Intramolecular Diels–Alder Reactions. 5 [1]

Facile Synthesis of an Octahydrobenzocycloheptenone Derivative Utilising Intramolecular Diels–Alder Reaction

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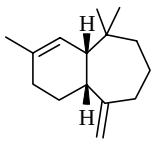
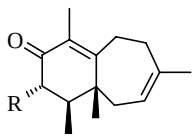
Abstract. Undecatrienone **4** was prepared in a short sequence *via* siloxycyclopropanes **1** and **3**. Intramolecular Diels–Alder reaction (IMDA) of **4** under various conditions afforded octahydrobenzocycloheptenone derivative **5** as a mixture of three or four diastereomers. High diastereoselectivities in favour of the *endo*-product *cis*-**5a** could be obtained with $TiCl_4$ as promoter. This selectivities were attributed to the formation of a seven-membered ring chelate as intermediate. The configurational assignment of all four diastereomers of **5** was based on isomerisation reactions and NMR analysis.

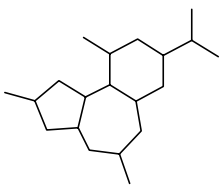
Carbocyclic molecules containing fused six- and seven-membered rings are found in a number of natural products [3], *e.g.* in himachalane and perforene sesquiterpenes such as α-himachalene [4] and perforenone A and B [5]. Of particular medicinal interest are the daphnane and tigliane derivatives, some of which can act as tumor promoters [6]. A number of syntheses of such fused 6/7 bicyclic ring systems [7] involved an IMDA reaction as the key step.



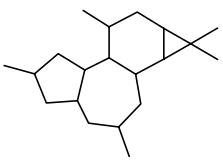
α-Himachalene



R = OH Perforenone A
R = Cl Perforenone B



Daphnane Skeleton



Tigliane Skeleton

We recently described syntheses and IMDA reactions of variably substituted 1,7,9-decatrien-3-ones to octahydronaphthalenones [1, 8]. The trienone substrates were assembled in fast and efficient sequences from simple precursors *via* siloxycyclopropanes. It was found that high stereocontrol of the cycloaddition step could be achieved by choice of the appropriate Lewis acid promoter [8c]. The use of strong Lewis acids with two free coordination sites led to the formation of the otherwise unfavoured *trans*-fused cycloadducts *via* a novel chelate-controlled cycloaddition reaction. The *trans*-fused octalone products, that were now available in good yields for the first time, were elaborated to the sesquiterpene α-eudesmol [8c], and, in a formal total synthesis, to the pharmaceutically important compound dihydromevinolin [1]. Here, we report the extension of the siloxycyclopropane route developed in our laboratory to undecatrienone substrates, and an IMDA reaction to furnish a fused 6/7 ring system. Since these 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.

Our approach to the undecatrienone substrate starts with the literature-known siloxycyclopropane **1** [9]. Deprotonation of **1** with LDA and subsequent reaction with *E*-1-iodo-3,5-hexadiene (**2**) [10] in presence of the lithium complexing agent 1,3-dimethylimidazolidin-2-one (DMEU) furnished the tetrasubstituted cyclopropane **3** in 44% yield with recovery of some starting material **1**. The modest yield of this reaction could not be explained in terms of low reactivity of the iodide **2** since analogous alkylation reactions with saturated iodides [11] generally proceed very smoothly (70–90% yield). It was found, however, that the yield was considerably lower (61%) when 1-iodo-3-butene was employed [12]. We therefore attribute the lower yields of the alkylation reactions with homoallylic iodides to the competing elimination reaction with either excess of LDA or the ester enolate acting as base. Due to the volatility and tenden-

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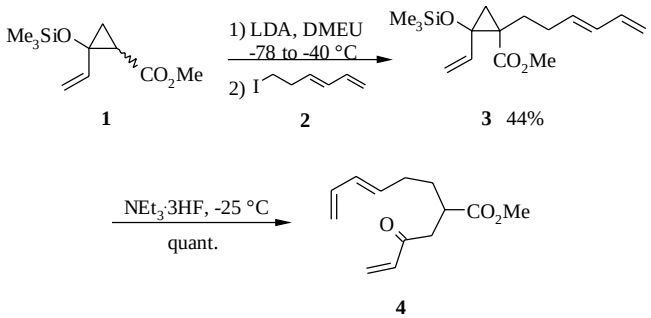
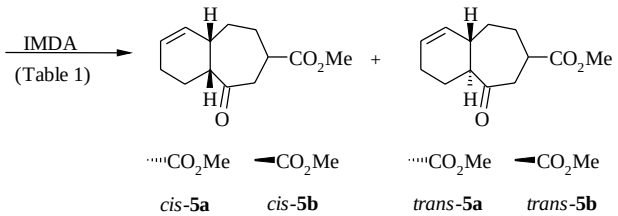
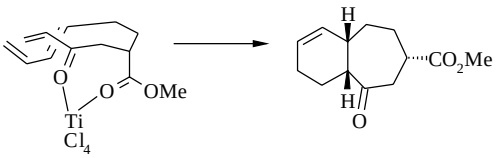
cy to polymerise the resulting 1,3,5-hexatriene could not be detected in the reaction mixture. Ring-opening of cyclopropane **3** by fluoride proceeded smoothly and furnished crude undecatrienone **4** in quantitative yield. This material was sufficiently pure to be employed in the subsequent cycloaddition reactions.





The IMDA reactions of trienone **4** under various conditions are summarised in Table 1. The thermal IMDA (entry 1) afforded **5** in a *cis*/*trans*-ratio of 4:1 with *cis*-**5b** being the major component. At this point we have to note the lower reactivity of undecatrienone **4** compared with the related decatrienone which undergoes intramolecular cycloaddition already at room temperature [8a]. The proton-catalysed reaction (entry 2) increased the *cis*/*trans*-ratio to 98:2, however, the major product of this reaction is *cis*-**5a**. The $TiCl_4$ promoted reaction (entry 3) yielded *cis*-**5a** almost exclusively. As in previous examples [1, 8c] this finding could be rationalised by the formation of a seven-membered ring chelate complex as intermediate preceding the cycloaddition. However, unlike in the earlier examples with the decatrienones where an *exo*-chelate transition conformation was favoured with $TiCl_4$, the undecatrienone derivative shows a strong preference for the *endo*-chelate transition state. The reason for this is unclear, but it seems likely that steric interactions of the chloride ligands with the diene, which disfavour the *endo*-chelate transition state of the decatrienones, do not play a role with the undecatrienone. Possibly, the longer chain linking diene and dienophile in **4** allows avoidance of steric repulsions in the chelate complex and hence the electronically favoured *endo*-approach dominates in this cycloaddition.



As in the corresponding reactions with the decatrienones [8c], **a**/**b**-epimerisation in the $TiCl_4$ promoted cycloaddition of **4** was observed upon work-up with NEt_3/H_2O (entry 4). The mechanism of this epimerisation involves formation of the ester enolate **6** which is subsequently protonated at C-7 to provide *cis*-**5** as an **a**/**b**-mixture [13]. It is interesting to note that under the conditions no epimerisation to *trans*-**5** could be observed. Thus presumably no enolate formation takes place at C-9a since reprotonation of such a bridgehead enolate only to *cis*-**5** seems unlikely. Furthermore, the reprotonation at C-7 of **6** to *cis*-**5a** and *cis*-**5b** (≈2.5:1) appears to be a kinetically controlled process as the thermodynamic *cis*-**5a**/**b** ratio was found to be about 8:1 (see below).

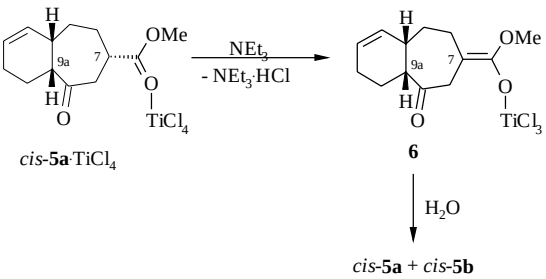
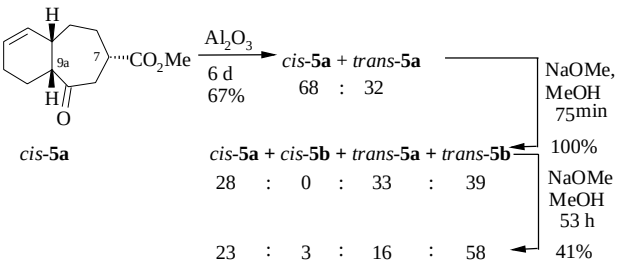


Table 1 Intramolecular Diels–Alder reactions of trienone **4** to cycloadduct **5**

Entry	Conditions [a])	Yield [b]) (%) (Conversion)	Diastereomeric Ratio [c]) *cis*-**5a** : *cis*-**5b** : *trans*-**5a** : *trans*-**5b**
1	benzene reflux, 22 h	52	30 : 50 : 10 : 10
2	1.9 equiv. CF_3CO_2H –78 °C to room temp., 19 h	77	62 : 36 : 2 : 0
3	1.2 equiv. $TiCl_4$ –78 °C, 0.5 h [d])	97 [e]) (85)	94 : 0 : 3 : 3
4	2.7 equiv. $TiCl_4$ –78 °C to room temp., 6 h [f])	54	67 : 28 : 1 : 4

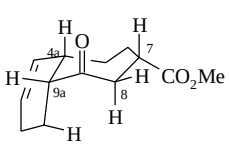
[a]) Reactions were conducted in CH_2Cl_2 in entries 2–4. [b]) Yield of purified product unless stated otherwise. [c]) Diastereomeric ratio of the crude product as determined by ^1H NMR analysis. [d]) Reaction was stopped by addition of water. [e]) Yield of crude product. [f]) Reaction was stopped by fast successive addition of NEt_3 and water.

For NMR analysis, diastereomer *cis*-**5a** could be separated and obtained in pure form out of a diastereomeric mixture. The proton signal assignments of this isomer were based on a $^1H/^1H$-COSY spectrum and homonuclear decoupling experiments. Diastereomer *cis*-**5b** was obtained and characterised in 86% diastereomeric purity after the thermal cycloaddition and careful chromatography. To secure the configurational assignments of all four isomers of cycloadduct **5** we also performed equilibration experiments on this compound. Specific epimerisation at C-9a of *cis*-**5a** by alumina produced a 2:1 mixture of *cis*-**5a** and *trans*-**5a**. The latter was characterised and stereochemically assigned in this mixture based on the significant signals. Equilibration of this mixture under stronger basic conditions with NaOMe afforded after 75 min a mixture of *cis*-**5a**, *trans*-**5a** and *trans*-**5b**, whereas all four diastereomers of **5** with *trans*-**5b** being the major component were obtained after a longer reaction period. This isomer was also characterised and assigned in the mixture.



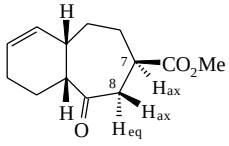
The assignments of the four isomers of **5** to the *cis* or *trans*-series was based on their ^{13}C NMR spectra. The bridgehead carbons of *trans*-fused 6/7-ring systems usually show absorption at higher ppm values than their *cis*-fused counterparts [14]. Thus, we assigned the two isomers with downfield bridgehead carbons to the *trans*-series. In addition, 9a-H of *cis*-**5a** exhibited only one diaxial coupling, which confirmed the *cis*-configuration and the depicted conformation of this isomer. The position of the methoxycarbonyl group in both *cis*-isomers is pseudoequatorial, which can be deducted from the diaxial couplings of 8-H_{ax} (albeit small in *cis*-**5a**) in both compounds. The assignment of both *cis*-isomers to the **a**- or **b**-series was based on the assignment of their respective 9a-epimers *trans*-**5a** and *trans*-**5b**. It was evident from the Dreiding models of both isomers that in *trans*-**5b** the methoxycarbonyl group should possess pseudoequatorial and in *trans*-**5a** rather pseudoaxial position. Thus, we identified the diastereomer with one large diaxial coupling of 8-H_{ax} (J=12.5 Hz) as *trans*-**5b**. The other *trans*-isomer that emerged from *cis*-**5a** after epimerisation at C-9a was assigned as *trans*-**5a**.

Our synthesis of the fused 6/7-ring system **5** *via* siloxycyclopropanes with an intramolecular Diels–Alder reaction as the key step exemplifies that this route can



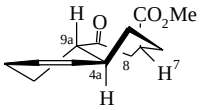
cis-**5a**

δ (C-4a) = 35.1
δ (C-9a) = 50.8
δ (9a-H) = 2.26 (ddd, J = 3, 6, 9 Hz)
δ (8-H_{ax}) = 2.75 (br. dd, J = 8, 12 Hz)
δ (8-H_{eq}) = 2.51 (dd, J = 3.5, 12 Hz)



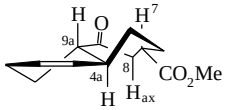
cis-**5b**

δ (C-4a) = 35.4
δ (C-9a) = 50.5
δ (8-H_{ax}) = 2.98 (dd, J = 11, 12.5 Hz)



trans-**5a**

δ (C-4a) = 38.5
δ (C-9a) = 52.2
δ (8-H) = 3.10 (ddd, J = 1.5, 4, 16 Hz)
2.57 (dd, J = 6.5, 16 Hz)



trans-**5b**

δ (C-4a) = 39.3 (or 41.1)
δ (C-9a) = 52.0
δ (8-H_{eq}) = 2.84 (ddd, J = 2, 4.5, 17 Hz)
δ (8-H_{ax}) = 2.70 (dd, J = 12.5, 17 Hz)

be potentially extended to the production of larger sized rings. The introduction of the diene moiety with the alkylation agent 1-iodo-3,5-hexadiene (**2**), however, proved to be troublesome as hydrogen iodide elimination from this substrate seems to be an inevitable side reaction. Once more, high stereocontrol of the cycloaddition reaction could be achieved with chelate forming $TiCl_4$, as was demonstrated in earlier examples with decatrienones [1, 8c].

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Experimental

All instrumentation has been described previously [8b].– ^1H (^{13}C) NMR spectra were recorded at 300 (75.5) MHz. – 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 mm.

Synthesis of Trienone 4

Methyl 1-[(3E,5)-Hexadienyl]-t-2-(trimethylsiloxy)-c-2-vinyl-r-1-cyclopropanecarboxylate (**3**)

To a solution of LDA (13.9 mmol, generated from diisopropylamine and *n*-BuLi at –78 °C, 20 min reaction time) in THF

(40 ml) at –78 °C was added methyl cyclopropanecarboxylate **1** (2.00 g, 9.33 mmol). After stirring for 2 h at –78 °C, 1,3-dimethylimidazolidin-2-one (DMEU, 3.20 g, 28.0 mmol) and (*E,E*)-1-iodo-3,5-hexadiene (**2**) (4.00 g, 19.2 mmol) were added, and stirring was continued at –78 °C for 14 h. The reaction was then warmed to –40 °C within 4 h, and stirred at this temperature for further 6 h. The reaction was quenched with satd. aqueous NH_4Cl solution (50 ml) and extracted with Et_2O (3 ×100 ml). The combined organic extracts were washed with water (300 ml), dried ($MgSO_4$) and concentrated. The residue was taken up in pentane (130 ml) to precipitate the diisopropylammonium salts. The colourless precipitate was filtered off, and the filtrate was concentrated. The residue (4.26 g) was chromatographed on alumina (hexane/EtOAc, 20:1) to afford a mixture (2.72 g) of the product **3**, iodo-hexadiene **2** and cyclopropane **1**. The mixture was separated by kugelrohr distillation. The starting materials **1** and **2** were removed at 60 °C/0.02 Torr, and the tetrasubstituted cyclopropane **3** was obtained at 100–150 °C/0.015 Torr as a colourless oil (1.20 g, 44%). – IR (neat): ν/cm^{-1} = 3095, 3010 (=C–H), 1725 (CO_2Me), 1650, 1600 (C=C), 1250 (Si–C). – ^{1}H NMR ($CDCl_3$): δ/ppm = 6.29 (dt, *J* = 10.5, 17 Hz, 1H, 5'-H), 6.05 (dd, *J* = 10.5, 15.5 Hz, 1H, 4'-H), 5.76 (dd, *J* = 10.5, 17 Hz, 1H, 1''-H), 5.70 (td, *J* = 7, 15.5 Hz, 1H, 3'-H), 5.27 (dd, *J* = 1.5, 17 Hz, 1H, *cis*-6'-H), 5.10 (dd, *J* = 1.5, 10.5 Hz, 1H, *trans*-6'-H), 5.09 (dd, *J* = 1.5, 17 Hz, 1H, *cis*-2''-H), 4.95 (dd, *J* = 1.5, 10.5 Hz, 1H, *trans*-2''-H), 3.63 (s, 3H, CO_2Me), 2.30–2.15, 1.59–1.50 (2 m, 3H, 1H, 1'-H, 2'-H), 1.80 (dd, *J* = 1.5, 6 Hz, 1H, *cis*-3-H), 1.03 (d, *J* = 6 Hz, 1H, *trans*-3-H), 0.15 (s, 9H, $SiMe_3$). – ^{13}C NMR ($CDCl_3$): δ/ppm = 172.3 (s, $\underline{C}O_2Me$), 137.0, 137.0, 134.3, 131.2 (4 d, C-1'', C-3', C-4', C-5'), 114.9, 114.4 (2 t, C-2'', C-6'), 65.2 (s, C-2), 51.8 (q, $CO_2\underline{Me}$), 37.1 (s, C-1), 30.5, 28.7, 24.6 (3 t, C-1', C-2', C-3), 0.8 (q, $SiMe_3$).

$C_{16}H_{26}O_3Si$	Calcd.:	C 65.26	H 8.90
(294.5)	Found:	C 64.70	H 9.03.

Methyl 2-[2-Oxo-3-butenyl]-(5E,7)-octadienoate (**4**)

To a solution of siloxycyclopropane **3** (1.00 g, 3.40 mmol) in CH_2Cl_2 (40 ml) was added at –25 °C $NEt_3 \cdot 3HF$ (2.60 g, 16.1 mmol). After stirring for 2 h at –25 °C the reaction was quenched with water (40 ml). The aqueous layer was extracted with CH_2Cl_2 (3 × 20 ml), and the combined organic phases were washed with water (100 ml), dried ($MgSO_4$) and concentrated. Trienone **4** was obtained as a pale yellow oil (0.755 g, 100%), which was used without further purification. – IR (neat): ν/cm^{-1} = 3080–3010 (=C–H), 2990–2860 (C–H), 1730 (CO_2Me), 1695, 1690 (C=O), 1610 (C=C). – ^{1}H NMR ($CDCl_3$): δ/ppm = 6.36 (dd, *J* = 10, 18 Hz, 1 H, 3'-H), 6.29 (td, *J* = 10.3, 17 Hz, 1H, 7-H), 6.24 (dd, *J* = 1.5, 18 Hz, 1H, *cis*-4'-H), 6.06 (ddd, *J* = 0.5, 10.3, 15 Hz, 1H, 6-H), 5.87 (dd, *J* = 1.5, 10 Hz, 1H, *trans*-4'-H), 5.65 (td, *J*=7, 15 Hz, 1H, 5-H), 5.14–4.97 (m, 2H, 8-H), 3.69 (s, 3H, CO_2Me), 3.08 (dd, *J* = 9, 17 Hz, 1H, 1'-H), 3.00–2.91 (m, 1H, 2-H), 2.69 (dd, *J* = 4.5, 17 Hz, 1H, 1'-H), 2.12 (dt, *J* = 7, 7.5 Hz, 2H, 4-H), 1.82–1.56 (m, 2H, 3-H). – ^{13}C NMR (75.5 MHz): δ/ppm = 198.4 (s, C=O), 175.6 (s, $\underline{C}O_2Me$), 137.2, 136.4 (2 d, C-3', C-7), 133.4 (d, C-6), 131.9 (d, C-5), 128.6 (t, C-4'), 115.4 (t, C-8), 51.6 (q, $CO_2\underline{Me}$), 39.5 (t, C-1'), 38.0 (d, C-2), 31.4, 30.0 (2 t, C-4, C-3).

Intramolecular Diels–Alder Reactions of Trienone 4 to Methyl 2,4a,5,6,7,8,9,9a-Octahydro-9-oxo-1*H*-benzocycloheptene-7-carboxylate (5)

Thermal Intramolecular Diels–Alder Reaction: A solution of trienone **4** (374 mg, 1.68 mmol) in benzene (80 ml) was refluxed for 22 h. After evaporation of the solvent *in vacuo*, the diastereomeric ratio of the crude product was determined by ^{1}H NMR analysis as *cis*-**5a**:*cis*-**5b**:*trans*-**5a**:*trans*-**5b** = 30:50:10:10. The crude product was subjected to distillation (kugelrohr, 120 °C/0.015 Torr) and repeated chromatography (chromatotron, first pentane/EtOAc, 4:1; second 10:1) to afford compound **5** in two fractions as colourless oils: the diastereomeric ratio of the first fraction was determined as *cis*-**5b**:*trans*-**5a**:*trans*-**5b** = 86:1:13 (65 mg, 17%); the second fraction contained all four isomers of **5** (129 mg, 35%).

Proton-catalysed Intramolecular Diels–Alder Reaction: To a solution of trienone **4** (240 mg, 1.08 mmol) in CH_2Cl_2 (40 ml) at –78 °C was added CF_3CO_2H (236 mg, 2.07 mmol). The reaction mixture was warmed slowly to room temp., and was left at this temperature for 12 h. The reaction was stopped by fast successive addition of NEt_3 (2 ml) and water (20 ml). The aqueous layer was extracted with CH_2Cl_2 (3 × 20 ml), the combined organic phases were washed with water (100 ml), dried ($MgSO_4$), and concentrated. Residual NEt_3 was removed *in vacuo*, and the resulting crude oil was filtered through a plug of silica gel (Et_2O). The diastereomeric ratio of the crude product was determined by ^{1}H NMR analysis as *cis*-**5a**:*cis*-**5b**:*trans*-**5a** = 62:36:2. Purification by distillation (kugelrohr, 120 °C/0.015 Torr) furnished product **5** as colourless oil (184 mg, 77%).

$TiCl_4$-catalysed Intramolecular Diels–Alder Reaction with aqueous work-up: To a solution of trienone **4** (300 mg, 1.35 mmol) in CH_2Cl_2 (30 ml) at –78 °C was added $TiCl_4$ (300 mg, 1.58 mmol). The reaction mixture was stirred for 0.5 h at this temperature, then quenched by addition of water (30 ml). The aqueous phase was extracted with CH_2Cl_2 (3 × 30 ml), the combined organic layers were washed with water (120 ml), dried ($MgSO_4$), and concentrated to afford crude **5** (291 mg, 85% conversion of **4**, *cis*-**5a**:*trans*-**5a**:*trans*-**5b** = 94:3:3).

$TiCl_4$-catalysed Intramolecular Diels–Alder Reaction with NEt_3 work-up: Trienone **4** (376 mg, 1.69 mmol) was treated with $TiCl_4$ (885 mg, 4.66 mmol) in CH_2Cl_2 (35 ml) as described above in the proton-catalysed reaction. The mixture was worked up after 6 h by addition of NEt_3 (2 ml) and water (20 ml) following the same procedure to afford crude cycloadduct **5** (*cis*-**5a**:*cis*-**5b**:*trans*-**5a**:*trans*-**5b** = 67:28:1:4). Pure **5** (204 mg, 54%) was obtained after chromatography (chromatotron, pentane/EtOAc, 4:1) as colourless oil.

*Isolation of pure cis-**5a***: Pure *cis*-**5a** could be obtained from a crude mixture of **5** (*cis*-**5a**:*cis*-**5b** ≈ 70:30), impurified with precursor **4** and polymers, after column chromatography on silica gel (hexane/EtOAc, 8:1).

Isomerisation of Cycloadduct 5

cis/trans Equilibration on Alumina: A mixture of *cis*-**5a** (150 mg, 0.675 mmol) and alumina (5 g) in CH_2Cl_2 (20 ml)

was stirred at room temp. for 6 d. After this period, the alumina was filtered off and washed with CH_2Cl_2 (100 ml). The filtrate was concentrated to afford a mixture of *cis*-**5a** and *trans*-**5a** (68:32, 100 mg, 67%).

Equilibration with NaOMe: Cycloadduct **5** (*cis*-**5a**:*trans*-**5a** = 68:32, 100 mg, 0.450 mmol) was stirred with NaOMe (0.36M in MeOH, 1.25 ml, 0.45 mmol) at room temp. for 75 min. After this period the reaction was stopped by addition of satd. aqueous NH_4Cl (3 ml). The mixture was extracted with Et_2O (3 × 6 ml), the combined organic phases were washed with water (18 ml), dried ($MgSO_4$), and concentrated to afford **5** (100 mg, 100%) as a mixture of diastereomers *cis*-**5a**, *trans*-**5a** and *trans*-**5b** (28:33:39). This mixture was again treated with NaOMe (0.36M in MeOH, 2.50 ml, 0.90 mmol) for 53 h, and provided after the same work-up procedure an equilibrium mixture of isomers *cis*-**5a**, *cis*-**5b**, *trans*-**5a** and *trans*-**5b** (23:3:16:58, 41mg, 41%).

Analytical and Spectroscopic Data of Cycloadduct 5

Obtained from a mixture of isomers.
IR (neat): ν/cm^{-1} = 3020 (=C–H), 2940, 2840 (C–H), 1735 (CO_2Me), 1700 (C=O).

$C_{13}H_{18}O_3$	Calcd.:	C 70.24	H 8.16
(222.3)	Found:	C 70.41	H 8.32.

^{1}H NMR (C_6D_6) of *Methyl (4aβ,7α,9aβ)-2,4a,5,6,7,8,9,9a-Octahydro-9-oxo-1H-benzocycloheptene-7-carboxylate* (*cis*-**5a**)

Assignments are based on a ^{1}H/^{1}H COSY spectrum and homodecoupling experiments: δ/ppm = 5.59–5.52 (m, 1H, 3-H), 5.39 (tdd, J = 2, 4, 10 Hz, 1H, 4-H), 3.39 (s, 3H, CO_2Me), 2.75 (br.dd, J = 8, 12 Hz, 1H, 8-H_{ax}), 2.51 (dd, J = 3.5, 12 Hz, 1H, 8-H_{eq}), 2.51–2.43 (m, 1H, 7-H), 2.26 (ddd, J = 3, 6, 9 Hz, 1H, 9a-H), 2.13 (m_c, 1H, 4a-H), 1.98–1.78, 1.77–1.49, 1.41–1.27 (3 m, 3H, 3H, 2H, 1-H, 2-H, 5-H, 6-H).

^{1}H NMR ($CDCl_3$) of *Methyl (4aβ,7β,9aβ)-2,4a,5,6,7,8,9,9a-Octahydro-9-oxo-1H-benzocycloheptene-7-carboxylate* (*cis*-**5b**)

Characterised in a mixture of diastereomers *cis*-**5b**:*trans*-**5a**:*trans*-**5b** = 86:1:13: δ/ppm = 5.81–5.67 (partially obscured m, 2H, 3-H, 4-H), 3.69 (s, 3H, CO_2Me), 2.98 (dd, J = 11, 12.5 Hz, 1H, 8-H_{ax}), 2.62 (td, J = 2, 11 Hz, 1H, 8-H_{eq}), 2.75–2.59 (partially obscured m, 2H), 2.49 (ddt, J = 2, 4.5, 12.5 Hz, 1H, 7-H), 2.18–1.88 (m, 3H), 1.99 (ddd, J = 2.5, 5.5, 11 Hz, 1H), 1.80–1.65, 1.26–1.13 (2 m, 2H, 1H), 1.28 (ddd, J = 5.5, 11.5, 13.5 Hz, 1H).

^{1}H NMR ($CDCl_3$) of *Methyl (4aα,7β,9aβ)-2,4a,5,6,7,8,9,9a-Octahydro-9-oxo-1H-benzocycloheptene-7-carboxylate* (*trans*-**5a**)

Characterised in a mixture of diastereomers *cis*-**5a**:*trans*-**5a** = 68:32: δ/ppm = 5.71–5.68, 5.41 (obscured m, br. d, J = 10 Hz, 1H each, 3-H, 4-H), 3.74 (s, 3H, CO_2Me), 3.10 (ddd, J = 1.5, 4, 16 Hz, 1H, 8-H), 3.01–2.95 (m, 1H, 7-H), 2.57 (dd, J = 6.5, 16 Hz, 1H, 8-H), 1.80–1.65, 1.36, 1.26–1.13 (m, br. q, m, J = 12.5 Hz, 2H, 7 H, 1H, 9a-H, 4a-H, 1-H, 2-H, 5-H, 6-H).

^{1}H NMR ($CDCl_3$) of *Methyl (4aα,7β,9aα)-2,4a,5,6,7,8,9,9a-Octahydro-9-oxo-1H-benzocycloheptene-7-carboxylate* (*trans*-**5b**)

Characterised in a mixture of diastereomers *cis*-**5a**:*cis*-**5b**:*trans*-**5a**:*trans*-**5b** = 23:3:16:58: δ/ppm = 5.75–5.70, 5.45–5.39 (2 partially obscured m, 1H each, 3-H, 4-H), 3.70 (s, 3H, CO_2Me), 2.84 (ddd, J = 2, 4.5, 17 Hz, 1H, 8-H_{eq}), 2.70 (dd, J = 12.5, 17 Hz, 1H, 8-H_{ax}), 2.65–2.36, 2.32–2.21, 2.15–1.19, 1.53 (3 partially obscured m, br. q, J = 12.5 Hz, 1H, 1H, 8H, 1H, 7-H, 9a-H, 4a-H, 1-H, 2-H, 5-H, 6-H).
For ^{13}C-NMR data of all four diastereomers of **5** see Table 2.

Table 2 ^{13}C NMR (75.5 MHz) data of cycloadduct **5**; δ

C	*cis*-**5a**	*cis*-**5b**	*trans*-**5a**	*trans*-**5b**
C-9 (s)	212.5	211.5	212.6	212.6
CO_2Me (s)	174.3	174.5	174.7	175.0
C-4 (d)	130.0	130.5	131.3	130.9
C-3 (d)	126.7	126.7	126.9	126.7
CO_2*Me* (q)	51.5	51.7	51.8	51.9
C-9a (d)	50.8	50.5	52.2	52.0
C-8 (t)	43.2	43.2	44.1	46.3
C-7 (d)	40.2	43.3	38.53 [a])	41.1 [a])
C-4a (d)	35.1	35.4	38.47 [a])	39.3 [a])
C-5, C-1, C-6, C-2 (4 t)	29.4, 29.3, 23.4, 22.6	33.0, 30.4, 24.3, 18.8	34.0, 29.8, 23.9, 23.7	37.3, 31.3, 23.9, 23.8

[a]) Assignments are interchangeable within the column.

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