Intramolecular Diels–Alder Reactions, 3[+]

Variable Stereocontrol in Cycloadditions of 1,7,9-Decatrien-3-ones by Different Lewis Acidic Promoters – Application to a Short Synthesis of α-Eudesmol

Barbara Frey,[a][1] Jürgen Schnaubelt,[a][2] and Hans-Ulrich Reißig*[a]

Keywords: Intramolecular Diels–Alder reaction / 1,7,9-Decatrien-3-ones / α-Eudesmol / Lewis acids / Chelates

Trienones **1**–**3** were subjected to Lewis acid-promoted intramolecular Diels–Alder reactions. It was shown that with monocoordinating Lewis acids the *endo* selectivity of the cycloaddition was generally high. The preference for either of the two possible *endo* products *cis*-**a** and *cis*-**b**, however, was shown to be highly dependent on the nature of the Lewis acid, and on the substitution pattern of the trienone substrates. Lewis acids with two coordination sites furnished predominantly the *exo* product *trans*-**b** via seven-membered ring chelate intermediates. The chelate-controlled intramolecular Diels–Alder reaction was then utilised as the key step in a stereocontrolled synthesis of the sesquiterpene α-eudesmol. This reaction mode, performed on a model trienone, also paved the way for the synthesis of the pharmaceutically important natural product dihydromevinolin.

Introduction

Natural products with bicyclo[4.4.0]decene entities are very common, and there have been numerous syntheses towards these compounds. A very elegant way to build the fused ring system and to install up to four new stereogenic centres in one step is provided by the intramolecular Diels−Alder reaction.[3] Within our studies on the synthesis of natural products with the bicyclo[4.4.0]decene skeleton, we recently described[4][5] the uncatalysed intramolecular Diels−Alder reactions of 1,7,9-decatrien-3-ones **1**−**3** to the octalones **4**−**6**. These compounds are of particular interest as octalone **5** is a direct precursor of the sesquiterpene α-eudesmol,[6] while octalone **6** serves as a model compound for the intramolecular cycloaddition in the synthesis towards the natural product dihydromevinolin.[5][6] The des-methyl analogue **1** was included in the studies to examine the influence of the 8-methyl group on the stereoselectivity of the cycloaddition. Both natural products require *trans*-fusion of the rings in the octalone precursors with the ester groups standing *cis* (isomer *trans*-**b**, for dihydromevinolin) or *trans* (isomer *trans*-**a**, for α-eudesmol), respectively, in relation to 8a-H. As reported earlier, the uncatalysed intramolecular cycloaddition reaction afforded the desired isomers *trans*-**5a** and *trans*-**6b** in unsatisfactory yields.[5] However, Lewis acid catalysis was expected to change the stereochemical outcome of the cycloaddition reaction considerably, as had been demonstrated on a number of earlier examples on intramolecular Diels−Alder reactions.[3] As the trienone esters **1**−**3** possess two ligating sites for Lewis acids, the use of chelating Lewis acids seemed particularly interesting. In the intramolecular Diels−Alder reaction[3][7] Lewis acids are not only used to accelerate the reaction but also to enhance the formation of *endo*-products (noninduced diastereoselectivity[8]). These promoters usually coordinate with dienophile-activating substituents. In singular cases, Lewis acids that are coordinated to the dienophile are known to interact with other substituents on the triene chain.[7d−7f] The nature of these interactions can be steric or coordinating, and can strongly affect the rate and stereochemical outcome of the reaction. Systematic investigations on the interactions of Lewis acids (attractive or repulsive) with substituents on the tether that links diene and dienophile (induced diastereoselectivity[8]) are rare.[9] In this paper we describe the application of various Lewis acids on the intramolecular Diels−Alder reaction of methoxycarbonyl-substituted 1,7,9-decatrien-3-ones **1**−**3** and their influence on the diastereoselectivity (induced and noninduced) of the reaction. Since all syntheses were performed with racemates, all chiral compounds are provided as mixtures of both enantiomers; for clarity, only one enantiomer is depicted in the schemes.

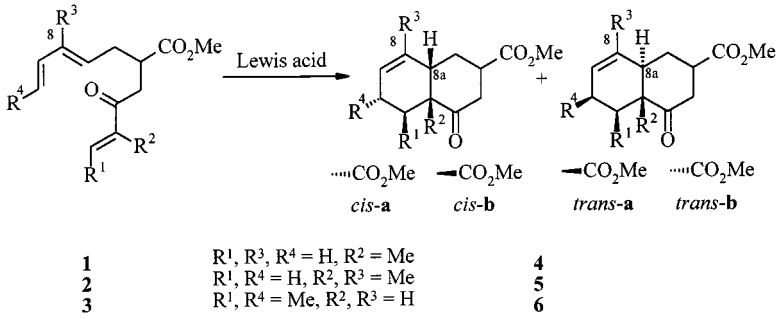
Results and Discussion

The Lewis acid promoters of the intramolecular Diels−Alder reactions of the trienones **1**−**3** were divided into monocoordinating (Table 1) and chelating (Table 2) Lewis acids. The monocoordinating Lewis acids, usually with one coordination site, influence the reaction only by binding to the enone carbonyl group of the trienone, whereas chelating

[+] Part 2: Ref.[5]

[a] Institut für Organische Chemie der Technischen Universität Dresden,
D-01062 Dresden, Germany
Fax: (internat.) +49 (0)351/ 463 7030
E-mail: Hans.Reissig@chemie.tu-dresden.de

  1434−193X/99/0606−1385 $ 17.50+.50/0



1 R^1, R^3, R^4 = H, R^2 = Me — **4**
2 R^1, R^4 = H, R^2, R^3 = Me — **5**
3 R^1, R^4 = Me, R^2, R^3 = H — **6**

Lewis acids possess two free sites and therefore can bind to both the enone carbonyl and methoxycarbonyl groups of the substrate to form chelate complexes.

Monocoordinating Lewis Acids

The intramolecular Diels−Alder reactions of the trienones **1**−**3** promoted by monocoordinating Lewis acids are grouped in Table 1. Some of the catalysts, like $ZnBr_2$ (entry 5), $ZnCl_2$ (footnote [f]) and TiI_4 (footnote [g]) principally possess two free coordination sites, but in this study, they behave like catalysts with one coordination site.

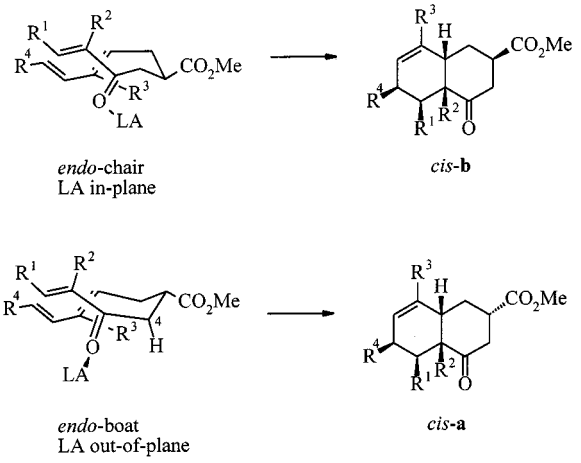
As expected, all monocoordinating Lewis acids promote the formation of the *endo*-products *cis*-**a** and *cis*-**b**, however, the **a**/**b** ratio differs with the nature of the substrate and the Lewis acid. This was demonstrated in the extensive investigations on trienones **1** and **2**, which provide nearly identical diastereomeric ratios in the uncatalysed intramolecular Diels−Alder reactions[4][5], but differ remarkably in the Lewis acid promoted reactions (Table 1). This finding suggests a significant steric effect of the 8-methyl group on the transition state of the cycloaddition. Trienone **1** forms predominantly *cis*-**4b** with all monocoordinating Lewis acids that were tested (entries 1−3). With trienone **2**, however, the **a**/**b** ratio depends on the nature of the Lewis acid. Here, Lewis acids with alkyl residues, such as $EtAlCl_2$ and TBDMS−OTf, promote the formation of *cis*-**5a** (entries 6 and 7), whereas Lewis acids with halide ligands only, like BF_3 or $ZnBr_2$, provide *cis*-**5b** as the major product (entries 4 and 5). Two possible *endo*-transition states leading to the *cis*-isomers are depicted in Scheme 1. The transition state with chairlike folding of the tether that links diene and dienophile leads to *cis*-**b**. It is preferred by trienone **1** with all Lewis acids, and by **2** only with the pure halide Lewis acids. The *cis*-**a** forming *endo*-boat transition state is favoured by **2** only with the alkylated Lewis acids. This *endo*-boat transition state is also the one that is energetically favoured in the uncatalysed cycloaddition of both trienones, **1** and **2**.[4][5] Based on the results so far obtained with **1** and **2**, it seems likely that mainly steric effects of the Lewis acid govern the course of the reaction. Looking at the geometry of the enone−Lewis acid complexes, it has (based on thermodynamic arguments) generally been assumed that the reactive geometries involve coordination of the Lewis acid in the plane of the carbonyl.[10] However, recent work by Corcoran et al. suggests that, in some cases, out-of-plane coordinated enone−Lewis acid complexes cannot be ruled out in Lewis acid mediated Diels−Alder reactions.[11] Whether these different coordination geometries are responsible for our findings is speculative (Scheme 1). The conclusions we draw from the diastereomeric ratios of the octalone products are very tentative, and the rather small energetic differences between the individual transition states

Table 1. Intramolecular Diels−Alder reactions promoted by monocoordinating Lewis acids

Entry	Trienone	Octalone	Lewis Acid	Conditions[a]	Yield[b] [%]	Diastereomeric Ratio[c] *cis*-**a**/*cis*-**b**/*trans*-**a**/*trans*-**b**
1	**1**	**4**	2.5 equiv. $BF_3{\cdot}OEt_2$	−78 to +20°C, 12 h	83[d]	20 : 74 : 6 : −
2	**1**	**4**	1 equiv. $EtAlCl_2$	−78°C, 19 h	89	24 : 47 : 15 : 14[e]
3	**1**	**4**	2 equiv. TBDMS−OTf	−78 to +10°C, 15 h	43	27 : 59 : 14 : −
4	**2**	**5**	2 equiv. $BF_3{\cdot}OEt_2$	−78 to −10°C, 12 h	53	34 : 55 : 8 : 3[f]
5	**2**	**5**	1.3 equiv. $ZnBr_2$	−78 to +20°C, 24 h	89[d]	4 : 79 : 3 : 14[g]
6	**2**	**5**	1 equiv. $EtAlCl_2$	−78°C, 18 h	79	67 : 20 : 8 : 5[h]
7	**2**	**5**	2 equiv. TBDMS−OTf	−78 to +10°C, 18 h	79	78 : 20 : 2 : −[i]
8	**7**[j]	**5**	1.2 equiv. $TiCl_4$	−78 to +10°C, 21 h	64	63 : 24 : 6 : 7
9	**3**	**6**	1.4 equiv. $BF_3{\cdot}OEt_2$	−10°C;[k] then r. t., 19 h	90[d]	73 : 18 : 9 : −

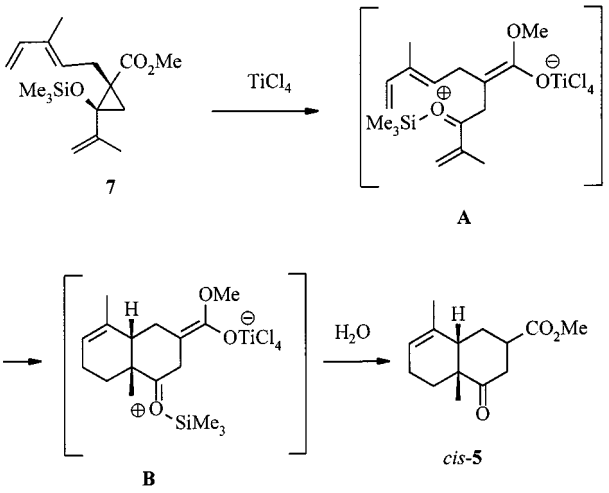
[a] All reactions were conducted in CH_2Cl_2 and stopped by addition of water, or satd. aqueous $NaHCO_3$ solution, or by fast successive addition of NEt_3 and water; control reactions[1] showed that in case of the monocoordinating Lewis acids the different workup procedures did not affect the diastereomeric ratios. − [b] Yield of the purified product unless stated otherwise. − [c] Diastereomeric ratio of the crude products; determined by ^{1}H-NMR analysis. − [d] Yield of the crude product. − [e] A similar diastereomeric ratio[1] was obtained with $(Me_3O)BF_4$. − [f] Similar diastereomeric ratios[1] were obtained with $AlCl_3$ and $ZnCl_2$. − [g] A similar diastereomeric ratio[1] was obtained with TiI_4. − [h] Similar diastereomeric ratios[1] were obtained with TMS−OTf, $Sn(OTf)_2$ and $CpTiBrCl_2$. − [i] A similar diastereomeric ratio[1] was obtained with Et_2AlCl. − [j] See Scheme 2. − [k] Temperature at which trienone and Lewis acid were combined.

should always be taken into account. However, it can be assumed that in out-of-plane complexes, steric interactions of the Lewis acid with R^3 and the substituents on the folded chain should not play an important role. With in-plane complexes, steric interactions of the catalyst with R^3, and, in a boatlike folded chain, with 4-H are to be expected. This might explain why the 8-methyl substituted (R^3 = Me) trienone **2** prefers the regularly energetically more favoured *endo*-boat transition state with bulky Lewis acids and the *endo*-chair transition state with the less bulky catalysts. It might also account for the high *endo*-chair preference of des-8-methyl trienone **1** (R^3 = H) with *all* Lewis acids.

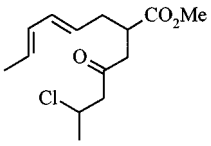


Scheme 1

A different mechanism to those described above is found in entry 8 where siloxycyclopropane **7**[4] was directly treated with (normally chelate-forming) $TiCl_4$. In this reaction, however, the titanium salt merely promotes the ring opening of the cyclopropane to intermediate **A** (Scheme 2).[12] The cyclisation step is then presumably promoted by "Me_3Si^+" to form the Diels–Alder product **B**. After hydrolysis, octalone **5**, enriched in *cis*-isomers, was obtained. In this context, this reaction fits in with the other Lewis acid-promoted cycloadditions in Table 1, albeit the **a/b** ratio is decided here *after* the cycloaddition by protonation of C-2 of intermediate **B**.

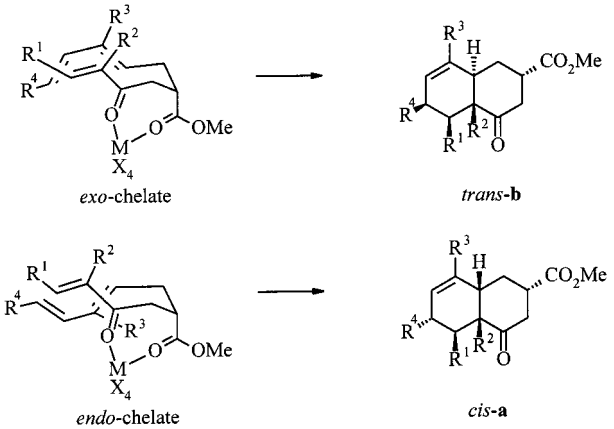


Scheme 2



Chelate Controlled Reactions

NMR investigations of complexes of simple γ-oxoesters with $TiCl_4$ show that the Lewis acid binds to the carbonyl **and** the methoxycarbonyl group in a seven-membered ring chelate complex.[13] With trienones **1**–**3** the formation of such chelate complexes would only allow the two chairlike transition conformations with the methoxycarbonyl group in axial position as depicted in Scheme 3. As shown in Table 2, strong Lewis acids with two free coordination sites like $TiCl_4$, $TiBr_4$, and $SnCl_4$ could be employed successfully in the cycloaddition of trienones **1** and **2**. Trienone **3**, however, produced mainly polymers and a small amount of the HCl adduct **8** upon treatment with $TiCl_4$ (entry 6), but could be reacted successfully with $SnCl_4$ (entries 7 and 8). It was found that, with the chelate forming Lewis acids, the primary product of the cycloaddition reactions is *trans*-**b**. This isomer is formed via the *exo*-chelate transition state (Scheme 3) and appeared as the main product in all reactions with solely aqueous workup (entries 3 and 7, Table 2). It is believed that steric interactions of the Lewis acid ligands X with the diene render the *endo*-chelate transition state less favourable. It is unclear, however, in how far the *cis*-**a** isomers result from the *endo*-chelate transition state (Scheme 3), or from the monocoordinated trienone *via* the *endo*-boat transition state (Scheme 1).



Scheme 3

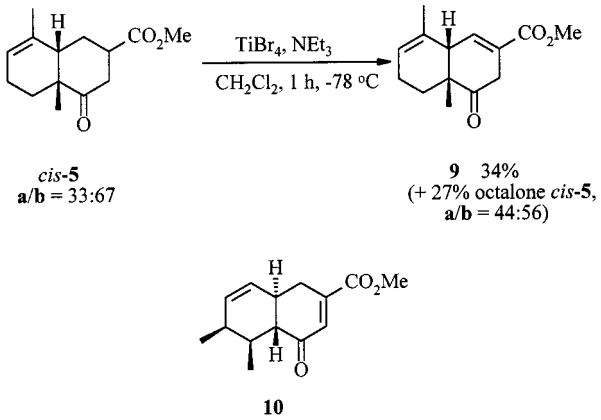
Work-up of the reactions with NEt_3/H_2O (which was done to avoid the presence of protons, which can also catalyse the cycloaddition reaction[4]), however, resulted in partial epimerisation to *trans*-**a** (Table 2, entries 1, 2, and 4). In two cases (entries 4 and 8, Table 2) these conditions also

Table 2. Chelate-controlled intramolecular Diels–Alder reactions

Entry	Pre-cursor	Prod.	Lewis Acid	Conditions[a]	Work-up Procedure	Yield[b] [%]	Diastereomeric ratio[c] *cis*-**a**/*cis*-**b**/*trans*-**a**/*trans*-**b**
1	**1**	**4**	1.2 equiv. $TiCl_4$	−78°C, 18 h[d]	NEt_3, H_2O[e]	47	14 : 31 : 12 : 43
2	**2**	**5**	1.2 equiv. $TiCl_4$	−78°C, 8 h[d]	NEt_3, H_2O[e]	58	15 : 11 : 23 : 51
3	**2**	**5**	1.5 equiv. $TiBr_4$	−78°C, 10 min	H_2O[f]	100[g]	11 : 15 : 9 : 65
4	**2**	**5**	2 equiv. $TiBr_4$	−78°C, 1 h	NEt_3, H_2O[e]	51[h]	7 : 8 : 52 : 33
5	**2**	**5**	2 equiv. $SnCl_4$	−78°C, 19 h[d]	NEt_3, H_2O[e]	60	1 : 32 : 1 : 66
6	**3**	**8**	1.2 equiv. $TiCl_4$	−78°C, 18 h	H_2O[f]	13[i]	– : – : – : –
7	**3**	**6**	1.5 equiv. $SnCl_4$	−78°C, 12 h; then −40°C, 7 h	H_2O[f]	73	45 : – : – : 55
8	**3**	**6**	2 equiv. $SnCl_4$	−78°C, 12 h; then −40°C, 7 h	NEt_3, 17 h; then H_2O[j]	46[k]	71 : – : – : 29

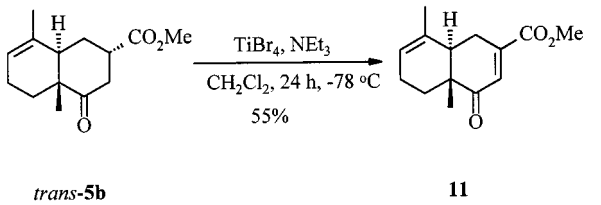
[a] All reactions were conducted in CH_2Cl_2; the trienone was added to a solution of the Lewis acid unless stated otherwise. – [b] Isolated yield unless stated otherwise. – [c] Diastereomeric ratio of the crude products; determined by ^{1}H-NMR analysis. – [d] The Lewis acid was added to a solution of the trienone. – [e] Reaction was stopped by fast successive addition of NEt_3 and water. – [f] Reaction was stopped by addition of water. – [g] Yield of the crude product, 85% conversion. – [h] Plus hexalone **9** (8%). – [i] Impurified. – [j] After addition of NEt_3, the reaction mixture was stirred for 17 h at −78°C before water was added. – [k] Plus hexalone **10** (24%).

produced the hexalones **9** and **10** in a subsequent oxidation reaction. This unexpected reaction also caused a change in the diastereomeric ratios. The MX_4-induced epimerisation and hexalone formation will be discussed below. It is interesting to note that the excess of Lewis acid did not affect the diastereomeric ratio (application of 1 equivalent MX_4 provided essentially the same results[1]), which would be expected from the formation of trienone · 2 MX_4 complexes. Less than stoichiometric amounts of MX_4, however, changed or even reversed the diastereomeric ratio towards the *cis* fused products, thus suggesting formation of (trienone)$_2$ · MX_4 complexes (data not shown).[1]

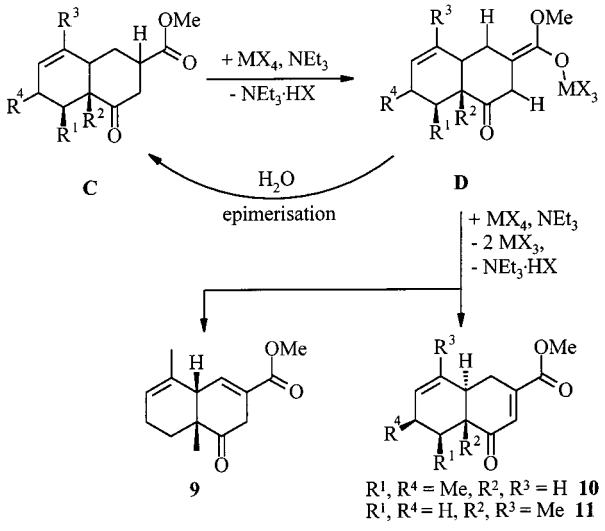


Epimerisation and Oxidation of the Octalones 5 and 6 Mediated by MX_4/NEt_3

As mentioned above, in some of the NEt_3 quenched reactions the octalone products were accompanied by the oxidation products **9** or **10**, respectively (Table 2, entries 4 and 8). It was found that hexalone **9** could also be synthesised directly from *cis*-**5** (**a**/**b** mixture) with $TiBr_4$/NEt_3. When the same reaction conditions were applied to the *trans*-**5b** isomer, the hexalone **11** with the new double bond in $\Delta^{2,3}$-position was formed. This compound could never be detected before in the cycloaddition reactions with NEt_3 workup, thus must form much slower than **9**. Apparently, remarkable stereoelectronic effects are responsible for the different behaviour of the stereoisomers of **5**.



The formation of the hexalones **9**–**11**, as well as the epimerisation to *trans*-**5a** during workup with NEt_3, can be rationalised by the reaction mechanism outlined below. Addition of NEt_3 to the reaction mixture of the MX_4-promoted reactions (or reaction of MX_4/NEt_3 with the pure octalones **C**) presumably leads to the formation of an ester enolate **D**, which, after hydrolysis, provides **C** as a mixture of *trans*-**a** and *trans*-**b** (or *cis*-**a**/**b** if **D** is *cis*-fused). Enolate **D** can also be oxidised by a second equivalent MX_4[14] to afford, after hydrolysis, a product with a second double bond in $\Delta^{1,2}$-position (as in **9**), or in conjugation with the

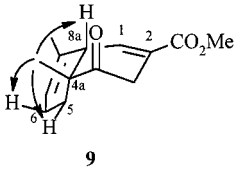


carbonyl group (as in **10** or **11**). With respect to the position of the new double bond, in each case the thermodynamically more stable product seems to be formed.[15]

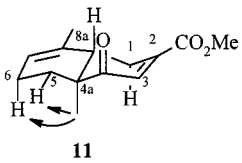
Configurational Assignment

The spectroscopic data of all diastereomers of octalone **6** have been published.[5] The isomers *cis*-**a/b** and *trans*-**a** of octalones **4** and **5** are also literature-known,[4] but most of them were characterised in a mixture of isomers. Due to the high diastereoselectivities of the Lewis acid-catalysed reactions, the individual isomers of **4** and **5** could be isolated in pure form and spectroscopically characterised (see Experimental Section). Octalones *trans*-**4b** and *trans*-**5b** are new and have been assigned in analogy to the compounds published recently.[5]

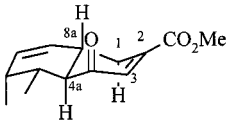
Structure and conformation of the hexalones **9**, **10**, and **11** could be confirmed by their NMR spectra and NOE experiments. ^{1}H-NMR assignments of **9** were made on the basis of decoupling experiments. As for compound **9** the $\Delta^{1,2}$-position of the new double bond was evident from the NMR spectra. A strong NOE of 4a-Me with 8a-H, and weak NOEs of 4a-Me with 5-H$_{eq}$ and 6-H$_{ax}$ confirm the *cis*-fusion of the rings and the conformation as depicted. The $\Delta^{2,3}$-position of the new double bond in hexalone **11** was deduced from the NMR spectra. The NOE experiments indicated but did not prove unambiguously that **11** is *trans* fused. A large *trans*-diaxial coupling of 8a-H and 1-H$_{ax}$ (J = 12 Hz) proves the axial position of 8a-H on the B-ring, whereas weak NOEs of the 4a-Me with 5-H$_{eq}$ and 6-H$_{ax}$ confirm the axial position of the 4a-Me on the A-ring. Assignment of the structure of **10** was made by comparison with the NMR data of **11**. In addition, two large *trans*-diaxial couplings (J = 12 Hz each) of 8a-H with 1-H$_{ax}$ and 4a-H proved in this case the *trans*-fusion of the rings.



9



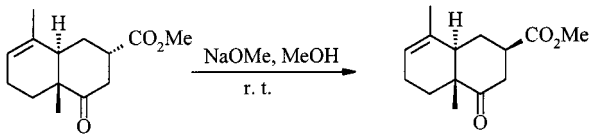
11



10

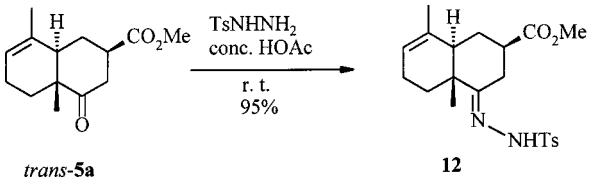
Synthesis of α-Eudesmol

For the synthesis of α-eudesmol we required the isomer *trans*-**5a** in pure form. The chelate-controlled intramolecular Diels–Alder reactions with NEt$_3$ workup produced the desired isomer in satisfactory yields. After separation and repeated chromatography,[1] further amounts of *trans*-**5a** could be obtained by a base-catalysed epimerisation reaction of *trans*-**5b**. Treatment of pure *trans*-**5b** with NaOMe in methanol furnished an equilibrium mixture of both *trans* isomers with *trans*-**5a** being formed in 61% isolated yield. The combined total yield of pure *trans*-**5a** after cycloaddition, repeated chromatography, epimerisation, and crystallisation was 21% in the end.[1]

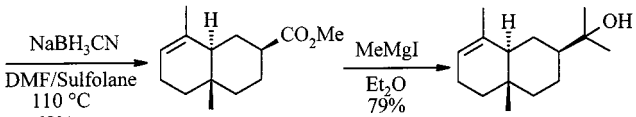


trans-**5b** *trans*-**5a** 61% (+ *trans*-**5b** 16%)

Octalone *trans*-**5a** was readily converted into α-eudesmol in three steps as outlined. Reduction of the carbonyl group was achieved by treatment of the tosylhydrazone **12** of octalone *trans*-**5a** with NaBH$_3$CN[16] and reaction of the resulting octaline **13** with an excess of MeMgI furnished analytically pure racemic α-eudesmol in 51% overall yield from *trans*-**5a**.



trans-**5a** **12**



13 α-Eudesmol

Conclusion

It was shown that the diastereoselectivity of the intramolecular Diels–Alder reactions of trienone esters could be controlled efficiently by the application of Lewis acids. Those with one free coordination site preferentially provide *cis*-octalones. In several instances high preferences for either of the *cis*-fused isomers, *cis*-**a** or *cis*-**b**, was found. This was strongly dependent on the nature of the substrate and the Lewis acid. Strong Lewis acids with two free coordination sites led preferentially to isomer *trans*-**b** as the primary product. This could be rationalised by the formation of a seven-membered ring chelate complex as the reactive transition conformation. It was shown that addition of NEt$_3$ in the workup procedure led to partial epimerisation to *trans*-**a** and to partial oxidation of the octalones to hexalones. The novel chelate-controlled intramolecular Diels–Alder reaction provided the basis for a short synthesis of the sesquiterpene α-eudesmol. The *trans*-**b** isomer of octalone **6**, which served as a model system for the synthesis of dihydromevinolin, was also obtained in good yields from a chelate-controlled cycloaddition reaction. This achievement paved the way for the formal total syn-

thesis of dihydromevinolin, which will be reported in due course.[17]

Experimental Section

General: All instrumentation has been described previously.[5] − A chromatotron (Harrison Research, 7924 T) was used for preparative TLC with centrifugal separation. The diameter of the disc was 24 cm, the thickness of the silica gel coat (Merck−Schuchardt, Silica gel 60 PF_{254} containing gypsum) was 2 cm.

General Procedures for the Lewis Acid Catalysed Intramolecular Diels−Alder Reactions of the Trienones 1−3 to the Octalones 4−6

Reaction Procedures. − Method A: A solution of the trienone in CH_2Cl_2 was placed in a flask, and the Lewis acid was added in one portion; for reaction times and temperatures see Table 3. − **Method B:** A solution of the Lewis acid in CH_2Cl_2 was placed in a flask and treated with the trienone; for reaction times and temperatures see Table 3.

Workup Procedures. − Method A: The reaction was quenched by fast successive addition of NEt_3 (0.5−1 mL/mmol Lewis acid) and water (2−10 mL/mmol Lewis acid). The aqueous layer was extracted three times with CH_2Cl_2, and the combined organic layers were washed with satd. aqueous NH_4Cl solution and water. If necessary, the combined aqueous phases were neutralised with 2 N HCl solution and backextracted with CH_2Cl_2. The combined organic extracts were dried ($MgSO_4$) and concentrated. The NEt_3 was removed in vacuo. If necessary, hydrolysis products of the Lewis acid were removed by filtration of the crude product through a plug of silica gel with Et_2O. − **Method B:** The reaction was quenched by addition of water (15 mL/mmol Lewis acid). The aqueous layer was extracted three times with CH_2Cl_2, the combined organic layers were washed with satd. aqueous $NaHCO_3$ solution and brine, dried ($MgSO_4$), and concentrated. If necessary, hydrolysis products of the Lewis acid were removed by filtration of the crude product through a plug of silica gel with Et_2O. − **Method C:** The reaction was quenched by addition of satd. aqueous $NaHCO_3$ solution (5 mL/mmol Lewis acid). The aqueous layer was extracted three times with CH_2Cl_2, dried ($MgSO_4$), and concentrated. − **Method D:** After addition of NEt_3 (0.3 mL/mmol Lewis acid) the reaction mixture was stirred for 17 h before water (7 mL/mmol Lewis acid) was added. The aqueous layer was extracted three times with CH_2Cl_2, the combined organic layers were washed with water, dried (Na_2SO_4), and concentrated. Hydrolysis products of the Lewis acid were removed by filtration of the crude product through a plug of silica gel with Et_2O.

Purification Procedures. − Method A: Kugelrohr distillation at 90−120°C/0.02 Torr. − **Method B:** Chromatotron chromatography (pentane/EtOAc, 8:1). − **Method C:** Conventional column chromatography on silica gel (hexane/EtOAc, 10:1). − **Method D:** Flash chromatography (hexane/EtOAc, 8:1). − **Method E:** Flash chromatography (hexane/EtOAc, 10:1).

Reaction of Methyl *trans*-2-Isopropenyl-1-[(*E*)-3-methyl-2,4-pentadienyl]-2-(trimethylsiloxy)cyclopropanecarboxylate (7) with $TiCl_4$: To a solution of the siloxycyclopropane **7** (300 mg, 0.972 mmol) in CH_2Cl_2 (30 mL) at −78°C was added $TiCl_4$ (221 mg, 1.17 mmol). Upon addition, the colour of the solution changed from pale yellow to a reddish brown. The reaction mixture was warmed to +10°C during which time its colour changed to brown. After fast successive addition of NEt_3 (1 mL) and water (10 mL) the aqueous layer was extracted with CH_2Cl_2 (3× 10 mL), the combined organic layers were washed with water (60 mL), dried ($MgSO_4$), and concentrated. Residual NEt_3 was removed in vacuo. The diastereomeric ratio of crude octalone **5** (245 mg, 100%) was determined as *cis*-**5a**/*cis*-**5b**/*trans*-**5a**/*trans*-**5b** = 63:24:6:7 by ^{1}H NMR. Purification by distillation (kugelrohr, 100°C/0.02 Torr) yielded octalone **5** (147 mg, 64%) as an oil. For analytical data of octalone **5** see ref.[5] For ^{1}H-NMR data see Table 5. For ^{13}C-NMR data see Table 6.

Spectroscopic Data of Methyl (4*E*,6*E*)-2-(4-Chloro-2-oxopentyl)-4,6-octadienoate (8): ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 6.07−5.93 (m, 2 H, 5-H, 6-H), 5.63, 5.40 (2 m_c, 2× 1 H, 7-H, 4-H), 4.45 (sext.,

Table 3. Lewis-acid catalysed intramolecular Diels−Alder reactions of the trienones **1**−**3** to the octalones **4**[a], **5**,[a] and **6**[b]

Trienone	Amount Used [mg (mmol)]	Lewis acid	Amount Used [mg[c] (mmol)]	CH_2Cl_2 [ml]	Reaction Method	Temperature, Time	Work-up Method	Purification Method	Product	Amount [mg]	Yield, (Conversion), [%]
1	400 (1.80)	$BF_3{\cdot}OEt_2$	640 (4.51)	40	A	−78 to +20°C, 12 h	A		**4**	415[d]	83[d]
1	200 (0.900)	$EtAlCl_2$, 1 M in *n*-hexane	1 mL (1.00)	20	A	−78°C, 19 h	B	A	**4**	178	89
1	130 (0.585)	TBDMS−OTf	310 (1.17)	10	A	−78 to +10°C, 15 h	C	A	**4**	56	43
2	247 (1.05)	$BF_3{\cdot}OEt_2$	300 (2.11)	20	A	−78 to −10°C, 12 h	A	A	**5**	132	53
2	100 (0.423)	$ZnBr_2$	125 (0.555)	10	B	−78 to +20°C, 24 h	A		**5**	89[d]	89[d] (90)
2	300 (1.27)	$EtAlCl_2$, 1 M in *n*-hexane	1.3 mL (1.3)	20	A	−78°C, 18 h	B	A	**5**	237	79
2	267 (1.13)	TBDMS−OTf	600 (2.27)	20	A	−78 to +10°C, 18 h	A	A	**5**	210	79
3	147 (0.622)	$BF_3{\cdot}OEt_2$	127 (0.871)	15	A	−10°C;[e] then r. t., 19 h	C		**6**	133[d]	90[d]
1	500 (2.25)	$TiCl_4$	510 (2.69)	40	A	−78°C, 18 h	A	A, B[f]	**4**	199[f]	47[f]
2	3070 (13.0)	$TiCl_4$	3000 (15.8)	100	A	−78°C, 8 h	A	A	**5**	1780	58
2	100 (0.423)	$TiBr_4$, 0.0320 M in CH_2Cl_2	20.0 mL (0.640)	2	B	−78°C, 10 min	B		**5**	100[d]	100[d] (85)
2	2670 (11.3)	$TiBr_4$, 0.270 M in CH_2Cl_2	85.0 mL (23.0)	10	B	−78°C, 1 h	A	C	**5**	1347[g]	51[g]
2	200 (0.846)	$SnCl_4$	440 (1.69)	20	A	−78°C, 19 h	A	A	**5**	120	60
3	230 (0.974)	$TiCl_4$	222 (1.17)	30	B	−78°C, 18 h	B	D	**8**	35	13[h]
3	586 (2.48)	$SnCl_4$	970 (3.72)	186	B	−78°C, 12 h; then −40 °C, 7 h	B	E	**6**	430	73
3	130 (0.550)	$SnCl_4$	287 (1.10)	55	B	−78°C, 12 h; then −40 °C, 7 h	D	E	**6**	60[i]	46[i]

[a] For analytical data see ref.[4], for ^{1}H-NMR data see Tables 4 and 5, for ^{13}C-NMR data see Table 6. − [b] For analytical and spectroscopic data see ref.[5]. − [c] Unless stated otherwise. − [d] Yield of crude product. − [e] Temperature at which trienone and Lewis acid were combined. − [f] A fraction of the crude material was purified. − [g] Plus hexalone **9** (216 mg, 8%, purity approx. 88%). − [h] Impurified. − [i] Plus hexalone **10** (31 mg, 24%).

Table 4. ^{1}H NMR (300 MHz) data [δ values, *J* (Hz)] of octalones **4**

H[a]	*cis*-**4a**	*cis*-**4b**	*trans*-**4a**	*trans*-**4b**
8-H	5.77 (m_c)	5.66 (m_c)	5.65 (m_c)	5.38 (td, *J* = 1.5, 10)
7-H	5.40 (br. qd, *J* = 2, 10)	5.66 (m_c)	5.37 (qd, *J* = 2, 10)	5.36 (td, *J* = 2, 10)
CO_2Me	3.70 (s)	3.69 (s)	3.72 (s)	3.69 (s)
2-H	2.80 (ddt, *J* = 4, 4.5, 12)	2.59−2.47 (m)	2.80 (ddt, *J* = 4.5, 5, 12)	3.16 (dddd, *J* = 3, 3.5, 6, 7)
3-H_{ax}	2.65 (dd, *J* = 12, 15.5)	2.75−2.68 (m)	2.98 (dd, *J* = 13, 14)	2.81 (dd, *J* = 7, 15.5)
3-H_{eq}	2.45 (ddd, *J* = 2, 4.5, 15.5)	2.75−2.68 (m)	2.46 (ddd, *J* = 1.5, 5, 14)	2.64 (ddd, *J* = 1, 3, 15.5)
8a-H	2.56−2.51 (m)	2.25−2.08 (m)	2.32−2.06[b] (m)	2.01 (dd, *J* = 5.5, 12)
6-H_{ax}	2.25−2.07[b] (m)	2.25−2.08 (m)	2.01−1.85[b] (m)	2.15−1.95 (m)
6-H_{eq}	2.25−2.07[b] (m)	2.25−2.08 (m)	2.32−2.06[b] (m)	2.15−1.95 (m)
5-H_{ax}	2.25 (br. ddd, *J* = 4.5, 12, 13.5)	1.96 (br. dd, *J* = 8, 12.5)	1.55 (ddd, *J* = 7.5, 11.5, 13.5)	1.52[b] (br. ddd, *J* = 7, 11, 13.5)
1-H_{eq}	2.01−1.89[b] (m)	2.25−2.08 (m)	2.32−2.06[b] (m)	2.46−2.39[c] (m)
1-H_{ax}	2.01−1.89[b] (m)	1.82−1.70 (m)	2.01−1.85[b] (m)	2.15−1.95[b] (m)
5-H_{eq}	1.25−1.19[b] (m)	1.30−1.23 (m)	2.01−1.85[b] (m)	1.89[c] (br. dd, *J* = 6, 13.5)
4a-Me	1.21 (s)	1.12 (s)	1.11 (s)	1.08 (s)

[a] Integrals are in accordance with the expected values. − [b,c] Assignments are interchangeable within the column.

Table 5. ^{1}H NMR (300 MHz) data [δ values, *J* (Hz)] of octalones **5**

H[a]	*cis*-**5a**	*cis*-**5b**[b]	*trans*-**5a**[b]	*trans*-**5b**[b]
8-Me	1.69 (s)	1.73 (q, *J* = 2)	1.69 (br. s)	1.68 (br. s)
7-H	5.40 (br. s)	5.39 (m_c)	5.40 (br. s)	5.39 (m_c)
CO_2Me	3.71 (s)	3.71 (s)	3.73 (s)	3.70 (s)
2-H	2.75 (tt, *J* = 5, 9)	2.73−2.63 (m)	2.74 (ddt, *J* = 4.5, 5, 13)	3.15 (tt, *J* = 3.5, 7)
3-H_{ax}	2.66 (dd, *J* = 9, 15.5)	2.75[e] (t, *J* = 13.5)	2.98 (dd, *J* = 13.5, 14.5)	2.77 (dd, *J* = 7, 15.5)
3-H_{eq}	2.50 (ddd, *J* = 1.5, 5, 15.5)	2.52 (br. td, *J* = 2.5, 13.5)	2.45 (ddd, *J* = 1.5, 5, 14.5)	2.66 (ddd, *J* = 1.5, 3.5, 15.5)
8a-H	2.20 (dd, *J* = 4, 9)	1.87[e] (m_c)	2.30−2.21 (m)	2.43−2.36 (m)
6-H_{ax}	2.15−1.90[e] (m)	2.12−2.01 (m)	2.12−2.00 (m)	2.07−2.01 (m)
6-H_{eq}	2.15−1.90[e] (m)	2.12−2.01 (m)	2.12−2.00 (m)	2.07−2.01 (m)
5-H_{ax}	2.15−1.90[c] (m)	1.92 (br. dd, *J* = 8.5, 11.5)	1.52 (ddd, *J* = 8, 11.5, 13.5)	1.53−1.23[c] (m)
1-H_{eq}	2.30−2.23[d] (m)	2.33 (qd, *J* = 3.5, 13.5)	2.30−2.21 (m)	2.40−2.31[d] (m)
1-H_{ax}	2.15−1.90[d] (m)	1.70−1.62 (m)	1.77 (dt, *J* = 12.5, 14)	1.96−1.85[d] (m)
5-H_{eq}	1.30−1.15[c] (m)	1.26−1.20 (m)	1.87−1.80 (m)	1.96−1.85[c] (m)
4a-Me	1.16 (s)	1.06 (s)	1.11 (s)	1.08 (s)

[a] Integrals are in accordance with the expected values. − [b] Signal assignments are based on a ^{1}H/^{1}H COSY spectrum. − [c,d] Assignments are interchangeable within the column. − [e] Signal is partially obscured.

Table 6. ^{13}C NMR (75.5 MHz) data (δ values) of the octalones **4** and **5**

C	*cis*-**4a**	*cis*-**5a**	*cis*-**4b**	*cis*-**5b**	*trans*-**4a**	*trans*-**5a**	*trans*-**4b**	*trans*-**5b**
C-4 (s)	212.5	213.1	213.4	214.1	212.1	213.3	212.5	213.1
CO_2Me (s)	174.3	174.8	174.0	174.1	173.7	174.2	174.8	174.8
C-7 (d)	127.1	124.8	125.7	120.8	127.0	122.2	127.1	122.1
C-8 [d (**4**) or s (**5**)]	128.9	133.2	128.6	134.6	129.7	132.0	127.7	132.3
C-4a (s)	46.3	47.2	46.5	47.3	45.9	46.7	46.2	46.8
CO_2*Me* (q)	51.8	52.0	52.0	52.1	51.7	51.1	52.1	52.2
C-2 (d)	42.6	39.1	42.3[a]	41.6	41.8[a]	42.9	42.8[a]	39.8[a]
C-3 (t)	39.8	39.6	39.6	39.9	38.1	38.5	37.6	37.4
C-8a (d)	39.2	45.2	40.9[a]	46.9	42.1[a]	45.6	40.3[a]	42.1[a]
C-5[b] (t)	29.8	29.8	32.2	31.3	30.6	28.6	28.4	28.6
C-1[b] (t)	28.2	23.9	27.3	26.4	29.8	26.1	27.7	24.7
C-6[b] (t)	22.4	22.3	21.7	21.8	22.6	22.2	22.8	22.1
8-Me (q)		23.9[a]		22.8		21.5		21.3
4a-Me (q)	25.2	21.7[a]	19.6	18.6	15.1	16.0	15.5	16.2

[a,b] Assignments are interchangeable within the column.

J = 7 Hz, 1 H, 4′-H), 3.68 (s, 3 H, CO_2Me), 3.05−2.20 (m, 7 H, 2-H, 3′-H, 3-H, 1′-H), 1.73 (d, *J* = 6 Hz, 3 H, 8-H), 1.52 (d, *J* = 7 Hz, 3 H, 5′-H). − ^{13}C NMR ($CDCl_3$, 75.5 MHz): δ = 204.3 (s, C=O), 174.8 (s, *C*O_2Me), 133.2, 130.9, 128.4, 126.5 (4 d, C-4, C-5, C-6, C-7), 52.5 (t, C-3′), 51.9 (d, C-4′), 51.8 (q, CO_2*Me*), 43.6 (t, C-1′), 39.8 (d, C-2), 34.8 (t, C-3), 25.0 (q, C-5′), 18.0 (q, C-8).

Methyl (4aβ,8aβ)-3,4,4a,5,6,8a-Hexahydro-4a,8-dimethyl-4-oxo-2-naphthalenecarboxylate (9): To a solution of $TiBr_4$ (780 mg, 2.12 mmol) at −78 °C in CH_2Cl_2 (20 mL) was added a solution of octalone **5** (200 mg, 0.846 mmol, *cis*-**5a**/*cis*-**5b** = 33:67) in CH_2Cl_2 (5 mL), followed by NEt_3 (350 mg, 3.46 mmol). After 1 h at −78 °C, more NEt_3 (2 mL), and water (20 mL) were added, and

the mixture was warmed to room temp. The aqueous phase was extracted with CH_2Cl_2 (3× 25 mL), the combined organic layers were washed with water (100 mL), dried ($MgSO_4$), and concentrated. After filtration through a plug of silica gel (Et_2O), 162 mg of a mixture of octalone **5** (*cis*-**5a**/*cis*-**5b** = 46:54) and hexalone **9** (**5**/**9** = 53:47) was obtained. Separation on silica gel (hexane/EtOAc, 10:1) furnished a fraction of pure hexalone **9** (52 mg, 26%) as a yellow oil, and a second fraction (69 mg) of **9** mixed (23:77) with recovered octalone **5** (*cis*-**5a**/*cis*-**5b** = 44:56). − IR (neat): $\tilde{\nu}$ = 3015 cm^{-1} (=C−H), 2950−2840 (C−H), 1730−1700 (br. s, C=O, CO_2Me), 1650 (C=C). − ^1H NMR (acetone-d_6, 300 MHz): δ = 7.06 (td, *J* = 2, 4 Hz, 1 H, 1-H), 5.50 (m_c, 1 H, 7-H), 3.74 (s, 3 H, CO_2Me), 3.17 (ddd, *J* = 2, 2.5, 21.5 Hz, 1 H, 3-H_{eq}*), 3.04 (ddd, *J* = 2, 2.5, 21.5 Hz, 1 H, 3-H_{ax}*), 2.90 (m_c, 1 H, 8a-H), 2.09−1.99 (m, 2 H, 5-H_{eq}, 6-H_{ax}), 1.94−1.86 (m, 1 H, 5-H_{ax}), 1.79 (m_c, 3 H, 8-Me), 1.28−1.20 (m, 1 H, 6-H_{eq}), 1.08 (s, 3 H, 4a-Me), * assignments are interchangeable. − ^{13}C NMR ($CDCl_3$, 75.5 MHz): δ = 211.4 (s, C-4), 166.0 (s, *C*O_2Me), 139.4 (d, C-1), 130.9 (s, C-8), 125.4 (s, C-2), 122.7 (d, C-7), 51.6 (q, CO_2*Me*), 47.8 (d, C-8a), 45.5 (s, C-4a), 36.6 (t, C-3), 27.6, 21.3 (2 t, C-5, C-6), 21.9 (q, 8-Me), 19.9 (q, 4a-Me). − $C_{14}H_{18}O_3$ (234.3): calcd. C 71.77, H 7.76; found C 71.80, H 7.67.

Methyl (4aβ,5β,6β,8aα)-1,4,4a,5,6,8a-Hexahydro-5,6-dimethyl-4-oxo-2-naphthalenecarboxylate (10): IR (neat): $\tilde{\nu}$ = 3020 cm^{-1} (=C−H), 2950, 2880 (C−H), 1720 (CO_2Me), 1680 (C=O), 1635 (C=C). − ^1H NMR ($CDCl_3$, 300 MHz): δ = 6.69 (d, *J* = 3 Hz, 1 H, 3-H), 5.79 (ddd, *J* = 3, 5, 10 Hz, 1 H, 7-H), 5.43 (td, *J* = 1.5, 10 Hz, 1 H, 8-H), 3.82 (s, 3 H, CO_2Me), 2.80 (dd, *J* = 4.5, 19 Hz, 1 H, 1-H_{eq}), 2.48 (br. dt, *J* = 1.5, 12 Hz*, 1 H, 8a-H), 2.25 (ddd, *J* = 3, 12, 19 Hz, 1 H, 1-H_{ax}), 2.21−2.00 (m, 3 H, 4a-H, 5-H, 6-H), 1.22 (d, *J* = 7 Hz, 3 H, 6-Me), 0.88 (d, *J* = 7 Hz, 3 H, 5-Me), * further coupling constants could not be determined. − ^{13}C NMR ($CDCl_3$, 75.5 MHz): δ = 202.4 (s, C-4), 166.9 (s, *C*O_2Me), 145.2 (s, C-2), 134.7 (d, C-3, C-7), 126.5 (d, C-8), 52.5 (q, CO_2*Me*), 49.5 (d, C-4a), 39.2 (d, C-8a), 35.1 (d, C-6), 33.4 (t, C-1), 30.8 (d, C-5), 16.8, 15.7 (2 q, 5-Me, 6-Me). − $C_{14}H_{18}O_3$ (234.3): calcd. C 71.77, H 7.76; found C 71.18, H 7.68.

Methyl (4aβ,8aα)-1,4,4a,5,6,8a-Hexahydro-4a,8-dimethyl-4-oxo-2-naphthalenecarboxylate (11): Following the procedure for the preparation of **9**, hexalone **11** was obtained from octalone *trans*-**5b** (20 mg, 0.085 mmol), $TiBr_4$ (78 mg, 0.21 mmol), and NEt_3 (34 mg, 0.34 mmol) in CH_2Cl_2 (3 mL), 24 h reaction time, as a yellow oil (11 mg, 55%). − IR (neat): $\tilde{\nu}$ = 3020 cm^{-1} (=C−H), 2940−2830 (C−H), 1720 (CO_2Me), 1675 (C=O), 1625 (C=C). − ^1H NMR ($CDCl_3$, 300 MHz): δ = 6.72 (dd, *J* = 0.5, 3 Hz, 1 H, 3-H), 5.46 (m_c, 1 H, 7-H), 3.85 (s, 3 H, CO_2Me), 2.89 (dd, *J* = 4.5, 19 Hz, 1 H, 1-H_{eq}), 2.56 (br. d, *J* = 12 Hz*, 1 H, 8a-H), 2.26 (ddd, *J* = 3, 12, 19 Hz, 1 H, 1-H_{ax}), 2.12−2.05 (m, 2 H, 5-H_{eq}, 6-H_{ax}), 2.04 (td, *J* = 3.5, 17.5 Hz, 1 H, 6-H_{eq}), 1.74 (quint., *J* = 1.5 Hz, 3 H, 8-Me), 1.43 (td, *J* = 9, 13 Hz, 1 H, 5-H_{ax}), 1.00 (s, 3 H, 4a-Me), * further coupling constants could not be determined. − ^{13}C NMR ($CDCl_3$, 75.5 MHz): δ = 204.9 (s, C-4), 167.1 (s, *C*O_2Me), 146.1 (s, C-2), 131.8 (d, C-3, C-8), 122.6 (d, C-7), 52.6 (q, CO_2*Me*), 43.4 (s, C-4a), 42.7 (d, C-8a), 28.0, 26.0, 22.0 (3 t, C-1, C-5, C-6), 20.7 (q, 8-Me), 14.3 (q, 4a-Me). − An elemental analysis could not be obtained due to the small amount of **11** available.

Epimerisation of *trans*-5b to *trans*-5a: Octalone *trans*-**5b** (353 mg, 1.48 mmol) was stirred in 0.36 M NaOMe solution in MeOH (8.0 ml, 2.9 mmol) for 25 h at room temp. The reaction mixture was quenched with satd. NH_4Cl solution (30 mL) and extracted with Et_2O (3× 80 mL). The combined organic extracts were washed with water (150 mL), dried ($MgSO_4$), and concentrated to provide 282 mg (80%) of an equilibrium mixture of *trans*-**5a** and *trans*-**5b** (78:22). Separation on silica gel (hexane/EtOAc, 10:1) furnished *trans*-**5a** as a pale yellow oil (215 mg, 61%), followed by *trans*-**5b** as a colourless oil (56 mg, 16% recovered).

Tosylhydrazone 12: A solution of *trans*-**5a** (511 mg, 2.16 mmol) and *p*-toluenesulfonylhydrazine (800 mg, 4.29 mmol) in glacial acetic acid (5 mL) was stirred for 25 h at room temp. The reaction mixture was diluted with water (50 mL) and extracted with CH_2Cl_2 (3× 50 mL). The combined organic extracts were neutralised with solid $NaHCO_3$, washed with water (125 mL) and brine (125 mL), and dried ($MgSO_4$). After concentration and purification on silica gel (Et_2O), tosylhydrazone **12** was obtained as a colourless amorphous solid (828 mg, 95%), m.p. 68−71°C. − IR (KBr): $\tilde{\nu}$ = 3500 cm^{-1} (N−H), 3100 (=C−H), 2850 (C−H), 1740 (CO_2Me), 1600 (C=N, C=C). − ^1H NMR ($CDCl_3$, 300 MHz): δ = 8.02 (br. s, 1 H, NH), 7.85−7.82 (m, 2 H, ortho-Ar-H), 7.30−7.28 (m, 2 H, *meta*-Ar-H), 5.37 (br. s, 1 H, 7-H), 3.67 (s, 3 H, CO_2Me), 2.90 (dd, *J* = 4.5, 14.5 Hz, 1 H, 3-H_{eq}), 2.66−1.11 (m, 9 H, 1-H, 2-H, 3-H_{ax}, 5-H, 6-H, 8a-H), 2.42 (s, 3 H, Ar-Me), 1.61 (br. s, 3 H, 8-Me), 0.91 (s, 3 H, 4a-Me). − ^{13}C NMR ($CDCl_3$, 75.5 MHz): δ = 174.6 (s, *C*O_2Me), 164.3 (s, C-4), 143.8, 135.4 (2 s, aromatic *ipso*-C, Ar-*para*-C), 132.5 (s, C-8), 129.3, 128.2 (2 d, Ar-ortho-C, Ar-*meta*-C), 122.3 (d, C-7), 52.0 (q, CO_2*Me*), 46.0 (d, C-8a), 42.1 (d, C-2), 40.9 (s, C-4a), 30.6, 26.2, 24.4, 22.6 (4 t, C-1, C-3, C-5, C-6), 21.6 (q, Ar-Me), 21.3 (q, 8-Me), 17.1 (q, 4a-Me). − $C_{21}H_{28}N_2O_4S$ (404.5): calcd. C 62.33, H 6.97, N 6.95; found C 61.76, H 7.02, N 6.70.

Methyl (2β,4aβ,8aα)-1,2,3,4,4a,5,6,8a-Octahydro-4a,8-dimethyl-2-naphthalenecarboxylate (13): To a solution of tosylhydrazone **12** (800 mg, 1.98 mmol) in DMF/sulfolane (1:1, 20 mL) at room temp. was added $NaBH_3CN$ (750 mg, 11.9 mmol), followed by *p*TsOH · H_2O (160 mg, 0.841 mmol). The reaction mixture was heated to 110°C. After 2 h, the reaction mixture was cooled to room temp., treated with another batch of $NaBH_3CN$ and *p*TsOH · H_2O (same amounts as above), and then heated again for 2 h at 110°C. This procedure was repeated three more times, after which the cooled reaction mixture was buffered with satd. NH_4Cl solution to pH 8 and extracted with pentane (6× 100 mL). The combined organic extracts were washed with water (150 mL), dried ($MgSO_4$), and concentrated. Column chromatography on silica gel (hexane/EtOAc, 40:1) furnished octaline **13** as a colourless oil (300 mg, 68%). − IR (neat): $\tilde{\nu}$ = 3020 cm^{-1} (=C−H), 2950−2850 (C−H), 1730 (CO_2Me). − ^1H NMR ($CDCl_3$, 300 MHz): δ = 5.33 (br. s, 1 H, 7-H), 3.68 (s, 3 H, CO_2Me), 2.40−2.29 (m, 1 H, 2-H), 2.17−1.97 (m, 2 H), 2.00 (ddd, *J* = 3, 3.5, 13 Hz, 1 H), 1.90 (br. d, *J* = 14 Hz, 1 H), 1.81−1.73 (m, 2 H), 1.61 (br. s, 3 H, 8-Me), 1.48 (td, *J* = 3.5, 13 Hz, 1 H), 1.38−1.29 (m, 3 H), 1.18 (ddd, *J* = 8, 10, 13 Hz, 1 H, 1-H_{ax}), 0.82 (s, 3 H, 4a-Me). − ^{13}C NMR ($CDCl_3$, 75.5 MHz): δ = 176.4 (s, *C*O_2Me), 134.2 (s, C-8), 121.3 (d, C-7), 51.4 (q, CO_2*Me*), 46.0 (d, C-8a), 44.3 (d, C-2), 39.2, 37.7, 26.4, 24.0, 22.7 (5 t, C-1, C-3, C-4, C-5, C-6), 32.0 (s, C-4a), 21.0 (q, 8-Me), 15.3 (q, 4a-Me). − $C_{14}H_{22}O_2$ (222.3): calcd. C 75.63, H 9.97; found C 75.64, H 10.14.

(±)-α-Eudesmol: To a solution of octaline **13** (250 mg, 1.12 mmol) at 0°C in THF (50 mL) was added over a period of 20 min MeMgI (3.0 M in Et_2O, Aldrich, 4.0 ml, 12.0 mmol). After stirring at room temp. for 2 h, the reaction mixture was cooled to 0°C and hydrolysed carefully with MeOH (10 mL), followed by satd. aqueous NH_4Cl solution (10 mL). The aqueous phase was extracted with Et_2O (3× 50 mL), the combined organic extracts were washed with satd. aqueous $Na_2S_2O_3$ solution (10 mL) and water (10 mL), and dried ($MgSO_4$). After removal of the solvents in vacuo neat (±)-α-eudesmol was obtained as a colourless solid (220 mg, 88%). Chro-

matography on alumina (hexane/EtOAc, 10:1) provided analytically pure (±)-α-eudesmol (198 mg, 79%), m.p. 78−79°C (ref.[6d] 78−79°C). − All spectroscopic data[1] correspond to those reported.[6e]

Acknowledgments

Financial support by the Fonds der Chemischen Industrie is gratefully appreciated. We thank Dr. Reinhold Zimmer and Dr. David Owen for their valuable help during preparation of the manuscript.

[1] B. Frey, Dissertation, Technische Hochschule Darmstadt, **1992**.
[2] J. Schnaubelt, Dissertation, Technische Universität Dresden, **1995**.
[3] For reviews about the intramolecular Diels−Alder reaction, see: [3a] W. R. Roush in *Comprehensive Organic Synthesis* (Eds.: B. M. Trost, I. Fleming), Pergamon Press, Oxford, **1991**, Vol. 5, p. 513−550. − [3b] W. R. Roush, *Advances in Cycloaddition*, JAI Press Inc., **1990**, Vol. 2, p. 91. − [3c] D. Craig, *Chem. Soc. Rev.* **1987**, *16*, 187−238. − [3d] D. Craig in *Stereoselective Synthesis, Methods of Organic Chemistry* (Eds.: G. Helmchen, R. W. Hoffmann, J. Mulzer, E. Schaumann), Georg Thieme Verlag, **1995**, Vol. E 21c, p. 2872−2904.
[4] R. Zschiesche, B. Frey, E. Grimm, H.-U. Reißig, *Chem. Ber.* **1990**, *123*, 363−374.
[5] B. Frey, J. Schnaubelt, H.-U. Reißig, *Eur. J. Org. Chem*. **1999**, 1377−1384, preceding paper.
[6] For isolation of α-eudesmol, dihydromevinolin, and related compounds, see references cited in ref.[5]; for syntheses of α-eudesmol involving an intramolecular Diels−Alder reaction as the key step, see: [6a] D. C. Humber, A. R. Pinder, R. A. Williams, *J. Org. Chem.* **1967**, *32*, 2335−2340. − [6b] D. F. Taber, S. A. Saleh, *Tetrahedron Lett.* **1982**, *23*, 2361−2364. − [6c] J. P. Kutney, A. K. Singh, *Can. J. Chem.* **1984**, *62*, 1407−1409. − [6d] M. A. Schwartz, A. M. Willbrand, *J. Org. Chem.* **1985**, *50*, 1359−1365. − [6e] T. Chou, S.-J. Lee, N.-K. Yao, *Tetrahedron* **1989**, *45*, 4113−4124.
[7] For increase of the *endo*-selectivity of trienone analogs by the application of Lewis acids, see:[7a] A. I. Meyers, T. K. Highsmith, P. T. Buonora, *J. Org. Chem.* **1991**, *56*, 2960−2964. − [7b] S. F. Martin, T. Rein, J. Liao, *Tetrahedron Lett.* **1991**, *32*, 6481−6484. − [7c] P. A. Grieco, S. T. Handy, J. P. Beck, *Tetrahedron Lett.* **1994**, *35*, 2663−2666. − For steric substituent effects, see: [7d] A. Alexakis, D. Jachiet, L. Toupet, *Tetrahedron* **1989**, *45*, 6203−6210. − [7e] Ref.[3c], p. 202. − For chelate complexes of trienone analoga, see: [7f] T. Takebayashi, N. Iwasawa, T. Mukaiyama, T. Hata, *Bull. Chem. Soc. Jpn.* **1983**, *56*, 1669−1677, and references cited therein.
[8] For the definition of induced/noninduced diastereoselectivity, see: L. F. Tietze, U. Beifuß, *Angew. Chem.* **1985**, *97*, 1067−1068; *Angew. Chem. Int. Ed. Engl.* **1985**, *24*, 1042−1043.
[9] [9a] M. Koch, Dissertation, Universität Würzburg, **1990**. − [9b] B. Frey, M. Koch, S. Hünig, H.-U. Reißig, *Synlett* **1991**, 854−856.
[10] [10a] S. E. Denmark, N. G. Almstead, *J. Am. Chem. Soc.* **1993**, *115*, 3133−3139, and references cited therein. − [10b] S. Shambayati, S. L. Schreiber in *Comprehensive Organic Synthesis* (Eds.: B. M. Trost, I. Fleming), Pergamon Press, Oxford, **1991**, Vol. 1, p. 283−324. − For X-ray structures of Lewis acid complexes with carbonyl and carboxyl compounds, see: [10c] S. Shambayati, W. E. Crowe, S. L. Schreiber, *Angew. Chem.* **1990**, *102*, 273−290; *Angew. Chem. Int. Ed. Engl.* **1990**, *29*, 256.
[11] [11a] D. K. Singh, J. B. Springer, P. A. Goodson, R. C. Corcoran, *J. Org. Chem.* **1996**, *61*, 1436−1442. − [11b] J. B. Springer, R. C. Corcoran, *J. Org. Chem.* **1996**, *61*, 1443−1448.
[12] For a similar ring-opening reaction, see: H.-U. Reißig, H. Holzinger, G. Glomsda, *Tetrahedron* **1989**, *45*, 3139−3150, and references cited therein.
[13] [13a] T. Kunz, A. Janowitz, H.-U. Reißig, *Chem. Ber.* **1989**, *122*, 2165−2175. − [13b] For an X-ray structure of a similar 7-membered ring chelate complex, see: T. Poll, J. O. Metter, G. Helmchen, *Angew. Chem.* **1985**, *97*, 116−118; *Angew. Chem. Int. Ed. Engl.* **1985**, *24*, 112−114.
[14] The generation of ester enolates with $TiCl_4$/amine is literature-known and has been exploited in the oxidative coupling of esters: [14a] I. Ojima, S. M. Brandstadter, R. J. Donovan, *Chem. Lett.* **1992**, 1591−1594 − [14b] N. Kise, K. Tokioka, Y. Aoyama, Y. Matsumura, *J. Org. Chem.* **1995**, *60*, 1100−1101. − [14c] Y. Matsumura, M. Nishimura, H. Hiu, M. Watanabe, N. Kise, *J. Org. Chem.* **1996**, *61*, 2809−2812.
[15] Attempts to isomerise the $\Delta^{1,2}$-double-bond of **9** into conjugation with the carbonyl group failed.[1]
[16] R. O. Hutchins, C. A. Milewski, B. E. Maryanoff, *J. Am. Chem. Soc.* **1973**, *95*, 3662−3668.
[17] J. Schnaubelt, B. Frey, H.-U. Reißig, *Helv. Chim. Acta*, in press.

Received December 7, 1998
[O98548]