isomer **36** in 45% overall yield. This compound **39** became the intermediate in the finally settled synthetic route to (±)-nominine.[4]

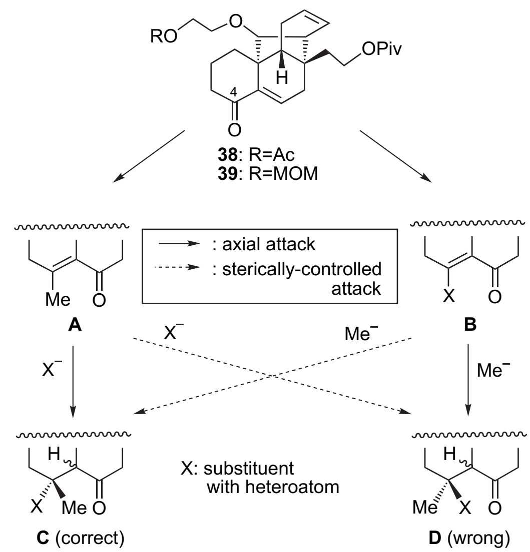
Using compound **38**, we attempted to introduce a nitrogen function at C6 (Scheme 4). Reduction of the enones **38** and **39** with sodium borohydride ($NaBH_4$) and cerium chloride ($CeCl_3$) was found to afford stereoselectively the 4β-OH derivatives **40** and **41**, respectively. Although the stereochemistry of **40** was unclear at this point, it was confirmed after derivation of **40** to **42** as follows. Thus, **40** was reacted with trichloroacetonitrile (CCl_3CN) and DBU[18] in order to



Scheme 4. Dehydrogenative oxidation of **22**, **32**, and **3** to form the $\Delta_{5,6}$-enone and attempted introduction of nitrogen function at C6. Reagents and conditions: (a) Ac_2O, pyridine, CH_2Cl_2, **23** 96% from **22**, **37** 95% from **3**; (b) MOMCl, *i*-Pr_2NEt, CH_2Cl_2, **24** 94% from **22**; (c) *p*-TsOH, acetone, **25** 96% from **23**, **26** 95% from **24**, **33** 94% from **32**; (d) TMSCl, NaI, HMDS, CH_3CN; (e) NBS, THF, **28** 33% overall from **25**, **29** 21% overall from **25**, **34** 70% overall from **33**; (f) DBU, benzene, **30** 87% from **28**, **30** 80% from **29**, **30** 62% overall from **25**, **31** 27% overall from **26**, **35** 69% from **34**, **38** 64% overall from **37**, **39** 57% overall from **3**, **39** 45% overall from **36**; (g) *i*-Pr_2NMgBr, TMSCl, Et_3N, Et_2O-HMPA; (h) 0.2% HCl, THF–H_2O (12:1); (i) $NaBH_4$, $CeCl_3\cdot7H_2O$, MeOH, **40** 92% from **38**, **41** 93% from **39**; (j) CCl_3CN, DBU, CH_2Cl_2, **42** 57% from **40**.

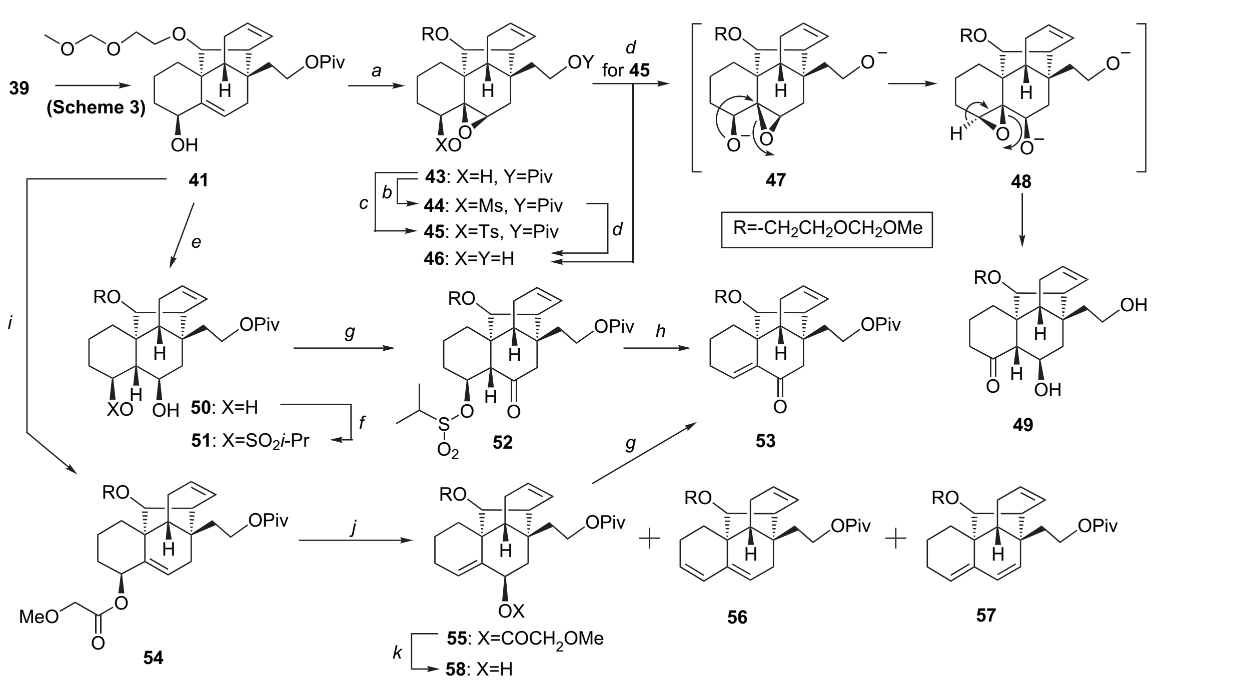
introduce a N-function at C6, affording **42**, whose stereochemistry was proved to be the undesired unnatural β-configuration by means of NOE experiments: 12% NOE enhancement was observed at H6 (δ 4.74–4.87, m) in the ^{1}H NMR NOE difference spectrum on irradiation at H20 (δ 3.91, d, J=6 Hz) of **42**. As this rearrangement reaction proceeds with stereoretention, this means that the stereochemistry of the hydroxy group at C4 of **40** is β. The stereoselectivity is consistent with the 'axial attack of small nucleophiles to cyclohexanone carbonyl group' reported by Cieplak.[19] The knowledge that small nucleophiles attack the C4 carbonyl not from the less-hindered β-side, but from the apparently congested α-side is very important for the subsequent synthetic route toward (±)-nominine, as described below.

2.1.3. Efforts aiming at carbonyl 1,3-transposition from 39. Our next task was to construct the pyrrolidine ring with the correct C4 stereochemistry from the above enone **38** or **39**. The fact that simple reduction of the C4 carbonyl group of **38** and **39** gave stereoselectively the 4β-hydroxy compounds **40** and **41** provided an important clue (Scheme 4). That is, if the 'axial attack of the small nucleophile' was also applicable to the enone **A** or **B** derived from **38** or **39**, the desired **C** with the correct C4 stereochemistry could be secured by the Michael addition of X to the enone **A** carrying a methyl group at C4, where X is a substituent with a heteroatom (Scheme 5). On the other hand, if the sterically controlled attack took precedence over the axial attack, **D** with the wrong stereochemistry would be formed from **A**, and so we would have to allow the enone **B** to react with methyl carbanion in a 1,4-addition manner to obtain compound **C**.



Scheme 5. Construction of C4 quaternary carbon with correct stereochemistry.

With this in mind, we first sought to obtain the 6-oxo-4-ene compound from **39** by means of 1,3-carbonyl transposition reaction (Scheme 6). The allyl alcohol **41** derived from **39** was oxidized with m-chloroperbenzoic acid (m-CPBA) to afford **43** in 90% yield together with the enone **39** in 4% yield. The stereochemistry of **43** was confirmed by observation of a weak NOE enhancement (1.4%) at H6 (δ 3.25, d, J=3.5 Hz) on irradiation at H20 (δ 3.83, d, J=6 Hz) in the ^{1}H NMR spectrum. Then, **43** was readily led to the mesylate **44** with methanesulfonyl chloride (MsCl) and triethylamine



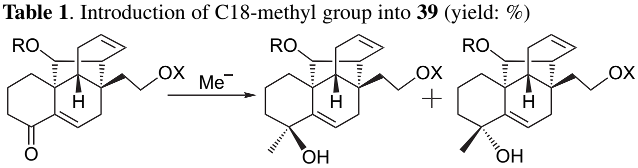
Scheme 6. Efforts aiming at carbonyl 1,3-transposition from **41** to form **53**. Reagents and conditions: (a) m-CPBA, CH_2Cl_2, **43** 90%, **39** 4%; (b) MsCl, Et_3N, CH_2Cl_2, **44** 86%; (c) p-TsCl, Et_3N, CH_2Cl_2, **45** 94%; (d) Na, liq. NH_3, THF, **46** 78% from **44**, **46** 54% from **45**, **49** 36% from **45**; (e) $BH_3\cdot SMe_2$, THF; then H_2O_2, NaOH, **50** 50%, recovery of **41** 20%; (f) i-$PrSO_2Cl$, Et_3N, CH_2Cl_2, **51** 86%; (g) Dess–Martin periodinane, CH_2Cl_2, **52** quant. from **51**, **53** quant. from **58**; (h) DBU, benzene, **53** 91% from **52**; (i) $MeOCH_2COCl$, pyridine, CH_2Cl_2, **54** 86%; (j) $Eu(fod)_3$, $CHCl_3$, **55** 33%, **56** 20%, **57** 20%; (k) K_2CO_3, MeOH, **58** 77%.

(Et_3N). Although we tried to transform **44** to the 6-hydroxy-4-ene derivative under the Birch reduction conditions according to the literature,[20] the sole product was epoxy-diol **46**. This compound was also obtained from tosylate **45** under the same conditions, but in this case, the 6-hydroxy-4-one derivative **49** was also isolated as another product. It is likely that not the C4-oxygen bond, but the sulfone–oxygen bond was cleaved to form **47** due to steric congestion around C4, then intramolecular epoxy-alcohol rearrangement (**48**) and subsequent epoxy-ketone rearrangement took place during post-treatment to yield **49**.

The hydroboration–oxidation protocol afforded the 4,6-di-β-hydroxy compound **50** when an appropriate amount of borane–methyl sulfide complex ($BH_3 \cdot SMe_2$) was used. Selective protection of the 4-hydroxy group was attained by using isopropylsulfonyl chloride (*i*-$PrSO_2Cl$) and Et_3N to furnish **51** in 86% yield. Reaction of **50** with MsCl, Et_3N or TsCl, Et_3N resulted in a dimesylate or recovery of **50**, respectively. Compound **52**, obtained from **51** quantitatively by means of the Dess–Martin oxidation,[21] was led to the desired enone **53** by treatment with DBU. Alternatively, compound **53** was also prepared from **41** as follows. The methoxyacetyl derivative **54** was prepared from **41**, and was subjected to 1,3-allylic rearrangement[22] catalyzed with tris(6,6,7,7,8,8,8-heptafluoro-2,2-dimethyl-3,5-octanedionato)europium(III) [Eu(fod)$_3$] to yield the desired **55**, though in only 33% yield, along with dienes **56** and **57** in 20% yield each. The methoxyacetyl group of **55** was removed and the resulting allyl alcohol **58** was oxidized with Dess–Martin periodinane to yield **53**.

2.1.4. Preparation of the β-methylenone 4 from 39. Since the preparation of **53** from **39** was difficult, as described in Scheme 6, we sought to obtain **4** in a more straightforward manner. Reaction of **39** with methylmagnesium iodide (MeMgI) in THF stereoselectively afforded the 4α-methyl derivative **59** in 38% yield together with recovery of **39** in 30% yield (Table 1, run b). The direction of the methyl carbanion attack is also in accordance with the above-mentioned 'axial attack of small nucleophile'. The recovery of **39** is attributable to enolization of **39** brought about by proton abstraction from C3 or C7 with MeMgI. With the more nonpolar solvent toluene, the enolization is liable to increase (run a). Employment of methyl lithium (MeLi) in place of MeMgI in diethyl ether (Et_2O) provided **59** (48%), its stereoisomer **60** (16%), and recovery of **39** (25%) (run c). Reaction of MeLi in THF, meanwhile, involved cleavage of the pivaloyl group to give **61** (59%), **62** (11%), and **63** (6%), corresponding to recovered enone (run d). The obtained **63** could be reused to furnish **61** (60%) and **62** (12%) (run e). The stereochemistry of **59** and **61** was confirmed by the observation of a NOESY cross peak between C4-α-methyl (axial) and H20 in the ^{1}H NMR spectra. On the other hand, in the ^{1}H NMR spectra of **60** and **62**, a NOESY cross peak was observed between C4-β-methyl (equatorial) and H6 olefin proton. We adopted the reaction conditions of runs d and e in Table 1 for this step toward the hetisine-type aconite alkaloids.

Table 1. Introduction of C18-methyl group into **39** (yield: %)



39: X=Piv
63: X=H

59: X=Piv
61: X=H

60: X=Piv
62: X=H

R=-$CH_2CH_2OCH_2OMe$

Run	Substrate	Me^-	Solvent	59	60	61	62	39	63
a	**39**	MeMgI	Toluene	19	—	—	—	50	—
b	**39**	MeMgI	THF	38	—	—	—	30	—
c	**39**	MeLi	Et_2O	48	16	—	—	25	—
d	**39**	MeLi	THF	—	—	59	11	—	6
e	**63**	MeLi	THF	—	—	60	12	—	—

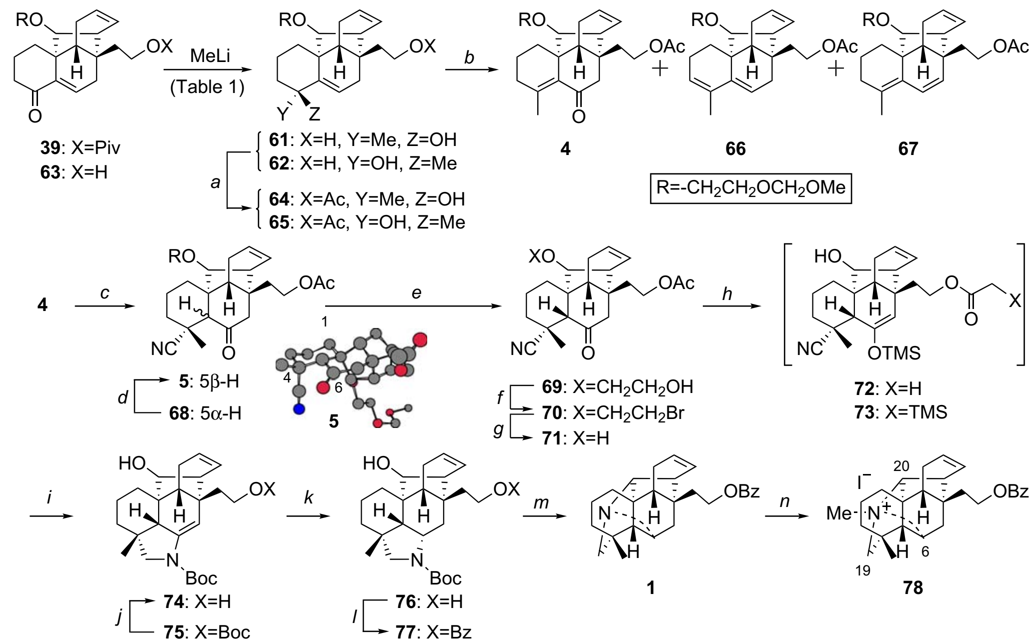
The intermediates **61** and **62** were acetylated as usual to afford **64** and **65** in yields of 93% and 90%, respectively (Scheme 7). Although the resulting tertiary allyl alcohols **64** and **65** were subjected to conventional PCC oxidation in dichloromethane (CH_2Cl_2), the desired enone **4** was obtained only in a trace amount and the major products were the dehydrated dienes **66** and **67**. An extensive search for the optimum oxidizing agent and reaction solvent led to oxidation with 20 wt % PCC–Al_2O_3 in benzene as the conditions of choice. With these conditions, the desired compound **4** was obtained in 63% and 65% yields from **64** and **65** with concomitant formation of **66** and **67** in yields of over 10% each, respectively.

2.2. Transformation of 4 to 1 by way of 5

Our remaining tasks from the intermediate **4** are formation of a pyrrolidine ring bridging between C4 and C6, construction of the azabicyclic ring, and creation and elaboration of the C-ring. Among these, we first focused on the pyrrolidine ring formation by use of the hydrocyanation reaction.

2.2.1. Stereoselective hydrocyanation reaction of 4. Hydrocyanation reaction[23] with diethylaluminum cyanide (Et_2AlCN) in toluene converted **4** to afford the trans isomer **5** with the desired C4 stereochemistry in 94% yield, together with its C5-stereoisomer **68** in 2% yield (Scheme 7). The structure of **5** was proved by the observation of a NOESY cross peak between H5 and C4-methyl as well as between H5 and H9. In the ^{1}H NMR spectrum of **68**, a NOESY cross peak was observed between H5 and H20. No C4-stereoisomer was formed, in complete concordance with the above-described 'axial attack of small nucleophile'. Use of tetrahydrofuran (THF) in place of toluene as the solvent resulted in an intractable reaction mixture. The minor isomer **68** was readily isomerized to thermodynamically more stable **5** on treatment with DBU in boiling benzene.

The 2-(methoxymethoxy)ethyl group at the C20-hydroxy group of **5** was removed at this stage according to the established procedure described in the preceding paper.[3] Thus, the MOM group was first cleaved to **69** with TMSI prepared in situ from chlorotrimethylsilane (TMSCl) and sodium iodide (NaI) in acetonitrile (CH_3CN). HCl treatment of **5** resulted in concomitant cleavage of the acetyl group. The obtained primary alcohol was brominated with carbon tetrabromide (Br_4C) and triphenylphosphine (Ph_3P) to afford **70**, and the

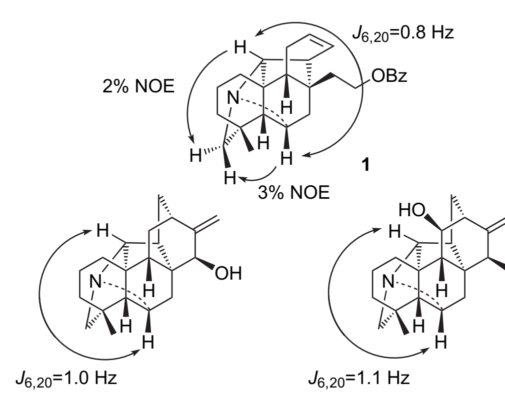


Scheme 7. Preparation of **1** from **61** and **62** by way of stereoselective hydrocyanation of **4** to form **5**. Reagents and conditions: (a) Ac_2O, pyridine, CH_2Cl_2, **64** 93% from **61**, **65** 90% from **62**; (b) 20 wt % PCC–Al_2O_3, benzene, **4** 63%, **66** 16%, **67** 13% from **64**; **4** 65%, **66** 15%, **67** 15% from **65**; (c) Et_2AlCN, toluene, **5** 94%, **68** 2%; (d) DBU, benzene, **5** 92% from **68**; (e) TMSCl, NaI, CH_3CN, **69** 92%; (f) Br_4C, Ph_3P, CH_2Cl_2, **70** 93%; (g) Zn, NH_4Cl, *i*-PrOH–H_2O (14:1), **71** 95%; (h) TMSCl, LDA, THF; (i) $LiAlH_4$, THF; Boc_2O, Et_3N, CH_2Cl_2, **74** 31% overall from **71**, **75** 25% overall from **71**; (j) K_2CO_3, MeOH, **74** 89% from **75**; (k) $NaBH_3CN$, 1% HCl, MeOH–H_2O (8:1), **76** 85%; (l) BzCl, pyridine, CH_2Cl_2, **77** 95%; (m) CF_3COOH, CH_2Cl_2; $SOCl_2$, pyridine, CH_2Cl_2, **1** 78% overall; (n) MeI, MeOH, **78** 73%.

resulting bromide was exposed to zinc (Zn) in the presence of ammonium chloride (NH_4Cl) in 2-propanol–H_2O (14:1) to afford **71** in the high yield of 95%.

2.2.2. Pyrrolidine ring formation from 71. It is necessary to protect the C6 carbonyl group of **71** prior to reduction of the cyano group. However, usual acetalization conditions such as ethylene glycol, *p*-TsOH in boiling benzene or methyl orthoformate, *p*-TsOH in MeOH ended in recovery of **71**, probably due to steric hindrance around the C6 carbonyl group. So the carbonyl group of **71** was protected as the silyl enol ether **72** by reaction with TMSCl and lithium diisopropylamide (LDA) (Scheme 7). At this juncture, formation of a small amount of **73** was observed, but the mixture of **72** and **73** was subjected without further purification to the next step, as the ester function would be cleaved under the reduction conditions of the cyano group. The mixture of **72** and **73** was reduced with lithium aluminum hydride (LAH) in boiling THF. Quenching of the reaction with water-saturated Et_2O involved concomitant cleavage of the silyl enol ether and the resulting amino-carbonyl compound cyclized spontaneously to an intermediary imine compound. The products after stirring the imine with di-*tert*-butyl dicarbonate (Boc_2O) and Et_3N were enamino-carbamates **74** (31% from **71**) and **75** (25% from **71**). The latter carbonate **75** was easily led to the former alcohol **74** on treatment with K_2CO_3 in MeOH. Then, the alkene conjugated to the nitrogen was reduced with sodium cyanoborohydride ($NaBH_3CN$) in a weak acid medium to provide **76** with the pyrrolidine ring.

2.2.3. Synthesis of 1 and its quaternization. Now the synthesis of **1** is in its final stage. After protection of the primary hydroxy group of **76** as the benzoate, the Boc group of the resulting **77** was cleaved with trifluoroacetic acid (CF_3COOH) to give an amino-alcohol (Scheme 7). This was exposed to thionyl chloride ($SOCl_2$) and pyridine[24] in CH_2Cl_2 at an ambient temperature to secure **1** in a good yield. In the ^1H NMR spectrum of **1**, the observations of long-range coupling (0.8 Hz) between H6 and H20 as well as the NOE enhancements at 19β-H and 19α-H on irradiation at H6 and H20, respectively, substantiated the structure (Scheme 8). Long-range coupling between H6 and H20 is also observed in the ^1H NMR spectra of the natural alkaloids nominine and kobusine. All other spectral data of **1** are also consistent with the structure depicted, but nevertheless, definitive structure proof is not an easy matter. The nitrogen involved in the azabicyclo ring system is known to be highly basic. So, the obtained **1** was led to the quaternary salt with methyl iodide (MeI) to get **78** in order to prove the complex



Scheme 8. Long-range coupling and NOE enhancement of **1**.

structure of **1**. In the ^{1}H and ^{13}C NMR spectra of **78**, the proton and carbon signals assigned to positions adjacent to the quaternary nitrogen, H6, H19 (×2), H20, and C6, C19, C20 were all shifted downfield, as described in the experimental section, giving explicit support to the azabicyclic ring structure of **1**.

3. Conclusion

In summary, we have synthesized compound **1** bearing the essential structural features of the hetisine-type aconite alkaloids, by utilizing the following key reactions: (i) dehydrogenative carbonyl 1,3-transposition reaction (**3**→**4**), (ii) stereoselective hydrocyanation reaction to form the natural-type C4 quaternary carbon (**4**→**5**), and (iii) construction of the azabicyclic ring system from **5**. The first total synthesis of hetisine-type aconite alkaloid is still in mid-course. In the subsequent paper, we show how our project was brought to a conclusion, culminated in a total synthesis of (±)-nominine from the intermediate **5**.

4. Experimental

Melting points were determined on a Yanagimoto micromelting point apparatus (hot plate), and are not corrected. MS and high-resolution MS (HRMS) were recorded on a Hitachi M-80B spectrometer in direct inlet mode at an ionizing voltage of 70 eV, and figures in parentheses indicate the relative intensities. IR spectra were measured on a Hitachi 215 or Shimadzu IR-460 spectrophotometer. ^{1}H NMR spectra were obtained on a Varian Mercury 300 (300 MHz) in $CDCl_3$ unless otherwise specified and coupling constants (*J* values) are rounded to the nearest 0.5 Hz. ^{13}C NMR spectra were measured on a Varian Mercury 300 (75 MHz) in $CDCl_3$ and ^{13}C multiplicities are shown in parentheses as CH_3 (primary), CH_2 (secondary), CH (tertiary), and C (quaternary). The NMR signals were assigned using proton decoupling techniques as well as gCOSY, DEPT, gHSQC, gHMBC, and/or NOESY spectra. Some characteristic signals for ^{1}H and ^{13}C NMR were selected and assigned as HX and CX, respectively, where X stands for hetisan carbon numbering. Column chromatography was conducted on silica gel (SiO_2, Fuji Davison BW 200), and the weight of SiO_2 and the eluting solvent are indicated in parentheses. Preparative TLC (PTLC) was carried out on glass plates (20×20 cm) coated with Merck silica gel $60PF_{254}$ (0.8 mm thick) unless otherwise specified, and the developing solvent is indicated in parentheses. Usual work-up refers to washing of the organic layers with water or brine, drying over anhydrous Na_2SO_4, and evaporating off the solvents under reduced pressure. Tetrahydrofuran (THF) was distilled from sodium/benzophenone ketyl prior to use.

4.1. Seeking a method for the C-ring formation (Scheme 3)

4.1.1. Protection of 6 with MOMCl to form 7. MOMCl (64 µl, 0.843 mmol) was added during 1 min to a cooled (−18 °C) solution of **6** (25 mg, 55.8 µmol) and *i*-Pr_2NEt (0.24 ml, 1.38 mmol) in CH_2Cl_2 (4 ml) under an Ar atmosphere. The solution was stirred for 15 h at −18 to 15 °C, then saturated $NaHCO_3$–H_2O was added and the mixture was extracted with CH_2Cl_2. The organic layer was washed successively with saturated $CuSO_4$–H_2O and saturated $NaHCO_3$–H_2O, and was treated as usual. The resulting residue was separated by PTLC [hexane–EtOAc (3:1)] to give **7** (27 mg, 98%) as a colorless glass. HRMS Calcd for $C_{28}H_{44}O_7$: 492.3085. Found: 492.3073. MS *m*/*z*: 492 (M^+, 3), 477 (2), 447 (1), 431 (2), 423 (1), 407 (2), 403 (10), 386 (3), 285 (5), 257 (4), 112 (19), 99 (100), 89 (21), 57 (47), 45 (73). IR ($CHCl_3$) cm^{-1}: 1709. ^{1}H NMR δ: 0.99 (1H, ddd, *J*=13, 13, 4 Hz), 1.10 (9H, s), 1.16–1.27 (2H, m), 1.46–1.90 (9H, m), 2.01–2.13 (2H, m), 2.15 (1H, dddd, *J*=19, 5, 3, 2.5 Hz), 2.33 (1H, br d, *J*=19 Hz), 2.47 (1H, ddd, *J*=7, 6, 1.5 Hz), 3.37 (3H, s, CH_2OCH_3), 3.45 (1H, ddd, *J*=11, 5.5, 5.5 Hz), 3.54 (1H, ddd, *J*=11, 6, 4.5 Hz), 3.58–3.71 (2H, m), 3.73–3.83 (1H, m), 3.84–3.98 (3H, m), 3.99 (1H, ddd, *J*=11, 8.5, 6.5 Hz), 4.13 (1H, ddd, *J*=11, 9, 6 Hz), 4.26 (1H, d, *J*=6 Hz), 4.64 (1H, d, *J*=6.5 Hz, OCH_2OCH_3), 4.67 (1H, d, *J*=6.5 Hz, OCH_2OCH_3), 5.53 (1H, ddd, *J*=9.5, 3, 3 Hz), 5.64 (1H, br dd, *J*=9.5, 7 Hz). ^{13}C NMR δ: 18.3 (CH_2), 20.9 (CH_2), 26.9 (CH_2), 27.2 (CH_3×3), 28.9 (CH_2), 33.7 (CH_2), 34.4 (CH_2), 34.9 (CH_2), 38.6 (C), 42.4 (C), 47.8 (CH), 48.6 (C), 50.8 (CH), 54.8 (CH), 55.0 (CH_3, CH_2OCH_3), 62.7 (CH_2), 63.8 (CH_2), 65.4 (CH_2), 66.7 (CH_2, CH_2OMOM), 68.8 (CH_2), 81.5 (CH), 96.4 (CH_2, OCH_2OCH_3), 110.3 (C), 125.3 (CH), 127.8 (CH), 178.4 (C).

4.1.2. Oxidation of 7 to form 8 and 9. In the same manner as reported in the preceding paper,[3] **7** (48 mg, 97.6 µmol) was oxidized with CrO_3 (146 mg, 1.46 mmol) and 3,5-dimethylpyrazole (169 mg, 1.76 mmol) in CH_2Cl_2 (5 ml) at −18 to 22 °C for 63 h. The same work-up as before and purification by PTLC [hexane–DME (5:1)] provided **8** (21 mg, 43%) and **9** (18.5 mg, 37%) in order of decreasing polarity. **8**: Colorless glass. HRMS Calcd for $C_{28}H_{42}O_8$: 506.2877. Found: 506.2875. MS *m*/*z*: 506 (M^+, 18), 417 (4), 299 (3), 271 (6), 243 (3), 99 (100), 89 (14), 57 (38), 45 (59), 41 (14). IR ($CHCl_3$) cm^{-1}: 1716, 1662. ^{1}H NMR δ: 1.17 (9H, s), 1.22–1.33 (2H, m), 1.45–1.83 (9H, m), 1.86–1.98 (2H, m), 2.09 (1H, br s, H9), 3.10 (1H, ddd, *J*=7, 6, 2 Hz, H14), 3.35 (3H, s), 3.54–3.60 (2H, m), 3.61–3.66 (2H, m), 3.76–3.86 (1H, m), 3.88–4.04 (5H, m), 4.62 (2H, s), 4.62 (1H, br d, *J*=6 Hz), 6.12 (1H, dd, *J*=9.5, 1.5 Hz, H12), 7.09 (1H, dd, *J*=9.5, 7 Hz, H13). ^{13}C NMR δ: 18.0 (CH_2), 20.5 (CH_2), 27.1 (CH_3×3), 29.6 (CH_2), 34.2 (CH_2), 34.4 (CH_2), 34.8 (CH_2), 38.5 (C), 48.1 (C), 50.0 (CH, C9), 50.1 (CH, C14), 50.7 (C), 55.0 (CH_3), 61.6 (CH_2), 64.0 (CH_2), 65.4 (CH_2), 66.6 (CH_2), 69.6 (CH_2), 74.0 (CH), 79.8 (CH), 96.4 (CH_2), 109.6 (C), 129.7 (CH, C12), 151.8 (CH, C13), 178.2 (C), 201.6 (C, C11). **9**: Colorless glass. HRMS Calcd for $C_{28}H_{42}O_8$: 506.2877. Found: 506.2881. MS *m*/*z*: 506 (M^+, 6), 417 (28), 405 (8), 299 (7), 271 (5), 112 (10), 99 (100), 89 (22), 57 (53), 45 (87), 41 (17). IR ($CHCl_3$) cm^{-1}: 1718, 1679. ^{1}H NMR δ: 1.16 (9H, s), 1.21 (1H, ddd, *J*=13, 13, 5 Hz), 1.32 (1H, ddd, *J*=13.5, 13.5, 5 Hz), 1.46–1.57 (3H, m), 1.57–1.83 (7H, m), 1.98–2.06 (1H, m), 2.01 (1H, dd, *J*=6.5, 1.5 Hz, H9), 3.07 (1H, ddd, *J*=6.5, 1.5, 1.5 Hz, H14), 3.33 (3H, s), 3.39–3.47 (1H, m), 3.49–3.63 (3H, m), 3.77–3.86 (1H, m), 3.89–4.02 (5H, m), 4.58 (1H, d, *J*=6.5 Hz), 4.59 (2H, s), 6.12 (1H, dd, *J*=9.5, 1.5 Hz, H12), 6.96 (1H, dd, *J*=9.5, 6.5 Hz, H11).

^{13}C NMR δ: 17.9 (CH_2), 20.3 (CH_2), 27.1 ($CH_3\times3$), 29.8 (CH_2), 32.9 (CH_2), 34.3 (CH, C9), 35.1 (CH_2), 38.5 (C), 49.7 (CH), 50.3 (C), 53.3 (C), 55.0 (CH_3), 57.3 (CH), 61.6 (CH_2), 64.1 (CH_2), 65.4 (CH_2), 65.6 (CH, C14), 66.2 (CH_2), 70.4 (CH_2), 77.8 (CH), 96.3 (CH_2), 109.6 (C), 131.8 (CH, C12), 148.7 (CH, C11), 178.2 (C), 200.0 (C, C13).

4.1.3. Transformation of 8 to 10 by (i) hydrogenation, (ii) alcoholysis, and (iii) oxidation. (i) *Hydrogenation*: A solution of **8** (21 mg, 41.5 μmol) in MeOH (5 ml) was hydrogenated over 10% Pd–C (5 mg, 4.7 μg atom) under a hydrogen atmosphere (1 atm) at 20 °C for 1.5 h. The mixture was filtered through a Celite pad and the pad was rinsed with CH_2Cl_2. Evaporation of the combined organic layers followed by separation by PTLC [hexane–EtOAc (2:1)] furnished the *dihydro derivative* (20 mg, 95%) as a colorless glass. HRMS Calcd for $C_{28}H_{44}O_8$: 508.3034. Found: 508.3020. MS *m/z*: 508 (M^+, 5), 447 (5), 419 (19), 407 (3), 301 (4), 99 (100), 57 (40), 45 (56), 41 (13). IR ($CHCl_3$) cm^{-1}: 1718, 1687. ^{1}H NMR δ: 1.04 (1H, ddd, J=13, 13, 4.5 Hz), 1.17 (9H, s), 1.23–1.42 (2H, m), 1.45–1.88 (11H, m), 1.78 (1H, s, H9), 2.01 (1H, ddd, J=13, 10, 3 Hz, H13), 2.27 (1H, dd, J=18.5, 7.5 Hz, H12), 2.40–2.47 (1H, m), 2.63 (1H, ddd, J=18.5, 10, 9.5 Hz, H12), 3.36 (3H, s), 3.60–3.85 (5H, m), 3.87–4.01 (3H, m), 4.05 (1H, ddd, J=11, 8.5, 6 Hz), 4.47 (1H, d, J=6.5 Hz, H20), 4.65 (2H, s). ^{13}C NMR δ: 17.8 (CH_2), 20.2 (CH_2), 20.5 (CH_2, C13), 27.1 ($CH_3\times3$), 27.3 (CH_2), 33.8 (CH_2), 34.6 (CH_2), 35.1 (CH_2), 36.5 (CH_2, C12), 38.6 (C, *C*Me$_3$), 44.6 (CH, C14), 45.2 (C), 49.0 (C), 49.8 (CH), 55.0 (CH_3), 60.7 (CH_2), 63.9 (CH_2), 65.4 (CH_2), 66.8 (CH_2), 71.0 (CH_2), 73.4 (CH), 78.3 (CH), 96.4 (CH_2), 109.7 (C), 178.4 (C), 214.1 (C). (ii) *Alcoholysis*: A solution of the above dihydro derivative (44 mg, 86.6 μmol) in 2% w/v K_2CO_3–MeOH (5 ml) was stirred under reflux for 2 h. After the mixture had been cooled, saturated NH_4Cl–H_2O was added and the mixture was extracted with CH_2Cl_2. Usual work-up and PTLC [benzene–EtOAc (2:3)] yielded the *primary alcohol* (36 mg, 98%) as a colorless glass. HRMS Calcd for $C_{23}H_{36}O_7$: 424.2459. Found: 424.2456. MS *m/z*: 424 (M^+, 4), 363 (5), 335 (18), 319 (3), 99 (100), 55 (14), 45 (67). IR ($CHCl_3$) cm^{-1}: 1683. ^{1}H NMR δ: 1.03 (1H, ddd, J=13, 13, 4 Hz), 1.28 (1H, ddd, J=13, 13, 4 Hz), 1.33–1.44 (1H, m), 1.46–1.80 (12H, m, including OH), 1.80 (1H, s, H9), 1.99 (1H, ddd, J=13.5, 10, 3 Hz), 2.26 (1H, dd, J=18.5, 7.5 Hz), 2.37–2.44 (1H, m), 2.62 (1H, ddd, J=18.5, 10, 9.5 Hz), 3.36 (3H, s), 3.59–3.85 (7H, m), 3.87–3.99 (3H, m), 4.45 (1H, d, J=6.5 Hz), 4.65 (2H, s). ^{13}C NMR δ: 17.9 (CH_2), 20.2 (CH_2), 20.5 (CH_2), 27.4 (CH_2), 33.8 (CH_2), 35.1 (CH_2), 36.5 (CH_2), 38.9 (CH_2, *C*H$_2$CH$_2$OH), 45.2 (CH), 45.3 (C), 49.1 (C), 49.7 (CH), 55.0 (CH_3), 58.9 (CH_2, CH_2OH), 63.9 (CH_2), 65.4 (CH_2), 66.8 (CH_2), 71.0 (CH_2), 73.1 (CH), 78.2 (CH), 96.4 (CH_2), 109.7 (C), 214.5 (C). (iii) *Oxidation*: PCC–Al_2O_3 (20 wt %, 252 mg, 0.234 mmol) was added to a cooled (0 °C) solution of the above alcohol (33 mg, 77.8 μmol) in CH_2Cl_2 (5 ml) and the mixture was stirred at 0 °C for 30 min and at 18 °C for 1 h. Saturated $NaHCO_3$–H_2O was added and the whole was extracted with CH_2Cl_2. Usual work-up and PTLC [hexane–EtOAc (4:3)] provided **10** (28 mg, 85%) as a colorless glass. HRMS Calcd for $C_{23}H_{34}O_7$: 422.2303. Found: 422.2304. MS *m/z*: 422 (M^+, 2), 361 (5), 333 (13), 99 (100), 89 (8), 55 (14), 45 (77). IR ($CHCl_3$) cm^{-1}: 1717, 1686. ^{1}H NMR δ: 1.06 (1H, ddd, J=13, 13, 4.5 Hz), 1.23–1.41 (2H, m), 1.47–1.81 (8H, m), 1.87 (1H, br s, H9), 1.95–2.04 (1H, m), 2.06 (1H, ddd, J=13.5, 9.5, 3.5 Hz), 2.26 (1H, dd, J=19, 7.5 Hz), 2.37 (1H, d, J=2 Hz, C*H$_2$*CHO), 2.68 (1H, ddd, J=19, 9.5, 9.5 Hz), 2.72–2.78 (1H, m), 3.36 (3H, s), 3.62–3.83 (5H, m), 3.87–4.02 (3H, m), 4.50 (1H, d, J=7 Hz), 4.64 (2H, s), 9.76 (1H, t, J=2 Hz, C*H*O). ^{13}C NMR δ: 17.9 (CH_2), 20.1 (CH_2), 20.9 (CH_2), 27.3 (CH_2), 34.9 (CH_2), 35.0 (CH_2), 36.4 (CH_2), 44.4 (CH), 45.4 (C), 49.0 (C), 49.5 (CH), 50.0 (CH_2, *C*H$_2$CHO), 55.1 (CH_3), 63.9 (CH_2), 65.5 (CH_2), 66.8 (CH_2), 71.1 (CH_2), 72.7 (CH), 78.0 (CH), 96.4 (CH_2), 109.6 (C), 200.4 (CH, CHO), 213.5 (C).

4.1.4. Transformation of 9 to 11. In the same manner as described for the preparation of **10** from **8** (Section 4.1.3), **9** (43 mg, 85.0 μmol) was hydrogenated to the dihydro derivative (42 mg, 97%). This compound (24 mg, 47.2 μmol) was subjected to alcoholysis to get the primary alcohol (19 mg, 95%), which was then oxidized to **11** (17 mg, 90%). The *dihydro derivative*: colorless glass. HRMS Calcd for $C_{28}H_{44}O_8$: 508.3034. Found: 508.3050. MS *m/z*: 508 (M^+, 3), 493 (2), 463 (2), 419 (23), 317 (6), 301 (8), 99 (100), 57 (47), 45 (73), 41 (17). IR ($CHCl_3$) cm^{-1}: 1714, 1699. ^{1}H NMR δ: 1.08–1.20 (1H, m), 1.17 (9H, s), 1.23–1.35 (1H, m), 1.42–1.46 (1H, m, H9), 1.46–1.91 (11H, m), 1.96–2.11 (1H, m), 2.11 (1H, br d, J=13 Hz), 2.21 (1H, dd, J=18, 9 Hz, H12), 2.66 (1H, ddd, J=18, 10, 10 Hz, H12), 2.83 (1H, d, J=7 Hz, H14), 3.35 (3H, s), 3.43–3.63 (4H, m), 3.75–3.85 (1H, m), 3.88–4.00 (3H, m), 4.01 (1H, ddd, J=11, 8, 6.5 Hz), 4.13 (1H, ddd, J=11, 8, 7 Hz), 4.47 (1H, d, J=7 Hz, H20), 4.60 (1H, d, J=6.5 Hz), 4.62 (1H, d, J=6.5 Hz). ^{13}C NMR δ: 18.0 (CH_2), 19.2 (CH_2, C11), 20.2 (CH_2), 27.1 ($CH_3\times3$), 28.1 (CH_2), 33.3 (CH_2), 33.5 (CH_2), 34.8 (CH_2), 35.5 (CH_2, C12), 38.5 (C), 45.8 (C), 48.0 (C), 50.2 (CH), 53.5 (CH, C9), 54.9 (CH_3), 60.9 (CH_2), 63.9 (CH_2), 65.1 (CH, C14), 65.4 (CH_2), 66.3 (CH_2), 69.9 (CH_2), 77.3 (CH), 96.1 (CH_2), 109.8 (C), 178.2 (C), 210.7 (C). The *primary alcohol*: colorless glass. HRMS Calcd for $C_{23}H_{36}O_7$: 424.2459. Found: 424.2453. MS *m/z*: 424 (M^+, 3), 409 (3), 335 (30), 319 (7), 112 (11), 99 (100), 55 (20), 45 (90). IR ($CHCl_3$) cm^{-1}: 1696. ^{1}H NMR δ: 1.08–1.19 (1H, m), 1.23–1.34 (1H, m), 1.38–1.43 (1H, m), 1.43–1.83 (9H, m, including OH), 1.53 (2H, t, J=7.5 Hz, C*H$_2$*CH$_2$OH), 1.85 (1H, dddd, J=14.5, 10, 9, 4.5 Hz, H11), 2.01 (1H, br dd, J=14.5, 10 Hz, H11), 2.20 (1H, dd, J=18, 9 Hz), 2.67 (1H, ddd, J=18, 10, 10 Hz), 2.89 (1H, d, J=7 Hz), 3.35 (3H, s), 3.43–3.63 (4H, m), 3.68 (2H, t, J=7.5 Hz, C*H$_2$*OH), 3.75–3.84 (1H, m), 3.87–3.98 (3H, m), 4.46 (1H, d, J=7 Hz, H20), 4.59 (1H, d, J=6.5 Hz), 4.63 (1H, d, J=6.5 Hz). ^{13}C NMR δ: 18.0 (CH_2), 19.3 (CH_2), 20.2 (CH_2), 28.1 (CH_2), 33.7 (CH_2, *C*H$_2$CH$_2$OH), 34.9 (CH_2), 35.7 (CH_2), 37.7 (CH_2), 46.1 (C), 47.7 (C), 50.3 (CH), 54.3 (CH), 55.0 (CH_3), 59.0 (CH_2, CH_2OH), 63.9 (CH_2), 64.7 (CH), 65.4 (CH_2), 66.3 (CH_2), 69.9 (CH_2), 77.6 (CH), 96.2 (CH_2), 109.9 (C), 211.9 (C). **11**: Colorless glass. HRMS Calcd for $C_{23}H_{34}O_7$: 422.2303. Found: 422.2302. MS *m/z*: 422 (M^+, 3), 407 (4), 333 (26), 112 (20), 99 (100), 89 (12), 86 (13), 55 (16), 45 (90). IR ($CHCl_3$) cm^{-1}: 1717, 1700. ^{1}H NMR δ: 1.11–1.23 (1H, m), 1.24–1.36 (1H, m), 1.43–1.83 (10H, m), 2.02–2.17 (2H, m), 2.22 (1H, dd, J=18, 9 Hz), 2.27 (1H, dd,

J=16, 2.5 Hz, CH_2CHO), 2.37 (1H, dd, J=16, 2 Hz, CH_2CHO), 2.73 (1H, ddd, J=18, 10.5, 10.5 Hz), 3.02 (1H, d, J=7 Hz, H14), 3.35 (3H, s), 3.46–3.64 (4H, m), 3.75–3.85 (1H, m), 3.88–3.99 (3H, m), 4.51 (1H, d, J=7 Hz, H20), 4.61 (1H, d, J=6.5 Hz), 4.63 (1H, d, J=6.5 Hz), 9.73 (1H, dd, J=2.5, 2 Hz, CHO). ^{13}C NMR δ: 18.0 (CH_2), 19.5 (CH_2), 20.2 (CH_2), 28.0 (CH_2), 34.7 (CH_2), 34.8 (CH_2), 35.5 (CH_2), 46.1 (C), 47.7 (C), 48.7 (CH_2, CH_2CHO), 50.1 (CH), 53.3 (CH), 55.0 (CH_3), 63.9 (CH_2), 64.5 (CH, C14), 65.4 (CH_2), 66.3 (CH_2), 70.1 (CH_2), 77.1 (CH, C20), 96.2 (CH_2), 109.8 (C), 200.6 (CH, CHO), 210.5 (C).

4.1.5. Preparation of acetylene 12 from 10. K_2CO_3 (18 mg, 0.130 mmol) was added to a solution of **10** (14 mg, 33.2 μmol) and dimethyl (1-diazo-2-oxopropyl)-phosphonate (38 mg, 0.198 mmol) in MeOH (3 ml) and the mixture was stirred at 19 °C under an Ar atmosphere for 3.5 h. Saturated NH_4Cl–H_2O was added and the whole was extracted with CH_2Cl_2. Usual work-up and separation by PTLC [hexane–EtOAc (3:2)] afforded **12** (11.5 mg, 83%) and **13** (1 mg, 7%) in order of increasing polarity. **12**: Colorless glass. HRMS Calcd for $C_{24}H_{34}O_6$: 418.2353. Found: 418.2348. MS m/z: 418 (M^+, 11), 357 (6), 329 (21), 99 (100), 55 (16), 45 (76). IR ($CHCl_3$) cm^{-1}: 2116, 1686. ^{1}H NMR δ: 1.05 (1H, ddd, J=13, 13, 4.5 Hz), 1.23–1.43 (2H, m), 1.47–1.85 (8H, m), 1.77 (1H, br s, H9), 1.97 (1H, dd, J=2.5, 2.5 Hz, C≡CH), 1.97–2.17 (4H, m), 2.26 (1H, dd, J=18.5, 7.5 Hz, H12), 2.51–2.57 (1H, m), 2.65 (1H, ddd, J=18.5, 9.5, 9.5 Hz, H12), 3.37 (3H, s), 3.60–3.84 (5H, m), 3.88–4.00 (3H, m), 4.47 (1H, d, J=7 Hz, H20), 4.65 (2H, s). ^{13}C NMR δ: 17.9 (CH_2), 20.2 (CH_2), 20.6 (CH_2), 26.2 (CH_2, CH_2C≡CH), 27.4 (CH_2), 34.4 (CH_2), 35.1 (CH_2), 36.5 (CH_2), 44.5 (CH), 46.3 (C), 49.7 (CH), 50.1 (C), 55.1 (CH_3), 63.9 (CH_2), 65.5 (CH_2), 66.8 (CH_2), 70.1 (C, *C*≡CH), 71.0 (CH_2), 72.0 (CH), 77.9 (CH), 80.7 (CH, C≡*C*H), 96.4 (CH_2), 109.7 (C), 213.8 (C). **13**: Colorless glass. HRMS Calcd for $C_{23}H_{34}O_7$: 422.2303. Found: 422.2303. MS m/z: 422 (M^+, 2), 407 (3), 361 (9), 333 (33), 99 (100), 69 (18), 55 (16), 45 (71). IR ($CHCl_3$) cm^{-1}: 1701. ^{1}H NMR δ: 1.21–1.95 (15H, m, including OH), 1.52 (1H, dd, J=14.5, 6 Hz, H15), 1.91 (1H, dd, J=14.5, 9.5 Hz, H15), 2.27–2.31 (1H, m), 2.35 (1H, dddd, J=7, 7, 2, 2 Hz, H14), 3.35 (3H, s), 3.40–3.48 (1H, m), 3.54–3.71 (3H, m), 3.74–3.84 (1H, m), 3.86–3.98 (3H, m), 3.99–4.07 (1H, m, H16), 4.20 (1H, d, J=7 Hz, H20), 4.62 (2H, s). ^{13}C NMR δ: 12.7 (CH_2, C13), 17.8 (CH_2, C6), 20.0 (CH_2, C2), 28.1 (CH_2, C1), 34.5 (CH_2, C7), 35.2 (CH_2, C3), 37.4 (CH_2, C15), 43.0 (C, C8), 45.2 (CH, C14), 49.2 (C, C10), 50.1 (CH, C5), 52.5 (CH, C12), 55.0 (CH_3), 63.9 (CH_2), 65.1 (CH, C9), 65.4 (CH_2), 66.5 (CH_2), 67.8 (CH, C16), 70.3 (CH_2), 77.7 (CH, C20), 96.4 (CH_2), 110.0 (C), 214.1 (C).

4.1.6. Preparation of acetylene 14 from 11. In the same manner as above (Section 4.1.5), **11** (40 mg, 94.8 μmol) was led to **14** (39 mg, 98%) as a colorless glass. HRMS Calcd for $C_{24}H_{34}O_6$: 418.2353. Found: 418.2334. MS m/z: 418 (M^+, 6), 329 (36), 313 (10), 112 (12), 99 (100), 89 (17), 55 (14), 45 (85). IR ($CHCl_3$) cm^{-1}: 2122, 1698. ^{1}H NMR δ: 1.09–1.21 (1H, m), 1.23–1.35 (1H, m), 1.43–1.67 (5H, m), 1.71–2.15 (9H, m), 1.99 (1H, dd, J=2.5, 2.5 Hz, C≡CH), 2.21 (1H, dd, J=18, 9 Hz, H12), 2.68 (1H, ddd, J=18, 10.5, 10.5 Hz, H12), 2.83 (1H, d, J=6.5 Hz, H14), 3.35 (3H, s), 3.43–3.63 (4H, m), 3.76–3.86 (1H, m), 3.88–4.01 (3H, m), 4.51 (1H, d, J=6.5 Hz, H20), 4.60 (1H, d, J=6.5 Hz), 4.62 (1H, d, J=6.5 Hz). ^{13}C NMR δ: 17.9 (CH_2), 19.3 (CH_2), 20.2 (CH_2), 25.2 (CH_2), 28.1 (CH_2), 33.9 (CH_2), 34.9 (CH_2), 35.7 (CH_2), 46.8 (C), 47.9 (C), 50.2 (CH), 52.5 (CH), 55.0 (CH_3), 63.9 (CH_2), 64.3 (CH, C14), 65.4 (CH_2), 66.3 (CH_2), 70.0 (CH_2), 70.3 (C, *C*≡CH), 77.8 (CH, C20), 80.7 (CH, C≡*C*H), 96.2 (CH_2), 109.9 (C), 210.6 (C).

4.1.7. Carbomercuration of 12 to form 16 and 17. BuLi (1.57 M, 0.55 ml, 0.864 mmol) was added to a cooled (−18 °C) solution of diisopropylamine (151 μl, 1.08 mmol) in THF (2 ml) under an Ar atmosphere and the mixture was stirred at the same temperature for 10 min. The resulting solution was cooled to −78 °C and to this were added TMSCl (0.27 ml, 2.13 mmol) and then a THF (2 ml) solution of **12** (9 mg, 21.5 μmol). The mixture was stirred at −78 °C for 30 min, then Et_3N (0.60 ml, 4.31 mmol) was added, and the resulting mixture was further stirred for 5 min. Saturated $NaHCO_3$–H_2O was added and the whole was extracted with CH_2Cl_2. The organic layer was successively washed with saturated $CuSO_4$–H_2O, saturated $NaHCO_3$–H_2O and H_2O, and treated as usual to give crude **15** (15 mg). Aside from this, trifluoromethanesulfonic anhydride (Tf_2O, 8 μl, 47.6 μmol) was added to a slurry of mercury(II) oxide (HgO, 10.5 mg, 48.5 μmol) in CH_3CN (1.5 ml) at 0 °C and the mixture was stirred at the same temperature under an Ar atmosphere for 3 min. *N*,*N*,*N*′,*N*′-Tetramethylurea (TMU, 12 μl, 0.100 mmol) was further added, and the whole was stirred at 0 °C for 3 min and at 20 °C for 10 min, then cooled again in an ice bath. The crude **15** (15 mg) in CH_2Cl_2 (2 ml) was added and the resulting mixture was stirred at 0 °C for 1 h and at 22 °C for 15 h. After the mixture had been cooled to 0 °C, 2.5% HCl–H_2O (0.48 ml, 0.324 mmol) was added and the mixture was stirred at 0 °C for 10 min and at 18 °C for 2 h. Saturated $NaHCO_3$–H_2O was added and the whole was extracted with CH_2Cl_2. Usual work-up and PTLC [hexane–EtOAc (3:2)] afforded **16** (2 mg) and a mixture of organo-mercury compounds (12 mg). The latter was dissolved in MeOH (2 ml), and to this was added p-TsOH·H_2O (10 mg, 52.6 μmol). The resulting solution was stirred at 19 °C for 1.5 h. Quenching with saturated $NaHCO_3$–H_2O, extraction with CH_2Cl_2, usual work-up, and PTLC [hexane–EtOAc (5:2)] gave a further crop of **16** (2 mg, total 4 mg, 50%) and **17** (1 mg, 12%) in order of increasing polarity. **16**: Colorless glass. HRMS Calcd for $C_{22}H_{30}O_5$: 374.2092. Found: 374.2088. MS m/z: 374 (M^+, 0.5), 342 (1), 329 (4), 268 (6), 239 (14), 91 (14), 45 (100). IR ($CHCl_3$) cm^{-1}: 1704, 1693, 1646. ^{1}H NMR δ: 1.37–1.47 (1H, m, H7), 1.54 (1H, dd, J=13, 9 Hz, H13), 1.59–1.81 (5H, m), 1.84 (1H, br s, H9), 1.94–2.03 (1H, m, H2), 2.06–2.14 (1H, m, H1), 2.20 (1H, ddd, J=16.5, 1.5, 1.5 Hz, H15), 2.21–2.43 (4H, m), 2.23 (1H, dd, J=13, 5 Hz, H13), 2.52 (1H, ddd, J=16.5, 3, 3 Hz, H15), 2.89 (1H, d, J=5 Hz, H12), 3.28 (1H, ddd, J=10, 5.5, 4 Hz), 3.33 (3H, s), 3.42 (1H, dd, J=6.5, 0.5 Hz, H20), 3.49 (1H, ddd, J=10, 6, 4 Hz), 3.53–3.64 (2H, m), 4.58 (2H, s), 4.72 (1H, br s, C=CH_2), 4.91 (1H, br s, C=CH_2). ^{13}C NMR δ: 19.1 (CH_2, C6), 20.9 (CH_2, C13), 23.7 (CH_2, C2), 28.1 (CH_2, C1), 33.6 (CH_2, C7), 35.6 (CH_2, C15), 41.9 (CH_2, C3), 43.4 (C, C8), 44.1 (CH, C14), 53.1 (C, C10), 54.3 (CH, C12), 55.1 (CH_3), 55.7 (CH, C5), 64.8 (CH, C9), 66.3 (CH_2), 70.3 (CH_2), 79.0 (CH, C20), 96.3 (CH_2), 109.0 (CH_2, C17), 143.8 (C, C16), 209.5 (C, C11), 211.4 (C, C4). **17**: Colorless glass. HRMS Calcd for $C_{22}H_{32}O_6$: 392.2197. Found: 392.2207. MS *m/z*: 392 (M^+, 1), 360 (1), 347 (7), 302 (5), 289 (4), 91 (10), 89 (9), 73 (10), 59 (13), 55 (12), 45 (100), 43 (49). IR ($CHCl_3$) cm^{-1}: 1696. ^1H NMR δ: 1.20 (1H, ddd, J=13, 13, 7 Hz, H7), 1.41–1.90 (5H, m), 1.91–2.47 (8H, m), 2.01 (1H, br s, H9), 2.11 (3H, s, $COCH_3$), 2.38 (1H, d, J=18 Hz, CH_2COMe), 2.47 (1H, d, J=18 Hz, CH_2COMe), 2.67 (1H, ddd, J=19, 9.5, 9.5 Hz), 2.96–3.02 (1H, m), 3.34 (3H, s), 3.33–3.51 (1H, m), 3.59–3.70 (3H, m), 3.70 (1H, d, J=6.5 Hz, H20), 4.60 (2H, s). ^{13}C NMR δ: 18.7 (CH_2), 20.9 (CH_2), 23.9 (CH_2), 27.5 (CH_2), 31.4 (CH_3, $COCH_3$), 33.4 (CH_2), 36.6 (CH_2), 41.8 (CH_2, C3), 43.8 (CH), 45.7 (C), 48.9 (CH_2, CH_2COMe), 52.9 (C), 55.1 (CH_3), 55.3 (CH, C5), 66.7 (CH_2), 71.1 (CH_2), 72.0 (CH), 79.2 (CH), 96.3 (CH_2), 206.1 (C, *C*OMe), 210.6 (C, C4), 213.2 (C, C11).

4.1.8. Aldol reaction of 11 to form 18 and 19. A solution of **11** (8 mg, 19.0 μmol) in K_2CO_3–MeOH (2% w/v, 2 ml) was stirred at 50 °C for 4 h. After the mixture had been cooled, saturated NH_4Cl–H_2O was added and the whole was extracted with CH_2Cl_2. Usual work-up and PTLC [hexane–EtOAc (1:2)] afforded **18** (4.5 mg, 56%) and **19** (2.5 mg, 31%) in order of decreasing polarity. **18**: Colorless glass. HRMS Calcd for $C_{23}H_{34}O_7$: 422.2303. Found: 422.2325. MS *m/z*: 422 (M^+, 1), 333 (38), 317 (21), 99 (100), 55 (19), 45 (91). IR ($CHCl_3$) cm^{-1}: 1710. ^1H NMR δ: 0.98 (1H, ddd, J=13, 13, 4 Hz), 1.19–1.72 (11H, m), 1.74–1.84 (2H, m, including OH), 2.07 (1H, dd, J=15, 9.5 Hz), 2.14–2.24 (2H, m), 2.34 (1H, br d, J=13 Hz), 2.72 (1H, dd, J=7, 2 Hz, H14), 3.35 (3H, s), 3.38–3.46 (1H, m), 3.54–3.60 (2H, m), 3.74–3.84 (2H, m), 3.88–3.99 (3H, m), 4.00–4.09 (1H, m, H16), 4.38 (1H, dd, J=7, 1.5 Hz, H20), 4.62 (2H, s). **19**: Colorless glass. HRMS Calcd for $C_{23}H_{34}O_7$: 422.2303. Found: 422.2292. MS *m/z*: 422 (M^+, 2), 407 (3), 377 (4), 333 (44), 317 (14), 99 (100), 55 (16), 45 (77). IR ($CHCl_3$) cm^{-1}: 1714. ^1H NMR δ: 0.98 (1H, ddd, J=12.5, 12.5, 4 Hz), 1.17–1.72 (10H, m, including OH), 1.39 (1H, dd, J=15.5, 2.5 Hz, H15), 1.79 (1H, br d, J=13 Hz), 1.89 (1H, dd, J=15.5, 9.5 Hz, H15), 1.89–1.95 (1H, m), 2.11 (1H, ddd, J=14, 10, 1.5 Hz), 2.26–2.31 (1H, m, H12), 2.36 (1H, br d, J=12.5 Hz), 2.57 (1H, dd, J=7.5, 2 Hz, H14), 3.35 (3H, s), 3.37–3.46 (1H, m), 3.52–3.62 (2H, m), 3.72–3.83 (2H, m), 3.88–3.98 (3H, m), 4.01–4.10 (1H, m, H16), 4.38 (1H, dd, J=7.5, 1.5 Hz, H20), 4.62 (2H, s).

4.1.9. Hydration of 14 to form 20. Tf_2O (8 μl, 47.6 μmol) was added to a cooled (0 °C) slurry of HgO (10.5 mg, 48.5 μmol) in CH_3CN (2 ml) and the mixture was stirred for 3 min. TMU (11.5 μl, 96.3 μmol) was added to this and the resulting mixture was stirred at 0 °C for 3 min and at 20 °C for 5 min. This solution of $Hg(OTf)_2(TMU)_2$ in CH_3CN (0.20 ml) was added to a solution of **14** (20 mg, 47.8 μmol) in CH_2Cl_2 (1 ml). H_2O (9 μl, 0.50 mmol) and CH_3CN (0.8 ml) were further added and the whole was stirred at 22 °C for 40 h. Quenching with saturated $NaHCO_3$–H_2O, extraction with CH_2Cl_2, usual work-up, and PTLC [hexane–EtOAc (1:1)] yielded **20** (15 mg, 80%) as a colorless glass. HRMS Calcd for $C_{22}H_{32}O_6$: 392.2197. Found: 392.2181. MS *m/z*: 392 (M^+, 1), 347 (10), 303 (6), 245 (6), 229 (8), 91 (10), 89 (8), 73 (16), 45 (100), 43 (54). IR ($CHCl_3$) cm^{-1}: 1699. ^1H NMR δ: 1.50–1.57 (1H, m), 1.61–1.93 (6H, m), 2.00–2.14 (3H, m), 2.10 (3H, s), 2.17–2.44 (5H, m), 2.29 (1H, d, J=17.5 Hz, CH_2Ac), 2.44 (1H, d, J=17.5 Hz, CH_2Ac), 2.69 (1H, ddd, J=18.5, 10.5, 10 Hz, H12), 2.96 (1H, d, J=6.5 Hz, H14), 3.28–3.37 (1H, m), 3.32 (3H, s), 3.46–3.53 (3H, m), 3.68 (1H, d, J=6.5 Hz, H20), 4.56 (2H, s). ^{13}C NMR δ: 18.9 (CH_2), 19.7 (CH_2), 24.0 (CH_2), 28.0 (CH_2), 31.9 (CH_3), 32.7 (CH_2), 35.7 (CH_2), 41.4 (CH_2), 46.5 (C), 47.5 (CH_2, CH_2Ac), 51.4 (CH), 52.7 (C), 55.0 (CH_3), 55.9 (CH), 65.0 (CH), 66.3 (CH_2), 70.0 (CH_2), 78.0 (CH), 96.1 (CH_2), 206.4 (C, *C*OMe), 210.0 (C, C13), 211.5 (C, C4).

4.1.10. Aldol reaction of 20 with LDA to form 21. BuLi (1.57 M, 0.97 ml, 1.52 mmol) was added to a cooled (−18 °C) solution of i-Pr_2NH (0.28 ml, 2.00 mmol) in THF (2 ml) and the mixture was stirred under an Ar atmosphere for 10 min. After the mixture had been cooled to −78 °C, a solution of **20** (12 mg, 30.6 μmol) in THF (2 ml) was added and the whole was stirred for 1 h. Saturated NH_4Cl–H_2O was added and the whole was extracted with CH_2Cl_2. Usual work-up and purification by PTLC [hexane–EtOAc (2:3)] provided a recovery of **20** (2.5 mg, 21%) and **21** (5.5 mg, 46%) as a colorless glass in order of increasing polarity. HRMS Calcd for $C_{22}H_{32}O_6$: 392.2197. Found: 392.2177. MS *m/z*: 392 (M^+, 0.2), 329 (5), 287 (12), 241 (15), 105 (10), 91 (10), 55 (14), 45 (100), 43 (29). IR ($CHCl_3$) cm^{-1}: 1702. ^1H NMR δ: 1.21–1.78 (9H, m, including OH), 1.36 (3H, s), 1.60 (1H, d, J=15.5 Hz, H15), 1.68 (1H, d, J=15.5 Hz, H15), 1.83 (1H, ddd, J=15, 10.5, 1.5 Hz, H11), 2.14 (1H, ddd, J=15, 4, 2 Hz, H11), 2.00 (1H, dd, J=4, 1.5 Hz, H12), 2.25–2.42 (3H, m), 2.46 (1H, br ddd, J=13, 3, 3 Hz), 2.72 (1H, dd, J=7.5, 2 Hz, H14), 3.23–3.37 (1H, m), 3.33 (3H, s), 3.45–3.56 (2H, m), 3.59 (1H, dd, J=7.5, 1.5 Hz, H20), 3.80 (1H, ddd, J=10.5, 4, 4 Hz), 4.57 (2H, s). ^{13}C NMR δ: 19.1 (CH_2), 19.9 (CH_2), 23.2 (CH_2), 27.3 (CH_2), 28.7 (CH_3), 34.1 (CH_2), 41.6 (CH_2), 44.8 (C), 45.2 (CH_2), 48.8 (CH, C9), 54.2 (CH, C12), 55.0 (C), 55.1 (CH_3), 55.5 (CH, C5), 61.4 (CH, C14), 66.5 (CH_2), 71.0 (CH_2), 72.3 (C), 81.5 (CH, C20), 96.2 (CH_2), 211.4 (C), 212.0 (C).

4.2. Oxidation of 22, 32, and 3 to form the $\Delta_{5,6}$ enone and attempted introduction of nitrogen function at C6 (Scheme 4)

4.2.1. Acetylation of 22 to form 23. A solution of **22** (18 mg, 44.4 μmol), Ac_2O (0.30 ml, 0.277 mmol), and pyridine (0.50 ml, 0.510 mmol) in CH_2Cl_2 (1.5 ml) was stirred at 27 °C for 4 h. Saturated $NaHCO_3$–H_2O was added and the mixture was extracted with CH_2Cl_2. Usual work-up and separation by PTLC [hexane–DME (2:1)] gave **23** (19 mg, 96%) as a colorless glass. HRMS Calcd for $C_{25}H_{37}NO_6$: 447.2619. Found: 447.2621. MS *m/z*: 447 (M^+, 23), 402 (4), 388 (8), 360 (30), 343 (19), 273 (9), 257 (13), 256 (12), 99 (53), 87 (100), 72 (14), 55 (9), 43 (42). IR ($CHCl_3$) cm^{-1}: 1727, 1630. ^1H NMR δ: 1.00 (1H, ddd, J=13, 13, 4 Hz, H1), 1.22 (1H, ddd, J=13, 13, 3.5 Hz, H3), 1.41 (1H, br d, J=5 Hz, H9), 1.49–1.79 (7H, m), 1.86–1.98 (1H, m), 2.05 (3H, s, $COCH_3$), 2.06 (1H, br d, J=13 Hz, H1), 2.17 (1H, dddd, J=19, 5, 3, 2 Hz, H11), 2.36 (1H, br d, J=19 Hz, H11), 2.46 (1H, d, J=15.5 Hz, CH_2CON), 2.69 (1H, d, J=15.5 Hz, CH_2CON), 2.89 (1H, ddd, J=7.5, 6.5, 1.5 Hz, H14), 2.92 (3H, s), 3.00 (3H, s), 3.49 (1H, ddd, J=11.5, 6, 4 Hz), 3.62 (1H, ddd, J=11.5, 6.5, 4 Hz), 3.73–3.83 (1H, m), 3.83–3.98 (3H, m), 4.15 (1H, ddd, J=11.5, 6, 4 Hz, CH_2OAc), 4.25 (1H, ddd, J=11.5, 6.5, 4 Hz, CH_2OAc), 4.30 (1H, d, J=6.5 Hz, H20), 5.54 (1H, ddd, J=9.5, 3, 3 Hz), 5.66 (1H, dddd, J=9, 5, 7.5, 2, 1.5 Hz). ^{13}C NMR δ: 18.3 (CH_2), 20.8 (CH_2), 21.0 (CH_3, COCH_3), 27.1 (CH_2), 28.8 (CH_2), 34.0 (CH_2), 35.0 (CH_2), 35.3 (CH_3), 37.5 (CH_2), 37.8 (CH_3), 43.7 (C), 48.1 (CH), 48.4 (C), 50.6 (CH), 54.5 (CH), 63.4 (CH_2, CH_2OAc), 67.0 (CH_2), 80.9 (CH), 110.3 (C), 125.2 (CH), 128.9 (CH), 170.8 (C, OCOCH$_3$), 172.6 (C, CONMe$_2$).

4.2.2. Methoxymethylation of 22 to form 24. MOMCl (42 μl, 0.553 mmol) was added to a solution of **22** (44 mg, 0.109 mmol) and *N*,*N*-diisopropylethylamine (*i*-Pr$_2$NEt) in CH_2Cl_2 (4 ml) at 0 °C under an Ar atmosphere. The mixture was stirred at that temperature for 30 min, and at 27 °C for 19 h. Saturated $NaHCO_3$–H_2O was added and the mixture was extracted with CH_2Cl_2. The organic layer was successively washed with saturated $CuSO_4$–H_2O and saturated $NaHCO_3$–H_2O. Usual work-up and separation by PTLC [hexane–DME (3:1)] furnished **24** (46 mg, 94%) as a colorless glass. HRMS Calcd for $C_{25}H_{39}NO_6$: 449.2775. Found: 449.2790. MS *m/z*: 449 (M$^+$, 38), 404 (11), 388 (9), 360 (39), 343 (66), 257 (39), 99 (100), 87 (55), 72 (25), 45 (80). IR ($CHCl_3$) cm^{-1}: 1625. ^{1}H NMR δ: 1.00 (1H, ddd, J=13, 13, 4 Hz, H1), 1.22 (1H, ddd, J=13, 13, 3.5 Hz), 1.41 (1H, br d, J=5 Hz), 1.48–1.77 (7H, m), 1.85–2.00 (1H, m), 2.07 (1H, br d, J=13 Hz), 2.17 (1H, dddd, J=19, 5, 2.5, 2.5 Hz), 2.35 (1H, br d, J=19 Hz), 2.46 (1H, d, J=15.5 Hz), 2.70 (1H, d, J=15.5 Hz), 2.88 (1H, ddd, J=7, 6.5, 1.5 Hz), 2.92 (3H, s), 3.00 (3H, s), 3.36 (3H, s, OCH$_2$OCH_3), 3.42–3.50 (1H, m), 3.52–3.60 (1H, m), 3.62–3.71 (2H, m, CH_2OMOM), 3.73–3.81 (1H, m), 3.83–3.97 (3H, m), 4.28 (1H, d, J=6.5 Hz), 4.64 (1H, d, J=6.5 Hz, OCH_2OCH$_3$), 4.67 (1H, d, J=6.5 Hz, OCH_2OCH$_3$), 5.52 (1H, ddd, J=9.5, 3, 2.5 Hz), 5.68 (1H, br dd, J=9.5, 7 Hz). ^{13}C NMR δ: 18.3 (CH_2), 20.9 (CH_2), 27.1 (CH_2), 28.8 (CH_2), 34.0 (CH_2), 35.0 (CH_2), 35.3 (CH_3), 37.5 (CH_2), 37.8 (CH_3), 43.7 (C), 48.3 (CH), 48.4 (C), 50.7 (CH), 54.6 (CH), 55.0 (CH_3, OCH_3), 63.8 (CH_2), 65.4 (CH_2), 66.7 (CH_2, CH_2OMOM), 68.7 (CH_2, CH_2CH$_2$OMOM), 81.3 (CH), 96.4 (CH_2, OCH_2OMe), 110.3 (C), 125.0 (CH), 129.1 (CH), 172.6 (C).

4.2.3. Deacetalization of 23, 24 to form 25, 26, respectively. The procedure for the preparation of **23** is described as a representative example. *p*-TsOH·H_2O (2 mg, 10.5 μmol) was added to a cooled (0 °C) solution of **48** (18 mg, 40.3 μmol) in acetone (3 ml) and the mixture was stirred at 26 °C for 3.5 h. Saturated $NaHCO_3$–H_2O was added and the mixture was extracted with CH_2Cl_2. Usual work-up and purification by PTLC [hexane–DME (5:2)] provided **25** (15.5 mg, 96%) as a colorless glass. HRMS Calcd for $C_{23}H_{33}NO_5$: 403.2357. Found: 403.2351. MS *m/z*: 403 (M$^+$, 16), 344 (8), 316 (30), 299 (12), 87 (100), 72 (16), 45 (21), 43 (42). IR ($CHCl_3$) cm^{-1}: 1733, 1695, 1630. ^{1}H NMR δ: 1.49 (1H, ddd, J=13, 13, 4.5 Hz, H1), 1.56–2.06 (7H, m), 2.20–2.34 (5H, m), 2.04 (3H, s), 2.42 (1H, br d, J=19.5 Hz), 2.56 (1H, d, J=15.5 Hz), 2.63 (1H, d, J=15.5 Hz), 2.84 (1H, br ddd, J=7.5, 6, 1.5 Hz), 2.93 (3H, s), 3.01 (3H, s), 3.31 (1H, ddd, J=11, 6, 4.5 Hz), 3.47 (1H, ddd, J=11, 4, 4 Hz), 3.61 (1H, d, J=6 Hz, H20), 4.03–4.20 (2H, m), 5.57 (1H, br ddd, J=9.5, 3, 2.5 Hz), 5.64 (1H, dddd, J=9.5, 7, 1.5, 1.5 Hz). ^{13}C NMR δ: 19.0 (CH_2), 20.9 (CH_3), 24.7 (CH_2), 27.4 (CH_2), 28.6 (CH_2), 33.3 (CH_2), 35.3 (CH_3), 37.4 (CH_2), 37.8 (CH_3), 41.6 (CH_2, C3), 43.8 (C), 48.8 (CH), 53.1 (CH), 53.8 (C), 56.5 (CH, C5), 63.5 (CH_2), 66.9 (CH_2), 81.9 (CH), 126.0 (CH), 127.6 (CH), 170.7 (C), 172.3 (C), 212.5 (C, C4). In the same manner, **24** (18 mg, 95%) was obtained as a colorless glass from **26** (21 mg, 46.8 mmol) after PTLC [hexane–DME (3:1)]. HRMS Calcd for $C_{23}H_{35}NO_5$: 405.2513. Found: 405.2520. MS *m/z*: 405 (M$^+$, 31), 373 (22), 344 (10), 316 (59), 299 (40), 87 (100), 72 (34), 45 (98). IR ($CHCl_3$) cm^{-1}: 1698, 1635. ^{1}H NMR δ: 1.49 (1H, ddd, J=13, 12, 4.5 Hz, H1), 1.50–2.03 (7H, m), 2.16–2.35 (5H, m), 2.47 (1H, br d, J=19.5 Hz), 2.57 (1H, d, J=15.5 Hz), 2.63 (1H, d, J=15.5 Hz), 2.84 (1H, ddd, J=7, 6.5, 1.5 Hz), 2.93 (3H, s), 3.01 (3H, s), 3.24–3.35 (1H, m), 3.34 (3H, s), 3.40–3.49 (1H, m), 3.55–3.60 (2H, m), 3.63 (1H, d, J=6.5 Hz, H20), 4.59 (1H, d, J=6.5 Hz), 4.62 (1H, d, J=6.5 Hz), 5.57 (1H, ddd, J=9.5, 3, 3 Hz), 5.67 (1H, dddd, J=9.5, 7, 1.5, 1.5 Hz). ^{13}C NMR δ: 19.1 (CH_2), 24.8 (CH_2), 27.4 (CH_2), 28.7 (CH_2), 33.3 (CH_2), 35.3 (CH_3), 37.5 (CH_2), 37.8 (CH_3), 41.5 (CH_2, C3), 43.8 (C), 48.9 (CH), 53.1 (CH), 53.7 (C), 55.0 (CH_3), 56.5 (CH, C5), 66.6 (CH_2), 68.6 (CH_2), 81.9 (CH), 96.3 (CH_2), 125.8 (CH), 128.0 (CH), 172.4 (C), 212.5 (C, C4).

4.2.4. Preparation of 28 and 29 from 25. NaI (42 mg, 0.280 mmol) and TMSCl (35 μl, 0.276 mmol) were added successively to a cooled (0 °C) solution of **25** (14 mg, 34.7 μmol) and HMDS (110 μl, 0.529 mmol) in CH_3CN (3 ml) under an Ar atmosphere. After having been stirred at that temperature for 10 min, the mixture was refluxed with stirring for 2 h. Saturated $NaHCO_3$–H_2O was added and the mixture was extracted with CH_2Cl_2. Consecutive washing of the organic layer with saturated $CuSO_4$–H_2O and saturated $NaHCO_3$–H_2O, and usual work-up gave a crude enol silyl ether (**27**, 19 mg). The residue was dissolved in THF (2.5 ml) at 0 °C and NBS (10 mg, 56.2 μmol) was added to this. The mixture was stirred at 0 to 27 °C for 4 h. Saturated $NaHCO_3$–H_2O and saturated $Na_2S_2O_3$–H_2O were added and the whole was extracted with CH_2Cl_2. Usual work-up and separation by PTLC [hexane–EtOAc (1:1)] provided crude **29** (5 mg) and **28** (5.5 mg, 33%) in order of increasing polarity. The crude **29** was further purified by PTLC (CH_2Cl_2) to give **29** (3.5 mg, 21%). ^{1}H NMR of crude **27** δ: 0.15 (9H, s), 1.29–1.40 (1H, m), 1.52–2.50 (12H, m), 2.04 (3H, s), 2.59 (1H, d, J=16 Hz), 2.65 (1H, d, J=16 Hz), 2.76 (1H, br dd, J=6, 5 Hz), 2.93 (3H, s), 3.00 (3H, s), 3.46 (1H, ddd, J=11, 6, 4 Hz), 3.56 (1H, ddd, J=11, 5, 4 Hz), 3.89 (1H, d, J=6 Hz, H20), 4.09–4.24 (2H, m), 5.51–5.66 (2H, m). **28**: Colorless glass. HRMS Calcd for $C_{23}H_{32}BrNO_5$: 483.1443, 481.1463. Found: 483.1456, 481.1459. MS *m/z*: 483, 481 (M$^+$, 1, 1), 402 (9), 397, 395 (4, 5), 314 (10), 297 (8), 211 (11), 87 (100), 72 (17), 45 (15), 43 (44). IR ($CHCl_3$) cm^{-1}: 1737, 1713, 1634. ^{1}H NMR δ: 1.50–1.67 (3H, m), 1.88 (1H, ddd, J=13.5, 8, 2 Hz), 1.90–2.00 (2H, m), 2.05–2.15 (1H, m), 2.08 (3H, s), 2.17–2.31 (3H, m), 2.37 (1H, br d, J=15 Hz), 2.39 (1H, d,

J=15.5 Hz), 2.70 (1H, d, J=15.5 Hz), 2.86 (1H, ddd, J=15, 7.5, 2 Hz), 2.91 (3H, s), 2.96 (3H, s), 3.12 (1H, ddd, J=7, 6.5, 1.5 Hz, H14), 3.35 (1H, ddd, J=15, 13, 7.5 Hz), 3.69 (2H, dd, J=5, 5 Hz), 4.16–4.29 (2H, m), 4.19 (1H, dd, J=6.5, 1 Hz, H20), 5.57 (1H, ddd, J=9.5, 3.5, 3 Hz), 5.72 (1H, dddd, J=9.5, 7, 2, 2 Hz). ^{13}C NMR δ: 21.0 (CH_3), 21.7 (CH_2), 24.8 (CH_2, C6), 27.0 (CH_2), 31.4 (CH_2, C1), 34.0 (CH_2), 35.3 (CH_3), 35.8 (CH_2), 37.3 (CH_2), 37.7 (CH_3), 43.7 (C), 45.5 (CH), 46.5 (CH), 56.3 (C), 63.5 (CH_2), 67.7 (CH_2), 80.3 (C, Br–C), 85.8 (CH), 124.4 (CH), 128.6 (CH), 170.7 (C), 171.6 (C), 203.4 (C). **29**: Colorless glass. HRMS Calcd for $C_{23}H_{32}BrNO_5$: 483.1443, 481.1463. Found: 483.1461, 481.1457. MS m/z: 483, 481 (M^+, 0.4, 0.4), 401 (3), 314 (4), 297 (4), 227 (5), 211 (7), 87 (100), 72 (10), 45 (11), 43 (27). IR ($CHCl_3$) cm^{-1}: 1737, 1709, 1629. ^{1}H NMR δ: 1.76 (1H, ddd, J=12.5, 12.5, 4.5 Hz), 1.78–2.14 (6H, m), 2.04 (3H, s), 2.22–2.44 (4H, m), 2.47–2.52 (1H, m), 2.48 (1H, d, J=15.5 Hz), 2.74 (1H, d, J=15.5 Hz), 2.94 (3H, s), 3.01 (3H, s), 3.16 (1H, ddd, J=7, 6, 1.5 Hz, H14), 3.28 (1H, dt, J=11, 5.5 Hz), 3.40–3.53 (1H, m), 3.46 (1H, dt, J=11, 4 Hz), 3.60 (1H, dd, J=6, 1 Hz, H20), 4.10 (2H, dd, J=5.5, 4 Hz), 5.59 (1H, ddd, J=9.5, 3, 3 Hz, H12), 5.67 (1H, dddd, J=9.5, 7, 1.5, 1.5 Hz, H13).

4.2.5. Dehydrobromination of 28 and 29 to form 30. DBU (9 μl, 60.3 μmol) was added to a solution of **28** (5.5 mg, 11.4 μmol) in benzene (2 ml) and the mixture was refluxed with stirring for 1 h. Saturated NH_4Cl–H_2O was added and the mixture was extracted with CH_2Cl_2. Usual work-up and purification by PTLC [hexane–DME (2:1)] afforded **30** (4 mg, 87%) as a colorless glass. HRMS Calcd for $C_{23}H_{31}NO_5$: 401.2200. Found: 401.2197. MS m/z: 401 (M^+, 5), 314 (7), 297 (19), 227 (12), 211 (18), 87 (100), 72 (20), 45 (15), 43 (57). IR ($CHCl_3$) cm^{-1}: 1735, 1674, 1638, 1604. ^{1}H NMR δ: 1.44 (1H, ddd, J=13, 11.5, 3.5 Hz, H1), 1.69–1.91 (3H, m), 2.03 (3H, s), ca. 2.12–2.22 (2H, m), 2.23 (1H, ddd, J=18, 12.5, 6.5 Hz, H3), 2.36 (1H, br d, J=19 Hz), 2.48 (1H, dddd, J=18, 4.5, 3.5, 2 Hz, H3), 2.57 (1H, d, J=16 Hz), 2.61 (2H, d, J=4 Hz, H7×2), 2.82 (1H, d, J=16 Hz), ca. 2.92–3.03 (1H, m), 2.94 (3H, s), 3.01 (3H, s), 3.43 (1H, ddd, J=11, 6.5, 4 Hz), 3.54 (1H, ddd, J=11, 5, 4 Hz), 3.74 (1H, d, J=6 Hz), 4.09–4.23 (2H, m), 5.52–5.69 (2H, m), 6.84 (1H, t, J=4 Hz, H6). ^{13}C NMR δ: 19.7 (CH_2), 20.9 (CH_3), 25.8 (CH_2), 26.4 (CH_2), 35.3 (CH_3), 36.9 (CH_2), 37.6 (CH_3), 39.2 (CH_2, C3), 39.6 (CH_2, C7), 40.8 (C), 48.7 (C), 49.3 (CH), 50.4 (CH), 63.4 (CH_2), 67.4 (CH_2), 91.3 (CH), 125.2 (CH), 128.0 (CH), 137.6 (CH, C6), 148.3 (C, C5), 170.6, (C), 171.4 (C), 197.3 (C, C4). In the same manner, **30** (2 mg, 80%) was obtained from **29** (3 mg, 6.22 μmol) on treatment with DBU (5 μl, 33.5 μmol) in boiling benzene (2 ml) for 2 h.

4.2.6. Preparation of 30 from 25 without isolation of the intermediates. A solution of **25** (60 mg, 0.149 mmol) and HMDS (0.38 ml, 1.83 mmol) in CH_3CN (5 ml) was stirred as above with NaI (179 mg, 1.19 mmol) and TMSCl (151 μl, 1.19 mmol) under an Ar atmosphere at 0 °C for 5 min, and at reflux for 2 h. The same work-up gave a residue (73 mg). This was dissolved in THF (4 ml) and the solution was stirred with NBS (40 mg, 0.225 mmol) at 0–20 °C for 4 h. The same work-up afforded a mixture of bromides (87 mg), which was then treated with DBU (89 μl, 0.596 mmol) in refluxing benzene (5 ml) for 1 h to give **30** (37 mg, 62% overall) after purification by PTLC as above.

4.2.7. Preparation of 31 from 26. Methylmagnesium bromide (MeMgBr, 3 M in Et_2O, 0.35 ml, 1.05 mmol) was added to a solution of diisopropylamine (i-Pr_2NH, 0.15 ml, 1.07 mmol) in Et_2O (6 ml) under an Ar atmosphere. After the mixture had been stirred at 27 °C for 14 h, a solution of **26** (17 mg, 42.0 μmol) in Et_2O (4 ml) was added and the resulting mixture was stirred for 10 min. TMSCl (0.32 ml, 2.52 mmol), Et_3N (0.41 ml, 2.95 mmol), and hexamethylphosphoramide (HMPA, 73 μl, 0.420 mmol) were added and the whole was further stirred at 27 °C for 4 h and at reflux for 1.5 h. After the mixture had been cooled in an ice bath, saturated $NaHCO_3$–H_2O was added and the whole was extracted with EtOAc. Consecutive washing of the organic layer with saturated $CuSO_4$–H_2O and saturated $NaHCO_3$–H_2O, and usual work-up gave a crude enol silyl ether (28 mg). The residue was dissolved in THF (3 ml) at 0 °C and NBS (15 mg, 84.3 μmol) was added to this, then the mixture was stirred under an Ar atmosphere at 0–27 °C for 14 h. Saturated $NaHCO_3$–H_2O and saturated $Na_2S_2O_3$–H_2O were added and the whole was extracted with CH_2Cl_2 to give a residue (33 mg). A solution of the residue (33 mg) was stirred with DBU (12 μl, 80.4 μmol) at reflux for 1 h. The same work-up as before and purification by PTLC [hexane–EtOAc (1:1)] provided **31** (4.5 mg, 27% overall) as a colorless glass. HRMS Calcd for $C_{23}H_{33}NO_5$: 403.2357. Found: 403.2364. MS m/z: 403 (M^+, 3), 316 (5), 297 (24), 271 (11), 227 (16), 211 (25), 210 (20), 87 (69), 72 (39), 45 (100). IR ($CHCl_3$) cm^{-1}: 1673, 1637, 1604. ^{1}H NMR δ: 1.39–1.50 (1H, m), 1.73–1.89 (3H, m), 2.11–2.26 (3H, m), 2.36 (1H, br d, J=19.5 Hz, H11), 2.47 (1H, dddd, J=18, 4, 4, 2 Hz, H3), 2.61 (2H, d, J=4 Hz, H7×2), 2.57 (1H, d, J=16 Hz), 2.82 (1H, d, J=16 Hz), 2.94 (3H, s), ca. 2.94–3.01 (1H, m), 3.01 (3H, s), 3.34 (3H, s), 3.36–3.44 (1H, m), 3.47–3.55 (1H, m), 3.58–3.68 (2H, m), 3.75 (1H, d, J=6 Hz), 4.63 (2H, s), 5.55–5.67 (2H, m), 6.83 (1H, t, J=4 Hz, H6). ^{13}C NMR δ: 19.7 (CH_2), 25.9 (CH_2), 26.4 (CH_2), 35.3 (CH_3), 37.0 (CH_2), 37.6 (CH_3), 39.1 (CH_2, C3), 39.6 (CH_2, C7), 40.8 (C), 48.7 (C), 49.4 (CH), 50.5 (CH), 55.0 (CH_3), 67.0 (CH_2), 69.1 (CH_2), 91.6 (CH), 96.4 (CH_2), 125.0 (CH), 128.3 (CH), 137.5 (CH, C6), 148.4, (C, C5), 171.5 (C), 197.4 (C, C4).

4.2.8. Deacetalization of 32 to form 33. In the same manner as described for the preparation of **25** from **23** (Section 4.2.3), **32** (28 mg, 78.0 μmol) was stirred with p-TsOH·H_2O (3 mg, 15.8 μmol) in acetone (3 ml) to afford **33** (23 mg, 94%) as a colorless glass after PTLC [hexane–DME (3:2)]. HRMS Calcd for $C_{19}H_{25}NO_3$: 315.1833. Found: 315.1830. MS m/z: 315 (M^+, 3), 287 (11), 259 (13), 201 (8), 172 (8), 129 (14), 87 (100), 72 (21), 45 (35). IR ($CHCl_3$) cm^{-1}: 1728, 1707 (sh), 1633. ^{1}H NMR δ: 1.54–1.72 (2H, m), 1.76–2.10 (6H, m), 2.27 (1H, ddd, J=13.5, 13.5, 6, 1 Hz, H3), 2.32–2.64 (5H, m), 2.45 (1H, d, J=15.5 Hz), 2.58 (1H, d, J=15.5 Hz), 2.83 (1H, dd, J=7, 2 Hz, C14), 2.95 (3H, s), 3.03 (3H, s), 5.67–5.75 (1H, m), 5.77–5.84 (1H, m). ^{13}C NMR δ: 20.1 (CH_2), 22.6 (CH_2), 26.4 (CH_2), 29.5 (CH_2), 33.2 (CH_2), 35.0 (CH_2), 35.4 (CH_3), 37.8 (CH_3), 40.6 (CH_2, C3), 41.1 (C), 50.2 (CH), 54.4 (CH, C5), 56.9 (CH), 58.1 (C), 124.8 (CH), 129.0 (CH), 171.3 (C), 209.5 (C, C4), 211.0 (C, C20).

4.2.9. Preparation of 34 from 33. In the same manner as described for the preparation of **28** and **29** from **25** (Section 4.2.4), **33** (23 mg, 73.0 μmol) was treated with NaI (88 mg, 0.587 mmol), TMSCl (74 μl, 58.4 μmol), and HMDS (0.23 ml, 1.11 mmol) in CH_3CN (3 ml) to give a crude silyl enol ether (30 mg), which was then stirred with NBS (20 mg, 0.112 mmol) in THF (3 ml) to provide **34** (20 mg, 70%) as a colorless glass after PTLC (CH_2Cl_2). HRMS Calcd for $C_{19}H_{24}BrNO_3$: 395.0919, 393.0939. Found: 395.0910, 393.0949. MS *m/z*: 395, 393 (M^+, 2, 2), 367, 365 (1, 1), 314 (18), 286 (46), 227 (19), 199 (100), 87 (53), 72 (35), 45 (50). IR ($CHCl_3$) cm^{-1}: 1729, 1715 (sh), 1636. ^1H NMR δ: 1.82–2.05 (4H, m), 2.07–2.29 (3H, m), 2.30 (1H, br d, J=19.5 Hz), 2.35–2.43 (1H, m, H3), 2.41–2.52 (1H, m), 2.53 (2H, s), 2.54–2.72 (1H, m), 2.93–2.99 (1H, m, H9), 2.96 (3H, s), 3.04 (3H, s), 3.17 (1H, dd, J=7.5, 2.5 Hz), 3.36 (1H, ddd, J=14.5, 14.5, 6.5 Hz, H3), 5.76 (1H, br ddd, J=9, 7.5, 1.5 Hz), 5.83 (1H, ddd, J=9, 3, 2.5 Hz). ^{13}C NMR δ: 21.0 (CH_2), 26.2 (CH_2), 26.6 (CH_2), 30.6 (CH_2), 30.9 (CH_2), 34.5 (CH_2), 34.8 (CH_2), 35.4 (CH_3), 37.8 (CH_3), 41.0 (C), 47.3 (CH), 56.5 (CH), 62.1 (C, C10), 73.5 (C, Br–C), 125.0 (CH), 128.8 (CH), 170.8 (C), 202.7 (C, C4), 208.0 (C, C20).

4.2.10. Dehydrobromination of 34 to form 35. In the same manner as described for the preparation of **30** from **28** and **29** (Section 4.2.5), **34** (20 mg, 50.8 μmol) was stirred with DBU (38 μl, 0.255 mmol) in refluxing benzene (3 ml) for 1 h to afford **35** (11 mg, 69%) as a colorless glass after PTLC [hexane–DME (2:1)]. HRMS Calcd for $C_{19}H_{23}NO_3$: 313.1677. Found: 313.1678. MS *m/z*: 313 (M^+, 8), 285 (3), 226 (58), 198 (81), 170 (26), 154 (47), 141 (33), 87 (100), 72 (39), 45 (77). IR ($CHCl_3$) cm^{-1}: 1725, 1678, 1636. ^1H NMR δ: 1.77–1.94 (2H, m), 2.12–2.21 (1H, m), 2.12–2.32 (1H, m), 2.32–2.59 (5H, m), 2.48 (1H, dd, J=21, 3.5 Hz, H7), 2.56 (1H, d, J=16.5 Hz), 2.63 (1H, d, J=16.5 Hz), 2.81 (1H, dd, J=21, 4.5 Hz, H7), 2.94 (3H, s), 3.02 (1H, br dd, J=7, 1.5 Hz), 3.02 (3H, s), 5.76 (1H, ddd, J=9, 7, 1.5 Hz), 5.83 (1H, ddd, J=9, 2.5, 2.5 Hz), 6.99 (1H, dd, J=4.5, 3.5 Hz, H6). ^{13}C NMR δ: 19.0 (CH_2), 25.9 (CH_2), 27.2 (CH_2), 34.7 (CH_2), 35.3 (CH_3), 37.6 (CH_3), 38.2 (CH_2, C7), 38.9 (CH_2, C3), 39.1 (C), 46.5 (CH), 54.1 (C), 58.4 (CH), 125.8 (CH), 128.4 (CH), 136.5 (C, C5), 138.5 (CH, C6), 170.6 (C), 195.8 (C, C4), 204.8 (C, C20).

4.2.11. Acetylation of 3 to form 37. In the same manner as described for the preparation of **23** from **22** (Section 4.2.1), **3** (37 mg, 91.6 μmol) was stirred with Ac_2O (0.20 ml, 2.12 mmol) and pyridine (0.30 ml, 3.88 mmol) in CH_2Cl_2 (1.5 ml) at 16 °C for 6 h. The same work-up and separation by PTLC [hexane–EtOAc (3:1)] gave **37** (39 mg, 95%) as a colorless glass. HRMS Calcd for $C_{26}H_{38}O_6$: 446.2666. Found: 446.2637. MS *m/z*: 446 (M^+, 0.1), 359 (0.2), 344 (0.4), 342 (0.4), 317 (0.3), 257 (1), 240 (8), 213 (2), 91 (6), 87 (100), 57 (22), 43 (29). IR ($CHCl_3$) cm^{-1}: 1719, 1701. ^1H NMR δ: 1.18 (9H, s), 1.42–2.11 (10H, m), 2.04 (3H, s), 2.19–2.34 (5H, m), 2.41 (1H, br d, J=19 Hz), 2.50 (1H, br dd, J=6, 6 Hz), 3.30 (1H, ddd, J=11, 5.5, 5.5 Hz, CH_2CH$_2$OAc), 3.45 (1H, ddd, J=11, 4, 4 Hz, CH_2CH$_2$OAc), 3.59 (1H, d, J=6 Hz), 4.00 (1H, ddd, J= 11, 8.5, 6.5 Hz, CH_2OPiv), 4.07–4.15 (2H, m, CH_2OAc), 4.13 (1H, ddd, J=11, 9, 6 Hz, CH_2OPiv), 5.53–5.66 (2H, m). ^{13}C NMR δ: 19.1 (CH_2), 20.8 (CH_3), 24.7 (CH_2), 27.2 ($CH_3\times3$ and CH_2, Piv and C11), 28.7 (CH_2), 33.6 (CH_2), 33.9 (CH_2), 38.6 (C), 41.5 (CH_2), 42.6 (C), 47.8 (CH), 53.8 (CH), 54.0 (C), 56.5 (CH), 62.5 (CH_2, *C*H$_2$OPiv), 63.4 (CH_2, *C*H$_2$OAc), 66.9 (CH_2, *C*H$_2$CH$_2$OAc), 82.0 (CH), 126.0 (CH), 126.4 (CH), 170.7 (C, *C*OMe), 178.4 (C, *C*OMe$_3$), 212.2 (C, C4).

4.2.12. Preparation of 38 from 37. In the same manner as described for the preparation of **30** from **25** (Section 4.2.6), **37** (44 mg, 98.7 μmol) was led to the enone **38** (64% overall) in three steps. **38**: Colorless glass. HRMS Calcd for $C_{26}H_{36}O_6$: 444.2510. Found: 444.2509. MS *m/z*: 444 (M^+, 0.4), 340 (2), 315 (1), 238 (2), 211 (10), 87 (100), 57 (27), 43 (39). IR ($CHCl_3$) cm^{-1}: 1721, 1678, 1607. ^1H NMR δ: 1.20 (9H, s), 1.43 (1H, ddd, J=13, 12, 3 Hz), 1.55 (1H, br d, J=5 Hz, H9), 1.67–1.91 (3H, m), 2.04 (3H, s), 2.11–2.30 (4H, m), 2.33 (1H, dd, J=21, 3 Hz, H7), 2.35 (1H, br d, J=19 Hz), 2.43–2.56 (2H, m), 2.66 (1H, dd, J=21, 5 Hz, H7), 3.42 (1H, ddd, J=11, 6.5, 4.5 Hz), 3.52 (1H, ddd, J=11, 5, 4 Hz), 3.69 (1H, d, J=6 Hz), 4.03–4.23 (4H, m), 5.54–5.64 (2H, m), 6.83 (1H, dd, J=5, 3 Hz, H6). ^{13}C NMR δ: 19.6 (CH_2), 20.9 (CH_3), 25.8 (CH_2), 26.3 (CH_2), 27.2 ($CH_3\times3$), 33.2 (CH_2), 38.6 (C), 39.1 (CH_2), 39.8 (CH_2, C7), 40.3 (C), 48.9 (C), 49.5 (CH, C9), 50.0 (CH), 61.9 (CH_2), 63.3 (CH_2), 67.4 (CH_2), 91.6 (CH), 125.5 (CH), 126.6 (CH), 136.7 (CH, C6), 148.6 (C, C5), 170.6 (C), 178.3 (C), 197.2 (C).

4.2.13. Preparation of 39 from 3. In the same manner as described for the preparation of **28** and **29** from **25** (Section 4.2.4), **3** (525 mg, 1.30 μmol) was led to the crude α-bromoketone (802 mg) on treatment with NaI (585 mg, 3.90 mmol), TMSCl (0.49 ml, 3.98 mmol), and HMDS (1.10 ml, 6.23 mmol) in CH_3CN (22 ml), and then with NBS (462 mg, 2.60 mmol) in THF (25 ml). The crude bromoketone was dissolved in THF (12 ml) and 2.5% HCl–H_2O (1.00 ml) was added to this at 0 °C. After the mixture had been stirred at 0 °C for 10 min, saturated $NaHCO_3$–H_2O was added and the whole was extracted with CH_2Cl_2. Usual work-up gave a residue (766 mg). The residue was dissolved in CH_2Cl_2 (25 ml) and to this was added *i*-Pr$_2$NEt (3.38 ml, 19.4 mmol). The resulting mixture was cooled to −20 °C under an Ar atmosphere, and a solution of MOMCl (0.74 ml, 9.74 mmol) in CH_2Cl_2 (5 ml) was slowly added to this during 30 min. The mixture was stirred at −20 to 0 °C for 16 h, and the reaction was quenched by the addition of saturated $NaHCO_3$–H_2O. The whole was extracted with CH_2Cl_2. The organic layer was successively washed with saturated $CuSO_4$–H_2O and saturated $NaHCO_3$–H_2O, and then was treated as usual to afford a residue, which was roughly purified by SiO_2 column chromatography [25 g, hexane–EtOAc (7:1 to 4:1)] to give a mixture of two stereoisomers (511 mg). The mixture (511 mg) was dissolved in benzene (30 ml) and DBU (289 μl, 1.02 mmol) was added to this. The resulting mixture was stirred under reflux for 1 h, and was treated as before. Purification by PTLC [hexane–EtOAc (4:1)] yielded **39** (331 mg, 57% overall from **3**) as a colorless viscous syrup. HRMS Calcd for $C_{26}H_{38}O_6$: 446.2666. Found: 446.2678. MS *m/z*: 446 (M^+, 2), 414 (2), 401 (2), 340 (6), 317 (3), 285 (5), 255 (6), 211 (35), 73 (18), 57 (62), 45 (100), 41 (22). IR ($CHCl_3$) cm^{-1}: 1719, 1675, 1606. ^1H NMR δ: 1.20 (9H, s), 1.38–1.47 (1H, m), 1.54 (1H, br d, J=5 Hz), 1.74 (1H, ddd, J=13.5, 8, 6 Hz), 1.78–1.88 (2H, m), 2.15–2.33 (5H, m), 2.33 (1H, dd, J=21, 3 Hz, H7), 2.48 (1H, dddd, J=18.5, 4, 4, 2 Hz, H3), 2.52–2.58 (1H, m), 2.65 (1H, dd, J=21, 5 Hz, H7), 3.35 (3H, s), 3.40 (1H, ddd, J=10.5, 6, 4.5 Hz), 3.50 (1H, ddd, J=10.5, 4.5, 4.5 Hz), 3.58–3.69 (2H, m), 3.71 (1H, d, J=6 Hz), 4.08 (1H, ddd, J=11, 8, 6.5 Hz), 4.19 (1H, ddd, J=11, 8, 6 Hz), 4.63 (2H, s), 5.56–5.66 (2H, m), 6.82 (1H, dd, J=5, 3 Hz, H6). ^{13}C NMR δ: 19.7 (CH_2), 25.9 (CH_2), 26.3 (CH_2), 27.2 ($CH_3\times3$), 33.2 (CH_2), 38.6 (C), 39.1 (CH_2, C3), 39.8 (CH_2, C7), 40.3 (C), 48.9 (C), 49.6 (CH), 50.1 (CH), 55.1 (CH_3), 61.9 (CH_2), 66.7 (CH_2), 69.1 (CH_2), 91.9 (CH), 96.4 (CH_2), 125.3 (CH), 127.0 (CH), 136.7 (CH, C6), 148.8 (C, C5), 178.4 (C), 197.3 (C, C4). In the same manner, **36** (22 mg, 54.5 μmol) was converted to **39** (11 mg, 45% overall from **36**) in five steps.

4.2.14. Reduction of 38, 39 to form 40, 41, respectively. Preparation of **40** from **38** is described as a representative example. $CeCl_3\cdot7H_2O$ (29 mg, 77.9 μmol) and $NaBH_4$ (3 mg, 78.9 μmol) were added in this order to a cooled (0 °C) solution of **38** (26 mg, 58.6 μmol) in MeOH (3 ml). After the mixture had been stirred at 0 °C for 10 min, saturated NH_4Cl–H_2O and saturated$NaHCO_3$–H_2O were added and the mixture was extracted with CH_2Cl_2. Usual work-up and PTLC [hexane–EtOAc (7:4)] provided **40** (24 mg, 92%) as a slightly unstable colorless glass. HRMS Calcd for $C_{26}H_{38}O_6$: 446.2666. Found: 446.2674. MS m/z: 446 (M^+, 1), 428 (1), 340 (1), 324 (1), 222 (9), 157 (15), 87 (100), 57 (41), 43 (57). IR ($CHCl_3$) cm^{-1}: 1721. ^1H NMR δ: 1.20 (9H, s), 1.36–1.49 (2H, m), 1.49–1.66 (4H, m, including OH), 1.73 (1H, ddd, J=13.5, 8.5, 6 Hz), 1.86–1.98 (2H, m), 2.05 (3H, s), 2.11–2.28 (3H, m), 2.31 (1H, br d, J=18.5 Hz), ca. 2.47–2.53 (1H, m), 2.49 (1H, ddd, J=18.5, 4.5, 2 Hz, H7), 3.45 (1H, ddd, J=11, 5.5, 4.5 Hz), 3.52 (1H, ddd, J=11, 5, 4.5 Hz), 3.68 (1H, d, J=6 Hz), 4.07 (1H, ddd, J=11, 8.5, 6.5 Hz), ca. 4.10–4.21 (2H, m), 4.19 (1H, ddd, J=11, 8.5, 6 Hz), 4.21–4.29 (1H, m, H4), 5.49–5.53 (1H, m, H6), 5.53–5.64 (2H, m). ^{13}C NMR δ: 18.8 (CH_2), 20.9 (CH_3), 23.8 (CH_2), 26.4 (CH_2), 27.2 ($CH_3\times3$), 31.4 (CH_2), 33.7 (CH_2), 38.6 (C), 38.7 (CH_2), 40.5 (C), 48.9 (C), 49.4 (CH), 50.2 (CH), 62.2 (CH_2), 63.4 (CH_2), 67.5 (CH_2), 69.1 (CH, C4), 92.5 (CH), 117.8 (CH, C6), 125.4 (CH), 127.2 (CH), 152.7 (C, C5), 170.6 (C), 178.4 (C). In the same manner, **41** (15 mg, 93%) was obtained from **39** (16 mg, 35.9 μmol) as a colorless glass. HRMS Calcd for $C_{26}H_{40}O_6$: 448.2823. Found: 448.2804. MS m/z: 448 (M^+, 0.2), 430 (0.6), 416 (2), 403 (3), 342 (2), 258 (3), 240 (8), 222 (16), 195 (17), 157 (19), 57 (64), 45 (100), 41 (22). IR ($CHCl_3$) cm^{-1}: 1719. ^1H NMR δ: 1.20 (9H, s), 1.33–1.48 (2H, m), 1.55–1.70 (4H, m, including OH), 1.72 (1H, ddd, J=13.5, 8.5, 6 Hz), 1.88–2.00 (2H, m), 2.11–2.34 (4H, m), 2.48 (1H, ddd, J=19, 4.5, 2 Hz, H7), 2.50 (1H, dd, J=6, 6 Hz), 3.35 (3H, s), 3.42 (1H, dt, J=11, 5 Hz), 3.49 (1H, dt, J=11, 5 Hz), 3.62 (2H, dd, J=5, 5 Hz), 3.70 (1H, d, J=6 Hz), 4.08 (1H, ddd, J=11, 8.5, 6.5 Hz), 4.19 (1H, ddd, J=11, 8.5, 6 Hz), 4.21–4.31 (1H, m, H4), 4.63 (2H, s), 5.47–5.52 (1H, m, H6), 5.52–5.65 (2H, m). ^{13}C NMR δ: 18.9 (CH_2), 23.8 (CH_2), 26.4 (CH_2), 27.2 ($CH_3\times3$), 31.5 (CH_2, C3), 33.7 (CH_2), 38.6 (C), 38.7 (CH_2, C7), 40.4 (C), 49.0 (C), 49.4 (CH, C9), 50.3 (CH, C14), 55.1 (CH_3), 62.2 (CH_2), 66.8 (CH_2), 69.0 (CH, C4), 69.3 (CH_2), 92.8 (CH), 96.4 (CH_2), 117.5 (CH, C6), 125.2 (CH), 127.5 (CH), 152.9 (C, C5), 178.4 (C).

4.2.15. Rearrangement of 40 to form 42. DBU (40 μl, 0.268 mmol) and CCl_3CN (54 μl, 0.538 mmol) were added to a solution of **40** (12 mg, 26.9 μmol) in CH_2Cl_2 (3 ml) and the mixture was stirred at 22 °C for 15 h. Saturated NH_4Cl–H_2O was added and the mixture was extracted with CH_2Cl_2. Usual work-up and PTLC [benzene–EtOAc (34:1)] gave crude **42** (10 mg), which was further purified by PTLC [hexane–EtOAc (5:1)] to yield **42** (9 mg, 57%) as a colorless glass. HRMS Calcd for $C_{28}H_{38}Cl_3NO_6$: 589.1762. Found: 589.1742. MS m/z: 595, 593, 591, 589 (M^+, 0, 0, 0.1, 0.1), 558, 556, 554 (0.2, 0.7, 1), 491, 489, 487, 485 (0, 0.5, 1, 1), 454, 452, 450 (0.5, 1, 2), 362, 360, 358, 356 (0.1, 1, 2, 2), 222 (6), 195 (7), 87 (100), 57 (35), 43 (46). IR ($CHCl_3$) cm^{-1}: 1718. ^1H NMR δ: 1.18 (9H, s), 1.33–1.43 (1H, m), 1.40 (1H, dd, J=13.5, 10 Hz, H7), 1.59–1.85 (5H, m), 1.96–2.14 (3H, m), 2.07 (3H, s), 2.20 (1H, dd, J=19, 5 Hz), 2.36 (1H, dd, J=13.5, 7.5 Hz, H7), 2.36 (1H, br d, J=19 Hz), 2.66 (1H, br dd, J=6, 6 Hz), 3.48 (1H, ddd, J=11, 6, 4 Hz), 3.54 (1H, ddd, J=11, 5, 4 Hz), 3.91 (1H, d, J=6 Hz), 4.05 (1H, ddd, J=11, 7.5, 6.5 Hz), 4.10–4.24 (3H, m), 4.74–4.87 (1H, m, H6), 5.33 (1H, ddd, J=4, 4, 2 Hz, H4), 5.56–5.68 (2H, m), 6.50 (1H, d, J=9 Hz, NH). ^{13}C NMR δ: 19.8 (CH_2), 20.9 (CH_3), 25.0 (CH_2), 25.4 (CH_2), 26.5 (CH_2), 27.2 ($CH_3\times3$), 33.1 (CH_2), 38.6 (C), 43.0 (C), 43.5 (CH_2), 47.5 (CH), 49.3 (CH, C6), 50.2 (C), 50.5 (CH), 62.2 (CH_2), 63.5 (CH_2), 67.8 (CH_2), 86.8 (CH), 92.6 (C, CCl_3), 116.5 (CH, C4), 125.7 (CH), 126.6 (CH), 142.4 (C, C5), 161.1 (C, NH*C*OCCl_3), 170.7 (C), 178.3 (C).

4.3. Efforts aiming at carbonyl 1,3-transposition from 39 to form 53 (Scheme 6)

4.3.1. Epoxidation of 41 to form 43. m-CPBA (16 mg, 92.8 μmol) was added to a cooled (0 °C) solution of **41** (14 mg, 31.3 μmol) in CH_2Cl_2 (3 ml) and the mixture was stirred at 0 °C for 10 min and at 27 °C for 1 h. Saturated $NaHCO_3$–H_2O and saturated $Na_2S_2O_3$–H_2O were added and the whole was extracted with CH_2Cl_2. Usual work-up and separation by PTLC [hexane–EtOAc (7:4)] afforded **39** (0.5 mg, 4%) and **43** (13 mg, 90%) in order of increasing polarity. **43**: Colorless glass. HRMS Calcd for $C_{26}H_{40}O_7$: 464.2772. Found: 464.2784. MS m/z: 464 (M^+, 0.3), 446 (3), 401 (1), 358 (1), 340 (3), 303 (3), 256 (7), 229 (9), 211 (17), 89 (24), 73 (13), 57 (68), 45 (100). IR ($CHCl_3$) cm^{-1}: 1719. ^1H NMR δ: 1.14–1.31 (2H, m), 1.19 (9H, s), 1.55–1.75 (3H, m), 1.77 (1H, d, J=11.5 Hz, OH), 1.82 (1H, dd, J=16.5, 3.5 Hz, H7), 1.90–2.01 (2H, m), 2.05–2.20 (4H, m), 2.25 (1H, d, J=16.5 Hz, H7), 2.47 (1H, br dd, J=6, 5.5 Hz), 3.25 (1H, d, J=3.5 Hz, H6), 3.37 (3H, s), 3.45 (1H, ddd, J=10.5, 6, 4.5 Hz), 3.56 (1H, ddd, J=10.5, 4.5, 4.5 Hz), 3.64–3.69 (2H, m), 3.83 (1H, d, J=6 Hz), 3.84 (1H, ddd, J=12, 11.5, 4.5 Hz, changed to dd, J=12, 4.5 Hz with D_2O, H4), 4.03 (1H, ddd, J=11, 8, 6.5 Hz), 4.13 (1H, ddd, J=11, 8, 6 Hz), 4.65 (2H, s), 5.52–5.63 (2H, m). ^{13}C NMR δ: 21.4 (CH_2), 26.3 (CH_2), 27.2 ($CH_3\times3$, CH_2), 32.3 (CH_2), 33.7 (CH_2), 34.9 (CH_2), 38.6 (C), 40.5 (C), 43.6 (CH), 47.3 (C), 48.3 (CH), 53.3 (CH, C6), 55.1 (CH_3), 62.1 (CH_2), 65.6 (CH, C4), 66.9 (CH_2), 67.2 (C, C5), 69.0

(CH_2), 87.8 (CH), 96.5 (CH_2), 125.9 (CH), 126.8 (CH), 178.3 (C).

4.3.2. Mesylation of 43 to form 44. MsCl (10 μl, 0.129 mmol) was added to a cooled (−20 °C) solution of **43** (3 mg, 6.47 μmol) and Et_3N (46 μl, 0.331 mmol) in CH_2Cl_2 (1.5 ml) under an Ar atmosphere. After the mixture had been stirred at that temperature for 40 min, saturated $NaHCO_3$–H_2O was added and the whole was extracted with CH_2Cl_2. The organic layer was successively washed with saturated $CuSO_4$–H_2O and saturated $NaHCO_3$–H_2O. Usual work-up and separation by PTLC [hexane–EtOAc (2:1)] yielded **44** (3 mg, 86%) as a colorless glass. MS *m/z*: 497 (M^+−CH_2OMe, 0.3), 446 (3), 401 (1), 340 (2), 299 (2), 238 (6), 211 (14), 89 (29), 73 (17), 57 (67), 45 (100), 41 (19). IR ($CHCl_3$) cm^{-1}: 1713. ^1H NMR δ: 1.19 (9H, s), ca. 1.30–1.41 (2H, m), ca. 1.51–1.84 (3H, m), 1.85 (1H, dd, *J*=16, 5, 4 Hz, H7), 1.94–2.20 (6H, m), 2.22 (1H, d, *J*=16.5 Hz, H7), 2.50 (1H, dd, *J*=6, 5 Hz), 3.03 (3H, s, SO_2CH_3), 3.19 (1H, d, *J*=4 Hz, H6), 3.38 (3H, s), 3.47 (1H, ddd, *J*=11, 6.5, 4.5 Hz), 3.57 (1H, ddd, *J*=11, 4.5, 4 Hz), 3.65–3.71 (2H, m), 3.91 (1H, d, *J*=6 Hz), 4.03 (1H, ddd, *J*=11, 7.5, 7 Hz), 4.11 (1H, ddd, *J*=11, 8, 6 Hz), 4.66 (1H, d, *J*=6.5 Hz), 4.70 (1H, d, *J*=6.5 Hz), 5.07 (1H, dd, *J*=12, 4.5 Hz, H4), 5.53–5.63 (2H, m).

4.3.3. Tosylation of 43 to form 45. In a similar manner to that described above (Section 4.3.2), **43** (6 mg, 12.9 μmol) was treated with *p*-toluenesulfonyl chloride (TsCl, 25 mg, 0.131 mmol) and Et_3N (0.50 ml, 3.59 mmol) in CH_2Cl_2 (1.5 ml) at 27 °C for 23 h. The same work-up as above and purification by PTLC [hexane–EtOAc (3:1)] yielded **45** (7.5 mg, 94%) as a colorless glass. MS *m/z*: 446 (M^+−TsOH, 4), 340 (3), 255 (6), 238 (6), 211 (12), 91 (33), 89 (28), 57 (65), 45 (100), 41 (17). IR ($CHCl_3$) cm^{-1}: 1718. ^1H NMR δ: 1.14–1.24 (1H, m), 1.19 (9H, s), 1.51–1.81 (5H, m), 1.75 (1H, dd, *J*=16.5, 3.5 Hz, H7), 1.93 (1H, br d, *J*=13.5 Hz), 2.03–2.17 (4H, m), 2.18 (1H, d, *J*=16.5 Hz, H7), 2.42–2.50 (1H, m), 2.45 (3H, s), 3.09 (1H, d, *J*=3.5 Hz, H6), 3.40 (3H, s), 3.47 (1H, ddd, *J*=11, 5.5, 4.5 Hz), 3.59 (1H, ddd, *J*=11, 4.5, 4 Hz), 3.66–3.73 (2H, m), 3.84 (1H, d, *J*=6 Hz), 4.01 (1H, ddd, *J*=11, 7.5, 7 Hz), 4.08 (1H, ddd, *J*=11, 8, 6 Hz), 4.69 (1H, d, *J*=6.5 Hz), 4.73 (1H, d, *J*=6.5 Hz), 4.96 (1H, dd, *J*=12, 4.5 Hz, H4), 5.51–5.62 (2H, m), 7.30–7.36 (2H, m), 7.75–7.81 (2H, m). ^{13}C NMR δ: 21.6 (CH_3), 21.8 (CH_2), 26.2 (CH_2), 26.4 (CH_2), 27.2 ($CH_3\times3$), 28.8 (CH_2), 33.7 (CH_2), 34.6 (CH_2), 38.6 (C), 40.6 (C), 43.4 (CH), 48.3 (CH), 48.4 (C), 52.6 (CH, C6), 55.2 (CH_3), 62.0 (CH_2), 65.3 (C, C5), 67.0 (CH_2), 68.8 (CH_2), 75.5 (CH, C4), 87.6 (CH), 96.5 (CH_2), 126.0 (CH), 126.7 (CH), 127.4 (CH×2), 129.6 (CH×2), 134.0 (C), 144.5 (C), 178.3 (C).

4.3.4. Attempted Birch reduction of 44 and 45. Reduction of **45** is described as a representative example. Na (33 mg, 1.43 mg atom) was added in small portions to a cooled (−78 °C) solution of **45** (4.5 mg, 7.28 μmol) in liq. NH_3 (ca. 3 ml) and THF (1.5 ml) under an Ar atmosphere. After the mixture had been stirred for 1 h, NH_4Cl (powder, 115 mg, 2.15 mmol) was added and the cooling bath was removed. The mixture was stirred at ambient temperature for 20 min. Saturated NH_4Cl–H_2O was added and the whole was extracted with CH_2Cl_2. Usual work-up and purification by PTLC [CH_2Cl_2–DME (5:1)] gave **46** (1.5 mg, 54%) and **49** (1 mg, 36%) in order of increasing polarity. **46**: Colorless glass. MS *m/z*: 362 (M^+−H_2O, 1), 344 (3), 317 (2), 303 (2), 274 (3), 256 (7), 229 (6), 211 (9), 105 (10), 91 (16), 89 (11), 73 (9), 59 (11), 45 (100), 41 (11). ^1H NMR δ: 1.12–1.31 (2H, m), 1.58 (1H, ddd, *J*=13.5, 8.5, 5.5 Hz), 1.59–1.89 (4H, m, including OH×2), 1.82 (1H, dd, *J*=16.5, 4 Hz, H7), 1.90–2.11 (4H, m), ca. 2.13–2.20 (2H, m), 2.21 (1H, d, *J*=16.5 Hz, H7), 2.48 (1H, br dd, *J*=6, 5 Hz), 3.24 (1H, d, *J*=4 Hz, H6), 3.37 (3H, s), 3.44 (1H, ddd, *J*=10.5, 6, 4.5 Hz), 3.57 (1H, ddd, *J*=10.5, 4.5, 4.5 Hz), 3.62–3.77 (2H, m), 3.69–3.89 (2H, m, C*H*$_2$OH), 3.78–3.89 (1H, m, H4), 3.82 (1H, d, *J*=6 Hz), 4.65 (2H, s), 5.52–5.63 (2H, m). ^{13}C NMR δ: 21.4 (CH_2), 26.4 (CH_2), 27.2 (CH_2), 32.3 (CH_2), 35.1 (CH_2), 38.1 (CH_2), 40.5 (C), 43.7 (CH), 47.2 (C), 48.4 (CH), 53.4 (CH, C6), 55.1 (CH_3), 60.1 (CH_2, CH_2OH), 65.5 (CH, C4), 66.9 (CH_2), 67.3 (C, C5), 69.0 (CH_2), 87.9 (CH), 96.5 (CH_2), 126.0 (CH), 126.9 (CH). For structure confirmation, **46** (1.5 mg) was treated with PivCl in pyridine to yield the pivaloate (1.5 mg), whose ^1H NMR was identical with that of **43**. **49**: Colorless glass. HRMS Calcd for $C_{21}H_{32}O_6$: 380.2197. Found: 380.2183. MS *m/z*: 380 (M^+, 1), 348 (2), 335 (3), 303 (7), 275 (5), 273 (6), 256 (6), 211 (11), 91 (19), 73 (14), 45 (100), 41 (11). IR ($CHCl_3$) cm^{-1}: 1691. ^1H NMR δ: 1.42–1.64 (3H, m), 1.72 (1H, ddd, *J*=13.5, 9, 5.5 Hz), ca. 1.88–2.08 (3H, m, including), 2.08 (1H, d, *J*=9 Hz, H5), 2.15–2.43 (6H, m), 2.57 (1H, br dd, *J*=6, 6 Hz), 2.85 (1H, d, *J*=2.5 Hz, OH), 3.24 (1H, ddd, *J*=10.5, 5.5, 5 Hz), 3.34 (3H, s), 3.41 (1H, ddd, *J*=10.5, 4.5, 4.5 Hz), ca. 3.53–3.60 (2H, m), 3.54 (1H, d, *J*=6 Hz), 3.61–3.82 (2H, m, C*H*$_2$OH), 4.25 (1H, dddd, *J*=10.5, 9, 7.5, 2.5 Hz, changed to ddd, *J*=10.5, 9, 7.5 Hz with D_2O, H6), 4.58 (1H, d, *J*=6.5 Hz), 4.61 (1H, d, *J*=6.5 Hz), 5.54–5.65 (2H, m). In the same manner, **46** (2 mg, 78%) was obtained from **44** (3 mg, 5.54 μmol).

4.3.5. Hydroboration–oxidation of 41 to form 50. $BH_3\cdot SMe_2$ (11 μl, 0.186 mmol) was added to a cooled (0 °C) solution of **41** (20 mg, 44.6 μmol) in THF (2.5 ml) under an Ar atmosphere and the mixture was stirred at 0 °C for 30 min, and at 22 °C for 15 h. EtOH (20 μl, 0.533 mmol) was gradually added and the resulting mixture was stirred for 10 min. After the mixture had been cooled in an ice bath, NaOH–H_2O (1 N, 180 μl, 0.180 mmol) and H_2O_2–H_2O (30%, 40 μl, 0.353 mmol) were further added, and the whole was stirred at 0 °C for 20 min, and at 22 °C for 8 h. Saturated NH_4Cl–H_2O and saturated $Na_2S_2O_3$–H_2O were added and the whole was extracted with CH_2Cl_2. Usual work-up and purification by PTLC [hexane–DME (3:1)] provided **50** (10.5 mg, 50%) and recovered **41** (4 mg, 20%) in order of decreasing polarity. **50**: Colorless glass. HRMS Calcd for $C_{26}H_{42}O_7$: 466.2928. Found: 466.2933. MS *m/z*: 466 (M^+, 1), 448 (2), 337 (7), 305 (7), 275 (6), 259 (7), 240 (7), 213 (10), 117 (12), 105 (13), 57 (85), 45 (100), 41 (27). IR ($CHCl_3$) cm^{-1}: 1716. ^1H NMR δ: 0.98 (1H, ddd, *J*=13, 12, 5.5 Hz), 1.19 (9H, s), 1.21 (1H, dd, *J*=10, 10 Hz, H5), 1.40–1.45 (1H, m), ca. 1.53 (1H, dd, *J*=14, 10 Hz, H7), 1.75 (1H, ddd, *J*=13.5, 8, 6 Hz), 1.82–1.93 (2H, m), 2.00 (1H, br d, *J*=13 Hz), 2.09 (1H, ddd, *J*=13.5, 8.5, 6.5 Hz), 2.21 (1H, dd, *J*=21, 4.5 Hz), 2.26 (1H, dd, *J*=14, 7 Hz, H7), 2.31 (1H, br d, *J*=21 Hz), 2.50–2.57 (2H, m, including OH, changed to δ 2.54, 1H, dd,

J=6, 5.5 Hz, H14), 3.28–3.37 (1H, m), 3.36 (3H, s), 3.42–3.47 (1H, br, OH), 3.47 (1H, dt, J=10.5, 5 Hz), ca. 3.58–3.66 (2H, m), ca. 3.65–3.75 (1H, m, H4), 3.71 (1H, d, J=6 Hz), ca. 3.98–4.08 (1H, m, H6), 4.06 (1H, ddd, J=10.5, 8, 6.5 Hz), 4.14 (1H, ddd, J=10.5, 8.5, 6 Hz), 4.63 (2H, s), 5.53–5.65 (2H, m). ^{13}C NMR δ: 21.5 (CH_2), 27.0 (CH_2), 27.2 ($CH_3\times3$), 29.0 (CH_2), 33.3 (CH_2), 35.1 (CH_2), 38.6 (C), 42.3 (C, C8), 44.0 (CH_2, C7), 47.5 (CH), 49.5 (C), 53.2 (CH), 55.1 (CH_3), 57.5 (CH, C5), 62.3 (CH_2), 66.8 (CH_2), 68.7 (CH_2), 71.3 (CH, C6), 75.4 (CH, C4), 83.7 (CH), 96.5 (CH_2), 126.1 (CH), 126.5 (CH), 178.3 (C).

4.3.6. *i*-Propylsulfonylation of 50 to form 51. *i*-$PrSO_2Cl$ (8 μl, 71.3 μmol) was added to a cooled (−18 °C) solution of **50** (9 mg, 19.3 μmol) and Et_3N (31 μl, 0.223 mmol) in CH_2Cl_2 (2 ml) under an Ar atmosphere and the mixture was stirred for 30 min. Saturated $NaHCO_3$–H_2O was added and the whole was extracted with CH_2Cl_2. The organic layer was washed successively with saturated $CuSO_4$–H_2O and saturated $NaHCO_3$–H_2O and then treated as usual. Separation by PTLC [benzene–EtOAc (5:2)] afforded **51** (9.5 mg, 86%) as a colorless glass. MS *m/z*: 404 (M^+−CH_2OMe−*i*-$PrSO_3$, 1), 386 (1), 342 (6), 240 (15), 222 (15), 195 (14), 157 (17), 129 (19), 91 (23), 71 (25), 57 (100), 45 (92), 43 (53), 41 (53). IR ($CHCl_3$) cm^{-1}: 1717. ^{1}H NMR δ: 1.01 (1H, ddd, J=13, 12.5, 5 Hz), 1.11 (9H, s), 1.38–1.62 (4H, m), 1.44 (6H, d, J=7 Hz, SO_2CHMe_2), 1.64–1.81 (3H, m), 1.98 (1H, br ddd, J=13, 3, 3 Hz), 2.04–2.16 (2H, m), 2.18–2.34 (2H, m), 2.28 (1H, dd, J=14.5, 8 Hz), 2.58 (1H, br dd, J=6, 6 Hz), 3.13 (1H, d, J=3.5 Hz, OH), 3.27 (1H, sep, J=7 Hz, SO_2CHMe_2), 3.37 (3H, s), 3.39 (1H, ddd, J=11, 5.5, 5 Hz), 3.51 (1H, ddd, J=11, 4.5, 4 Hz), ca. 3.58–3.70 (2H, m), 3.81 (1H, d, J=6 Hz), 4.01–4.19 (3H, m), 4.64 (1H, d, J=6.5 Hz), 4.69 (1H, d, J=6.5 Hz), 4.80 (1H, ddd, J=11, 10.5, 4.5 Hz, H4), 5.53–5.66 (2H, m). ^{13}C NMR δ: 16.5 (CH_3), 16.6 (CH_3), 21.4 (CH_2), 27.0 (CH_2), 27.2 ($CH_3\times3$), 29.0 (CH_2), 32.8 (CH_2), 33.3 (CH_2), 38.6 (C), 41.9 (C), 43.8 (CH_2), 47.4 (CH), 50.4 (C), 52.9 (CH), 53.1 (CH, SO_2CHMe_2), 55.1 (CH_3), 56.9 (CH, C5), 62.2 (CH_2), 67.0 (CH_2), 68.5 (CH_2), 69.4 (CH, C6), 83.5 (CH), 84.7 (CH, C4), 96.5 (CH_2), 125.7 (CH), 126.9 (CH), 178.3 (C).

4.3.7. Dess–Martin oxidation of 51 to form 52. A solution of **51** (7 mg, 12.2 μmol) and Dess–Martin periodinane (52 mg, 0.123 mmol) in CH_2Cl_2 (3 ml) was heated under reflux with stirring for 18 h. After the mixture had been cooled, saturated $Na_2S_2O_3$–H_2O was added and the mixture was extracted with CH_2Cl_2. Usual work-up followed by PTLC [hexane–EtOAc (3:2)] afforded **52** (7 mg, quant.) as a colorless glass. MS *m/z*: 446 (M^+−*i*-$PrSO_3H$, 2), 414 (3), 317 (3), 285 (5), 256 (5), 238 (6), 211 (15), 91 (15), 89 (17), 73 (45), 57 (76), 45 (100), 43 (43), 41 (41). IR ($CHCl_3$) cm^{-1}: 1719. ^{1}H NMR δ: ca. 1.14–1.22 (1H, m), 1.19 (9H, s), 1.33 (3H, d, J=6.5 Hz), 1.44 (3H, d, J=7 Hz), ca. 1.44–1.55 (1H, m), 1.55–1.69 (2H, m), 1.88 (1H, ddd, J=14, 7, 7 Hz), 1.93–1.97 (1H, m), ca. 2.02–2.11 (1H, m), 2.07 (1H, ddd, J=14, 7, 7 Hz), 2.28–2.48 (3H, m), 2.47 (1H, d, J=16.5 Hz, H7), 2.47 (1H, d, J=9.5 Hz, H5), 2.54 (1H, d, J=16.5 Hz, H7), 2.64 (1H, br dd, J=6, 5.5 Hz), ca. 3.32–3.39 (1H, m), 3.35 (3H, s), 3.45 (1H, ddd, J=10.5, 4.5, 4.5 Hz), 3.50 (1H, d, J=6 Hz), ca. 3.54–3.65 (2H, m), 3.66 (1H, qq, J=7, 6.5 Hz), 4.04 (1H, ddd, J=11.5, 7, 7 Hz), 4.14 (1H, ddd, J=11.5, 7, 7 Hz), 4.61 (1H, d, J=6.5 Hz), 4.64 (1H, d, J=6.5 Hz), 4.74 (1H, ddd, J=11, 9.5, 5.5 Hz, H4), 5.55–5.66 (2H, m). ^{13}C NMR δ: 16.3 (CH_3), 17.0 (CH_3), 20.3 (CH_2), 27.2 ($CH_3\times3$, CH_2), 28.6 (CH_2), 32.3 (CH_2), 32.7 (CH_2), 38.6 (C), 44.3 (C), 48.4 (CH), 50.6 (C), 51.7 (CH_2, C7), 52.8 (CH), 53.7 (CH), 55.1 (CH_3), 61.6 (CH_2), 62.9 (CH, C5), 66.6 (CH_2), 68.8 (CH_2), 78.1 (CH, C4), 84.7 (CH), 96.4 (CH_2), 125.6 (CH), 126.2 (CH), 178.2 (C), 207.4 (C, C6).

4.3.8. DBU treatment of 52 to form 53. A solution of **52** (7 mg, 12.3 μmol) and DBU (9 μl, 60.3 μmol) in benzene (2.5 ml) was heated under reflux with stirring for 2 h. After the mixture had been cooled, saturated NH_4Cl–H_2O was added and the mixture was extracted with CH_2Cl_2. Usual work-up and separation by PTLC [hexane–EtOAc (2:1)] afforded **53** (5 mg, 91%) as a colorless glass. HRMS Calcd for $C_{26}H_{38}O_6$: 446.2666. Found: 446.2648. MS *m/z*: 446 (M^+, 4), 414 (4), 317 (5), 285 (8), 255 (5), 211 (19), 73 (56), 57 (57), 45 (100), 41 (20). IR ($CHCl_3$) cm^{-1}: 1716, 1676, 1617. ^{1}H NMR δ: 1.20 (9H, s), 1.41 (1H, ddd, J=12.5, 9.5, 5 Hz), 1.50–1.66 (2H, m), 1.67–1.72 (1H, m), 1.76 (1H, ddd, J=13.5, 7.5, 6.5 Hz), 1.99–2.44 (4H, m), 2.28–2.35 (2H, m), 2.50 (1H, d, J=20 Hz, H7), 2.61 (1H, br dd, J=6, 6 Hz), 2.62 (1H, d, J=20 Hz, H7), 3.35 (3H, s), 3.39–3.47 (1H, m), 3.55 (1H, ddd, J=10.5, 4.5, 4.5 Hz), 3.62–3.67 (2H, m), 3.75 (1H, d, J=6 Hz), 4.07 (1H, ddd, J=11, 7, 7 Hz), 4.15 (1H, ddd, J=11, 7.5, 6 Hz), 4.63 (2H, s), 5.59–5.69 (2H, m), 6.69 (1H, dd, J=5, 3.5 Hz, H4). ^{13}C NMR δ: 19.7 (CH_2), 25.2 (CH_2, C3), 25.8 (CH_2), 26.5 (CH_2), 27.2 ($CH_3\times3$), 33.0 (CH_2), 38.6 (C), 40.5 (C), 46.3 (C), 48.0 (CH), 49.0 (CH), 50.0 (CH_2, C7), 55.1 (CH_3), 61.7 (CH_2), 66.7 (CH_2), 69.5 (CH_2), 89.3 (CH), 96.4 (CH_2), 125.1 (CH), 127.0 (CH), 131.2 (CH, C4), 145.4 (C, C5), 178.3 (C), 199.2 (C, C6).

4.3.9. Methoxyacetylation of 41 to form 54. Methoxyacetyl chloride (49 μl, 0.536 mmol) was added to a cooled (0 °C) solution of **41** (8 mg, 17.9 μmol) in CH_2Cl_2 (1.5 ml) and pyridine (0.3 ml) under an Ar atmosphere. After the mixture had been stirred at 0 °C for 45 min, saturated $NaHCO_3$–H_2O was added and the whole was stirred at 19 °C for 20 min. Extraction with CH_2Cl_2, usual work-up, and separation by PTLC [hexane–EtOAc (2:1)] provided **54** (8 mg, 86%) as a colorless glass. MS *m/z*: 475 (M^+−CH_2OMe, 0.5), 430 (3), 414 (1), 398 (2), 324 (3), 222 (24), 195 (19), 157 (28), 57 (43), 45 (100), 41 (18). IR ($CHCl_3$) cm^{-1}: 1743, 1720. ^{1}H NMR δ: 1.19 (9H, s), 1.39–1.50 (1H, m), ca. 1.55–1.70 (4H, m), 1.72 (1H, ddd, J=11, 8, 6.5 Hz), 1.82–1.92 (1H, m), 1.98 (1H, ddd, J=13.5, 5, 5 Hz), 2.10–2.26 (3H, m), 2.30 (1H, br d, J=19.5 Hz), 2.46 (1H, ddd, J=18, 4, 2 Hz), 2.51 (1H, dd, J=6, 6 Hz), 3.36 (3H, s), 3.42 (1H, dt, J=10.5, 5 Hz), 3.46 (3H, s, $COCH_2OCH_3$), 3.49 (1H, dt, J=10.5, 5 Hz), 3.63 (2H, dd, J=5, 5 Hz), 3.71 (1H, d, J=6 Hz), 4.04 (2H, s, $COCH_2OMe$), 4.08 (1H, ddd, J=11, 8, 6.5 Hz), 4.17 (1H, ddd, J=11, 8.5, 6 Hz), 4.63 (1H, d, J=6.5 Hz), 4.65 (1H, d, J=6.5 Hz), 5.36–5.41 (1H, m, H6), 5.48–5.55 (1H, m, H4), 5.52–5.65 (2H, m). ^{13}C NMR δ: 18.1 (CH_2), 23.3 (CH_2), 26.3 (CH_2), 27.2 ($CH_3\times3$), 27.4 (CH_2), 33.6 (CH_2), 38.6 (C), 38.7 (CH_2), 40.5 (C), 48.7 (C), 49.5 (CH), 50.3 (CH), 55.1 (CH_3), 59.3 (CH_3, $COCH_2OCH_3$), 62.2 (CH_2), 66.9 (CH_2), 69.2 (CH_2), 69.9 (CH_2, $COCH_2OMe$), 72.0

(CH, C4), 92.7 (CH), 96.4 (CH_2), 120.7 (CH, C6), 125.2 (CH), 127.4 (CH), 147.5 (C, C5), 169.5 (C, *C*OCH$_2$OMe), 178.4 (C).

4.3.10. Europium-catalyzed rearrangement of 54 to form 55–57. Eu(fod)$_3$ (1.5 mg, 1.59 μmol) was added to a solution of **54** (6 mg, 11.5 μmol) in $CHCl_3$ (2 ml) under an Ar atmosphere and the mixture was stirred at 22 °C for 24 h. Saturated $NaHCO_3$–H_2O was added and the whole was extracted with CH_2Cl_2. Usual work-up and separation by PTLC [benzene–EtOAc (15:1)] yielded **55** (2 mg, 33%), **56** (1 mg, 20%), and **57** (1 mg, 20%) in order of decreasing polarity. **55**: Colorless glass. MS *m/z*: 430 (M^+–MeOCH$_2$COOH, 2), 414 (2), 386 (2), 324 (3), 222 (20), 195 (16), 157 (24), 89 (17), 73 (19), 57 (49), 45 (100), 41 (20). IR ($CHCl_3$) cm^{-1}: 1743, 1719. ^{1}H NMR δ: 1.18 (9H, s), 1.48–2.36 (9H, m), 1.77 (1H, dd, *J*=15, 5.5 Hz, H7), 2.09 (1H, dd, *J*=15, 7 Hz, H7), 2.22–2.26 (2H, m), 2.47–2.54 (1H, m), 3.36 (3H, s), 3.39–3.55 (2H, m), 3.46 (3H, s), 3.65 (2H, dd, *J*=5, 5 Hz), 3.79 (1H, d, *J*=6 Hz), 4.00–4.19 (2H, m), 4.04 (2H, s, COC*H*$_2$OMe), 4.64 (2H, s), 5.11 (1H, ddd, *J*=3.5, 3.5, 1.5 Hz, H4), 5.55–5.65 (2H, m), 5.69 (1H, ddd, *J*=7, 5.5, 1.5 Hz, H6). **56**: Colorless glass. HRMS Calcd for $C_{26}H_{38}O_5$: 430.2717. Found: 430.2701. MS *m/z*: 430 (M^+, 2), 398 (1), 324 (2), 222 (39), 157 (44), 91 (18), 89 (13), 73 (13), 57 (66), 45 (100), 41 (23). IR ($CHCl_3$) cm^{-1}: 1717. ^{1}H NMR δ: 1.20 (9H, s), ca. 1.56–1.61 (1H, m), 1.37 (1H, ddd, *J*=12.5, 12.5, 5 Hz), 1.73 (1H, ddd, *J*=13.5, 8.5, 5.5 Hz), 1.97–2.36 (6H, m), 2.36 (1H, br d, *J*=19 Hz), 2.48–2.58 (2H, m), 3.35 (3H, s), 3.38 (1H, dd, *J*=10.5, 5 Hz), 3.47 (1H, dt, *J*=10.5, 5 Hz), 3.62 (2H, dd, *J*=5, 5 Hz), 3.78 (1H, d, *J*=6.5 Hz), 4.07 (1H, ddd, *J*=10.5, 8.5, 6.5 Hz), 4.19 (1H, ddd, *J*=10.5, 9, 6 Hz), 4.63 (2H, s), 5.21 (1H, dd, *J*=4, 3.5 Hz, H6), 5.55–5.67 (2H, m), 5.77 (1H, br dd, *J*=9.5, 5 Hz, H3), 5.93 (1H, dd, *J*=9.5, 2.5 Hz, H4). **57**: Colorless glass. HRMS Calcd for $C_{26}H_{38}O_5$: 430.2717. Found: 430.2713. MS *m/z*: 430 (M^+, 1), 398 (1), 324 (5), 222 (40), 157 (45), 89 (32), 73 (21), 57 (41), 45 (100), 41 (20). IR ($CHCl_3$) cm^{-1}: 1720. ^{1}H NMR δ: 1.19 (9H, s), 1.25–1.36 (1H, m), 1.39–1.70 (2H, m), 1.68 (1H, br d, *J*=4.5 Hz), 1.84 (1H, ddd, *J*=14, 8, 6.5 Hz), 1.96–2.09 (3H, m), 2.15 (1H, br d, *J*=13 Hz), 2.19–2.30 (1H, m), 2.36 (1H, br d, *J*=19 Hz), 2.64 (1H, br dd, *J*=7, 6 Hz), 3.35 (3H, s), ca. 3.35–3.43 (1H, m), 3.50 (1H, ddd, *J*=10.5, 5, 5 Hz), 3.61–3.66 (2H, m), 3.79 (1H, d, *J*=6 Hz), 4.05–4.17 (2H, m), 4.64 (2H, s), 5.40 (1H, br dd, *J*=5, 3.5 Hz, H4), 5.64 (1H, ddd, *J*=9.5, 3, 3 Hz), 5.55 (1H, dddd, *J*=9.5, 6.5, 1.5, 1.5 Hz), 5.77 (1H, d, *J*=9.5 Hz, H6), 5.90 (1H, d, *J*=9.5 Hz, H7).

4.3.11. Alcoholysis of 55 to form 58. K_2CO_3 (10 mg, 72.5 μmol) was added to a cooled (0 °C) solution of **55** (1.5 mg, 2.88 μmol) in MeOH (2 ml) and the mixture was stirred for 1.5 h. Saturated NH_4Cl–H_2O was added and the whole was extracted with CH_2Cl_2. Usual work-up and separation by PTLC [hexane–EtOAc (2:1)] gave **58** (1 mg, ca. 77%) as a colorless glass. HRMS Calcd for $C_{26}H_{40}O_6$: 448.2823. Found: 448.2824. MS *m/z*: 448 (M^+, 0.4), 342 (4), 258 (7), 240 (13), 213 (22), 174 (18), 91 (18), 57 (78), 45 (100), 41 (27). IR ($CHCl_3$) cm^{-1}: 1720. ^{1}H NMR δ: 1.19 (9H, s), 1.35 (1H, d, *J*=5 Hz, OH), 1.42–1.88 (5H, m), 1.65 (1H, dd, *J*=14.5, 6.5 Hz, H7), 1.90–1.94 (1H, m), 1.95–2.08 (3H, m), 2.08 (1H, dd, *J*=14.5, 6.5 Hz, H7), ca. 2.16–2.30 (2H, m), 2.45–2.52 (1H, m), 3.36 (3H, s), 3.37–3.44 (1H, m), 3.50 (1H, ddd, *J*=10.5, 5, 5 Hz), ca. 3.60–3.69 (2H, m), 3.73 (1H, d, *J*=6 Hz), 4.10 (1H, ddd, *J*=11, 8.5, 6.5 Hz), 4.18 (1H, ddd, *J*=11, 8.5, 6.5 Hz), 4.35–4.44 (1H, m, H6), 4.64 (2H, s), 5.54 (1H, ddd, *J*=4, 3.5, 1.5 Hz, H4), 5.55–5.65 (2H, m).

4.3.12. Dess–Martin oxidation of 58 to form 53. In the same manner as described for the preparation of **52** from **51** (Section 4.3.7), **58** (1 mg, 2.23 mmol) was oxidized with Dess–Martin periodinane (10 mg, 23.7 μmol) to afford **53** (1 mg, quant.) after PTLC [hexane–EtOAc (3:1)].

4.4. Introduction of the C18-methyl group into 39 (Table 1)

4.4.1. Reaction of 39 with MeMgI (runs a and b). The reaction procedure in THF (run b) is described as a representative example. MeMgI (0.37 M in Et_2O, 0.30 ml, 0.117 mmol) was added to a cooled (0 °C) solution of **39** (5 mg, 11.2 μmol) in THF (2.5 ml) under an Ar atmosphere and the mixture was stirred at that temperature for 20 min. Saturated NH_4Cl–H_2O was added and the whole was extracted with CH_2Cl_2. Usual work-up and purification by PTLC [benzene–EtOAc (7:1)] yielded **59** (2 mg, 38%) and recovered **39** (1.5 mg, 30%) in order of decreasing polarity. **59**: Colorless glass. MS *m/z*: 444 (M^+−H_2O, 2), 356 (1), 338 (3), 236 (31), 171 (48), 57 (82), 45 (100), 41 (35). IR ($CHCl_3$) cm^{-1}: 1713. ^{1}H NMR δ: 1.19 (9H, s), 1.32–1.74 (7H, m, including OH), 1.34 (3H, s), 2.01–2.10 (1H, m), 2.10–2.20 (1H, m), 2.15 (1H, dd, *J*=18.5, 3 Hz, H7), 2.24 (1H, ddd, *J*=13.5, 8.5, 7 Hz), 2.33 (1H, br d, *J*=19.5 Hz, H11), 2.49 (1H, br dd, *J*=6, 6 Hz, H14), 2.49 (1H, dd, *J*=18.5, 4 Hz, H7), 3.36 (3H, s), 3.40 (1H, ddd, *J*=11, 5.5, 5.5 Hz), 3.51 (1H, ddd, *J*=11, 4.5, 4.5 Hz), ca. 3.59–3.68 (2H, m), 3.66 (1H, d, *J*=6 Hz, H20), 4.08 (1H, ddd, *J*=10.5, 8.5, 7 Hz), 4.18 (1H, ddd, *J*=10.5, 8.5, 6 Hz), 4.64 (2H, s), 5.52–5.64 (2H, m), 5.69 (1H, dd, *J*=4, 3 Hz, H6). ^{13}C NMR δ: 19.8 (CH_2), 25.9 (CH_2), 26.5 (CH_2), 27.2 (CH_3×3), 31.7 (CH_3), 33.7 (CH_2), 38.6 (C), 38.8 (CH_2, C7), 39.0 (CH_2), 40.3 (C), 48.4 (C, C10), 50.3 (CH), 50.8 (CH, C9), 55.1 (CH_3), 62.2 (CH_2), 66.9 (CH_2), 69.1 (CH_2), 71.7 (C, C4), 92.6 (CH), 96.5 (CH_2), 118.7 (CH, C6), 125.4 (CH), 127.3 (CH), 156.1 (C), 178.4 (C). In a similar manner, **39** (5 mg, 11.2 μmol) was reacted with MeMgI in toluene at −18 to 0 °C to afford **59** (1 mg, 19%) and a recovery of **39** (2.5 mg, 50%).

4.4.2. Reaction of 39 with MeLi in Et_2O (run c). MeLi (1.1 M, 0.31 ml, 0.341 mmol) was added to a cooled (−78 °C) solution of **39** (6 mg, 13.5 μmol) in Et_2O (3 ml) under an Ar atmosphere and the mixture was stirred for 30 min. Quenching with saturated NH_4Cl–H_2O, extraction with CH_2Cl_2, usual work-up, and PTLC [benzene–EtOAc (6:1)] yielded **60** (1 mg, 16%), **59** (3 mg, 48%), and recovered **39** (1.5 mg, 25%) in order of decreasing polarity. **60**: Colorless glass. MS *m/z*: 444 (M^+−H_2O, 2), 356 (3), 338 (2), 236 (19), 171 (33), 57 (67), 45 (100), 41 (23). IR ($CHCl_3$) cm^{-1}: 1707. ^{1}H NMR δ: 1.20 (9H, s), ca. 1.22–1.85 (7H, m), 1.36 (3H, s), 2.09–2.36 (4H, m), 2.15 (1H, dd, *J*=19, 3.5 Hz, H7), 2.49 (1H, dd, *J*=6, 6 Hz, H14), 2.49 (1H, dd, *J*=19, 4.5 Hz, H7), 3.35 (3H, s), 3.46–3.68 (4H, m), 3.86 (1H, d, *J*=6 Hz, H20), 4.06 (1H, ddd, *J*=11, 8.5, 6.5 Hz), 4.16 (1H, ddd, J=11, 8.5, 6 Hz), 4.63 (1H, d, J=6.5 Hz), 4.65 (1H, d, J=6.5 Hz), 5.52–5.65 (2H, m), 5.69 (1H, dd, J=4.5, 3.5 Hz, H6).

4.4.3. Reaction of 39 or 63 with MeLi in THF (runs d and e). The reaction procedure of run d is described as a representative example. MeLi (1.1 M in Et_2O, 1.37 ml, 1.51 mmol) was slowly added during 1 min to a cooled (−78 °C) solution of **39** (84 mg, 0.188 mmol) in THF (8 ml) under an Ar atmosphere and the mixture was stirred at that temperature for 20 min. Saturated NH_4Cl–H_2O was added and the whole was extracted with CH_2Cl_2. Usual work-up and purification by PTLC [benzene–EtOAc (1:1)] furnished crude-**63** (10 mg), **61** (42 mg, 59%), and **62** (8 mg, 11%) in order of increasing polarity. The crude-**63** was further separated by PTLC (2% MeOH–CH_2Cl_2) to give **63** (4 mg, 6%). **61**: Slightly labile colorless glass. MS m/z: 360 (M^+−H_2O, 2), 315 (1), 272 (4), 254 (15), 209 (17), 189 (21), 171 (22), 45 (100). ^{1}H NMR δ: 1.31–1.76 (9H, m, including OH×2), 1.34 (3H, s), 2.05 (1H, ddd, J=12.5, 3.5, 3.5 Hz), 2.09–2.24 (2H, m), 2.13 (1H, dd, J=19, 3 Hz, H7), 2.33 (1H, br d, J=19 Hz), 2.47 (1H, dd, J=19, 4 Hz, H7), 2.49 (1H, dd, J=6, 6 Hz), 3.36 (3H, s), 3.40 (1H, dt, J=10.5, 5 Hz), 3.51 (1H, dt, J=10.5, 5 Hz), 3.64 (2H, dd, J=5, 5 Hz), ca. 3.64–3.82 (2H, m), 3.65 (1H, d, J=6 Hz), 4.64 (2H, s), 5.51–5.63 (2H, m), 5.68 (1H, dd, J=4, 3 Hz, H6). ^{13}C NMR δ: 19.8 (CH_2), 25.9 (CH_2), 26.6 (CH_2), 31.7 (CH_3), 38.3 (CH_2), 39.0 (CH_2), 39.1 (CH_2), 40.3 (C), 48.3 (C), 50.3 (CH), 50.8 (CH), 55.1 (CH_3), 60.3 (CH_2), 66.9 (CH_2), 69.1 (CH_2), 71.7 (C, C4), 92.6 (CH), 96.5 (CH_2), 118.8 (CH, C6), 125.6 (CH), 127.3 (CH), 156.1 (C, C5). **62**: Slightly labile colorless glass. MS m/z: 360 (M^+−H_2O, 2), 315 (1), 272 (3), 254 (13), 209 (14), 189 (18), 171 (17), 45 (100). ^{1}H NMR δ: 1.24–1.38 (1H, m), 1.36 (3H, s), 1.42–1.67 (3H, m), 1.59–1.88 (5H, m, including OH×2), 2.08–2.24 (3H, m), 2.13 (1H, dd, J=19, 3 Hz, H7), 2.31 (1H, br d, J=20 Hz), 2.45–2.51 (1H, m), 2.46 (1H, dd, J=19, 4.5 Hz, H7), 3.35 (3H, s), 3.45–3.83 (6H, m), 3.85 (1H, d, J=6 Hz), 4.63 (1H, d, J=6.5 Hz), 4.65 (1H, d, J=6.5 Hz), 5.52–5.65 (2H, m), 5.68 (1H, dd, J=4.5, 3 Hz, H6). ^{13}C NMR δ: 18.0 (CH_2), 25.3 (CH_2), 26.5 (CH_2), 28.9 (CH_3), 37.9 (CH_2), 38.2 (CH_2), 39.2 (CH_2), 40.1 (C), 47.8 (C), 50.0 (CH), 50.4 (CH), 55.1 (CH_3), 60.3 (CH_2), 67.2 (CH_2), 69.3 (CH_2), 70.8 (C, C4), 93.8 (CH), 96.4 (CH_2), 119.0 (CH, C6), 125.2 (CH), 127.9 (CH), 155.5 (C, C5). **63**: Colorless glass. HRMS Calcd for $C_{21}H_{30}O_5$: 362.2092. Found: 362.2109. MS m/z: 362 (M^+, 0.5), 330 (1), 317 (2), 285 (2), 273 (2), 256 (20), 211 (27), 185 (11), 91 (12), 73 (13), 45 (100). ^{1}H NMR δ: 1.43 (1H, ddd, J=13, 10, 5 Hz), 1.53 (1H, br d, J=5 Hz), 1.68 (1H, ddd, J=13.5, 8.5, 5.5 Hz), 1.77–1.88 (2H, m), 2.13–2.27 (5H, m, including OH), 2.28–2.39 (1H, m), 2.33 (1H, dd, J=21, 3 Hz, H7), 2.48 (1H, dddd, J=18.5, 4, 4, 2 Hz, H3), 2.56 (1H, br dd, J=6, 6 Hz), 2.62 (1H, dd, J=21, 5 Hz, H7), 3.35 (3H, s), 3.39 (1H, ddd, J=10.5, 6, 4.5 Hz), 3.51 (1H, ddd, J=10.5, 4.5, 4.5 Hz), 3.58–3.68 (2H, m), ca. 3.68–3.84 (2H, m), 3.70 (1H, d, J=6 Hz), 4.63 (2H, s), 5.55–5.65 (2H, m), 6.82 (1H, dd, J=5, 3 Hz, H6). ^{13}C NMR δ: 19.7 (CH_2), 25.9 (CH_2), 26.4 (CH_2), 37.5 (CH_2), 39.1 (CH_2, C3), 40.0 (CH_2, C7), 40.2 (C), 48.8 (C), 49.7 (CH), 50.2 (CH), 55.1 (CH_3), 60.1 (CH_2, CH_2OH), 66.7 (CH_2), 69.1 (CH_2), 91.9 (CH), 96.4 (CH_2), 125.4 (CH), 127.0 (CH), 136.9 (CH, C6), 148.8 (C, C5), 197.4 (C, C4). In the same manner, **63** (4 mg, 11.0 μmol) was reacted with MeLi (1.1 M in Et_2O, 0.08 ml, 88.1 μmol) to give **61** (2.5 mg, 60%) and **62** (0.5 mg, 12%) (Table 1, run e).

4.5. Preparation of 1 from 61 and 62 (Scheme 7)

4.5.1. Acetylation of 61, 62 to form 64, 65, respectively. The preparation of **64** from **61** is described as a typical procedure. Ac_2O (0.20 ml, 2.12 mmol) was added to a cooled (0 °C) solution of **61** (35 mg, 92.6 μmol) in pyridine (0.30 ml, 3.71 mmol) and CH_2Cl_2 (1.5 ml), and the mixture was stirred at 0 °C for 5 min and at 25 °C for 5 h. Saturated $NaHCO_3$–H_2O was added and the whole was extracted with CH_2Cl_2. Usual work-up and purification by PTLC [hexane–EtOAc (2:1)] provided **64** (36 mg, 93%) as a slightly labile colorless glass. MS m/z: 402 (M^+−H_2O, 2), 357 (2), 314 (8), 296 (5), 236 (15), 209 (23), 171 (29), 45 (100), 43 (59). IR ($CHCl_3$) cm^{-1}: 1720. ^{1}H NMR δ: 1.31–1.43 (1H, m), 1.34 (3H, s), 1.44–1.79 (7H, m), 2.01–2.20 (2H, m), 2.04 (3H, s), 2.14 (1H, dd, J=19, 3 Hz), 2.23 (1H, ddd, J=13.5, 9.5, 6.5 Hz), 2.33 (1H, br d, J=18.5 Hz), 2.47 (1H, dd, J=19, 4 Hz), 2.48 (1H, dd, J=6, 6 Hz), 3.36 (3H, s), 3.40 (1H, dt, J=10.5, 5 Hz), 3.51 (1H, dt, J=10.5, 5 Hz), 3.64 (2H, dd, J=5, 5 Hz), 3.66 (1H, d, J=6 Hz), 4.07 (1H, ddd, J=10.5, 9, 6.5 Hz, CH_2OAc), 4.21 (1H, ddd, J=10.5, 9.5, 5.5 Hz, CH_2OAc), 4.64 (2H, s), 5.51–5.63 (2H, m), 5.69 (1H, dd, J=4, 3 Hz). ^{13}C NMR δ: 19.8 (CH_2), 21.1 (CH_3, COCH_3), 25.9 (CH_2), 26.5 (CH_2), 31.7 (CH_3), 33.8 (CH_2), 38.8 (CH_2), 39.0 (CH_2), 40.2 (C), 48.3 (C), 50.2 (CH), 50.7 (CH), 55.1 (CH_3), 62.2 (CH_2, CH_2OAc), 66.9 (CH_2), 69.1 (CH_2), 71.7 (C, C4), 92.5 (CH), 96.4 (CH_2), 118.6 (CH), 125.5 (CH), 127.2 (CH), 156.1 (C), 170.9 (C, COCH_3). In the same manner, **62** (8 mg, 21.2 μmol) was led to **65** (8 mg, 90%), a slightly labile colorless glass. MS m/z: 402 (M^+−H_2O, 2), 357 (1), 314 (2), 296 (3), 236 (13), 209 (11), 171 (32), 45 (100), 43 (51). IR ($CHCl_3$) cm^{-1}: 1724. ^{1}H NMR δ: 1.25–1.38 (1H, m), 1.36 (3H, s), 1.41–1.56 (3H, m), 1.62–1.89 (4H, m, including OH), 2.04 (3H, s), ca. 2.05–2.21 (2H, m), 2.14 (1H, dd, J=19, 2.5 Hz), 2.23 (1H, ddd, J=13, 9.5, 6.5 Hz), 2.32 (1H, br d, J=20 Hz), 2.44–2.51 (1H, m), 2.46 (1H, dd, J=19, 4.5 Hz), 3.35 (3H, s), 3.46–3.60 (2H, m), 3.60–3.71 (2H, m), 3.86 (1H, d, J=6 Hz), 4.07 (1H, ddd, J=10.5, 9.5, 6.5 Hz, CH_2OAc), 4.21 (1H, ddd, J=10.5, 9.5, 6 Hz, CH_2OAc), 4.63 (1H, d, J=6.5 Hz), 4.65 (1H, d, J=6.5 Hz), 5.52–5.64 (2H, m), 5.68 (1H, dd, J=4.5, 2.5 Hz). ^{13}C NMR δ: 17.9 (CH_2), 21.1 (CH_3, COCH_3), 25.3 (CH_2), 26.4 (CH_2), 28.9 (CH_3), 33.7 (CH_2), 37.9 (CH_2), 38.9 (CH_2), 40.0 (C), 47.9 (C), 49.8 (CH), 50.4 (CH), 55.1 (CH_3), 62.2 (CH_2, CH_2OAc), 67.2 (CH_2), 69.4 (CH_2), 70.7 (C, C4), 93.7 (CH), 96.4 (CH_2), 118.9 (CH), 125.1 (CH), 127.8 (CH), 155.5 (C), 170.9 (C, COCH_3).

4.5.2. Oxidation of 64 and 65 to form 4, 66, and 67. The oxidation procedure of **64** is presented as a representative example. PCC–Al_2O_3 (20 wt %, 346 mg, 0.321 mmol) was added in one portion to a cooled (5 °C) solution of **64** (45 mg, 0.107 mmol) in benzene (8 ml), and the mixture was stirred at that temperature for 15 min and at 25 °C for 2 h. Saturated $NaHCO_3$–H_2O was added and the whole was filtered under reduced pressure. The filtered Al_2O_3 was washed with CH_2Cl_2. The filtrate was extracted with CH_2Cl_2 and the organic layer was treated as usual.

Purification by PTLC [hexane–EtOAc (9:1)] afforded **4** (28 mg, 63%), **66** (7 mg, 16%), and **67** (5.5 mg, 13%) in order of decreasing polarity. **4**: Colorless glass. HRMS Calcd for $C_{24}H_{34}O_6$: 418.2353. Found: 418.2359. MS *m/z*: 418 (M^+, 2), 386 (3), 373 (7), 299 (6), 237 (9), 225 (23), 187 (14), 73 (30), 45 (100), 43 (45). IR ($CHCl_3$) cm^{-1}: 1727, 1668. ^1H NMR δ: 1.46–1.72 (3H, m), 1.78 (1H, ddd, J=14, 8, 6.5 Hz), 1.83–1.94 (2H, m), 2.03 (3H, s), 2.03–2.17 (3H, m), 2.04 (3H, s), 2.22–2.38 (2H, m), 2.46 (1H, d, J=19.5 Hz, H7), 2.52 (1H, d, J=19.5 Hz, H7), 2.56–2.62 (1H, m), 3.35 (3H, s), 3.43 (1H, ddd, J=10.5, 5.5, 4.5 Hz), 3.53 (1H, ddd, J=10.5, 4.5, 4.5 Hz), 3.61–3.66 (2H, m), 3.69 (1H, d, J=6 Hz), 4.07 (1H, ddd, J=11, 8, 6.5 Hz), 4.17 (1H, ddd, J=11, 8, 6.5 Hz), 4.62 (2H, s), 5.54–5.68 (2H, m). ^{13}C NMR δ: 19.7 (CH_2), 21.0 (CH_3), 21.9 (CH_3), 26.1 (CH_2), 26.6 (CH_2), 32.6 (CH_2), 34.2 (CH_2), 41.0 (C), 47.96 (C), 48.00 (CH), 49.6 (CH), 51.8 (CH_2, C7), 55.0 (CH_3), 61.7 (CH_2), 66.7 (CH_2), 69.5 (CH_2), 90.1 (CH), 96.4 (CH_2), 125.1 (CH), 127.1 (CH), 140.1 (C, C5), 143.4 (C, C4), 170.7 (C), 201.1 (C, C6). **66**: Slightly unstable colorless glass. HRMS Calcd for $C_{24}H_{34}O_5$: 402.2404. Found: 402.2410. MS *m/z*: 402 (M^+, 1), 342 (1), 236 (16), 209 (10), 208 (12), 171 (27), 45 (100), 43 (53). IR ($CHCl_3$) cm^{-1}: 1729. ^1H NMR δ: 1.36 (1H, ddd, J=12.5, 12.5, 5 Hz), ca. 1.52–1.61 (1H, m), 1.73 (3H, br s), 1.74 (1H, ddd, J=13, 9, 6 Hz), 1.92–2.31 (6H, m), 2.05 (3H, s), 2.49 (1H, dd, J=6, 5.5 Hz), 2.55 (1H, dd, J=19, 4.5 Hz, H7), 3.34 (3H, s), 3.38 (1H, dt, J=10.5, 5 Hz), 3.47 (1H, dt, J=10.5, 5 Hz), 3.61 (2H, dd, J=5, 5 Hz), 3.79 (1H, d, J=6 Hz), 4.09 (1H, ddd, J=10.5, 9, 6.5 Hz), 4.22 (1H, ddd, J=10.5, 9.5, 6 Hz), 4.82 (2H, s), 5.35 (1H, dd, J=4.5, 3 Hz, H6), 5.54–5.67 (3H, m). ^{13}C NMR δ: 19.3 (CH_3), 21.1 (CH_3), 23.0 (CH_2), 25.0 (CH_2), 26.5 (CH_2), 33.9 (CH_2), 39.3 (CH_2), 40.3 (C), 47.1 (C), 49.5 (CH), 50.1 (CH), 55.1 (CH_3), 62.2 (CH_2), 66.8 (CH_2), 68.9 (CH_2), 91.9 (CH), 96.4 (CH_2), 117.0 (CH, C6), 125.4 (CH), 126.3 (CH, C3), 127.5 (CH), 129.2 (C, C4), 148.5 (C, C5), 170.9 (C). **67**: Slightly unstable colorless glass. HRMS Calcd for $C_{24}H_{34}O_5$: 402.2404. Found: 402.2384. MS *m/z*: 402 (M^+, 1), 342 (1), 296 (6), 236 (16), 209 (11), 171 (48), 45 (100), 43 (40). IR ($CHCl_3$) cm^{-1}: 1722. ^1H NMR δ: 1.24 (1H, ddd, J=12.5, 12.5, 3.5 Hz), 1.46–1.70 (3H, m), 1.68 (3H, br s), 1.84 (1H, dt, J=14, 7.5 Hz), 1.88–2.11 (3H, m), 2.03 (3H, s), 2.12 (1H, br d, J=12.5 Hz), 2.20 (1H, dddd, J=19.5, 5, 2.5, 2.5 Hz), 2.36 (1H, br d, J=19.5 Hz), 2.62 (1H, dd, J=6, 6 Hz), 3.35 (3H, s), 3.38 (1H, ddd, J=10.5, 5, 4.5 Hz), 3.49 (1H, ddd, J=10.5, 4.5, 4.5 Hz), 3.60–3.66 (2H, m), 3.78 (1H, d, J=6 Hz), 4.13 (2H, dd, J=7.5, 7.5 Hz), 4.64 (2H, s), 5.53 (1H, dddd, J=9.5, 6.5, 1.5, 1.5 Hz), 5.61 (1H, ddd, J=9.5, 2.5, 2.5 Hz), 5.74 (1H, d, J=9.5 Hz, H7), 6.29 (1H, d, J=9.5 Hz, H6). ^{13}C NMR δ: 18.8 (CH_3), 20.4 (CH_2), 21.1 (CH_3), 26.7 (CH_2), 27.0 (CH_2), 31.3 (CH_2), 32.0 (CH_2), 43.4 (C), 48.7 (C), 48.8 (CH), 49.4 (CH), 55.0 (CH_3), 62.4 (CH_2), 66.8 (CH_2), 69.2 (CH_2), 89.5 (CH), 96.5 (CH_2), 124.8 (CH, C6), 125.6 (CH), 125.9 (CH), 126.7 (CH, C4), 135.1 (CH, C7), 137.6 (C, C5), 170.9 (C). In the same manner, oxidation of **65** (14 mg, 33.3 μmol) provided **4** (9 mg, 65%), **66** (2 mg, 15%), and **67** (2 mg, 15%).

4.5.3. Hydrocyanation of 4 to form 5 and 68. Et_2AlCN (1 M in toluene, 1.03 ml, 1.03 mmol) was added to a cooled (−18 °C) solution of **4** (54 mg, 0.129 mmol) in toluene (8 ml) under an Ar atmosphere and the mixture was stirred at that temperature for 30 min, and at 24 °C for 1.5 h. Saturated NH_4Cl–H_2O was added and the whole was extracted with CH_2Cl_2. Usual work-up and separation by PTLC [hexane–EtOAc (7:4)] afforded **5** (54 mg, 94%) and **68** (1 mg, 2%) in order of increasing polarity. **5**: Colorless glass. HRMS Calcd for $C_{25}H_{35}NO_6$: 445.2462. Found: 445.2443. MS *m/z*: 445 (M^+, 1), 413 (2), 400 (5), 385 (1), 356 (2), 326 (2), 296 (2), 280 (4), 252 (4), 175 (5), 117 (6), 105 (9), 89 (20), 73 (16), 59 (17), 45 (100), 43 (38). IR ($CHCl_3$) cm^{-1}: 1733, 1706. ^1H NMR δ: 1.14–1.29 (2H, m), 1.56 (3H, s), 1.56–1.68 (2H, m), 1.76–1.81 (1H, m), 1.80–2.15 (3H, m), 2.04 (3H, s), 2.15 (1H, s, H5), 2.21 (1H, br d, J=13 Hz), 2.25–2.35 (1H, m), 2.43 (1H, br d, J=20 Hz), 2.45 (1H, d, J=17.5 Hz, H7), 2.63 (1H, d, J=17.5 Hz, H7), 2.68 (1H, br dd, J=6, 6 Hz), 3.35 (3H, s), 3.46–3.74 (4H, m), 3.88 (1H, d, J=6 Hz), 4.05 (1H, ddd, J=11.5, 7.5, 7 Hz), 4.17 (1H, ddd, J=11.5, 7.5, 6.5 Hz), 4.62 (1H, d, J=6.5 Hz), 4.66 (1H, d, J=6.5 Hz), 5.57–5.68 (2H, m). ^{13}C NMR δ: 20.1 (CH_2), 21.0 (CH_3), 27.0 (CH_2), 28.3 (CH_3, C4-methyl), 29.4 (CH_2), 32.2 (CH_2), 33.3 (C, C4), 38.5 (CH_2), 43.1 (C), 47.9 (C), 48.3 (CH), 51.6 (CH_2, C7), 54.1 (CH), 55.0 (CH_3), 61.6 (CH_2), 66.1 (CH, C5), 66.5 (CH_2), 68.8 (CH_2), 84.0 (CH), 96.2 (CH_2), 122.8 (C, CN), 125.1 (CH), 126.9 (CH), 170.6 (C), 206.0 (C, C6). **68**: Colorless glass. HRMS Calcd for $C_{25}H_{35}NO_6$: 445.2462. Found: 445.2466. MS *m/z*: 445 (M^+, 1), 413 (1), 400 (3), 385 (1), 371 (2), 340 (3), 326 (3), 296 (3), 280 (3), 252 (6), 105 (8), 89 (15), 73 (17), 59 (13), 45 (100), 43 (37). IR ($CHCl_3$) cm^{-1}: 2234, 1729, 1702. ^1H NMR δ: 1.25–1.46 (2H, m), 1.37 (3H, s), 1.66–1.85 (3H, m), 1.91 (1H, ddd, J=13, 12.5, 3.5 Hz, H3), 1.97–2.05 (2H, m), 2.04 (3H, s), 2.16 (1H, ddd, J=14, 7.5, 7 Hz), 2.21 (1H, br d, J=19 Hz), 2.34 (1H, dd, J=19, 5 Hz), 2.47 (1H, d, J=20 Hz, H7), 2.52–2.58 (1H, m), 2.63 (1H, d, J=20 Hz, H7), 2.73 (1H, s, H5), 3.37 (3H, s), 3.44–3.61 (2H, m), 3.52 (1H, d, J=6 Hz), 3.62–3.68 (2H, m), 4.06 (1H, ddd, J=11, 7.5, 7 Hz), 4.16 (1H, ddd, J=11.5, 7.5, 6.5 Hz), 4.63 (1H, d, J=6.5 Hz), 4.66 (1H, d, J=6.5 Hz), 5.58–5.68 (2H, m). ^{13}C NMR δ: 17.9 (CH_2), 21.0 (CH_3), 21.2 (CH_3, C4-methyl), 26.1 (CH_2), 27.5 (CH_2), 32.7 (CH_2), 34.8 (C, C4), 37.6 (CH_2), 40.2 (C), 43.0 (CH), 45.5 (CH), 47.2 (C), 52.0 (CH_2, C7), 55.2 (CH_3), 61.3 (CH_2), 63.2 (CH, C5), 66.7 (CH_2), 69.9 (CH_2), 93.6 (CH), 96.4 (CH_2), 124.8 (CH), 125.1 (C, CN), 127.3 (CH), 170.6 (C), 209.7 (C, C6).

4.5.4. Isomerization of 68 to 5 with DBU. A solution of **68** (6 mg, 13.5 μmol) and DBU (10 μl, 67.0 μmol) in benzene (2.5 ml) was refluxed with stirring for 0.5 h. After the mixture had been cooled, saturated NH_4Cl–H_2O was added and the whole was extracted with CH_2Cl_2. Usual work-up and separation by PTLC [hexane–EtOAc (7:4)] yielded a product with lower polarity than **68,** which was identical with **5** (5.5 mg, 92%).

4.5.5. Deprotection of 5 with TMSI to form 69. TMSCl (26 μl, 0.206 mmol) was added to a cooled (0 °C) slurry of **5** (18 mg, 40.4 μmol) and NaI (17 mg, 0.227 mmol) in CH_3CN (2.5 ml) under an Ar atmosphere and the mixture was stirred at 0 °C for 40 min. Saturated $NaHCO_3$–H_2O was added and the whole was extracted with CH_2Cl_2. Usual work-up and separation by PTLC [hexane–EtOAc (1:1)] furnished **69** (15 mg, 94%) as a colorless glass.

HRMS Calcd for $C_{23}H_{31}NO_5$: 401.2200. Found: 401.2191. MS *m/z*: 401 (M^+, 15), 356 (3), 341 (6), 314 (8), 279 (10), 252 (15), 194 (12), 175 (11), 117 (16), 105 (27), 91 (44), 45 (41), 43 (100). IR ($CHCl_3$) cm^{-1}: 2230, 1725, 1705. ^1H NMR δ: 1.17–1.30 (2H, m), 1.57 (3H, s), 1.59–1.72 (1H, m), 1.78–2.15 (5H, m), 2.05 (3H, s), 2.17 (1H, s, H5), 2.21 (1H, br d, J=13 Hz), 2.32 (1H, dd, J=19, 4.5 Hz), 2.45 (1H, br d, J=19 Hz), 2.47 (1H, d, J=17.5 Hz), 2.63 (1H, d, J=17.5 Hz), 2.67–2.73 (1H, m), 3.47 (1H, ddd, J=10, 7.5, 3 Hz, OCH_2CH_2OH), 3.54 (1H, ddd, J=10, 4.5, 3 Hz, OCH_2CH_2OH), 3.58–3.69 (1H, m, changed to δ 3.63, ddd, J=10, 4.5, 3 Hz with D_2O), 3.71–3.82 (1H, m, changed to δ 3.76, ddd, J=10, 7.5, 3 Hz with D_2O), 3.97 (1H, d, J=6 Hz), 4.05 (1H, ddd, J=11.5, 7, 7 Hz), 4.18 (1H, ddd, J=11.5, 7.5, 6.5 Hz), 5.57–5.73 (2H, m). ^{13}C NMR δ: 20.2 (CH_2), 21.0 (CH_3), 27.1 (CH_2), 28.0 (CH_3, C4-methyl), 29.3 (CH_2), 32.2 (CH_2), 33.4 (C, C4), 38.4 (CH_2), 43.2 (C), 47.9 (C), 48.1 (CH), 51.6 (CH_2), 54.1 (CH), 61.5 (CH_2), 61.9 (CH_2, CH_2OH), 66.0 (CH, C5), 70.0 (CH_2, OCH_2CH_2OH), 83.2 (CH), 123.0 (C, CN), 125.7 (CH), 126.4 (CH), 170.6 (C), 205.8 (C).

4.5.6. Bromination of 69 to form 70. A solution of **69** (14 mg, 34.9 μmol), Ph_3P (56 mg, 0.214 mmol), and CBr_4 (58 mg, 0.175 mmol) in CH_2Cl_2 (4 ml) was stirred at 0 °C for 5 min and at 24 °C for 1.5 h. Saturated $NaHCO_3$–H_2O was added and the whole was extracted with CH_2Cl_2. Usual work-up and purification by PTLC [hexane–EtOAc (2:1)] provided **70** (15 mg, 93%) as a colorless glass. HRMS Calcd for $C_{23}H_{30}BrNO_4$: 465.1337, 463.1357. Found: 465.1355, 463.1370. MS *m/z*: 465, 463 (M^+, 6, 5), 405, 403 (3, 2), 384 (8), 378, 376 (4, 5), 279 (23), 109, 107 (36, 37), 91 (51), 43 (100). IR ($CHCl_3$) cm^{-1}: 2237, 1728, 1707. ^1H NMR δ: 1.15–1.29 (2H, m), 1.56 (3H, s), ca. 1.57–1.70 (1H, m), 1.77–1.82 (1H, m), 1.85–2.04 (2H, m), 1.88 (1H, ddd, J=14, 7.5, 6.5 Hz), 2.05 (3H, s), 2.09 (1H, ddd, J=14, 7.5, 7 Hz), 2.16 (1H, s), 2.23 (1H, dddd, J=13, 3.5, 3.5, 1.5 Hz), 2.31 (1H, dd, J=19, 5 Hz), 2.45 (1H, br d, J=19 Hz), 2.46 (1H, d, J=17.5 Hz), 2.64–2.70 (1H, m), 2.63 (1H, d, J=17.5 Hz), 3.43 (1H, ddd, J=10.5, 6.5, 6 Hz, CH_2Br), 3.48 (1H, ddd, J=10.5, 6, 6 Hz, CH_2Br), 3.63 (1H, ddd, J=10.5, 6.5, 6 Hz), 3.76 (1H, ddd, J=10.5, 6, 6 Hz), 3.93 (1H, d, J=6 Hz), 4.05 (1H, ddd, J=11, 7.5, 7 Hz), 4.17 (1H, ddd, J=11, 7.5, 6.5 Hz), 5.55–5.71 (2H, m). ^{13}C NMR δ: 20.2 (CH_2), 21.0 (CH_3), 27.0 (CH_2), 28.1 (CH_3), 29.3 (CH_2), 30.5 (CH_2, CH_2Br), 32.2 (CH_2), 33.3 (C), 38.4 (CH_2), 43.2 (C), 48.1 (C), 48.3 (CH), 51.6 (CH_2), 54.2 (CH), 61.5 (CH_2), 66.1 (CH), 69.0 (CH_2), 83.6 (CH), 122.8 (C, CN), 125.4 (CH), 126.5 (CH), 170.6 (C), 205.8 (C).

4.5.7. Zinc reduction of 70 to form 71. Zn (784 mg, 12.0 mg atom) and NH_4Cl (43 mg, 0.804 mmol) were added to a solution of **70** (37 mg, 79.7 μmol) in 2-PrOH–H_2O (14:1, 12 ml) and the mixture was refluxed with stirring for 12 h. Saturated NH_4Cl–H_2O was added and the whole was extracted with CH_2Cl_2. Usual work-up and separation by PTLC [hexane–EtOAc (4:3)] afforded **71** (27 mg, 95%) as colorless prisms, mp 138–139 °C (CH_2Cl_2–hexane). Anal. Calcd for $C_{21}H_{27}NO_4$: C, 70.56; H, 7.61; N, 3.92. Found: C, 70.49; H, 7.70; N, 3.93. HRMS Calcd for $C_{21}H_{27}NO_4$: 357.1939. Found: 357.1938. MS *m/z*: 357 (M^+, 3), 339 (3), 297 (8), 279 (8), 270 (8), 252 (11), 242 (14), 105 (28), 91 (35), 43 (100). IR (KBr) cm^{-1}: 2238, 1734, 1694. ^1H NMR δ: 1.25 (1H, ddd, J=13.5, 13.5, 3.5 Hz), 1.30 (1H, ddd, J=13, 13, 4 Hz), 1.57 (3H, s), 1.68 (1H, ddddd, J=14, 3.5, 3.5, 3.5, 3.5 Hz), 1.78–2.12 (6H, m), 2.04 (3H, s), 2.14 (1H, d, J=10 Hz, OH), 2.18 (1H, s), 2.35 (1H, dddd, J=19.5, 4.5, 3, 2 Hz), 2.45 (1H, br d, J=19.5 Hz), 2.45 (1H, d, J=17 Hz), 2.63 (1H, d, J=17 Hz), 2.68 (1H, ddd, J=6.5, 6.5, 2 Hz), 4.05 (1H, ddd, J=11.5, 7, 7 Hz), 4.18 (1H, ddd, J=11.5, 7.5, 7.5 Hz), 4.37 (1H, dd, J=10, 6.5 Hz, changed to d, J=6.5 Hz with D_2O, H20), 5.71 (1H, dddd, J=9.5, 6.5, 2, 1.5 Hz), 5.83 (1H, ddd, J=9.5, 3, 3 Hz). ^{13}C NMR δ: 20.2 (CH_2), 21.0 (CH_3), 27.3 (CH_2), 28.0 (CH_3), 29.6 (CH_2), 32.2 (CH_2), 33.3 (C), 38.4 (CH_2), 42.9 (C), 48.1 (C), 50.2 (CH), 51.4 (CH_2), 54.1 (CH), 61.4 (CH_2), 65.8 (CH), 76.0 (CH, C20), 122.7 (C, CN), 127.3 (CH), 128.0 (CH), 170.6 (C), 205.8 (C).

4.5.8. Pyrrolidine ring formation from 71 to form 74 and 75. BuLi (1.56 M in hexane, 1.44 ml, 2.26 mmol) was added to a cooled (−18 °C) solution of *i*-Pr_2NH (0.48 ml, 3.43 mmol) in THF (5 ml) under an Ar atmosphere and the mixture was stirred at the same temperature for 10 min. The mixture was then cooled to −78 °C and TMSCl (0.72 ml, 5.68 mmol) was added. A solution of **71** (20 mg, 56.0 μmol) in THF (3 ml) was added dropwise to this, and the resulting mixture was stirred at −78 °C for 30 min. Et_3N (1.56 ml, 11.2 mmol) was added to the mixture and the whole was further stirred at −78 °C for 15 min. Saturated $NaHCO_3$–H_2O was added and the resulting mixture was extracted with CH_2Cl_2. The organic layer was washed successively with saturated $CuSO_4$–H_2O and saturated $NaHCO_3$–H_2O and then treated as usual to give a mixture of **72** and **73** (34 mg). This was dissolved in THF (8 ml), $LiAlH_4$ (106 mg, 2.79 mmol) was added, and the whole was vigorously stirred under reflux for 1.5 h under an Ar atmosphere. The reaction mixture was cooled in an ice bath and Et_2O saturated with H_2O (4 ml) was slowly added. The volatile materials were removed under reduced pressure and the residue was dried over P_2O_5 for 3 h. A slurry of the residue in CH_2Cl_2 (6 ml) and Et_3N (0.98 ml, 7.04 mmol) was cooled in an ice bath and Boc_2O (328 μl, 1.43 mmol) was added to this under an Ar atmosphere. After the mixture had been stirred at 22 °C for 7 h, saturated $NaHCO_3$–H_2O was added and the whole was extracted with CH_2Cl_2. Usual work-up and purification by PTLC [benzene–EtOAc (6:1)] yielded **74** (7 mg, 31%) and **75** (7 mg, 25%) in order of decreasing polarity. **74**: Colorless glass. HRMS Calcd for $C_{24}H_{35}NO_4$: 401.2564. Found: 401.2578. MS *m/z*: 401 (M^+, 4), 344 (9), 317 (14), 300 (18), 261 (29), 246 (13), 244 (15), 91 (13), 57 (100), 41 (46). IR ($CHCl_3$) cm^{-1}: 1681. ^1H NMR δ: 1.13 (3H, s), 1.30–1.70 (5H, m, including OH), 1.51 (9H, s), 1.67 (1H, ddd, J=14, 7.5, 6.5 Hz, CH_2CH_2OH), 1.77–1.90 (2H, m), 1.95–2.00 (1H, m), 2.02 (1H, ddd, J=14, 7.5, 6.5 Hz, CH_2CH_2OH), 2.07 (1H, d, J=12.5 Hz, OH), 2.23–2.39 (2H, m), 2.47 (1H, ddd, J=7, 7, 1.5 Hz, H14), 2.51 (1H, d, J=3 Hz, H5), 3.13 (1H, d, J=11 Hz, H19), 3.58 (1H, d, J=11 Hz, H19), 3.71–3.86 (2H, m), 4.11 (1H, dd, J=12.5, 7 Hz, changed to d, J=7 Hz with D_2O, H20), 5.39 (1H, br s, H7), 5.58 (1H, dddd, J=9.5, 7, 2, 2 Hz, H13), 5.83 (1H, ddd, J=9.5, 3, 3 Hz, H12). ^{13}C NMR δ: 17.3 (CH_2, C2), 22.3 (CH_2, C1), 27.2 (CH_2, C11), 28.4 ($CH_3\times3$), 30.5 (CH_3, C18), 31.3 (CH_2, C3), 34.5 (C, C4), 35.2 (CH_2, CH_2CH_2OH), 45.1

(C, C8), 48.4 (C, C10), 50.9 (CH, C9), 52.7 (CH, C14), 60.9 (CH, C5), 61.0 (CH_2, CH_2OH), 64.3 (CH_2, C19), 79.2 (CH, C20), 80.4 (C, COO*C*Me_3), 110.1 (CH, C7), 126.5 (CH, C13), 129.6 (CH, C12), 139.8 (C, C6), 152.5 (C, *C*OOCMe_3). **75**: Colorless glass. HRMS Calcd for $C_{29}H_{43}NO_6$: 501.3088. Found: 501.3101. MS *m/z*: 501 (M^+, 2), 400 (6), 344 (16), 317 (6), 261 (10), 244 (8), 200 (6), 91 (6), 57 (100), 41 (30). IR ($CHCl_3$) cm^{-1}: 1730, 1681. ^1H NMR δ: 1.12 (3H, s), 1.17–1.26 (1H, m), 1.43–1.68 (3H, m), 1.47 (9H, s), 1.51 (9H, s), 1.75 (1H, ddd, J=13.5, 9, 6.5 Hz), ca. 1.77–1.89 (2H, m), 1.93–1.98 (1H, m), 2.06 (1H, d, J=12 Hz, OH), 2.09 (1H, ddd, J=13.5, 9, 6.5 Hz), 2.27–2.33 (2H, m), 2.48 (1H, ddd, J=7, 6, 1.5 Hz), 2.50 (1H, d, J=3 Hz, H5), 3.13 (1H, d, J=11 Hz), 3.58 (1H, d, J=11 Hz), 4.04–4.25 (2H, m), 4.10 (1H, dd, J=12, 6 Hz, changed to d, J=6 Hz with D_2O), 5.35 (1H, br s), 5.57 (1H, dddd, J=9.5, 7, 2, 2 Hz), 5.82 (1H, ddd, J=9.5, 3, 3 Hz). ^{13}C NMR δ: 17.3 (CH_2), 22.3 (CH_2), 27.1 (CH_2), 27.7 ($CH_3\times3$), 28.4 ($CH_3\times3$), 30.5 (CH_3), 31.3 ($CH_2\times2$, C3 and *C*H_2CH_2OBoc), 34.5 (C, C4), 44.8 (C), 48.4 (C), 50.8 (CH), 52.6 (CH), 60.9 (CH, C5), 64.4 (CH_2, C19), 65.1 (CH_2, *C*H_2OBoc), 79.2 (CH), 80.4 (C, NCOO*C*Me_3), 81.6 (C, OCOO*C*Me_3), 109.3 (CH, C7), 126.3 (CH), 129.6 (CH), 140.0 (C, C6), 152.5 (C), 153.3 (C).

4.5.9. Alcoholysis of 75 to form 74. K_2CO_3 (15 mg, 0.109 mmol) was added to a solution of **75** (7 mg, 14.0 μmol) in MeOH (3 ml) and the mixture was gently refluxed with stirring for 6 h. After the mixture had been cooled, saturated NH_4Cl–H_2O was added and the whole was extracted with CH_2Cl_2. Usual work-up and separation by PTLC [hexane–EtOAc (1:1)] provided **74** (5 mg, 89%).

4.5.10. $NaBH_3CN$ reduction of 74 to form 76. $NaBH_3CN$ (22 mg, 0.349 mmol) and HCl–H_2O (2.5%, 0.50 ml, 0.342 mmol) were successively added in this order to a cooled (0 °C) solution of **74** (7 mg, 17.5 μmol) in MeOH (2 ml) and the mixture was stirred at the same temperature for 10 min and at 19 °C for 2.5 h. Saturated $NaHCO_3$–H_2O was added and the whole was extracted with CH_2Cl_2. Usual work-up and separation by PTLC [benzene–EtOAc (1:1)] afforded **76** (6 mg, 85%) as a colorless glass. HRMS Calcd for $C_{24}H_{37}NO_4$: 403.2721. Found: 403.2719. MS *m/z*: 403 (M^+, 1), 347 (5), 303 (32), 258 (11), 105 (13), 91 (15), 57 (100), 41 (44). IR ($CHCl_3$) cm^{-1}: 1674. ^1H NMR (at 50 °C) δ: 0.94 (3H, s), 1.03 (1H, ddd, J=13, 11.5, 4.5 Hz, H1), 1.19–1.34 (2H, m), ca. 1.45–1.55 (1H, m), 1.46 (9H, s), ca. 1.59–1.75 (2H, m), 1.60 (1H, d, J=7 Hz, H5), 1.76 (1H, ddd, J=13, 4, 4 Hz, H1), 1.85–2.05 (3H, m, including OH), 2.15 (1H, dd, J=16.5, 8.5 Hz, H7), 2.21–2.28 (2H, m), 2.29 (1H, br d, J=16.5 Hz, H7), 2.44 (1H, br dd, J=7, 6.5 Hz, H14), 3.10–3.24 (1H, m, H19), 3.39 (1H, d, J=11 Hz, H19), 3.61–3.83 (2H, m), 4.11 (1H, br dd, J=8.5, 7 Hz, H6), 4.46 (1H, dd, J=12, 6.5 Hz, changed to d, J=6.5 Hz with D_2O, H20), 5.64 (1H, dddd, J=9.5, 7, 2, 2 Hz, H13), 5.79 (1H, ddd, J=9.5, 3, 3 Hz, H12).

4.5.11. Benzoylation of 76 to form 77. Benzoyl chloride (44 μl, 0.379 mmol) was added to a solution of **76** (5 mg, 12.4 μmol) in pyridine (0.8 ml) and the mixture was stirred at 19 °C for 14 h. Saturated $NaHCO_3$–H_2O was added and the whole was extracted with CH_2Cl_2. Usual work-up and separation by PTLC [hexane–EtOAc (5:1)] gave **77** (6 mg, 95%) as a colorless glass. HRMS Calcd for $C_{31}H_{41}NO_5$: 507.2982. Found: 507.2987. MS *m/z*: 507 (M^+, 0.5), 451 (1), 423 (2), 407 (39), 389 (4), 379 (4), 325 (4), 302 (5), 285 (9), 258 (9), 185 (10), 105 (47), 77 (22), 57 (100), 41 (31). IR ($CHCl_3$) cm^{-1}: 1708, 1676. ^1H NMR (at 50 °C) δ: 0.95 (3H, s), 1.05 (1H, ddd, J=12.5, 11, 4 Hz), 1.23–1.35 (2H, m), ca. 1.44–1.56 (1H, m), 1.46 (9H, s), 1.62 (1H, d, J=7 Hz, H5), 1.66–2.20 (5H, m), 2.02 (1H, d, J=12 Hz, OH), 2.23 (1H, dd, J=16, 8.5 Hz), 2.25–2.30 (2H, m), 2.31 (1H, br d, J=16 Hz), 2.52 (1H, br dd, J=7, 6 Hz), 3.10–3.26 (1H, m), 3.40 (1H, d, J=11 Hz), 4.14 (1H, br dd, J=8.5, 7 Hz), 4.36 (1H, ddd, J=11, 8, 7 Hz, C*H_2*OBz), 4.46 (1H, ddd, J=11, 8, 5.5 Hz, C*H_2*OBz), 4.50 (1H, dd, J=12, 6 Hz, changed to d, J=6 Hz with D_2O, C20), 5.63 (1H, dddd, J=9.5, 7, 2, 2 Hz), 5.80 (1H, ddd, J=9.5, 3, 3 Hz), 7.38–7.44 (2H, m), 7.50–7.57 (1H, m), 7.99–8.04 (2H, m).

4.5.12. Completion of the synthesis of 1 from 77. CF_3COOH (0.10 ml, 1.30 mmol) was added to a cooled (0 °C) solution of **77** (5 mg, 9.86 μmol) in CH_2Cl_2 (0.9 ml) and the mixture was stirred at the temperature for 2 h. Saturated $NaHCO_3$–H_2O was added and the whole was extracted with CH_2Cl_2. Usual work-up gave a residue (5 mg). The residue was dissolved in CH_2Cl_2 (3 ml) and the solution was cooled in an ice bath. Pyridine (32 μl, 0.396 mmol) and $SOCl_2$ (14 μl, 0.192 mmol) were added in this order under an Ar atmosphere and the mixture was stirred at 0 °C for 30 min and at 19 °C for 22 h. Saturated $NaHCO_3$–H_2O was added and the resulting mixture was stirred for 15 min. Extraction with CH_2Cl_2, usual work-up, and separation by Al_2O_3–PTLC (Merck-type E, 0.1% MeOH–CH_2Cl_2) provided **1** (3 mg, 78%) as a colorless glass. HRMS Calcd for $C_{26}H_{31}NO_2$: 389.2353. Found: 389.2353. MS *m/z*: 389 (M^+, 100), 374 (5), 284 (13), 254 (48), 240 (17), 160 (37), 105 (81), 91 (27), 77 (64), 41 (24). IR ($CHCl_3$) cm^{-1}: 1708. ^1H NMR δ: 0.96 (3H, s, H18), 1.16–1.55 (4H, m), 1.43 (1H, br s, H5), 1.56–1.66 (2H, m), 1.66–1.70 (1H, m, H9), 1.75 (1H, dd, J=13.5, 2.5 Hz, H7), 1.89–2.01 (2H, m, C*H_2*CH_2OBz), 2.01 (1H, dd, J=13.5, 3 Hz, H7), 2.14 (1H, br d, J=19 Hz, H11), 2.25 (1H, dddd, J=19, 4, 2.5, 2.5 Hz, H11), 2.26 (1H, br d, J=7 Hz, H14), 2.38 (1H, d, J=12.5 Hz, H19-α), 2.52 (1H, d, J=12.5 Hz, H19-β), 2.76 (1H, d, J=1 Hz, H20), 3.23–3.28 (1H, m, H6), 4.34 (1H, ddd, J=11, 7, 7 Hz, C*H_2*OBz), 4.44 (1H, ddd, J=11, 7.5, 6.5 Hz, C*H_2*OBz), 5.52 (1H, dddd, J=9.5, 4, 2.5, 1 Hz, H12), 5.72 (1H, dddd, J=9.5, 7, 2, 1.5 Hz, H13), 7.40–7.47 (2H, m), 7.52–7.58 (1H, m), 8.00–8.04 (2H, m). ^{13}C NMR δ: 19.6 (CH_2, C2), 26.3 (CH_2, C11), 28.0 (CH_2, C1), 28.7 (CH_3, C18), 30.9 (CH_2, *C*H_2CH_2OBz), 34.0 (CH_2, C3), 35.4 (CH_2, C7), 38.0 (C, C4), 41.6 (C, C8), 48.5 (CH, C14), 49.88 (CH, C9), 49.91 (C, C10), 59.6 (CH, C5), 62.5 ($CH_2\times2$, C19 and *C*H_2OBz), 65.1 (CH, C6), 72.9 (CH, C20), 125.9 (CH, C12), 128.1 (CH×2, Bz), 129.0 (CH, C13), 129.3 (CH×2, Bz), 130.2 (C, Bz), 132.6 (CH, Bz), 166.4 (C, *C*OPh).

4.5.13. Quaternization of 1 to form 78. MeI (96 μl, 1.54 mmol) was added to a solution of **1** (1.5 mg, 3.86 μmol) in MeOH (1 ml) and the mixture was stirred at 22 °C for 50 h. Volatile materials were removed and the resulting residue was subjected to PTLC (10% MeOH–CH_2Cl_2) to afford **78** (1.5 mg, 73%) as a colorless glass.

MS m/z: 389 (M^+−MeI, 56), 374 (3), 284 (9), 267 (51), 254 (28), 160 (30), 142 (58), 127 (26), 122 (40), 105 (100), 91 (26), 77 (91), 51 (35). IR ($CHCl_3$) cm^{-1}: 1710. ^{1}H NMR δ: 1.30 (3H, s, H18), 1.16–1.87 (6H, m), 1.96 (1H, br s, H5), 1.91–1.95 (1H, m, H9), ca. 1.96–2.15 (3H, m), 2.21 (1H, br d, J=20 Hz, H11), 2.30–2.40 (1H, m, H11), 2.37 (1H, dd, J=15, 3 Hz, H7), 2.76 (1H, dd, J=6, 1 Hz, H14), 3.47 (1H, d, J=12.5 Hz, H19-α), 3.53 (3H, s, N^+–CH_3), 3.93 (1H, d, J=12.5 Hz, H19-β), 3.98 (1H, d, J=1.5 Hz, H20), 4.32–4.37 (1H, m, H6), 4.40 (1H, ddd, J=11.5, 6.5, 6.5 Hz), 4.47 (1H, ddd, J=11.5, 6.5, 6.5 Hz), 5.77 (1H, br d, J=9.5 Hz, H12), 5.96 (1H, br dd, J=9.5, 6 Hz, H13), 7.44–7.51 (2H, m), 7.56–7.63 (1H, m), 7.98–8.03 (2H, m). ^{13}C NMR δ: 18.6 (CH_2, C2), 25.7 (CH_2, C11), 27.9 (CH_2, C1), 28.5 (CH_3, C18), 29.9 (CH_2, CH_2CH_2OBz), 31.2 (CH_2, C7), 32.9 (CH_2, C3), 36.6 (C, C4), 41.8 (CH_3, N^+–CH_3), 42.4 (C, C8), 43.6 (CH, C14), 49.8 (CH, C9), 50.6 (C, C10), 57.1 (CH, C5), 61.4 (CH_2, CH_2CH_2OBz), 70.8 (CH_2, C19), 71.7 (CH, C6), 76.7 (CH, C20), 124.8 (CH, C12), 128.4 (CH×2, Bz), 128.9 (CH, C13), 129.2 (CH×2, Bz), 129.4 (CH, Bz), 133.1 (CH, Bz), 166.2 (C, *C*OPh).

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