Intramolecular Diels–Alder reaction of functionalized trienes: synthesis of medium-ring lactones †

Annamaria Deagostino,[a] Jacques Maddaluno,*[,b] Mariella Mella,[c] Cristina Prandi[a] and Paolo Venturello*[,a]

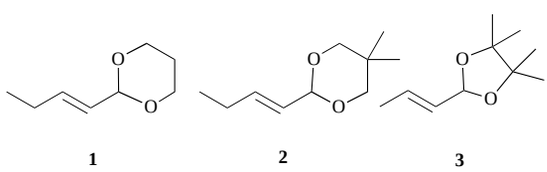
[a] *Dipartimento di Chimica Generale ed Organica Applicata dell'Università, Corso Massimo D'Azeglio, 48-I 10125 Torino, Italy. E-Mail: venturello@silver.ch.unito.it*
[b] *Laboratoire des Fonctions Azotées et Oxygénées Complexes l'IRCOF, UPRES-A 6014 Université de Rouen, 76821-Mont St Aignan Cedex, France*
[c] *Dipartimento di Chimica Organica dell'Università, Viale Taramelli, 10-I 27100 Pavia, Italy*

A simple preparative procedure has been developed for trienic systems, starting from cyclic α,β-unsaturated acetals derived from crotonaldehyde and (*E*)-pent-2-enal. The reaction is initiated by a regioselective metallation at the γ site of the unsaturated system that immediately induces 1,4-eliminative ring fission, and stereoselectively affords hydroxy-functionalized *E*-1,3-dienes. The esterification of those hydroxy dienes with acryloyl chloride gives activated trienes, suitable for intramolecular Diels–Alder reaction that yields medium-ring lactones. This method is relatively versatile with respect to the length and the substitution of the tether between the diene and the dienophile. The presence of additional stereogenic centres in the tether induces interesting selectivities during the cycloaddition step that are reported and discussed.

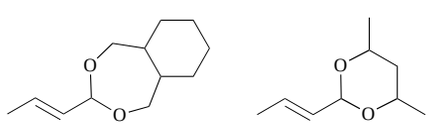
Introduction

The Diels–Alder[1] reaction is one of the most widely used methods in organic synthesis owing to its connective nature. A six-membered ring is produced, and up to four stereogenic centres can be introduced in a stereocontrolled manner. In particular, the intramolecular Diels–Alder reaction (IMDA),[2] where the diene and the dienophile are constrained in the same structure, allows the simultaneous formation of two rings and, in a single step, complex structures such as those contained in many drugs and natural products can be assembled. In connection with studies directed to explore the usefulness of α,β-unsaturated acetals as acyl-anion equivalents,[3] we have demonstrated that these derivatives undergo simple 1,4-elimination when treated with an equimolar mixture of butyllithium and potassium *tert*-butoxide (Schlosser's reagent LICKOR).[4] In particular, cyclic α,β-unsaturated acetals derived from propane-1,3-diol undergo 1,4-eliminative ring fission that gives hydroxy-functionalized *E*-buta-dienes that can be readily transformed into the requisite trienes for IMDA reaction, by esterification with an α,β-unsaturated acyl chloride. We have recently reported preliminary results that were principally focused on the regioselectivity of the cycloaddition, a problem worth discussing considering the length of the link between diene and dienophile moieties, that could lead to fused and/or bridged macrolactones.[5] The method set up in the course of our work can be of interest, as it gives selective access to *E*-alkoxydienes that are to be regarded as potent synthons, since: (i) *E* dienes are known to be more reactive than *Z* dienes; (ii) the accelerating and polarizing effects of electron-donating diene substituents on the rate of the intramolecular cyclization has been established for a long time. The method allows, moreover, some flexibility about length and substitution of the bridging chain, as well as substitution of the diene. This approach also suits the introduction of stereogenic centres in the linking chain, which can be an efficient way to control the newly created asymmetric centres.[6]

Here we report the results obtained starting from α,β-unsaturated acetals **1**–**5** that afford trienic intermediates in which diene substitution, ring size (*viz*. number of atoms bridging the diene and the dienophile), and bridge substituents have been varied.



1 **2** **3**



4 **5**

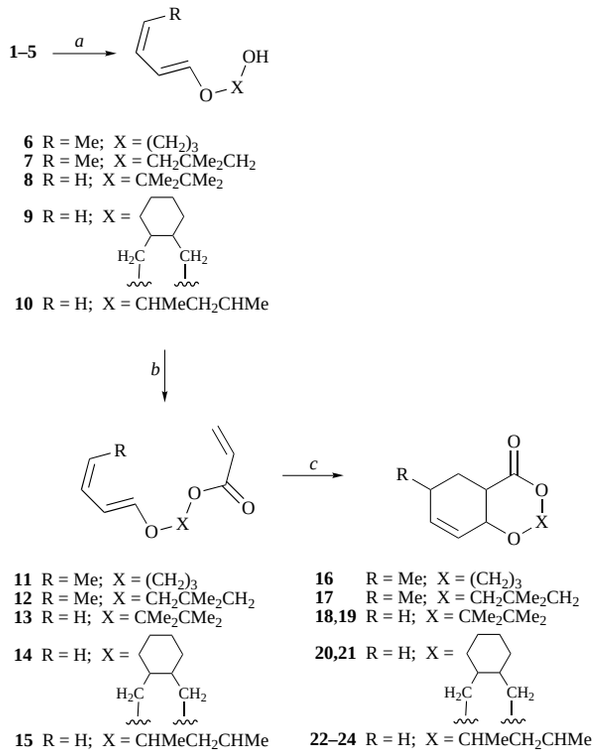
Results and discussion

Structure of the diene

The structure of the diene depends on the choice of the starting aldehyde [crotonaldehyde, R = H, and (*E*)-pent-2-enal, R = Me in Scheme 1], unsubstituted and 4-methyl-substituted (1*E*)-1-alkoxybuta-1,3-dienes are here described.‡ Moreover, elimination products **6** and **7** (Scheme 1), derived respectively from acetals **1** and **2**, result, by ^{1}H NMR analysis, as a mixture of the 5*E*,7*Z* and 5*E*,7*E* stereoisomers. The *Z*-configuration of the C(7)–C(8) double bond of the major isomer has been deduced from the irradiation of the signal corresponding to the allyl (δ 1.70 for **6**; δ 1.68 for **7**) C(8)Me group, that gives rise to a

† Partly taken from the Ph.D. Thesis of A. D.

‡ The case of 3-methyl-substituted 1,3-diene has been previously reported (see ref. 5). The *E*-configuration in the alkoxy-substituted double bond has been deduced in previous works (see ref. 3) from the J_{trans} coupling constants between the α and β olefinic hydrogen atoms in the ^{1}H NMR spectra, and by NOE experiments. In this work the value of the coupling constant in dienic derivatives confirms the *E*-configuration.



Scheme 1 *Reagents and conditions*: *a* LICKOR (1.5–2.5 mol equiv.), THF (10 cm^3), *T* −95 °C; *b* pyridine (2.5 mol equiv.), acryloyl chloride (2.2 mol equiv.), Et_2O (30 cm^3), *T* 25 °C; *c* refluxing benzonitrile or toluene, in the presence of hydroquinone

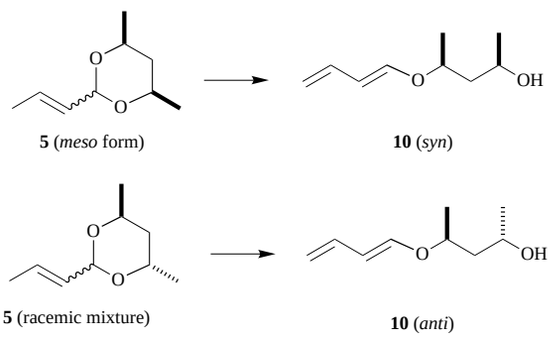
nuclear Overhauser enhancement (NOE) of the signal assigned to the C(5)H of the conjugate double bond (δ 6.54 for **6**, δ 6.57 for **7**). Indeed, the value of the coupling constant ($J_{7,8}$ 11.5 for **6**, *J* 12.0 for **7**) does not allow an unequivocal assignment of the configuration.§ The two isomers can be separated (5*E*,7*Z*:5*E*,7*E*, 9:1) by column chromatography on silica gel (diethyl ether–light petroleum, 10:90),¶ and the subsequent steps were carried out on the pure 5*E*,7*Z* major isomer.

Structure of the tether

The ring size and the substituents on the tether have been varied using acetals obtained from propane-1,3-diol (**1**), 2,2-dimethylpropane-1,3-diol (**2**), 2,3-dimethylbutane-2,3-diol (**3**), *cis*-cyclohexane-1,2-dimethanol (**4**), and pentane-2,4-diol (**5**). When ethylene glycol, instead of 2,3-dimethylbutane-2,3-diol, was used in order to obtain a five-atom tether, the 1,4-elimination reaction proceeds with lower yields. Indeed, in 1,3-dioxolane derivatives a metallation competes α to the oxygen ring, and promotes a cycloelimination which affords acetaldehyde enolate and starting carbonyl compound.‖

The reactions related to acetals **4** and **5**, obtained by reaction of crotonaldehyde with *cis*-cyclohexane-1,2-dimethanol and pentane-2,3-diol, respectively, need some additional comment. In spite of the presence of two stereocentres, *cis*-cyclohexane-1,2-dimethanol is optically inactive since it is a *meso* compound, the ring closure giving rise to a pseudoasymmetric carbon. The metallation-promoted 1,4-elimination on 4-(prop-1-enyl)-3,5-dioxabicyclo[5.4.0]undecane **4** triggers the acetalic ring fission, and thus breaks the symmetry of the starting diol. Worthy of note is the presence of two racemic but *syn*-substituted asymmetric centres in triene **14** that could lead to the formation of up to four diastereoisomeric adducts (two derived from the *endo* approach and two from the *exo* one).

The situation is slightly different in the case of 4,6-dimethyl-2-(prop-1-enyl)-1,3-dioxane (**5** and **5**′), as starting material pentane-2,4-diol was purchased as a mixture of isomers [*meso*:(2*S*,4*S* + 2*R*,4*R*) = 55:45].** The formation of the 1,3-dioxane ring adds also, in this case, a pseudoasymmetric carbon, leading to four isomers, that are two diastereomeric *meso* forms and one pair of enantiomers. Only two isomers (one *meso* form and a couple of enantiomers) are detected by ^{13}C, ^1H NMR, and GLC analysis.†† Upon dioxane fragmentation, the *meso* compound leads to an alcohol presenting a *syn* '**u**' arrangement of its methyl group (Scheme 2) while the enantiomers yield an *anti* 'l' (racemic) situation.



Scheme 2 Dioxane ring opening in the case of *meso* and racemic forms of acetal **5**

Finally, the dienophile can be introduced by esterification of the terminal alcohol with different acyl chlorides: acryloyl chloride, but also crotonoyl or methacryloyl chlorides. However, only the acrylates thus obtained present a significant reactivity in the cycloaddition conditions tested here.‡‡ We have therefore limited our investigations to the case of those esters.

IMDA reaction

Intramolecular cycloaddition of trienes **11**–**15** has been carried out in refluxing toluene and benzonitrile; the results are reported in Table 1. Stereochemical analysis of the cycloadducts **16**–**24** was determined after accurate measurement of coupling constants and complete attribution of the signals, thanks to a set of chemical-shift correlation (COSY) and NOE spectroscopy (NOESY) experiments, and the stereochemistry of the junction was assigned by considering the coupling pattern of bridgehead protons.[5],§§

In the case of trienes **11** and **12** that lead respectively to cycloadducts **16** and **17** it must be pointed out that they exhibit completely opposite stereochemistry at the junction. In particular, triene **11** selectively affords the *endo* addition product **16** (deduced from the *cis* pattern of the signals centred at δ 2.75 and 4.22, coupled with a $J_{\text{axial-equatorial}}$ value of 3.0 Hz; see Experimental section); on the other hand, compound **12** leads to the *exo* adduct **17**, exhibiting a clear *trans* junction pattern (the signals centred at δ 2.92 and 3.95 are coupled with $J_{\text{axial-axial}}$ 9.0 Hz; see Experimental section). The *endo*/*exo* selectivity switch between substrates **11** and **12** is somewhat puzzling, especially with respect to previous results obtained with closely

** We thank Aldrich Chimica for this communication.

†† The presence of pairs of enantiomers was checked in this and in all the required cases by the use of a chiral capillary column (25 m × 0.2 mm × 0.33 μm film thickness) of Megadex-5®.

‡‡ Crotonates and methacrylates do not undergo cyclization below the bp of toluene (111 °C), where they begin to decompose: A. Deagostino and P. Venturello, unpublished data. See also ref. 9.

§§ The different macrolactonic structures that account for stereochemical assignments on the basis of ^1H NMR spectra have been discussed in ref. 5.

§ This high *Z* selectivity is to be compared with that observed in a closely related case, see ref. 7.

¶ Light petroleum refers to the fraction with distillation range 30–60 °C.

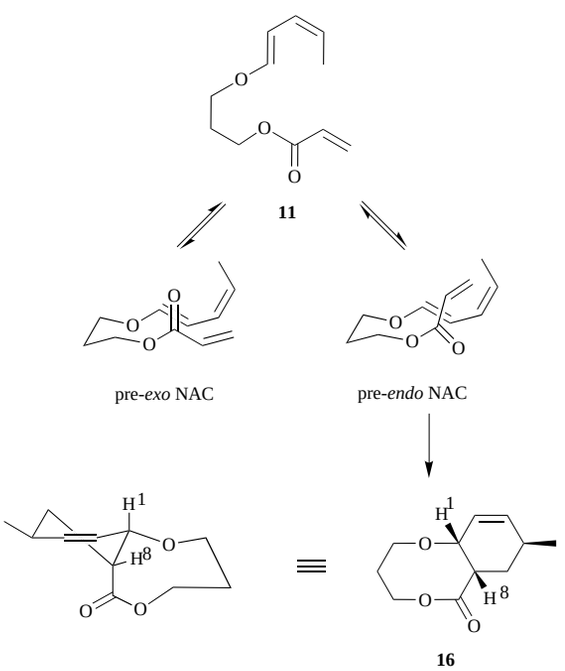
‖ Similar reactivity has been previously reported for the dioxolane ring obtained from cyclohex-2-enone, see ref. 8.

Table 1 Thermal cycloaddition of trienes **11**–**15**

		Toluene			Benzonitrile		
Triene	Adduct	*trans*:*cis*[a]	Yield[b] (%)	Reaction time (*t*/*h*)	*trans*:*cis*[a]	Yield[b] (%)	Reaction time (*t*/*h*)
11	**16**				<1:>99	30	2
12	**17**				>99:<1	50	2
13	**18**, **19**	72:28	60	60	65:35	55	0.3•
14	**20**, **21**	10:90	67	3.5	10:90	70	0.5
15[c]	**22**–**24**	>99:<1[c]	57	4	>99:<1[c]	40	0.5
		50:50[c]			50:50[c]		

[a] On the basis of the yield of the isolated isomers. [b] Yield of products isolated by column chromatography. [c] The triene derived from the *meso* form of pentane-2,4-diol selectively affords the *trans* adduct **22**, while the triene coming from the racemic mixture shows no selectivity and yields a 50:50 mixture of *cis* (**23**) and *trans* (**24**) adducts.

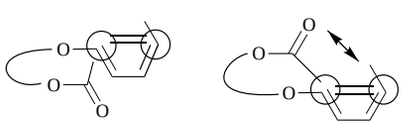
related systems.[5]¶¶ Within the framework of an early transition state, it can be tentatively rationalized by considering that in the case of triene **11** a 'flexible' tether connects dienic and dienophilic moieties, allowing the formation of two relatively loose Near Attack Conformations[10] (NAC) that show comparable weak steric interactions (Scheme 3). Such a situation might

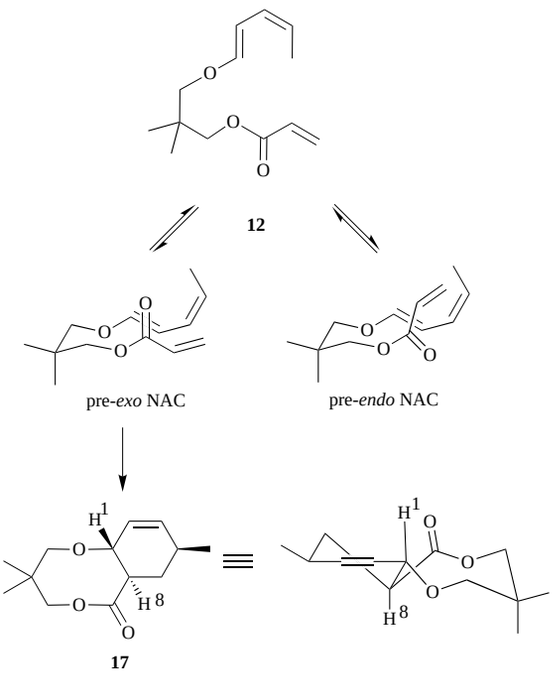


Scheme 3 Schematic representation of the *exo* and *endo* approaches for compound **11**

favour the *endo* approach on the basis of orbital factors similar to those that control the intermolecular cycloaddition. By contrast, in the case of triene **12** the *gem*-dimethyl substitution leads to more compact[11] NAC (Scheme 4) in which orbital factors cannot cope with the unfavourable pseudo-axial orientation of the ester vinyl group, occurring in the *endo* transition structure. The results obtained with trienes **14** and **15** are quite

¶¶ The following interaction in the *endo* transition structure could explain the selectivity switch linked to the terminal substitution of the diene by a methyl group (compare triene **11** in this work with triene **3a** in ref. 5). The unfavourable interaction is shown (↔).



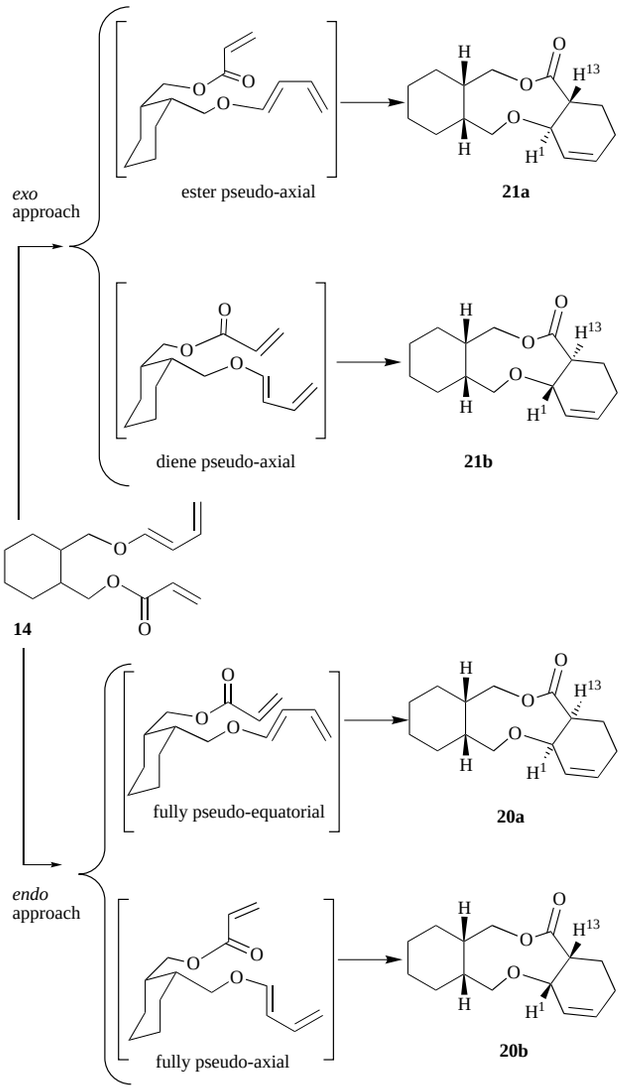


Scheme 4 Schematic representation of the *exo* and *endo* approaches for compound **12**

interesting and deserve come comment. Here again, the stereochemical outcome of the cyclization step seems to be strongly influenced by the elements bridging the diene and the dienophile, in particular by the presence of a rigid skew in the bridge (in the case of compound **14**), and by remote chiral centres (in the case of compound **15**).‖‖

Starting from the racemic pair of trienes **14**, a mixture of diastereoisomeric adducts **20** and **21** was obtained. ^{1}H NMR analysis indicates that the two major isomers (present as a 50:50 ratio) feature a C(1)–C(13)H *cis*-relationship (Scheme 5); they thus derive from an *endo* approach. The well known flexibility of medium-size systems renders the analysis of their NAC particularly questionable. Keeping this in mind, we have represented (Scheme 5) four possible threshold conformations that may be regarded as favourable precursors for the *endo* and *exo* cyclization modes. Such a 'graphical' analysis suggests that a single *endo* isomer should be obtained, derived from a preferred fully pseudo-equatorial situation (leading to product **20a**). The recovery of a mixture totally contradicts this statement. In fact, the large and flexible tether in compound **14** can turn the IMDA into an intermolecular-like cyclization, in which orbital controls would recover some significance. To these kinetic arguments in favour of the *endo* adducts can also be added thermodynamic ones, the harsh thermal conditions employed

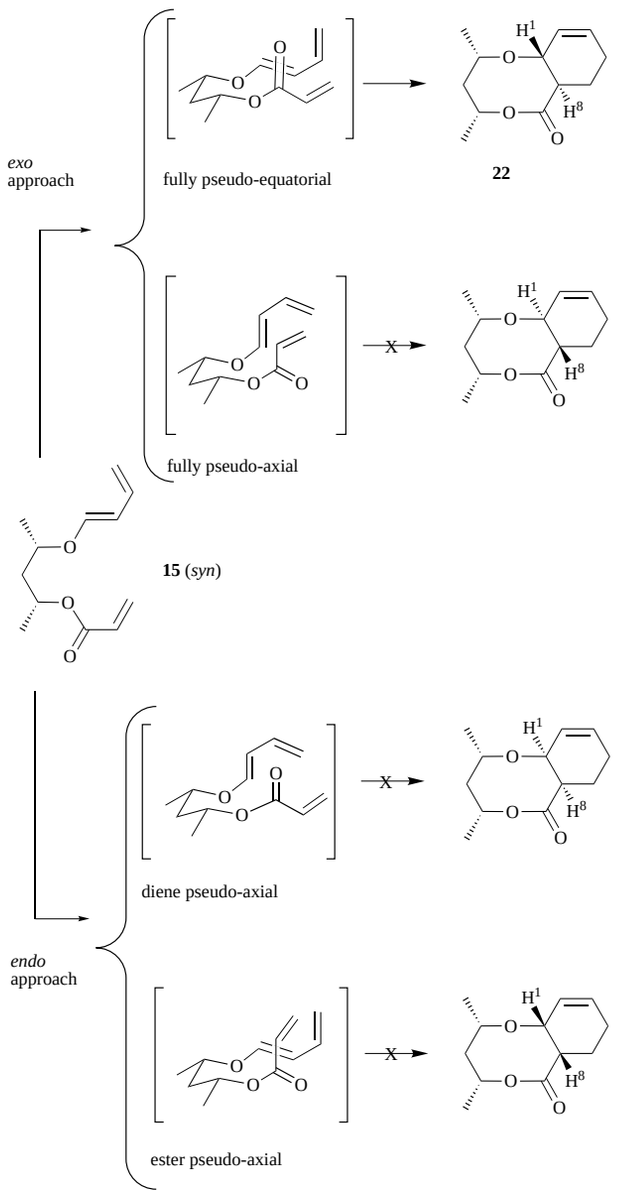
‖‖ For successful examples of such a strategy see ref. 12.



Scheme 5 Schematic representation of the *exo* and *endo* approaches for compound **14**

possibly giving some reversibility to the ring-closing process. The newly formed lactone is indeed nine-membered and surely does not constrain cycloadducts **20** and **21** to assume a rigid arrangement, and thus cyclohexane and cyclohexene rings can fairly freely interconvert assuming different conformations.*** Would such a flopping take place on the *exo* adduct, it would force the stable diequatorial *trans*-fused lactone to assume a diaxial arrangement that appears prohibitively strained. In contrast, the *cis*-fused isomers show two axial-equatorial conformations of comparable influences and should thus benefit from more conformational liberty.

By contrast, the methyl substituents borne by the tether of triene **15** seem to exert an important control on the stereochemical outcome to lactones **22**–**24**. The NAC-type analysis can, to some extent, be now considered as more reliable, since the shorter system is expected to be much less flexible. This is especially true for the *syn* disubstituted linker (*viz.* derived from the *meso* diol) for which a single pseudo-chair folding with both equatorial methyl groups is to be considered. The threshold forms in Scheme 6 strongly suggest that a single *exo* cyclization



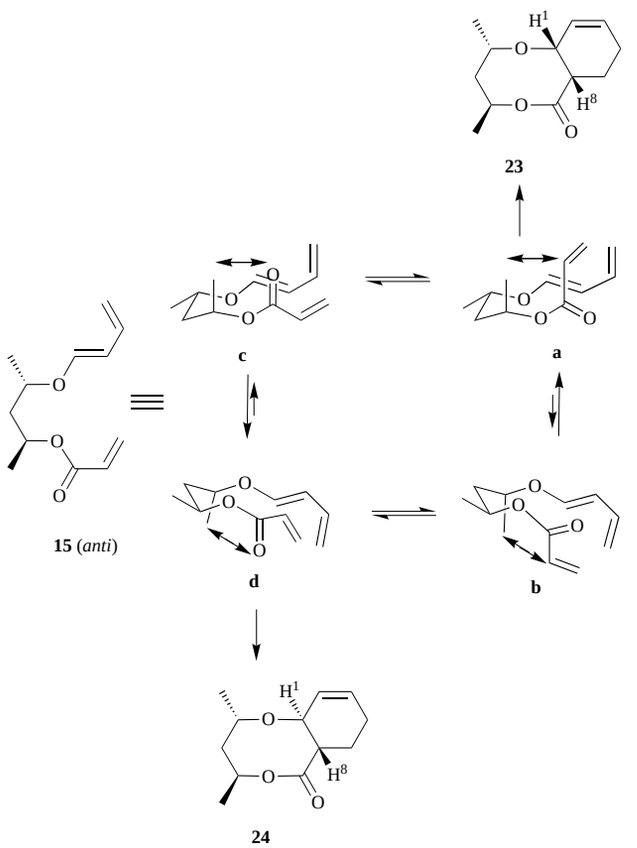
Scheme 6 Schematic representation of the *exo* and *endo* approaches for compound **15** (*meso*)

mode, corresponding to a fully pseudoequatorial arrangement, can be expected. Adduct **22** is indeed the only diastereoisomer derived from *syn*-**15** that could be identified. This conformation meets the *syn* relationship between C(1)H and C(3)H, and also takes into account the relative control of methyl groups on rings junction.††† By contrast, in the case of the *anti*-**15** derivative many conformers have to be considered, and all show unfavourable axial–axial steric interactions. Consequently cyclo-

*** The ^{1}H NMR spectrum of the mixture of isomers of **20** and **21** appears confused in $CDCl_3$, while in $CD_3C_6D_5$ (80 °C) we were able to single out two isomers (50:50) for the **20** *cis* product. Indeed, the bridgehead protons, C(1)H and C(13)H (Scheme 3), show a pattern corresponding to a *cis* ring-junction situation for both isomers, with no large coupling constant (peaks centred at δ 2.52 and 3.84 for one isomer, and δ 2.48 and 3.89 for the other. See Experimental section). Moreover, when the same analysis was carried out in CD_3CN, one of the *cis* isomers shows a well defined pattern that clearly displays an axial–equatorial coupling constant (J 6.0 Hz). In the ^{1}H NMR spectrum of the **21** *trans* isomer both C(1)H (2.42) and C(13)H (4.05) are axial as C(1)H displays a large axial–axial coupling constant (J 10.0).

††† The suggested *trans*-relationship in cycloadduct **22** was deduced from the large axial–axial coupling-constant value (J 9.5 Hz) between C(1)H (δ 4.08) and C(8)H (δ 2.60), and confirmed by NOE experiments. Moreover, the *syn* relationship between the methyl substituents [on C(3) and C(5)] and between C(1)H and C(3)H was assigned considering that the irradiation of C(3)H (δ 3.55) causes an intense NOE of C(5)H (δ 5.28) and of C(1)H.

addition affords a mixture (50 : 50) of two diastereoisomers **23** (*endo*) and **24** (*exo*) (Scheme 7). Moreover, considering the NOE experiments carried out on compound **23** we have established that the irradiation of C(3)H (δ 3.85) causes a strong NOE on C(1)H (δ 4.30), but no effect on C(5)H (δ 5.11). These data indicate: (i) the *anti* relationship between methyl groups on C(3) and C(5); (ii) the *syn* relationship between C(3)H and C(1)H, suggesting that the equilibrium between **a** and **b** NAC is decidedly shifted towards the **a** form (Scheme 7). In the case of adduct **24** the *trans*-fused structure was deduced from the large coupling-constant value (J 9.0 Hz) between C(1)H (δ 4.05) and C(8)H (δ 2.70), while the *anti* relationship between methyl groups was deduced by the NOE experiment that shows NOE of the signal pertinent to C(3)H (δ 4.42), by irradiation of the C(5) methyl group (δ 1.45). Moreover, the absence of an NOE on C(1)H by irradiation of C(3)H suggests the relative *anti* relationship and the prevalence of the **d**-form in the equilibrium shown in Scheme 7.



Scheme 7 Schematic representation of the *exo* and *endo* approaches for compound **15** (racemic); the unfavourable interaction is shown (↔)

Conclusions

The results we present indicate that the δ-elimination–acetal ring-fission cascade provides efficient access to dienic alcohols that can, in turn, be esterified to yield activated trienic systems. The thermal [4 + 2] intramolecular cycloaddition undergone by these systems offers a fairly general route to seven- to nine-membered lactonic rings. The *endo–exo* selectivity of the cyclization step is very sensitive to the substitution pattern of the connecting chain, the *exo*-process seeming favoured by sterically demanding tethers. We have also been able to show in one case that the newly created asymmetric centres can be controlled with respect to those eventually borne by the tether, suggesting possible extensions in the direction of other chiral diols such as *trans*-cyclohexanediol.

Experimental

General

Air- and moisture-sensitive reagents were protected by and handled under argon, in flame-dried equipment. The temperature of slush liquid nitrogen–acetone is consistently indicated as −95 °C, that of an ice-bath as 0 °C, and 'room temperature' as 25 °C. Purification by column chromatography was performed on Merck silica gel 60 as stationary phase and light petroleum (distillation range 30–60 °C)–diethyl ether as eluent. ^{1}H NMR spectra were recorded at 60, 300 or 400 MHz. Chemical shifts were determined using $SiMe_4$ as internal standard (60 MHz) or (300, 400 MHz) relative to the residual solvent peak ($CHCl_3$: δ 7.26). Coupling constants (J) are given in Hz, and coupling patterns are described by abbreviations: s (singlet), d (doublet), t (triplet), q (quartet), p (pentet), hex (hextet), br s (broad singlet), br d (broad doublet), br t (broad triplet). ^{13}C NMR spectra were recorded at 75.5 or 100.4 MHz. Chemical shifts were determined relative to the residual solvent peak ($CHCl_3$ δ_C 77.0). A cross-linked methyl silicone capillary column [25 × 0.2 mm × 0.33 μm film thickness; oven temperature = 70 ⟶ 250 °C, 20 °C min^{-1}; flow rate (He) 5 cm^3 min^{-1}] was used for GLC-mass spectra that were obtained at a 70 eV ionization potential.

Materials

Starting materials commercially available were reagent grade and were used without further purification. Anhydrous tetrahydrofuran (THF) was obtained by distillation over sodium wire after the persistence of the blue colour of sodium diphenylketyl.[13] Anhydrous diethyl ether was distilled from $LiAlH_4$ and then stored over 4-Å molecular sieves.

Synthesis of acetals 1–5

α,β-Unsaturated acetals were synthesized according to the standard method in a Dean–Stark apparatus, using toluene as solvent and pyridinium toluene-*p*-sulfonate (PPTS) as catalyst.

2-(But-1-enyl)-1,3-dioxane 1. (*E*)-Pent-2-enal (8.4 g, 0.1 mol) and propane-1,3-diol (7.6 g, 0.1 mol) furnished compound **1**, which was purified by distillation (bp 70 °C, 12 mmHg; 10 g, 70%), δ_H(60 MHz) 1.00 (3 H, t, J 7.0), 1.85 (4 H, m), 3.95 (4 H, m), 4.80 (1 H, br d, J 4.0), 5.50 (1 H, dd, J 12.0 and 4.0) and 5.80 (1 H, dt, J 12.0 and 6.0).

2-(But-1-enyl)-5,5-dimethyl-1,3-dioxane 2. (*E*)-Pent-2-enal (8.4 g, 0.1 mol) and 2,2-dimethylpropane-1,3-diol (10.4, 0.1 mol) afforded, after distillation (bp 90 °C, 15 mmHg), 12.7 of title product **2** (75%), δ_H(60 MHz) 1.20 (3 H, s), 1.25 (3 H, t, J 6.0), 1.30 (3 H, s), 1.85 (2 H, pent, J 6.0), 4.80 (1 H, d, J 6.0), 5.35 (1 H, dd, J 16.0 and 6.0) and 5.77 (1 H, dt, J 16.0 and 6.0).

4,4,5,5-Tetramethyl-2-(prop-1-enyl)-1,3-dioxolane 3. Crotonaldehyde (7.0 g, 0.1 mol) and 2,3-dimethylbutane-2,3-(diol (11.8 g, 0.1 mol) yielded compound **3**. Distillation of the crude reaction mixture (bp 95 °C, 15 mmHg) afforded 15.3 g of pure acetal **3** (90%), δ_H(60 MHz) 1.15 (12 H, s), 1.70 (3 H, d, J 6.0), 4.80 (1 H, d, J 6.0), 5.35 (1 H, dd, J 16.0 and 6.0) and 5.77 (1 H, dq, J 16.0 and 6.0).

4-(Prop-1-enyl)-3,5-dioxabicyclo[5.4.0]undecane 4. Crotonaldehyde (7.0 g, 0.1 mol) and *cis*-cyclohexane-1,2-dimethanol (14.4 g, 0.1 mol) afforded compound **4** as a mixture of diastereomers (50 : 50) that was purified by distillation (bp 96 °C, 0.3 mm Hg; 12.5 g, 64%), δ_H(300 MHz) (bold figures used to distinguish between isomers) 1.35–1.85 (20 H, m), **1.72** (3 H, ddd, J 7.0, 1.5 and 1.0), **1.74** (3 H, ddd, J 7.0, 1.5 and 1.0), 3.52 (2 H, dd, J 6.0 and 1.5), 3.65 (2 H, dd, J 6.0 and 3.0), 3.72 (2 H, dd, J 6.0 and 1.5), 3.85 (2 H, dd, J 6.0 and 3.0), **5.07** (1 H, dpent, J 5.0 and 1.0), **5.10** (1 H, dpent, J 5.0 and 1.0), 5.55 (2 H, ddq, J 15.0, 5.0 and 1.5), **5.80** (1 H, dqd, J 15.0, 7.0 and 1.0), **5.85** (1 H, dqd, J 15.0, 7.0 and 1.0); δ_C(75.5 MHz) 17.3, 24.0, 26.5, 26.8, 39.3, 39.4, 67.0, 67.1, 100.1, 100.5, 128.4, 128.6 and 128.7;

m/*z* (EI, 7.0 eV) (rel. int.) 196 (M^+, 1%), 81 (59), 67 (100), 55 (60) and 41 (97).

4,6-Dimethyl-2-(prop-1-enyl)-1,3-dioxane 5 and 5′. Crotonaldehyde (7.0 g, 0.1 mol) and pentane-2,4-diol (10.4 g, 0.1 mol) afforded products **5** and **5′**. The mixture was distilled (bp 82 °C, 20 mmHg), and 10.1 g (65%) of a diastereomeric mixture (diastereomeric ratio = 60:40). Isomer **5**: δ_H(300 MHz) 1.24 (6 H, d, *J* 6.0), 1.52 (2 H, dt, *J* 13.0 and 2.5), 1.73 (3 H, dd, *J* 7.0 and 1.5), 3.80 (2 H, dqd, *J* 11.0, 6.0 and 2.5), 4.95 (1 H, br d, *J* 5.5), 5.58 (1 H, ddq, *J* 16.0, 5.5 and 1.5) and 5.92 (1 H, ddq, *J* 16.0, 7.0 and 1.5); δ_C(75.5 MHz) 21.4, 21.5, 21.7, 40.1, 72.2, 72.3, 100.4, 130.1 and 130.4; *m*/*z* (EI, 70 eV) (rel. int.) 156 (M^+, 2%), 71 (98), 69 (100), 45 (98) and 43 (100).

Isomer **5′**: δ_H(300 MHz) 1.22 (6 H, d, *J* 6.0), 1.74 (3 H, dd, *J* 7.0 and 1.5), 1.87 (2 H, ddd, *J* 13.0, 1.5 and 6.0), 4.03 (2 H, q br d, *J* 6.0 and 2.5), 5.24 (1 H, br d, *J* 5.5), 5.52 (1 H, ddq, *J* 16.0, 5.5 and 1.5) and 5.75 (1 H, ddq, *J* 16.0, 7.0 and 1.5). δ_C(75.5 MHz) 17.0, 17.4, 17.5, 36.5, 67.2, 67.9, 93.4, 128.3 and 128.7; *m*/*z* (EI, 70 eV) (rel. int.) 156 (M^+, 1%), 71 (98), 69 (100), 68 (98) and 45 (98).

Synthesis of alkoxydienes 6–10. Typical procedure

Under an inert atmosphere, Bu^{n}Li (1.6 mol dm^{-3}; 9.4 cm^3, 15.0 mmol) was added dropwise to a stirred, cooled (−95 °C) solution of sublimed Bu^{t}OK (1.68 g, 15.0 mmol) and acetal **3** (1.70 g, 10.0 mmol) in anhydrous THF (10 cm^3). After a few seconds the solution turned purple and was stirred at −95 °C for 2 h. After this time the reaction was quenched with a THF solution of water (10 cm^3), and the colour was discharged. The two phases were separated, and the aqueous one was extracted with Et_2O (3 × 20 cm^3). The combined organic phases were washed with brine (2 × 15 cm^3), dried (Na_2SO_4), and concentrated to give crude compound **8**, which was purified by chromatography.

(5*E*,7*Z*)-4-Oxanona-5,7-dien-1-ol 6.‡‡‡ (Isomers mixture 9:1). Purification: eluent light petroleum–Et_2O (80:20) (90% yield; ν_{max}(film)/cm^{-1} 3560–3300 and 1650; δ_H(300 MHz) 1.70 (3 H, dd, *J* 7.0 and 2.0), 1.85 (2 H, m), 2.30 (1 H, br s), 3.75 (2 H, m), 3.90 (2 H, m), 5.28 (1 H, dq, *J* 11.0 and 6.5), 5.80 (1 H, t, *J* 11.5), 5.87 (1 H, tq, *J* 11.0 and 1.5) and 6.54 (1 H, d, *J* 11.5); *m*/*z* (EI, 70 eV) (rel. int.) 142 (M^+, 25%), 84 (95), 83 (59), 56 (48) and 55 (100) (Found: C, 65.49; H, 9.98. Calc. for $C_8H_{14}O_2$: C, 65.57; H, 9.92%).

(5*E*,7*Z*)-2,2-Dimethyl-4-oxanona-5,7-dien-1-ol 7.‡‡‡ Purification: eluent light petroleum–Et_2O (80:20) (96% yield); ν_{max}(film)/cm^{-1} 3580–3225 and 1655; δ_H(300 MHz) 0.95 (6 H, s), 1.68 (3 H, dd, *J* 7.0 and 1.5), 2.20 (1 H, br s), 3.43 (2 H, s), 3.61 (2 H, s), 5.30 (1 H, dq, *J* 12.0 and 7.0), 5.76 (1 H, t, *J* 12.0), 5.86 (1 H, tq, *J* 12.0 and 1.5) and 6.57 (1 H, br d, *J* 12.0); δ_C(75.5 MHz) 13.0, 21.4, 21.9, 36.2, 69.4, 76.4, 102.1, 120.8, 125.0 and 150.0; *m*/*z* (EI, 70 eV) (rel. int.) 170 (M^+, 16%), 84 (100), 55 (96), 41 (96) and 39 (79) (Found: C, 70.63; H, 10.53. Calc. for $C_{10}H_{18}O_2$: C, 70.55; H, 10.66%).

(*E*)-2,3,3-Trimethyl-4-oxaocta-5,7-dien-2-ol 8. Purification: eluent light petroleum–Et_2O (70:30) (86% yield); ν_{max}(film)/cm^{-1} 3550–3325 and 1648; δ_H(300 MHz) 1.15 (6 H, s), 1.40 (6 H, s), 2.30 (1 H, br s), 4.80 (1 H, dd, *J* 11.0 and 1.5), 5.00 (1 H, dd, *J* 17.0 and 1.5), 5.74 (1 H, t, *J* 11.5), 6.24 (1 H, dt, *J* 17.0 and 11.0) and 6.62 (1 H, d, *J* 11.5); *m*/*z* (EI, 70 eV) (rel. int.) 170 (M^+, 10%), 101 (43), 83 (97), 59 (76) and 55 (100) (Found: C, 70.47; H, 10.52. Calc. for $C_{10}H_{18}O_2$: C, 70.55; H, 10.66%).

2-[(*E*)-Buta-1,3-dienyloxymethyl]cyclohexylmethanol 9. Purification: eluent light petroleum–Et_2O (80:20) (98% yield); ν_{max}(film)/cm^{-1} 3550–3325 and 1651; δ_H(60 MHz) 1.50 (8 H, m), 2.10 (2 H, m), 3.90 (1 H, br s), 4.00 (4 H, m), 4.75 (1 H, dd, *J* 11.0 and 1.5), 5.00 (1 H, dd, *J* 16.0 and 1.5), 5.60 (1 H, t, *J* 11.5), 6.15 (1 H, dt, *J* 16.0 and 11.5) and 6.50 (1 H, br d, *J* 12.0) (Found: C, 73.67; H, 10.54. Calc. for $C_{12}H_{20}O_2$: C, 73.43; H, 10.27%).

(*E*)-4-Methyl-5-oxanona-6,8-dien-2-ol (*syn*-10 and *anti*-10′). Purification: eluent light petroleum–Et_2O (70:30) as a mixture of two diastereoisomers in 60:40 ratio (88% yield). Compound *syn*-**10** δ_H(60 MHz) 1.18 (3 H, d, *J* 6.0), 1.25 (3 H, d, *J* 6.0), 1.70 (2 H, dd, *J* 6.5 and 6.0), 2.90 (1 H, br s) 3.90 (2 H, m), 4.75 (1 H, dd, *J* 11.5 and 1.5), 5.0 (1 H, dd, *J* 16.0 and 1.5), 5.60 (1 H, t, *J* 11.5), 6.15 (1 H, dt, *J* 16.0 and 11.5) and 6.50 (1 H, br d, *J* 12.0); isomer *anti*-**10′** δ_H(60 MHz) 1.18 (3 H, d, *J* 6.0), 1.25 (3 H, d, *J* 6.0), 1.60 (1 H, ddd, *J* 15.0, 6.0 and 5.0), 1.95 (1 H, ddd, *J* 15.0, 8.0 and 6.0), 2.90 (1 H, br s), 3.90 (2 H, m), 4.75 (1 H, dd, *J* 11.5 and 1.5), 5.00 (1 H, dd, *J* 16.0 and 1.5), 5.60 (1 H, t, *J* 11.5), 6.15 (1 H, dt, *J* 16.0 and 11.5) and 6.50 (1 H, br d, *J* 12.0) (Found: C, 69.35; H, 10.37. Calc. for $C_9H_{16}O_2$: C, 69.19; H, 10.32%).

Synthesis of trienes 11–15. Typical procedure

Compound **6** (0.71 g, 5.0 mmol) was dissolved in Et_2O (50 cm^3) and treated with H_2C=CHCOCl (0.90 g, 10.0 mmol) in the presence of pyridine (0.87 g, 11.0 mmol) at 25 °C. After 10 min the reaction mixture was treated with 5% aq. $NaHCO_3$ (15 cm^3). The two phases were separated and the aqueous phase was extracted with Et_2O (3 × 15 cm^3). The combined organic phases were then washed with brine (15 cm^3), dried (K_2CO_3), filtered and concentrated to give crude compound **11**.

(5*E*,7*Z*)-4-Oxanona-5,7-dienyl acrylate 11. Purification: eluent light petroleum–Et_2O (95:5) (60% yield); ν_{max}(film)/cm^{-1} 1724, 1652 and 1617; δ_H(400 MHz) 1.75 (3 H, br d, *J* 8.0), 2.10 (2 H, m), 3.91 (2 H, br t, *J* 6.0), 4.34 (2 H, br t, *J* 6.5), 5.30 (1 H, dq, *J* 10.5 and 8.0), 5.82 (1 H, t, *J* 10.5), 5.85 (1 H, dd, *J* 10.5 and 2.0), 5.90 (1 H, dd, *J* 12.6 and 10.5), 6.15 (1 H, dd, *J* 16.8 and 10.5), 6.45 (1 H, dd, *J* 16.8 and 2.0) and 6.55 (1 H, d, *J* 12.6); δ_C(75.5 MHz) 13.0, 28.2, 60.2, 65.1, 102.0, 120.0, 125.2, 128.0, 130.2, 150.3 and 165.1; *m*/*z* (EI, 70 eV) (rel. int.) 196 (M^+, 6%), 113 (100), 85 (73), 56 (42) and 55 (98) (Found: C, 67.25; H, 8.17. Calc. for $C_{11}H_{16}O_3$: C, 67.32; H, 8.22%).

(5*E*,7*Z*)-2,2-Dimethyl-4-oxanona-5,7-dienyl acrylate 12. Purification: eluent light petroleum–Et_2O (95:5) (53% yield); ν_{max}(film)/cm^{-1} 1727, 1653 and 1607; δ_H(300 MHz) 1.10 (6 H, s), 1.70 (3 H, dd, *J* 7.0 and 1.5), 3.50 (2 H, s), 4.00 (2 H, s), 5.35 (1 H, dq, *J* 10.0 and 7.0), 5.63 (1 H, dd, *J* 10.0 and 1.5), 5.72 (1 H, td, *J* 12.0 and 1.5), 5.84 (1 H, ddq, *J* 12.0, 10.0 and 1.5), 6.13 (1 H, dd, *J* 17.0 and 10.5), 6.41 (1 H, dd, *J* 17.0 and 1.5) and 6.54 (1 H, d, *J* 12.0); *m*/*z* (EI, 70 eV) (rel. int.) 224 (M^+, 4%), 141 (37), 84 (39), 69 (94) and 55 (100) (Found: C, 69.55; H, 8.87. Calc. for $C_{13}H_{20}O_3$: C, 69.61; H, 8.99%).

(*E*)-1,1,2,2-Tetramethyl-3-oxahepta-4,6-dienyl acrylate 13. Purification: eluent light petroleum–Et_2O (90:10) (50% yield); ν_{max}(film)/cm^{-1} 1724 and 1649; δ_H(300 MHz) 1.15 (6 H, s), 1.30 (6 H, s), 4.80 (1 H, ddd, *J* 11.0, 2.0 and 1.0), 5.00 (1 H, ddd, *J* 17.0, 2.0 and 1.0), 5.74 (1 H, t, *J* 11.5), 5.77 (1 H, dd, *J* 10.0 and 1.5), 6.05 (1 H, dd, *J* 17.5 and 10.0), 6.25 (1 H, dt, *J* 17.0 and 11.0), 6.30 (1 H, dd, *J* 17.5 and 1.5) and 6.67 (1 H, d, *J* 12.0); δ_C(75.5 MHz) 20.2, 21.2, 81.8, 82.0, 85.8, 100.7, 110.8, 111.3, 129.4, 129.9, 133.2, 145.2 and 164.7; *m*/*z* (EI, 70 eV) (rel. int.) 155 (224 − $CH_2CHCHCHO$, 2%), 111 (47), 83 (100), 69 (49) and 55 (98) (Found: C, 69.59; H, 8.93%).

2-[(*E*)-Buta-1,3-dienyloxymethyl]cyclohexylmethyl acrylate 14. Purification: eluent light petroleum–Et_2O (90:10) (48% yield); ν_{max}(film)/cm^{-1} 1724 and 1640; δ_H(400 MHz) 1.50 (8 H, br s), 2.10 (2 H, m), 3.69 (1 H, dd, *J* 9.2 and 6.0), 3.73 (1 H, dd, *J* 9.2 and 2.0), 4.15 (2 H, d, *J* 6.5), 4.80 (1 H, dd, *J* 9.2 and 1.5), 4.95 (1 H, dd, *J* 18.4 and 1.5), 5.60 (1 H, t, *J* 12.3), 5.80 (1 H, dd, *J* 12.0 and 1.5), 6.10 (1 H, dd, *J* 18.4 and 12.0), 6.22 (1 H, dt, *J* 18.4 and 10.0), 6.40 (1 H, dd, *J* 18.4 and 1.5) and 6.65 (1 H, d, *J* 12.3); δ_C(75.5 MHz) 23.1, 23.3, 26.2, 26.8, 37.0, 38.0, 64.2,

‡‡‡ It is advantageous to strip off the hexanes from Bu^{n}Li and to use a higher concentration of LICKOR base, in order to increase the strength of the reagent. In this case metallation takes place at a less acidic site, namely an allylic methylene group. For analogous elimination promoted by metallation at a CH_2 group see, for example, ref. 14.

70.0, 107.2, 113.0, 128.5, 132.00, 145.4, 152.1 and 165.0; *m/z* (EI, 70 eV) (rel. int.) 181 (250 − $CH_2CHCHCHO$, 3%), 109 (43), 67 (47), 55 (100) and 53 (12) (Found: C, 72.03; H, 8.77. Calc. for $C_{15}H_{22}O_3$: C, 71.97; H, 8.86%).

(*E*)-1,3-Dimethyl-4-oxaocta-5,7-dienyl acrylate 15. Purification: eluent light petroleum–Et_2O (90:10), as a mixture of two diastereoisomers in a 60:40 ratio (55% yield); for *syn*-**15** ν_{max}(film)/cm^{-1} 1735 and 1640; δ_H(300 MHz) 1.19 (3 H, d, *J* 6.0), 1.22 (3 H, d, *J* 6.0), 1.72 (2 H, dd, *J* 6.0 and 6.5), 3.90 (1 H, ept, *J* 6.0), 4.72 (1 H, dd, *J* 10.0 and 2.0), 4.88 (1 H, dd, *J* 17.0 and 2.0), 5.01 (1 H, m), 5.55 (1 H, dd, *J* 13.0 and 10.5), 5.76 (1 H, dd, *J* 11.0 and 1.5), 6.05 (1 H, dd, *J* 17.0 and 11.0), 6.15 (1 H, dt, *J* 17.0 and 10.0), 6.32 (1 H, dd, *J* 17.0 and 1.5) and 6.35 (1 H, dd, *J* 13.0 and 1.5); δ_C(75.5 MHz) 19.9, 20.1, 42.2, 68.2, 73.9, 108.9, 111.2, 128.7, 130.3, 133.5, 149.6 and 165.4; *m/z* (EI, 70 eV) (rel. int.) 141 (210 − $CH_2CHCHCHO$, 12%), 70 (13), 69 (50), 55 (100) and 53 (7).

For *anti*-**15** ν_{max}(film)/cm^{-1} 1735 and 1640; δ_H(300 MHz) 1.19 (3 H, d, *J* 6.0), 1.22 (3 H, d, *J* 6.0), 1.58 (1 H, ddd, *J* 15.0, 6.0 and 5.0), 2.00 (1 H, ddd, *J* 15.0, 8.0 and 6.0), 3.90 (1 H, hex, *J* 6.0), 4.72 (1 H, dd, *J* 10.0 and 2.0), 4.88 (1 H, dd, *J* 17.0 and 2.0), 5.01 (1 H, m), 5.55 (1 H, dd, *J* 13.0 and 10.5), 5.76 (1 H, dd, *J* 11.0 and 1.5), 6.05 (1 H, dd, *J* 17.0 and 11.0), 6.15 (1 H, dt, *J* 17.0 and 10.0), 6.32 (1 H, dd, *J* 16.0 and 2.0) and 6.35 (1 H, dd, *J* 13.0 and 1.5); δ_C(75.5 MHz) 20.1, 20.4, 43.0, 68.1, 73.9, 107.9, 111.2, 128.9, 130.2, 133.2, 149.2 and 165.4; *m/z* (EI, 70 eV) (rel. int.) 141 (210 − $CH_2CHCHCHO$, 12%), 70 (13), 69 (53), 55 (100) and 53 (6) (Found: C, 68.66; H, 8.57. Calc. for $C_{12}H_{18}O_3$: C, 68.55; H, 8.63%).

Representative procedure for intramolecular Diels–Alder cycloaddition (products 16–24)

A solution of triene (2.0 mmol) in toluene (5.0 cm^3) or benzonitrile (5.0 cm^3) was degassed with argon. The solution was refluxed in the presence of hydroquinone under inert atmosphere, and the reaction was followed by TLC (eluent light petroleum–Et_2O). After the time indicated in Table 1 the mixture was washed with 10% aq. NaOH, the organic solvent was removed *in vacuo* and, after column chromatography [Et_2O–light petroleum (10:90)], the cycloadduct was isolated.

10-Methyl-2,6-dioxa-1α,8α-bicyclo[6.4.0]dodec-11-en-7-one 16. Needles, mp 105–107 °C (from light petroleum–Et_2O); ν_{max}($CHCl_3$)/cm^{-1} 1730; δ_H(300 MHz) 1.05 (3 H, d, *J* 7.0), 1.40 (1 H, dt, *J* 13.0 and 11.0), 1.62 (1 H, m), 1.95 (1 H, dt, *J* 12.5 and 4.5), 2.08 (1 H, m), 2.29 (1 H, m), 2.75 (1 H, ddd, *J* 13.0, 5.0 and 3.0), 3.56 (1 H, dd, *J* 12.0 and 10.0), 3.88 (1 H, ddd, *J* 12.0, 11.0 and 6.0), 4.20 (1 H, ddm, *J* 18.0 and 4.0), 4.22 (1 H, br d, *J* 3.0), 4.80 (1 H, dd, *J* 11.0 and 7.5) and 5.75 (2 H, s); δ_C(75.5 MHz) 21.0, 27.5, 30.0, 30.1, 45.3, 63.9, 72.4, 79.2, 125.4, 137.9 and 176.2; *m/z* (EI, 70 eV) (rel. int.) 196 (M^+, 3%), 113 (100), 79 (21), 77 (20) and 55 (100) (Found: C, 67.28; H, 8.19. Calc. for $C_{11}H_{16}O_3$: C, 67.32; H, 8.22%).

4,4,10-Trimethyl-2,6-dioxa-1β,8α-bicyclo[6.4.0]dodec-11-en-7-one 17. Purification: eluent light petroleum–Et_2O (70:30); ν_{max}(film)/cm^{-1} 1731; δ_H(300 MHz) 0.92 (3 H, s), 0.94 (3 H, s), 1.10 (3 H, d, *J* 7.0), 1.60 (1 H, ddt, *J* 14.0, 2.5 and 1.5), 2.10 (1 H, ddd, *J* 14.0, 13.0 and 6.0), 2.40 (1 H, m), 2.92 (1 H, ddd, *J* 13.0, 9.0 and 2.5), 3.06 (1 H, d, *J* 12.5), 3.58 (1 H, dd, *J* 12.5 and 1.0), 3.71 (1 H, dd, *J* 12.0 and 1.0), 3.95 (1 H, dq, *J* 9.0 and 1.5), 4.5 (1 H, d, *J* 12.0), 5.55 (1 H, dt, *J* 10.0 and 2.0) and 5.75 (1 H, dddd, *J* 10.0, 4.0, 2.0 and 1.5); δ_C(75.5 MHz) 20.1, 20.8, 21.8, 28.2, 30.6, 37.9, 39.0, 72.7, 75.9, 81.2, 127.6, 134.5 and 176.8; *m/z* (EI, 70 eV) (rel. int.) 224 (M^+, 2%), 141 (48), 79 (47), 69 (48) and 55 (100) (Found: C, 69.57; H, 8.89. Calc. for $C_{13}H_{20}O_3$: C, 69.61; H, 8.99%).

3,3,4,4-Tetramethyl-2,5-dioxa-1α,7α-bicyclo[5.4.0]undec-10-en-6-one 18. Needles, mp 118–121 °C (from eluent light petroleum–Et_2O); ν_{max}($CHCl_3$)/cm^{-1} 1735; δ_H(300 MHz) 1.24 (3 H, s), 1.34 (3 H, s), 1.47 (3 H, s), 1.48 (3 H, s), 2.06–2.08 (2 H, m), 2.22–2.30 (2 H, m), 2.79 (1 H, dt, *J* 12.0 and 4.5), 4.45 (1 H, br t, *J* 4.0), 5.77 (1 H, dddd, *J* 10.0, 4.5, 2.5 and 1.2) and 5.95 (1 H, ddm, *J* 10.0 and 5.0); δ_C(75.5 MHz) 20.6, 21.4, 23.6, 26.0, 26.3, 26.9, 48.5, 62.6, 79.8, 89.0, 126.4, 131.4 and 178.4; *m/z* (EI, 70 eV) (rel. int.) 138 (24 − $CO_2CCH_3CH_3$, 2%), 80 (100), 79 (44), 77 (13) and 55 (19) (Found: C, 69.65; H, 8.91%).

3,3,4,4-Tetramethyl-2,5-dioxa-1β,7α-bicyclo[5.4.0]undec-10-en-6-one 19. Purification: eluent light petroleum–Et_2O (90:10); ν_{max}(film)/cm^{-1} 1735; δ_H(300 MHz) 1.24 (6 H, s), 1.40 (3 H, s), 1.41 (3 H, s), 1.73–1.76 (2 H, m), 2.15–2.20 (2 H, m), 2.79 (1 H, ddd, *J* 13.0, 10.0 and 3.0), 4.32 (1 H, ddd, *J* 10.0, 4.5 and 2.0), 5.50 (1 H, ddt, *J* 10.0, 4.5 and 2.0) and 5.89 (1 H, dm, *J* 10.0); δ_C(75.5 MHz) 19.3, 22.2, 23.7, 24.1, 27.3, 27.8, 46.8, 67.5, 79.0, 87.5, 128.7, 129.9 and 174.9; *m/z* (EI, 70 eV) (rel. int.): 138 (224 − $CO_2CCH_3CH_3$, 2%), 80 (100), 79 (48), 77 (12) and 59 (12).

2,11-Dioxa-1α,4α,9α,13α-tricyclo[11.4.0.0^{4,9}]heptadec-16-en-12-one 20b and 2,11-dioxa-1β,4α,9α,13β-tricyclo[11.4.0.0^{4,9}]-heptadec-16-en-12-one 20a (see footnote***). Purification: eluent light petroleum–Et_2O (95:5); δ_H($CD_3C_6D_5$; 80 °C; 300 MHz) 1.00–2.00 (14 H, m), 2.52 (1 H, m), 3.28 (1 H, dd, *J* 11.0 and 1.5), 3.75 (1 H, br dd, *J* 11.0 and 5.0), 3.84 (1 H, m), 3.98 (1 H, dd, *J* 11.0 and 5.0), 5.05 (1 H, br t, *J* 11.0) and 5.70 (2 H, m); δ_C($CD_3C_6D_5$; 80 °C; 75.5 MHz) 21.6, 24.5, 25.5, 26.6, 28.1, 29.1, 35.0, 41.1, 46.1, 68.0, 77.4, 79.3, 128.4, 131.0 and 174.7; *m/z* (EI, 70 eV) (rel. int.) 181 (M^+ − $CHCHOCH_2CH$, 11%), 109 (100), 95 (50), 80 (51) and 55 (81).

For isomer **20** δ_H($CD_3C_6D_5$; 80 °C; 300 MHz) 1.00–2.00 (14 H, m), 3.35 (1 H, dd, *J* 11.0 and 10.0), 3.79 (1 H, dd, *J* 11.0 and 5.0), 3.89 (1 H, m), 3.90 (1 H, br t, *J* 11.0), 4.65 (1 H, dd, *J* 11.0 and 4.0) and 5.70 (2 H, m); δ_C($CD_3C_6D_5$; 80 °C; 75.5 MHz) 21.8, 23.0, 25.4, 25.8, 27.3, 30.5, 40.7, 44.7, 46.9, 66.3, 76.8, 79.1, 128.0, 131.4 and 174.2; *m/z* (EI, 70 eV) (rel. int.) 250 (M^+, 2%), 109 (100), 79 (33), 55 (100) and 41 (34).

For isomer **20** δ_H(CD_3CN; 300 MHz) 1.50 (2 H, m), 1.80 (1 H, m), 2.10 (2 H, m), 2.30 (1 H, m), 2.79 (1 H, ddd, *J* 10.0, 6.0 and 3.5), 3.50 (1 H, dd, *J* 12.0 and 10.0), 3.95 (1 H, dd, *J* 10.0 and 5.0), 4.02 (1 H, m), 4.17 (1 H, t, *J* 10.5), 4.55 (1 H, dd, *J* 10.5 and 3.5), 5.80 (1 H, m) and 5.95 (1 H, m).

2,11-Dioxa-1β,4α,9α,13α-tricyclo[11.4.0.0^{4,9}]heptadec-16-en-12-one 21a and 21b (see footnote***). Purification: eluent light petroleum–Et_2O (95:5); ν_{max}(film)/cm^{-1} 1740; δ_H(CD_3CN; 300 MHz) 1.25–1.70 (8 H, m), 1.80 (2 H, m), 1.90 (1 H, m), 2.10 (2 H, m), 2.20 (1 H, m), 2.42 (1 H, ddd, *J* 13.0, 10.0 and 2.5), 3.25 (1 H, t, *J* 11.0), 3.94 (1 H, dd, *J* 11.0 and 5.0), 4.05 (1 H, m), 4.30 (1 H, m), 4.40 (1 H, m), 5.55 (1 H, m) and 5.65 (1 H, m); δ_C($CD_3C_6D_5$; 75.5 MHz) 24.7, 25.1, 26.5, 27.5, 30.6, 37.6, 40.7, 50.6, 63.7, 68.4, 77.8, 78.5, 127.9, 132.7 and 177.1; *m/z* (EI, 70 eV) (rel. int.) 181 (M^+ − $CHCHOCH_2CH$,11%), 109 (100), 80 (51), 79 (50) and 55 (84) (Found: C, 71.86; H, 8.93. Calc. for $C_{15}H_{22}O_3$: C, 71.97; H, 8.86%).

3α,5α-Dimethyl-2,6-dioxa-1β,8α-bicyclo[6.4.0]dodec-11-en-7-one 22. Purification: eluent light petroleum–Et_2O (95:5); ν_{max}(film)/cm^{-1} 1735; δ_H(300 MHz) 1.15 (3 H, d, *J* 7.0), 1.30 (3 H, d, *J* 7.0), 1.60–1.90 (2 H, m), 1.75–1.90 (2 H, m), 2.10 (2 H, m), 2.60 (1 H, ddd, *J* 12.0, 9.0 and 3.0), 3.55 (1 H, dq, *J* 10.0 and 6.5), 3.55 (1 H, dq, *J* 10.0 and 6.5), 4.09 (1 H, dm, *J* 9.5), 5.28 (1 H, ddq, *J* 12.0, 6.5 and 3.0) and 5.60 (2 H, br s); δ_C(75.5 MHz) 20.7, 21.5, 24.0, 24.1, 47.7, 48.8, 75.5, 79.7, 86.4, 127.9, 131.0 and 180.4; *m/z* (EI, 70 eV) (rel. int.) 141 (M^+ − $CH_2CHCHCHO$, 40%), 79 (80), 69 (100), 55 (100) and 41 (61) (Found: C, 68.61; H, 8.60. Calc. for $C_{12}H_{18}O_3$: C, 68.55; H, 8.63%).

3β,5α-Dimethyl-2,6-dioxa-1α,8α-bicyclo[6.4.0]dodec-11-en-7-one 23. Purification: eluent light petroleum–Et_2O (95:5); ν_{max}(film)/cm^{-1} 1748; δ_H(300 MHz) 1.25 (3 H, d, *J* 7.0), 1.31 (3 H, d, *J* 7.0), 1.60–1.75 (4 H, m), 2.05–2.30 (2 H, m), 2.74 (1 H, ddd, *J* 13.0, 5.5 and 3.0), 3.85 (1 H, dq, *J* 9.0 and 6.5), 4.30 (1 H, m), 5.11 (1 H, pent, *J* 6.5), 5.75 (1 H, m) and 5.95 (1 H, m); δ_C(75.5 MHz) 20.7, 21.5, 24.0, 24.1, 47.8, 48.7, 75.5, 79.7, 86.4, 127.9, 131.0 and 180.4; *m/z* (EI, 70 eV) (rel. int.) 210 (M^+,

40%), 141 (95), 68 (100), 55 (100) and 41 (98) (Found: C, 68.43; H, 8.70%).

3β,5α-Dimethyl-2,6-dioxa-1β,8α-bicyclo[6.4.0]dodec-11-en-7-one 24. Purification: eluent light petroleum–Et_2O (95:5); ν_{max}(film)/cm^{-1} 1747; δ_H(300 MHz) 1.15 (3 H, d, *J* 6.5), 1.30 (1 H, m), 1.45 (3 H, d, *J* 6.5), 1.70–2.20 (4 H, m), 2.22 (1 H, ddd, *J* 13.0, 4.5 and 4.0), 2.70 (1 H, ddd, *J* 12.0, 9.0 and 2.5), 4.05 (1 H, dm, *J* 9.0), 4.42 (1 H, qd, *J* 6.5 and 3.0), 5.00 (1 H, m), 5.50 (1 H, dq, *J* 10.0 and 2.0) and 5.75 (1 H, dm, *J* 10.0); and δ_C (75.5 MHz) 18.2, 19.1, 20.2, 21.7, 29.6, 37.8, 48.0, 66.4, 72.7, 128.7, 131.7 and 176.6 (Found: C, 68.65; H, 8.55%).

Acknowledgements

This work was supported by grants from Italian CNR and MURST. A. D. warmly thanks Dr L. Duhamel, director of the 'Laboratoire des Fonctions Azotées & Oxygénées Complexes de l'IRCOF' (UPRES-A 6014 CNRS) for kind hospitality and access to the high-field NMR spectrometer.

References

1 O. Diels and K. Alder, *Justus Liebigs Ann. Chem.*, 1928, **460**, 98.
2 Reviews: W. Oppolzer, *Angew. Chem.*, *Int. Ed. Engl.*, 1977, **16**, 10; G. Brieger and J. N. Bennett, *Chem. Rev.*, 1980, **80**, 63; D. F. Taber, *Intramolecular Diels–Alder and Alder Ene Reactions*, Springer, Berlin, 1984; A. G. Fallis, *Can. J. Chem.*, 1984, **62**, 183; D. Craig, *Chem. Soc. Rev.*, 1987, **16**, 187; W. R. Roush, *Comprehensive Organic Synthesis*, ed. B. Trost and J. Fleming, Pergamon Press, Oxford, 1991, vol. 5, p. 513.
3 P. Venturello, *J. Chem. Soc.*, *Chem. Commun.*, 1992, 1032; C. Prandi and P. Venturello, *J. Org. Chem.*, 1994, **59**, 5458; A. Deagostino, C. Prandi and P. Venturello, *Tetrahedron*, 1996, **52**, 1433, and references therein.
4 M. Schlosser, *Organomet. Chem.*, 1967, **8**, 9. For reviews see: M. Schlosser, *Mod. Synth. Methods*, 1992, **6**, 227; A. Mordini, *Advances in Carbanion Chemistry*, ed. V. Snieckus, JAI Press, Greenwich, CT, 1992, vol. 1, p. 1; M. Schlosser, F. Faigl, L. Franzini, H. Geneste, G. Katsoulos and G.-f. Zhong, *Pure Appl. Chem.*, 1994, **66**, 1439.
5 A. Deagostino, J. Maddaluno, C. Prandi and P. Venturello, *J. Org. Chem.*, 1996, **61**, 7597. For other access to comparable lactones see: I. Collins, *Contemp. Org. Synth.*, 1997, **4**, 281; M. P. Doyle and C. S. Peterson, *Tetrahedron Lett.*, 1997, **38**, 5265.
6 P. J. Ainsworth, D. Craigh, A. J. P. White and D. J. Williamson, *Tetrahedron*, 1966, **52**, 8937; W. R. Roush, J. A. Champoux and B. C. Peterson, *Tetrahedron Lett.*, 1996, **37**, 8989.
7 A. Guillam, J. Maddaluno and L. Duhamel., *Chem. Commun.*, 1996, 1295.
8 C. Miuskowski, S. Manna and J. R. Falck, *Tetrahedron Lett.*, 1984, **25**, 519.
9 S. R. Wilson and D. T. Mao, *J. Org. Chem.*, 1979, **44**, 3093; J. J. S. Bajorek and J. K. Sutherland, *J. Chem. Soc.*, *Perkin Trans. 1*, 1975, 1559; G. A. Kraus and M. J. Tauschner, *J. Am. Chem. Soc.*, 1980, **102**, 1974.
10 F. C. Lightstone and T. C. Bruice, *J. Am. Chem. Soc.*, 1994, **116**, 10 789.
11 C. Giessner-Prettre, S. Hückel, J. Maddaluno and M. E. Jung, *J. Org. Chem.*, 1997, **62**, 1439.
12 M. J. Lilly and M. S. Sherburn, *Chem. Commun.*, 1997, 967 and references cited therein.
13 W. Schlenk and E. Bergmann, *Justus Liebigs Ann. Chem.*, 1928, **464**, 22.
14 A. Mordini, E. Ben Rayana, C. Margot and M. Schlosser, *Tetrahedron*, 1990, **46**, 2401.

Paper 7/07913C
Received 3rd *November* 1997
Accepted 18*th November* 1997