Pergamon

Tetrahedron 56 (2000) 4027–4042

TETRAHEDRON

Diels–Alder Reactions of 5,6-Dihydro-2(1*H*)-pyridones

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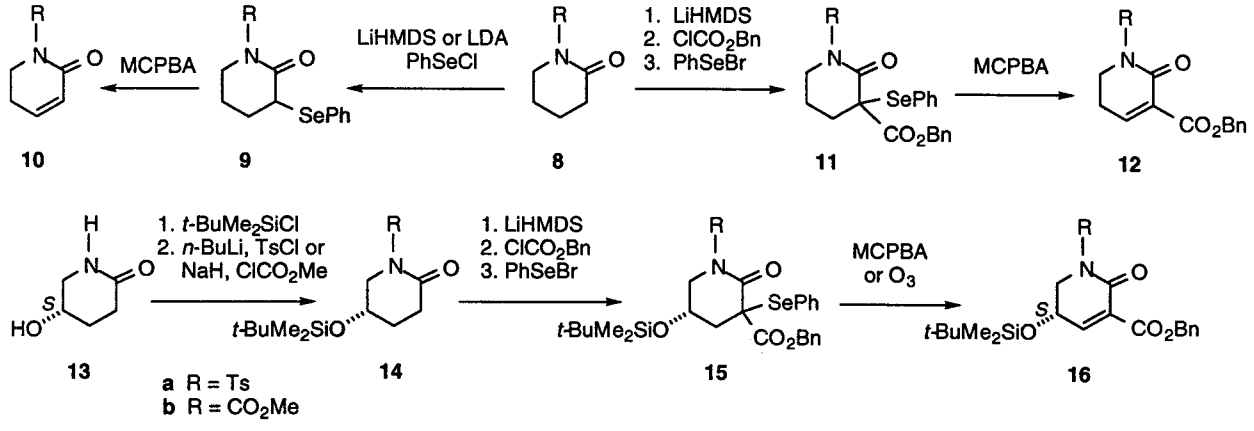
Received 16 December 1999; revised 27 March 2000; accepted 13 April 2000

Abstract—The Diels–Alder reaction of achiral 5,6-dihydro-2(1*H*)-pyridones **12a**,**b** and enantiopure 5,6-dihydro-2(1*H*)-pyridones **16a**,**b** with a variety of diversely substituted buta-1,3-dienes under thermal or catalytic conditions, to give partially reduced isoquinolones **18**–**33** and **35**–**37**, is reported.

The partially reduced isoquinoline moiety is present in a large number of alkaloids belonging to different structural types, most of them displaying notable pharmacological activities.[1] We present here a straightforward synthetic entry to this structural unit, both in the racemic series and in enantiopure form, that involves the Diels–Alder reaction of 5,6-dihydro-2(1*H*)-pyridones as dienophiles with diversely substituted buta-1,3-dienes **1**–**7** (see Table 1).[2,3]

As the starting dihydropyridones we used **10a**,**b**, **12a**,**b** and **16a**,**b**, which were prepared from 2-piperidone or (*S*)-5-hydroxy-2-piperidone (**13**),[4] as outlined in Scheme 1. All of these dihydropyridones bear an electron-withdrawing group on the piperidine nitrogen atom in order to enhance the reactivity of the carbon–carbon double bond as a dienophile. In dihydropyridones **12** and **16** an additional activating benzyloxycarbonyl group is present at the pyridone 3 position.

The results of the Diels–Alder reactions between dihydropyridones **10**, **12** and **16** and dienes **1**–**7**, under a variety of experimental conditions, either thermal or with Lewis-acid catalysis,[5] are summarized in Table 1. The products obtained are shown in Figs. 1–3. The stereochemical assignment of the Diels–Alder adducts was effected from their NMR data, with the aid of bidimensional (COSY and HETCOR), ^{1}H–^{1}H decoupling, and NOE difference experiments, when necessary. Diagnostic ^{1}H NMR data to determine the *anti* or *syn* stereochemistry in the chiral non-racemic series were the *J* values of H-3, H-4 and H-4a of the isoquinoline nucleus. Table 2 shows significant ^{13}C NMR chemical shifts for the Diels–Alder adducts.



Scheme 1.

Keywords: Diels–Alder reaction; pyridones; isoquinolines.
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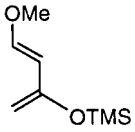
PII: S0040-4020(00)00317-3

Table 1. Diels–Alder reactions of 5,6-dihydro-2(1*H*)-pyridones

Diene	Dienophile	Conditions[a]	Products[b] (yield%)
 **1**	**10a**	A[c]	**17a** (34)
	12a	A[c]	**18a** (58)
	12a	B[c]	**18a** (41)
			19a (30)
	12b	A[c]	**18b** (15)
			19b (21)
	12b	B[c]	**18b** (17)
			19b (62)
	16a	A	**20a** (14)
			22a (18)
	16a	B	**20a**[d] (40)
			21a (13)
	16a	C	**20a**[d] (20)
	16b	B[c]	**20b**[d] (29)
			21b (11)
	16b	C	**21b** (28)
			22b (19)
 **2**	**12a**	C	**23a** (65)
	12b	C	**23b** (67)
	16a	C	**25a** (18)
			27a (52)
	16b	C	**25b**+**27b** (1:6, 82)
 **3**	**12a**	A	**24a** (25)
	12a	C	**24a** (69)
	12b	A	**24b** (11)
	12b	C	**24b** (73)
	16a	C	**26a** (27)
			28a (55)
	16b	C	**26b**+**28b** (1:3, 75)

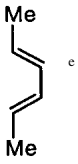
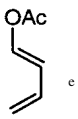
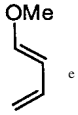
Thermal induced Diels–Alder reactions from **10** only succeeded, although in moderate yield, using the *N*-tosyldihydropyridone **10a** and the highly reactive Danishefsky's diene **1**[6] in refluxing *p*-cymene. Treatment of the initially formed adduct with camphorsulfonic acid brought about both the hydrolysis of the silyl enol ether functionality and elimination of methanol to give **17a** (Fig. 1). When using either **10b**, a less reactive dienophile, or other dienes, or solvents with a lower boiling point, the reactants were recovered unchanged. The reaction of dienophiles **12a**,**b**, which incorporate an additional activating group at the 3 position, with diene **1** under thermal conditions proceeded with higher yields to give the adducts **18** and **19**, the latter arising from elimination of methanol. It is worth mentioning that when using benzene as the solvent the yield was higher, probably because the starting dihydropyridones **12** decompose at the *p*-cymene reflux temperature to give the less reactive dihydropyridones **10** and their 3,6-dihydro isomers (see Experimental). The elimination of methanol from the initially formed 8-methoxy substituted adducts takes place more easily from the *exo* diastereomers, in which the methoxy group is in an axial disposition, than in the *endo* isomers. In fact, attempts to perform this elimination from ***endo*-18a** under acidic conditions (CSA or *p*-TsOH) were unsuccessful.[7] Diagnostic ^{13}C NMR data for adducts ***endo*-18a** and its C-8 epimer ***exo*-18a** are shown in Fig. 1. With the enantiopure dihydropyridones **16a**,**b**, Danishefsky's diene reacted under both thermal and catalytic conditions to afford adducts **20** (*anti*, minor amounts of other diastereomers were also formed), **21** and **22** in moderate to low yields.

The Diels–Alder reaction of dienophiles **12a**,**b** and **16a**,**b** with alkyl substituted buta-1,3-dienes **2** and **3** took place in low yields under thermal conditions but in quite good yields when using $ZnBr_2$ or $ZnCl_2$ as a catalyst to give the corresponding adducts **23**–**28** (Fig. 2). With enantiopure dihydropyridones **16a**,**b** as the dienophiles, mixtures of stereoisomeric adducts *anti* (**25** and **26**) and *syn* (**27** and **28**) were obtained, the latter being the major products. Diagnostic ^{1}H NMR data for these *anti* and *syn* adducts are shown in Fig. 2. The absolute configuration of **27a** was confirmed by X-ray crystallography.

Similarly, cycloadditions of **12a**,**b** and **16a**,**b** with an *E*,*Z* mixture of hexa-2,4-diene (**4**) in the presence of $ZnBr_2$ as catalyst afforded the respective adducts **29a**,**b** and **30a**,**b** in good yields as mixtures of diastereomers of undetermined configuration at C-5 and C-8. As in the above alkyl substituted butadienes, the major diastereomers **30a**,**b** formed in the reaction of enantiopure dihydropyridones **16a**,**b** possessed a *syn* stereochemistry ($J_{4-4a}\approx$5.5 Hz).

Dihydropyridones **12a**,**b** and **16a**,**b** were also allowed to react with *O*-substituted 1-hydroxybuta-1,3-dienes **5** (*Z*/*E*

Table 1 (*continued*)

Diene	Dienophile	Conditions[a]	Products[b] (yield%)
 **4**	**12a**	A	**29a** (17)
	12a	C	**29a** (70)
	12b	C	**29b** (63)[f]
	16a	C	**30a**[d] (73)
	16b	C	**30b**[d] (67)
 **5**	**12a**	A	**31a** (38)
	12a	C	**31a** (51)
	12b	A	**31b** (9)
	12b	C	**31b** (32)
			34b (14)
	12b	D	**31b** (67)
	16a	C	**35a**[g] (67)
			38a (19)[f]
	16b	C	**35b** (46)
			38b (10)
 **6**	**12a**	A	**32a** (48)
	12a	C	**32a** (89)
	12b	A	**32b** (12)
			32c (24)
	12b	C	**32b** (32)
			34b (34)
	16a	C	**36a** (68)
 **7**	**12a**	A[c]	**33a** (28)
	12a	C	**33a** (4)
			34a (50)
	12b	A	**33b** (31)
	12b	D	**34b** (47)
	16a	C	**37a** (4)
			38a (14)

[a] A: *p*-cymene, reflux. B: benzene, reflux. C: $ZnBr_2$ or $ZnCl_2$, CH_2Cl_2. D: $EtAlCl_2$, CH_2Cl_2.
[b] For the stereochemistry at C-5 and C-8, see Experimental.
[c] Followed by CSA treatment.
[d] Accompanied by a minor stereoisomer.
[e] Commercial mixture of isomers.
[f] Mixture of two diastereomers.
[g] Accompanied by two minor diastereomers.

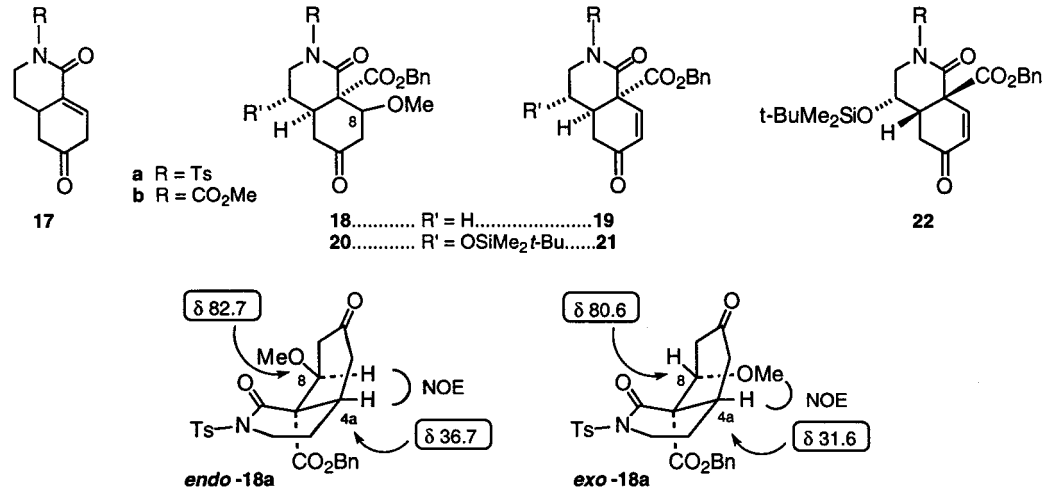


Figure 1. Diels–Alder adducts from Danishefsky's diene and diagnostic ^{13}C NMR data for adducts ***endo*-18a** and ***exo*-18a**.

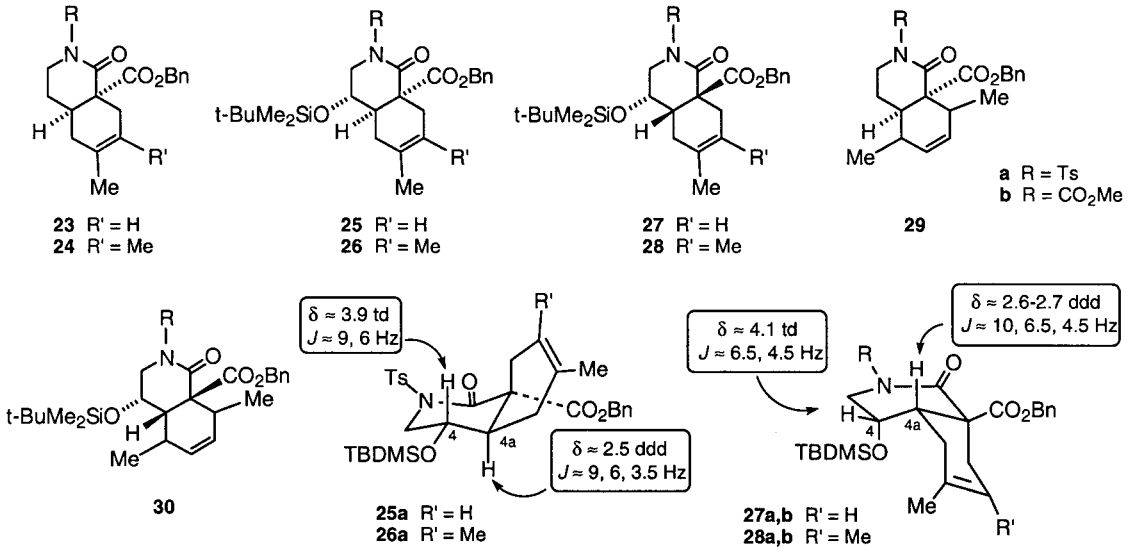


Figure 2. Diels–Alder adducts from alkyl substituted buta-1,3-dienes and diagnostic ^{1}H NMR data for adducts **25**–**28**.

mixture), **6** (*Z*/*E* mixture), and **7** under a variety of reaction conditions. The thermal cycloaddition reactions of **12a**,**b** with these dienes gave moderate yields of the corresponding adducts **31a**,**b**–**33a**,**b** as mixtures of *endo*/*exo* isomers (Fig. 3). Deprotection of the *N*-methoxycarbonyl substituent, probably during purification, occurred to some extent in the reaction of diene **6** with dihydropyridone **12b** to give the *N*-unsubstituted bicyclic adduct **32c**. The yields were clearly higher when the reactions using dienes **5** and **6** were performed in the presence of a Lewis acid catalyst ($ZnCl_2$ or $ZnBr_2$), although in series **b** aldehyde **34b**, resulting from a Michael-type addition of the activated diene to the conjugated C–C double bond of the dienophile, was also formed. This problem was circumvented using $EtAlCl_2$ as the Lewis acid catalyst. Under these conditions dihydropyridone **12b** afforded adduct **31b** (6:1 *endo*/*exo* mixture) in 67% yield as the only isolable product. However, the Michael addition was the preponderant or exclusive process when operating from the *O*-silyl diene **7**, and no synthetically useful Diels–Alder reactions were produced with this diene. In general, with *O*-substituted 1-hydroxybutadienes the yields were slightly higher in the more reactive *N*-tosyl

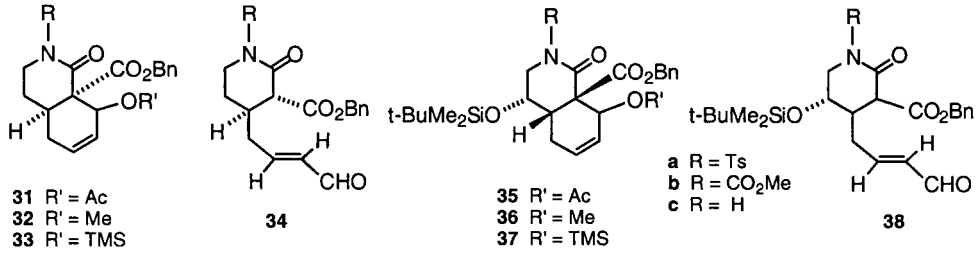


Figure 3. Diels–Alder adducts from *O*-substituted 1-hydroxybuta-1,3-dienes.

Table 2. Significant ^{13}C NMR chemical shifts of Diels–Alder adducts **17–37** (values with an asterisk are interchangeable)

	C-3	C-4	C-4a	C-5	C-6	C-7	C-8	C-8a	Other[a]
17a	45.5	29.8	34.1	44.4	206.2	40.0	136.8	131.5	
***endo*-18a**	44.6	26.4	36.7	42.5	207.2	41.4	82.7	59.0	57.6
***exo*-18a**	44.1	26.4	31.6	40.4	206.2	42.1	80.6	60.3	56.9
18b	44.6	25.6	36.6	42.5	-	41.3	82.6	59.6	57.9,
19a	45.1	26.0	36.5	39.9	200.0	130.6	143.9	–	
19b	45.1	25.3	36.4	39.9	195.4	130.3	144.4	58.3	
20a	51.0	65.1	45.2	37.8	206.4	42.0	83.4	59.2	57.6
20b	51.8	64.7	45.0	38.0	206.9	41.9	83.4	60.0	57.8
21a	50.6	66.1	44.1	35.7	194.6	131.2	144.0	58.0	
21b	51.3	65.7	44.1	35.9	195.0	131.1	144.7	58.8	
22a	50.6	66.9	42.0	36.6	194.9	131.0	144.0	56.5	
22b	50.7	66.8	42.1	36.8	195.4	130.8	144.6	57.2	
23a	44.6	25.3	32.8	32.5	130.8	116.9	28.8	55.3	23.2
23b	45.0	24.9	33.0	32.7	130.8	117.1	29.0	55.9	23.4
24a	44.7	25.4	33.0	34.4	121.9*	122.6*	34.4	56.5	18.4, 18.8
24b	44.9	25.0	33.1	34.4*	122.0*	122.5*	34.6*	57.0	18.4, 18.8
25a	50.9	65.6	41.0	27.5	130.7	117.3	29.5	54.6	23.2
26a	50.9	65.9	41.3	29.5	122.4*	122.5*	35.1	55.7	18.4, 18.8,
27a	50.0	65.7	39.1	26.5	131.1	117.9	30.7	54.6	23.1
27b	50.1	65.2	39.4	26.4	131.2	118.0	30.9	55.2	23.2
28a	49.9	65.9	39.3	28.1	122.9*	123.0*	36.2	55.6	18.4, 18.6
28b	50.1	65.4	39.6	28.1	122.8*	123.0*	36.6	56.2	18.5, 18.7
29a	46.2	18.2	38.3	28.9	129.5	127.1	32.5	59.5	17.6, 18.6
29b[b]	46.4	18.0	38.7	32.5	129.6	127.3	29.1	60.3	17.5, 19.1
29b[c]	41.6	23.7	32.5	34.0	129.2	129.8	34.2	59.7	17.5, 19.6
30a	51.5	65.0	48.3	30.9	130.5*	131.2*	35.2	59.9	17.2, 18.2
30b	51.4	64.9	48.1	30.9	130.2*	131.4*	34.8.	61.0	17.5, 18.2
***endo*-31a**	46.0	24.1	31.8	27.5	122.9	127.8	66.9	59.5	20.4,
***exo*-31a**	41.6	25.8	27.2	30.2	123.2	130.4	67.0	59.0	20.6
***endo*-31b**	46.0	23.7	32.1	27.7	123.1	127.7	67.5	59.3	20.9
***exo*-31b**	41.8	25.1	27.2	30.2	123.5	130.3	67.6	59.5	20.6
***endo*-32a**	46.3	24.0	31.7	27.7	123.5	125.8	74.9	59.7	58.6,
***endo*-32b**	46.2	23.5	31.9	27.8	123.7	125.9	74.9	60.4	58.8
***exo*-32b**	41.6	25.4	26.7	30.7	123.4	125.7	73.8	60.6	57.0
***endo*-32c**	41.3	23.3	32.0	28.1	124.0	125.9	74.3	57.7	59.1
***endo*-33a**	46.1	23.7	31.7	27.6	124.8	127.0	65.9	60.2	-0.1
***exo*-33a**	41.8	26.5	26.4	30.9	125.1	127.3	66.2	61.5	0.6
***endo*-33b**	46.2	23.5	32.1	27.8	124.8	127.1	66.5	60.7	0.1
***exo*-33b**	41.7	25.4	26.3	30.5	127.4	127.6	66.4	61.5	0.3
***endo*-35a**	49.3	65.7	40.5	22.3	126.5*	127.9*	70.8	58.6	20.7
***endo*-35b**	49.5	65.0	41.2	22.4	126.9*	127.7*	71.6	59.3	20.9
***exo*-35b**	49.7	64.4	34.4	22.5	130.6	123.0	67.6	58.6	20.6
***exo*-36a**	49.6	65.2	33.5	22.2	129.6	122.9	73.7	59.7	57.0
***endo*-37a**	49.9	65.5	32.8	22.2	126.5*	127.8*	66.2	60.7	0.3

[a] Substituents on the carbocyclic ring.
[b] Less polar diastereomer.
[c] More polar diastereomer.

(**a**) series under both thermal conditions and with Lewis acid catalysis.

Finally, taking into account the above results, Diels–Alder reactions from the chiral non-racemic dienophiles **16a**,**b** were only studied in the presence of Lewis acids. Thus, dienes **5** and **6** again gave satisfactory results, and the corresponding adducts **35a**,**b** and **36a**,**b** were obtained in good yields. In the former case, minor amounts of the respective aldehydes **38a**,**b** were also formed. As in the above racemic series, diene **7** was not synthetically useful to obtain Diels–Alder adducts.

Concerning the *syn*/*anti* stereoselectivity with enantiopure dienophiles **16a** and **16b**, it is worth mentioning that the *syn* adducts **35**, **36**, and **37a**,**b** were formed as the major diastereomers, accompanied in some cases by minor amounts of other diastereomers of undetermined configuration. The *endo*/*exo* and *syn*/*anti* stereochemistry for adducts **31–33** and **35–37** was inferred from their ^{1}H and ^{13}C NMR spectra. Fig. 4 shows selected diagnostic NMR data for these adducts. The ^{13}C chemical shift of the olefinic 6 and 7 carbons is of diagnostic value[8] to establish the pseudoequatorial or pseudoaxial disposition of the substituent at C-8 in adducts **35–37** derived from **16**. The configuration of isoquinolone ***endo*-35b** was confirmed by X-ray crystallography.

In summary, the Diels–Alder reaction between 5,6-dihydro-2(1*H*)-pyridones and substituted buta-1,3-dienes provides a general entry to the partially reduced isoquinolone system, both in the racemic series and in enantiopure form. Except for the more reactive Danishefsky's diene, the best yields are obtained when the cycloaddition is carried out using Lewis acid catalysis. For each particular reaction the highest yield is normally in the range 50–85%, although in general both the *endo*/*exo* and *syn*/*anti* stereoselectivities are low.

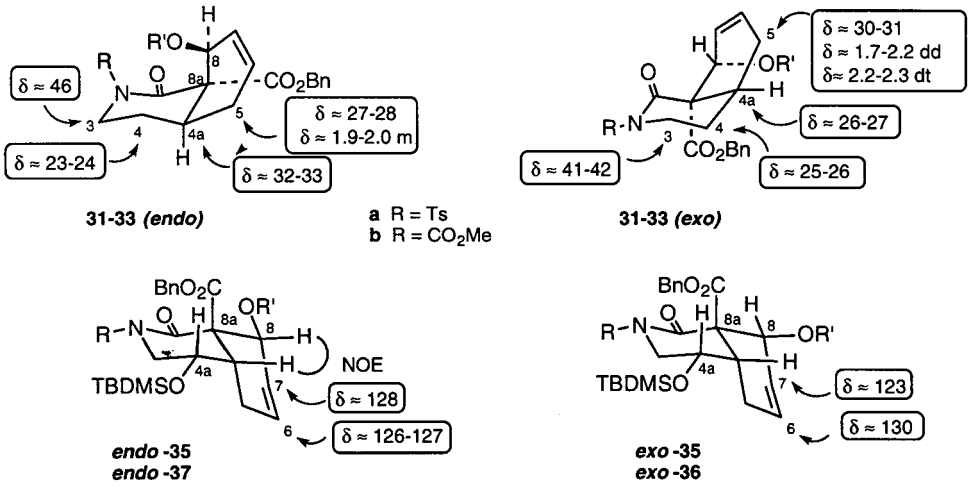


Figure 4. Diagnostic NMR data for adducts **31**–**33** and **35**–**37**.

Experimental

General

Melting points were determined in a capillary tube on a Büchi apparatus and are uncorrected. ^{1}H and ^{13}C NMR spectra were recorded in $CDCl_3$ solution on a Varian Gemini 200 (200 and 50.3 MHz, respectively), a Varian Gemini 300 (300 and 75 MHz, respectively), or a VX R-500 (500 MHz) instrument. Chemical shifts are expressed in parts per million (δ) relative to internal Me_4Si. IR spectra were recorded on a Nicolet 205 FT-IR spectrophotometer. Mass spectra were determined on a Hewlett–Packard 5988A mass spectrometer or on a Autospec-VG (HRMS). Column and flash chromatography were carried out on SiO_2 (silica gel 60 SDS, 70–200 μm and 35–70 μm, respectively) or Al_2O_3 (aluminiumoxid 90 Merck, activity II–III, 70–230 mesh ASTM). Drying of organic extracts during the work-up of reactions was performed over anhydrous Na_2SO_4. Microanalyses were performed on a Carlo Erba 1106 analyzer by the Centro de Investigación y Desarrollo (CSIC), Barcelona.

1-(*p*-Toluenesulfonyl)-5,6-dihydro-2(1*H*)-pyridone (10a). A solution of LHMDS (1 M in THF, 15 ml, 15 mmol) was diluted in anhydrous THF (40 ml) under N_2 at −20°C, and a solution of δ-valerolactam (1 g, 10 mmol) in THF (10 ml) was slowly added. After 10 min, TsCl (1.9 g, 10 mmol) was added, and the mixture was stirred at −20°C for 2 h. Finally, H_2O (20 ml) was added, and the aqueous layer was extracted with Et_2O. The combined organic extracts were washed with brine, dried, and concentrated to give, after chromatography (flash, SiO_2, 1:1 hexane–AcOEt), **1-(*p*-toluenesulfonyl)-2-piperidone (8a)** (1.28 g, 50%): mp 141–143°C (Et_2O) (Lit.[9] 144–145°C); IR (KBr) 1686, 1350, 1173 cm^{-1}; ^{1}H NMR (200 MHz) 1.80 (m, 2H, 5-H), 1.89 (m, 2H, 4-H), 2.42 (t, *J*=6.6 Hz, 2H, 3-H), 2.43 (s, 3H, Me), 3.92 (t, *J*=6.2 Hz, 2H, 6-H), 7.31 (d, 2H, Ts-*m*-H), 7.61 (d, 2H, Ts-*o*-H); ^{13}C NMR (50.3 MHz) 20.2 (C-4), 21.5 (Me), 23.1 (C-5), 33.9 (C-3), 46.8 (C-6), 128.6 (C-*o*-Ph), 129.6 (C-*m*-Ph), 135.9 (C-*p*-Ph), 144.6 (C-*i*-Ph), 170.2 (C-2); MS, *m*/*z* (rel intensity) 254 (M^++1, 1), 189 (47), 133 (89), 120 (38), 108 (23), 91 (100), 65 (80), 56 (27), 55 (43). A solution of LHMDS (1 M in THF, 7.8 ml, 7.8 mmol) in anhydrous THF (40 ml) was slowly added (30 min) under N_2 to a solution of **8a** (1.8 g, 7.08 mmol) in anhydrous THF (40 ml) cooled at −78°C, and stirring was continued at −78°C for 1 h. A solution of PhSeCl (1.5 g, 7.8 mmol) in anhydrous THF (40 ml) was next added, and the mixture was stirred at 0°C for 30 min, poured into H_2O, and extracted with Et_2O. The combined organic extracts were washed with brine, dried, and concentrated to give, after chromatography (flash, SiO_2, 1:1 hexane–AcOEt), **3-(phenylselanyl)-1-(*p*-toluenesulfonyl)-2-piperidone (9a)** (1.7 g, 60%): mp 125–127°C (Et_2O); IR (NaCl) 1683, 1349, 1168 cm^{-1}; ^{1}H NMR (200 MHz) 1.74–2.23 (m, 4H, 4-H and 5-H), 2.45 (s, 3H, Me), 3.77–3.89 (m, 2H, 3-H and 6-H), 3.94–4.06 (m, 1H, 6-H), 7.17–7.46 (m, 7H, Ph-H and Ts-*m*-H), 7.92 (d, *J*=8.4 Hz, 2H, Ts-*o*-H); ^{13}C NMR (50.3 MHz) 21.5 (C-5), 21.6 (Me), 28.0 (C-4), 43.5 (C-3), 46.4 (C-6), 127.7 (C-*i*-Ph), 128.6 (C-*p*-Ph), 128.8, 129.0 and 129.2 (C-Ph), 135.6 (C-*p*-Ts and C-*o*-Ph), 144.6 (C-*i*-Ts), 169.2 (C-2); MS, *m*/*z* (rel intensity) 409 (M^++1, 1), 407 (M^+−1, 1), 264 (67), 157 (43), 155 (37), 91 (100), 69 (36), 65 (40), 57 (35), 55 (45). A solution of MCPBA (78%, 4 g, 18.1 mmol) in anhydrous CH_2Cl_2 (20 ml) was added to a solution of **9a** (5 g, 12.2 mmol) in anhydrous CH_2Cl_2 (30 ml) cooled at 0°C. The mixture was allowed to rise to 25°C, and stirring was continued for 3 h. Saturated aqueous $NaHCO_3$ was added, and the aqueous layer was extracted with CH_2Cl_2. The extracts were dried and concentrated, and the resulting solid was crystallized from Et_2O to give pure dihydropyridone **10a** (2.4 g, 78%): IR (KBr) 1677, 1341, 1170 cm^{-1}; ^{1}H NMR (200 MHz) 2.37 (s, 3H, Me), 2.48 (m, 2H, 5-H), 4.00 (t, *J*=6.3 Hz, 2H, 6-H), 5.78 (dt, *J*=9.9 and 1.8 Hz, 1H, 3-H), 6.75 (dt, *J*=9.9, 4.2 Hz, 1H, 4-H), 7.26 (d, *J*=8.4 Hz, 2H, Ts-*m*-H), 7.87 (d, *J*=8.4 Hz, 2H, Ts-*o*-H); ^{13}C NMR (50.3 MHz) 21.5 (Me), 25.2 (C-5), 44.0 (C-6), 125.0 (C-4), 128.4 (C-*o*-Ts), 129.3 (C-*m*-Ts), 135.8 (C-*p*-Ts), 144.5 (C-3), 144.7 (C-*i*-Ts), 162.9 (C-2); MS, *m*/*z* (rel intensity) 252 (M^++1, 1), 187 (59), 119 (100), 91 (63), 68 (32), 65 (41).

1-(Methoxycarbonyl)-5,6-dihydro-2(1*H*)-pyridone (10b). A dispersion of NaH (60% in mineral oil, 4.5 g, 108 mmol) under N_2 was washed with anhydrous hexane and suspended

in anhydrous CH_2Cl_2 (100 ml). δ-Valerolactam (10.3 g, 100 mmol) was slowly added at 0°C, and the mixture was stirred for 15 min. Then, methyl chloroformate (15.5 ml, 200 mmol) was slowly added, and stirring was continued at 25°C for 3 h. After addition of H_2O, the mixture was extracted with CH_2Cl_2, and the combined organic extracts were washed with brine, dried, and concentrated to give, after chromatography (flash, SiO_2, 1:1 hexane–AcOEt), **1-(methoxycarbonyl)-2-piperidone (8b)**[3a] (12.4 g, 79%): IR (NaCl) 1785, 1716 cm^{-1}; ^1H NMR (200 MHz) 1.85 (m, 4H, 4-H and 5-H), 2.54 (m, 2H, 3-H), 3.74 (m, 2H, 6-H), 3.86 (s, 3H, OMe); ^{13}C NMR (50.3 MHz) 20.1 (C-4), 22.3 (C-5), 34.5 (C-3), 46.3 (C-6), 53.5 (OMe), 154.6 (CO_2Me), 171.0 (C-2). Operating as in the preparation of **9a**, from LDA (1.5 M in cyclohexane, 31.8 ml, 1.5 equiv.) in anhydrous THF (40 ml), piperidone **8b** (5 g, 31.8 mmol) in anhydrous THF (40 ml), and PhSeCl (6.1 g, 31.8 mmol) in anhydrous THF (40 ml), **1-(methoxycarbonyl)-3-(phenylselanyl)-2-piperidone (9b)** (3.7 g, 38%) was obtained after flash chromatography (SiO_2, 1:1 hexane–AcOEt): IR (NaCl) 1724, 1667 cm^{-1}; ^1H NMR (200 MHz) 1.52–1.88 (m, 4H, 4-H and 5-H), 3.60–3.90 (m, 2H, 6-H), 3.58 (t, J=7.8 Hz, 1H, 3-H), 3.67 (s, 3H, OMe), 7.26–7.34 (m, 3H, PhH), 7.62 (m, 2H, PhH); ^{13}C NMR (50.3 MHz) 20.8 (C-5), 28.5 (C-4), 44.7 (C-3), 46.3 (C-6), 53.8 (OMe), 128.3 (C-*i*-PhSe), 128.5 (C-*p*-PhSe), 129.1 (C-*m*-PhSe), 135.3 (C-*o*-PhSe), 155.0 (CO_2Me), 170.5 (C-2). Operating as in the preparation of **10a**, from MCPBA (77%, 10 g, 58.13 mmol) in anhydrous CH_2Cl_2 (60 ml), and piperidone **9b** (10.7 g, 34.18 mmol) in anhydrous CH_2Cl_2 (60 ml) for 18 h, dihydropyridone **10b** (3.42 g, 65%) was obtained after flash chromatography (SiO_2, 1:1 hexane–AcOEt): IR (NaCl) 1780, 1716 cm^{-1}; ^1H NMR (200 MHz) 2.44 (m, 2H, 5-H), 3.89 (s, 3H, OMe), 3.96 (t, J=6.6 Hz, 2H, 6-H), 5.99 (dt, J=9 and 2 Hz, 1H, 3-H), 6.84 (dt, J=9 and 4 Hz, 1H, 4-H); ^{13}C NMR (50.3 MHz) 24.4 (C-5), 43.6 (C-6), 53.6 (OMe), 125.5 (C-3), 144.2 (C-4), 154.5 (CO_2Me), 163.2 (C-2).

3-(Benzyloxycarbonyl)-1-(*p*-toluenesulfonyl)-5,6-dihydro-2(1*H*)-pyridone (12a). LHMDS (1 M in THF, 14 ml, 14 mmol) was slowly added to a solution of piperidone **8a** (1.61 g, 6.36 mmol) in anhydrous THF (90 ml) cooled at −78°C, and the mixture was stirred for 1 h. Then, benzyl chloroformate (0.9 ml, 6.36 mmol) was added, stirring was continued for 20 min, and PhSeBr, generated from Ph_2Se_2 (1.49 g, 4.77 mmol) and Br_2 (0.228 ml, 4.44 mmol) in anhydrous THF, was added. The mixture was stirred at −78°C for 30 min, allowed to rise to 25°C, poured into 0.1 N aqueous HCl, and extracted with AcOEt. The combined organic extracts were washed with saturated aqueous $NaHCO_3$, dried, and concentrated to give, after chromatography (flash, SiO_2, 3:1 hexane–AcOEt), **3-(benzyloxycarbonyl)-3-(phenylselanyl)-1-(*p*-toluenesulfonyl)-2-piperidone (11a)** (2.3 g, 67%): IR (NaCl) 1731, 1699, 1355, 1170 cm^{-1}; ^1H NMR (200 MHz) 1.64–1.75 (m, 1H, 4-Hax), 1.83–2.00 (m, 2H, 5-H), 2.20 (dt, J=14, 5.3 Hz, 1H, 4-Heq), 2.41 (s, 3H, Me), 3.70–3.79 (m, 2H, 6-H), 5.08 (s, 2H, CH_2Ph), 7.20–7.45 (m, 12H, PhH), 7.90 (d, J=8.4 Hz, 2H, Ts-*o*-H); ^{13}C NMR (50.3 MHz): 21.2 (C-5), 21.6 (Me), 31.3 (C-4), 45.7 (C-6), 55.5 (C-3), 67.7 (CH_2Ph), 125.8 (C-*i*-PhSe), 128.0, 128.2, 128.4, 128.7, 128.8, 129.3 and 129.8 (C-Ph), 134.9 (C-*i*-Bn), 135.3 (C-*p*-Ts), 138.3 (C-*o*-PhSe), 144.8 (C-*i*-Ts), 166.7 and 168.8 (C-2 and CO_2Bn); MS, *m*/*z* (rel intensity) 543 (M^++1, 0.1), 91 (100), 78 (26), 65 (23). A solution of MCPBA (77%, 2.31 g, 12.5 mmol) in anhydrous CH_2Cl_2 (80 ml) was slowly added under N_2 to a solution of piperidone **11a** (3.2 g, 5.89 mmol) in anhydrous CH_2Cl_2 (50 ml) cooled at 0°C. The mixture was allowed to rise to 25°C and stirred for 3 h, poured into saturated aqueous $NaHCO_3$, and extracted with CH_2Cl_2. The combined organic extracts were washed with brine, dried and concentrated to give dihydropyridone **12a** (2.1 g, 93%), which was used in the next reaction without further purification. An analytical sample was obtained by crystallization: mp 94–95°C (Et_2O); IR (NaCl) 1741, 1692, 1355, 1168 cm^{-1}; ^1H NMR (200 MHz) 2.40 (s, 3H, Me), 2.61 (td, J=6.4, 4.5 Hz, 2H, 5-H), 4.06 (t, J=6.4 Hz, 2H, 6-H), 5.18 (s, 2H, CH_2Ph), 7.24–7.36 (m, 7H, PhH and Ts-*m*-H), 7.56 (t, J=4.4 Hz, 1H, 4-H), 7.93 (d, J=8.4 Hz, 2H, Ts-*o*-H); ^{13}C NMR (50.3 MHz) 21.2 (Me), 25.1 (C-5), 43.0 (C-6), 66.6 (CH_2Ph), 127.9, 128.0, 128.2 and 129.1 (C-Ph), 135.0 (C-*i*-Bn), 135.3 (Ts-*p*-C), 144.6 (Ts-*i*-C), 151.4 (4-C), 159.1 and 162.2 (2-C and CO_2Bn); MS, *m*/*z* (rel intensity) 386 (M^++1, 0.3), 97 (36), 83 (65), 71 (50), 69 (71), 57 (100), 55 (89). Anal. Calcd for $C_{20}H_{19}O_5NS$: C, 62.32; H, 4.97; N, 3.63; S, 8.39. Found: C, 62.48; H, 4.96; N, 3.60; S, 8.19.

3-(Benzyloxycarbonyl)-1-(methoxycarbonyl)-5,6-dihydro-2(1*H*)-pyridone (12b). Operating as in the preparation of **11a**, from LHMDS (1 M in THF, 30 ml, 30 mmol), piperidone **8b** (2 g, 12.8 mmol) in anhydrous THF (60 ml), benzyl chloroformate (1.8 ml, 12.8 mmol), and PhSeBr, generated from Ph_2Se_2 (2.96 g, 9.48 mmol) and Br_2 (0.456 ml, 8.87 mmol) in anhydrous THF, **3-(benzyloxycarbonyl)-1-(methoxycarbonyl)-3-(phenylselanyl)-2-piperidone (11b)** (3.8 g, 68%) was obtained after flash chromatography (SiO_2, 1:1 hexane–AcOEt): IR (NaCl) 1776, 1725 cm^{-1}; ^1H NMR (300 MHz) 1.65 (m, 1H, 5-Heq), 1.83 (m, 1H, 5-Hax), 2.00 (ddd, J=13.8, 10, 5.8 Hz, 1H, 4-Hax), 2.25 (dddd, J=13.8, 7.9, 5.3, 0.9 Hz, 1H, 4-Heq), 3.45 (dddd, J=13.3, 6.5, 5.9, 0.9 Hz, 1H, 6-Heq), 3.70 (ddd, J=13.3, 8.1 5.5 Hz, 1H, 6-Hax), 3.86 (s, 3H, OMe), 5.15 and 5.24 (2d, J=12.3 Hz, 1H each, CH_2Ph), 7.25 (m, 3H, PhH), 7.35 (m, 5H, PhH), 7.49 (d, J=8 Hz,2H, PhH); ^{13}C NMR (50.3 MHz) 20.6 (C-5), 31.4 (C-4), 45.5 (C-6), 54.1 (OMe), 57.0 (C-3), 67.7 (CH_2Ph), 128.2, 128.4, 128.7 and 129.7 (C-Ph), 135.0 (C-*i*-Bn), 138.4 (C-*i*-PhSe), 154.7 (CO_2Me), 167.8 and 169.0 (C-2 and CO_2Bn); MS, *m*/*z* (rel intensity) 447 (M^+1), 284 (22), 91 (100); 77 (17); 65 (17). Anal. Calcd for $C_{21}H_{21}NO_5Se$: C, 56.51; H, 4.74; N, 3.14. Found: C, 56.46; H, 4.81; N, 3.12. Piperidone **11b** was oxidized by two different methods. *Method A:* Ozone was bubbled through a stirred solution of **11b** (2.45 g, 5.49 mmol) in anhydrous CH_2Cl_2 (50 ml) at −78°C until the solution turned to a characteristic pale blue color. Then, the solution was purged with N_2 and stirred at 25°C for 30 min. The solvent was removed, and the residue was chromatographed (flash, SiO_2, 3:2 hexane–AcOEt) to yield dihydropyridone **12b** (1.4 g, 87%): IR (KBr) 1773, 1717, 1704 cm^{-1}; ^1H NMR (300 MHz) 2.54 (q, 2H, 5-H), 3.89 (s, 3H,OMe), 3.96 (t, J=6.5 Hz, 2H, 6-H), 5.27 (s, 2H, CH_2Ph), 7.37 (m, 5H, Ph-H), 7.57 (t, J=4.4 Hz, 1H, 4-H); ^{13}C NMR (75 MHz) 24.6 (C-5), 43.3 (C-6), 54.1 (OMe), 67.1

(CH_2Ph), 128.2 and 128.5 (C-Ph), 135.3 and 135.4 (C-3 and C-*i*-Ph), 149.9 (C-4), 154.6 (CO_2Me), 159.6 and 163.5 (C-2 and CO_2Bn); MS, *m*/*z* (rel intensity) 183 (23), 157 (21), 155 (50), 112 (17), 91 (100), 65 (28). Anal. Calcd for $C_{15}H_{15}NO_5$: C, 62.28; H, 5.23; N, 4.84. Found: C, 62.12; H, 5.29; N, 4.77. *Method B:* Operating as in the preparation of **12a**, a solution of MCPBA (80%, 1.6 g, 7.6 mmol) and piperidone **11b** (3.4 g, 7.6 mmol) in anhydrous CH_2Cl_2 (60 ml) was allowed to react for 1 h 30 min. After workup and crystallization from hexane–AcOEt, dihydropyridone **12b** (1.64 g, 74%), was obtained. When an excess of MCPBA was used, **3-(benzyloxycarbonyl)-3,4-epoxy-1-(methoxycarbonyl)-2-piperidone** was isolated as the major compound: IR (KBr) 1780, 1751, 1731 cm^{-1}; ^1H NMR (300 MHz) 2.22 (ddd, *J*=15.2, 12.7, 5.7 Hz, 1H, 5-Hax), 2.41 (dm, *J*=15.3 Hz, 1H, 5-Heq), 3.48 (td, *J*=13, 4 Hz, 1H, 6-Hax), 3.80 (d, *J*=2.7 Hz, 1H, 4-H), 4.08 (s, 3H, Me), 4.12 (dd, *J*=13.2, 5.6 Hz, 1H, 6-Heq), 5.3 and 5.8 (2d, *J*=12.2 Hz, 1H each, CH_2Ph), 7.38 (m, 5H, PhH); ^{13}C NMR (75 MHz) 23.3 (C-5), 38.9 (C-6), 54.3 (OMe), 57.9 (C-4), 58.2 (C-3), 67.8 (CH_2Ph), 128.3, 128.4 and 128.5 (C-Ph), 134.6 (C-*i*-Ph), 153.8 (CO_2Me), 163.7 and 164.5 (C-2 and CO_2Bn); MS, *m*/*z* (rel intensity) 171 (39), 112 (34), 91 (100), 65 (18). Anal. Calcd for $C_{16}H_{14}NO_6$: C, 59.01; H, 4.95; N, 4.59. Found: C, 58.98; H, 5.08; N, 4.56.

(*S*)-(−)-5-(*tert*-Butyldimethylsilyloxy)-1-(*p*-toluenesulfonyl)-2-piperidone (14a). A mixture of (*S*)-(−)-5-hydroxy-2-piperidone (**13**)[4] (2 g, 17.3 mmol), *tert*-butyldimethylsilyl chloride (3.14 g, 20.8 mmol), and imidazole (2.94 g, 43.4 mmol) in DMF (14 ml) was stirred under N_2 at 25°C for 1 h. The solvent was evaporated, and AcOEt (100 ml) and 5% aqueous citric acid (50 ml) were added. The mixture was extracted with AcOEt, and the organic extracts were washed with 5% aqueous citric acid and saturated aqueous $NaHCO_3$. The combined organic extracts were dried and concentrated, and the resulting oil was chromatographed (Al_2O_3, CH_2Cl_2) to give **(*S*)-(−)-5-(*tert*-butyldimethylsilyloxy)-2-piperidone** (3.64 g, 91%): $[\alpha]_D^{20}=-12.09$ (*c* 2, MeOH); IR (KBr) 3145, 3043, 1644 cm^{-1}; ^1H NMR (300 MHz) 0.07 and 0.08 (2s, 3H each, Me_2Si), 0.88 (s, 9H, *t*-Bu), 1.87 (q, *J*=6 Hz, 2H, 4-H), 2.31 (dt, *J*=17.6, 6.1 Hz, 1H, 3-H), 2.58 (dt, *J*=17.6, 7.5 Hz, 1H, 3-H), 3.18 (ddd, *J*=12.5, 5, 2.5 Hz, 1H, 6-Hax), 3.39 (ddd, *J*=12.5, 3.9, 2.1 Hz, 1H, 6-Heq), 4.08 (qn, *J*=4.5 Hz, 1H, 5-Hax), 6.45 (br s, 1H, NH); ^{13}C NMR (75 MHz) −4.9 and −4.8 (Me_2Si), 17.9 (C–Si), 25.6 (*t*-Bu), 27.4 and 28.8 (C-3 and C-4), 49.2 (C-6), 64.0 (C-5), 172.1 (C-2). *n*-BuLi (1.6 M in hexane, 8.9 ml, 14.2 mmol) was added to a solution of the above protected piperidone (3 g, 13.1 mmol) in anhydrous THF (120 ml) cooled at 0°C, and the solution was stirred at 0°C for 25 min. Then, TsCl (3.75 g, 19.6 mmol) and DMAP (0.37 g, 3 mmol) were added, and the mixture was allowed to rise to 25°C, stirred for 3 h, poured into saturated aqueous $NaHCO_3$, and extracted with AcOEt. Concentration of the dried organic extracts followed by flash chromatography (SiO_2, CH_2Cl_2) gave **14a** (5.68 g, 57%) as a yellow solid: mp 137–138°C (Et_2O); $[\alpha]_D^{20}=-10.3$ (*c* 1, $CHCl_3$); IR (KBr) 1686, 1355, 1167 cm^{-1}; ^1H NMR (300 MHz) 0.08 and 0.11 (2s, 3H each, Me_2Si), 0.85 (s, 9H, *t*-Bu), 1.85 (m, 2H, 4-H), 2.38 (ddd, *J*=17, 6.2, 4.4 Hz, 1H, 3-Heq), 2.41 (s, 3H, MeTs), 2.6 (ddd, *J*=17, 10, 7 Hz, 1H, 3-Hax), 3.83 (dd, *J*=12.4, 3 Hz, 1H, 6-Hax), 3.97 (ddd, *J*=12.4, 4, 1.4 Hz, 1H, 6-Heq), 4.26 (m, 1H, 5-H), 7.28 (d, *J*=8.8 Hz, 2H, Ts-*m*-H), 7.89 (d, *J*=8.4 Hz, 2H, Ts-*o*-H); ^{13}C NMR (75 MHz) −4.9 (Me_2Si), 17.8 (C–Si), 21.5 (MeTs), 25.5 (*t*-Bu), 28.1 and 29.4 (C-3 and C-4), 53.3 (C-6), 63.9 (C-5), 128.4 (C-*o*-Ts) 129.1 (C-*m*-Ts), 136.0 (C-*p*-Ts), 144.5 (C-*i*-Ts), 169.6 (C-2); MS, *m*/*z* (rel intensity) 326 (100), 262 (27), 229 (30), 155 (84), 91 (64), 73 (61). Anal. Calcd for $C_{18}H_{29}NO_4SiS$: C, 56.37; H, 7.63; N, 3.65; S, 8.35. Found: C, 56.60; H, 7.74; N, 3.60; S, 8.13.

(*S*)-(+)-3-(Benzyloxycarbonyl)-5-(*tert*-butyldimethylsilyloxy)-1-(*p*-toluenesulfonyl)-5,6-dihydro-2(1*H*)-pyridone (16a). Operating as in the preparation of **11a**, from LHMDS (1 M in THF, 12 ml, 12 mmol), piperidone **14a** (2.0 g, 5.21 mmol) in anhydrous THF (100 ml), benzyl chloroformate (0.77 ml, 5.73 mmol), and PhSeBr (1.59 g, 6.77 mmol) in anhydrous THF (25 ml), two epimeric **(*S*)-3-(benzyloxycarbonyl)-5-(*tert*-butyldimethylsilyloxy)-3-(phenylselanyl)-1-(*p*-toluenesulfonyl)-2-piperidones (15a)** (7:3, 2.97 g, 85%) were obtained after flash chromatography (SiO_2, 4:1 hexane–AcOEt). Major epimer (oil): $[\alpha]_D^{20}=-41.7$ (*c* 0.7, $CHCl_3$); IR (NaCl) 1730, 1708, 1361, 1172 cm^{-1}; ^1H NMR (300 MHz) −0.06 and 0.01 (2s, 3H each, Me_2Si), 0.83 (s, 9H, *t*-Bu), 1.85 (dd, *J*=14.6, 6.6 Hz, 1H, 4-H), 2.44 (s, 3H, MeTs), 2.49 (dd, *J*=14, 6.6 Hz, 1H, 4-H), 3.39 (dd, *J*=13.5, 3.8 Hz, 1H, 6-H), 3.80 (dd, *J*=13.5, 4.7 Hz, 1H, 6-H), 3.95 (m, 1H, 5-Hax), 5.06 and 5.15 (2d, *J*=12.1 Hz, 1H each, CH_2Ph), 7.2–7.4 (m, 12H, PhH), 7.95 (d, *J*=8.25 Hz, 2H, Ts-*o*-H); ^{13}C NMR (75 MHz) −5.0 and −4.9 (Me_2Si), 17.9 (C–Si), 21.7 (MeTs), 25.6 (*t*-Bu), 40.7 (C-4), 51.3 (C-6), 54.0 (C-3), 64.5 (C-5), 67.9 (CH_2Ph), 125.6 (C-*i*-Ph), 128.3, 128.5, 128.8, 129.1, 129.3 and 129.9 (C-Ph), 134.7 (C-*p*-Ts), 135.3 (C-*i*-SePh), 138.3 (C-*o*-SePh), 144.8 (C-*i*-Ts), 166.2 (CO_2Bn), 168.2 (C-2); MS, *m*/*z* (rel intensity) 352 (6), 229 (7), 155 (8), 91 (100), 79 (8), 78 (12), 77 (12). Anal. Calcd for $C_{32}H_{39}NO_6SSeSi$: C, 57.13; H, 5.84; N, 2.08; S, 4.77. Found: C, 57.08; H, 5.95; N, 2.03; S, 4.68. Minor epimer (solid): mp 104–106°C (Et_2O); $[\alpha]_D^{20}=+47.2$ (*c* 0.5, $CHCl_3$); IR (KBr) 1737, 1665, 1359, 1176 cm^{-1}; ^1H NMR (300 MHz) −0.02 and 0.02 (2s, 3H each, Me_2Si), 0.81 (s, 9H, *t*-Bu), 2.17 (dd, *J*=14.3, 3.6 Hz, 1H, 4-Hax), 2.36 (s, 3H, MeTs), 2.50 (ddd, *J*=14.3, 5.1, 1.3 Hz, 4-Heq), 3.78 (ddd, *J*=12.7, 5, 1.3 Hz, 1H, 6-Heq), 3.86 (dd, *J*=12.6, 3.6 Hz, 1H, 6-Hax), 4.19 (m, 1H, 5-Hax), 4.93 and 5.07 (2 d, *J*=12.8 Hz, 1H each, CH_2Ph), 7.1–7.4 (m, 10 H, PhH), 7.53 (d, *J*=8.3 Hz, 2H, Ts-*m*-H), 7.89 (d, *J*=8.3 Hz, 2H, Ts-*o*-H); ^{13}C NMR (75 MHz) −5.2 and −5.0 (Me_2Si), 18.0 (C–Si), 21.6 (MeTs), 25.6 (*t*-Bu), 39.7 (C-4), 52.4 (C-6), 63.8 (C-5), 67.4 (CH_2Ph), 126.4 (C-*i*-Ph), 127.4, 127.8, 128.2, 128.6, 128.7, 129.1 and 129.8 (C-Ph), 134.9 (C-*i*-Ts), 135.2 (C-*i*-SePh), 138.2 (C-*o*-SePh), 144.6 (C-*p*-Ts), 166.1 (CO_2Bn), 168.9 (C-2); MS, *m*/*z* (rel intensity) 352 (6), 229 (6), 255 (8), 91 (100), 79 (5), 78 (9), 77 (9). Anal. Calcd for $C_{32}H_{39}NO_6SSeSi$: C, 57.13; H, 5.84; N, 2.08; S, 4.77. Found: C, 56.77; H, 5.96; N, 2.03; S, 4.58. Operating as in the preparation of **12a**, a solution of selanides **15a** (118 mg, 0.17 mmol) and MCPBA (77%, 58 mg, 0.26 mmol) in anhydrous CH_2Cl_2 (7 ml) was stirred for 1.5 h to give pure dihydropyridone **16a** (61 mg, 67%) as a yellow solid after crystallization: mp 140–143°C (Et_2O); $[\alpha]_D^{20}=+10.7$ (*c* 1, $CHCl_3$); IR (KBr) 1714, 1679, 1352, 1166 cm^{-1}; ^1H NMR (300 MHz) 0.13 and 0.16 (2s, 3H

each, Me_2Si), 0.90 (s, 9H, *t*-Bu), 2.42 (s, 3H, MeTs), 3.88 (dd, *J*=12.9, 7.9 Hz, 1H, 6-Hax), 4.21 (ddd, *J*=12.7, 4.8, 0.9 Hz, 1H, 6-Heq), 4.63 (ddd, *J*=7.8, 4.8, 3 Hz, 1H, 5-Hax), 5.21 (s, 2H, CH_2Ph), 7.31 (m, 3H, 4-H and Ts-*m*-H), 7.93 (d, *J*=8Hz, 2H, Ts-*o*-H); ^{13}C NMR (75 MHz) −4.7 (Me_2Si), 17.9 (C–Si), 21.6 (MeTs), 25.5 (*t-Bu*-C–Si), 49.9 (C-6), 63.9 (C-5), 67.3 (CH_2Ph), 127.8, 128.2, 128.3 and 128.4 (C-Ph), 128.6 (C-*m*-Ts), 129.4 (C-*o*-Ts), 135.1 (C-3), 135.4 (C-*p*-Ts), 144.9 (C-*i*-Ts), 151.7 (C-4), 158.5 (CO_2Bn), 162.4 (C-2); MS, *m/z* (rel intensity) 275 (6), 155 (6), 108 (6), 92 (12), 91 (100). Anal. Calcd for $C_{26}H_{33}NO_6SSi$: C, 60.56; H, 6.45; N, 2.72; S, 6.22. Found: C, 60.37; H, 6.57; N, 2.62; S, 6.01.

(*S*)-(+)-3-(Benzyloxycarbonyl)-5-(*tert*- butyldimethylsilyloxy)-1-(methoxycarbonyl)-5,6-dihydro-2(1*H*)-pyridone (16b). Operating as in the preparation of **11a**, from LHMDS (1 M in THF, 3.8 ml, 3.8 mmol), piperidone **14b**[10] (0.5 g, 1.74 mmol) in anhydrous THF (10 ml), benzyl chloroformate (0.23 ml, 1.74 mmol), and PhSeBr (0.57 g, 2.41 mmol) in anhydrous THF (6 ml), an epimeric mixture of **(*S*)-3-(benzyloxycarbonyl)-5-(*tert*-butyldimethylsilyloxy)-1-(methoxycarbonyl)-3-(phenylselanyl)-2-piperidones (15b)** (2.5:1, 0.67 g, 67%) was obtained after flash chromatography (SiO_2, CH_2Cl_2). The major epimer could be separated: IR (NaCl) 1780, 1730 cm^{-1}; ^1H NMR (200 MHz) 0.02 (s, 6H, Me_2Si), 0.87 (s, 9H, *t*-Bu), 2.06 (dd, *J*=14, 6.6 Hz, 1H, 4-H), 2.50 (dd, *J*=14, 6.2 Hz, 1H, 4-H), 3.31 (dd, *J*=13.6, 4.8 Hz, 1H, 6-H), 3.82 (dd, *J*=13.7, 5.3 Hz, 1H, 6-H), 3.94 (s, 3H, CO_2Me), 3.96 (m, 1H, 5-H), 5.1 and 5.2 (2d, *J*=12.2 Hz, 1H each, CH_2Ph), 7.41 (m, 10H, PhH); ^{13}C NMR (50.3 MHz) −5.1 and −4.9 (Me_2Si), 17.8 (C–Si), 25.5 (*t*-Bu), 40.9 (C-4), 51.1 (C-6), 54.3 (CO_2Me), 55.1 (C-3), 64.0 (C-5), 67.9 (CH_2Ph), 128.4, 128.5, 128.8 and 129.8 (C-Ph), 134.8 (C-*i*-Bn), 138.4 (C-*o*-SePh), 154.4 (CO_2Me), 167.2 (CO_2Bn), 168.7 (C-2); MS, *m/z* (rel intensity) 577 (M^++1, 0.002), 520 (2), 272 (12), 91(100), 77 (5), 59 (6). Anal. Calcd for $C_{27}H_{35}NO_6SeSi{\cdot}1/4H_2O$: C, 55.8; H, 6.16; N, 2.41. Found: C, 55.55; H, 6.11; N, 2.63. Selanides **15b** (676 mg, 1.17 mmol) in anhydrous CH_2Cl_2 (5 ml) were treated with O_3 as in the preparation of **12b** (Method A). The crude mixture was poured into brine and extracted with CH_2Cl_2. The combined organic extracts were dried and concentrated, and the residue was chromatographed (flash, SiO_2, 7:3 hexane–AcOEt) to give dihydropyridone **16b** (386 mg, 78%): $[\alpha]_D^{20}$=+10.5 (*c* 1, $CHCl_3$); IR (KBr) 1780, 1727, 1389 cm^{-1}; ^1H NMR (200 MHz) 0.15 (s, 6H, Me_2Si), 0.92 (s, 9H, *t*-Bu), 3.67 (dd, *J*=12.8, 9.2 Hz, 1H, 6-Hax), 3.90 (s, 3H, OMe), 4.12 (ddd, *J*=12.8, 5.1, 1.5 Hz, 1H, 6-Heq), 4.63 (ddd, *J*=9, 5.1, 2.8 Hz, 1H, 5-Hax), 5.30 (s, 2H, CH_2Ph), 7.36 (m, 6H, 4-H, PhH); ^{13}C NMR (50.3 MHz) −5.0 (Me_2Si), 17.7 (C–Si), 25.3 (*t*-Bu), 50.0 (C-6), 54.0 (OMe), 63.6 (C-5), 67.1 (CH_2Ph), 127.9, 128.1 and 128.3, (C-Ph, C-3), 135.0 (C-*i*-Bn), 151.7 (C-4), 158.5 (CO_2Bn), 162.2 (C-2); MS, *m/z* (rel intensity) 240 (14), 91 (100). Anal. Calcd for $C_{21}H_{29}NO_6Si{\cdot}1/2H_2O$: C, 58.86; H, 7.06; N, 3.27. Found: C, 58.82; H, 7.08; N, 3.42.

General procedures for Diels–Alder cycloadditions

Method A: An excess of the diene was added to a solution of the 5,6-dihydro-2(1*H*)-pyridone in distilled and degased *p*-cymene, and the mixture was stirred at reflux temperature until disappearance of the dienophile by TLC. After evaporation of the solvent, the residue was chromatographed (flash, SiO_2) unless otherwise indicated.

Method B: An excess of the diene was added to a solution of the 5,6-dihydro-2(1*H*)-pyridone in anhydrous C_6H_6, and the mixture was stirred at reflux temperature until disappearance of the dienophile by TLC. After evaporation of the solvent, the residue was extracted with AcOEt or CH_2Cl_2. The organic extracts were dried and concentrated, and the crude product was chromatographed (flash, SiO_2) unless otherwise indicated.

Method C: A solution of the 5,6-dihydro-2(1*H*)-pyridone in anhydrous CH_2Cl_2 was slowly added to a suspension of anhydrous $ZnBr_2$ (1 equiv.) in anhydrous CH_2Cl_2 at 0°C. Then, an excess of the diene was added dropwise, and the mixture was stirred either at 0°C or at 25°C, depending on the reactivity of the dienophile, until disappearance of the dienophile by TLC. A saturated aqueous $NaHCO_3$ solution was added, and the mixture was extracted with CH_2Cl_2. The combined organic extracts were dried and concentrated, and the residue was chromatographed (flash, SiO_2) unless otherwise indicated.

Diels–Alder reactions from Danishefsky's diene 1

With dihydropyridone 10a. *Method A:* From **10a** (500 mg, 1.98 mmol) and diene **1** (1.34 ml, 6.94 mmol) in *p*-cymene (15 ml) for 6 h, a residue was obtained. Anhydrous THF (50 ml) and CSA (300 mg, 1.29 mmol) were added to the residue, and the resulting solution was stirred at 0°C for 1 h. After addition of saturated aqueous $NaHCO_3$, the mixture was extracted with AcOEt. Concentration of the dried organic extracts afforded, after chromatography (Et_2O), **1,6-dioxo-2-(*p*-toluenesulfonyl)-1,2,3,4,4a,5,6,7-octahydroisoquinoline (17a)** (217 mg, 34%): mp 156–159°C (Et_2O); IR (KBr) 1716, 1679, 1678, 1347, 1174 cm^{-1}; ^1H NMR (300 MHz) 1.65 (qd, *J*=12.7, 4.2 Hz, 1H, 4-Hax), 2.09 (m, 1H, 4-Heq), 2.15 (dd, *J*=14.6, 12.4 Hz, 1H, 5-Hax), 2.44 (s, 3H, Me), 2.54 (dd, *J*=14.7, 4.5 Hz, 1H, 5-Heq), 2.67–2.82 (m, 1H, 4a-H), 3.00 (dd, *J*=23.4, 3.1 Hz, 1H, 7-H), 3.07 (ddd, *J*=23.1, 4.8, 2.5 Hz, 1H, 7-H), 3.58 (td, *J*=12.7, 2.9 Hz, 1H, 3-Hax), 4.39 (ddd, *J*=12.7, 4.2, 3 Hz, 1H, 3-Heq), 7.08 (m, 1H, 8-H), 7.24 (d, *J*=8.0 Hz, 2H, Ts-*m*-H), 7.83 (d, *J*=8.3 Hz, 2H, Ts-*o*-H). Anal. Calcd for $C_{16}H_{17}O_4NS$: C, 60.17; H, 5.37; N, 4.39; S, 10.04. Found: C, 59.65; H, 5.27; N, 4.18; S, 9.62.

With dihydropyridone 12a. *Method A:* Dihydropyridone **12a** (500 mg, 1.29 mmol) was allowed to react with diene **1** (0.89 ml, 4.5 mmol) in *p*-cymene (10 ml) for 1 h. After CSA treatment (300 mg, 0°C, 1 h), as above, followed by chromatography (65:35 hexane–AcOEt), adducts ***endo*-18a** (250 mg, 40%) and its C-8 epimer ***exo*-18a** (115 mg, 18%) were obtained. **(4a*RS*,8*SR*,8a*SR*)-8a-(Benzyloxycarbonyl)-8-methoxy-1,6-dioxo-2-(*p*-toluenesulfonyl)perhydroisoquinoline (*endo*-18a)**: mp 90–91°C (Et_2O); IR (KBr) 1744, 1724, 1679, 1359, 1174 cm^{-1};^1H NMR (200 MHz) 1.97 (m, 1H, 4-Hax) 2.22 (m,1H, 4-Heq), 2.28 (dd, *J*=15, 6 Hz, 1H, 5-Hax), 2.41 (ddd, *J*=15, 3, 1.2 Hz, 1H, 5-Heq), 2.41 (s, 3H, MeTs), 2.65 (ddd, *J*=15.4, 3, 1.2 Hz, 1H, 7-Heq), 2.83 (m, 1H, 4a-H), 2.82 (s, 3H, OMe), 2.83 (dd,

J=16, 3.6 Hz, 1H, 7-Hax), 3.90 (ddd, J=12.6, 8.8, 4.5 Hz, 1H, 3-Hax), 4.09 (dt, J=12.7, 5 Hz, 1H, 3-Heq), 4.29 (td, J=2.8, 1 Hz, 1H, 8-Heq), 5.20 and 5.05 (2d, J=12.3 Hz, 1H each, CH_2Ph), 7.2–7.4 (m, 7H, PhH and Ts-*m*-H), 7.89 (d, J=8.3 Hz, 2H, Ts-*o*-H); MS, *m/z* (rel intensity) 286 (6), 256 (23), 91 (100), 65 (12). Anal. Calcd for $C_{25}H_{27}O_7NS$: C, 61.84; H, 5.60; N, 2.88; S, 6.60. Found: C, 61.84; H, 5.76; N, 2.70; S, 6.55. **(4a*RS*,8*RS*,8a*SR*)-Isomer (*exo*-18a)**: mp 150–151°C (Et_2O); IR (KBr) 1729, 1720, 1702, 1359, 1174 cm^{-1}; ^1H NMR (200 MHz) 1.64 (dtd, J=14.5, 7, 3.2 Hz, 1H, 4-H), 1.97 (t, J=14 Hz, 1H, 5-Hax), 2.34 (ddd, J=14.6, 5.3, 2 Hz, 1H, 5-Heq), 2.41 (s, 3H, MeTs), 2.43 (dd, J=15.5, 3 Hz, 1H, 7-Hax), 2.51 (m, 1H, 4-H), 2.58 (ddd, J=15.5, 3, 2 Hz, 1H, 7-Heq), 3.00 (s, 3H, OMe), 3.23 (m, 1H, 4a-H), 3.55 (ddd, J=13.6, 7.7, 6.2 Hz, 1H, 3-Hax), 4.14 (dt, J=13.6, 6.2 Hz, 1H, 3-Heq), 4.38 (t, J=3 Hz, 1H, 8-H), 5.24 and 4.96 (2d, J=12 Hz, 1H each, CH_2Ph), 7.20–7.35 (m, 7H, PhH), 7.86 (d, J=8.4 Hz, 2H, Ts-*o*-H); MS, *m/z* (rel intensity) 350 (7); 91 (100); 65 (12); 57 (10); 55 (10). Anal. Calcd for $C_{25}H_{27}O_7NS$: C, 61.84; H, 5.60; N, 2.88; S, 6.60. Found: C, 61.89; H, 5.69; N, 2.89; S, 6.60. *Method B:* Dihydropyridone **12a** (500 mg, 1.29 mmol) was allowed to react with diene **1** (0.5 ml, 2.6 mmol) in C_6H_6 (10 ml) for 30 min. After CSA treatment (300 mg, 0°C, 1 h) as above, followed by chromatography (3:1 hexane–AcOEt), adducts **18a** (250 mg, 41%) and **19a** (170 mg, 30%) were obtained. ***cis*-8a-(Benzyloxycarbonyl)-1,6-dioxo-2-(*p*-toluenesulfonyl)-1,2,3,4,4a,5,6,8a-octahydroisoquinoline (19a)**: mp 159–161°C (Et_2O); IR (KBr) 1739, 1687, 1676, 1354, 1167 cm^{-1}; ^1H NMR (200 MHz) 1.85 (dtd, J=14, 10 and 5 Hz, 1H, 4-Hax), 2.05 (dq, J=14 and 4.5 Hz, 1H, 4-Heq), 2.29 (dd, J=17 and 6 Hz, 1H, 5-H), 2.43 (s, 3H, Me), 2.47 (dd, J=17 and 5 Hz, 1H, 5-H), 2.97 (m, 1H, 4a-H), 3.75 (ddd, J=13, 9 and 4.5 Hz, 1H, 3-Heq), 4.19 (dt, J=13 and 5 Hz, 1H, 3-Hax), 5.06 and 5.17 (2d, J=12 Hz, 1H each, CH_2Ph), 6.14 and 6.77 (2d, J=10 Hz, 1H each, 7-H and 8-H), 7.3 (m, 8H, PhH and Ts-*m*-H), 7.88 (d, J=8.4 Hz, 2H, Ts-*o*-H); Anal. Calcd for $C_{24}H_{23}O_6NS$: C, 63.56; H, 5.11; N, 3.09; S, 7.07. Found: C, 63.57; H, 5.21; N, 3.28; S, 6.98. ***cis*-8a-(Benzyloxycarbonyl)-8-methoxy-1-oxo-2-(*p*-toluenesulfonyl)-6-(trimethylsilyloxy)-1,2,3,4,4a,5,6,8a-octahydroisoquinoline** was also isolated (55 mg, 8%): IR (KBr) 1735, 1687, 1366, 1177 cm^{-1}; ^1H NMR (300 MHz) 0.13 (m, 9H, Me_3Si), 1.65–1.69 (dm, J=12.5 Hz, 1H, 4-H), 1.84 (d, J=15.6 Hz, 1H, 5-Hax), 1.98 (dd, 15.6, 4.7 Hz, 1H, 5-Heq), 2.40 (s, 3H, Me-Ts), 2.51–2.66 (m, 1H, 4a-H), 2.67–2.75 (m, 1H, 4-H), 2.82 (s, 3H, OMe), 3.86 (td, J=12.1, 5.5 Hz, 1H, 3-Hax), 4.13 (m, 1H, 3-Heq), 4.31 (d, J=5.2 Hz, 1H, 8-H), 4.99 (d, J=12.4 Hz, 1H, CH_2Ph), 5.08–5.16 (m, 1H, 7-H), 5.22 (d, J=12 Hz, 1H, CH_2Ph), 7.26–7.31 (m, 7H, PhH), 7.89 (d, J=7.8 Hz, 2H, Ts-*o*-C); ^{13}C NMR (50.3 MHz): 0.2 (Me_3Si), 21.6 (MeTs), 24.6 (C-4), 32.7 (C-4a), 33.1 (C-5), 46.3 (C-3), 57.6 (OMe), 59.2 (C-8a), 67.4 (CH_2Ph), 76.0 (C-8), 100.9 (C-7), 128.0, 128.1, 128.3, 128.5, and 129.0 (C-Ph), 135.7 (C-*p*-Ts), 136.1 (C-*i*-Bn), 144.4 (C-*i*-Ts), 150.2 (C-6), 167.5 and 168.8 (C-1 and CO_2Bn). Anal. Calcd for $C_{29}H_{35}O_7NSSi$: C, 61.14; H, 6.19; N, 2.46; S, 5.63. Found: C, 60.53; H, 6.46; N, 2.55; S, 5.19.

With dihydropyridone 12b. *Method A:* From **12b** (500 mg, 1.73 mmol) and diene **1** (0.7 ml, 3.5 mmol) in *p*-cymene (8 ml) for 5 h, and then from CSA (140 mg, 0.6 mmol) in anhydrous THF (6 ml) at 25°C for 1 h, adducts **18b** (100 mg, 15%) and **19b** (130 mg, 21%) were obtained after chromatography (4:1 hexane–AcOEt). **(4a*RS*,8*SR*,8a*SR*)-8a-(Benzyloxycarbonyl)-8-methoxy-2-(methoxycarbonyl)-1,6-dioxoperhydroisoquinoline (*endo*-18b)**: IR (NaCl) 1775, 1725 cm^{-1}; ^1H NMR (300 MHz) 1.92 (dq, J=11, 4 Hz, 1H, 4-H), 2.15 (m, 1H, 4-H), 2.32 (dd, J=15, 6 Hz, 1H, 5-Hax), 2.46 (ddd, J=15, 6.3, 1.1 Hz, 1H, 5-Heq), 2.76 (ddd, J=16, 3, 1.1 Hz, 1H, 7-Heq), 2.81 (m, 1H, 4a-H), 2.91 (dd, J=16, 3.4 Hz, 1H, 7-Hax), 3.26 (s, 3H, OMe), 3.71 (ddd, J=13, 9, 5 Hz, 1H, 3-Heq), 3.87 (m, 1H, 3-Hax), 3.89 (s, 3H, CO_2Me), 4.51 (td, J=3.2, 1 Hz, 1H, 8-H), 5.20 and 5.24 (2d, J=12 Hz, 1H each, CH_2Ph), 7.35 (m, 5H, PhH). Anal. Calcd for $C_{20}H_{23}NO_7$: C, 61.69; H, 5.95; N, 3.60. Found: C, 61.59; H, 6.03; N, 3.53. ***cis*-8a-(Benzyloxycarbonyl)-2-(methoxycarbonyl)-1,6-dioxo-1,2,3,4,4a,5,6,8a-octahydroisoquinoline (19b)**: IR (NaCl) 1780, 1720, 1690 cm^{-1}; ^1H NMR (200 MHz) 1.91 (m, 2H, 4-H), 2.34 (dd, J=16.5, 6 Hz, 1H, 5-H), 2.51 (dd, J=16, 5 Hz, 5-H), 3.05 (m, 1H, 4a-H), 3.59 (ddd, J=13, 10.7, 4.5 Hz, 1H, 3-H), 3.88 (s, 3H, OMe), 3.97 (dt, J=13, 4.7 Hz, 1H, 3-H), 5.23 and 5.27 (2d, J=12.2 Hz, 1H each, CH_2Ph), 6.19 (d, J=10 Hz, 1H, 7-H), 6.93 (dd, J=10, 1.1 Hz, 1H, 8-H), 7.34 (m, 5H, PhH). Anal. Calcd for $C_{19}H_{19}NO_6$: C, 63.86; H, 5.36; N, 3.92. Found: C, 63.60; H, 5.40; N, 3.78. *Method B:* From **12b** (510 mg, 1.76 mmol) and diene **1** (0.7 ml, 3.5 mmol) in C_6H_6 (10 ml) for 2 h, and then from CSA (410 mg, 1.77 mmol) in anhydrous THF (10 ml) at 0°C for 1 h, adducts **18b** (122 mg, 17%) and **19b** (390 mg, 62%) were obtained after chromatography (4:1 hexane–AcOEt).

With dihydropyridone 16a. *Method A:* From **16a** (516 mg, 1 mmol) and diene **1** (0.67 ml, 3.5 mmol) in *p*-cymene (15 ml) for 1.5 h, adducts **20a** (14%, one diastereomer of unknown configuration at C-8) and **22a** (18%) were obtained after chromatography (CH_2Cl_2–1% MeOH). An analytical sample of **(4*S*,4a*R*,8a*S*)-8a-(benzyloxycarbonyl)-4-(*tert*-butyldimethylsilyloxy)-8-methoxy-1,6-dioxo-2-(*p*-toluenesulfonyl)perhydroisoquinoline (20a)** was obtained by chromatography (CH_2Cl_2–1% MeOH): IR (KBr) 1743, 1725, 1694, 1357, 1172 cm^{-1}; ^1H NMR (300 MHz) 0.13 (s, 6H, Me_2Si), 0.91 (s, 9H, *t*-Bu), 2.05 (dd, J=15, 7 Hz, 1H, 5-H), 2.40 (s, 3H, MeTs), 2.65 (m, 2H, 5-H, 7-H), 2.84 (m, 2H, 4-Ha and 7-H), 2.94 (s, 3H, OMe), 3.39 (dd, J=13.6, 11 Hz, 1H, 3-Hax), 4.30 (m, 3H, 3-Heq, 4-H and 8-H), 5.06 and 5.14 (2d, J=12.5 Hz, 1H each, CH_2Ph), 7.15–7.39 (m, 7H, PhH), 7.87 (d, J=8.2 Hz, 2H, Ts-*o*-H). **(4*S*,4a*S*,8a*S*)-8a-(Benzyloxycarbonyl)-4-(*tert*-butyldimethylsilyloxy)-1,6-dioxo-2-(*p*-toluenesulfonyl)-1,2,3,4,4a,5,6,8a-octahydroisoquinoline (22a):** mp 133–135°C (Et_2O); $[\alpha]_D^{20}$=−46.8 (*c* 0.25, $CHCl_3$); IR (KBr) 1748, 1698, 1686, 1359, 1176 cm^{-1}; ^1H NMR (300 MHz) −0.02 and 0.05 (2s, 3H each, Me_2Si), 0.75 (s, 9H, *t*-Bu), 2.23 (dd, J=17, 6 Hz, 1H, 5-H), 2.41 (s, 3H, MeTs), 2.62 (dd, J=17, 6.4 Hz, 1H, 5-H), 2.95 (td, J=6, 3 Hz, 1H, 4a-H), 3.84 (dd, J=12.7, 3.3 Hz, 1H, 3-H), 3.97 (dd, J=12.7, 5.1 Hz, 1H, 3-H), 4.20 (dt, J=5, 3.1 Hz, 1H, 4-Hax), 5.07 and 5.20 (2d, J=12.5 Hz, 1H each, CH_2Ph), 6.14 (d, J=10.3 Hz, 1H, 7-H), 6.93 (d, J=10.3 Hz, 1H, 8-H), 7.24–7.36 (m, 7H, PhH), 7.91 (d, J=8.4 Hz, 2H, Ts-*o*-H); MS, *m/z* (rel intensity) 583 (M+, 0.03), 526 (7), 228 (11), 91 (100), 73 (20). Anal. Calcd for $C_{30}H_{37}NO_7SSi$: C, 61.72; H, 6.39; N, 2.4; S, 5.49. Found: C, 61.66; H, 6.36; N, 2.43; S,

5.38. *Method B:* From **16a** (300 mg, 0.58 mmol) and diene **1** (0.34 ml, 1.74 mmol) in C_6H_6 (10 ml) for 1 h, adducts **20a** (one diastereomer of unknown configuration at C-8, accompanied by a minor diastereomer of unknown configuration, 4:1, 132 mg, 40%) and **21a** (46 mg, 13%) were obtained after chromatography (9:1 hexane–AcOEt). **(4*S*,4a*R*,8a*R*)-8a-(Benzyloxycarbonyl)-4-(*tert*-butyldimethylsilyloxy)-1,6-dioxo-2-(*p*-toluenesulfonyl)-1,2,3,4,4a,5,6,8a-octahydroisoquinoline (21a):** ^{1}H NMR (200 MHz) 0.07 and 0.11 (2s, 3H each, Me_2Si), 0.90 (s, 9H, t-Bu), 2.30 (dd, *J*=16.8, 5 Hz, 1H, 5-H), 2.41 (s, 3H, Me-Ts), 2.62 (dd, *J*=16.8, 5.2 Hz, 1H, 5-H), 2.92 (dt, *J*=9.2, 5.2 Hz, 1H, 4a-H), 3.51 (dd, *J*=12, 8.5 Hz, 1 H, 3-Hax), 3.88 (td, *J*=8.7, 4.7 Hz, 1H, 4-Hax), 4.22 (dd, *J*=12, 4.8 Hz, 1H, 3-Heq), 5.07 (s, 2H, CH_2Ph), 6.17 (d, *J*=10.2 Hz, 1H, 7-H), 6.75 (d, *J*=10.2 Hz, 1H, 8-H), 7.10–7.40 (m, 7H, PhH), 7.88 (d, *J*=8.4 Hz, 2H, Ts-*o*-H). *Method C:* From **16a** (70 mg, 0.13 mmol) in CH_2Cl_2 (2 ml), $ZnBr_2$ (30 mg, 0.13 mmol) in CH_2Cl_2 (2 ml), and diene **1** (0.07 ml, 0.41 mmol) at 25°C for 4 h, adducts **20a** (one diastereomer of unknown configuration at C-8, accompanied by traces of the same minor diastereomer as in Method B, 17 mg, 20%) were obtained after chromatography (9:1 hexane–AcOEt).

With dihydropyridone 16b. *Method B:* From **16b** (311 mg, 0.74 mmol) and diene **1** (0.28 ml, 1.47 mmol) in C_6H_6 (6 ml) for 2 h, and then from CSA (17 mg, 0.07 mmol) in THF (6 ml) at reflux for 2.5 h, a mixture of adducts was obtained after chromatography (9:1 hexane–AcOEt). Crystallization (pentane) gave adduct **21b** (40 mg, 11%). Evaporation of the mother liquor furnished adduct **20b** (one diastereomer of unknown configuration at C-8, accompanied by traces of a minor diastereomer, 100 mg, 29%). **(4*S*,4a*R*,8a*S*)-8a-(Benzyloxycarbonyl)-4-(*tert*-butyldimethylsilyloxy)-8-methoxy-2-(methoxycarbonyl)-1,6-dioxoperhydroisoquinoline (20b):** ^{1}H NMR (200 MHz) 0.01 and 0.05 (2s, 3H each, Me_2Si), 0.83,(s, 9H, *t*-Bu), 2.05 (dd, *J*=15, 6.6 Hz, 1H, 5-H), 2.63 (m, 2H, 5-H and 7-H), 2.80 (m, 1H, 4a-H), 2.89 (dd, *J*=16, 3.6 Hz, 1H, 7-H), 3.20 (s, 3H, OMe), 3.22 (dd, *J*=12.4, 9.6 Hz, 1H, 3-Hax), 3.82 (s, 3H, CO_2Me), 3.96 (dd, *J*=12.4, 5.4 Hz, 1H, 3-Heq), 4.20 (ddd, *J*=11, 9.2, 5.2 Hz, 1H, 4-H), 4.42 (m, 1H, 8-H), 5.13 and 5.21 (2d, *J*=12.8 Hz, 1H each, CH_2Ph), 7.29 (s, 5H, PhH). Anal. Calcd for $C_{26}H_{37}NO_8Si$: C, 60.09; H, 7.18; N, 2.70. Found: C, 60.16; H, 7.26; N, 2.78. **(4*S*,4a*R*,8a*R*)-8a-(Benzyloxycarbonyl)-4-(*tert*-butyldimethylsilyloxy)-2-(methoxycarbonyl)-1,6-dioxo-1,2,3,4,4a,5,6,8a-octahydroisoquinoline (21b):** mp 122–124°C (*n*-pentane). IR (KBr) 1743, 1726, 1711, 1687 cm^{-1}; ^{1}H NMR (200 MHz) 0.05 and 0.06 (2s, 3H, Me_2Si), 0.89 (s, 9H, *t*-Bu), 2.35 (dd, *J*=17, 5.2 Hz, 1H, 5-H), 2.67 (dd, *J*=17, 4.6 Hz, 1H, 5-H), 3.01 (dtd, *J*=8.8, 4.6, 1.5 Hz, 1H, 4a-H), 3.43 (dd, *J*=12.4, 8.8 Hz, 3-Hax), 3.84, (ddd, *J*=8.8, 4.8 Hz, 1H, 4-H), 3.89 (s, 3H, OMe), 4.00 (dd, *J*=12.4, 4.8 Hz, 1H, 3-Heq), 5.24 and 5.28 (2d, *J*=11 Hz, 1H each, CH_2Ph), 6.21 (d, *J*=10.4 Hz, 1H, 7-H), 6.90 (dd, *J*=10.3, 1.5 Hz, 1H, 8-H), 7.35 (s, 5H, PhH). *Method C:* From **16b** (200 mg, 0.47 mmol) in CH_2Cl_2 (4 ml), $ZnBr_2$ (106 mg, 0.47 mmol) in CH_2Cl_2 (2 ml), and diene **1** (0.27 ml, 1.42 mmol) at 25°C for 14 h, adducts **21b** (64 mg, 28%) and **22b** (44 mg, 19%) were obtained after chromatography (7:3 hexane–AcOEt). **(4*S*,4a*S*,8a*S*)-8a-(Benzyloxycarbonyl)-4-(*tert*-butyldimethylsilyloxy)-2-(methoxycarbonyl)-1,6-dioxo-1,2,3,4,4a,5,6,8a-octahydroisoquinoline (22b):** ^{1}H NMR (300 MHz) -0.02 and 0.02 (2s, 3H each, Me_2Si), 0.78 (s, 9H, *t*-Bu), 2.34 (dd, *J*=17, 6 Hz, 1H, 5-H), 2.65 (dd, *J*=17, 6.3 Hz, 1H, 5-H), 3.06 (td, *J*=5.8, 3.4 Hz, 1H, 4a-H), 3.60 (dd, *J*=13.4, 2.9 Hz, 3-H), 3.87 (s, 3H, OMe), 3.95 (dd, *J*=13.4, 5.1 Hz, 1H, 3-H), 4.19 (dt, *J*=5.2, 3 Hz, 1H, 4-H), 5.21 and 5.28 (2d, *J*=12.1 Hz, 1H each, CH_2Ph), 6.18 (d, *J*=10.3 Hz, 1H, 7-H), 7.07 (d, *J*=10.3 Hz, 1H, 8-H), 7.35 (s, 5H, PhH). Anal. Calcd for $C_{25}H_{33}NO_7Si$: C, 61.58; H, 6.82; N, 2.87. Found: C, 61.83; H, 6.95; N, 2.81.

Diels–Alder reactions from 2-methylbuta-1,3-diene (2)

With dihydropyridone 12a. *Method C:* From **12a** (500 mg, 1.29 mmol) in CH_2Cl_2 (5 ml), $ZnBr_2$ (290 mg, 1.29 mmol) in CH_2Cl_2 (10 ml), and diene **2** (0.9 ml, 9.0 mmol) at 25°C for 2.5 h, ***cis*-8a-(benzyloxycarbonyl)-6-methyl-1-oxo-2-(*p*-toluenesulfonyl)-1,2,3,4,4a,5,8,8a-octahydroisoquinoline (23a)** (390 mg, 65%) was obtained after crystallization from Et_2O: mp 114–115°C (Et_2O); IR (KBr) 1750, 1680, 1175 cm^{-1}; ^{1}H NMR (200 MHz) 1.56 (s, 3H, 6-Me), 1.72 (m, 1H, 5-H), 1.89 (m, 2H, 4-H), 1.95 (d, *J*=4.4 Hz, 1H, 5-H), 2.35 (m, 1H, 8-H), 2.41 (s, 3H, MeTs), 2.54 (m, 1H, 8-H), 2.63 (m, 1H, 4a-H), 3.53 (dt, *J*=12.2, 8.4 Hz, 1H, 3-H), 4.27 (dt, *J*=12.4, 5.2 Hz, 1H, 3-H), 5.02 and 5.13 (2d, *J*=12.6 Hz, 1H each, CH_2Ph), 5.27 (br s, 1H, 7-H), 7.24 (m, 7H, PhH and Ts-*m*-H), 7.85 (d, *J*=8.4 Hz, 2H, Ts-*o*-H); MS, *m/z* (rel intensity) 453 (M^+, 1), 320 (17), 319 (73), 254 (17), 190 (13), 119 (17), 91 (100). Anal. Calcd for $C_{25}H_{27}O_5NS{\cdot}1/2H_2O$: C, 64.92; H, 6.01; N, 3.03; S, 6.93. Found: C, 64.60; H, 5.88; N, 3.31; S, 6.93.

With dihydropyridone 12b. *Method C:* From **12b** (500 mg, 1.7 mmol) in CH_2Cl_2 (5 ml), $ZnBr_2$ (390 mg, 1.73 mmol) in CH_2Cl_2 (5 ml), and diene **2** (0.86 ml, 8.5 mmol) at 25°C for 1.5 h, ***cis*-8a-(benzyloxycarbonyl)-2-(methoxycarbonyl)-6-methyl-1-oxo-1,2,3,4,4a,5,8,8a-octahydroisoquinoline (23b)** (407 mg, 67%) was obtained after chromatography (1:1 hexane–AcOEt): IR (NaCl) 1775, 1725, 1680 cm^{-1}; ^{1}H NMR (300 MHz) 1.58 (s, 3H, 6-Me), 1.68 (dd, *J*=17.9, 3.8 Hz, 1H, 5-H), 1.80 (m, 2H, 4-H), 1.95 (ddd, *J*=18.3, 3.3, 0.8 Hz, 1H, 5-H), 2.49 (dm, *J*=17.3 Hz, 1H, 8-H), 2.68 (m, 3H, 8-H and 4a-H), 3.45 (dt, *J*=12.6, 5.4 Hz, 1H, 3-H), 3.81 (s, 3H, OMe), 3.95 (dt, *J*=13, 4.8 Hz, 1H, 3-H), 5.10 and 5.22 (2d, *J*=12.3 Hz, 1H each, CH_2Ph), 5.32 (br s, 1H, 7-H), 7.31 (s, 5H, PhH). Anal. Calcd for $C_{20}H_{23}NO_5{\cdot}1/2H_2O$: C, 65.56; H, 6.60; N, 3.82. Found: C, 65.54; H, 6.45; N, 4.10.

With dihydropyridone 16a. *Method C:* From **16a** (400 mg, 0.77 mmol) in CH_2Cl_2 (15 ml), $ZnBr_2$ (173 mg, 0.77 mmol) in CH_2Cl_2 (8 ml), and diene **2** (0.38 ml, 3.85 mmol) at 0°C for 3 h, adducts **25a** (80 mg, 18%) and **27a** (239 mg, 52%) were obtained after chromatography (CH_2Cl_2). **(4*S*,4a*R*,8a*R*)-8a-(Benzyloxycarbonyl)-4-(*tert*-butyldimethylsilyloxy)-6-methyl-1-oxo-2-(*p*-toluenesulfonyl)-1,2,3,4,4a,5,8,8a-octahydroisoquinoline (25a):** ^{1}H NMR (300 MHz) 0.09 and 0.15 (2s, 3H each, Me_2Si), 0.93 (s, 9H, *t*-Bu), 1.61 (s, 3H, 6-Me), 1.75 (dm, *J*=18.2 Hz, 1H, 5-H), 2.07 (dm, *J*=18.1 Hz, 1H, 5-H), 2.29 (dm, *J*=18.1 Hz, 1H, 8-H), 2.44 (s, 3H, MeTs), 2.58 (ddd, *J*=9, 5.8, 3.5 Hz, 1H, 4a-H), 2.76 (dm, *J*=18.2 Hz, 1H, 8-H), 3.35 (dd, *J*=12, 9 Hz, 1H, 3-Hax), 3.97 (td, *J*=9, 6.2 Hz, 1H, 4-Hax), 4.39 (dd,

J=12, 6.2 Hz, 1H, 3-Heq), 5.04 and 5.11 (2d, J=12.4 Hz, 1H each, CH_2Ph), 5.37 (br s, 1H, 7-H), 7.17 (m, 2H, PhH), 7.28–7.34 (m, 5H, PhH), 7.88 (d, J=8.4 Hz, 2H, Ts-*o*-H). **(4*S*,4a*S*,8a*S*)-isomer (27a):** mp 108–110°C (pentane); $[\alpha]_D^{20}$=+35.3 (c 1, $CHCl_3$); IR (KBr) 1750, 1688, 1354, 1176 cm^{-1}; ^1H NMR (200 MHz) 0.00 and 0.02 (2s, 3H each, Me_2Si), 0.89 (s, 9H, *t*-Bu), 1.55 (s, 3H, 6-Me), 1.73 (dd, J=19.4, 9.2 Hz, 1H, 5-H), 2.06 (dd, J=18.2, 6.6 Hz, 1H, 5-H), 2.30 (dm, J=17.2 Hz, 1H, 8-H), 2.43 (s, 3H, MeTs), 2.67 (ddd, J=10, 6.6, 4.4 Hz, 1H, 4a-H), 2.83 (dm, J=17.2 Hz, 1H, 8-H), 3.77 (dd, J=12.8, 7 Hz, 1H, 3-H), 3.85 (dd, J=12.6, 6 Hz, 1H, 3-H), 4.12 (td, J=6.5, 4.8 Hz, 1H, 4-Heq), 4.99 and 5.24 (2d, J=12 Hz, 1H each, CH_2Ph), 5.27 (br s, 1H, 7-H), 7.25–7.45 (m, 7H, PhH), 7.89 (d, J=8.6 Hz, 2H, Ts-*o*-H); MS, *m*/*z* (rel intensity) 91 (100), 448 (21), 526 (6). Anal. Calcd for $C_{31}H_{41}NO_6SiS$: C, 63.78; H, 7.08; N, 2.4; S, 5.49. Found: C, 63.80; H, 7.16; N, 2.39; S, 5.30.

X-Ray crystal structure of 27a. Crystal data: $C_{31}H_{41}NO_6SSi$, orthorhombic, space group $P2_12_12_1$, a=9.880 (2) Å, b=10.300 (1) Å, c=31.694 (6) Å, V=3225.3 (9) $Å^3$, Z=4, μ (MoKα)=0.178 mm^{-1}, D_c=1.202 mg m^{-3}. The experiment was done on an Enraf–Nonius CAD4 diffractometer using graphite monochromated MoKα radiation. The crystal had approximate dimensions of 0.52×0.45×0.15 mm. Data collection was up to a resolution of 2θ=49.96° producing 3310 reflections. The structure was solved by direct methods (SHELXS 86) after applying Lorentz, polarization and absorption (empirical psi scan method) corrections to the 3229 independent reflections. Full matrix least-squares refinement (SHELXL 93) using anisotropic thermal parameters for non-H atoms and a global isotropic temperature factor for the H-atoms (introduced at calculated positions) converged to a R factor of 0.136 (0.057 for reflections with $I>2\sigma(I)$). Maximum and minimum heights at the final difference Fourier synthesis were 0.31 and −0.29 e $Å^{-3}$. Complete data have been deposited at the Cambridge Crystallographic Data Centre.

With dihydropyridone 16b. *Method C:* From **16b** (300 mg, 0.71 mmol) in CH_2Cl_2 (12 ml), $ZnBr_2$ (160 mg, 0.71 mmol) in CH_2Cl_2 (6 ml), and diene **2** (0.36 ml, 3.57 mmol) at 0°C for 2 h, a mixture of adducts **25b** and **27b** (1:6, 288 mg, 82%) was obtained after chromatography (8:2 hexane–AcOEt). An analytical sample of **(4*S*,4a*S*,8a*S*)-8a-(benzyloxycarbonyl)-4-(*tert*-butyldimethylsilyloxy)-2-(methoxycarbonyl)-6-methyl-1-oxo-1,2,3,4,4a,5,8,8a-octahydroisoquinoline (27b)** was obtained by chromatography (8:2 hexane–AcOEt): $[\alpha]_D^{20}$=+70.4 (c 1, $CHCl_3$); IR (NaCl) 1782, 1727 cm^{-1}; ^1H NMR (200 MHz) 0.00 (s, 6H, Me_2Si), 0.86 (s, 9H, *t*-Bu), 1.66 (s, 3H, Me), 1.88 (dd, J=18, 10.4 Hz, 1H, 5-H), 2.12 (dd, J=18.4, 6.2 Hz, 1H, 5-H), 2.34 (dm, J=16.8 Hz, 1H, 8-H), 2.77 (ddd, J=10.2, 6.6, 4.4 Hz, 1H, 4a-Heq), 2.98 (ddm, J=17.2, 3.2 Hz, 1H, 8-H), 3.63 (d, J=7 Hz, 2H, 3-H), 3.86 (s, 3H, OMe), 4.13 (td, J=7, 4.1 Hz, 1H, 4-H), 5.10 and 5.32 (2d, J=12.2 Hz, 1H each, CH_2Ph), 5.38 (m, 1H, 7-H), 7.34 (m, 5H, PhH); MS, *m*/*z* (rel intensity) 353 (9), 352 (34), 91 (100), 73 (31), 59 (10). Anal. Calcd for $C_{26}H_{37}NO_6Si\cdot 1/4H_2O$: C, 63.45; H, 7.68; N, 2.85. Found: C, 63.19; H, 7.71; N, 3.02.

Diels–Alder reactions from 2,3-dimethylbuta-1,3-diene (3)

With dihydropyridone 12a. *Method A:* From **12a** (500 mg, 1.29 mmol) and diene **3** (0.7 ml, 6.2 mmol) in *p*-cymene (10 ml) for 6 h, adduct **24a** (150 mg, 25%) and dihydropyridone **10a** (50 mg) were obtained after chromatography (85:15 hexane–AcOEt). ***cis*-8a-(Benzyloxycarbonyl)-6,7-dimethyl-1-oxo-2-(*p*-toluenesulfonyl)-1,2,3,4,4a,5,8,8a-octahydroisoquinoline (24a):** mp 115–117°C (Et_2O); IR (KBr) 1736, 1691, 1362, 1170 cm^{-1}; ^1H NMR (300 MHz) 1.52 and 1.59 (2s, 3H each, 6- and 7-Me), 1.75 (dm, J=19 Hz, 1H, 5-H), 1.82–1.91 (m, 2H, 4-H), 1.97 (dm, J=19 Hz, 1H, 5-H), 2.34 (d, J=17 Hz, 1H, 8-H), 2.40 (s, 3H, MeTs), 2.48 (d, J=17 Hz, 1H, 8-H), 2.59 (qn, J=7 Hz, 1H, 4a-H), 3.53 (dt, J=12, 8 Hz, 1H, 3-H), 4.26 (dt, J=12, 5 Hz, 1H, 3-H), 5.03 and 5.08 (2d, J=12.4 Hz, 1H each, CH_2Ph), 7.13–7.20 (m, 2H, PhH), 7.23–7.34 (m, 5H, PhH), 7.85 (d, J=8.5 Hz, 2H, Ts-*o*-H); MS, *m*/*z* (rel intensity) 467 (M^+, 1), 333 (12), 332 (56), 176 (10), 133 (16), 91 (100), 65 (13). Anal. Calcd for $C_{26}H_{29}O_5NS$: C, 66.79; H, 6.25; N, 3.00; S, 6.86. Found: C, 66.70; H, 6.30; N, 3.00; S, 6.76. *Method C:* From **12a** (300 mg, 0.77 mmol) in CH_2Cl_2 (5 ml), $ZnBr_2$ (178 mg, 0.77 mmol) in CH_2Cl_2 (5 ml), and diene **3** (0.4 ml, 3.5 mmol) at 25°C for 2.5 h, adduct **24a** (250 mg, 69%) was obtained after crystallization from Et_2O.

With dihydropyridone 12b. *Method A:* From **12b** (500 mg, 1.73 mmol) and diene **3** (0.7 ml, 6.2 mmol) in *p*-cymene (5 ml) for 2 h, adduct **24b** (74 mg, 11%) was obtained after column chromatography (hexane–AcOEt, increasing polarity). ***cis*-8a-(Benzyloxycarbonyl)-2-(methoxycarbonyl)-6,7-dimethyl-1-oxo-1,2,3,4,4a,5,8,8a-octahydroisoquinoline (24b):** IR (NaCl) 1777, 1747, 1726 cm^{-1}; ^1H NMR (300 MHz) 1.56 and 1.63 (2s, 3H each, 6- and 7-Me), 1.80 (m, 2H, 4-H), 2.01 (dm, J=13.5 Hz, 2H, 5-H), 2.47 and 2.58 (2d, J=17 Hz, 1H each, 8-H), 2.68 (dq, J=8.4, 5.5 Hz, 1H, 4a-H), 3.45 (ddd, J=13, 10, 3.6 Hz, 1H, 3-Hax), 3.84 (s, 3H, OMe), 3.98 (ddd, J=13.3, 6, 4 Hz, 1H, 3-Heq), 5.14 and 5.22 (2d, J=12 Hz, 1H each, CH_2Ph), 7.32 (m, 5H, PhH). Anal. Calcd for $C_{21}H_{25}NO_5$: C, 67.91; H, 6.78; N, 3.77. Found: C, 67.75; H, 6.89; N, 3.61. *Method C:* From **12b** (1 g, 3.46 mmol) in CH_2Cl_2 (15 ml), $ZnBr_2$ (780 mg, 3.46 mmol) in CH_2Cl_2 (5 ml), and diene **3** (2.3 ml, 20.4 mmol) at 25°C for 2 h, adduct **24b** (946 mg, 73%) was obtained after chromatography (1:1 hexane–AcOEt).

With dihydropyridone 16a. *Method C:* From **16a** (400 mg, 0.77 mmol) in CH_2Cl_2 (15 ml), $ZnBr_2$ (173 mg, 0.77 mmol) in CH_2Cl_2 (8 ml), and diene **3** (0.61 ml, 5.39 mmol) at 0°C for 3 h, adducts **26a** (126 mg, 27%) and **28a** (253 mg, 55%) were obtained after chromatography (9:1 hexane–AcOEt). **(4*S*,4a*R*,8a*R*)-8a-(Benzyloxycarbonyl)-4-(*tert*-butyldimethylsilyloxy)-6,7-dimethyl-2-(*p*-toluenesulfonyl)-1-oxo-1,2,3,4,4a,5,8,8a-octahydroisoquinoline (26a):** IR (NaCl) 1739, 1699, 1361, 1172 cm^{-1}; ^1H NMR (200 MHz) 0.08 and 0.14 (2s, 3H each, Me_2Si), 0.93 (s, 9H, *t*-Bu), 1.61 and 1.62 (2s, 3H each, 6- and 7-Me), 1.81 (dm, J=18.3 Hz, 1H, 5-H), 2.08 (dm, J=18.2 Hz, 1H, 5-H), 2.28 (dm, J=16.8 Hz, 1H, 8-H), 2.44 (s, 3H, MeTs), 2.53 (m, 1H, 4a-H), 2.64 (dm, J=16.8 Hz, 1H, 8-H), 3.34 (dd, J=12, 8.8 Hz, 1H, 3-Hax), 3.96 (td, J=8.6, 6.2 Hz, 1H, 4-Hax), 4.39 (dd,

J=12, 6.2 Hz, 1H, 3-Heq), 5.06 (s, 2H, CH_2Ph), 7.12–7.39 (m, 7H, PhH), 7.88 (d, J=8.3 Hz, 2H, Ts-*o*-H). Anal. Calcd for $C_{32}H_{43}NO_6SSi\cdot 1/4H_2O$: C, 63.81; H, 7.28; N, 2.33; S, 5.32. Found: C, 63.70; H, 7.53; N, 2.31; S, 4.88. MS, *m/z* (rel intensity) 599 (M^++1, 42), 598 (M^+, 100), 91 (64). **(4*S*,4a*S*,8a*S*)-Isomer (28a):** IR (NaCl) 1740, 1704, 1362, 1171 cm^{-1}; ^1H NMR (300 MHz) 0.00 (s, 6H, Me_2Si), 0.87 (s, 9H, *t*-Bu), 1.52 (s, 6H, 6- and 7-Me), 1.81 (ddm, J=18.2, 8 Hz, 1H, 5-H), 2.06 (ddm, J=18.2, 6.8 Hz, 1H, 5-H), 2.29 (dm, J=16.4 Hz, 1H, 8-H), 2.42 (s, 3H, MeTs), 2.62 (ddd, J=9.5, 7, 4.4 Hz, 1H, 4a-H), 2.68 (dm, J= 15.9 Hz, 8-H), 3.78 (dd, J=12.4, 6.8 Hz, 1H, 3-H), 3.84 (dd, J=12.5, 5.9 Hz, 1H, 3-H), 4.13 (td, J=6.2, 4.6 Hz, 1H, 4-Heq), 5.00 and 5.18 (2d, J=12 Hz, 1H each, CH_2Ph), 7.20–7.40 (m, 7H, PhH), 7.89 (d, J= 8.4 Hz, 2H, Ts-*o*-H). Anal. Calcd for $C_{32}H_{43}NO_6SSi\cdot 1/2H_2O$: C, 63.34; H, 7.31; N, 2.31; S, 5.28. Found: C, 63.12; H, 7.41; N, 2.31; S, 4.82.

With dihydropyridone 16b. *Method C:* From **16b** (200 mg, 0.47 mmol) in CH_2Cl_2 (10 ml), $ZnBr_2$ (106 mg, 0.47 mmol) in CH_2Cl_2 (2 ml), and diene **3** (0.26 ml, 2.37 mmol) at 0°C for 3 h, a mixture of adducts **26b** and **28b** (1:3, 175 mg, 75%) was obtained after chromatography (8:2 hexane–AcOEt). An analytical sample of **(4*S*,4a*S*,8a*S*)-8a-(benzyloxycarbonyl)-4-(*tert*-butyldimethylsilyloxy)-2-(methoxycarbonyl)-6,7-dimethyl-1-oxo-1,2,3,4,4a,5,8,8a-octahydroisoquinoline (28b)** was obtained by chromatography (8:2 hexane–AcOEt): $[\alpha]_D^{20}$=+15.8 (*c* 0.4, $CHCl_3$); IR (NaCl) 1781, 1726 cm^{-1}; ^1H NMR (200 MHz) 0.00 (s, 6H, Me_2Si), 0.87 (s, 9H, *t*-Bu), 1.62 and 1.64 (2s, 3H each, 6- and 7-Me), 1.92 (ddm, J=18.2, 10 Hz, 1H, 5-H), 2.12 (dd, J=18.2, 6.3 Hz, 1H, 5-H), 2.35 (dm, J=16.2 Hz, 1H, 8-H), 2.72 (ddd, J=10.2, 7, 4.4 Hz, 1H, 4a-H), 2.84 (d, J=16.6 Hz, 1H, 8-H), 3.63 (d, J=7 Hz, 2H, 3-H), 3.87 (s, 3H, OMe), 4.13 (td, J=7, 4.4 Hz, 1H, 4-H), 5.13 and 5.32 (2d, J=12 Hz, 1H each, CH_2Ph), 7.37 (m, 5H, PhH); MS, *m/z* (rel intensity) 366 (100), 115 (10), 91 (69), 73 (78), 59 (18). Anal. Calcd for $C_{27}H_{39}NO_6Si\cdot H_2O$: C, 62.40; H, 7.95; N, 2.70. Found: C, 62.86; H, 7.83; N, 2.72.

Diels–Alder reactions from hexa-2,4-diene (4)

With dihydropyridone 12a. *Method A:* From **12a** (330 mg, 0.85 mmol) and diene **4** (commercial mixture of isomers, 0.34 ml, 2.97 mmol) in *p*-cymene (10 ml) for 10 h, adduct **29a** (67 mg, 17%, one diastereomer of unknown configuration at C-5 and C-8) and dihydropyridones **10a** and **12a** (traces) were obtained after chromatography (85:15 hexane–AcOEt). ***cis*-8a-(Benzyloxycarbonyl)-5,8-dimethyl-1-oxo-2-(*p*-toluenesulfonyl)-1,2,3,4,4a,5,8,8a-octahydroisoquinoline (29a):** mp 145–147°C (Et_2O); IR (KBr) 1745, 1684, 1352, 1169 cm^{-1}; ^1H NMR (300 MHz) 0.85 (d, J=7.8 Hz, 3H, 8-Me), 0.94 (d, J=7.4 Hz, 3H, 5-Me), 1.84 (m, 2H, 4-H), 1.96 (m, 1H, 5-H), 2.43 (s, 3H, MeTs), 2.49 (q, J=5 Hz, 1H, 4a-H), 3.18 (m, 1H, 8-H), 3.74 (td, J=12, 6.5 Hz, 1H, 3-Hax), 4.31 (ddd, J=12, 6, 2 Hz, 1H, 3-Heq), 5.02 and 5.11 (2d, J=8.2 Hz, 1H each, CH_2Ph), 5.27 (d, J=10 Hz, 1H, 7-H), 5.53 (dt, J=10, 3 Hz, 1H, 6-H), 7.18 (m, 2H, PhH), 7.29 (m, 5H, PhH and Ts-*o*-H), 7.89 (d, J=8 Hz, 2H, Ts-*m*-H); MS, *m/z* (rel intensity) 468 (M^++1, 1), 332 (40), 322 (12), 268 (24), 155 (17), 133 (19), 91 (100). Anal. Calcd for $C_{26}H_{29}O_5NS$: C, 66.79; H, 6.25; N, 3.00; S, 6.86. Found: C, 66.61; H, 6.32; N, 3.05; S, 6.95. *Method C:* From **12a** (500 mg, 1.29 mmol) in CH_2Cl_2 (5 ml), $ZnBr_2$ (290 mg, 1.3 mmol) in CH_2Cl_2 (10 ml), and diene **4** (commercial mixture of isomers, 0.8 ml, 9.1 mmol) at 25°C for 2.5 h, adduct **29a** (430 mg, 70%, the same diastereomer of unknown configuration at C-5 and C-8 obtained by method A) was obtained after crystallization from Et_2O.

With dihydropyridone 12b. *Method C:* From **12b** (300 mg, 1.03 mmol) in CH_2Cl_2 (5 ml), $ZnBr_2$ (230 mg, 1.03 mmol) in CH_2Cl_2 (5 ml), and diene **4** (commercial mixture of isomers, 0.8 ml, 7.21 mmol) at 25°C for 7 h, ***cis*-8a-(benzyloxycarbonyl)-2-(methoxycarbonyl)-5,8-dimethyl-1-oxo-1,2,3,4,4a,5,8,8a-octahydroisoquinoline (29b)** (255 mg, 63%, 1:1 mixture of two diastereomers of unknown configuration at C-5 and C-8) was obtained after chromatography (1:1 hexane–AcOEt). Analytical samples of both diastereomers were obtained by chromatography (1:1 hexane–AcOEt). Less polar diastereomer of **29b**: IR (NaCl) 1775, 1727, 1702 cm^{-1}; ^1H NMR (300 MHz) 0.92 (d, J=7.4 Hz, 3H, 5-Me), 1.12 (d, J=7.6 Hz, 3H, 8-Me), 1.73 (m, 2H, 4-H), 1.96 (m, 1H, 5-H), 2.49–2.60 (m, 1H, 4a-H), 3.30 (m, 1H, 8-H), 3.59 (m, 1H, 3-Hax), 3.85 (s, 3H, OMe), 3.95 (dt, J=12.6, 3.2 Hz, 1H, 3-Heq), 5.06 and 5.26 (2d, J=12.4 Hz, 1H each, CH_2Ph), 5.26–5.29 (m, 1H, 6-H), 5.58 (ddd, J=10.4, 3.5, 3 Hz, 1H, 7-H), 7.31 (s, 5H, PhH); MS, *m/z* (rel intensity) 232 (47), 214 (31), 188 (31), 91 (100), 65 (22), 55 (11). Anal. Calcd for $C_{21}H_{25}NO_5$: C, 67.91; H, 6.78; N, 3.77. Found: C, 67.33; H, 7.34; N, 3.11. More polar diastereomer of **29b**: IR (NaCl) 1775, 1729, 1703 cm^{-1}; ^1H NMR (300 MHz) 0.79 (d, J=7.4 Hz, 3H, 5-Me), 1.02 (d, J=7 Hz, 3H, 8-Me), 1.69–1.87 (m, 3H, 4-H and 5-H), 2.19–2.26 (m, 2H, 4-H and 4a-H), 3.08 (ddd, J=14.3, 8, 6 Hz, 1H, 3-Hax), 3.20 (m, 1H, 8-H), 3.84 (s, 3H, OMe), 4.1 (ddd, J=14.3, 8, 4 Hz, 1H, 3-Heq), 5.18 (s, 2H, CH_2Ph), 5.34 (dm, J=10 Hz, 1H, 6-H), 5.65 (ddd, J=10, 5, 2.5 Hz, 1H, 7-H), 7.34 (s, 5H, PhH); MS, *m/z* (rel intensity) 232 (47), 214 (31), 188 (31), 91 (100), 65 (22). Anal. Calcd for $C_{21}H_{25}NO_5$: C, 67.91; H, 6.78; N, 3.77. Found: C, 67.49; H, 7.30; N, 3.18.

With dihydropyridone 16a. *Method C:* From **16a** (300 mg, 0.58 mmol) in CH_2Cl_2 (12 ml), $ZnBr_2$ (130 mg, 0.58 mmol) in CH_2Cl_2 (6 ml), and diene **4** (commercial mixture of isomers, 0.33 ml, 2.9 mmol) at 0°C for 4 h, **(4*S*,4a*S*,8a*S*)-8a-(benzyloxycarbonyl)-4-(*tert*-butyldimethylsilyloxy)-5,8-dimethyl-2-(*p*-toluenesulfonyl)-1-oxo-1,2,3,4,4a,5,8,8a-octahydroisoquinoline (30a)** (unknown configuration at C-5 and C-8; accompanied by a minor diastereomer of unknown configuration, 3.5:1, 256 mg, 73%) was obtained after chromatography (CH_2Cl_2). An analytical sample of **30a** was obtained by chromatography (CH_2Cl_2): IR (NaCl) 1780, 1728, 1382 cm^{-1}; ^1H NMR (300 MHz) 0.00 and 0.02 (2s, 3H each, Me_2Si), 0.80 (s, 9H, *t*-Bu), 0.96 (d, J=7.4 Hz, 3H, 8-Me), 1.05 (d, J=7.6 Hz, 3H, 5-Me), 2.18 (m, 1H, 5-H), 2.36 (s, 3H, MeTs), 2.66, (t, J=5.6 Hz, 1H, 4a-H), 2.99 (m, 1H, 8-H), 3.51 (dd, J=12.6, 6.6 Hz, 1H, 3-H), 4.03 (dd, J=12.7, 5.3 Hz, 1H, 3-H), 4.24 (q, J=5.7 Hz, 1H, 4-H), 5.03 and 5.08 (2d, J=11.3 Hz, 1H each, CH_2Ph), 5.47 and 5.54 (2 dt, J=9.7, 2.7 Hz, 1H each, 6- and 7-H), 7.20–7.40 (m, 7H, PhH), 7.85 (d, J=8.5 Hz, 2H, H-*o*-Ts); MS, *m/z* (rel intensity) 599 (M+1, 42), 598 (M+, 100), 91 (64).

With dihydropyridone 16b. *Method C:* From **16b** (200 mg, 0.47 mmol) in CH_2Cl_2 (8 ml), $ZnBr_2$ (106 mg, 0.47 mmol) in CH_2Cl_2 (4 ml), and diene **4** (commercial mixture of isomers, 0.27 ml, 2.38 mmol) at 0°C for 5 h, after a second addition of the diene (2.5 equiv.) at 25°C for 1 h, **(4*S*,4a*S*,8a*S*)-8a-(benzyloxycarbonyl)-4-(*tert*-butyldimethylsilyloxy)-5,8-dimethyl-2-(methoxycarbonyl)-1-oxo-1,2,3,4,4a,5,8,8a-octahydroisoquinoline (30b)** (unknown configuration at C-5 and C-8; accompanied by traces of a diastereomer of unknown configuration, 160 mg, 67%) was obtained after chromatography (4:1 hexane–AcOEt). An analytical sample of **30b** was obtained by chromatography (4:1 hexane–AcOEt): IR (NaCl) 1780, 1727 cm^{-1}; ^1H NMR (200 MHz) 0.05 (s, 6H, Me_2Si), 0.85 (s, 9H, *t*-Bu), 1.05 and 1.15 (2d, *J*=7.5 Hz, 3H each, 5- and 8-Me), 2.20 (m, 1H, 5-H), 2.77 (t, *J*=5.5 Hz, 1H, 4a-H), 3.11 (m, 1H, 8-H), 3.50 (dd, *J*=13.6, 7 Hz, 1H, 3-H), 3.85 (s, 3H, CO_2Me), 3.86 (dd, *J*=13.6, 5.2 Hz, 1H, 3-H), 4.19 (dt, *J*=6.8, 5.2 Hz, 1H, 4-H), 5.10 and 5.31 (2d, *J*=12.6 Hz, 1H each, CH_2Ph), 5.49 and 5.62 (2dt, *J*=10, 2.6 Hz, 1H, 6- and 7-H), 7.33 (s, 5H, PhH). Anal. Calcd for $C_{27}H_{39}NO_6Si\cdot1/2H_2O$: C, 63.5; H, 7.89; N, 2.74. Found: C, 63.2; H, 7.7; N, 2.66.

Diels–Alder reactions from 1-acetoxybuta-1,3-diene (5)

With dihydropyridone 12a. *Method A:* From **12a** (500 mg, 1.29 mmol) and diene **5** (1:1 *cis–trans* mixture, 0.53 ml, 4.5 mmol) in *p*-cymene (15 ml) for 5 h, adducts ***endo*-31a** (51 mg, 8%) and ***exo*-31a** (190 mg, 30%) and dihydropyridone **10a** (traces) were obtained after chromatography (4:1 hexane–AcOEt). **(4a*RS*,8*RS*,8a*RS*)-8-Acetoxy-8a-(benzyloxycarbonyl)-1-oxo-2-(*p*-toluenesulfonyl)-1,2,3,4,4a,5,8,8a-octahydroisoquinoline (endo-31a):** mp 150–151°C (Et_2O); IR (KBr) 1747, 1688, 1358, 1171 cm^{-1}; ^1H NMR (200 MHz) 1.70 (s, 3H, MeCO), 1.75 (m, 1H, 4-H), 2.00 (m, 2H, 5-H), 2.41 (s, 3H, MeTs), 2.43 (m, 1H, 4-H), 2.68 (dq, *J*=13.5, 3.7 Hz, 1H, 4a-H), 3.81 (td, *J*=12, 5.4 Hz, 1H, 3-Hax), 4.20 (ddd, *J*=12, 6, 1.5 Hz, 1H, 3-Heq), 5.04 and 5.10 (2d, *J*=12 Hz, 1H each, CH_2Ph), 5.75–5.90 (m, 3H, 6-H, 7-H and 8-Heq), 7.14–7.38 (m, 7H, PhH), 7.92 (d, *J*=8.4 Hz, 2H, Ts-*o*-H); MS, *m/z* (rel intensity) 135 (10); 238 (10); 105 (12); 92 (10); 91 (100); 69 (13); 65 (13); 57 (17); 55 (19). Anal. Calcd for $C_{26}H_{27}O_7NS\cdot1/2H_2O$: C, 61.65; H, 5.57; N, 2.77; S, 6.33. Found: C, 61.55; H, 5.44; N, 2.78; S, 6.98. **(4a*RS*,8*SR*,8a*RS*)-Isomer (*exo*-31a):** IR (NaCl) 1739, 1730, 1713, 1359, 1170 cm^{-1}; ^1H NMR (200 MHz) 1.65–1.85 (m, 2H, 4-H), 1.71 (s, 3H, MeCO), 2.17 (m, 1H, 5-H), 2.32 (m, 1H, 5-H), 2.40 (s, 3H, MeTs), 2.78 (m, 1H, 4a-H), 3.16 (ddd, *J*=14, 9.5, 7.1 Hz, 1H, 3-Hax), 4.24 (ddd, *J*=14, 8.5, 3.4 Hz, 1H, 3-Heq), 4.90 and 4.97 (2d, *J*=12 Hz, 1H each, CH_2Ph), 5.70–5.74 (m, 2H, 6-H and 7-H), 5.79 (d, *J*=2.9 Hz, 1H, 8-Heq), 7.15–7.35 (m, 7H, PhH), 7.79 (d, *J*=8.4 Hz, 2H, Ts-*o*-H); MS, *m/z* (rel intensity) 320 (19); 346 (13); 91 (100); 65 (13). *Method C:* From **12a** (300 mg, 0.77 mmol) in CH_2Cl_2 (5 ml), $ZnBr_2$ (173 mg, 0.77 mmol) in CH_2Cl_2 (5 ml), and diene **5** (1:1 *cis–trans* mixture, 0.4 ml, 3.85 mmol) at 25°C for 4 h, adducts ***endo*-31a** (60 mg, 16%) and ***exo*-31a** (136 mg, 35%) were obtained after chromatography (7:3 hexane–AcOEt).

With dihydropyridone 12b. *Method A:* From **12b** (500 mg, 1.73 mmol) and diene **5** (1:1 *cis–trans* mixture, 0.4 ml, 3.46 mmol) in *p*-cymene (5 ml) for 2 h, adducts ***exo*-31b** (33 mg, 5%) and ***endo*-31b** (30 mg, 4%) were obtained after column chromatography (hexane–AcOEt, increasing polarity). **(4a*RS*,8*SR*,8a*RS*)-8-Acetoxy-8a-(benzyloxycarbonyl)-2-(methoxycarbonyl)- 1-oxo-1,2,3,4,4a,5,8,8a-octahydroisoquinoline (*exo*-31b):** IR (KBr) 1760, 1735, 1731 cm^{-1}; ^1H NMR (300 MHz) 1.64 (m, 1H, 4-Heq), 1.70 (s, 3H, MeCO), 1.91 (ddm, *J*=18, 11.5 Hz, 1H, 5-Hax), 2.30 (dt, *J*=18, 5.5 Hz, 1H, 5-Heq), 2.39 (ddd, *J*=14, 7.4, 4.4 Hz, 1H, 4-Hax), 2.90 (m, 1H, 4a-H), 3.21 (ddd, *J*=14.3, 8, 4.4 Hz, 1H, 3-Hax), 3.84 (s, 3H, OMe), 4.15 (ddd, *J*=14.3, 8.7, 7.2 Hz, 1H, 3-Heq), 5.10 and 5.20 (2d, *J*=12 Hz, 1H each, CH_2Ph), 5.86 (m, 1H, 6-H), 5.93 (m, 1H, 7-H), 5.98 (d, *J*=4.6 Hz, 1H, 8-H), 7.33 (s, 5H, PhH). Anal. Calcd for $C_{21}H_{23}NO_7$: C, 62.84; H, 5.78; N, 3.49. Found: C, 62.70; H, 5.93; N, 3.39. **(4a*RS*,8*RS*,8a*RS*)-Isomer (*endo*-31b):** IR (KBr) 1775, 1736, 1706 cm^{-1}; ^1H NMR (300 MHz) 1.68 (dm, *J*=14 Hz, 1H, 4-Heq), 1.96 (s, 3H, MeCO), 2.02 (m, 2H, 5-H), 2.36 (dq, *J*=13, 6 Hz, 1H, 4-H), 2.75 (dq, *J*=13, 4.4 Hz, 1H, 4a-H), 3.66 (td, *J*=13, 6 Hz, 1H, 3-Hax), 3.87 (s, 3H, OMe), 3.97 (ddd, *J*=13, 6, 2 Hz, 1H, 3-Heq), 5.13 and 5.27 (d, *J*=12 Hz, 1H each, CH_2Ph), 5.83 (dt, *J*=10, 4 Hz, 1H, 6-H), 5.93 (dm, *J*=10 Hz, 1H, 7-H), 5.97 (dd, *J*=4.2 Hz, allylic *J*, 1H, 8-H), 7.33 (m, 5H, PhH). Anal. Calcd for $C_{21}H_{23}NO_7\cdot1/2H_2O$: C, 61.46; H, 5.89; N, 3.41. Found: C, 61.6; H, 57.3; N, 3.48. *Method C:* From **12b** (500 mg, 1.73 mmol) in CH_2Cl_2 (5 ml), $ZnBr_2$ (389 mg, 1.73 mmol) in CH_2Cl_2 (5 ml), and diene **5** (1:1 *cis–trans* mixture, 0.65 ml, 6.06 mmol) at 25°C for 3.5 h, adducts ***exo*-31b** (80 mg, 11%) and ***endo*-31b** (134 mg, 20%) and aldehyde **34b** (86 mg, 14%) were obtained after chromatography (7:3 hexane–AcOEt). ***trans*-3-(Benzyloxycarbonyl)-1-(methoxycarbonyl)-4-[4-oxo-2(*E*)-butenyl]-2-piperidone (34b):** IR (NaCl) 1772, 1727, 1689 cm^{-1}; ^1H NMR (300 MHz) 1.55 (dtd, *J*=14.1, 10.4 and 4.8 Hz, 1H, 5-Hax), 2.06 (dq, *J*=14.1 and 4.5 Hz, 1H, 5-Heq), 2.29 (m, 1H, 1′-H), 2.39 (m, 1H, 1′-H), 2.54 (m, 1H, 4-H), 3.33 (d, *J*=9.9 Hz, 1H, 3-H), 3.61 (ddd, *J*=13.2, 10.7, 4.1 Hz, 1H, 6-Hax), 3.87 (s, 3H, OMe), 3.90 (dt, *J*=13.2, 4.8 Hz, 1H, 6-Heq), 5.16 and 5.24 (2d, *J*=12.1 Hz, 1H each, CH_2Ph), 6.09 (ddt, *J*=15.6, 7.7, 1.2 Hz, 1H, 3′-H), 6.66 (ddd, *J*=15.3, 8.1, 6.8 Hz, 1H, 2′-H), 7.35 (m, 5H, PhH), 9.46 (d, *J*=7.7 Hz, 1H, CHO); ^{13}C NMR (75 MHz) 27.1 (C-5), 35.1 (C-4), 37.4 (C-1′), 44.7 (C-6), 54.3 (OMe), 57.4 (C-3), 67.6 (CH_2Ph), 128.5 and 128.6, (C-Ph), 131.0 (C-*i*-Bn), 135.4 (C-3′), 150.8 (CO_2Me), 152.4 (C-2′), 166.4 and 168.7 (CO_2Bn and C-2), 193.1 (CHO). MS, *m/z* (rel intensity) 224 (25); 156 (54); 124 (16); 91 (100); 65 (12). Anal. Calcd for $C_{19}H_{21}O_6N\cdot1/3H_2O$: C, 62.47; H, 5.98; N, 3.83. Found: C, 62.53; H, 6.09; N, 3.52. *Method D:* A solution of **12b** (300 mg, 1.03 mmol) and diene **5** (1:1 *cis–trans* mixture, 0.23 ml, 1.03 mmol) in anhydrous CH_2Cl_2 (10 ml) cooled at −20°C was added to a solution of $EtAlCl_2$ (1 M in hexane, 0.5 ml) in anhydrous CH_2Cl_2 (5 ml) at the same temperature. The mixture was stirred at −20°C for 15 min and then allowed to rise to 0°C. More $EtAlCl_2$ (1 M in hexane, 1.5 ml) in anhydrous toluene was added, and stirring was continued at 0°C for 1 h and at 25°C for 30 min. After addition of H_2O and evaporation of the organic solvent, the residue was extracted with AcOEt. Concentration of the dried organic extracts afforded adducts ***exo*‴×+β** (36 mg, 9%) and ***endo*-31b** (240 mg, 58%) after column chromatography (hexane–AcOEt, increasing polarity).

With dihydropyridone 16a. *Method C:* From **16a** (400 mg, 0.77 mmol) in CH_2Cl_2 (15 ml), $ZnBr_2$ (173 mg, 0.77 mmol) in CH_2Cl_2 (5 ml), and diene **5** (1:1 *cis–trans* mixture, 0.45 ml, 3.85 mmol) at 0°C for 6 h, adduct ***endo*-35a** (accompanied by two minor diastereomers of undetermined configuration, 2.8:1, 325 mg, 67%) and aldehydes **38a** (86 mg, 19%, 2.9:1 mixture of two diastereomers of unknown configuration) were obtained after chromatography (4:1 hexane–AcOEt). An analytical sample of the major diastereomer **(4*S*,4a*S*, 8*R*, 8a*R*)-8-acetoxy-8a-(benzyloxycarbonyl)-4-(*tert*-butyldimethylsilyloxy)-1-oxo-2-(*p*-toluenesulfonyl)-1,2,3,4,4a,5,8,8a-octahydroisoquinoline (*endo*-35a)** was obtained by chromatography (4:1 hexane–AcOEt): mp 59–61°C (pentane); $[\alpha]_D^{20}=-8.3$ (*c* 1, $CHCl_3$); IR (KBr) 1746, 1696, 1355,1171 cm^{-1}; ^1H NMR (500 MHz) 0.00 and 0.03 (2s, 3H each, Me_2Si), 0.88 (s, 9H, *t*-Bu), 1.85 (s, 3H, MeCO), 1.98 (ddq, *J*=18.7, 10.5, 2.5 Hz, 1H, 5-Ha), 2.21 (dt, *J*=18.5, 5.5 Hz, 1H, 5-H), 2.42 (s, 3H, MeTs), 2.69 (dt, *J*=9.5, 6.5 Hz, 1H, 4a-H), 3.82 (d, *J*=6 Hz, 2H, 3-H), 4.17 (q, *J*=6 Hz, 1H, 4-H), 5.09 and 5.14 (2d, *J*=12 Hz, 1H each, CH_2Ph), 5.74 (m, 3H, 6-H, 7-H and 8-H), 7.20–7.35 (m, 7H, PhH), 7.91 (d, *J*=8.5 Hz, 2H, Ts-*o*-H). Anal. Calcd for $C_{32}H_{41}NO_8SSi\cdot 1/2C_5H_{12}$: C, 62.42; H, 7.14; N, 2.11; S, 4.83. Found: C, 62.25; H, 7.24; N, 2.37; S, 4.51. An analytical sample of the major aldehyde **(5*S*)-3-(benzyloxycarbonyl)-5-(*tert*-butyldimethylsilyloxy)-4-(4-oxo-2(*E*)-buten-1-yl)-1-(*p*-toluenesulfonyl)-2-piperidone (38a)** was obtained by chromatography (4:1 hexane–AcOEt): IR (NaCl) 1742, 1693, 1362, 1172 cm^{-1}; ^1H NMR (300 MHz) 0.07 and 0.13 (2s, 3H each, Me_2Si), 0.82 (s, 9H, *t*-Bu), 2.15 (m, 1H, 1′-H), 2.41 (s, 3H, MeTs), 2.42 (m, 2H, 4-H and 1′-H), 3.45 (d, *J*=11 Hz, 1H, 3-H), 3.71 (dd, *J*=12.2, 1.3 Hz, 1H, 6-H), 4.14 (br s, 1H, 5-H), 4.15 (masked dd, *J*=12.5, 3 Hz, 1H, 6-H), 5.08 and 5.17 (2d, *J*=12 Hz, 1H each, CH_2Ph), 6.02 (dd, *J*=15.5, 7.5 Hz, 1H, 3′-H), 6.58 (dt, *J*=15.6, 6.6 Hz, 1H, 2′-H), 7.20–7.40 (m, 7H, PhH), 7.90 (d, *J*=8.3 Hz, 2H, Ts-*o*-H), 9.40 (d, *J*=7.7 Hz, 1H, CHO); ^{13}C NMR (50.3 MHz) −4.9 and −4.2 (Me_2Si), 17.8 (C–Si), 21.6 (MeTs), 25.6 (*t*-Bu), 33.0 (C-1′), 40.9 (C-4), 52.4 (C-6), 52.9 (C-3), 64.7 (C-5), 67.7 (CH_2Ph), 128.4, 128.6, 128.8, and 129.4 (C-Ph), 134.5 (C-*i*-Bn, C-*i*-Ts and C-2′), 145.2 (C-*p*-Ts), 152.8 (C-3′), 165.1 and 168.6 (C-2 and CO_2Bn), 193.0 (CHO).

With dihydropyridone 16b. *Method C:* From **16b** (300 mg, 0.71 mmol) in CH_2Cl_2 (6 ml), $ZnBr_2$ (160 mg, 0.71 mmol) in CH_2Cl_2 (6 ml), and diene **5** (1:1 *cis–trans* mixture, 0.42 ml, 3.3 mmol) at 0°C for 4 h, a mixture of adducts ***endo*-35b** (140.8 mg, 37%) and ***exo*-35b** (35.2 mg, 9%) and aldehyde **38b** (one diastereomer of undetermined configuration, 35 mg, 10%) were obtained after chromatography (4:1 hexane–AcOEt). **(4*S*,4a*S*,8*R*,8a*R*)-8-Acetoxy-8a-(benzyloxycarbonyl)-4-(*tert*-butyldimethylsilyloxy)-2-(methoxycarbonyl)-1-oxo-1,2,3,4,4a,5,8,8a-octahydroisoquinoline (*endo*-35b):** mp 116–118°C (pentane); $[\alpha]_D^{20}=+25.7$ (*c* 2, $CHCl_3$); IR (KBr) 1747, 1724, 1372 cm^{-1}; ^1H NMR (500 MHz) 0.00 (s, 6H, Me_2Si), 0.87 (s, 9H, *t*-Bu), 1.98 (s, 3H, MeCO), 2.17 (ddm, *J*=17.3, 10.3 Hz, 1H, 5-H), 2.32 (ddm, *J*=18.8, 6.8 Hz, 1H, 5-H), 2.82 (ddd, *J*=10.3, 6.9, 5.1 Hz, 1H, 4a-H), 3.64 (dd, *J*=13.3, 7.6 Hz, 1H, 3-H), 3.69 (dd, *J*=13.3, 6.3 Hz, 1H, 3-H), 3.88 (s, 3H, OMe), 4.17 (br q *J*=6.3 Hz, 1H, 4-H), 5.16 and 5.28 (2d, *J*=12 Hz, 1H each, CH_2Ph), 5.82 (m, 3H, 6-H, 7-H and 8-H), 7.38 (s, 5H, PhH). Anal. Calcd for $C_{27}H_{37}NO_8Si$: C, 61.00; H, 7.01; N, 2.63. Found: C, 60.74; H, 7.17; N, 2.68. **(4*S*,4a*S*,8*S*,8a*R*)-Isomer (*exo*-35b)**: IR (KBr) 1783, 1737 cm^{-1}; ^1H NMR (300 MHz) 0.08 and 0.11 (2s, 3H each, Me_2Si), 0.89 (s, 9H, *t*-Bu), 1.72 (s, 3H, MeCO), 2.02 (ddm, *J*=18.6, 11.1 Hz, 1H, 5-H), 2.38 (dm, *J*=19.3 Hz, 1H, 5-H), 2.94 (dt, *J*=10.7, 6.3 Hz, 1H, 4a-H), 3.54 (dd, *J*=13.5, 6.4 Hz, 1H, 3-H), 3.64 (dd, *J*=13.5, 7 Hz, 1H, 3-H), 3.83 (s, 3H, OMe), 4.58 (br q, *J*=6.3 Hz, 1H, 4-H), 5.13 and 5.18 (2d, *J*=12 Hz, 1H each, CH_2Ph), 5.95 (m, 3H, 6-H, 7-H and 8-H), 7.33 (s, 5H, PhH). **(5*S*)-3 -(Benzyloxycarbonyl)-5-(*tert*-butyldimethylsilyloxy)-1-(methoxycarbonyl)-4-[4-oxo-2(*E*)-butenyl]-2-piperidone (38b):** ^1H NMR (200 MHz) 0.07 (s, 6H, Me_2Si), 0.86 (s, 9H, *t*-Bu), 2.06 (m, 1H, 1′-H), 2.27 (m, 1H, 4-H), 2.48 (m, 1H, 1′-H), 3.55 (dd, *J*=14.2, 3 Hz, 1H, 6-H), 3.59 (d, *J*=10.2 Hz, 1H, 3-H), 3.88 (s, 3H, OMe), 4.09 (masked dd, *J*=14.4, 3.2 Hz, 1H, 6-H), 4.10 (br s, 1H, 5-H), 5.14 and 5.26 (2d, *J*=12 Hz, 1H each, CH_2Ph), 6.08 (dd, *J*=15.6, 7.2 Hz, 1H, 3′-H), 6.63 (dt, *J*=15.4, 7.4 Hz, 1H, 2′-H), 7.37 (m, 5H, PhH), 9.43 (d, J=7.6 Hz, 1H, CHO); ^{13}C NMR (50.3 MHz) −4.9 and −4.5 (Me_2Si), 17.9 (C–Si), 25.6 (*t*-Bu), 33.5 (C-1′), 41.5 (C-4), 52.3 (C-6), 53.9 (C-3), 54.4 (OMe), 64.7 (C-5), 67.7 (CH_2Ph), 128.4, 128.5, and 128.6 (C-Ph), 135.0 (C-*i*-Bn and C-2′), 153.1 (C-3′), 154.7 (CO_2Me), 166.2 and 169.4 (C-2 and CO_2Bn), 193.2 (CHO).

X-Ray crystal structure of *endo*-35b. Crystal data: $C_{27}H_{37}NO_8Si$, orthorhombic, space group $P2_12_12_1$, a=7.8146 (12) Å, b=10.578 (2) Å, c=36.032 (5) Å, V=2978.5 (7) $Å^3$, Z=4, μ (MoKα)=0.124 mm^{-1}, D_c=1.186 mg m^{-3}. The experiment was done on an Enraf–Nonius CAD4 diffractometer using graphite monochromated MoKα radiation. The crystal had approximate dimensions of 0.40×0.16×0.15 mm. Data collection was up to a resolution of 2θ(=47.38°. producing 2600 reflections. The structure was solved by direct methods (SHELXS 86) after applying Lorentz, polarization and absorption (empirical psi scan method) corrections to the 2600 independent reflections. Full matrix least-squares refinement (SHELXL 93) using anisotropic thermal parameters for non-H atoms and a global isotropic temperature factor for the H-atoms (introduced at calculated positions) converged to a R factor of 0.246 (0.052 for reflection with $I>2\sigma(I)$). Maximum and minimum heights at the final difference Fourier synthesis were 0.23 and −0.21 e $Å^{-3}$. Complete data have been deposited at the Cambridge Crystallographic Data Centre.

Diels–Alder reactions from 1-methoxybuta-1,3-diene (6)

With dihydropyridone 12a. *Method A:* From **12a** (500 mg, 1.29 mmol) and diene **6** (1:1 *cis–trans* mixture, 0.4 ml, 3.96 mmol) in *p*-cymene (10 ml) for 2 h, adducts ***endo*-32a** and ***exo*-32a** (3:2 mixture, 293 mg, 48%) and dihydropyridone **10a** (traces) were obtained after chromatography (4:1 hexane–AcOEt). Isomer ***endo*-32a** was isolated by crystallization from Et_2O. **(4a*RS*,8*RS*,8a*RS*)-8a-(Benzyloxycarbonyl)-8-methoxy-1-oxo-2-(*p*-toluenesulfonyl)-1,2,3,4,4a,5,8,8a-octahydroisoquinoline (*endo*-32a):** mp 149–151°C (Et_2O); IR (KBr) 1737 1682, 1357, 1170 cm^{-1}; ^1H NMR (200 MHz) 1.62 (dm, *J*=13.4 Hz, 1H, 4-H), 1.93 (m, 2H, 5-H), 2.40 (s, 3H, MeTs), 2.48 (ddd, *J*=19, 12.3, 7 Hz,

1H, 4-H), 2.64 (dm, *J*=14 Hz, 1H, 4a-H), 2.87 (s, 3H, OMe), 3.82 (td, *J*=12, 5.6 Hz, 1H, 3-Hax), 4.09–4.18 (m, 2H, 8-H and 3-Heq), 5.01 and 5.19 (2d, *J*=12.4 Hz, 1H each, CH_2Ph), 5.70 (dt, *J*=10.2, 4 Hz, 1H, 6-H), 5.91 (ddt, *J*=10.2, 4.3, 2 Hz, 1H, 7-H), 7.21–7.35 (m, 7H, PhH), 7.90 (d, *J*=8.3 Hz, 2H, Ts-*o*-H); MS, *m/z* (rel intensity) 470 (M^+, 1); 321 (11); 270 (15); 240 (19); 187 (25); 91 (100); 84 (26); 65 (14). Anal. Calcd for $C_{25}H_{27}O_6NS$: C, 63.95; H, 5.80; N, 2.98; S, 6.83. Found: C, 63.86; H, 5.83; N, 2.98; S, 6.79. *Method C:* From **12a** (300 mg, 0.77 mmol) in CH_2Cl_2 (5 ml), $ZnBr_2$ (170 mg, 0.77 mmol) in CH_2Cl_2 (5 ml), and diene **6** (1:1 *cis–trans* mixture, 0.42 ml, 3.8 mmol) at 25°C for 1 h, a mixture of adducts ***endo*-32a** and ***exo*-32a** (1:1, 330 mg, 89%) was obtained after chromatography (7:3 hexane–AcOEt). Isomer ***endo*-32a** was isolated by crystallization from Et_2O.

With dihydropyridone 12b. *Method A:* From **12b** (500 mg, 1.73 mmol) and diene **6** (1:1 *cis–trans* mixture, 0.15 ml, 3.1 mmol) in *p*-cymene (8 ml) for 4 h, adducts **32b** (3:2 mixture of *endo* and *exo* adducts, 75 mg, 12%) and ***endo*-32c** (135 mg, 24%) were obtained after chromatography (4:1 hexane–AcOEt). The assignment of ^1H and ^{13}C NMR spectra of adducts **32b** was performed by comparison with spectra of other adducts of these series. **(4a*RS*,8*RS*, 8a*RS*)-8a-(Benzyloxycarbonyl)-8-methoxy-2-(methoxycarbonyl)-1-oxo-1,2,3,4,4a,5,8,8a-octahydroisoquinoline (*endo*-32b):** IR (KBr) 1770, 1727, 1640 cm^{-1}; ^1H NMR (200 MHz) 1.56 (dm, *J*=13.6 Hz, 1H, 4-H), 1.96 (br s, 2H, 5-H), 2.45 (m, 1H, 4-H), 2.65 (dq, *J*=13.6, 3.2 Hz, 1H, 4a-H), 3.17 (s, 3H, CO_2Me), 3.08–3.23 (m, 1H, 3-Hax), 3.61 (td, *J*=11.6, 5.8 Hz, 1H, 3-Heq), 3.84 (s, 3H, OMe), 4.45 (d, *J*=4.4 Hz, 1H, 8-H), 5.10 and 5.30 (2d, *J*=12.2 Hz, 1H each, CH_2Ph), 5.70–5.86 (m, 1H, 6-H), 6.01 (m, 1H, 7-H), 7.33 (m, 5H, PhH). Anal. Calcd for $C_{20}H_{23}NO_6 \cdot 1/4H_2O$: C, 63.57; H, 6.27; N, 3.71. Found: C, 63.6; H, 6.20; N, 3.56. **(4a*RS*,8*SR*,8a*RS*)-Isomer (*exo*-32b):** IR (KBr) 1770, 1727, 1650 cm^{-1}; ^1H NMR (200 MHz) 1.49–1.64 (m, 1H, 4-Heq), 1.78 (dd, *J*=18.4, 12 Hz, 2H, 5-Hax), 2.26 (dt, *J*=18.6, 5.4 Hz, 1H, 5-Heq), 2.34–2.56 (m, 1H, 4-Hax), 2.79–2.92 (m, 1H, 4a-H), 3.08–3.24 (m, 1H, 3-Hax), 3.36 (s, 3H, CO_2Me), 3.87 (s, 3H, OMe), 4.12 (ddd, *J*=14.4, 8, 4 Hz, 1H, 3-Heq), 4.35 (d, *J*=4 Hz, 1H, 8-H), 5.06 and 5.27 (2d, *J*=12.4 Hz, 1H each, CH_2Ph), 5.7–5.86 (m, 1H, 6-H), 6.01 (m, 1H, 7-H), 7.35 (m, 5H, PhH). Anal. Calcd for $C_{20}H_{23}NO_6 \cdot 1/4H_2O$: C, 63.57; H, 6.27; N, 3.71. Found: C, 63.6; H, 6.20; N, 3.56. **(4a*RS*,8*RS*,8a*RS*)-8a-(Benzyloxycarbonyl)-8-methoxy-1-oxo-1,2,3,4,4a,5,8,8a-octahydroisoquinoline (*endo*-32c):** IR (KBr) 3266, 1728, 1684, 1634 cm^{-1}; ^1H NMR (300 MHz) 1.43 (dt, *J*=13, 3.2 Hz, 1H, 4-Heq), 1.98 (m, 2H, 5-H), 2.44 (tdd, *J*=13.5, 11.7, 6.7 Hz, 1H, 4-Hax), 2.68 (ddt, *J*=13.7, 5, 3 Hz, 1H, 4a-H), 3.43 (m, 2H, 3-H), 3.41 (s, 3H, OMe), 4.38 (dd, *J*=4.4, 0.8 Hz, 1H, 8-H), 5.12 and 5.27 (2d, *J*=12 Hz, 1H each, CH_2Ph), 5.74 (dt, *J*=10.2, 4.2 Hz, 1H, 6-H), 6.03 (ddt, *J*=10.3, 4.4, 2.4 Hz, 1H, 7-H), 6.50 (br s, 1H, NH), 7.33 (m, 5H, PhH). Anal. Calcd for $C_{18}H_{21}NO_4$: C, 68.55; H, 6.71; N, 4.44. Found: C, 68.38; H, 6.69; N, 4.35. *Method C:* From **12b** (300 mg, 1.03 mmol) in CH_2Cl_2 (5 ml), $ZnBr_2$ (230 mg, 1.03 mmol) in CH_2Cl_2 (5 ml), and diene **6** (1:1 *cis–trans* mixture, 0.21 ml, 2 mmol) at 25°C for 7 h, adducts ***endo*-32b** and ***exo*-32b** (1:1 mixture, 125 mg, 32%) and aldehyde **34b** (150 mg, 34%) were obtained after chromatography (1:1 hexane–AcOEt).

With dihydropyridone 16a. *Method C:* From **16a** (300 mg, 0.58 mmol) in CH_2Cl_2 (12 ml), $ZnBr_2$ (130 mg, 0.58 mmol) in CH_2Cl_2 (6 ml), and diene **6** (1:1 *cis–trans* mixture, 0.29 ml, 2.9 mmol) at 0°C for 4 h, adduct ***exo*-36a** (239 mg, 68%, accompanied by traces of three minor diastereomers) was obtained after chromatography (4:1 hexane–AcOEt). An analytical sample of the major diastereomer **(4*S*,4a*S*,8*S*,8a*R*)-8a-(benzyloxycarbonyl)-4-(*tert*-butyldimethylsilyloxy)-8-methoxy-1-oxo-2-(*p*-toluenesulfonyl)-1,2,3,4,4a,5,8,8a-octahydroisoquinoline (*exo*-36a)** was obtained by chromatography (4:1 hexane–AcOEt): ^1H NMR (200 MHz) -0.04 and -0.03 (2s, 3H each, Me_2Si), 0.77 (s, 9H, *t*-Bu), 1.53 (ddm, *J*=18.5, 11.5 Hz, 1H, 5-H), 2.09 (dtm, *J*=19.2, 5.5 Hz, 1H, 5-H), 2.25 (s, 3H, MeTs), 2.73 (dt, *J*=11.4, 6.2 Hz, 1H, 4a-H), 2.94 (s, 3H, OMe), 3.55 (dd, *J*=13.3, 6.1 Hz, 1H, 3-H), 3.63 (dd, *J*=13.2, 5.6 Hz, 1H, 3-H), 4.15 (d, *J*=4.4 Hz, 1H, 8-H), 4.54 (q, *J*=6 Hz, 1H, 4-H), 4.87 and 5.12 (2d, *J*=12 Hz, 1H each, CH_2Ph), 5.61 (ddd, *J*=10, 4.6, 2 Hz, 1H, 7-H), 5.71 (dm, *J*=10 Hz, 1H, 6-H), 7.09–7.21 (m, 7H, PhH), 7.71 (d, *J*=8.4 Hz, 2H, Ts-*o*-H). Anal. Calcd for $C_{31}H_{41}NO_7SSi$: C, 62.08; H, 6.89; N, 2.34; S, 5.34. Found: C, 61.71; H, 6.83; N, 2.36; S, 5.11.

Diels–Alder reactions from (*E*)-1-(trimethylsilyloxy)-buta-1,3-diene (7)

With dihydropyridone 12a. *Method A:* From **12a** (500 mg, 1.29 mmol) and diene **(*E*)-7** (0.78 ml, 4.5 mmol) in *p*-cymene (10 ml) for 2 h, a residue was obtained after concentration of the solvent. Anhydrous THF (50 ml) and CSA (300 mg, 1.29 mmol) were added to the residue, and the resulting solution was stirred at 0°C for 1 h. After evaporation of the solvent and addition of saturated aqueous $NaHCO_3$, the mixture was extracted with AcOEt. Concentration of the dried organic extracts afforded a residue, which was chromatographed (85:15 hexane–AcOEt) to yield a mixture of adducts ***endo*-33a** and ***exo*-33a** (3:2, 190 mg, 28%) and dihydropyridone **10a** (traces). Isomer ***endo*-33a** was isolated by crystallization from Et_2O. **(4a*RS*, 8*RS*, 8a*RS*)-8a-(Benzyloxycarbonyl)-1-oxo-2-(*p*-toluenesulfonyl)-8-(trimethylsilyloxy)-1,2,3,4,4a,5,8,8a-octahydroisoquinoline (*endo*-33a):** mp 176–178°C (Et_2O); IR (KBr) 1747, 1676, 1345, 1163 cm^{-1}; ^1H NMR (200 MHz) 0.07 (s, 9H, Me_3Si); 1.64 (m, 1H, 4-H), 1.97 (m, 2H, 5-H), 2.40 (s, 3H, MeTs), 2.62 (dm, *J*=13.5 Hz, 1H, 4a-H), 2.73 (m, 1H, 4H), 3.85 (td, *J*=11.5, 6 Hz, 1H, 3-Hax), 4.03 (ddd, *J*=11.7, 5.2, 1.5 Hz, 1H, 3-Heq), 4.75 (d, *J*=4.3 Hz, 1H, 8-H), 5.09 and 4.96 (2d, *J*=12.5 Hz, 1H each, $PhCH_2$), 5.67 (dt, *J*=10.3, 3.8 Hz, 1H, 6-H), 5.78 (ddt, *J*=10.2, 4.5, 2.2 Hz, 1H, 7-H), 7.13–7.34 (m, 7-H, PhH and Ts-*m*-H), 7.93 (d, *J*=8.3 Hz, 2H, Ts-*o*-H); MS, *m/z* (rel intensity) 97 (45), 96 (39); 91 (51); 83 (60); 82 (41); 71 (51); 69 (75); 57 (100); 55 (81). Anal. Calcd for $C_{27}H_{33}O_6NSSi$: C, 61.45; H, 6.30; N, 2.65; S, 6.08. Found: C, 61.55; H, 6.31; N, 2.60; S, 6.07. Spectroscopic data of the **(4a*RS*, 8*SR*,8a*RS*)-isomer (*exo*-33a)** were inferred from an *endo*/*exo* mixture: ^1H NMR (200 MHz) −0.02 (s, 9H, Me_3Si); 1.20–3.20 (m, 5H, 4-H, 4a-H, 5-H), 2.44 (s, 3H, MeTs), 3.95–4.15 (m, 1H, 3-Hax), 4.25 (m, 1H, 3-Heq),

4.83 (d, J=4.3 Hz, 1H, 8-H), 4.95 and 5.15 (2d, J=12.5 Hz, 1H each, $PhCH_2$), 5.65–5.85 (m, 2H, 6-H, 7-H), 7.10–7.40 (m, 7-H, PhH and Ts-*m*-H), 7.78 (d, J=8.3 Hz, 2H, Ts-*o*-H). *Method C:* From **12a** (320 mg, 0.82 mmol) in CH_2Cl_2 (3 ml), $ZnBr_2$ (164 mg, 0.73 mmol) in CH_2Cl_2 (2 ml), and diene **(*E*)-7** (0.7 ml, 4.2 mmol) at 25°C for 30 min, adducts ***endo*-33a** and ***exo*-33a** (1:1 mixture, 27 mg, 4%) and aldehyde **34a** (266 mg, 50%) were obtained after chromatography (CH_2Cl_2–MeOH 1%). ***trans*-3-(Benzyloxycarbonyl)-4-[4-oxo-2(*E*)-butenyl]-1-(*p*-toluenesulfonyl)-2-piperidone (34a):** ^{1}H NMR (300 MHz) 1.63 (m, 1H, 5-H), 1.93–2.5 (m, 4H, 4-H, 1′-H, 5-H), 2.39 (s, 3H, MeTs), 3.18 (d, J=10 Hz, 1H, 3-H), 3.61 (m, 1H, 6-H), 3.98 (m, 1H, 6-H), 5.43 (m, 2H, CH_2Ph), 6.50 (m, 1H, 3′-H), 6.81 (m, 1H, 2′-H), 7.27 (d, J=7.6 Hz, 2H, Ts-*m*-H), 7.29 (m, 5H, PhH), 7.88 (d, J=7.6 Hz, 2H, Ts-*o*-H), 9.47 (d, J=7.7 Hz, 1H, CHO).

With dihydropyridone 12b. *Method A:* From **12b** (500 mg, 1.73 mmol) and diene **(*E*)-7** (1 ml, 5.7 mmol) in *p*-cymene (8 ml) for 2.5 h, adducts ***endo*-33b** and ***exo*-33b** (1:1, 230 mg, 31%) were obtained after chromatography (7:3 hexane–AcOEt). **(4a*RS*,8*RS*,8a*RS*)-8a-(Benzyloxycarbonyl)-2-(methoxycarbonyl)-1-oxo-8-(trimethylsilyloxy)-1,2,3,4,4a,5,8,8a-octahydroisoquinoline (*endo*-33b):** IR (NaCl) 1777, 1739, 1725 cm^{-1}; ^{1}H NMR (300 MHz) 0.08 (s, 9H, Me_3Si), 1.54 (m, 1H, 4-H), 1.95 (br s, 2H, 5-H), 2.66 (m, 2H, 4-H and 4a-H), 3.61 (m, 1H, 3-Hax), 3.86 (s, 3H, OMe), 3.75 (m, 1H, 3-Heq), 4.85 (d, J=5 Hz, 1H, 8-H), 5.23 and 5.28 (2d, J=12.4 Hz, 1H each, CH_2Ph), 5.69 (m, 1H, 6-H), 5.79 (m, 1H, 7-H), 7.25 (s, 5H, PhH); MS, *m*/*z* (rel intensity) 416 (32), 297 (20), 296 (95) 280 (47), 264 (31), 142 (37), 91 (100), 65 (22). Anal. Calcd for $C_{22}H_{29}NO_6Si$: C, 61.23; H, 6.77; N, 3.25. Found: C, 61.40; H, 6.88; N, 3.28. **(4a*RS*,8*SR*, 8a*RS*)-Isomer (*exo*-33b):** IR (NaCl) 1752, 1725 cm^{-1}; ^{1}H NMR (300 MHz) 0.08 (s, 9H, Me_3Si), 1.56 (dtd, J=13, 6.5, 1 Hz, 1H, 4-H), 1.79 (dd, J=18, 12 Hz, 1H, 5-Hax), 2.24 (dt, J=18, 6 Hz, 1H, 5-Heq), 2.34 (dtd, J=14, 7.5, 4.5 Hz, 1H, 4-H), 2.92 (m, 1H, 4a-H), 3.03 (ddd, J=14.5, 8, 7.5 Hz, 1H, 3-Hax), 3.82 (s, 3H, OMe), 4.06 (ddd, J=14.5, 8, 4 Hz, 1H, 3-Heq), 5.00 (d, J=4.4 Hz, 1H, 8-H), 5.08 and 5.29 (2d, J=12.4 Hz, 1H each, CH_2Ph), 5.73 (m, 1H, 6-H), 5.81 (m, 1H, 7-H), 7.34 (s, 5H, PhH); MS, *m*/*z* (rel intensity) 297 (12); 296 (60); 280 (18); 264 (24); 192 (12); 91 (100). Anal. Calcd for $C_{22}H_{29}NO_6Si$: C, 61.23; H, 6.77; N, 3.25. Found: C, 61.13; H, 6.75; N, 3.17. *Method D:* Operating as in the above method D, from dihydropyridone **12b** (289 mg, 1 mmol), diene **(*E*)-7** (0.35 ml, 2 mmol) and $EtAlCl_2$ (1 M in hexane, 0.5+1.5 ml), aldehyde **34b** (160 mg, 47%) was obtained after chromatography (CH_2Cl_2–MeOH 5%).

With dihydropyridone 16a. *Method C:* From **16a** (300 mg, 0.58 mmol) in CH_2Cl_2 (15 ml), $ZnBr_2$ (130 mg, 0.58 mmol) in CH_2Cl_2 (6 ml), and diene **(*E*)-7** (0.5 ml, 2.9 mmol) at 0°C for 4 h, adduct ***endo*-37a** (14 mg, 4%) and aldehyde **38a** (48 mg, 14%, the major aldehyde obtained from diene **5**) were obtained after chromatography (4:1 hexane–AcOEt). **(4*S*,4a*S*,8*R*,8a*R*)-8a-(Benzyloxycarbonyl)-4-(*tert*-butyldimethylsilyloxy)-1-oxo-2-(*p*-toluenesulfonyl)-8-(trimethylsilyloxy)-1,2,3,4,4a,5,8,8a-octahydroisoquinoline (*endo*-37a):** IR (NaCl) 1741, 1720, 1361, 1172 cm^{-1}, ^{1}H NMR (300 MHz) 0.00 (s, 9H, Me_3Si), 0.05 and 0.06 (2s, 3H each, Me_2Si), 0.89 (s, 9H, *t*-Bu), 1.60 (dd, J=18.7, 11.5 Hz, 1H, 5-H), 2.15 (ddd, J=18.7, 6.3, 3 Hz, 1H, 5-H), 2.36 (s, 3H, MeTs), 2.91 (dt, J=11.9, 6.5 Hz, 1H, 4a-H), 3.44 (dd, J=13.7, 5.9 Hz, 1H, 3-H), 3.76 (dd, J=13.7, 4.8 Hz, 1H, 3-H), 4.54 (q, J=5.8 Hz, 1H, 4-H), 4.81 (m, 1H, 8-H), 5.02 and 5.15 (2d, J=12.2 Hz, 1H each, CH_2Ph), 5.62 (br s, 2H, 6-H and 7-H), 7.20–7.32 (m, 7H, PhH), 7.83 (d, J=8 Hz, 2H, Ts-*o*-H). Anal. Calcd for $C_{33}H_{47}NO_7SSi_2$: C, 60.24; H, 7.20; N, 2.13; S, 4.87. Found: C, 60.24; H, 7.38; N, 2.10; S, 4.60.

Acknowledgements

Financial support from DGICYT, Spain (project PB94-0214) and the 'Comissionat per a Universitats i Recerca', Generalitat de Catalunya (Grant SGR99-00079) is gratefully acknowledged. Thanks are also due to the 'Ministerio de Educación y Cultura', Spain for a fellowship to V. L.

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