# Model Studies on the Synthesis of Medium-sized and Large Carbocycles using the Ireland Enolate Claisen Rearrangement

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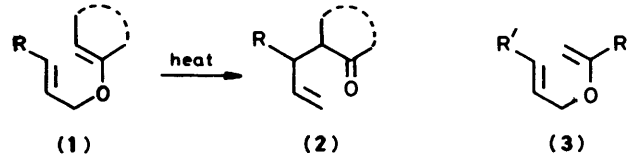
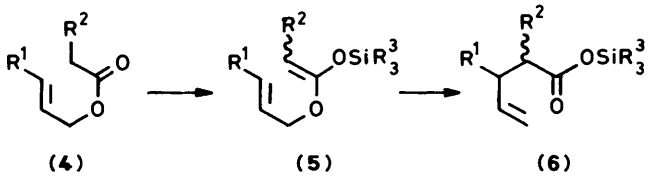
Model studies have shown that the enolate Claisen rearrangement, a modification (developed by R. E. Ireland *et al.*) of the original Claisen rearrangement, can successfully be applied to the elaboration of medium-sized and large carbocycles from *O*-silyl enolates of suitable unsaturated macrolides (Scheme). The rearrangements are largely *non*-stereoselective, a fact which can be rationalised in terms of the intermediacy of both chair- and boat-like transition states and possibly because, in some cases, both the (*E*)- and (*Z*)-enolate of the macrolides are involved.

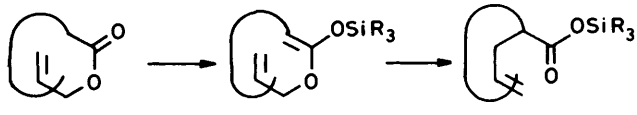
The Claisen rearrangement [(1) ⟶ (2)][1] was one of the first sigmatropic processes to be recognised and has subsequently gained an important position in synthetic methodology, especially in the elaboration of substituted phenols and related aromatics. Although originally discovered using an aliphatic precursor,[2] subsequent applications in this area were somewhat sporadic, partly due to the high temperatures required for such rearrangements and partly because of the relative inaccessibility of allyl vinyl ethers (**1**). However, during the past twenty years, a number of modifications to the original method have greatly enhanced the value of this pericyclic process. In general, these advances have focused on alternative ways to obtain the required vinyl ether function and were perhaps first stimulated by the work of Eschenmoser and co-workers[3] in which the key intermediates [(**3**; R = $NMe_2$)] were obtained by transetherifications of allylic alcohols with amide acetals. Subsequently, the use of acid-catalysed transetherifications with orthoethers, leading to acetals [(**3**; R = OEt)], was developed.[4] More recently, it has been shown[5] that acetals of this type can also be obtained by selenoxide eliminations. Claisen rearrangements of thioesters (so-called 'Thio-Claisens') have been developed,[6] and offer some advantages in suitable cases and, in some isolated examples, the vinyl group has been replaced by an imine function.[7] The idea of using an unsaturated acetal in place of the original vinyl ether function was further extended by Ireland *et al.*[8] in their use of *O*-silyl enolates (**5**), derived from the corresponding readily available esters (**4**). Overall, this process offers some crucial advantages, in particular the avoidance of the acidic conditions required in orthoester transetherifications and the fact that the key rearrangement step [(**5**) ⟶ (**6**)] proceeds rapidly at significantly lower temperatures, typically below 100 °C, compared with *ca.* 140 °C for longer periods required by the amide acetal and orthoester methods. Prior to this work, some examples of the direct rearrangement of enolates derived from allyl esters had been reported[9] although both the yields obtained and the conditions used made this method very limited (see also ref. 8). The use of zinc enolates (derived from allyl α-bromo esters in a Reformatsky–Claisen combination) and of enol phosphates in place of the vinyl ether function has also been briefly reported[10] but these methods have not been further developed. During the past few years it has been amply demonstrated, especially by Ireland's group,[11] that the overall sequence (**4**) ⟶ (**6**) represents one of the best and most general ways to effect a Claisen rearrangement and is now often referred to as an Ireland–Claisen or an Ireland (ester)enolate–Claisen rearrangement. In general, the optimum conditions consist of enolisation of the allyl esters using lithium di-isopropylamide (LDA) at −78 °C followed by *O*-silylation.[12] t-Butyldimethyl- or triethyl-silyl chloride are usually preferred as the intermediates are more stable, and *C*-silylation† of the ester enolates is usually avoided. We were attracted by the possibility of applying the Ireland–Claisen method to the synthesis of medium-sized and large carbocycles by rearrangements of macrolides as summarised in the Scheme. In general, the elaboration of such carbocycles directly from acyclic precursors suffers from the obvious problems associated with intra- *versus* inter-molecular reactions although some notable exceptions have been discovered, in addition to the classical acyloin condensation, such as $Ni(CO)_4$-induced intramolecular couplings of α,ω-bis-allylic bromides[13] and cyclisations of metallated allylic sulphides or cyanhydrins containing a distal electrophilic function such as an epoxide or halide.[14] Until fairly recently, similar limitations also applied to the syntheses of large lactones (macrolides) from ω-hydroxy acids or related precursors. However, stimulated by the occurrence in Nature of many macrolides with important pharmacological or odoriferous properties, a variety of methods are now available for the preparation of these lactones.[15] Thus, the sequence




(1) (2) (3)




(4) (5) (6)

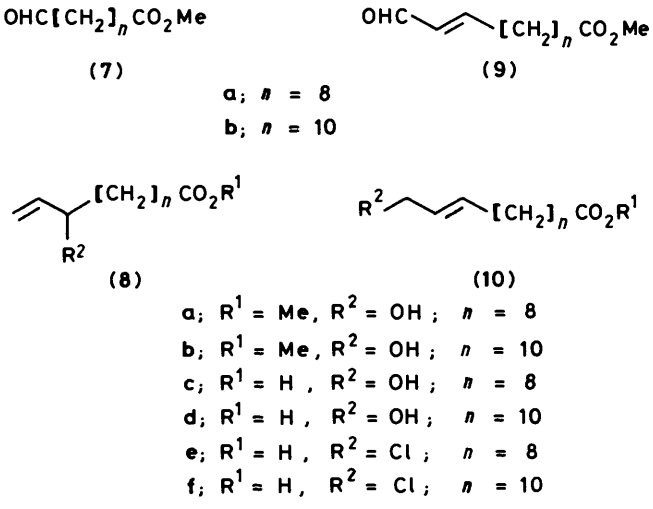



Scheme.

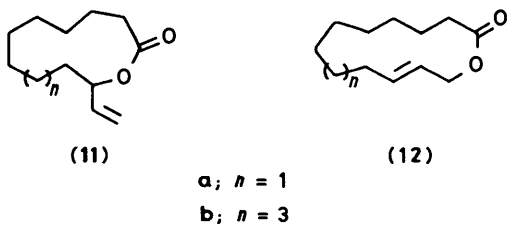
† Note that use of even bulkier silyl chlorides such as $Bu^tPh_2SiCl$ would probably result in extensive *C*-silylation: see G. Larson and L. M. Fuentes, *J. Am. Chem. Soc.*, 1981, **103**, 2418.

shown in the Scheme could provide a relatively brief and simple approach to large carbocycles which would contain both an olefinic and carboxylic acid function, both of which could be independently manipulated to provide access to further derivatives. At the outset of our studies, Danishefsky *et al.*[16] had shown that the key rearrangement (Scheme) could be applied to ω-vinyl-valerolactones and -caprolactones leading to cyclohexene- and cycloheptene-carboxylic acids respectively and, furthermore, had applied the method to an elegant synthesis of the sesquiterpene widdrol.[17] More recently, two other groups[18,19] have reported examples of such Ireland–Claisen rearrangements of unsaturated macrolides. Herein, we report in full[20] the successful outcome of our own model studies, based on the Scheme, a reaction which has been termed the alicyclic Claisen rearrangement,[18] and which we have utilised in an approach to some diterpenes.[21]

The ω-hydroxy acids used in our work were derived from readily available starting materials, using straightforward methodology. Methyl 10-oxodecanoate (**7a**) was obtained from methyl undec-10-enoate by ozonolysis,[22] while the two-carbon homologue (**7b**) was prepared from cyclododecanone by Baeyer–Villiger oxidation using the excellent large-scale procedure developed by Whiting and co-workers,[23] followed by methanolysis and oxidation with pyridinium chlorochromate (PCC).[24] Subsequent reactions between the aldehydo esters and vinylmagnesium bromide at −78 °C then provided the two

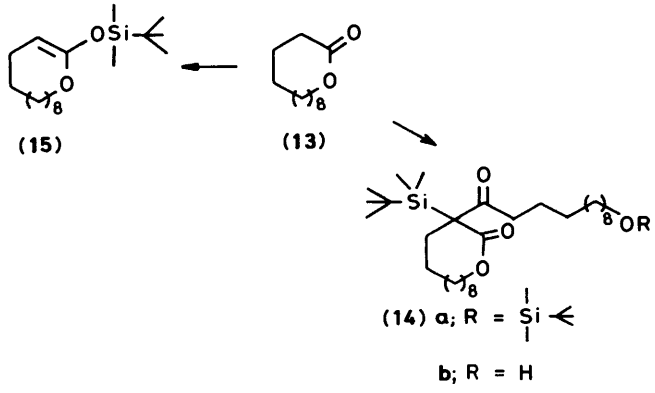



hydroxy esters (**8a**) and (**8b**) in excellent yields, saponification of which gave the required hydroxy acids [(**8c**) and (**8d**)]. The aldehydo esters (**7a**) and (**7b**) were also used as precursors for the ω-hydroxy acids (**10c**) and (**10d**) which were obtained following Wittig reactions with oxoethylidenetriphenylphosphorane,[25] leading to homologues (**9a**) and (**9b**), followed by sodium borohydride reduction and finally saponification. Several methods[15] were then examined for the direct preparation of the required macrolides (**11a, b**) and (**12a, b**)

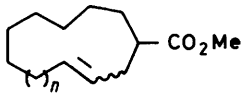



from the corresponding hydroxy acids. Although these were largely successful, g.l.c. analysis before and after isolation revealed that considerable losses were occurring during separation of the relatively volatile macrolides from the large quantities of solvents used in these high-dilution methods. A solution to this problem was found in the procedure of Galli and Mandolini,[26] developed from much earlier work, whereby ω-bromo acids can be lactonised using a suspension of potassium carbonate in hot dimethyl sulphoxide (DMSO). Crucially, the volatile, non-polar macrolides could be isolated simply by continuous extraction of the cooled reaction mixture with light petroleum (b.p. 40—60 °C). Separation of the macrolides was thus achieved with minimal loss and furthermore relatively large-scale lactonisations could be carried out without the need for a tedious and wasteful aqueous work-up or the use of expensive reagents; the residual DMSO can be recovered and reused simply by filtration and distillation. As the existing procedure could be applied to saturated ω-bromo acids, we needed only to convert our hydroxy acids into the corresponding allylic chlorides. Initially, this caused problems of regioselectivity when some of the more conventional reagents were used. For example, treatment of hydroxy acid (**8d**) with thionyl chloride gave a mixture of the allylic chlorides (**10f**) and (**8f**) in the ratio 77:23, according to $^1$H n.m.r. analysis. However, both of the primary alcohols (**10c**) and (**10d**) were cleanly converted into the corresponding primary chlorides (**10e**) and (**10f**) by treatment with hexachloroacetone and triphenylphosphine at −78 °C followed by warming to ambient temperature.[27] The same reagent combination was also found to be suitable for the preparation of the secondary chlorides (**8e**) and (**8f**); in these cases, however, the reactions were best carried out at 0 °C and provided the required chlorides contaminated with *ca.* 10% of the corresponding primary allylic chlorides. The regioselectivities were lower at −78 °C. The isomers were not separated but were immediately lactonised using $K_2CO_3$–DMSO, as the isomeric macrolides could be easily separated by column chromatography. This lactonisation procedure provided the required macrolides (**11a, b**) and (**12a, b**) in *ca.* 70% isolated yields. While traces (≤ 5%) of the corresponding diolides were observed, there was no evidence that isomeric macrolides were being produced by $S_N2'$ attack by the carboxylate anions.

Initial experiments to test the viability of enolisation and *O*-silylation of this type of macrolide were carried out using dodecan-12-olide (**13**)[23] as a model. It was found that use of at least a slight excess of LDA was essential, since if slightly less than one equivalent were used at −78 °C for 0.25 h, addition of an excess of t-butyldimethylsilyl chloride gave mainly the adduct (**14a**) [*m/z* 624 ($M^+$, 5%) and 567 ($M$ − Bu$^t$, 100)] which on brief treatment with aqueous hydrogen fluoride in acetonitrile underwent only *O*-desilylation to give (**14b**) [*m/z*



510 ($M^+$, 3%) and 453 ($M$ − Bu$^t$, 100)]. Both compounds exhibited i.r. and $^1$H n.m.r. data which were consistent with the proposed structures. The required *O*-silyl enolate (**15**) [$\delta_H$ 3.67 (t, *J* 7.5, C*H*=C)] was observed as a minor product under these conditions but was obtained free from any contamination by adduct (**14a**) when two equivalents of LDA in tetrahydrofuran–hexamethyl phosphoric triamide (THF–HMPA) were used, and could be isolated following a brief aqueous work-up. Further purification by chromatography was not possible as the compound was rapidly hydrolysed back to dodecan-12-olide (**13**). Subsequently, enolisation and trapping of the unsaturated macrolides (**11a, b**) and (**12a, b**) was found to be most efficiently carried out using two equivalents of hexane-free LDA in THF–HMPA (3:1) at −78 °C for 0.75 h, followed by addition of Bu$^t$Me$_2$SiCl. After isolation, the *O*-silyl enolates were refluxed in toluene for 5—8 h (t.l.c. monitoring), then the whole reaction product was desilylated using aqueous hydrogen fluoride in acetonitrile. Separation of the acidic products, followed routinely by diazomethylation and chromatography, finally gave the esters (**16a, b**) and (**17a, b**) in 63—80% isolated yields. This method therefore is a relatively brief and potentially widely applicable approach to medium-sized and large carbocycles.

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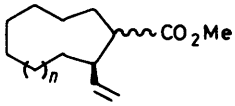
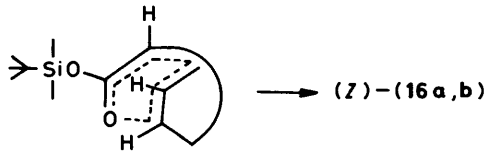



(17)

a; *n* = 1

b; *n* = 3

A disappointing feature of these rearrangements is the lack of stereospecificity, as in only one case [(**11a**) ⟶ (**16a**)] was a single isomer obtained. The complete isomeric purity of carbocycle (**16a**) was assured on the basis of $^1$H and particularly $^{13}$C n.m.r. data. We have assigned the (*Z*)-stereochemistry on the basis of the absence of a peak at *ca.* 970 cm$^{-1}$ in the i.r. spectrum of compound (**16a**); by contrast, a peak at 975 cm$^{-1}$ is present in the corresponding spectrum of the two-carbon homologue (**16b**) which was obtained as an isomeric mixture in the ratio 72:28 according to both $^1$H n.m.r. and g.l.c. data. On the basis of the respective $^{13}$C n.m.r. spectra, the major isomer of compound (**16b**) has the (*Z*)-stereochemistry. These data are also consistent with those reported[19] for (*E*)- and (*Z*)-3-methylcyclopentadec-3-enoic acid. In all cases, the (*E*)-isomers show an absence of resonances between 30 and 40 p.p.m. in their $^{13}$C spectra, whereas in the (*Z*)-isomers triplets are observed at $\delta_C$ *ca.* 31 and 34 p.p.m. Both *O*-silyl enolates derived from macrolides (**11a**) and (**11b**) were single isomers according to $^1$H n.m.r. analysis; from the deductions of Still and Galynker,[28] it is most probable that these have the (*E*)-stereochemistry derived from the kinetically more favoured (*Z*)-lithio-enolates. Therefore, the exclusive formation of (*Z*)-(**16a**) can be rationalised by assuming the intermediacy of the boat-like transition state (**18**), the usually more energetically favourable chair conformation (**19**) being excluded because of the constraints imposed by the remainder of the macrolide ring. Presumably, in the case of the larger 13-membered macrolide (**11b**), the carbon bridge is sufficiently long to allow some participation by this latter conformation. Consistent with this is the observation that a related 15-membered macrolide affords the corresponding carbocycles in an (*E*)/(*Z*) ratio of 8:1.[19] Based on these types of arguments, we had hoped that rearrangement of the (*E*)-macrolides (**12a**) and (**12b**) would give rise largely or exclusively to the *cis*-isomers of carbocycles (**17**), *via* the chair conformation (**20**), as both this and the corresponding boat conformation

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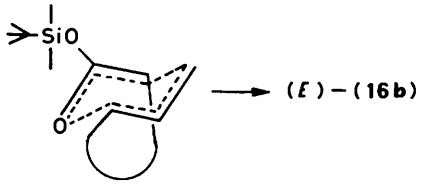


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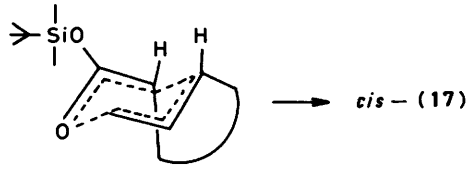
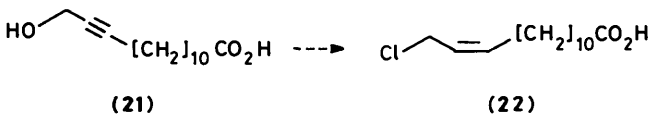



(20)

contain an axial–equatorial polymethylene bridge. However, carbocycle (**17a**) was obtained as two isomers in the ratio 56:44, while the homologue (**17b**) showed an isomeric ratio of 68:32. Both ratios were determined by integration of the two methyl ester resonances. The $^{13}$C n.m.r. data were also consistent with the proposed structures although not all the resonances were resolved. This lack of stereospecificity could be due to the intermediacy of both *O*-silyl enolate isomers, indicated by the occurrence of a pair of triplets [$\delta_H$ 3.65 and 3.68, both *J* 7.5, CH=C(O)OSi] in the $^1$H n.m.r. spectrum of the crude enolates, in the ratio *ca.* 1:2. As further purification was not possible however, this explanation must be regarded as tentative. If the (*Z*)-silyl enolate were formed, then this would probably rearrange largely *via* an alternative chair conformation [*cf.* (**20**)] with a diequatorial polymethylene bridge. Rearrangement of the (*Z*)-macrolide (**23**), isomeric with macrolide (**12b**), also gave an isomeric mixture of the carbocycles (**17b**), in the ratio 34:66, in 76% isolated yield. Macrolide (**23**) was obtained from the acetylenic acid (**21**)[29] by sequential Lindlar hydrogenation[29] and chlorination,[27] under the same conditions used for the (*E*)-isomer (**10d**), to give the chloro acid (**22**), which was then lactonised with $K_2CO_3$–DMSO. In this case, the intermediate *O*-silyl enolate appeared to be a single isomer [$\delta_H$ 3.67, t, *J* 7.5] which most probably was the (*E*)-isomer;[28] based on previous

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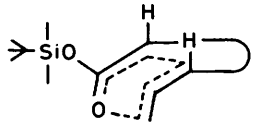


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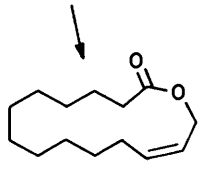


(23)

observations,[18] we have assigned the *cis*-stereochemistry to the major isomer obtained from macrolide (**23**), which would arise *via* the diequatorially bridged boat conformation (**24**). Presumably, the polymethylene bridge in this case is sufficiently long to allow some involvement of the corresponding diaxially substituted chair conformation, leading to the minor *trans*-isomer of carbocycle (**17b**). Based on the above assignment, the major isomers obtained from the (*E*)-macrolides (**12a**) and (**12b**) have a *trans*-stereochemistry.[18] It is highly probable that, in general, such rearrangements of smaller or more highly substituted macrolides will lead to single isomers, whose stereochemistries can be predicted on the basis of the above conformational arguments, thus further enhancing the utility of this method; some examples of this have already been documented.[16–18,21]

## Experimental

*General Details.*—M.p.s. were determined on a Kofler hot-stage apparatus and are uncorrected. I.r. spectra were determined using a Perkin-Elmer 710B spectrometer. $^1$H N.m.r. spectra were determined using dilute solutions in deuteriochloroform and a Perkin-Elmer R32 (90 MHz) or a Brucker WM-250 (250 MHz) spectrometer. $^{13}$C N.m.r. spectra were recorded using the latter instrument operating at 62.8 MHz. Tetramethylsilane was used as an internal standard throughout; splittings (*J*) are expressed in Hertz. Mass spectra were determined using either an A.E.I. MS 902 or VG 7070E spectrometer.

All reactions were conducted under a static atmosphere of dry nitrogen, and all organic solutions were dried over anhydrous magnesium sulphate.

*Methyl* 10-*Oxodecanoate* (**7a**).—Ozonolysis of methyl undec-10-enoate using the improved method of Dev and co-workers[22] gave the aldehydo ester (**7a**) (73%), an oil, b.p. 108—110 °C at 0.6 mmHg (lit.,[22] 119—121 °C at 2 mmHg; lit.,[30] 120—121 °C at 3 mmHg); $\delta_H$ 1.20—1.76 (12 H, m), 2.16—2.48 (4 H, m, 2 × C$H_2$C=O), 3.64 (3 H, $CO_2$Me), and 9.77 (1 H, t, *J* 2, CHO).

*Methyl* 12-*Oxododecanoate* (**7b**).—Baeyer–Villiger oxidation of cyclododecanone following the procedure of Whiting and co-workers[23] gave 12-dodecanolide (83%). A solution of this lactone (81.6 g, 0.408 mol) in methanolic sodium methoxide [from sodium (22.25 g) and methanol (1 100 ml)] was refluxed for 0.5 h, then cooled and evaporated to *ca.* 300 ml. Following acidification with excess of ice-cold 1M-hydrochloric acid, the mixture was extracted with ether (3 × 100 ml). The combined extracts were dried and evaporated; crystallisation of the residue from light petroleum gave methyl 12-hydroxydodecanoate (71.2 g, 75%), m.p. 34.5—35.5 °C (lit.,[31,32] 34—35 °C). A solution of methyl 12-hydroxydodecanoate (19 g, 82.6 mmol) in dry dichloromethane (50 ml) was slowly added to a vigorously stirred suspension of PCC[24] (45 g, 209 mmol) in dichloromethane (250 ml). After 1 h at room temperature, t.l.c. analysis (10% EtOAc–light petroleum) showed complete consumption of the alcohol. The mixture was filtered through silica gel, with dichloromethane as eluant. Evaporation of the filtrate gave the aldehydo ester (**7b**) (15.9 g, 83%) as a pale yellow oil, b.p. 109—110 °C at 0.1 mmHg (lit.,[33] 154 °C at 5 mmHg) which solidified on refrigeration (lit.,[33] m.p. 16 °C) and showed $\delta_H$ 1.24—1.35 (12 H, m), 1.41—1.74 (4 H, m), 2.20—2.50 (4 H, m, 2 × C$H_2$C=O), 3.66 (3 H, $CO_2$Me), and 9.81 (1 H, t, *J* 2, CHO).

10-*Hydroxydodec*-11-*enoic Acid* (**8c**).—Vinylmagnesium bromide (22.5 ml of 1.6M soln. in THF; 36 mmol) was added dropwise to a stirred solution of methyl 10-oxodecanoate (**7a**) (7 g, 35 mmol) in THF (100 ml) maintained at −78 °C. Ten minutes after the addition, saturated aqueous ammonium chloride (50 ml) was added and the mixture was allowed to reach ambient temperature. Following the addition of ether (50 ml), the aqueous layer was removed and the organic layer was shaken successively with saturated brine (25 ml) then with solid sodium chloride. After filtration, the filtrate was dried and evaporated and the residue was chromatographed over silica gel with 20% EtOAc–light petroleum as eluant to give methyl-10-hydroxydodec-11-enoate (**8a**) (3.68 g, 52%), $\nu_{max.}$(film) 3 400 and 1 735 cm$^{-1}$; $\delta_H$ 1.20—1.70 (14 H, m), 2.22 (2 H, t, *J* 7, C$H_2$$CO_2$Me), 3.65 (3 H, $CO_2$Me), 3.98 (1 H, br q, *J ca.* 6, 10-H), 4.98 (1 H, ddd, *J* 10, 2, and 1.5, CH=C$H_c$$H_t$), 5.14 (1 H, ddd, *J* 17, 2, and 1, CH=C$H_c$$H_t$), and 5.83 (1 H, ddd, *J* 17, 10, and 6, C$H$=$CH_2$). The material was pure by t.l.c. analysis.

A solution of the foregoing hydroxy ester (3.68 g, 16.1 mmol) in 10% methanolic potassium hydroxide (50 ml) and water (1 ml) was stirred overnight at room temperature, then evaporated. The residue was dissolved in water (50 ml) and the resulting solution was washed with ether (25 ml) then acidified with excess of conc. hydrochloric acid and extracted with ether (5 × 25 ml). The combined extracts were washed successively with water (10 ml) and brine (10 ml), then dried and evaporated. Crystallisation of the residue from light petroleum–ether gave the *hydroxy acid* (**8c**) (2.81 g, 82%), m.p. 43—44 °C; $\nu_{max.}$ ($CHCl_3$) 3 400, 3 200—2 600, and 1 720 cm$^{-1}$; $\delta_H$ 1.20—1.80 (14 H, m), 2.34 (2 H, t, *J* 7, C$H_2$$CO_2$H), 4.12 (1 H, br q, *J ca.* 6, 10-H), 5.10 (1 H, ddd, *J* 10, 2, and 1.5, CH=C$H_c$$H_t$), 5.22 (1 H, ddd, *J* 17, 2, and 1, CH=C$H_c$$H_t$), 5.89 (1 H, ddd, *J* 17, 10, and 6, C$H$=$CH_2$), and 6.90 (2 H, br, 2 × OH) (Found: C, 67.1; H, 10.2. $C_{12}H_{22}O_3$ requires C, 67.3; H, 10.3%).

12-*Hydroxytetradec*-13-*enoic Acid* (**8d**).—By the procedure detailed above, reaction between methyl 12-oxododecanoate (**7b**) (9.63 g, 38 mmol) and vinylmagnesium bromide (23.9 ml of 1.6M soln) gave *methyl* 12-*hydroxytetradec*-13-*enoate* (**8b**) (6.39 g, 66%), m.p. 36—38 °C; $R_F$ 0.28 (10% EtOAc–light petroleum); $\nu_{max.}$ ($CHCl_3$) 3 410 and 1 735 cm$^{-1}$; $\delta_H$ 1.20—1.70 (18 H, m), 2.20 (1 H, br, OH), 2.24 (2 H, t, *J* 7, C$H_2$$CO_2$Me), 3.64 (3 H, $CO_2$Me), 4.00 (1 H, br q, *J ca.* 6, 12-H), 5.01 (1 H, ddd, *J* 10, 2, and 1.5, CH=C$H_c$$H_t$), 5.16 (1 H, ddd, *J* 17, 2, and 1, CH=C$H_c$$H_t$), and 5.85 (1 H, ddd, *J* 17, 10, and 6, C$H$=$CH_2$) (Found: C, 70.5; H, 10.6. $C_{15}H_{28}O_3$ requires C, 70.3; H, 10.9%).

Hydrolysis of the hydroxy ester (**8b**) (6.39 g) using 10% methanolic potassium hydroxide then gave the *hydroxy acid* (**8d**) (5.68 g, 94%), m.p. 51—52 °C; $\nu_{max.}$(solid film) 3 350, 3 240, and 1 715 cm$^{-1}$; $\delta_H$ 1.20—1.80 (18 H, m), 2.33 (2 H, t, *J* 7, C$H_2$$CO_2$H), 4.11 (1 H, br q, *J ca.* 6, 12-H), 5.10 (1 H, ddd, *J* 10, 2, and 1.5, CH=C$H_c$$H_t$), 5.24 (1 H, ddd, *J* 17, 2, and 1, CH=C$H_c$$H_t$), 5.93 (1 H, ddd, *J* 17, 10, and 6, C$H$=$CH_2$), and 7.09 (2 H, br, 2 × OH) (Found: C, 69.3; H, 11.0. $C_{14}H_{26}O_3$ requires C, 69.4; H 10.7%).

(E)-*Methyl* 12-*Oxododec*-10-*enoate* (**9a**).—A solution of methyl 10-oxodecanoate (**7a**) (8 g, 40 mmol) and oxoethylidenetriphenylphosphorane[25] (13.52 g, 44.5 mmol) in dry chloroform (60 ml) was refluxed for 48 h. The cooled solution was mixed with silica gel (70—230 mesh; 20 g) and evaporated to dryness. The resulting powder was placed on a column of silica gel (150 g) and eluted with 20% EtOAc–light petroleum to give the *aldehyde* (**9a**) (7.75 g, 86%), which was pure according to t.l.c. and $^1$H n.m.r. analysis and was used as such in the subsequent steps. An analytical sample was obtained, with some loss, by Kugelrohr distillation and showed b.p. 145 °C (oven temp.) at 0.01 mmHg (lit.,[34,35] 109 °C at 0.01 mmHg; 119—121 °C at 0.23 mmHg); $\nu_{max.}$(film) 1 735 and 1 690 cm$^{-1}$; $\delta_H$ 1.21—1.80 (12 H, m), 2.22—2.45 (4 H, m), 3.68 (3 H, $CO_2$Me), 6.11 (1 H, ddt, *J* 16, 8, and *ca.* 1, CH=C$H$CHO), 6.89 (1 H, dt, *J*

16 and 7, C*H*=CHCHO), and 9.54 (1 H, d, *J* 8, CHO) (Found: C, 69.2; H, 9.4. $C_{13}H_{22}O_3$ requires C, 69.0; H, 9.7%).

(E)-*Methyl* 14-*Oxotetradec*-12-*enoate* (**9b**).—By the procedure described above, reaction between methyl 12-oxododecanoate (**7b**) (1.05 g) and oxoethylidenetriphenylphosphorane[25] (1.55 g) for 24 h gave the aldehyde (**9b**) (0.7 g, 66%), $\nu_{max.}$ (film) 1 735 and 1 690 $cm^{-1}$; $\delta_H$ 1.20—1.76 (16 H, m), 2.18—2.40 (4 H, m), 3.69 (3 H, $CO_2Me$), 6.14 (1 H, ddt, *J* 16, 8, and *ca.* 1, CH=C*H*CHO), 6.92 (1 H, dt, *J* 16 and 7, C*H*=CHCHO), and 9.54 (1 H, d, *J* 8, CHO). The $^1H$ n.m.r. data indicated that *ca.* 5% of the (*Z*)-isomer was present [$\delta_H$ 9.56 (d, CHO)]. Attempted distillation resulted in extensive loss. The chromatographed material [single spot, $R_F$ 0.7 (20% EtOAc–light petroleum)] showed C, 71.5; H, 10.0 ($C_{15}H_{26}O_3$ requires C, 70.9; H, 10.2%) and was used directly in the next step.

(E)-12-*Hydroxydodec*-10-*enoic Acid* (**10c**).—Sodium borohydride (1.15 g, 30.5 mmol) was added portionwise during 0.25 h to a stirred solution of (*E*)-methyl 12-oxododec-10-enoate (**9a**) (7.75 g, 30.3 mmol) in ethanol (50 ml) maintained at −30 °C. After a further 5 min, the solution was diluted with water (200 ml) and extracted with ether (4 × 50 ml). The combined extracts were washed successively with water (25 ml) and brine (25 ml), then dried and evaporated. Kugelrohr distillation of the residue gave (*E*)-methyl 12-hydroxydodec-10-enoate (**10a**) (7.13 g, 92%), b.p. 175 °C (oven temp.) at 0.1 mmHg; $\nu_{max.}$ (film) 3 440, 1 735, and 985 $cm^{-1}$; $\delta_H$ 1.20—1.75 (12 H, m), 1.90—2.16 (2 H, m, C$H_2$CH=), 2.18 (1 H, OH), 2.32 (2 H, t, *J* 7, C$H_2$$CO_2$Me), 3.66 (3 H, $CO_2$Me), 4.10 (2 H, m, C$H_2$OH), and 5.64—5.78 (m, 2 H, CH=CH). The ester was saponified using 10% methanolic hydroxide as previously described to give the *hydroxy acid* (**10c**) (90%) which showed m.p. 39—40 °C, after crystallisation from ether–light petroleum to remove a small amount of the corresponding saturated hydroxy acid [$\delta_H$ 3.66 (t, *J* 7, C$H_2$OH)], and $\nu_{max.}$ ($CHCl_3$) 3 400—2 500, 1 718, and 982 $cm^{-1}$; $\delta_H$ 1.25—1.75 (12 H, m), 1.90—2.17 (2 H, m, C$H_2$CH=), 2.34 (2 H, t, *J* 7, C$H_2$$CO_2$H), 4.11 (2 H, br d, *J ca.* 5, C$H_2$OH), 5.61—5.75 (2 H, m, CH=CH), and 7.37 (2 H, br, 2 × OH) (Found: C, 67.4; H, 10.1. $C_{12}H_{22}O_3$ requires C, 67.3; H, 10.3%).

(E)-14-*Hydroxytetradec*-12-*enoic Acid* (**10d**).—Reduction of (*E*)-methyl 14-oxotetradec-12-enoate (**9b**) (3.18 g) by sodium borohydride as described above gave (*E*)-methyl 14-hydroxytetradec-12-enoate (**10b**) (2.89 g, 89%), $\nu_{max.}$ (film) 3 440, 1 735, and 984 $cm^{-1}$; $\delta_H$ 1.21—1.75 (16 H, m), 1.90—2.13 (2 H, m, C$H_2$CH=), 2.32 (2 H, t, *J* 7, C$H_2$$CO_2$Me), 2.58 (1 H, OH), 3.68 (3 H, $CO_2$Me), 4.09 (2 H, m, C$H_2$OH), and 5.62—5.76 (2 H, m, CH=CH). Saponification using 10% methanolic potassium hydroxide then gave the *hydroxy acid* (**10d**) (88%), which contained *ca.* 5% of the corresponding saturated compound [$\delta_H$ 3.67 (t, *J* 7, C$H_2$OH)]. Crystallisation from ether–light petroleum gave the pure hydroxy acid, m.p. 47—48 °C; $\nu_{max.}$ ($CHCl_3$) 3 400—2 500, 1 718, and 981 $cm^{-1}$; $\delta_H$ 1.19—1.77 (16 H, m), 1.94—2.16 (2 H, m, C$H_2$CH=), 2.35 (2 H, t, *J* 7, C$H_2$$CO_2$H), 4.1 (2 H, br d, *J ca.* 5, C$H_2$OH), 5.63—5.77 (2 H, m, CH=CH), and 7.06 (2 H, br, 2 × OH) (Found: C, 69.7; H, 10.7. $C_{16}H_{26}O_3$ requires C, 69.4; H, 10.7%).

10-*Vinyldecan*-10-*olide* (**11a**).—Hexachloroacetone (4.08 ml, 26.9 mmol) was added dropwise to an ice-cold solution of 10-hydroxydodec-11-enoic acid (**8c**) (2.75 g, 12.8 mmol) and triphenylphosphine (6.96 g, 26.8 mmol) in a mixture of dry dichloromethane (25 ml) and dry ether (25 ml).[27] After the addition, the mixture was stirred without cooling for 1 h, then treated with 10% aqueous sodium carbonate (25 ml). After 10 min, water (25 ml) and ether (25 ml) were added and the aqueous layer was separated, washed with ether (25 ml), acidified with excess of dil. hydrochloric acid, and extracted with ether (3 × 50 ml). The combined extracts were washed successively with water (20 ml) and brine (20 ml), then dried and evaporated and the residue was chromatographed over silica gel with 30% EtOAc–light petroleum as eluant to give 10-chlorododec-11-enoic acid (**8e**) (1.93 g, 65%), $\delta_H$ 1.20—1.90 (14 H, m), 2.32 (2 H, t, *J* 7, C$H_2$$CO_2$H), 4.31 (1 H, q, *J* 7, C*H*Cl), 5.08 (1 H, ddd, *J* 10, 2, and 1.5, CH=C$H_c$$H_t$), 5.25 (1 H, ddd, *J* 17, 2, and 1, CH=CH$_c$$H_t$), 5.88 (1 H, ddd, *J* 17, 10, and 7, C*H*=$CH_2$), and 11.80 (br, $CO_2$H). The material was contaminated with 14% of the corresponding primary allylic chloride (**10e**) [$\delta_H$ 3.99 (dd, *J* 6 and *ca.* 1, $CH_2Cl$)]; the mixture was lactonised directly as separation of the isomeric macrolides was found to be easier and much more efficient than separation at this stage.

A solution of the foregoing allylic chloride (**8e**) (3.97 g, 17.06 mmol), containing 14% of the primary allylic chloride (**10e**), in DMSO (8 ml) was added during 6 h *via* a motor-driven syringe to a stirred suspension of anhydrous potassium carbonate (7.5 g, 54.3 mmol) in DMSO (1 500 ml), maintained at 100 °C.[26] After a further 0.5 h, the mixture was cooled and continuously extracted with light petroleum (b.p. 40—60 °C) overnight. The cooled extract was washed successively with water and saturated brine, then dried and evaporated ($t < 30$ °C). Chromatography of the residual oil over silica gel with 10% EtOAc–light petroleum as eluant gave the *decanolide* (**11a**) (2.11 g, 73%), b.p. 125—130 °C (oven temp.) at 10 mmHg; $\nu_{max.}$ (film) 1 735 $cm^{-1}$; $\delta_H$ 1.20—1.85 (14 H, m), 2.21—2.50 (2 H, m, $CH_2$C=O), 5.10 (1 H, dt, *J* 10 and *ca.* 1, CH=C$H_c$$H_t$), 5.20 (1 H, dt, *J* 17 and *ca.* 1, CH=CH$_c$$H_t$), 5.28—5.35 (1 H, m, C*H*CH=$CH_2$), and 5.80 (1 H, ddd, *J* 17, 10, and 6, C*H*=$CH_2$); *m/z* 196 (20%, $M^+$), 153 (10), 81 (42), 70 (51), 67 (80), and 55 (100) (Found: $M^+$, 196.1462. $C_{12}H_{20}O_2$ requires *M*, 196.1463).

Also isolated was the isomeric lactone (**12a**) (0.19 g).

12-*Vinyldodecan*-12-*olide* (**11b**).—Using the procedure detailed above, treatment of 12-hydroxytetradec-13-enoic acid (**8d**) (2.41 g, 9.96 mmol) with hexachloroacetone (3.19 ml, 21 mmol) and triphenylphosphine (5.5 g, 21 mmol)[27] gave the 12-chloro derivative (**8f**) (2.01 g, 77%) as a waxy solid, m.p. 34—36 °C; $\delta_H$ 1.51—1.90 (18 H, m), 2.32 (2 H, t, *J* 7, C$H_2$$CO_2$H), 4.32 (1 H, q, *J* 7, CHCl), 5.08 (1 H, ddd, *J* 10, 2, and 1.5, CH=C$H_c$$H_t$), 5.25 (1 H, ddd, *J* 17, 2, and 1, CH=CH$_c$$H_t$), 5.87 (1 H, ddd, *J* 17, 10, and 7, C*H*=$CH_2$), and 11.77 (br, $CO_2$H) contaminated with 10% of the primary allylic chloride (**10f**) [$\delta_H$ 4.00 (dd, *J* 6 and *ca.* 1, $CH_2Cl$)]. The mixture (2.01 g) was immediately lactonised as described above by dissolution in DMSO (20 ml) and addition during 4.5 h to anhydrous potassium carbonate (1.6 g) in DMSO (750 ml), to give the *macrolide* (**11b**) (1.08 g, 63%), b.p. 80 °C (oven temp.) at 0.1 mmHg; $\nu_{max.}$ (film) 1 738 $cm^{-1}$; $\delta_H$ 1.25—1.85 (18 H, m), 2.29 (1 H, ddd, *J* 14.1, 9.1, and 3.6, C$H_a$$H_b$C=O), 2.48 (1 H, ddd, *J* 14.1, 8.2, and 3.5, CH$_a$$H_b$C=O), 5.11 (1 H, dt, *J* 10.6 and 1.3, CH=C$H_c$$H_t$), 5.21 (1 H, dt, *J* 17.3 and 1.4, CH=CH$_c$$H_t$), 5.33 (1 H, m, C*H*CH=$CH_2$), and 5.81 (1 H, ddd, *J* 17.3, 10.6, and 5.8, C*H*=$CH_2$); $\delta_C$ 22.9, 24.5, 24.7, 25.2, 25.5, 26.2, 26.5, 26.8, 33.5, 34.9, 74.5 (*C*HCH=$CH_2$), 115.48 (=$CH_2$), 137.1 (=CH), and 173.4 p.p.m. (C=O); *m/z* 224 (26%, $M^+$), 181 (15), 109 (23), 98 (56), 95 (50), 81 (72), 67 (75), and 55 (100) (Found: $M^+$, 224.1778. $C_{14}H_{24}O_2$ requires *M*, 224.1776). Also isolated were the isomeric lactone (**12b**) (see below for data) (0.078 g) and a trace (*ca.* 20 mg) of the diolide, m.p. 108—110 °C, [*m/z* 448 (5%, $M^+$)], corresponding to (**11b**).

(E)-*Dodec*-10-*en*-12-*olide* (**12a**).—Hexachloroacetone (5.65 ml, 37.2 mmol) was added dropwise to a stirred solution of (*E*)-12-hydroxydodec-10-enoic acid (**10c**) (3.8 g, 17.7 mmol) and triphenylphosphine (9.65 g, 36.8 mmol) in dry dichloromethane–ether (1:1; 100 ml) maintained at −78 °C.[27] The cooling bath

was then removed and the solution was stirred for 1.25 h, then treated with saturated aqueous sodium carbonate (50 ml). After 5 min, water (50 ml) was added and the organic layer was separated and extracted with water (25 ml). The combined aqueous solutions were washed with ether (20 ml), then acidified with solid citric acid and extracted with ether (3 × 100 ml). These last three combined solutions were washed successively with water (20 ml) and brine (20 ml), then dried and evaporated; chromatography of the residue over silica gel with 30% EtOAc–light petroleum provided (*E*)-12-chlorododec-10-enoic acid (**10e**) (2.88 g, 70%), $\nu_{max.}$ (film) 1 715 and 970 $cm^{-1}$; $\delta_H$ 1.20—1.80 (12 H, m), 1.90—2.19 (2 H, m, $CH_2CH$=), 2.36 (2 H, t, *J* 7, $CH_2CO_2H$), 3.99 (2 H, dd, *J* 6 and *ca.* 1, $CH_2Cl$), and 5.48—5.96 (2 H, m, CH=CH). A correct microanalysis was not obtained (Found: C, 61.2; H, 8.7. $C_{12}H_{21}ClO_2$ requires C, 61.9; H, 9.0%); the compound was lactonised without further purification.

Addition of a solution of the allylic chloride (**10e**) (1.76 g, 7.56 mmol) in DMSO (8 ml) during 4 h to anhydrous potassium carbonate (2.5 g) in DMSO (1 000 ml) as described above gave the *macrolide* (**12a**) (1.05 g, 71%), b.p. 85 °C (oven temp.) at 0.1 mmHg; $\nu_{max.}$ (film) 1 735 and 970 $cm^{-1}$; $\delta_H$ 1.18—1.83 (12 H, m), 1.93—2.19 (2 H, m), 2.20—2.42 (2 H, m), 4.58 (2 H, d, *J* 6, $CH_2O$), and 5.53—6.04 (2 H, m, CH=CH); *m/z* 196 (24%, $M^+$), 153 (14), 99 (20), 95 (15), 81 (20), 68 (36), 67 (40), and 55 (100) (Found: $M^+$, 196.1460. $C_{12}H_{20}O_2$ requires *M*, 196.1463).

(E)-*Tetradec*-12-*en*-14-*olide* (**12b**).—Chlorination of (*E*)-14-hydroxytetradec-12-enoic acid (**10d**) (1.17 g) by the foregoing procedure gave the allylic chloride (**10f**) (0.78 g), $\nu_{max.}$ (film) 1 715 and 970 $cm^{-1}$; $\delta_H$ 1.20—1.80 (16 H, m), 1.90—2.16 (2 H, m, $CH_2CH$=), 2.34 (2 H, t, *J* 7, $CH_2CO_2H$), 4.02 (2 H, dd, *J* 6 and *ca.* 1, $CH_2Cl$), 5.43—5.97 (2 H, m, CH=CH), and 11.40 (1 H, br, $CO_2H$). The compound was immediately lactonised by the usual procedure to give the *macrolide* (**12b**) (0.47 g, 70%), b.p. 110 °C (oven temp.) at 0.01 mmHg; $\nu_{max.}$ (film) 1 736 and 970 $cm^{-1}$; $\delta_H$ 1.19—1.32 (12 H, m), 1.44 (2 H, m), 1.68 (2 H, m), 2.10 (2 H, m), 2.30 (1 H, dd, *J* 9.1 and 3.4, CHCO), 2.31 (1 H, t, *J* 7.6, CHCO), 4.53 (2 H, d, *J* 6.0, $CH_2O$), and 5.58—5.81 (2 H, m, CH=CH); $\delta_C$ 24.7, 26.3, 26.8, 26.9, 27.1, 27.4, 27.7, 28.6, 31.0, 34.5, 64.8, 125.0, 137.5, and 173.7 p.p.m.; *m/z* 224 (26%, $M^+$), 181 (12), 125 (15), 111 (25), 98 (56), 81 (68), 68 (84), and 55 (100) (Found: $M^+$, 224.1790. $C_{14}H_{24}O_2$ requires *M*, 224.1776).

The material exhibited a single peak on g.l.c., $R_t$ 4.1 min (SE 30 column; 160 °C) [*cf.* corresponding (*Z*)-isomer (**23**), $R_t$ 8.0 min, under identical conditions].

(Z)-*Tetradec*-12-*en*-14-*olide* (**23**).—14-Hydroxytetradec-12-ynoic acid (**21**), obtained by the literature method[29] from 11-bromoundecanoic acid and the dianion of propargyl alcohol (prop-2-yn-1-ol), showed m.p. 80—82 °C (from EtOAc) (lit.,[29] 82—83 °C). Lindlar hydrogenation in methanol gave (*Z*)-14-hydroxytetradec-12-enoic acid, m.p. 42.5—43.0 °C (from ether–light petroleum) (lit.,[29] 43—44 °C). Chlorination using the method described above[27] for the corresponding (*E*)-isomer gave (*Z*)-14-chlorotetradec-12-enoic acid (**22**) (72%), $\nu_{max.}$ ($CHCl_3$) 1 715 $cm^{-1}$; $\delta_H$ 1.20—1.80 (16 H, m), 2.03—2.22 (2 H, m, $CH_2CH$=), 2.38 (2 H, t, *J* 7, $CH_2CO_2H$), 4.14 (2 H, d, *J* 8, $CH_2Cl$), 5.50—5.85 (2 H, m, CH=CH), and 11.44 (1 H, br, $CO_2H$). Lactonisation as previously described then gave the *macrolide* (**23**) (83%), b.p. 110 °C (oven temp.) at 0.03 mmHg; $\nu_{max.}$ (film) 1 735, 1 650, and 725 $cm^{-1}$; $\delta_H$ (250 MHz) 1.21—1.38 (12 H, m), 1.46 (2 H, p, *J* 6.3), 1.69 (2 H, m), 2.17 (2 H, app. q, *J* 6.3, $CH_2CH$=), 2.32 (1 H, dd, *J* 9.0 and 3.5, CHCO), 2.33 (1 H, t, *J* 7.6, CHCO), 4.56 (2 H, dd, *J* 5.0 and 1.9, $CH_2O$), and 5.67—5.72 (2 H, m, CH=CH); *m/z* 224 (21%, $M^+$), 181 (11), 125 (12), 123 (12), 111 (25), 109 (27), 98 (58), 95 (53), 82 (72), 81 (78), 69 (50), 68 (94), 58 (78), and 55 (100) (Found: $M^+$, 224.1798. $C_{14}H_{24}O_2$ requires *M*, 224.1776).

The compound showed a single peak, $R_t$ 8.0 min (SE 30 column; 160 °C) [*cf.* (*E*)-isomer (**12b**), $R_t$ 4.1 min].

*Enolate Trapping and Claisen Rearrangement of Macrolides: General Procedure.*—n-Butyl-lithium (2.55 ml of a 1.6M solution in hexane; 4.08 mmol) was slowly added to dry di-isopropylamine (0.59 ml, 4.08 mmol) stirred under nitrogen at −5 °C. After 0.25 h, the reaction flask was evacuated to remove the solvent. The residue was cooled to −78 °C and dissolved in THF–HMPA (3:1; total 20 ml) and a solution of the macrolide (2 mmol) in THF (2 ml) was added dropwise during 5 min. After 0.75 h at −78 °C the mixture was treated with a solution of t-butyldimethylsilyl chloride (0.62 g, 4.12 mmol) in THF (1 ml). The resulting solution was stirred for a further 0.25 h at −78 °C, then poured into a mixture of water (100 ml) and ether (50 ml). The ether solution was separated and the aqueous layer was extracted with a further portion of ether. The combined ether solutions were washed successively with water (20 ml) and saturated brine, then shaken with solid sodium chloride and dried. After removal of the solvent, the residue was refluxed in toluene (5 ml) until t.l.c. analysis indicated completion of the rearrangement (usually 5—8 h). The cooled solution was evaporated and the residue was stirred with aqueous hydrogen fluoride (3 equiv.) in THF (5 ml) or acetonitrile (5 ml) for 5—15 min (t.l.c. monitoring). The solution was then diluted with 1M-sodium hydroxide (50 ml) and washed with ether (2 × 20 ml), then acidified with a slight excess of conc. hydrochloric acid and extracted with ether (3 × 20 ml). The combined organic extracts were washed with brine, then dried and treated with an excess of ethereal diazomethane. Evaporation gave the crude products which were purified as detailed below.

(Z)-*Methyl Cycloundec*-3-*enecarboxylate* (**16a**).—By the general procedure, rearrangement of 10-vinyldecan-10-olide (**11a**) (0.4 g, 2.04 mmol) gave, *via* a single silyl enolate according to $^1H$ n.m.r. spectroscopy {$\delta_H$ 3.67 [1 H, t, *J* 7.5, CH=C(O)OSi}, the *methyl ester* (**16a**) (0.317 g, 74%), b.p. 95 °C (oven temp.) at 0.5 mmHg; $\nu_{max.}$ (film) 1 735, 1 655, and 725 $cm^{-1}$; $\delta_H$ 1.20—1.80 (12 H, m), 1.98—2.15 (2 H, m), 2.30—2.55 (3 H, m), 3.67 (3 H, $CO_2Me$), and 5.38—5.61 (2 H, m, CH=CH); $\delta_C$ 24.3, 25.3, 25.8, 26.4, 26.8, 28.4, 33.9, 36.2, 43.7, 51.4, 127.8, 133.5, and 176.5 p.p.m.; *m/z* 210 (100%, $M^+$, FAB) (Found: C, 74.2; H, 10.3. $C_{13}H_{22}O_2$ requires C, 74.3; H, 10.5%).

(E)- and (Z)-*Methyl Cyclotridec*-3-*enecarboxylate* (**16b**).—By the general procedure, enolisation and trapping of 12-vinyldodecan-12-olide (**11b**) (0.336 g, 1.5 mmol) gave an intermediate silyl enolate which appeared to be a single isomer, $\delta_H$ 3.68 [1 H, t, *J* 7.5, CH=C(O)OSi], 4.34 (1 H, m, $CHCH=CH_2$), 5.08 (1 H, dt, *J* 10 and *ca.* 1, $CH=CH_cH_t$), 5.20 (1 H, dt, *J* 17 and *ca.* 1, $CH=CH_cH_t$), and 5.87 (1 H, ddd, *J* 17, 10, and 6, $CH=CH_2$). Claisen rearrangement and desilylation gave cyclotridec-3-enecarboxylic acid, after chromatography over silica gel with 20% EtOAc–light petroleum as eluant, which showed $\nu_{max.}$ 3 400—2 500, 1 705, 1 665, 1 655, 975, and 730 $cm^{-1}$; $\delta_H$ 1.19—1.79 (16 H, m), 1.95—2.17 (2 H, m), 2.22—2.60 (3 H, m), 5.36—5.55 (2 H, m, CH=CH), and 11.60 (1 H, br, $CO_2H$); *m/z* 224 (58%, $M^+$), 109 (65), 95 (90), 81 (95), and 67 (100). Esterification gave the *methyl esters* (**16b**) (0.25 g, 70%), b.p. 80—85 °C (oven temp.) at 0.1 mmHg; $\nu_{max.}$ (film) 1 735, 1 665, 1 655, 975, and 720 $cm^{-1}$; $\delta_H$ (250 MHz) 3.680 and 3.683 ($CO_2Me$); $\delta_C$ [(*Z*)-isomer] 24.6, 25.1, 25.1, 25.8, 26.0, 26.2, 27.5, 27.9, 31.5, 34.4, 44.3, 51.5, 128.6, 133.9, and 176.8 p.p.m.; [(*E*)-isomer] 24.1, 24.9, 25.5, 25.7, 26.1, 26.8, 27.7, 28.2, 28.4, 28.7, 44.0, 51.4, 127.1, 132.8, and 176.3 p.p.m. [Found: C, 75.6; H, 11.3. $C_{15}H_{26}O_2$ requires C, 75.6; H, 10.9%).

The isomer ratio was determined by both $^1H$ n.m.r. inte-

gration and g.l.c. to be 72:28 (*Z*:*E*). [G.l.c. (SE30; 170 °C) $R_t$ (*Z*) 6.4 min; $R_t$ (*E*) 5.4 min].

cis- *and* trans-*Methyl 2-Vinylcyclononanecarboxylate* (**17a**).—By the general procedure, enolisation and trapping of (*E*)-dodec-10-en-12-olide (**12a**) (0.4 g, 2.04 mmol) gave an intermediate *O*-silyl enolate which appeared to be a mixture of isomers [$\delta_H$ 3.65 and 3.68 (both t, *J* 7.5); ratio *ca.* 1:2]. After being heated in toluene, followed by desilylation and esterification, chromatography of the product using silica gel with 20% EtOAc–light petroleum as eluant gave the *carbocycle* (**17a**) (0.27 g, 63%), b.p. 90 °C (oven temp.) at 0.7 mmHg; $\nu_{max.}$ (film) 1 735 and 1 635 $cm^{-1}$; $\delta_H$ 1.25—1.95 (14 H, m), 2.42—2.75 (2 H, m), 3.54 (1.68 H, $CO_2Me$), 3.59 (1.32 H, $CO_2Me$), 4.80—5.00 (2 H, m, $=CH_2$), and 5.54–5.73 (1 H, m, =CH); $\delta_C$ 23.0, 23.4, 24.9, 25.6, 25.7, 26.8, 26.9, 27.1, 27.4, 29.7, 42.6, 43.4, 46.0, 51.3, 51.4, 114.5, 115.0, 139.6, 141.1, 176.3, and 176.4 p.p.m.; *m/z* 210 [Found: C, 74.4; H, 10.6. $C_{13}H_{22}O_2$ requires C, 74.3; H, 10.5%].

cis- *and* trans-*Methyl 2-Vinylcycloundecanecarboxylate* (**17b**).—(a) *From* (E)-*tetradecen*-14-*olide* (**12b**). Enolisation and *O*-silylation of the macrolide (0.26 g, 1.16 mmol) in the usual way appeared to give a mixture of isomers ($\delta_H$ 3.64 and 3.67, t, *J* 7.5) which, after the usual rearrangement procedure followed by chromatography over silica gel with 5% ether–light petroleum, gave the *carbocycle* (**17b**) (0.22 g, 80%), b.p. 105 °C (oven temp.) at 0.5 mmHg; $\nu_{max.}$ (film) 1 735 and 1 635 $cm^{-1}$; $\delta_H$ 1.20—1.85 (18 H, m), 2.40—2.78 (2 H, m), 3.61 (2.03 H, $CO_2Me$), 3.65 (0.97 H, $CO_2Me$), 4.91—5.04 (2 H, m, $=CH_2$), and 5.55—5.79 (1 H, m, =CH); $\delta_C$ 23.1, 23.7, 24.2, 24.6, 25.5, 25.7, 25.9, 26.0, 26.1, 26.2, 26.4, 26.8, 28.0, 28.9, 30.2, 44.2, 44.3, 46.3, 47.6, 51.1, 51.4, 114.6, 114.9, 140.1, 140.4, and 175.9 p.p.m.; *m/z* 238 (48%, $M^+$), 209 (16), 164 (20), 139 (39), 126 (28), 113 (42), 109 (38), 95 (62), 87 (100), 81 (77), 67 (75), and 55 (83) (Found: C, 75.4; H, 11.2. $C_{15}H_{26}O_2$ requires C, 75.6; H, 10.9%).

(b) *From* (Z)-*tetradec*-12-*en*-14-*olide* (**23**). Under the standard conditions, rearrangement of the macrolide (**23**) (0.2 g, 0.89 mmol), *via* a single *O*-silyl enolate [$\delta_H$ 3.67, t, *J* 7.5], followed by esterification gave the carbocycle (**17b**) (0.16 g, 76%) with spectral and analytical data [Found: C, 75.5; H, 11.1%] entirely consistent with the proposed structure, and differing only from the foregoing sample, obtained from the corresponding (*E*)-macrolide, in peak-height ratios. The isomeric ratio was determined by integration of the methyl ester resonances [$\delta_H$ 3.61 (1.02 H) and 3.65 (1.98 H)].

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