Cycloaddition behavior of unsymmetric cyclopentadienone. Peri- and regio-selectivities

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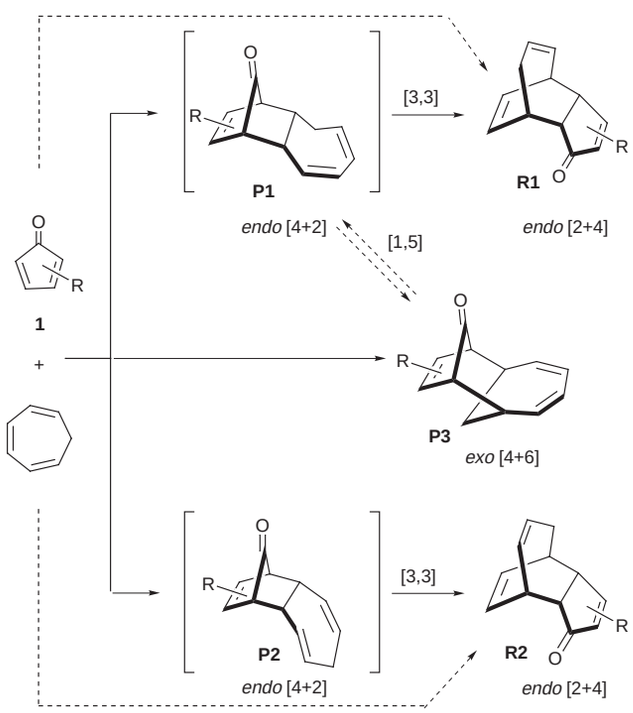
An asymmetrically substituted cyclopentadienone, 2-methoxycarbonyl-5-methyl-3,4-diphenylcyclopentadienone **1a**, was synthesized and cycloadditions of compound **1a** with various unsaturated compounds involving conjugated medium-ring polyenes were investigated. The cycloaddition behavior was analyzed by frontier molecular orbital (FMO) theory, indicating that the reactivity, stereo- and regio-selectivities observed are entirely consistent with the FMO predictions.

Introduction

Cyclopentadienones **1** are reactive and versatile diene components having very low lowest unoccupied molecular orbital (LUMO) energy levels. However, there are not many cyclopentadienones existing as monomers. Kanematsu and Harano made a systematic study of the pericyclic reactions of some monomeric cyclopentadienones with general dienophiles and conjugated medium-ring polyenes, establishing the possible reaction pathways as outlined in Scheme 1, which involve all of



Scheme 1

the thermally allowed cycloadducts from dienones **1** and conjugated seven-membered polyenes by either a direct or an indirect pathway.[1] The pericyclic reaction behavior has been rationalized in terms of frontier molecular orbital (FMO) interactions.[2]

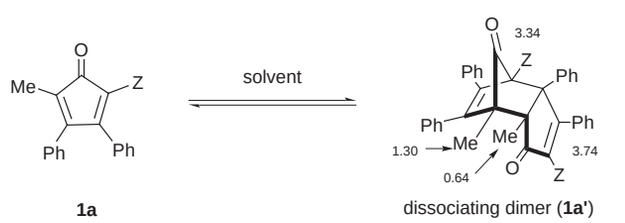
In these previous studies, the reaction behavior of symmetrically substituted cyclopentadienones has been extensively investigated. However, cycloadditions of asymmetrical cyclopentadienones have been investigated far less and their regioselectivities have not yet been clarified.[3]

These backgrounds prompted us to investigate the pericyclic reactions of asymmetrical cyclopentadienones with unsaturated compounds involving conjugated medium-ring polyenes. In the present investigation, we prepared an asymmetrical cyclopentadienone, 2-methoxycarbonyl-5-methyl-3,4-diphenylcyclopentadienone **1a**, and qualitatively analyzed its reaction behavior in terms of FMO theory. The results are discussed here in detail in comparison with previous works.

Results

Cycloaddition of dienone 1a with general olefins

The cyclopentadienone **1a** was prepared according to the synthetic method[4] for 2,5-bismethoxycarbonyl-3,4-diphenylcyclopentadienone **1b** by application of more severe reaction conditions than for analogue **1b** and isolated as a monomer (red solid), which, in solution at rt, gradually transformed into an equilibrium mixture (**1a** : **1a**′ = 2 : 1) of monomer **1a** and the [4 + 2] cycloadduct dimer **1a**′ (see Scheme 2). In comparison



Scheme 2

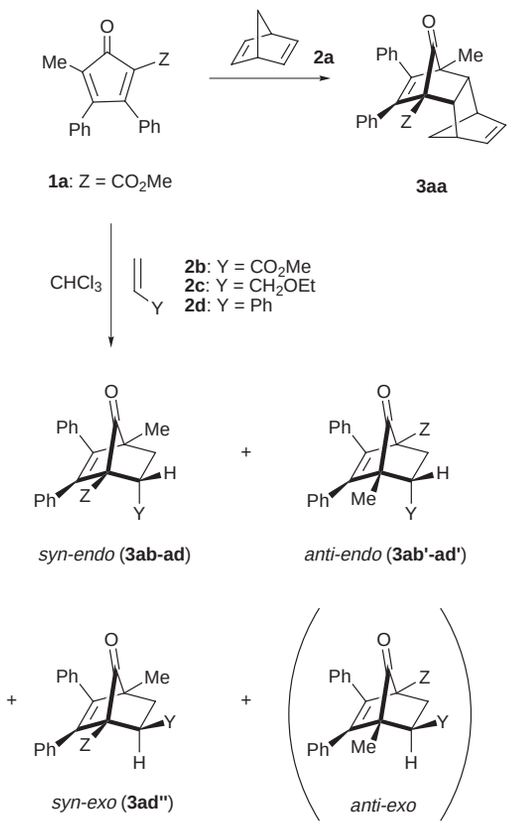
with the ^{1}H NMR spectral data of those of structurally analogous compounds, the ^{1}H NMR spectrum was interpreted as being due to a mixture of compounds **1a** and **1a**′. The *syn*-orientation of the phenyl and methyl groups at the ring juncture of dimer **1a**′ was determined on the basis of the high-field shift of the methyl group due to the phenyl ring-current effect.

Heating of a mixture of dienone **1a** and trinorbornadiene **2a** in $CHCl_3$ at 50 °C gave the *endo-exo* cycloadduct **3aa** in 94% yield (see Scheme 3). The IR spectrum of product **3aa** exhibited a strained-ring carbonyl and an ester carbonyl at 1772 cm^{-1} and 1728 cm^{-1}, respectively. The ^{1}H NMR spectrum showed an asymmetrical spectral pattern due to asymmetrically substituted cyclopentadienone moiety. The bridged methylene proton signals appeared as an AB quartet at δ 1.25 and 2.40 (J 9.2 Hz). The high-field shift of the former proton due to the stilbene ring-current effect suggested the structure of *endo-exo* [4 + 2] cycloadduct. The *exo*/*endo* nature of the cycloadducts was

Table 1 Reaction conditions and products for the reaction of dienone **1a** with dienophiles **2a**–**d** in $CHCl_3$

Dienophile	Temp. (*T*/°C)	Time (*t*/h)	Yield (%)	Product proportions[a]		
2a	50	1.0	94 (**3aa**)			
2b	50	0.5	67	1 (**3ab**)	8.8 (**3ab′**)	0
2c	reflux	12.0	75	8 (**3ac**)	1 (**3ac′**)	0
2d	50	1.5	54	7 (**3ad**)	2.5 (**3ad′**)	1 (**3ad″**)

[a] The product proportions were determined by integration of the ^1H signals of the 270 MHz NMR spectrum. See Scheme 3.



Scheme 3

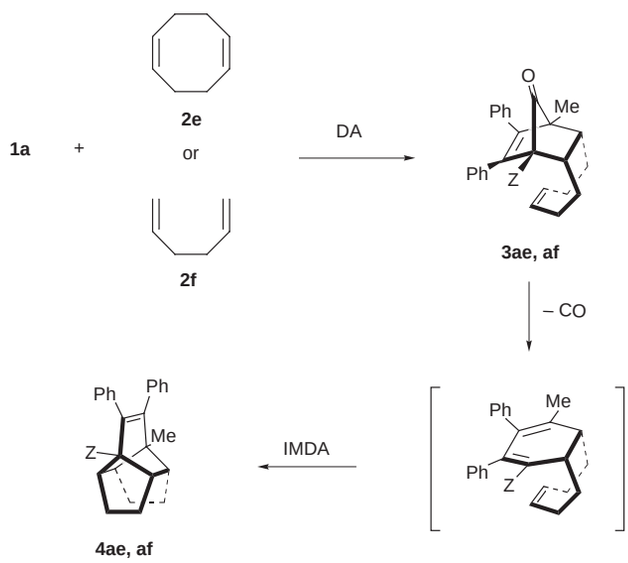
determined on the basis of the general rule of heteronuclear multiple-bond connectivity (HMBC) spectral correlation for the bicyclo[2.2.1]hepten-7-one skeleton.[5]

Similarly, the cycloadditions of substrate **1a** with methyl acrylate **2b**, allyl ethyl ether **2c** and styrene **2d** were carried out (Table 1). The structures of the cycloadducts were determined by comparison of the IR, ^{13}C NMR and ^1H NMR spectral data with those of the known cycloadducts of olefins **2b**–**d** and dienone **1b** or 2,5-diethyl-3,4-diphenylcyclopentadienone **1c**.[6] The *endo*/*exo* and *anti*/*syn* natures of the product were established by inspection of the HMBC spectrum.[5] The product proportions due to the *endo*/*exo* and *syn*/*anti* isomers were determined by inspection of the ^1H NMR spectra of the crude products (Table 1).

In the cycloadditions of dienone **1a** with olefin **2b**–**d**, regioisomeric product may be produced for the *endo* and *exo* isomers (Table 1). In the case of acrylate **2b**, the *syn*-*endo* **3ab** and *anti*-*endo* **3ab′** cycloadducts were formed in the ratio 1 : 8.8, wherein *syn* and *anti* are defined with regard to the arrangement of the ester groups of both addends. The ratio of the *syn*-*endo* **3ac** and *anti*-*endo* **3ac′** cycloadducts from **2c** is 8 : 1. The cycloaddition of dienone **1a** with styrene **2d** gave *syn*-*endo* **3ad**, *syn*-*exo* **3ad″** and *anti*-*endo* **3ad′** cycloadducts (**3ad** : **3ad″** : **3ad′** = 7 : 1 : 2.5 and *syn* : *anti* = 3.3 : 1).

Cycloaddition of 1a with nonoconjugated dienes

In our previous paper,[7] we reported that cycloaddition of compound **1b** with nonconjugated dienes such as cycloocta-1,5-diene **2e** and hexa-1,5-diene **2f** gave the Diels–Alder (DA) adducts, which on heating above 170 °C underwent sequential pericyclic reactions [decarbonylation and intramolecular DA (IMDA) reaction] to give the double DA (DDA) adducts. Similarly, dienone **1a** cycloadded to dienes **2e** and **2f** to give the DDA adducts **4ae** and **4af**, respectively (see Scheme 4).



Scheme 4

The decarbonylation rate of the DA adducts was affected by the bridgehead substituents. In the case of the DA adduct of dienone **1a**, prolonged or higher temperature heating was needed for the completion of decarbonylation leading to the DDA adduct. The DA adducts of compound **1c** and **2e** did not undergo decarbonylation under the reaction conditions with dienones **1a** and **1b**.

Table 2 shows the reaction conditions and yields of the DDA adducts prepared by one-pot procedures *via* three-step sequential pericyclic reactions.

Cycloaddition of dienone 1a with conjugated polyenes

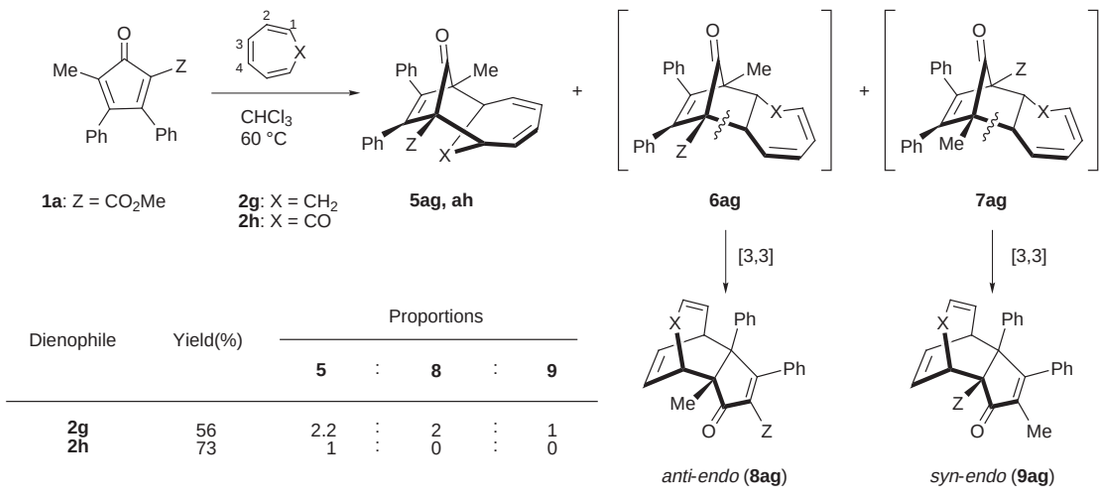
Cycloaddition of dienone **1a** with cycloheptatriene **2g** proceeded in $CHCl_3$ at 60 °C to afford the *exo* [4 + 6] **5ag**, *anti*-*endo* [2 + 4] **8ag** and *syn*-*endo* [2 + 4] **9ag** cycloadducts, in which *syn* and *anti* are defined in regard to the arrangement of the ester (Z) and the methylene (X) moieties. The cycloadducts **8ag** and **9ag** were considered to be formed from the [3,3]-sigmatropic rearrangement of the corresponding *anti*-*endo* [4 + 2] **6ag** and *syn*-*endo* [4 + 2] **7ag** cycloadducts, respectively (Scheme 5).

The formation proportions of the cycloadducts **5ag**, **8ag** and **9ag** are 2.2 : 2 : 1. The structures of the cycloadducts **5ag** and **8ag** were determined by comparison of their IR, ^1H and ^{13}C NMR spectral data with those of the known cycloadducts **5bg** and **8bg** derived from cycloaddition of dienone **1b** with cycloheptatriene **2g**.[1b] The important assignments of the ^1H and ^{13}C NMR spectral data of adducts **5ag** and **8ag** are shown here with the structural formulae.

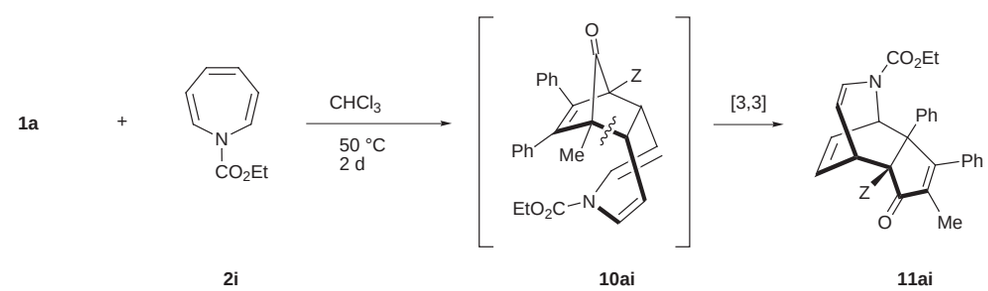
Cycloaddition of dienone **1a** with tropone **2h** only gave the *exo* [4 + 6] cycloadduct **5ah**.

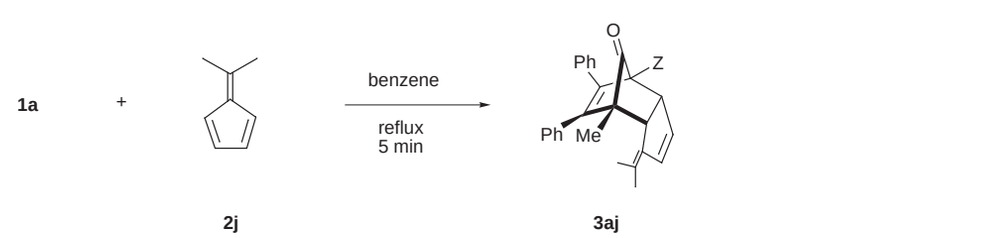
Table 2 Double Diels–Alder adducts from the cycloadditions of dienones **1** and dienophiles **2e**,**f** (Scheme 4)

Diene	Dienophile	Temp. (*T*/°C)	Time (*t*/h)	Product	Yield (%)	Ref.
1a	**2e**	180	10	**4ae**	25	
1b	**2e**	170	10	**4be**	58	7*a*
1c	**2e**	200	44	**4ce**	20	7*b*
1a	**2f**	180	5	**4af**	4	
1b	**2f**	150	8	**4bf**	70	7*a*



Dienophile	Yield(%)	Proportions 5 : 8 : 9
2g	56	2.2 : 2 : 1
2h	73	1 : 0 : 0





Scheme 5

Cycloaddition of dienone **1a** with *N*-ethoxycarbonyl-1*H*-azepine **2i** proceeded in $CHCl_3$ at 50 °C to afford the *endo* [2 + 4] cycloadduct **11ai**. The structure of the cycloadduct **11ai** was determined by comparison of the IR, ^1H and ^{13}C NMR spectral data with those of the known cycloadduct **11bi** derived from cycloaddition of dienone **1b** with carbamate **2i**.[1b] The important assignments of the ^1H and ^{13}C NMR spectral data of adduct **11ai** are shown above. The cycloadduct **11ai** was assumed to be formed *via* [3,3]-sigmatropic rearrangement of the corresponding *endo* [4 + 2] intermediate **10ai** at the C(3)–C(4) position (see Scheme 5).

Cycloaddition of dienone **1a** with 6,6-dimethylfulvene **2j** gave the *endo* [4 + 2] cycloadduct **3aj**.

Cycloaddition reactivity

To compare the cycloaddition reactivity of dienone **1a** with those of analogues **1b** and **1c**, the reaction rates were measured by following the decrease of dienone **1a** in its reaction with compound **2a**. The pseudo-first-order rate constants are summarized in Table 3 which includes the relative rates of dienones **1b** and **1c**. The reactivity of compound **1a** was found to be intermediate between those of dienones **1b** and **1c**.

Discussion

The reaction behavior of dienone **1a** is considered to fall under the category of inverse-type cycloaddition[8] in which the interaction between the LUMO of dienone **1a** and the HOMO of dienophiles is dominant (see Fig. 1). The cycloaddition reactivity of dienone **1a** deduced from the cycloaddition conditions and the kinetic data is clearly affected by the 2,5-substituents, being in accord with the FMO prediction (see Table 4).

The exclusive formation of the *endo-exo* cycloadduct **3aa**

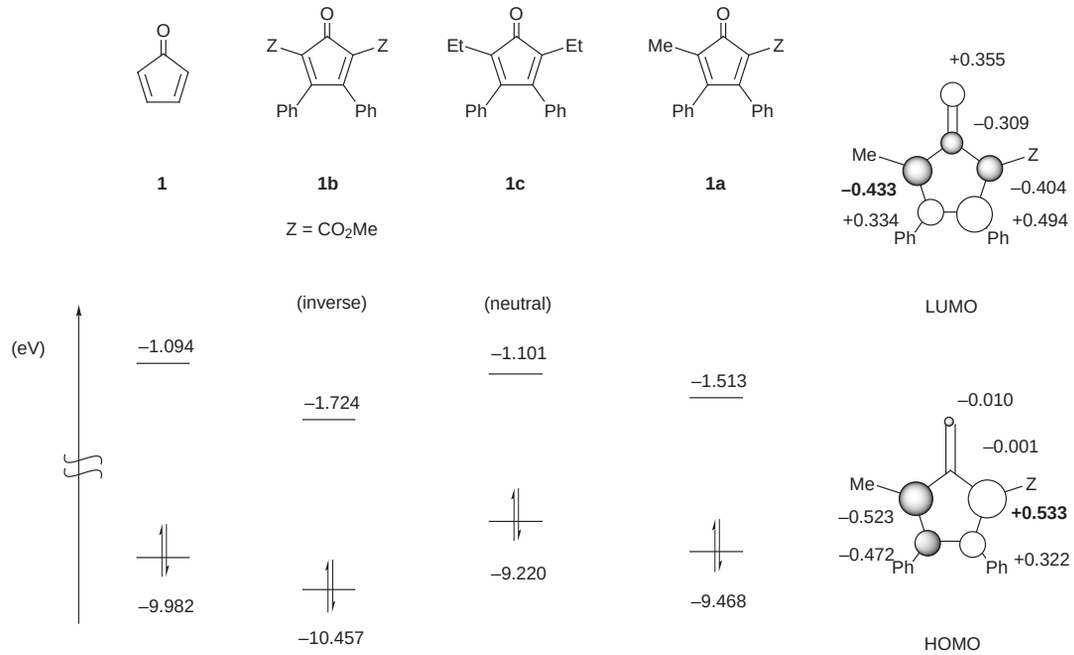
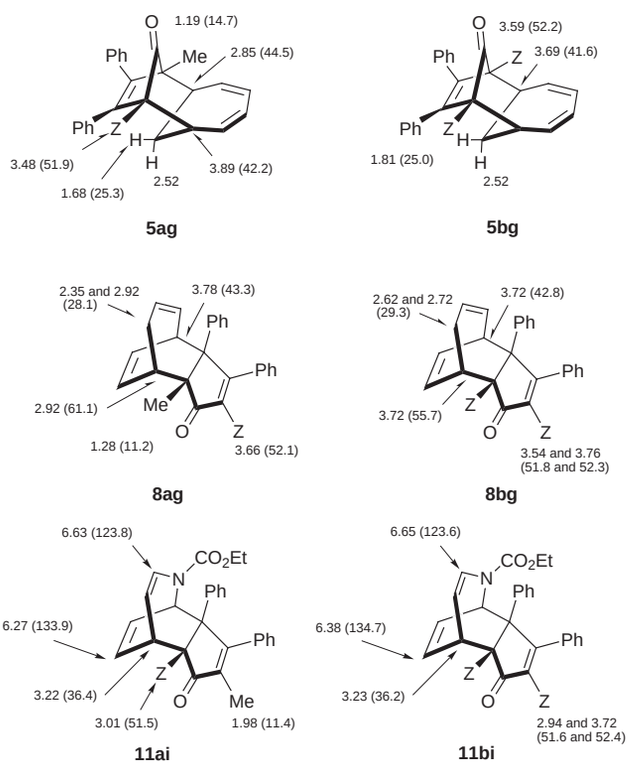


Fig. 1 PM3-Calculated FMO energy levels of cyclopentadienones **1a**–**c** and coefficients of compound **1a**.

Table 3 Pseudo-first-order rate constants (k) for cycloadditions of dienones **1a**–**c** with trinorbornadiene **2a** in benzene at 40 °C

Dienone	$k \times 10^{-4}$ (s^{-1})	k_{1b}/k_{1a}	k_{1c}/k_{1a}
1a	1.73		
1b	19.4	11.2	
1c	0.04		2.3×10^{-2}



Comparison of δ_H and δ_C NMR (in parentheses) spectral data of adducts **5ag**, **8ag** and **11ai** with those of analogues **5bg**, **8bg** and **11bi**.

from cycloaddition of dienone **1a** with compound **2a** can be accounted for by asymmetrical *p*-orbitals of dienophile **2a** in which the *exo*-oriented *p* lobes are larger than the *endo* ones owing to σ–π interactions between the adjacent strained σ bonds and the *p*-orbitals.[9]

In general, the regioselectivity obeyed the rule of large–large/small–small interaction of the coefficients at the reaction sites.[2b] In the cycloaddition with compound **2b**, the interaction between the HOMO of dienone **1a** and the LUMO of dienophile **2b** is dominant. Although the difference in the HOMO coefficients of the reaction site is small (C-2: −0.523 and C-5: 0.523), the *anti-endo* cycloadduct is dominant, in accord with the FMO prediction (Table 4). Involvement of the secondary orbital interaction[10] in the calculation of the perturbation equation also supports the FMO prediction based on the primary interactions.

In the cycloaddition with styrene **2d**, although the steric repulsion between the ester and phenyl substituents is operative, the cycloadduct with a *syn* relationship between the ester and phenyl groups is the main product. The dominant FMO interaction as inverse-type cycloaddition accounts for the regioselectivity observed (see Fig. 2).

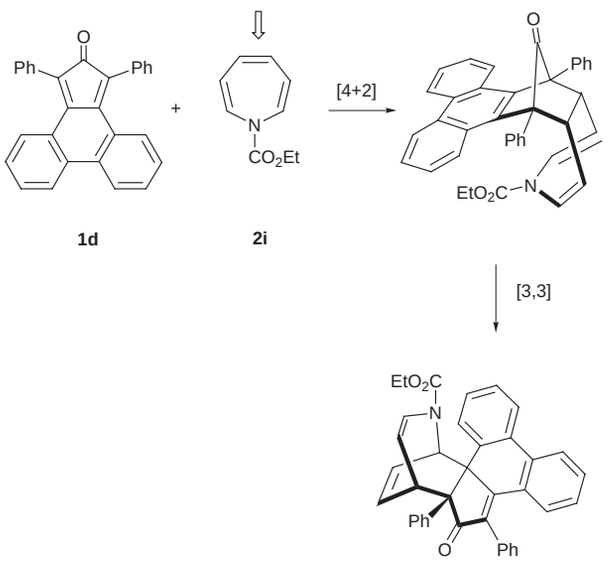
The regioselectivity observed in adducts **3ac** and **3af** can be explained in terms of the FMO theory.

As described above, the overall pericyclic reaction behavior of dienones **1** toward cycloheptatriene **2g** is still obscure. In Scheme 1, the **R1**-type cycloadduct has been isolated but the corresponding primary cycloadduct **P1** has not yet been isolated. On the other hand, in the reaction of phencyclone **1d** with carbamate **2i**, the primary [4 + 2] cycloadduct (**P2**-type) at the C(3)–C(4) position was isolated and its [3,3]-sigmatropic rearrangement to the [2 + 4] cycloadduct (**R2**-type) was studied (see Scheme 6).[1d] The same type of cycloadduct was isolated in the reaction of carbamate **2i** with dienones **1a** and **1b**.[1e]

To investigate the presence of the primary [4 + 2] cycloadduct (**P1**-type) derived from attack at the C(1)–C(2) position in the crude reaction mixture of substrates **1a**,**b** and **2g**, time-course experiments by ^{1}H NMR and TLC analyses were carried out. However, we could not recognize any intermediate ascribable to the primary cycloadduct even under very mild reaction conditions. At first, this result seemed to indicate that the [2 + 4] cycloadduct is formed from the direct cycloaddition of dienone **1a** and cycloheptatriene **2g**, in which dieone **1a** acts as 2π rather than, as is more usual, a 4π component (see Scheme 7). If this assumption is true, the site selectivity of compound **1a** should be reversed. Analysis of the LUMO coefficients of dienone **1a** predicts the dominant formation of a different type

Table 4 FMO energy levels of dienone **1a** and dienophiles **2** and reaction type of the corresponding cycloaddition

	Diene	Dienophile							
	1a	**2b**	**2c**	**2d**	**2f**	**2g**	**2h**	**2i**	**2j**
Orbital levels									
HOMO	−9.47	−11.06	−10.03	−9.13	−10.06	−8.95	−9.55	−8.82	−9.01
LUMO	−1.51	−1.43	1.08	−0.13	1.06	−0.04	−0.63	−0.47	−0.62
Reaction type		normal	inverse	inverse	inverse	inverse	inverse	inverse	inverse



1d **2i**

Scheme 6

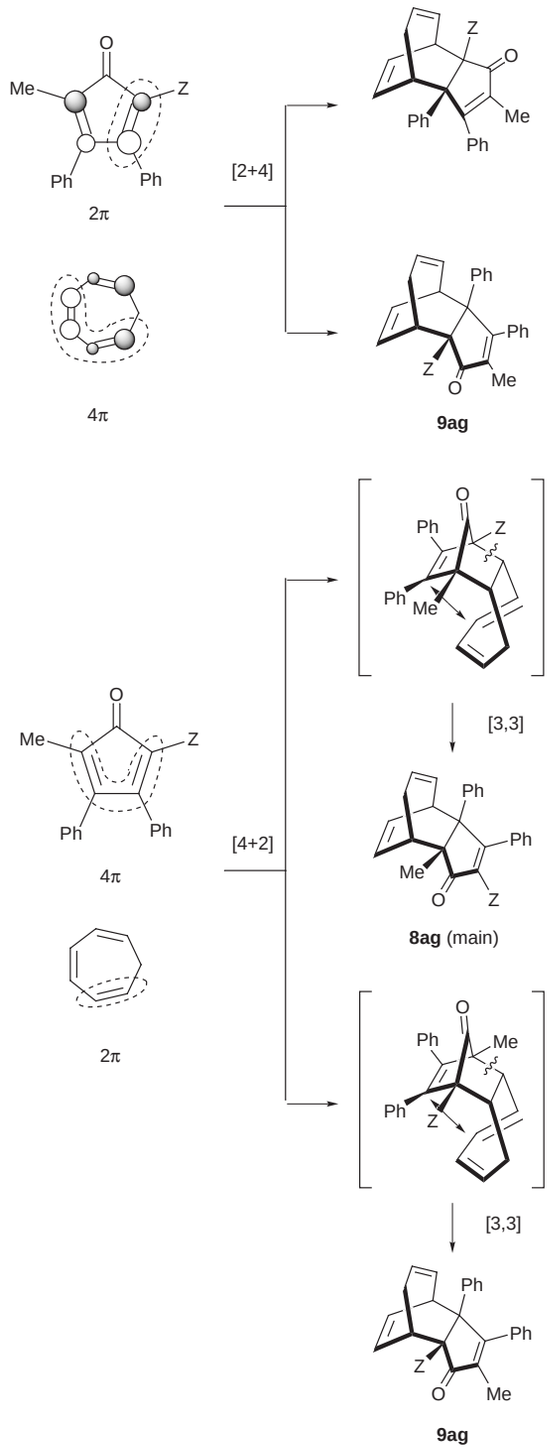
of [2 + 4] cycloadduct, compound **9ag**. In contrast, the predominant formation of [2 + 4] cycloadduct **8ag** *via* initial **P1**-type [4 + 2] cycloadduct at the C(1)–C(2) position is consistent with theoretical predictions as discussed above. These suggest that the **P1**-type cycloaddition occurs according to the large–large/small–small interaction rule followed by relatively fast [3,3]-sigmatropic rearrangement.

In the cycloaddition of dienone **1a** with cycloheptatriene **2g**, the *endo* [4 + 2] cycloaddition at the C(1)–C(2) position may produce the *syn* and *anti* regioisomers as shown in Scheme 5. The predominant formation of the *anti* isomer (with respect to the ester and methylene groups) can be explained by FMO theory.[10]

In the cycloaddition of cyclopentadienones with cycloheptatriene **2g**, the presence of the [3,3]-sigmatropic rearrangement product (**R2**-type) of the *endo* [4 + 2] cycloadduct at the C(3)–C(4) position (**P2**-type) is puzzling. Inspection of the coefficients of compound **2g** indicates that the magnitudes of the C(3) and C(4) coefficients (+0.429) are almost the same as those of C(1) and C(6) (−0.423), indicating that both *endo* [4 + 2] attack at the C(3)–C(4) position and *exo* [4 + 6] attack are similarly preferable (see Fig. 2). In the cycloadditions of dienones **1a**–**c** with triene **2g**, the absence of the **R2**-type cycloadduct is assumed to be due to the nonbonded H/H interaction between the methylene hydrogens of thiene **2g** and two phenyl *ortho*-hydrogens of dienones **1a**–**c** in the transition state (Fig. 3). This assumption is supported by the fact that the formation of similar types of [4 + 2] cycloadducts has been observed with carbamate **2i** which does not have sterically hindered methylene hydrogens at the 1-position.

In the formation of the *exo* [4 + 6] cycloadduct, the σ–π interaction[11] between the methylene hydrogen of cycloheptatriene **2g** and C(3) and C(4) seems to be operative in the transition state (Fig. 4).

In the case of tropone **2h**, the formation of the *exo* [4 + 6]



Scheme 7

cycloadduct can be accounted for in terms of FMO theory, in which the largest coefficients are found for the C(2) and C(7) positions.

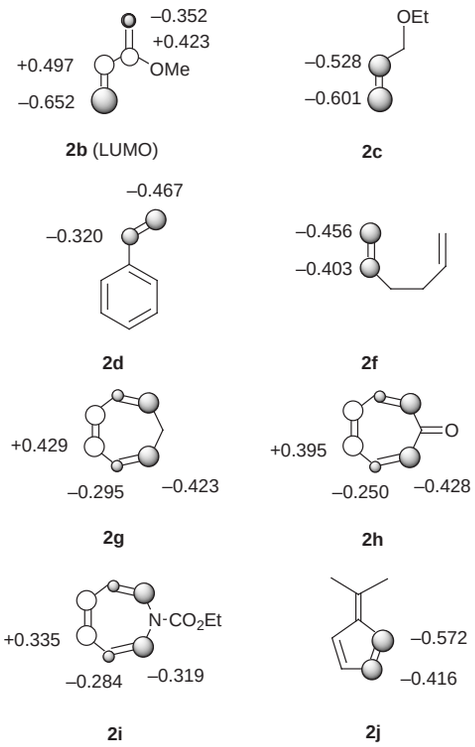


Fig. 2 HOMO coefficients of asymmetrical dienophiles **2b**–**d**, **2f**–**j** calculated by PM3.

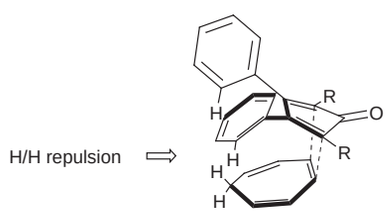


Fig. 3 Schematic representation of H/H interaction in the cycloaddition of dienones **1a**–**c** with cycloheptatriene **2g**.

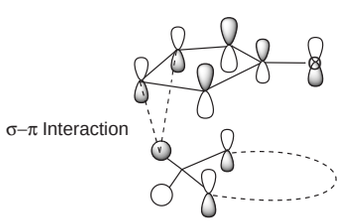


Fig. 4 Schematic representation of σ–π interaction in the cycloaddition of dienones **1a**–**c** with cycloheptatriene **2g**.

In summary, the regioselectivities in the cycloadditions of the cyclopentadienone **1a** with various unsaturated compounds involving conjugated medium-ring polyenes could be rationalized by FMO theory. The periselectivity toward cycloheptatriene **2g** is explained on the basis of FMO considerations plus additional factors. The site selectivity of dienone **1a** toward triene **2g** seems to give us a clue as to the formation mechanism of the [3,3]-sigmatropic rearrangement products.

Experimental

Mps were measured on a Yanagimoto MP-J2 apparatus and are uncorrected. IR spectra were taken with a Hitachi 270-30 spectrophotometer. High-resolution mass spectra (HRMS) were taken with a JEOL JMS-DX303HF spectrometer. ^{1}H NMR, ^{13}C NMR and HMBC spectra were taken with JEOL JNM-EX 270 (270 MHz) and JNM-A 500 (500 MHz) spectrometers for ~10% solutions with $SiMe_4$ (TMS) as an internal standard; chemical shifts are expressed as δ-values and the coupling constants (J) are expressed in Hz. UV spectra were recorded on a Simadzu UV-2500PC spectrophotometer.

Materials

2,5-Bis(methoxycarbonyl)-3,4-diphenylcyclopentadienone[4] **1b** and 2,5-diethyl-3,4-diphenylcyclopentadienone[12] **1c** were prepared according to the previously reported methods.

2-Methoxycarbonyl-5-methyl-3,4-diphenylcyclopentadienone 1a

A mixture of benzil (21.0 g, 0.1 mol), methyl propionylacetate (26.0 g, 0.2 mol) and potassium hydroxide (1.5 g) in 160 ml of methanol was stirred at reflux for 48 h. The solvent was then removed under reduced pressure. The residue was diluted with benzene and the solution was washed three times with water. The organic layer was dried ($MgSO_4$), filtered, and the solvent was removed under reduced pressure. The residual oils was then dehydrated as described in the following procedure.

The carbinol (30.2 g, 0.09 mol) was added to 54.4 ml of acetic anhydride containing 3 drops of concentrated sulfuric acid. The mixture were stirred for 5 min at rt. The solution was added to 610 ml of water with stirring. The precipitated oil was taken up in benzene. The organic layer was dried ($MgSO_4$), filtered, and the solvent was removed under reduced pressure. The solid was collected and red crystals of *title compound* **1a** (18.9 g, 69%) were obtained: red powder, mp 137–139 °C (Found: M^+, 304.1092. $C_{20}H_{16}O_3$ requires M, 304.1087); ν_{max}(KBr)/cm^{-1} 1708 (C=O); δ_H(500 MHz; $CDCl_3$) 1.89 (3H, s, Me), 3.69 (3H, s, OMe) and 6.89–7.36 (10H, m, ArH); δ_C(125 MHz; $CDCl_3$) 9.3 (Me), 52.0 (OMe), 127.8, 128.3, 128.9, 129.2, 129.3 and 130.3 (ArC), 117.6, 127.4, 132.3, 132.5, 151.8 and 163.3 (quaternary C), 167.8 (ester C=O) and 197.3 (C=O); *m*/*z* (EI) 304 (M^+, 58%); λ_{max}(*n*-hexane)/nm 428 (ε/dm^3 mol^{-1} cm^{-1} 13.8) and 312 (1394.4).

Compound **1a′**: δ_H(500 MHz; $CDCl_3$) 0.64 and 1.30 (6H, s, methyl × 2), 3.34 and 3.74 (6H, s, OMe × 2) and 7.00–7.39 (10H, m, ArH); δ_C(125 MHz; $CDCl_3$) 8.82 and 17.5 (methyl × 2), 51.3 and 51.6 (OMe × 2), 59.7, 62.1, 66.2 and 69.1 (quaternary carbon), 126.5, 126.8, 127.3, 127.4, 127.6, 128.3, 128.5, 128.7, 128.8, 129.4, 129.6, 129.9, 130.3, 130.8 and 131.5 (aromatic CH), 131.9, 132.0, 133.5, 138.2, 138.3, 143.1 and 143.6 (quaternary carbon), 165.3 and 171.3 (ester C=O), 194.1 (enone C=O) and 202.0 (bridge C=O).

Cycloadditions of dienone 1a with dienophiles (general procedure)

A mixture of dienone **1a** (0.5 g, 1.64 mmol) and an excess of dienophile (4.93–16.4 mmol) in $CHCl_3$ (1 ml) was heated at 50 °C until the red color disappeared. The solvent was removed under reduced pressure. The residual oil was treated with methanol to give a solid, which was collected, and recrystallized from EtOH to give the cycloadduct as prisms.

Each cycloadduct was isolated as a mixture of stereoisomers and its formation ratio was determined by 270 MHz ^{1}H NMR spectroscopy.

The following compounds were obtained by essentially the same procedure as described above.

(1α,4α,4aβ,5β,8β,8aβ)-5-Methoxycarbonyl-8-methyl-6,7-diphenyl-1,4,4a,5,8,8a-hexahydro-1,4:5,8-dimethanonaphthalen-9-one 3aa. *Prisms* (94%), mp 155–156 °C (from EtOH) (Found: C, 81.8; H, 6.1. $C_{27}H_{24}O_3$ requires C, 81.79; H, 6.10%); ν_{max}(KBr)/cm^{-1} 1772 (bridge C=O) and 1728 (ester C=O); δ_H(500 MHz; $CDCl_3$) 1.25 (1H, s, 10-H), 1.26 (3H, s, Me), 2.01 (1H, d, *J* 8.5, 8a-H), 2.40 (1H, d, *J* 9.2, 10-H), 2.80 (1H, d, *J* 8.5, 4a-H), 2.94 (1H, s, 1-H), 3.35 (1H, s, 4-H), 3.52 (3H, s, OMe), 6.30–6.31 (1H, m, 2-H), 6.40–6.41 (1H, m, 3-H) and 7.02–7.32 (10H, m, ArH); δ_C(125 MHz; $CDCl_3$) 13.1 (Me), 40.7 (C-10), 43.3 (C-1), 4.35 (C-4a), 45.1 (C-4), 48.3 (C-8a), 51.9

(OMe), 58.3 (C-8), 67.4 (C-5), 127.4, 127.6, 127.8, 128.0, 128.3 and 128.4 (ArC), 134.6, 136.5 and 139.1 (quaternary C), 140.9 (C-2), 141.1 (C-3), 169.3 (ester C=O) and 193.7 (bridge C=O); *m*/*z* (EI) 396 (M^+, 25%) and 368 ($M^+ - CO$, 12).

1,5*endo*-Bis(methoxycarbonyl)-4-methyl-2,3-diphenylbicyclo-[2.2.1]hept-2-en-7-one 3ab′. *Prisms* (67%) mp 129–130 °C (from EtOH) (Found: C, 73.8; H, 5.6. $C_{24}H_{22}O_5$ requires C, 73.83; H, 5.68%); ν_{max}(KBr)/cm^{-1} 1792 (bridge C=O) and 1738 (ester C=O); δ_H(500 MHz; $CDCl_3$) 1.52 (1H, s, Me), 2.73 (1H, dd, *J* 5.5 and 12.8, 6-H *endo*), 2.84 (1H, dd, *J* 9.8 and 12.8, 6-H *exo*), 3.05 (1H, dd, *J* 5.5 and 9.8, 5-H), 3.40 and 3.57 (6H, s, OMe × 2) and 6.94–7.22 (10H, m, ArH); δ_C(125 MHz; $CDCl_3$) 12.4 (Me), 29.3 (C-6), 45.6 (C-5), 51.7 and 52.1 (OMe), 58.3 (C-4), 63.5 (C-1), 127.2, 127.5, 127.6, 127.7, 128.0, 128.4, 128.7, 129.3 and 129.5 (ArC), 133.3, 133.4, 138.9 and 140.2 (quaternary C), 168.3 and 171.9 (ester C=O) and 196.5 (bridge C=O); *m*/*z* (EI) 390 (M^+, 7%), 362 ($M^+ - CO$, 13%).

Inspection of the NMR spectrum of the oily crude product from the filtrate indicated the presence of the *syn* DA adduct **3ab** besides **3ab′**. However, compound **3ab** could not be isolated because of cleavage of the strained ketonic bond during chromatography on silica gel.

5*endo*-Ethoxymethyl-4-methoxycarbonyl-1-methyl-2,3-diphenylbicyclo[2.2.1]hept-2-en-7-one 3ac. *Prisms* (75%), mp 110–112 °C (from EtOH) (Found: C, 76.85; H, 6.6. $C_{25}H_{26}O_4$ requires C, 76.9; H, 6.71%); ν_{max}(KBr)/cm^{-1} 1770 (bridge C=O) and 1736 (ester C=O); δ_H(500 MHz; $CDCl_3$) 1.19 (1H, t, *J* 7.32, $CH_2OCH_2CH_3$), 1.24 (3H, s, Me), 1.43 (1H, dd, *J* 6.7 and 12.2, 6-H *endo*), 2.04 (1H, dd, *J* 9.8 and 12.2, 6-H *exo*), 3.32–3.36 (1H, m, 5-H), 3.49 (1H, dd, *J* 9.2 and 7.3, $CH_2OCH_2CH_3$), 3.51–3.59 (2H, m, $CH_2OCH_2CH_3$), 3.60 (3H, s, OMe), 3.81 (1H, dd, *J* 6.7 and 9.2, $CH_2OCH_2CH_3$) and 7.01–7.31 (10H, m, ArH); δ_C(125 MHz; $CDCl_3$) 12.4 (Me), 15.1 ($CH_2OCH_2CH_3$), 34.9 (C-6), 37.7 (C-5), 51.9 (OMe), 52.0 (C-1), 54.8 (C-4), 66.3 ($CH_2OCH_2CH_3$), 72.1 ($CH_2OCH_2CH_3$), 127.1, 127.4, 127.6, 128.1, 128.2, 128.3, 128.6, 129.1, 129.4 and 129.5 (ArC), 134.2, 134.4, 136.3 and 143.1 (quaternary C), 168.7 (ester C=O) and 198.8 (bridge C=O); *m*/*z* (EI) 390 (M^+, 12%) and 362 ($M^+ - CO$, 39).

Inspection of the NMR spectrum of the oily crude product from the filtrate indicated the presence of the *anti* DA adduct **3ac′** besides **3ac**. However, adduct **3ac′** could not be isolated because of cleavage of the strained ketonic bond during chromatography on silica gel.

4-Methoxycarbonyl-1-methyl-2,3,5*endo*-triphenylbicyclo-[2.2.1]hept-2-en-7-one 3ad. *Needles* (50%), mp 165–166 °C (from EtOH) (Found: C, 82.4; H, 6.0. $C_{28}H_{24}O_3$ requires C, 82.33; H, 5.92%); ν_{max}(KBr)/cm^{-1} 1770 (bridge C=O) and 1736 (ester C=O); δ_H(500 MHz; $CDCl_3$) 1.37 (3H, s, Me), 2.17 (1H, dd, *J* 6.1 and 12.8, 6-H *endo*), 2.38 (1H, dd, *J* 9.8 and 12.8, 6-H *exo*), 3.44 (3H, s, OMe), 4.35 (1H, dd, *J* 6.1 and 9.8, 5-H) and 6.16–7.57 (15H, m, ArH); δ_C(125 MHz; $CDCl_3$) 12.7 (Me), 38.7 (C-6), 42.2 (C-5), 51.7 (OMe), 55.5 (C-1), 71.0 (C-4), 126.7, 127.2, 127.3, 127.4, 128.4, 128.5, 128.6, 129.2 and 129.5 (ArC), 133.9, 134.0, 136.9, 140.5 and 141.8 (quaternary C), 168.4 (ester C=O) and 198.5 (bridge C=O); *m*/*z* (EI) 408 (M^+, 37%) and 380 ($M^+ - CO$, 40).

4-Methoxycarbonyl-1-methyl-2,3,5*exo*-triphenylbicyclo-[2.2.1]hept-2-en-7-one 3ad″. *Prisms* (4%), mp 138–140 °C (from EtOH) (Found: C, 82.4; H, 6.05%); ν_{max}(KBr)/cm^{-1} 1771 (bridge C=O) and 1734 (ester C=O); δ_H(500 MHz; $CDCl_3$) 1.33 (3H, s, Me), 1.98 (1H, dd, *J* 5.5 and 12.2, 6-H *endo*), 2.56 (1H, dd, *J* 11.0 and 12.2, 6-H *exo*), 3.27 (3H, s, OMe), 3.57 (1H, dd, *J* 5.5 and 11.0, 5-H) and 7.07–7.38 (15H, m, ArH); δ_C(125 MHz; $CDCl_3$) 12.1 (Me), 42.3 (C-6), 46.5 (C-5), 51.4 (OMe), 54.0 (C-1), 67.2 (C-4), 126.7, 127.3, 127.5, 127.7, 128.1, 128.3, 128.5 and 129.0 (ArC), 133.5, 133.6, 141.1, 142.6 and 144.4 (quaternary C), 167.6 (ester C=O) and 200.0 (bridge C=O); *m*/*z* (EI) 408 (M^+, 7%) and 380 ($M^+ - CO$, 12).

Inspection of the NMR spectrum of the oily crude product from the filtrate indicated the presence of the *anti-endo* DA adduct **3ad′** besides **3ab**. However, adduct **3ab′** could not be isolated because of cleavage of the strained ketonic bond during chromatography on silica gel.

2-Methoxycarbonyl-5-methyl-3,4-diphenyltricyclo[4.4.1.1^{2,5}]-dodeca-3,7,9-trien-12-one 5ag. *Needles* (24%), mp 179–183 °C (from EtOH–AcOEt) (Found: C, 81.75; H, 6.0. $C_{27}H_{24}O_3$ requires C, 81.79; H, 6.10%); ν_{max}(KBr)/cm^{-1} 1764 (bridge C=O) and 1730 (ester C=O); δ_H(500 MHz; $CDCl_3$) 1.19 (3H, s, Me), 1.68 (1H, d, *J* 14.0, 11-H), 2.52–2.64 (1H, m, 11-H), 2.85–2.86 (1H, m, 6-H), 3.48 (3H, s, OMe), 3.89–3.90 (1H, m, 1-H), 6.05–5.96 (3H, m, 7-, 8- and 9-H), 6.39–6.43 (1H, m, 10-H) and 7.10–7.34 (10H, m, ArH); δ_C(125 MHz; $CDCl_3$) 14.7 (Me), 25.3 (C-11), 42.2 (C-6) 44.5 (C-1), 51.9 (OMe), 52.3 (C-5), 60.9 (C-2), 126.3, 126.4 and 132.8 (C-7, -8 and -9), 127.7, 127.8, 128.3, 128.4, 129.1 and 130.5 (ArC), 134.1 (C-10), 134.2, 134.8, 135.6 and 141.9 (quaternary C), 169.6 (ester C=O) and 203.0 (bridge C=O); *m*/*z* (EI) 396 (M^+, 33%) and 365 ($M^+ - OMe$, 22).

2-Methoxycarbonyl-8a-methyl-3,3a-diphenyl-4,7,8,8a-tetrahydro-4,8-ethenoazulen-1(3a*H*)-one 8ag. *Powder* (32%), mp 162–164 °C (from EtOH) (Found: C, 81.8; H, 6.0. $C_{27}H_{24}O_3$ requires C, 81.79; H, 6.10%); ν_{max}(KBr)/cm^{-1} 1764 (bridge C=O) and 1730 (ester C=O); δ_H(500 MHz; $CDCl_3$) 1.28 (3H, s, Me), 2.19–2.15 (1H, m, 7-H), 2.35–2.39 (1H, m, 7-H), 2.92–2.97 (1H, m, 8-H), 3.66 (3H, s, OMe), 3.78–3.82 (1H, m, 4-H), 5.94–6.23 (4H, m, 5-, 6-, 9- and 10-H) and 7.09–7.31 (10H, m, ArH); δ_C(125 MHz; $CDCl_3$) 11.2 (Me), 28.1 (C-7), 43.3 (C-4), 52.0 (OMe), 59.5 (C-8a), 61.1 (C-8), 67.9 (C-3a), 127.2, 127.3, 127.4, 127.7, 128.2, 128.5 and 128.6 (ArC), 128.9, 129.4, 129.8 and 134.5 (C-5, -6, -9 and -10), 134.7, 134.9, 138.5 and 142.8 (quaternary C), 168.6 (ester C=O) and 197.8 (enone C=O); *m*/*z* (EI) 396 (M^+, 36%) and 365 ($M^+ - OMe$, 55).

Inspection of the NMR spectrum of the oily crude product from the filtrate indicated the presence of the *syn-endo* DA adduct **9ag** besides **8ag**.

2-Methoxycarbonyl-5-methyl-3,4-diphenyltricyclo[4.4.1.1^{2,5}]-dodeca-3,7,9-triene-11,12-dione 5ah. *Needles* (73%), mp 152–154 °C (from EtOH) (Found: C, 78.95; H, 5.4. $C_{27}H_{22}O_4$ requires C, 79.01; H, 5.40%); ν_{max}(KBr)/cm^{-1} 1764 (bridge C=O) and 1736 (ester C=O); δ_H(500 MHz; $CDCl_3$) 1.21 (3H, s, Me), 3.46 (1H, dd, *J* 4.89 and 8.4, 6-H), 3.55 (3H, s, OMe), 4.35–4.38 (1H, m, 1-H), 5.61–5.62 (1H, m, 7-H), 6.05–6.08 (3H, m, 8-, 9- and 10-H) and 6.96–7.28 (10H, m, ArH); δ_C(125 MHz; $CDCl_3$) 12.9 (Me), 52.3 (OMe), 59.6 (C-6), 59.8 (C-5), 62.2 (C-1), 68.1 (C-2), 122.4 (C-7), 123.9, 126.4 and 127.0 (C-8, -9 and -10), 127.8, 128.1, 128.4, 128.9, 134.6, 136.0 and 142.1 (ArC), 132.8, 133.2, 138.0 and 144.4 (quaternary C), 167.8 (ester C=O) and 200.5 and 203.7 (bridge C=O); *m*/*z* (EI) 410 (M^+, 45%) and 379 ($M^+ - OMe$, 25).

(1α,5α,5aβ,8aβ)-7-Methyl-6-oxo-8,8a-diphenyl-1,2,5,5a,6,8a-hexahydro-1,5-ethenocyclopent[*c*]azepine-2,5a-dicarboxylic acid 2-ethyl 5a-methyl ester 11ai. Pale yellow *prisms* (84%) mp 159–160 °C (from EtOH) (Found: C, 74.2; H, 5.8; N, 3.0. $C_{29}H_{27}NO_5$ requires C, 73.99; H, 5.76; N, 2.94%); ν_{max}(KBr)/cm^{-1} 1742 (enone C=O) and 1692 (ester C=O); δ_H(500 MHz; $CDCl_3$) 1.21 (3H, t, *J* 7.33, CH_2CH_3), 1.98 (3H, s, Me), 3.01 (3H, s, OMe), 3.22 (1H, t, *J* 7.94, 5-H), 4.07 (2H, q, *J* 7.33, CH_2CH_3), 5.21–5.62 (3H, m, 1-, 4- and 10-H), 6.27 (1H, t, *J* 7.93, 9-H), 6.63 (1H, d, *J* 9.15, 3-H) and 7.24–7.41 (10H, m, ArH); δ_C(125 MHz; $CDCl_3$) 11.4 (Me), 14.5 (CH_2CH_3), 36.4 (C-5), 51.5 (OMe), 53.5 (C-1), 62.7 (CH_2CH_3), 63.1 (C-8a), 71.4 (C-5a), 109.4 (C-10),

122.9 (C-4), 123.8 (C-3), 133.9 (C-9), 124.1, 127.2, 127.6, 128.5, 129.4, 129.7, 129.9 and 130.3 (ArC), 138.5, 140.6 and 154.0 (quaternary C), 170.2 and 171.0 (ester C=O) and 204.1 (enone C=O); *m*/*z* (EI) 469 (M^+, 19%), 410 ($M^+ - CO_2Me$, 14), 304 (M^+ − **2i**, 32) and 165 (M^+ − **1a**, 100).

(3aα,4α,7α,7aα)-1-Isopropylidene-4-methoxycarbonyl-7-methyl-5,6-diphenyl-3a,4,7,7a-tetrahydro-1*H*-4,7-methanoinden-8-one 3aj. *Needles* (74%), mp 154–156 °C (from EtOH) (Found: C, 81.5; H, 6.1. $C_{28}H_{26}O_3$ requires C, 81.92; H, 6.38%); ν_{max}(KBr)/cm^{-1} 1778 (bridge C=O) and 1728 (ester C=O); δ_H(500 MHz; $CDCl_3$) 1.43 (3H, s, Me), 1.59 and 1.67 (6H, s, Me × 2), 3.32 (1H, d, *J* 7.3, 7a-H), 3.61 (3H, s, OMe), 4.25 (1H, d, *J* 7.3, 3a-H), 6.04 (1H, d, *J* 7.0, 2-H), 6.64 (1H, d, *J* 7.3, 3-H) and 6.90–7.25 (10H, m, ArH); δ_C(125 MHz; $CDCl_3$) 14.5, 21.3 and 23.3 (Me × 3), 46.9 (C-7a), 50.9 (OMe), 52.1 (C-3a), 60.1 (C-7), 66.0 (C-4), 127.1, 127.7, 127.8, 128.8 and 131.4 (ArC), 129.9 (C-2), 137.6 (C-3), 131.4, 134.1, 134.8, 136.8, 138.1 and 141.3 (quaternary C), 169.2, (ester C=O) and 198.4 (bridge C=O); *m*/*z* (EI) 410 (M^+, 25%) and 382 (M^+ − CO, 36).

Thermolysis of the [4 + 2] cycloadducts of nonconjugated dienes (general procedure). Formation of DNA adduct

A mixture of compounds **1a** (0.5 g, 1.64 mmol) and **2e** (0.89 g, 8.2 mmol) was heated at 180 °C for 10 h in a sealed tube. The resulting oil was purified by chromatography on silica gel with AcOEt–benzene (1:20) to give the DDA adduct as needles.

The following compounds were obtained by essentially the same procedure as above.

9-Methoxycarbonyl-12-methyl-10,11-diphenyltetracyclo-[6.4.0.0^{4,12}.0^{5,9}]dodec-10-ene 4ae. *Needles* (25%), mp 152–154 °C (from EtOH) (Found: C, 84.65; H, 7.6. $C_{27}H_{28}O_2$ requires C, 84.34; H, 7.34%); ν_{max}(KBr)/cm^{-1} 1722 (ester C=O); δ_H(500 MHz; $CDCl_3$) 0.94 (3H, s, Me), 1.48–1.54 (2H, m, 2- and 3-H), 1.73–1.75 (2H, m, 6- and 7-H), 1.84–1.86 (2H, m, 1- and 4-H), 1.90–1.94 (4H, m, 2-, 3-, 6- and 7-H), 2.50–2.59 (2H, m, 5-H and 8-H), 3.03 (3H, s, OMe) and 6.81–7.26 (10H, m, ArH); δ_C(125 MHz; $CDCl_3$) 22.4 (Me), 24.4, 25.1, 25.6 and 25.7 (C-2, -3, -6 and -7), 44.3 and 45.6 (C-5 and -8), 45.9 and 46.8 (C-1 and -4), 50.9 (OMe), 61.3 (quaternary C), 125.6, 125.7, 126.6, 126.8, 127.3, 129.4, 129.8, 130.1 and 130.3 (ArC), 137.6, 139.5, 140.8 and 143.1 (quaternary C) and 175.4 (ester C=O); *m*/*z* (EI) 384 (M^+, 100%) and 325 ($M^+ - CO_2Me$, 58).

7-Methoxycarbonyl-1-methyl-8,9-diphenyltricyclo[4.3.1.0^{3,7}]-dec-8-ene 4af. *Powder* (4%), mp 135–137 °C (EtOH) (Found: C, 83.6; H, 7.0. $C_{25}H_{26}O_2$ requires C, 83.76; H, 7.31%); ν_{max}(KBr)/cm^{-1} 1726 (ester C=O); δ_H(500 MHz; $CDCl_3$) 0.88 (3H, s, Me), 1.27 (2H, d, *J* 11.6, 2- and 10-H), 1.58 (2H, d, *J* 8.6, 4- and 5-H), 1.93–1.97 (4H, m, 2-, 4-, 5- and 10-H), 2.69–2.70 (2H, m, 3- and 6-H), 3.11 (3H, s, OMe) and 6.86–7.24 (10H, m, ArH); δ_C(125 MHz; $CDCl_3$) 24.7 (Me), 31.0 (C-2 and -10), 36.4 (C-1), 39.5 (C-3 and -6), 47.3 (C-4 and -5), 51.1 (OMe), 62.9 (C-7), 125.7, 125.9, 127.0, 127.2, 129.2, 129.4 and 129.8 (ArC), 136.6, 138.9, 139.4 and 147.7 (quaternary C) and 175.2 (ester C=O); *m*/*z* (EI) 358 (M^+, 100%) and 299 ($M^+ - CO_2Me$, 73).

Kinetics

The pseudo-first-order conditions were maintained by using a 100:1 ratio of dienophiles to dienones **1a**, **1b** and **1c** in benzene. The reaction rate was followed at 40.0 ± 0.1 °C by measuring the loss of the long-wavelength absorption (428 nm) of dienone **1a** by using a 10 × 10 mm quartz cell sealed with a ground-glass stopper, which was thermostatted at constant temperature. Pseudo-first-order rate constants were determined by a least-squares method. The results are listed in Table 3.

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