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Stereocontrolled synthesis of acyclic terpenoids *via N*-ylide [2,3]rearrangement of ammonium salts with the stereodefined isoprene unit

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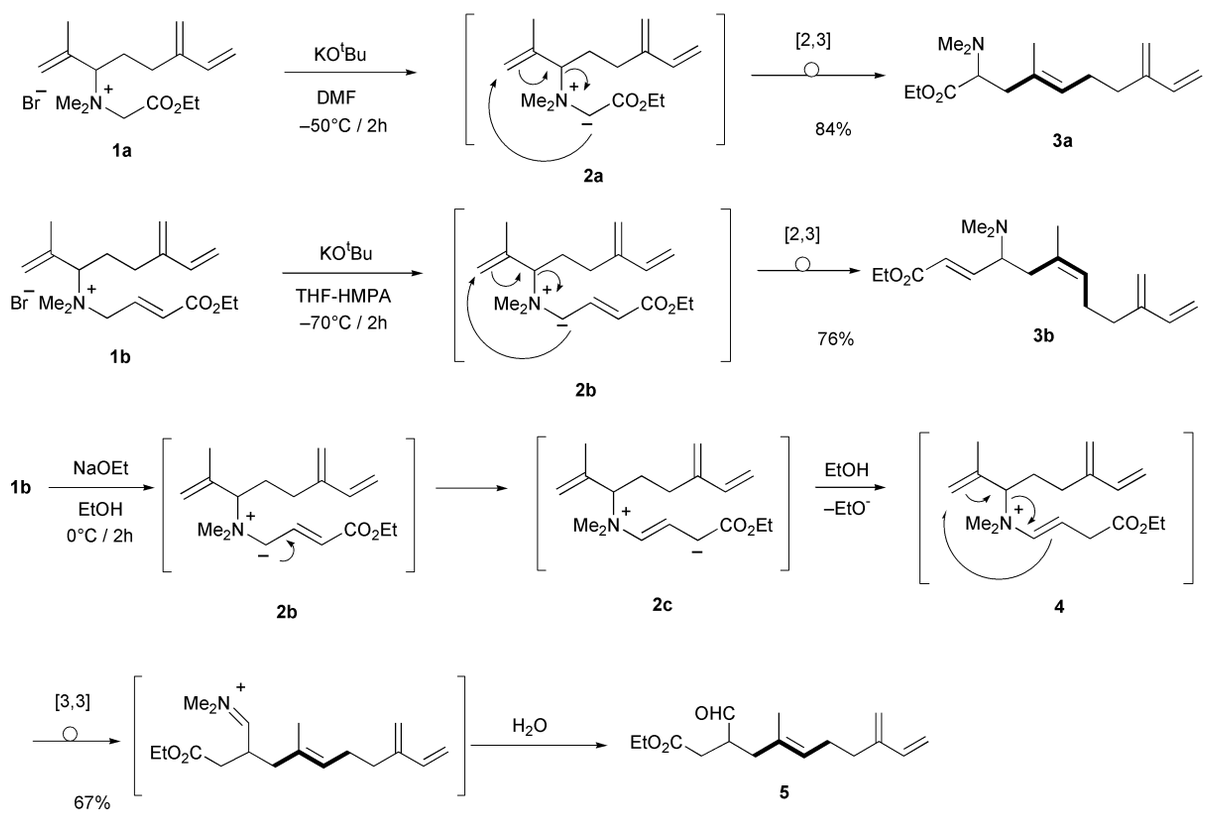
Stereocontrolled elongation of a functionalized isoprene unit on the *E* or *Z* terminal methyl of terpenoids was achieved by *N*-ylide rearrangement of the common ammonium salts under selected reaction conditions. A 1,5-diene or conjugated triene skeleton can be furnished by reductive or oxidative removal of the amino group of the rearrangement product, respectively. As an application to natural-product synthesis, all-(*E*)-terpenoid (*E*)-**11d** and (*E,Z*)-terpenoid (*Z*)-**11c** were converted into *β*-sinensal and (13*Z*)-retinol, respectively. General aspects of these transformations and a plausible transition state for the *N*-ylide rearrangement are discussed.

Introduction

[2,3]- and [3,3]sigmatropic rearrangements are often used for the stereoselective preparation of di- and trisubstituted olefins.[1] Treatment of a quaternary ammonium salt with a base may bring about the formation of an ammonium ylide species followed by spontaneous [2,3]sigmatropic rearrangement to give a homoallylic tertiary amine.[2] The [2,3]sigmatropic rearrangement is occasionally accompanied by Hofmann elimination and other side reactions including [1,2]sigmatropic rearrangement.[2,3] Therefore reaction selectivity as well as stereoselectivity must be attained for the synthetic application.

We reported a [2,3]sigmatropic *N*-ylide rearrangement that provided (*Z*)- or (*E*)-homoallylic dimethylamines with high stereoselectivity in good yields.[4] Furthermore, as shown in Scheme 1, [2,3]sigmatropic rearrangement of ylide **2a** with a powerful electron-withdrawing substituent (*e.g.*, CO_2Et) in the α-position and of ylide **2b** with a vinyl group carrying an ester



Scheme 1

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Table 1 Reaction of *N*-(3-ethoxycarbonylbut-2-enoyl)-*N*-*β*-methallyldimethylammonium salt **9a**

Run	Base	Solvent	Conditions (*T*/°C/C/*t*/h)	Yield (%)[a]	*Z* : *E*[b]
1	KO^{t}Bu	THF–HMPA[c]	−70/2	41	27 : 73
2	KO^{t}Bu	THF–DMPU[d]	−70/2	46	28 : 72
3	KO^{t}Bu	THF	−70/2	45	30 : 70
4	KO^{t}Bu	DME	−70/2	55	39 : 61
5	KO^{t}Bu	CH_2Cl_2	−70 to rt/3	52	42 : 58
6	LDA	THF	−70/2	45	43 : 57
7	DBU[e]	THF	−70 to rt/12	66	40 : 60
8	DBU	EtOH	0/2	60	72 : 28
9	$NaNH_2$	NH_3	−65/4	36	73 : 27
10	LHMDS[f]	NH_3	−65/4	46	72 : 28
11	KOEt	EtOH	0/1	68	80 : 20
12	NaOEt	EtOH	0/1	56	81 : 19
13	LiOEt	EtOH	0/1	41	87 : 13

[a] Combined yield. [b] The stereochemistry of the products was confirmed by ^{1}H-NMR ($CDCl_3$). [c] HMPA content was 20 vol%. [d] 1,3-Dimethyl-3,4,5,6-tetrahydropyrimidin-2(*1H*)-one [e] 1,8-Diazabicyclo[5.4.0]undec-7-ene [f] Lithium hexamethyldisilazide

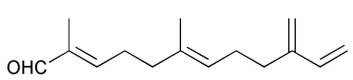
Table 2 Reaction of *N*-(3-ethoxycarbonylbut-2-enoyl)-*N*-*β*-methallyldimethylammonium salts **9b** and **9c**

Run	Substrate	Base	Solvent	Conditions (*T*/°C/C/*t*/h)	Yield (%)[a]	*Z* : *E*
1	**9b**	KO^{t}Bu	THF–HMPA[b]	−70/2	41	100 : 0[c]
2	**9b**	LiOEt	EtOH	−70/2	37	100 : 0[c]
3	**9b**	NaOEt	EtOH	−70/2	32	100 : 0[c]
4	**9b**	KOEt	EtOH	−70/4	43	100 : 0[c]
5	**9c**	KOEt	EtOH	−70/4	56	92 : 8[d]
6	**9c**	KOEt	EtOH	−78/4	71[e]	95 : 5[d]

[a] Combined yield. [b] HMPA content was 20 vol%. [c] An examination of the chemical shifts of olefinic methyl protons in ^{1}H NMR ($CDCl_3$) [δ 1.82 (3H, s)] suggested that a single stereoisomer (*Z*)-**11b** is produced. [d] The ratio of *Z* : *E* was determined by capillary GC analysis. Each of these compounds was separated carefully by column chromatography on silica gel. Stereochemistry of the isolated stereoisomers was analyzed by ^{1}H-NMR spectroscopy. [e] Besides [2,3]sigmatropic rearrangement products (*Z*)-**11c** and (*E*)-**11c**, [1,2]- and [3,3]rearrangement products were obtained in 10% and 7% yield, respectively.

moiety at the *β*-position afford exclusively (*E*)-olefin **3a** and (*Z*)-olefin **3b**, respectively.[5] On the other hand, treatment of salt **1b** with an alkoxide base in a protic solvent resulted in the formation of enammonium salt **4** *via* the isomerization of ylide **2b** to more stable carbanion **2c** followed by spontaneous [3,3]sigmatropic rearrangement at 0 °C to give, with complete stereoselectivity, trisubstituted (*E*)-olefin **5** possessing a formyl group on the homoallylic carbon.[6]

Herein we report a unique [2,3]sigmatropic *N*-ylide rearrangement that provides predominantly the *Z*- or *E*-trisubstituted olefin (according to the reaction conditions) from the common ammonium salts having a stereodefined isoprene unit. This new stereoselective reaction will play an important role in natural-product synthesis, especially in the terpenoid field. *E*-Selectivity and *Z*-selectivity of the rearrangement were applied to a stereoselective synthesis of *β*-sinensal (**6**) and reach (13*Z*)-retinol (**7**), respectively.



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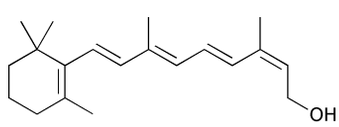

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Results and discussion

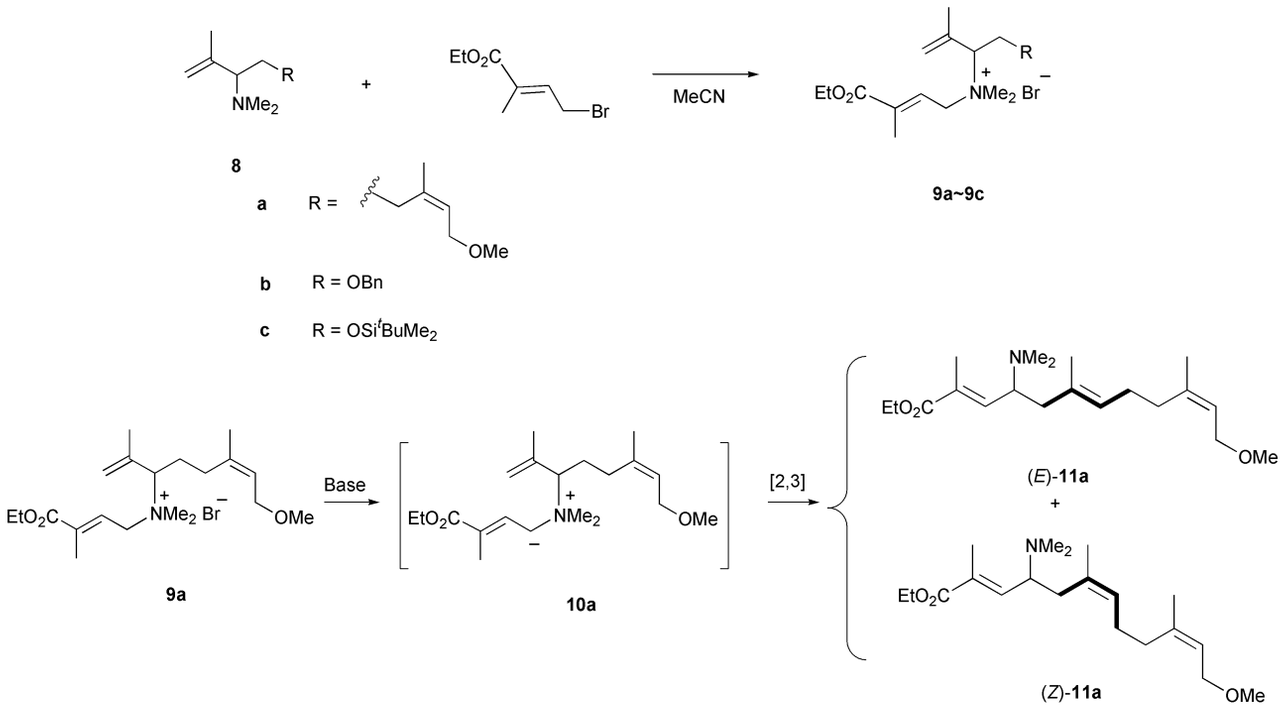
Quaternization of the internal amines **8a**–**8c** with ethyl (*E*)-γ-bromo-α-methylbut-2-enoate[7] furnished ammonium bromides **9a**–**9c** quantitatively (Scheme 2). These quaternary ammonium salts were treated with various bases under a variety of reaction conditions. The results are summarized in Tables 1 and 2.

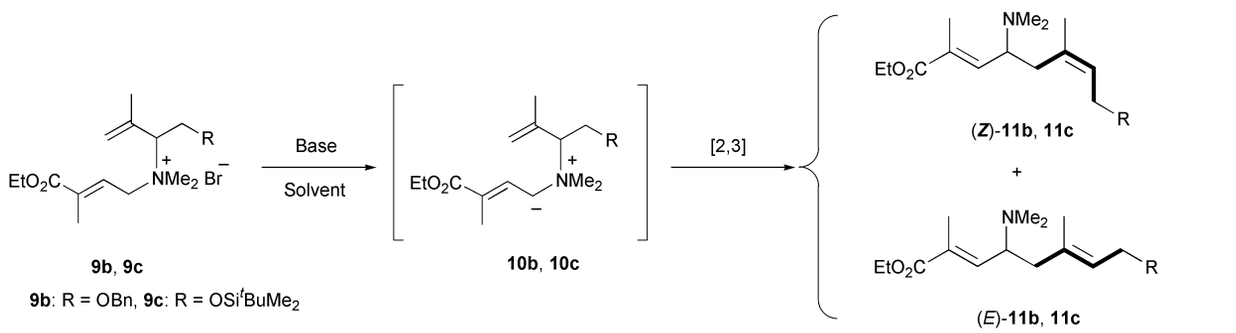
Treatment of **9a** with potassium *tert*-butoxide in a mixture of THF–HMPA gave (*E*)-**11a** predominantly (Table 1, run 1). This result is a sharp contrast to that of the rearrangement of salt **1b** shown above. Similarly, the reaction of **9a** with potassium *tert*-butoxide in aprotic solvents afforded (*E*)-**11a** predominantly (Table 1, runs 2, 3). Higher polarity of the solvent seems to increase the *E*-selectivity of the rearrangement (Table 1, runs 1–7).

In clear contrast, very interestingly, (*Z*)-**11a** formed predominantly when the salt **9a** was treated with an alkoxide base in ethanol at 0 °C, without isomerization of the parent *E* double bond in the (*E*)-2-methylbut-2-enoate ester moiety (Table 1, runs 8–13). Presumably the formed ammonium ylide intermediate **10a** rapidly underwent [2,3]sigmatropic rearrangement without isomerization to give a sort of enammonium salt **4** as observed in the case of **1b** in protic solvents. Furthermore, lower basisity increased the *Z*-selectivity of the rearrangement (Table 1, run 13). Lithium ethoxide is the best base for *Z*-selectivity we have found up to the present.

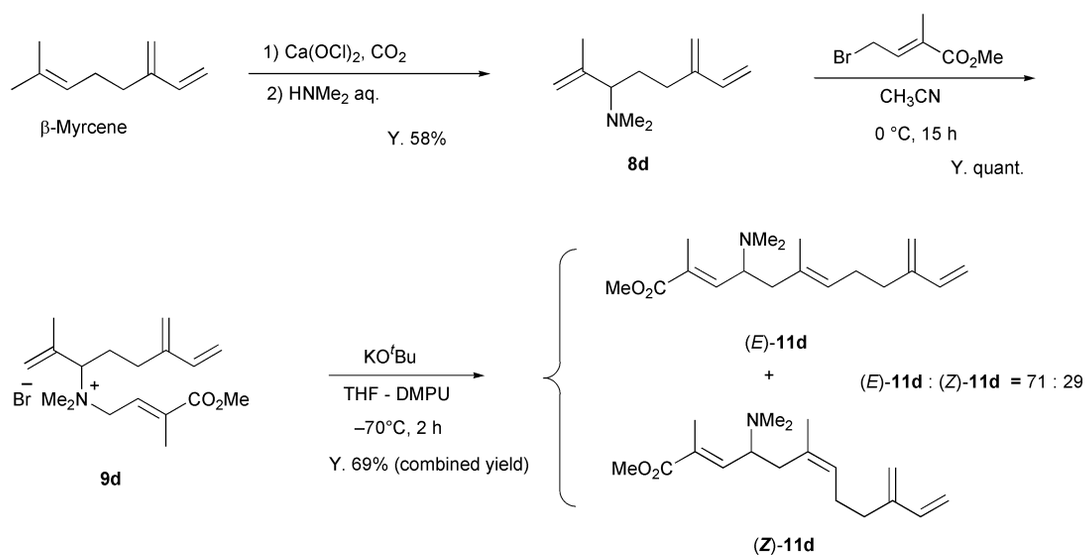
Interestingly, treatment of **9b** gave (*Z*)-**11b** with complete stereoselectivity under both the following reaction conditions; with potassium *tert*-butoxide in a mixture of THF–HMPA, and with alkoxide in ethanol (Table 2, runs 1–4). Similarly, the reaction of **9c** with potassium ethoxide in ethanol afforded (*Z*)-**11c** in good yield (runs 5, 6).

This unique stereoselective reaction will play an important role in natural-product synthesis, especially in the terpenoid field. *E*-Selectivity of the rearrangement was applied to a stereoselective synthesis of *β*-sinensal (**6**), which is a characteristic flavor component of the essential oil of the China orange (*citrus sinensls*) (Scheme 3). *β*-Myrcene was converted *via* ene-type chlorination[8] followed by amination[9] into internal allylamine **8d**. Quaternization[10] of **8d** with methyl (*E*)-γ-bromo-α-methylbut-2-enoate in MeCN gave ammonium salt **9d**. Treatment of **9d** with potassium *tert*-butoxide in a mixture of THF–DMPU resulted in a 71 : 29 mixture of (*E*)-**11d**

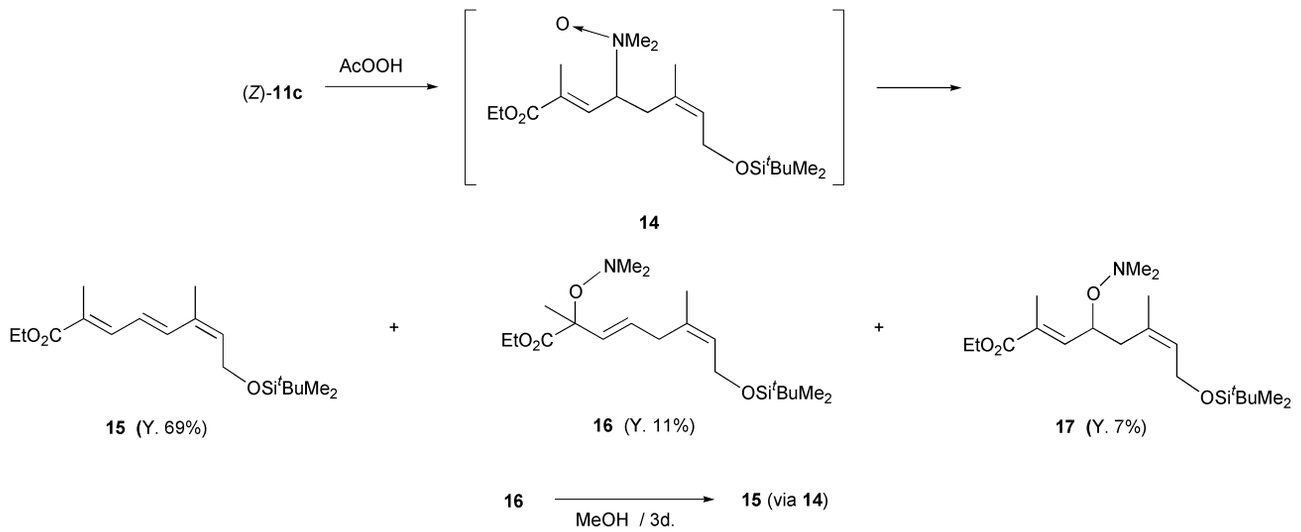




Scheme 2



Scheme 3



Scheme 4

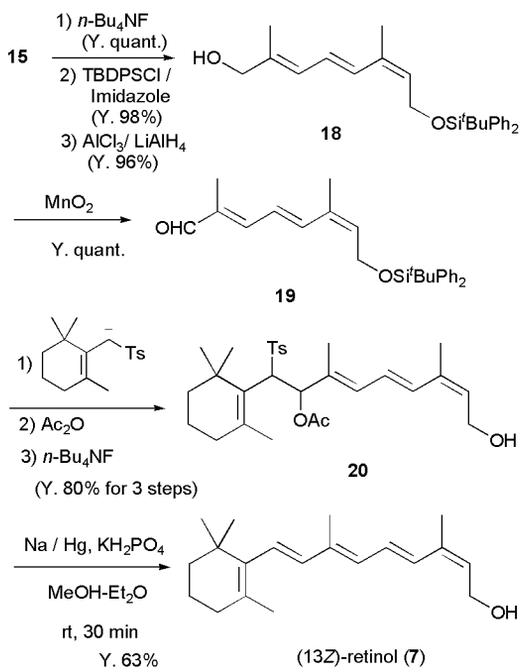
and (*Z*)-**11d** in a 69% combined yield. Notably, purification of (*E*)-**11d** was easily achieved by column chromatography on silica gel.

A reductive removal of the dimethylamino group in (*E*)-**11d** was achieved by quaternization with MeI, followed by treatment with sodium amalgam in a buffer solution without any conjugate reduction, to give *α,β*-unsaturated ester **12**. The subsequent reduction of **12** was most effectively carried out with AlH_3[11] prepared *in situ* from aluminium chloride and lithium aluminium hydride to give the corresponding unsaturated alcohol **13** in 90% yield. Treatment of **13** with active manganese(IV) oxide in hexane at 0 °C for 3 h furnished the desired *β*-sinensal (**6**) in 72% yield.

On the other hand, *Z*-selectivity of the rearrangement was applied to a stereoselective synthesis of reach (13*Z*)-retinol (**7**), of which only a few syntheses have been reported.[12] This synthesis involves the preparation of the triene **15** as a building block which was prepared by the oxidative cleavage of the amino group of the desired [2,3]rearrangement product (*Z*)-**11c**. Treatment of (*Z*)-**11c** with peracetic acid in dichloromethane at −60 °C in the presence of sodium carbonate resulted in the formation of the *N*-oxide intermediate **14**, which spontaneously underwent Cope elimination during warming to 0 °C for 30 min to give triene **15** in 69% yield. The *E* stereochemistry of the newly formed double bond was confirmed by the ^{1}H-NMR spectrum (*δ* 6.85, d, 1H, *J* = 15 Hz). Besides this Cope elimination, [2,3]sigmatropic rearrangement product **16** and [1,2]rearrangement product **17** were obtained in 11 % and 7% yield, respectively. Furthermore, **16** was gradually converted into triene **15** presumably *via N*-oxide **14** in MeOH. This unique transformation was completed within 3 d in MeOH at ambient temperature (Scheme 4).

Because of its lability to $AlCl_3$, the *tert*-butyldimethylsilyl protecting group was then replaced by a *tert*-butyldiphenylsilyl group (Scheme 5). Transformation of the ester group to a formyl group was carried out by treatment with AlH_3, followed by active manganese(IV) oxide. *β*-Cyclogeranyl *p*-tolyl sulfone[13] was converted with *n*-BuLi into its carbanion, which reacted with the triene aldehyde **19** and was quenched with acetic anhydride[14] to give *β*-acetoxy sulfone **20** after desilylation, which underwent smooth reductive cleavage with sodium amalgam to furnish the desired (13*Z*)-retinol (**7**). The structure of the synthetic (13*Z*)-retinol was confirmed by a comparison of its spectral data with those in the literature.[12]

In order to find the reason why the rearrangement afforded *Z* or *E* olefins stereoselectively under the selected conditions, the following experiments were undertaken. Treatment of **9e** having a (*Z*)-α-methylbut-2-enonitrile moiety with potassium *tert*-butoxide in THF at −30 °C gave the rearrangement

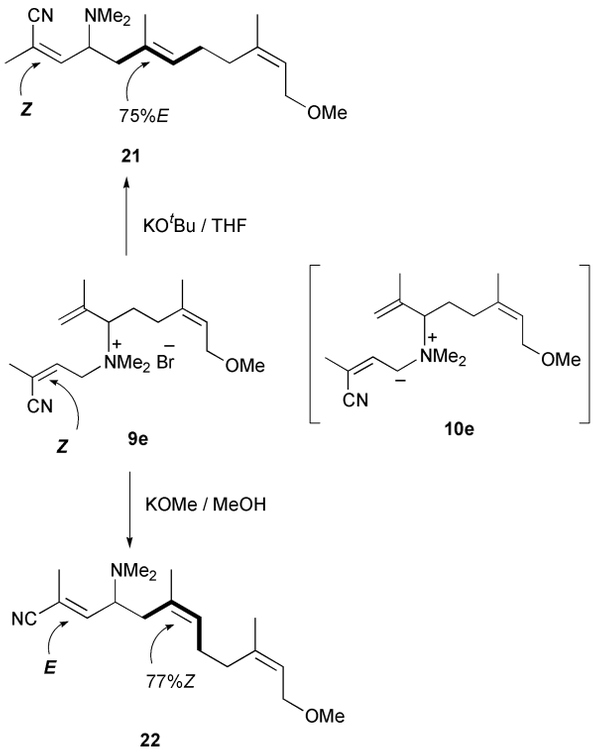


Scheme 5

product **21** with 75% *E* selectivity, without isomerization of the parent *Z* double bond on the methylbutenonitrile moiety. On the other hand, treatment of **9e** with potassium methoxide in methanol at −30 °C gave the rearrangement product **22** with 77% *Z* selectivity along with complete isomerization on the *Z* methylbut-2-enoyl moiety into the stable *E* double bond (Scheme 6).

[2,3]Sigmatropic rearrangement of ylide **2a** having an electron-withdrawing group may have the usual concerted transition state of a doubly suprafacial mode[15] and a more energetically favorable conformation, in which the R^1CH_2 group occupied mainly the equatorial position, exerting no vicinal repulsion between R^1CH_2 and the vinyl methyl group, which leads to an *E* olefin. On the other hand, the [2,3]sigmatropic rearrangement of ylides **2b**, **10a**, **10b**, **10c** and **10e** seems to have an earlier (*i.e.*, reactant-like) transition state than that of the above-mentioned stable ylide **2a**. Thus another envelope conformation can be postulated as a plausible transition state, leading to either *Z* or *E* olefin as depicted in Scheme 7.

Judging from the above-mentioned results from [2,3]-rearrangement of ylide **10e**, we would like to propose two types of carbanion generated on ylide formation, *viz*, a non-conjugated anion and a conjugated one. The term non-

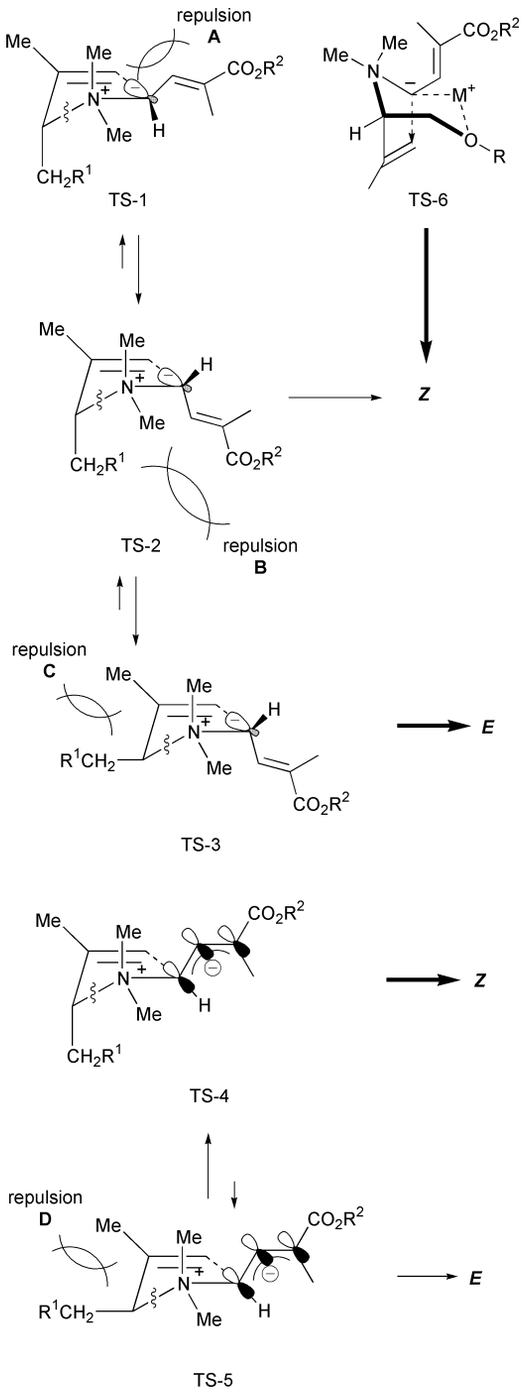


Scheme 6

conjugated anion means the ylide carbanion undergoes [2,3]rearrangement more quickly than enolate conjugation as soon as a proton is removed by a base. And the term conjugated anion means the ylide carbanion undergoes [2,3]rearrangement slowly after enolate stabilization.

The non-conjugated anion type includes transition states having three kinds of major steric repulsions: TS-1, TS-2 and TS-3 include the synclinal repulsion **A** between one of the *N*-methyls and the methyl butenoyl moiety, 1,3-diaxial repulsion **B** between R^1CH_2 and the methyl butenoyl group, and vicinal repulsion **C** between R^1CH_2 and the vinyl methyl group, respectively. The conformational preference of TS-2 over TS-1 may result from the synclinal repulsion **A** being larger than the 1,3-diaxial repulsion **B**. In addition, the conformational preference of TS-3 over TS-2 may result from the 1,3-diaxial repulsion **B** being larger than the vicinal repulsion **C**, which may be an important factor in the *E*-selective rearrangement. In the case of R^1 being a benzyloxy or siloxy group, which increases steric bulkiness, vicinal repulsion may become larger than 1,3-diaxial repulsion. Another plausible mechanism could be chelation control by the internal oxygen functionality, metal cation and ylide carbanion which together form a six-membered chair ring. The conformer having the isopropenyl group in an axial position could rearrange smoothly to give the *Z*-olefin, because of a suitable distance between the isopropenyl group and the ylide carbanion as shown in TS-6. The other conformer having the isopropenyl group in an equatorial position could not rearrange because of the remote distance from the ylide carbanion. Thus *Z*-selective rearrangement is predominantly achieved in the rearrangement of salt **9b** or **9c**. However, the conjugated-anion type includes only TS-4 and TS-5, exerting neither synclinal repulsion **A** nor 1,3-diaxial repulsion **B** due to the interconversion of the sp^3 ylide carbanion into an sp^2 ylide carbanion. The conformational preference of TS-4 over TS-5 may result from the critical vicinal repulsion **D**, which may be an important factor in the *Z*-selective rearrangement.

As summary, stereocontrolled elongation of a functionalized *E* isoprene unit on the *E* or *Z* terminal methyl of terpenoids was achieved by the *N*-ylide rearrangement of the common ammonium salts under selected reaction conditions. Highly



Scheme 7

stereoselective elongation of a functionalized isoprene unit on the *Z* terminal methyl of the prenol unit was achieved by the rearrangement of the *N*-3-caboxybut-2-enyl-*β*-methallyldimethylammonium salt. A 1,5-diene or conjugated triene skeleton can be obtained by reductive or oxidative removal of the amino group of the rearrangement product, respectively. The present method is useful for the construction of (*E,E*) and (*E,Z*)-1,5-diene sesquiterpenoid synthons or conjugated (*E,E,Z*)-triene monoterpenoid synthons.

Experimental

Melting points were determined on a Büchi 535 capillary melting point apparatus without correction. Infrared spectra (IR) were recorded on a Hitachi 260–10 IR spectrometer or a Perkin–Elmer Paragon 1000 FTIR spectrometer. ^{1}H-NMR (270 MHz) and ^{13}C-NMR (68 MHz) spectra were recorded on a JEOL EX-270 spectrometer in $CDCl_3$, using tetramethylsilane

as internal standard (δ = 0.00). For samples *J*-Values are given in Hz. GC-Mass spectra were recorded with a Perkin–Elmer Q-Mass 910 mass spectrometer. Gas chromatographic determination was performed on a Shimadzu GC-14A. Thin-layer chromatography (TLC) was performed on precoated Merck TLC plates with silica gel 60 F-254. Column chromatography was carried out with silica gel BW-127ZH or NH-DM1020 (100–200 mesh, Fuji Silysia Chemical Industries) or Cica-Merck Silica gel 60 (Kanto Chemical Industries). All reagents were obtained from commercial suppliers and were used as received unless otherwise indicated.

4-*tert*-Butyldimethylsiloxy-3-dimethylamino-2-methylbut-1-ene 8c

To a mixture of sodium (2.1 g, 91.3 mmol) in liquid ammonia (*ca.* 70 cm^3) at −65 °C was added dropwise a solution of 2 g (9.1 mmol) of 4-benzyloxy-3-dimethylamino-2-methylbut-1-ene (**8b**)[9] in anhydrous diethyl ether (20 cm^3) over a period of 10 min. After stirring of the mixture for an additional 20 min at −60 °C, isoprene (10 cm^3) and methanol (10 cm^3) were added successively. The solution was allowed to gradually warm to room temperature and then was poured into brine (50 cm^3). After the aqueous solution had been extracted with a mixture of ethyl acetate and diethyl ether (50 : 50), the organic phase was washed with brine, dried ($MgSO_4$), filtered, and concentrated by a rotary evaporator to give 1.2 g of crude 2-dimethylamino-3-methylbut-3-en-1-ol. A solution of the crude alcohol (0.13 g, 1 mmol), imidazole (0.14 g, 2 mmol), and *tert*-butylchlorodimethylsilane (0.2 g, 1.3 mmol) in anhydrous DMF (4 cm^3) was stirred for 2 h at room temperature. Water (10 cm^3) was added to the reaction mixture. The organic layer was separated and the aqueous layer was extracted with ethyl acetate. The combined organic layer were washed with brine, dried ($MgSO_4$), filtered, and evaporated. The residual material was purified by column chromatography to give **8c** (0.15 g, 63%) as a colorless oil (Found: C, 64.05; H, 12.11; N, 5.66. $C_{13}H_{29}NOSi$ requires C, 64.13; H, 12.01; N, 5.75%); ν_{max}(neat)/cm^{-1} 2950, 1470, 1260, 1120, 900, 840, 780 and 680; δ_H (270 MHz; $CDCl_3$; Me_4Si) 0.06 (6H, s, 2 × Me), 0.84 (9H, s, 3 × Me), 1.66 (3H, s, Me), 2.20 (6H, s, 2 × NMe), 2.54 (1H, m, CHN), 3.59 (1H, dd, *J* 10.2 and 5.9, CH*H*O), 3.77 (1H, dd, *J* 10.2 and 5.9, C*H*HO), 4.83 (2H, m, CH_2=C).

[(2*E*)-3-Methoxycarbonylbut-2-enyl](1-isopropenyl-4-methylene hex-5-enyl)dimethylammonium bromide (9d)

A solution of 3-dimethylamino-2-methyl-6-methyleneocta-1,7-diene (**8d**)[9] (0.18 g, 1 mmol) in anhydrous acetonitrile (30 cm^3) and methyl (*E*)-γ-bromo-α-methybut-2-enoate[10] (0.29 g, 1.5 mmol) was stirred for 2 d at room temperature. The solvent was evaporated off to give an oil, which was purified by washing with anhydrous diethyl ether several times. The residual material was dried under reduced pressure to give salt **9d** (0.35 g, 98%) as a pale yellow viscous oil (Found: C, 57.89; H, 8.34; N, 3.68. $C_{18}H_{30}BrNO_2$ requires C, 58.06; H, 8.12; N, 3.76%); ν_{max}(neat)/cm^{-1} 3400, 2950, 1730, 1660, 1610, 1480, 1210, 1040 and 920; δ_H (270 MHz; $CDCl_3$; Me_4Si) 2.00 (3H, s, Me), 2.10 (3H, s, Me), 2.1–3.0 (4H, m, CH_2CH_2), 3.28, 3.36 (6H, each s, 2 × NMe), 3.78 (3H, s, OMe), 4.0–4.3 (1H, m, CHN), 4.6–4.9 (2H, m, CH_2N), 5.1–5.2 (2H, m, 4-CH_2), 5.13 (1H, d, *J* 10.6, CH*H*=CH), 5.25 (1H, d, *J* 17.5, C*H*H=CH), 5.64 (2H, m, CH_2=C), 6.36 (1H, dd, *J* 10.6 and 17.5, CH_2=C*H*), 6.79 (1H, m, CH=C).

Similary, [(2*E*)-3-ethoxycarbonylbut-2-enyl][(4*Z*)-1-isopropenyl-6-methoxy-4-methylhex-4-enyl]dimethylammonium bromide (**9a**), [(2*E*)-3-ethoxycarbonylbut-2-enyl](1-isopropenyl-2-benzyloxyethyl)dimethylammonium bromide (**9b**), and [(2*E*)-3-ethoxycarbonylbut-2-enyl][1-isopropenyl-2-(*tert*-butyldimethylsiloxy)ethyl]dimethylammonium bromide (**9c**) were prepared quantitatively from (6*Z*)-8-methoxy-3-dimethylamino-2,6-dimethylocta-1,6-diene (**8a**),[9] 4-benzyloxy-3-dimethylamino-2-methylbut-1-ene (**8b**),[9] and 4-*tert*-butyldimethylsiloxy-3-dimethylamino-2-methylbut-1-ene (**8c**) as starting material, respectively.

9a: Pale yellow viscous oil (Found: C, 57.11; H, 8.99; N, 3.01. $C_{20}H_{36}BrNO_3$ requires C, 57.41; H, 8.67; N, 3.35%); ν_{max}(neat)/cm^{-1} 3400, 2950, 1730, 1660, 1610, 1470, 1210 and 920; δ_H (270 MHz; $CDCl_3$; Me_4Si) 1.32 (3H, t, *J* 7.0, CH_2CH_3), 1.77 (3H, s, 6-Me), 1.81 (3H, s, Me), 2.01 (3H, s, Me), 1.9–2.4 (4H, m, CH_2CH_2), 3.30 (3H, s, OMe), 3.33, 3.43 (6H, each s, 2 × NMe), 3.83 (2H, m, CH_2O), 4.23 (2H, q, *J* 7.0, CH_2CH_3), 4.3–4.5 (1H, m, CHN), 4.7–4.9 (2H, m, CH_2N), 5.4–5.6 (1H, m, CH=C), 5.6–5.7 (2H, m, CH_2=C), 6.9–7.0 (1H, m, CH=C). **9b**: Pale yellow viscous oil (Found: C, 58.79; H, 7.90; N, 3.01. $C_{21}H_{32}BrNO_3$ requires C, 59.15; H, 7.56; N, 3.28%); ν_{max}(neat)/cm^{-1} 3400, 2950, 1730, 1660, 1460, 1270, 1130, 970, 760 and 700; δ_H (270 MHz; $CDCl_3$; Me_4Si) 1.32 (3H, t, *J* 7.0, CH_2CH_3), 1.98 (3H, s, Me), 2.02 (3H, s, Me), 3.31, 3.38 (6H, each s, 2 × NMe), 3.9–4.2 (2H, m, CH_2O), 4.23 (2H, q, *J* 7.0, CH_2CH_3), 4.63 (2H, s, CH_2Ph), 4.8–4.9 (1H, m, CHN), 5.0–5.2 (2H, m, CH_2N), 5.4–5.7 (2H, m, CH_2=C), 6.7–6.9 (1H, m, CH=C), 7.3–7.4 (5H, m, Ph). **9c**: Pale yellow viscous oil (Found: C, 53.24; H, 9.15; N, 3.05. $C_{20}H_{40}BrNO_3Si$ requires C, 53.32; H, 8.95; N, 3.11%); ν_{max}(neat)/cm^{-1} 3400, 2950, 1700, 1650, 1480, 1460, 1430, 1250, 1120, 940, 860, 830, 770 and 740; δ_H (270 MHz; $CDCl_3$; Me_4Si) 0.06 (6H, s, 2 × Me), 0.91 (9H, s, 3 × Me), 1.32 (3H, t, *J* 7.0, CH_2CH_3), 2.05 (3H, s, Me), 2.16 (3H, s, Me), 3.34, 3.46 (6H, each s, 2 × NMe), 4.0–4.1 (1H, m, CHN), 4.23 (2H, q, *J* 7.0, CH_2CH_3), 4.3–4.4 (1H, m, CH*H*O), 4.82 (2H, t, *J* 7.6, CH_2N), 4.9–5.1 (1H, m, C*H*HO), 5.5–5.7 (2H, m, CH_2=C), 6.79 (1H, t, *J* 7.6, CH=C).

General procedure for the rearrangement reaction of *N*-3-ethoxycarbonylbut-2-enyl-*N*-β-methallyldimethylammonium salts 9a, 9b and 9c with bases

To a solution of 1 mmol of ammonium salt in 45 cm^3 of the selected solvent (THF, DMF, EtOH, or mixed solvent THF–HMPA) was added 2 mmol of base (potassium *tert*-butoxide, sodium ethoxide, potassium ethoxide, or lithium ethoxide) at −70 to 0 °C under the conditions as shown in Tables 1 and 2. After stirring of the mixture for 1–4 h at the same temperature, water (5 cm^3) was added to the reaction mixture, which was extracted with diethyl ether. The combined organic layer was washed with brine, dried ($MgSO_4$), filtered, and evaporated. The residual material was purified by column chromatography to give the [2,3]sigmatropic rearrangement product (**11a**, **11b**, or **11c**) as shown in Tables 1 and 2.

11a: Colorless oil ν_{max}(neat)/cm^{-1} 2940, 1710, 1450, 1250, 1100 and 750; δ_H (270 MHz; $CDCl_3$; Me_4Si) 1.29 (3H, t, *J* 7.3, CH_2CH_3), 1.61, 1.69 (3H, each s, 6-Me, *E*-isomer and *Z*-isomer, respectively), 1.74 (3H, s, 10-Me), 1.84 (3H, s, 2-Me), 2.0–2.4 (6H, m, 3 × CH_2), 2.29 (6H, s, 2 × NMe), 3.31 (3H, s, OMe), 3.3–3.4 (1H, m, CHN), 3.89 (2H, d, *J* 6.9, CH_2O), 4.19 (2H, q, *J* 7.3, CH_2CH_3), 5.15 (1H, m, CH_2=C), 5.35 (1H, t, *J* 6.9, CH=C), 6.68 (1H, d, *J* 10.2, CH=C). (*Z*)-**11b**: Colorless oil (Found: C, 72.95; H, 9.26; N, 3.81. $C_{21}H_{31}NO_3$ requires C, 73.01; H, 9.04; N, 4.05%); ν_{max}(neat)/cm^{-1} 2950, 1720, 1450, 1260, 1100, 750 and 700; δ_H (270 MHz; $CDCl_3$; Me_4Si) 1.27 (3H, t, *J* 7.3, CH_2CH_3), 1.76 (3H, s, 6-Me), 1.82 (3H, s, 2-Me), 2.28 (6H, s, 2 × NMe), 2.2–2.6 (2H, m, CH_2), 3.3–3.4 (1H, m, CHN), 3.97 (2H, m, CH_2O), 4.15 (2H, q, *J* 7.3, CH_2CH_3), 4.48 (2H, m, CH_2Ph), 5.48 (1H, t, *J* 6.8, CH=C), 6.64 (1H, d, *J* 10.2, CH=C), 7.3–7.4 (5H, m, Ph). (*Z*)-**11c**: Colorless oil (Found: C, 64.78; H, 10.86; N, 3.59. $C_{20}H_{39}NO_3Si$ requires C, 64.99; H, 10.63; N, 3.79%); ν_{max}(neat)/cm^{-1} 2950, 1705, 1460, 1250, 1100, 1055, 835 and 785; δ_H (270 MHz; $CDCl_3$; Me_4Si) 0.06 (6H, s, 2 × Me), 0.89 (9H, s, 3 × Me), 1.30 (3H, t, *J* 7.3, CH_2CH_3), 1.73 (3H, s, 6-Me), 1.82 (3H, s, 2-Me), 2.28 (6H, s, 2 × NMe), 2.2–2.4 (2H, m, CH_2), 3.3–3.4 (1H, m, CHN), 4.0–4.3 (2H, m, CH_2O), 4.19

(2H, q, *J* 7.3, C*H*$_2$CH$_3$), 5.35 (1H, t, *J* 6.1, CH=C), 6.63 (1H, d, *J* 10.4, CH=C). (*E*)-**11c**: Colorless oil (Found: C, 64.89; H, 10.72; N, 3.69. $C_{20}H_{39}NO_3Si$ requires C, 64.99; H, 10.63; N, 3.79%); ν_{max}(neat)/cm^{-1} 2950, 1710, 1465, 1250, 1100, 1060, 840 and 790; δ_H (270 MHz; $CDCl_3$; Me_4Si) 0.06 (6H, s, 2 × Me), 0.89 (9H, s, 3 × Me), 1.26 (3H, t, *J* 7.3, CH$_2$C*H*$_3$), 1.62 (3H, s, 6-Me), 1.82 (3H, s, 2-Me), 2.28 (6H, s, 2 × NMe), 2.0–2.3 (2H, m, CH$_2$), 3.2–3.4 (1H, m, CHN), 3.9–4.2 (2H, m, CH$_2$O), 4.12 (2H, q, *J* 7.3, C*H*$_2$CH$_3$), 5.31 (1H, t, *J* 6.3, CH=C), 6.67 (1H, d, *J* 10.2, CH=C).

Methyl (2*E*,6*E*)-2,6-dimethyl-4-dimethylamino-10-methylenedodeca-2,6,11-trienoate ((*E*)-11d)

To a solution of ammonium salt **9d** (0.39 g, 1 mmol) in a mixture of THF (36 cm^3) and 1,3-dimethyl-3,4,5,6-tetrahydropyrimidin-2(1*H*)-one (DMPU) (9 cm^3) was added potassium *tert*-butoxide (0.224 g, 2 mmol) at −70 °C. After stirring of the mixture for 2 h at the same temperature, water (5 cm^3) was added to the reaction mixture, which was extracted with diethyl ether. The combined organic layers were washed with brine, dried ($MgSO_4$), filtered, and evaporated. The residual material was purified by column chromatography to give the desired rearrangement product (*E*)-**11d** (142.6 mg, 49%) and (*Z*)-**11d** (58 mg, 20%) as colorless oils. (*E*)-**11d** (Found: C, 74.02; H, 10.26; N, 4.71. $C_{18}H_{29}NO_2$ requires C, 74.18; H, 10.03; N, 4.81%); ν_{max}(neat)/cm^{-1} 1740, 1450, 1160, 1040, 900, 800 and 770; δ_H (270 MHz; $CDCl_3$; Me_4Si) 1.60 (3H, s, 6-Me), 1.82 (3H, s, 2-Me), 2.0–2.4 (6H, m, 3 × CH$_2$), 2.29 (6H, s, 2 × NMe), 3.3–3.4 (1H, m, CHN), 3.73 (3H, s, OMe), 4.9–5.0 (2H, m, CH$_2$=C), 5.04 (1H, d, *J* 10.9, CH*H*=CH), 5.1–5.3 (1H, m, CH=C), 5.20 (1H, d, *J* 17.8, C*H*H=CH), 6.36 (1H, dd, *J* 10.9 and 17.8, C*H*=CH$_2$), 6.67 (1H, d, *J* 10.2, CH=C). (*Z*)-**11d** (Found: C, 74.12; H, 10.14; N, 4.75. $C_{18}H_{29}NO_2$ requires C, 74.18; H, 10.03; N, 4.81%); ν_{max}(neat)/cm^{-1} 1740, 1450, 1160, 1040, 900, 800 and 770; δ_H (270 MHz; $CDCl_3$; Me_4Si) 1.70 (3H, s, 6-Me), 1.82 (3H, s, 2-Me), 2.0–2.4 (6H, m, 3 × CH$_2$), 2.28 (6H, s, 2 × NMe), 3.3–3.4 (1H, m, CHN), 3.74 (3H, s, OMe), 4.9–5.0 (2H, m, CH$_2$=C), 5.03 (1H, d, *J* 10.9, CH*H*=CH), 5.1–5.3 (1H, m, CH=C), 5.20 (1H, d, *J* 17.8, C*H*H=CH), 6.36 (1H, dd, *J* 10.9 and 17.8, C*H*=CH$_2$), 6.67 (1H, d, *J* 10.3, CH=C).

Methyl (2*E*,6*E*)-2,6-dimethyl-10-methylenedodeca-2,6,11-trienoate (12)

A solution of amine (*E*)-**11d** (0.31 g, 1 mmol) in anhydrous diethyl ether (30 cm^3) and MeI (0.21 g, 1.5 mmol) was stirred for 2 d at room temperature. The solvent was evaporated off to give a solid, which was purified by washing with anhydrous diethyl ether several times. The residual material was dried under reduced pressure to give 0.45 g of the crude desired ammonium salt quantitatively. To a solution of the ammonium salt (0.45 g, 1 mmol) and potassium dihydrogen phosphate (2.2 g, 16.2 mmol) in methanol (10 cm^3) was added 5% sodium amalgam (2.2 g, 4.8 mmol) and the mixture was stirred for 30 min at room temperature. Water (5 cm^3) was added to the reaction mixture, which was extracted with diethyl ether. The combined organic layers were washed with brine, dried ($MgSO_4$), filtered, and evaporated. The residual material was purified by column chromatography to give **12** (0.18 g, 68%) as a colorless oil (Found: C, 77.25; H, 9.94. $C_{16}H_{24}O_2$ requires C, 77.38; H, 9.74%); ν_{max}(neat)/cm^{-1} 1720, 1600, 1260, 1160 and 900; δ_H (270 MHz; $CDCl_3$; Me_4Si) 1.62 (3H, s, 6-Me), 1.84 (3H, s, 2-Me), 2.0–2.7 (8H, m, 4 × CH$_2$), 3.73 (3H, s, OMe), 5.0–5.1 (2H, m, CH$_2$=C), 5.06 (1H, d, *J* 10.9, CH*H*=CH), 5.1–5.3 (1H, m, CH=C), 5.24 (1H, d, *J* 17.8, C*H*H=CH), 6.38 (1H, dd, *J* 10.9 and 17.8, C*H*=CH$_2$), 6.75 (1H, t, *J* 10, CH=C).

(2*E*,6*E*)-2,6-Dimethyl-10-methylenedodeca-2,6,11-trien-1-ol (13)

A suspension of lithium aluminium hydride (LAH) (0.17 g, 4.4 mmol)) in anhydrous diethyl ether (2 cm^3) was added to a solution of aluminium trichloride (0.23 g, 1.7 mmol) in anhydrous diethyl ether (3 cm^3) and the mixture was stirred at 0 °C for 1 h under argon. After dropwise addition of a solution of the ester **12** (0.26 g, 1 mmol) in anhydrous diethyl ether (1.5 cm^3), stirring was continued at 0 °C for 3 h. The reaction mixture was then diluted with diethyl ether (5 cm^3), acidified with 10% hydrochloric acid, and extracted with diethyl ether (4 × 10 cm^3). The combined organic layers were washed successively with saturated aq. sodium hydrogen carbonate and then with brine, dried ($MgSO_4$), filtered, and concentrated. The residue was purified by column chromatography to give tetraene alcohol **13** (0.20 g, 90%) as a colorless oil (Found: C, 81.56; H, 11.15. $C_{15}H_{24}O$ requires C, 81.76; H, 10.98%); ν_{max}(neat)/cm^{-1} 3350, 1040, 990 and 900; δ_H (270 MHz; $CDCl_3$; Me_4Si) 1.2–1.3 (1H, br s, OH), 1.61 (3H, s, 6-Me), 1.67 (3H, s, 2-Me), 2.0–2.7 (8H, m, 4 × CH$_2$), 3.99 (2H, s, CH$_2$O), 5.0–5.1 (2H, m, CH$_2$=C), 5.06 (1H, d, *J* 10.9, CH*H*=CH), 5.1–5.3 (1H, m, CH=C), 5.24 (1H, d, *J* 17.8, C*H*H=CH), 5.40 (1H, t, *J* 8, CH=C), 6.38 (1H, dd, *J* 10.9 and 17.8, C*H*=CH$_2$).

β-Sinensal (6)

To a solution of alcohol **13** (0.20 g, 0.9 mmol) in hexane (120 cm^3) was added manganese(IV) oxide (2.6 g, 29.9 mmol) and the mixture was stirred for 3 h at 0 °C. After filtration, the solution was evaporated to give an oil, which was purified by column chromatography to give *β*-sinensal (**6**) (0.14 g, 72%) as a colorless oil, ν_{max}(neat)/cm^{-1} 1690, 1650 and 900; δ_H (270 MHz; $CDCl_3$; Me_4Si) 1.63 (3H, s, 6-Me), 1.75 (3H, s, 2-Me), 2.1–2.6 (8H, m, 4 × CH$_2$), 5.00 (2H, m, CH$_2$=C), 5.06 (1H, d, *J* 10.9, CH*H*=CH), 5.1–5.3 (1H, m, CH=C), 5.24 (1H, d, *J* 17.8, C*H*H=CH), 6.38 (1H, dd, *J* 10.9 and 17.8, C*H*=CH$_2$), 6.48 (1H, t, *J* 8.9, CH=C), 9.39 (1H, s, CHO).

Ethyl (2*E*,4*E*,6*Z*)-8-*tert*-butyldimethylsiloxy-2,6-dimethylocta-2,4,6-trienoate (15)

To a suspension of the allylamine (*Z*)-**11c** (0.99 g, 2.68 mmol) and sodium carbonate (0.31 g, 2.92 mmol) in dichloromethane (30 cm^3) was added dropwise 40% peracetic acid (0.56 g, 2.94 mmol) at −60 °C. After stirring for 30 min at −60 °C, the reaction mixture was allowed to warm to 0 °C over a period of 30 min. Saturated aqueous sodium hydrogen carbonate (10 cm^3) was poured into the reaction mixture. After stirring for 10 min at room temperature, the layers were separated and the aqueous layer was extracted with ethyl acetate (4 × 10 cm^3). The combined organic layers were washed with brine, dried ($MgSO_4$), filtered, and evaporated under reduced pressure. The residue was purified by column chromatography to give **15** (0.60 g, 69%), **16** (0.11g, 11%) and **17** (0.07g, 7%). **15**: Colorless oil (Found: C, 66.44; H, 10.16. $C_{18}H_{32}O_3Si$ requires C, 66.62; H, 9.94%); ν_{max}(neat)/cm^{-1} 1710, 1620, 1245, 1100 and 1070; δ_H (270 MHz; $CDCl_3$; Me_4Si) 0.09 (6H, s, 2 × Me), 0.91 (9H, s, 3 × Me), 1.32 (3H, t, *J* 7, CH$_2$C*H*$_3$), 1.92 (3H, s, 6-Me), 1.99 (3H, s, 2-Me), 4.22 (2H, q, *J* 7, C*H*$_2$CH$_3$), 4.39 (2H, d, *J* 6.3, CH$_2$O), 5.63 (1H, t, *J* 6.3, CH=C), 6.50 (1H, dd, *J* 11 and 15, C*H*=CH), 6.85 (1H, d, *J* 15, C*H*=CH), 7.26 (1H, d, *J* 11, CH=C). **16**: Colorless oil (Found: C, 62.17; H, 10.47; N, 3.57. $C_{20}H_{39}NO_4Si$ requires C, 62.29; H, 10.19; N, 3.63%); ν_{max}(neat)/cm^{-1} 1740, 1245, 1100 and 1070; δ_H (270 MHz; $CDCl_3$; Me_4Si) 0.06 (6H, s, 2 × Me), 0.90 (9H, s, 3 × Me), 1.28 (3H, t, *J* 7.3, CH$_2$C*H*$_3$), 1.54 (3H, s, 2-Me), 1.67 (3H, s, 6-Me), 2.5–2.6 (2H, m, CH$_2$), 2.61 (6H, s, 2 × NMe), 4.16 (2H, d, *J* 6.6, CH$_2$O), 4.20 (2H, q, *J* 7.3, C*H*$_2$CH$_3$), 5.39 (1H, t, *J* 6.6, CH=C), 5.5–5.7 (2H, m, CH=CH). **17**: Colorless oil (Found: C, 61.91; H, 10.44; N, 3.46. $C_{20}H_{39}NO_4Si$ requires C, 62.29; H, 10.19; N, 3.63%); ν_{max}(neat)/cm^{-1} 1716, 1472, 1255, 1065, 836 and 777; δ_H (270 MHz; $CDCl_3$; Me_4Si) 0.06 (6H, s, 2 × Me), 0.90 (9H, s, 3 × Me), 1.29 (3H, t, *J* 7.3, CH$_2$C*H*$_3$), 1.77 (3H, s, 6-Me), 1.87 (3H, s, 2-Me), 2.0–2.5 (2H, m, CH$_2$), 2.54 (6H, s, 2 × NMe),

4.16 (2H, d, *J* 6.3, CH_2O), 4.19 (2H, q, *J* 7.3, CH_2CH_3), 4.51 (1H, q, *J* 6.9, CHON), 5.39 (1H, t, *J* 6.3, CH=C), 6.66 (1H, d, *J* 6.9, CH=C).

(2*E*,4*E*,6*Z*)-8-*tert*-Butyldiphenylsiloxy-2,6-dimethylocta-2,4,6-trien-1-ol (18)

A solution of triene ester **15** (0.36 g, 1.1 mmol) in THF (4 cm^3) and tetra-*n*-butylammonium fluoride (TBAF) (1.0 M solution in THF; 2.2 cm^3, 2.2 mmol) was stirred for 30 min at room temperature. Water (5 cm^3) was added to the reaction mixture, which was then extracted with diethyl ether. The combined organic layers were washed with brine, dried ($MgSO_4$) and evaporated to give crude ethyl (2*E*,4*E*,6*Z*)-8-hydroxy-2,6-dimethylocta-2,4,6-trienoate 0.25 g, quantitative. A solution of 0.25 g of crude ethyl (2*E*,4*E*,6*Z*)-8-hydroxy-2,6-dimethylocta-2,4,6-trienoate, imidazole (0.18 g, 2.2 mmol), and *tert*-butylchlorodiphenylsilane (TBDPSCL) (0.37 g, 1.35 mmol) in anhydrous DMF (3 cm^3) was stirred for 1 h at room temperature. Water (10 cm^3) was added to the reaction mixture. The organic layer was separated and the aqueous layer was extracted with ethyl acetate. The combined organic layers were washed with brine, dried ($MgSO_4$), filtered, and evaporated. The residual material was purified by column chromatography to give ethyl (2*E*,4*E*,6*Z*)-8-*tert*-butyldiphenylsiloxy-2,6-dimethylocta-2,4,6-trienoate (0.48 g, 98%) as a colorless liquid (Found: C, 74.94; H, 8.11. $C_{28}H_{36}O_3Si$ requires C, 74.95; H, 8.09%); ν_{max}(neat)/cm^{-1} 1705, 1620, 1240, 1105, 1060, 970 and 710; δ_H (270 MHz; $CDCl_3$; Me_4Si) 1.06 (9H, s, 3 × Me), 1.32 (3H, t, *J* 6.9, CH_2CH_3), 1.89 (3H, s, 6-Me), 1.96 (3H, s, 2-Me), 4.21 (2H, q, *J* 6.9, CH_2CH_3), 4.39 (2H, d, *J* 6.6, CH_2O), 5.70 (1H, t, *J* 6.6, CH=C), 6.45 (1H, dd, *J* 11 and 15, C*H*=CH), 6.59 (1H, d, *J* 15, C*H*=CH), 7.12 (1H, d, *J* 11, CH=C), 7.3–7.7 (10H, m, 2 × Ph). A suspension of LAH (56 mg, 1.47 mmol) in anhydrous diethyl ether (1 cm^3) was added to a mixture of $AlCl_3$ (66 mg, 0.495 mmol) in anhydrous diethyl ether (2 cm^3) and the whole was stirred at 0 °C for 1 h under argon. After dropwise addition of a solution of ethyl (2*E*,4*E*,6*Z*)-8-*tert*-butyldiphenylsiloxy-2,6-dimethylocta-2,4,6-trienoate (0.18 g, 0.4 mmol) in anhydrous diethyl ether (3 cm^3), stirring was continued at 0 °C for 3 h. The reaction mixture was then diluted with diethyl ether (15 cm^3), 1 M NaOH (3 cm^3) was added, and the mixture was extracted with diethyl ether (4 × 10 cm^3). The combined extract was washed with brine (3 cm^3), dried ($MgSO_4$), filtered, and concentrated. The residue was purified by column chromatography to give triene alcohol **18** (0.157 g, 96%) as a colorless oil (Found: C, 76.56; H, 8.67. $C_{26}H_{34}O_2Si$ requires C, 76.80; H, 8.43%); ν_{max}(neat)/cm^{-1} 3300, 1100, 1060 and 700; δ_H (270 MHz; $CDCl_3$; Me_4Si) 1.05 (9H, s, 3 × Me), 1.26 (1H, br s, OH), 1.81 (3H, s, 6-Me), 1.87 (3H, s, 2-Me), 4.08 (2H, br s, CH_2OH), 4.37 (2H, d, *J* 6.3, CH_2O), 5.56 (1H, t, *J* 6.3, CH=C), 6.02 (1H, d, *J* 9.9, C*H*=CH), 6.32 (1H, d, *J* 15.2, CH=C), 6.39 (1H, dd, *J* 9.9 and 15.2, C*H*=CH), 7.3–7.7 (10H, m, 2 × Ph).

(2*E*,4*E*,6*Z*)-8-*tert*-Butyldiphenylsiloxy-2,6-dimethylocta-2,4,6-trienal (19)

To a solution of triene alcohol **18** (107.2 mg, 0.26 mmol) in a mixture of hexane (30 cm^3) and chloroform (7 cm^3) was added active manganese(IV) oxide (1.5 g, 17.3 mmol) and the mixture was stirred for 12 h at room temperature. After filtration, the solvent was evaporated off to give an oil, which was purified by column chromatography to give **19** (106.6 mg, quant.) as a colorless oil (Found: C, 76.85; H, 8.19. $C_{26}H_{32}O_2Si$ requires C, 77.18; H, 7.97%); ν_{max}(neat)/cm^{-1} 1680, 1610, 1105, 1060 and 700; δ_H (270 MHz; $CDCl_3$; Me_4Si) 1.06 (9H, s, 3 × Me), 1.86 (3H, s, 6-Me), 1.92 (3H, s, 2-Me), 4.42 (2H, d, *J* 6.3, CH_2O), 5.81 (1H, t, *J* 6.3, CH=C), 6.57 (1H, dd, *J* 12 and 15, C*H*=CH), 6.73 (1H, d, *J* 15, C*H*=CH), 6.75 (1H, d, *J* 12, CH=C), 7.3–7.7 (10H, m, 2 × Ph), 9.42 (1H, s, CHO).

9-(2′,6′,6′-Trimethylcyclohex-1′-enyl)-8-acetoxy-3,7-dimethyl-9-(*p*-tolylsulfonyl)nona-2*Z*,4*E*,6*E*-trien-1-ol (20)

To a stirred solution of *β*-cyclogeranyl *p*-tolyl sulfone (244.8 mg, 0.838 mmol) in anhydrous THF (4 cm^3) was added at −78 °C slowly, under nitrogen, *n*-BuLi (a 1.6 M hexane solution, 0.5 cm^3, 0.8 mmol) over a period of 10 min. After stirring of the mixture for 1 h, a solution of aldehyde **19** (80.9 mg, 0.2 mmol) in anhydrous THF (1.2 cm^3) was added slowly at −78 °C. After stirring of the mixture for 3 h, acetic anhydride (0.15 cm^3, 1.6 mmol) was added, and the reaction mixture was allowed to warm to room temperature. Saturated aq. ammonium chloride was poured into the flask, and the reaction mixture was extracted with diethyl ether (4 × 20 cm^3). The combined organic layer was washed with brine (5 cm^3), dried ($MgSO_4$), filtered, and evaporated under reduced pressure. The residue was purified by column chromatography with hexane and ethyl acetate (85 : 15) to give 9-(2′,6′,6′-trimethylcyclohex-1′-enyl)-8-acetoxy-1-*tert*-butyldiphenylsiloxy-3,7-dimethyl-9-(*p*-tolylsulfonylnona-2*Z*,4*E*,6*E*-triene (118.2 mg, 80%) as a colorless liquid (Found: C, 73.18; H, 7.95. $C_{45}H_{58}O_5SSi$ requires C, 73.13; H, 7.91%); ν_{max}(neat)/cm^{-1} 1750, 1450, 1375, 1310, 1135, 960 and 700; δ_H (270 MHz; $CDCl_3$; Me_4Si) 0.67 (3H, s, Me), 1.03 (9H, s, 3 × Me), 1.10 (3H, s, Me), 1.3–1.7 (4H, m, CH_2CH_2), 1.68 (3H, s, 2′-Me), 1.98 (3H, s, 3-Me), 2.04 (3H, s, COMe), 1.9–2.2 (2H, m, CH_2), 2.08 (3H, s, 7-Me), 2.46 (3H, s, *Me*Ar), 4.16 (1H, d, *J* 11, CHS), 4.33 (2H, d, *J* 6.3, CH_2O), 5.54 (1H, t, *J* 6.3, CH=C), 5.8–5.9 (1H, m, C*H*=CH), 5.96 (1H, d, *J* 11, C*H*OAc), 6.1–6.3 (2H, m, C*H*=CH + CH=C), 7.2–7.9 (14H, m, Ar). A solution of 9-(2′,6′,6′-trimethylcyclohex-1′-enyl)-8-acetoxy-1-*tert*-butyldiphenylsiloxy-3,7-dimethyl-9-(*p*-tolylsulfonyl)nona-2*Z*,4*E*,6*E*-triene (14.3 mg, 0.0194 mmol) in THF (3 cm^3) containing TBAF (1.0 M solution in THF; 0.1 cm^3, 0.1 mmol) was stirred for 30 min at room temperature. Water (1 cm^3) was added to the reaction mixture, which was extracted with diethyl ether (4 × 20 cm^3). The combined extract was washed with brine (5 cm^3), dried ($MgSO_4$), filtered, and evaporated. The residual material was purified by column chromatography to give the alcohol **20** (9.68 mg, 99%) as a colorless oil (Found: C, 69.52; H, 8.25. $C_{29}H_{40}O_5S$ requires C, 69.57; H, 8.05%); ν_{max}(neat)/cm^{-1} 3300, 1750, 1450, 1375, 1310, 1230, 1140 and 960; δ_H (270 MHz; $CDCl_3$; Me_4Si) 0.72 (3H, s, Me), 1.11 (3H, s, Me), 1.3–1.7 (4H, m, CH_2CH_2), 1.64 (1H, br s, OH), 1.71 (3H, s, 2′-Me), 1.86 (3H, s, 3-Me), 2.01 (3H, s, COMe), 2.0–2.2 (2H, m, CH_2), 2.11 (3H, s, 7-Me), 2.47 (3H, s, *Me*Ar), 4.19 (1H, d, *J* 10.6, CHS), 4.27 (2H, d, *J* 7, CH_2OH), 5.58 (1H, t, *J* 7, CH=C), 5.99 (1H, d, *J* 11, C*H*=CH), 6.02 (1H, d, *J* 10.6, C*H*OAc), 6.33 (1H, dd, *J* 11 and 15, C*H*=CH), 6.51 (1H, d, *J* 15, CH=C), 7.3–7.9 (4H, m, Ar).

(13*Z*)-Retinol (7)

To a solution of the alcohol **20** (4.5 mg, 0.009 mmol) and potassium dihydrogen phosphate (20 mg, 0.15 mmol) in a mixture of ethanol (1 cm^3) and diethyl ether (1 cm^3) was added 5% sodium amalgam (20 mg, 0.043 mmol) and the mixture was stirred for 30 min at room temperature in the dark. Water (5 cm^3) was added to the reaction mixture, which was then extracted with diethyl ether (4 × 10 cm^3). The combined extract was washed with brine (2 cm^3), dried ($MgSO_4$), filtered, and evaporated. The residual material was purified by column chromatography to give (13*Z*)-retinol (**7**) (1.62 mg, 63%); ν_{max}(neat)/cm^{-1} 3400, 1720, 1340, 1270, 1180, 1080, 1020 and 970; δ_H (270 MHz; $CDCl_3$; Me_4Si) 1.00 (6H, s, 2 × Me), 1.5–1.7 (5H, m, CH_2CH_2 + OH), 1.71 (3H, s, Me), 1.92 (3H, s, 3-Me), 1.95 (3H, s, 7-Me), 1.9–2.1 (2H, m, CH_2), 4.32 (2H, d, *J* 8, CH_2OH), 5.55 (1H, d, *J* 8, CH=C), 6.10 (1H, d, *J* 11, CH=C), 6.11 (1H, d, *J* 16, C*H*=CH), 6.15 (1H, d, *J* 16, C*H*=CH), 6.62 (1H, d, *J* 16, C*H*=CH), 6.65 (1H, dd, *J* 11 and 16, C*H*=CH).

(2*Z*)-1-Bromo-3-cyanobut-2-ene

To a solution of 2-methylbutene-2-nitrile (15.2 g, 187 mmol) in tetrachloromethane (100 cm^3) containing *N*-bromosuccinimide (50 g, 281 mmol) was added a catalytic amount of benzoyl peroxide. After refluxing for 5 h, the reaction mixture was filtered and poured into saturated aqueous sodium hydrogen carbonate (30 cm^3). The organic phase was separated and the aqueous layer was extracted with dichloromethane (4 × 30 cm^3). The combined organic layers were washed with brine, dried ($MgSO_4$), filtered, and evaporated under reduced pressure. The residue was purified by distillation under reduced pressure to give 12.5 g of a mixture of (2*Z*)- and (2*E*)-1-bromo-3-cyanobut-2-ene (bp 40–47 °C, 0.9 mmHg) and further purified by column chromatography with hexane and ethyl acetate (95 : 5, R_f = 0.25) to give pure (2*Z*)-1-bromo-3-cyanobut-2-ene (9 g, 30%) as a colorless liquid (Found: C, 37.45; H, 3.85; N, 8.58. C_5H_6BrN requires C, 37.53; H, 3.78; N, 8.75%); ν_{max}(neat)/cm^{-1} 3047, 2220, 1639, 1440, 1207 and 738; δ_H (270 MHz; $CDCl_3$; Me_4Si) 2.02 (3H, s, Me), 4.12 (2H, d, *J* 8.3, CH_2Br), 6.35 (1H, t, *J* 8.3, CH=C); δ_C (68 MHz; $CDCl_3$; Me_4Si) 20.1, 27.1, 113.2, 135.8, 141.3; NOE experiment: irradiation of vinyl proton caused 3.0% enhancement of methyl proton.

[(2*Z*)-3-Cyanobut-2-enyl]-[(4*Z*)-1-isopropenyl-6-methoxy-4-methylhex-4-enyl] dimethylammonium bromide (9e)

A solution of **8a** (2.11 g, 10 mmol) in anhydrous acetonitrile (106 cm^3) containing (2*Z*)-1-bromo-3-cyanobut-2-ene (1.6 g, 10 mmol) was stirred for 2 d at room temperature with protection from light. The solution was evaporated to give a residue, which was washed several times with diethyl ether and recrystallized from methyl acetate–diethyl ether to give **9e** (3.32 g, 89%) as white crystals (Found: C, 58.10; H, 8.42; N, 7.38. $C_{18}H_{31}BrN_2O$ requires C, 58.22; H, 8.41; N, 7.54%); mp 102.5–104.4 °C; ν_{max}(KBr)/cm^{-1} 2942, 2218, 1670 and 1446; δ_H (270 MHz; $CDCl_3$; Me_4Si) 1.81 (3H, s, 4-Me), 2.02 (3H, s, 1′-Me), 2.22 (3H, s, Me), 1.8–2.2 (4H, m, CH_2CH_2), 3.33 (3H, s, OMe), 3.36, 3.39 (6H, each s, 2 × NMe), 3.84 (2H, d, *J* 6.9, CH_2O), 4.3–4.5 (2H, m, CH_2N), 4.5–4.7 (1H, m, CHN), 5.50 (1H, t, *J* 6.9, CH=C), 5.6–5.7 (2H, m, CH_2=C), 7.17 (1H, t, *J* 7.3, CH=C).

(2*Z*,6*E*,10*Z*)-11-Cyano-3,7-dimethyl-9-dimethylamino-1-methoxydodeca-2,6,10-triene ((2*Z*,6*E*,10*Z*)-21) and its C-6 epimer ((2*Z*,6*Z*,10*Z*)-21)

To a solution of ammonium salt **9e** (131.6 mg, 0.35 mmol) in THF (18 cm^3) was added potassium *tert*-butoxide (78.4 mg, 0.7 mmol) at −30 °C. After stirring of the mixture for 1 h at the same temperature, water was added, and the reaction mixture was extracted with ethyl acetate (4 × 10 cm^3). The combined extract was washed with brine (3 cm^3), dried ($MgSO_4$), filtered, and concentrated. The residue was purified by column chromatography (silica gel NH-DM1020) with hexane–ethyl acetate (9 : 1) to give (2*Z*,6*E*,10*Z*)-**21** (46.2 mg, 45%) and (2*Z*,6*Z*,10*Z*)-**21** (15.4 mg, 15%). (2*Z*,6*E*,10*Z*)-**21**: Colorless liquid (Found: C, 74.40; H, 10.45; N, 9.69. $C_{18}H_{30}N_2O$ requires C, 74.44; H, 10.41; N, 9.65%); ν_{max}(neat)/cm^{-1} 2933, 2217, 1668, 1451 and 1097; δ_H (270 MHz; $CDCl_3$; Me_4Si) 1.66 (3H, s, 7-Me), 1.75 (3H, s, 3-Me), 1.97 (3H, s, Me), 2.0–2.2 (5H, m, CH_2CH_2 + CH*H*CH), 2.29 (6H, s, 2 × NMe), 2.3–2.5 (1H, m, C*H*HCH), 3.32 (3H, s, OMe), 3.3–3.5 (1H, m, CHN), 3.90 (2H, d, *J* 6.9, CH_2O), 5.0–5.2 (1H, m, CH=C), 5.36 (1H, t, *J* 6.9, CH=C), 5.99 (1H, d, *J* 10.2, CH=C); δ_C (68 MHz; $CDCl_3$; Me_4Si) 16.2, 20.3, 23.4, 26.7, 31.9, 41.8, 43.0, 57.9, 63.8, 68.6, 112.0, 118.0, 121.7, 127.5, 131.6, 140.4, 146.9; NOE experiments: irradiation of C-6 vinyl proton caused 14% enhancement of methylene proton of C-8 and no enhancement of methyl proton on C-7. Thus this NOE analysis shows the stereochemistry of the double bond between C-6 and C-7 is the *E*-configuration. Furthermore, irradiation of vinyl proton of C-10 caused 14% enhancement of methyl proton on C-11. Thus this NOE analysis shows the stereochemistry of methylbutenonitrile moiety is the *Z*-configuration. (2*Z*,6*Z*,10*Z*)-**21**: Colorless liquid (Found: C, 74.45; H, 10.35; N, 9.71. $C_{18}H_{30}N_2O$ requires C, 74.44; H, 10.41; N, 9.65%); ν_{max}(neat)/cm^{-1} 2933, 2217, 1665, 1450 and 1095; δ_H (270 MHz; $CDCl_3$; Me_4Si) 1.75 (3H, s, 3-Me), 1.88 (3H, s, 7-Me), 1.97 (3H, s, Me), 2.0–2.2 (5H, m, CH_2CH_2 + CH*H*CH), 2.29 (6H, s, 2 × NMe), 2.3–2.5 (1H, m, C*H*HCH), 3.32 (3H, s, OMe), 3.3–3.5 (1H, m, CHN), 3.90 (2H, d, *J* 6.9, CH_2O), 5.1–5.3 (1H, m, CH=C), 5.36 (1H, t, *J* 6.9, CH=C), 5.99 (1H, d, *J* 10.2, CH=C); δ_C (68 MHz; $CDCl_3$; Me_4Si) 20.3, 23.4, 23.9, 26.9, 32.0, 34.3, 41.9, 57.9, 63.8, 68.6, 112.0, 118.0, 121.7, 127.5, 131.6, 140.4, 147.0; NOE experiments: irradiation of C-6 vinyl proton caused 14% enhancement of methyl proton on C-7. Thus this NOE analysis shows the stereochemistry of the double bond between C-6 and C-7 is the *Z*-configuration. Furthermore irradiation of vinyl proton of C-10 caused 14% enhancement of methyl proton on C-11. Thus this NOE analysis shows the stereochemistry of methyletenonitrile moiety is the *Z*-configuration.

(2*Z*,6*Z*,10*E*)-11-Cyano-3,7-dimethyl-9-dimethylamino-1-methoxydoddeca-2,6,10-triene ((2*Z*,6*Z*,10*E*)-22) and its C-6 epimer ((2*Z*,6*E*,10*E*)-22)

To a solution of ammonium salt **9e** (132.3 mg, 0.36 mmol) in methanol (18 cm^3) was added potassium methoxide (49.9 mg, 0.71 mmol) at −30 °C. After stirring of the mixture for 2 h at the same temperature, water was added, and then methanol was evaporated off under reduced pressure. The water layer was extracted with ethyl acetate (4 × 20 cm^3). The combined extract was washed with brine (5 cm^3), dried ($MgSO_4$), filtered, concentrated. The residue was purified by column chromatography (silica gel NH-DM1020) with hexane–ethyl acetate (9 : 1) to give (2*Z*,6*Z*,10*E*)-**22** (47.7 mg, 46%) and (2*Z*,6*E*,10*E*)-**22** (14.2 mg, 14%): (2*Z*,6*Z*,10*E*)-**22**: Colorless liquid (Found: C, 74.42; H, 10.46; N, 9.58. $C_{18}H_{30}N_2O$ requires C, 74.44; H, 10.41; N, 9.65%); ν_{max}(neat)/cm^{-1} 2932, 2218, 1702, 1450 and 1098; δ_H (270 MHz; $CDCl_3$; Me_4Si) 1.69 (3H, s, Me), 1.76 (3H, s, 3-Me), 1.88 (3H, s, 7-Me), 2.0–2.2 (5H, m, CH_2CH_2 + CH*H*CH), 2.28 (6H, s, 2 × NMe), 2.3–2.5 (1H, m, C*H*HCH), 3.32 (3H, s, OMe), 3.3–3.5 (1H, m, CHN), 3.90 (2H, d, *J* 6.9, CH_2O), 5.1–5.3 (1H, m, CH=C), 5.38 (1H, t, *J* 6.9, CH=C), 6.27 (1H, d, *J* 10.2, CH=C); δ_C (68 MHz; $CDCl_3$; Me_4Si) 15.5, 23.5, 24.0, 26.8, 32.1, 34.4, 41.6, 57.8, 60.3, 68.6, 111.7, 120.1, 122.0, 127.6, 131.1, 140.0, 146.9; NOE experiments: irradiation of C-6 vinyl proton caused 6.5% enhancement of methyl proton on C-7 and no enhancement of methylene proton of C-8. Thus this NOE analysis shows the stereochemistry of the double bond between C-6 and C-7 is the *Z*-configuration. Furthermore, irradiation of vinyl proton of C-10 caused 5.9% enhancement of methyne proton of C-9 and no enhancement of methyl proton on C-11. Thus this NOE analysis shows the stereochemistry of the methylbutenonitrile moiety is the *E*-configuration. (2*Z*,6*E*,10*E*)-**22**: Colorless liquid (Found: C, 74.40; H, 10.48; N, 9.68. $C_{18}H_{30}N_2O$ requires C, 74.44; H, 10.41; N, 9.65%); ν_{max}(neat)/cm^{-1} 2933, 2218, 1702, 1450 and 1098; δ_H (270 MHz; $CDCl_3$; Me_4Si) 1.66 (3H, s, 7-Me), 1.69 (3H, s, Me), 1.76 (3H, s, 3-Me), 2.0–2.2 (5H, m, CH_2CH_2 + CH*H*CH), 2.28 (6H, s, 2 × NMe), 2.3–2.5 (1H, m, C*H*HCH), 3.32 (3H, s, OMe), 3.3–3.5 (1H, m, CHN), 3.90 (2H, d, *J* 6.9, CH_2O), 5.0–5.2 (1H, m, CH=C), 5.38 (1H, t, *J* 6.9, CH=C), 6.27 (1H, d, *J* 10.2, CH=C); δ_C (68 MHz; $CDCl_3$; Me_4Si) 15.5, 16.1, 23.4, 27.0, 32.0, 42.0, 43.0, 57.9, 60.3, 68.6, 111.7, 120.3, 122.2, 127.6, 131.3, 140.0, 146.9; NOE experiments: irradiation of C-6 vinyl proton caused 7% enhancement of methylene proton of C-8. Thus this NOE analysis shows the stereochemistry of the double bond between C-6 and C-7 is the *E*-configuration.

Furthermore, irradiation of vinyl proton of C-10 caused no enhancement of methyl proton on C-11. Thus this NOE analysis shows the stereochemistry of the methylbutenonitrile moiety is the *E*-configuration.

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