Tetrahedron Vol. 48, No. 13, pp. 2659-2680, 1992
Printed in Great Britain

0040-4020/92 $3.00+.00

Diastereofacial Selectivity in Uncatalyzed Diels-Alder Cycloadditions Involving α,β-Unsaturated Esters and Lactones with Stereogenic Centers Containing Oxygen Functionalities&

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(*Received in UK* 25 *November* 1991)

Abstract. Both experimental and theoretical studies on the Diels-Alder cycloadditions of dienophiles **1**, **2** and **3** to different dienes show that the observed diastereofacial selectivity results from a combination of electronic and steric interactions. The traditional Felkin-Anh model is not appropriate for these cases. Several new chiral synthetic building blocks have been prepared.

INTRODUCTION

The control of diastereofacial selectivity in Diels-Alder cycloadditions involving chiral dienophiles has stimulated a great interest during the last years. A bold general solution to this problem has been proposed by Hehre,[1] with a theoretical approach which assumes that the selectivity is mainly influenced by electrostatic interactions, independent of topological distortions involving the participant molecular orbitals[2] and steric effects.[3] Although several examples have been reported which follow this rule,[1,4,5] some other cases have been found which do not.[4,6]

A particular class of chiral dienophiles, the α,β-unsaturated esters possessing a heteroatom at a chiral allylic carbon, have received much attention. Thus, Franck[7] and Horton[8] have carried out the Diels-Alder reactions of chiral unsaturated esters obtaining adducts produced through the anti-attack of dienes at the diastereotopic π-face of dienophiles, as shown in Figure 1. In agreement with the theory enounced by Houk,[9] Franck assumed that the orbital interaction of a syn-alkoxy group in the cycloaddition transition state is more unfavorable than the syn-alkyl interaction, despite the bulk of the sugar moiety. As a consequence, the incoming group would bind to the face opposite to the allylic oxygen function to minimize secondary orbital antibonding effects. This model can

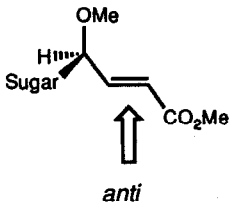
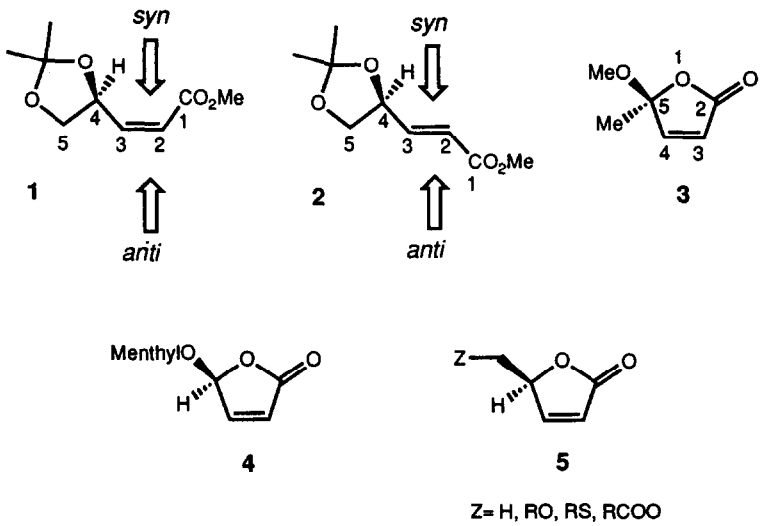


Fig 1. Conformational model (ref. 7) showing the anti attack.

be considered as an extension of that of Felkin-Anh,[10,11] and possesses a conformational preference, shown in Figure 1, based only on orbital interactions.

Diastereofacial selectivity of several reported Diels-Alder cycloadditions can be interpreted satisfactorily by means of this theory.[7b,8a] Processes involving quite rigid cyclic dienophiles, such as pseudoester **4** (Chart I) could be also understood in this manner.[12]

Chart I

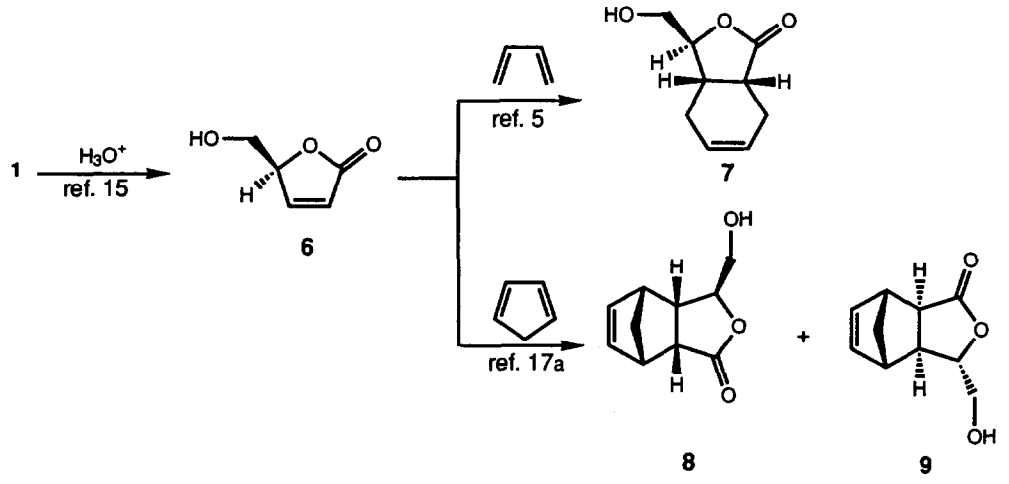


However, in many instances the formation of the major adduct is reported to occur via the anti-Felkin-Anh active conformer rather than via the Felkin-Anh conformer, due to repulsive dipole-dipole and non-bonding interactions,[13] or steric hindrance.[3,13]

Among these last examples, the results described by Mulzer[14] were particularly interesting for us. This author reported the Diels-Alder reactions of cyclopentadiene with the (Z)- and the (E)-enoates **1** and **2**[15] (Chart I), respectively, to give a mixture of endo/exo adducts according to a syn-alkoxy diastereoselection in both cases.

This selectivity is opposite to that observed in the Diels-Alder cycloadditions of several dienes to chiral butenolides 5,[5,16,17] which are dienophiles largely studied in our laboratory. For instance, we found that hydroxymethylbutenolide 6 reacts with butadiene and cyclopentadiene giving the adducts 7 and 8/9, respectively, with 100% anti-facial selectivity[5,17a] (Scheme 1). This behavior is extensive to other butenolides represented by the general structure 5 (Chart I). However, in these cases there is not a heteroatom directly attached to the stereogenic center.

Scheme 1



Since the butenolide 6 can be synthesized from (Z)-enoate 1,[15] (Scheme 1) it seemed interesting to investigate and rationalize the facial selectivity in the Diels-Alder reactions of esters 1 and 2 with different kinds of dienes. The pseudoester 3[18] (in racemic form, one enantiomer shown in Chart I) was also investigated in order to verify if disfavorable interactions due to the methoxyl group could direct the syn-methyl face orientation toward the dienes. In this case, the orientation of the heteroatom attached to the chiral center is fixed relative to the π-face of the dienophile. The control of the diastereofacial selection in the cycloadditions of the esters 1 and 2, jointly with chiral butenolides, could provide an efficient entry to a set of isomeric adducts which could serve as useful precursors in asymmetric synthesis.

RESULTS and DISCUSSION

I. Diels-Alder cycloadditions: Production and identification of the adducts.

Dienophiles **1**, **2** and **3** were allowed to react with butadiene, cyclopentadiene, and 1-trimethylsilyloxy-1,3-butadiene, as examples of acyclic and cyclic C-dienes, and heterosubstituted dienes, respectively. Reactions with butadiene and cyclopentadiene were performed under the non-catalyzed thermal activation conditions shown in Table I. Adducts were obtained in high yields, the structures being represented in Chart II. Cycloaddition of these dienophiles to 1-trimethylsilyloxy-1,3-butadiene were attempted at 110 and 150 °C using toluene as solvent, but no reaction took place. However, the expected adducts were obtained in good yields when the reactions were performed under high pressure conditions (Table I).

(a) Reactions with butadiene.

Reaction between the (Z)-enoate **1** and butadiene was carried out at 170 °C for 17 h, affording a 93:7 mixture (GLC, ^{1}H NMR) of the two possible stereoisomeric adducts **10** and **11** in 62% yield, with a 32% recovery of starting material (Table I, entry 1). Column chromatography allowed the isolation of the major isomer **10** which was converted into the lactone derivative **34** through acid methanolysis (Chart II). Compound **34** is a solid mp 66-67 °C, $(\alpha)_D$ -75.2 ° whose structure was confirmed by spectroscopic means. Stereochemical assignment of **34** as a result of syn-diastereoface selection was accomplished by comparing it with the diastereomeric adduct **7** (Lit.[5] liquid, oven temperature 160 °C (0.035 Torr), $(\alpha)_D$ -6.5 °), obtained from furanone **6** (Scheme 1), and previously identified.[5] By exclusion, the minor isomer obtained was assigned to be **11**.

The (E)-enoate **2** was allowed to react with butadiene at 170 °C for 18 h giving a 60:40 mixture of adducts **12** and **13**, in 92% yield (Table I, entry 2). The relative proportion of these isomers was determined by capillary G.C. analysis of the mixture, obtained as a liquid whose mass spectrum and elemental analysis were consistent with the expected structure. However, the two isomers could not be isolated by using the habitual chromatographic techniques. The slightly major isomer was tentatively assigned to be **12** in accordance with the predominant syn-diastereoface selection observed in the cycloaddition of **2** with cyclopentadiene (*vide infra*).

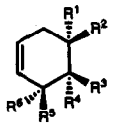
Reaction of the pseudoester **3** at 140 °C for 17 h did not afford the expected adducts. Instead of them, a 10:1 mixture of (±)-**14** and (±)-**15** was

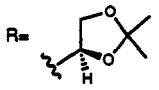
Table I. Diels-Alder Cycloadditions of Dienophiles **1**, **2**, and **3** with Butadiene, Cyclopentadiene, and 1-trimethylsilyloxy-1,3-butadiene.[a]

			conditions			adducts (% ratio)				
						syn[b]		anti[b]		
entry	diene	dienophile	temp °C	pressure kbar[c]	time h	endo	exo	endo	exo	yield %
1[d]	butadiene	**1**	170	--	17	**10** (93)		**11** (7)		62
2[e]	butadiene	**2**	170	--	18	**12** (60)		**13** (40)		92
3[d]	cyclopentadiene	**1**	100	--	16	**21** (78)	**22** (15)	**23** (7)		94
4[e]	cyclopentadiene	**1**	80	--	8	**21** (80)	**22** (15)	**23** (5)		95
5[d]	cyclopentadiene	**2**	95	--	17	**24** (27)	**25** (58)	**26** + **27** (15)		98
6[e]	cyclopentadiene	**2**	80	--	8	**24** (27)	**25** (60)	**26** + **27** (13)		95
7[e]	cyclopentadiene	**3**	140	--	5	**30** (40)	**33** (23)	**31** (21)	**32** (16)	85
8[e]	cyclopentadiene	**3**	120	--	15	**30** (39)	**33** (25)	**31** (22)	**32** (14)	66
9[e]	cyclopentadiene	**3**	100	--	5	**30** (37)	**33** (24)	**31** (22)	**32** (17)	64
10[d]	1-(TMSO)butadiene	**1**	40	12	64	**16** (100)				100
11[e]	1-(TMSO)butadiene	**2**	50	14	65	**17** (25)	**18** (25)	**19** (25)	**20** (25)	99
12[e]	1-(TMSO)butadiene	**3**	40	12	70	**28** (50)		**29** (50)		65

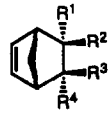
[a] 1-(TMSO)butadiene. [b] Respect to the oxygen-substituent (see Chart I). [c] Only for high-pressure-induced reactions. [d] Yield and isomer ratio on isolated products. [e] Yield and isomer ratio from GC and/or ^{1}H NMR analysis of the reaction crude.

Chart II

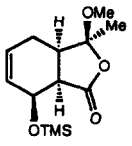




	R^1	R^2	R^3	R^4	R^5	R^6
10	H	R	CO_2Me	H	H	H
11	R	H	H	CO_2Me	H	H
12	H	R	H	CO_2Me	H	H
13	R	H	CO_2Me	H	H	H
14	COMe	H	H	CO_2Me	H	H
15	COMe	H	CO_2Me	H	H	H
16	H	R	CO_2Me	H	OTMS	H
17	H	R	H	CO_2Me	H	OTMS
18	H	R	H	CO_2Me	OTMS	H
19	R	H	CO_2Me	H	OTMS	H
20	R	H	CO_2Me	H	H	OTMS



	R^1	R^2	R^3	R^4
21	CO_2Me	H	H	R
22	H	R	CO_2Me	H
23	R	H	H	CO_2Me
24	H	R	H	CO_2Me
25	H	CO_2Me	H	R
26	CO_2Me	H	R	H
27	R	H	CO_2Me	H



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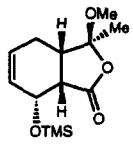

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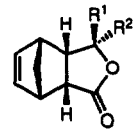
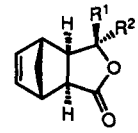
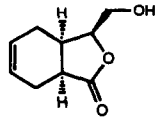


	R^1	R^2
30	Me	MeO
31	MeO	Me



	R^1	R^2
32	Me	MeO
33	MeO	Me



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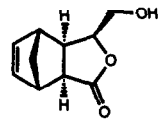


35

obtained in 57% yield (Chart II). These products[19] resulted from cycloaddition of butadiene to methyl (Z)- and (E)-4-oxo-2-pentenoate, respectively, produced *in situ* through ring-opening and rearrangement of **3**, accompanied by partial (Z)-(E) double bond isomerization. Compounds **14** and **15** could be isolated by column chromatography and were unequivocally

identified by their representative spectral data. MS: m/e 183 (M+1), and 182 (M); ^{1}H NMR: Me-CO- at 2.1 and 2.2 ppm, respectively; ^{13}C NMR: ketone carbonyl at 209 and 210 ppm, respectively.

(b) Reactions with cyclopentadiene.

Diels-Alder reaction between **1** and cyclopentadiene at 100 °C for 16 h, afforded a 78:15:7 mixture of the diastereoisomers **21, 22,** and **23** in 94% yield (Table I, entry 3). A very similar result was obtained when the reaction was performed at 80 °C for 8 h (entry 4), showing a predominance for the (syn-endo)-diastereoselection in this cycloaddition. It is notewhorty that the facial selectivity of **1** is identical for both butadiene and cyclopentadiene.

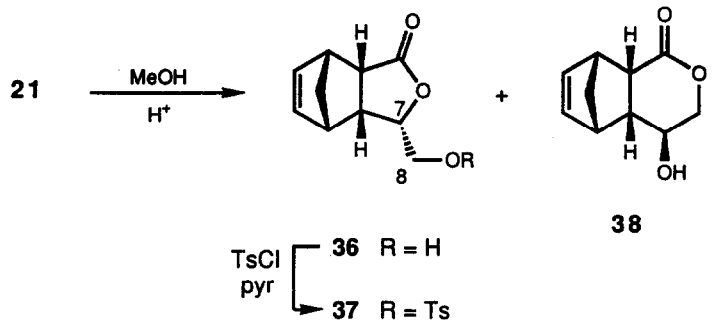
Mulzer and coworkers reported this reaction, performed at 80 °C for 8 h, giving a 85:15 mixture of **21** and **22** in 95% yield, without mention of the anti-adducts.[14] These authors distinguished between endo- and exo-isomers on the basis of considering ^{1}H-^{1}H coupling constants. The syn-diastereoselection was verified in that work[14] by saponification of adduct **21**, with concomitant epimerization at the α-carbonyl position, to produce a carboxylic acid whose configuration was determined by X-ray analysis. Nevertheless, the configuration of **22** remained uncertain.

We wished to assign unambigously the configuration of every adduct **21, 22** and **23** obtained in our laboratory. Since NMR coupling constant analysis did not appear to definitively identify each isomer, we transformed these products into the tricyclic lactone derivatives **36, 35** and **8**, respectively. These lactones are rigid systems whose stereochemistry was easier to study by NMR techniques or by chemical correlation with other previously known compounds. Thus, since lactone **8** was identical to the endo-isomer obtained as a major product in the reaction between butenolide **6** and cyclopentadiene (Scheme 1),[17a] (anti-endo)-stereochemistry could be assigned to adduct **23**.

Acid methanolysis of **21** afforded the γ-lactone **36** and the δ-lactone **38** in 4.5:1 equilibrium ratio (Scheme 2). Since ^{1}H NMR and IR spectral data were not enough to identify unequivocally each lactone, the tosyl derivative **37** was prepared. The absorption of the protons at C-8 as an ABX system, centered at 3.8 ppm in **36**, was shifted to 4.2 ppm in the tosylate **37**. However, the absorption due to the proton at C-7 rested unchanged at 4.6 ppm. These results confirmed the structure of **36** as the γ-lactone.

In turn, adduct **22** gave the lactone derivative **35**, through acid methanolysis. The configuration of lactones **35** and **36** was elucidated by

Scheme 2



using the differential NOE technique and long range ^{1}H-^{13}C coupling constant values.[20]

Ester **2** underwent cycloaddition with cyclopentadiene at 95 °C for 17 h to afford a 27:58:15 mixture of the isomeric adducts **24**, **25** and **26+27**, in 98% yield, as evidenced by GC-MS and NMR analysis of the reaction crude. The same result was obtained from the reaction carried out at 80 °C for 8 h (Table I, entries 5 and 6, respectively). Column chromatography allowed the isolation of **24** and **25**, and the mixture **26+27**. The major product **25** was identified as the (syn-exo)-isomer by correlation with the product resultant from base-induced epimerization of **21**, which was identical to **25**. In a similar manner, compound **24** was assigned to be the (syn-endo)-isomer by correlation of its epimer with the previously known adduct **22**. By exclusion, the mixture **26+27** must correspond to the (anti-endo/exo)-isomers. Mulzer[14] reported the reaction of **2** with cyclopentadiene at 80 °C for 8 h to produce only adducts **24** and **25** in 40:60 ratio.

In turn, pseudoester **3** reacted with cyclopentadiene at 140 °C for 5 h, to give a 40:21:16:23 mixture of the racemic isomers **30**, **31**, **32**, and **33** along with 15 % unaltered starting material. The relative proportion of these stereoisomers was essentially the same when the reaction was performed at lower temperatures. However, the yield of adducts decreased in these cases (compare entry 7 with entries 8 and 9, Table I). The four products could be isolated by column chromatography and characterized. Their anti/syn and endo/exo stereochemistry was unambigously assigned on the basis of considering ^{1}H and ^{13}C NMR data concerning to long range ^{1}H-^{13}C coupling constants and differential NOE measurements.[20]

(c) Reactions with 1-trimethylsilyloxy-1,3-butadiene.

(Z)-Enoate **1** reacted with 1-trimethylsilyloxy-1,3-butadiene in dichloromethane under 12 kbar pressure at 40 °C for 64 h to give quantitatively adduct **16**, solid mp 58-60 °C, $(\alpha)_D$ +64.5° (Table I, entry 10). This compound was hydrolyzed to produce the bicyclic dihydroxylactone **39**, mp 97-99 °C, $(\alpha)_D$ +15.8 °. ^1H-^1H and ^1H-^{13}C 2D NMR spectra, differential NOE experiments, and coupling constant analysis permitted the stereochemical assignment of product **39**, and consequently adduct **16** was identified as the (syn-endo)-isomer. Significant NMR data are shown in Figure 2.

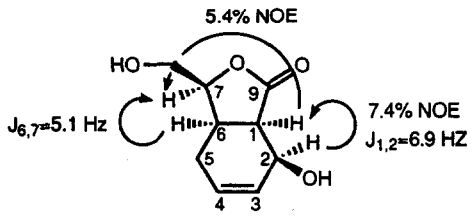


Fig 2. NOE between H_1/H_7 and H_2/H_1, and significant ^1H-^1H J's in compound **39**.

The (E)-enoate **2** underwent cycloaddition to the title diene in dichloromethane at 14 kbar pressure and 50 °C for 65 h, affording a liquid containing the mixture of the four possible isomers **17**, **18**, **19**, and **20** in roughly equal proportion, without recovering of the starting material (Table I, entry 11). Since the four isomers could not be separated, their relative proportion was determined through integration of the signals as singlets at 3.45, 3.50, 3.55, and 3.60 ppm, corresponding to the four $\underline{Me}O_2C$ groups in the ^1H NMR spectrum of the mixture. Further purification was not possible owing to its unstability under the usual chromatographic conditions. Regiochemistry of the adducts was assigned assuming the preferred orientation of this diene to be similar to that observed in the cycloaddition to enoate **4** and to unsaturated lactones and ketones.[17b,c]

This last result is in agreement with the reported result for the thermal reaction between **2** and 1-methoxymethyloxy-3-trimethylsilyloxy-1,3-cyclohexadiene that afforded a mixture of the four possible syn/anti and endo/exo-diastereoisomers, but as a single regioisomer each. Reaction of **1** with this diene also gave a mixture of both (endo-syn/anti)-diastereoisomers,[21] showing no face diastereo-selection in contrast with

the high pressure induced reaction described above between **1** and the title diene.

Finally, pseudoester **3** reacted with 1-trimethylsilyloxy-1,3-butadiene under 12 kbar pressure at 40 °C for 70 h, giving a 50:50 mixture of adducts **28** and **29**, along with about 35% unreacted **3** (Table I, entry 12). Adducts could not be isolated, and their relative proportion was determined through integration of the absorptions of the methyl groups (1.73, 1.76, and 1.82 (product **3**) ppm) and of those of the methoxy groups (3.40 (product **3**), 3.50, and 3.55 ppm) in the ^{1}H NMR spectrum of the mixture. The Mass spectrum of the reaction crude showed peaks at m/e 271 (M + 1) and 270 (M) which confirmed the presence of adducts. Their structural assignment was tentatively made on the basis of the excellent regiospecificity exhibited by the diene in high pressure-induced reactions with related butenolides[17b,c] and with ester **1**. Moreover, it is known that the formation of an endo-adduct has a lower volume of activation at the transition state than the corresponding exo-isomer, and consequently the former product is favored under high-pressure conditions.[22] With these considerations in mind, and due to the scarce anti/syn diastereoselection observed in the cycloaddition of **3** to cyclopentadiene, the obtained adducts were identified as the (syn-endo)-isomer **28** and the (anti-endo)-isomer **29**.

II. η-Face Diastereoselection

(a) Acyclic Dienophiles.

The results listed in Table I show a better η-face diastereoselection in the cycloadditions involving the (Z)-enoate **1** than those involving **2** as dienophile.

Conformational enthalpies have been calculated by using the AM1 method and they are indicated in Figure 3. The position of the ester group with respect to the C-C double bond has been fixed to be s-cis,[23] and the rotation around the C_3-C_4 bond have been considered. In any reaction of **1** the major isomer was not produced via the active conformer **B**, in which the attack of the diene to the double bond would be directed along the trajectory anti to the neighbouring oxygen atom. Conversely, this attack on the Felkin-Anh active conformer **A** would be seriously hindered due to the steric congestion between the diene, C_5 and the ester group. Moreover, conformer **A** presents severe nonbonded interactions and an unfavorable dipole-dipole effect. The absolute energy minimum corresponds to the conformation represented by **C**, in which the C_2-C_3-C_4-O dihedral angle is

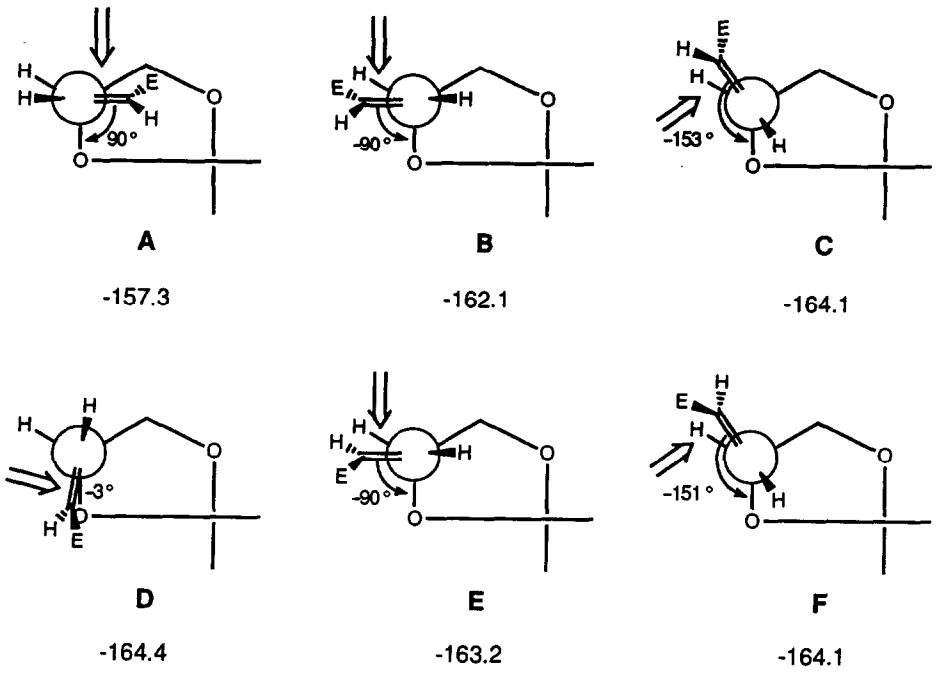


Fig 3. Heats of formation (kcal/mol) and dihedral angles for conformations **A–C** (ester **1**) and **D–F** (ester **2**).

-153° (Fig 3). The calculated enthalpy differences between **C** and the conformers **A** and **B** are H_A-H_C = 6.8 kcal/mol and H_B-H_C = 2.0 kcal/mol (Fig 5a). Actually, the formation of the major products **10**, **21/22** and **16** in the reactions between **1** and butadiene, cyclopentadiene and 1-trimethylsilyloxy-1,3-butadiene, respectively, can be predicted <u>via</u> the active conformer **C**. Similar conformers had been previously invoked to explain the stereochemical outcome of either (4+2)[14] or (3+2)[24] cycloadditions, but neither experimental nor theoretical quantitative data had been given.

The geometry of the possible transition states for the reaction between **1** and butadiene has been determined, showing that the conformational bias in the ground state is retained. Both conformers **A** and **C** lead to the same transition state, (1)-<u>syn</u>, with a dihedral angle equal to -169.7 ° (Fig 4a). The difference between the enthalpy barrier for this transition state and that associated with the antiperiplanar attack at conformer **B**, (1)-<u>anti</u>, has been estimated to be 2.9 kcal/mol (Fig 5a), thus explaining the distribution of the isomeric adducts obtained experimentally.

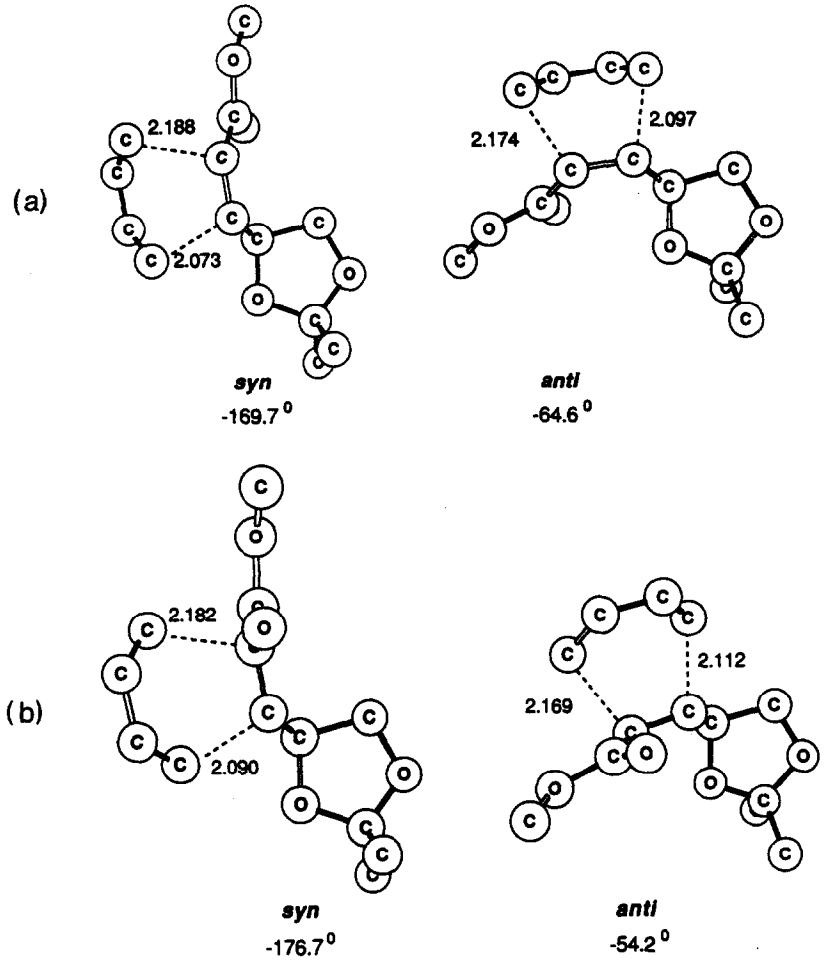


Fig 4. Transition states for the reactions between butadiene and: (a) ester 1, and (b) ester 2, leading to syn- and anti-adducts. Lenghts of the forming bonds (Å) and dihedral angles (see Fig 3 for their definition) are given.

In the case of ester 2, the Felkin-Anh conformation equivalent to **A** in the former case corresponds to the absolute energy maximum. Formation of syn-adducts can be explained considering the active conformer **F**, which is very similar to **C**, while anti-adducts can be produced either from **E** or **D**. This last conformer corresponds to the absolute energy minimum, being H_F-H_D = 0.3 kcal/mol, which is a value much smaller than the calculated differen-

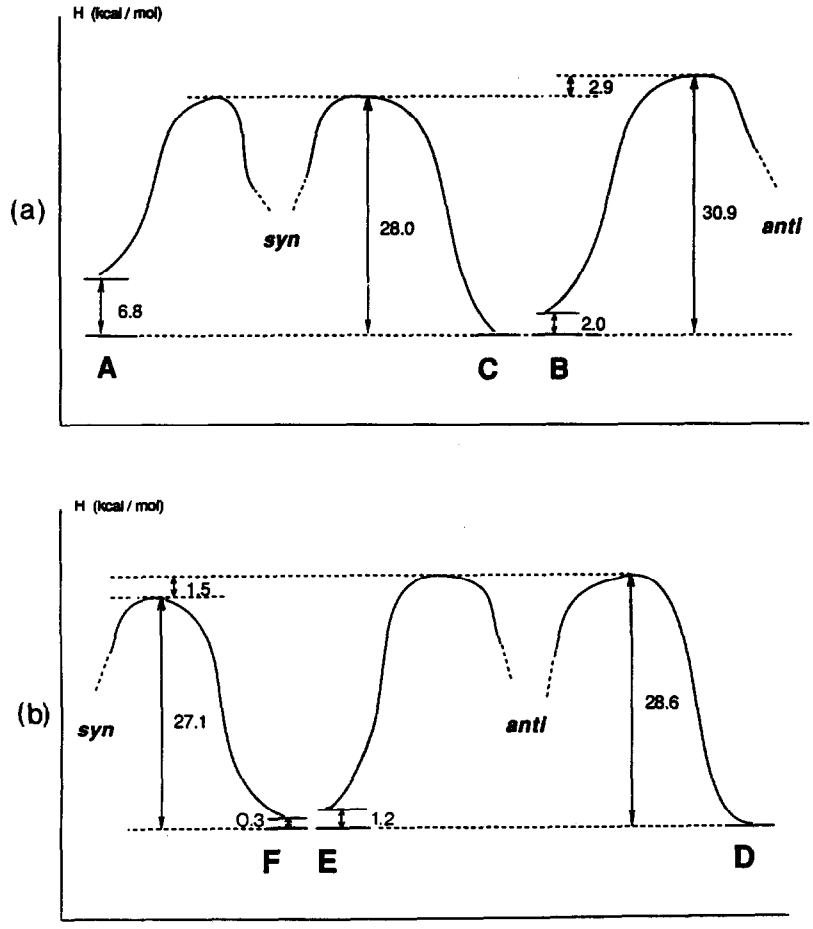


Fig 5. AM1 Computed enthalpy diagrams for the active conformers evaluated, and for the barriers involved in the reactions between butadiene and: (a) ester **1**, and (b) ester **2**. In both cases, the endo orientation of the diene is considered.

ce between **B** and **C** for compound **1**. Actually, the difference between enthalpy barriers for the formation of syn- and anti-adducts is only 1.5 kcal/mol (Fig 5). These low increment explains the slight diastereoselectivity observed in the (4+2) cycloadditions of **2**, in contrast with the behavior of the (Z)-isomer **1**. It is noticeable that the geometry of the lower transition state for **2** is closely related to the geometry of the lower transition state for **1**, and reproduces better the ground-state conformation **F** than the more stable conformation **D**.

Dannenberg and Frank have recently evaluated the effect of a noncyclic stereogenic center, located at the allylic position in chiral 1,3-pentadienes, on π-face selectivity in the Diels-Alder reactions with acyclic dienophiles.[25] These authors reported that no single effect seems to dominate the predicted selectivities. Rather, they appear to result from a combination of electronic and steric interactions. Moreover, they concluded that the conformations of the ground states of the reactants do not always provide good indications of the eventual transition-state geometries. Consequently, predictions made regarding such conformations are not uniformely correct. The calculations in our work support and complement this statement. It is significant that Dannenberg's calculations and our results predict the same type of transition state for these Diels-Alder reactions even though one involves chiral dienes and one involves chiral dienophiles. The traditional Felkin-Ahn correlation of raising or lowering appropriate molecular orbitals via a particular conformation at the adjacent chiral center is not suitable for these cases.

(b) **Cyclic dienophiles.**

Conformational rotations are very restricted in cyclic pseudoester **3**, and this molecule can be considered as essentially rigid. Feringa has reported the facial selectivity in the Diels-Alder cycloadditions to pseudoester **4** (Chart I) to occur exclusively anti to the bulky menthyloxy substituent.[12] In our case, the volumes of the two substituents, methyl and methoxyl, are quite similar.[26,27] Experimental results from the reactions of **3** with cyclopentadiene and 1-trimethylsilyloxy-1,3-butadiene show a π-face distereoselection much lower than that observed in the Diels-Alder cycloadditions of other cyclic chiral dienophiles, such as monosubstituted pseudoesters[12] and butenolides.[5,17] On the other hand, our results point out a predominant role of the methyl group in directing the most favorable attack of the diene. Theoretical predictions are also in accordance with these findings, as can be deduced from the data in Table II.[28,29] In the reaction of **3** with cyclopentadiene the difference between the computed enthalpy barriers for the endo-stereoisomers through a syn- or an anti-MeO attack is 4.3 kcal/mol. This difference is only 1.5 kcal/mol for exo-stereoisomers, in very good agreement with the experimental isomer distribution shown in Table I (compare the ratios **30:31** =2 and **33:32**=1.4 in entry 7). A similar face diastereoselection was theoretically predicted for the reaction of **3** and butadiene, but in this case experimental results cannot corroborate this predicition due to the side-reaction mentioned

Table II. AM1 calculated enthalpy barriers and lenghts of the forming bonds at the transition state, for the reactions of 3 with butadiene and cyclopentadiene.

Diene	endo/exo orientation	syn-face orientation	$\Delta H^{\#a}$	r_1[b]	r_2[b]
Butadiene	endo	Me	27.1	2.141	2.177
		MeO	26.1	2.124	2.185
	exo	Me	26.0	2.143	2.160
		MeO	23.5	2.141	2.160
Cyclopen-tadiene	endo	Me	36.5	2.127	2.142
		MeO	32.2	2.100	2.167
	exo	Me	33.7	2.124	2.143
		MeO	32.2	2.104	2.164

[a] kcal/mol. [b] Distance (Å) involving C_4 (r_1) and C_3 (r_2) in compound 3 (see Chart I).

above, which led to the obtention of monocyclic adducts. Then, it seems clear that steric hindrance owing to the methyl group dominates over the possible disfavorable non-bonding interactions due to the methoxyl group, which would orient the anti-alkoxy diastereoselection.

CONCLUSIONS

We have investigated the facial selectivity in Diels-Alder cycloadditions involving representative acyclic and cyclic dienophiles with allylic stereogenic centers containing oxygen functionalities. The results obtained can be rationalized on the basis of the influence that both steric and electronic factors exert on the orientation of the dienophile-diastereotopic face offered to the attacking diene. The Felkin-Anh model is not of general application for the cycloadditions to chiral acyclic dienophiles. In these cases, steric repulsions and dipole-dipole effects play an important role in determining the transition-state geometries and energies. For rigid cyclic dienophiles, our results show that steric

effects are at least as important as secondary orbital interactions.

Fifteen new mono-, bi-, and tricyclic polyfunctionalized compounds have been synthesized in the course of this work. These products are important chiral synthetic building blocks whose applications are being explored in our laboratory.

EXPERIMENTAL SECTION

Melting points were determined on a hot stage and are uncorrected. Distillation of small amounts was effected in a bulb-to-bulb distillation apparatus; only the oven temperatures (ot) are given. Electron-impact mass spectra were recorded at 70 eV.

General Procedures for Thermal Diels-Alder Cycloadditions. A mixture of the dienophile (6-47 mmol) and the diene (15 mL, 25 equiv of butadiene; 5-36 mL, 10 equiv of cyclopentadiene) was introduced into a glass reactor fitted with a teflon stopper, and heated in an oil bath (see Table I for the particular reaction temperature and time conditions). The reaction mixture was cooled, diluted with CH_2Cl_2 and filtered to remove polymeric materials. The solvent and excess diene were evaporated under reduced pressure. The residue was chromatographed on silica gel (mixtures of hexane-ethyl acetate as eluents) to afford the corresponding adducts. The relative proportions of stereoisomers were determined by means of capillary GLC and ^1H NMR analysis.

General Procedures for High Pressure-Induced Cycloadditions. The particular conditions for each reaction are given in Table I. The dienophile (1.2-2.7 mmol) and 1.5 equiv of the diene (2.5 M solution of diene in CH_2Cl_2) were introduced, by means of a syringe, into a 1- or 3-mL pyrex glass cells (1.5-mm wall-thickness) fitted with a 1 mm inner diameter capillary orifice. All reactions were performed in a piston-cylinder high pressure apparatus for pressures up to 20 kbar. Cells were immersed into hexane, used as piezotransmitter liquid which was contained in the high pressure apparatus, closed on the bottom side with a steel stopper. Then the mobile piston was inserted and the whole assembly was placed between the pistons of a hydraulic press. The pressure was raised depending on the reaction conditions used in each case, and the reaction mixture was kept under these conditions for the convenient time. After decompression the solvent was removed and the residue analyzed using NMR techniques.

General Procedure for Acid Hydrolysis of Adducts. A 0.1-0.3 M solution of adduct in methanol, containing some drops of HCl or H_2SO_4, was stirred at rt. The progress of the reaction was monitored by TLC until dissapearence of the starting material. The solvent was removed at reduced pressure and the residue was purified by column chromatography on silica gel using mixtures of hexane-ethyl acetate as eluents.

Base-Induced Epimerization of Ester 21 to Ester 25. A 1.6 M solution of sodium methoxide in methanol (28 mL, 45 mmol) was added to a stirred solution of **21** (4.4 g, 17.6 mmol) in 130 mL of methanol. The mixture was stirred at room temperature for 72 h. Then, the solvent was evaporated and the residue was poured into dichloromethane. The solution was washed successively with saturated aqueous ammonium chloride until pH<7. The organic layer was dried and the solvent was removed. The reaction crude was chromatographed on silica gel (9:1 hexane-ethyl acetate as eluent) to afford ester **25** (88% yield), which was identical to the major isomer obtained in the reaction between pentenoate **2** and cyclopentadiene.

General Procedures for Theoretical Calculations. The AM1[30] method was used in the energy calculations. Total geometry optimization was performed throughout. Transition states were directly located through minimization of the root mean square gradient and have been characterized through the computation of the force constant matrix.[31] For a transition state this

matrix must have only one negative eigenvalue. Calculations of the conformational energies have been performed considering the rotation around the C_3-C_4 bond (see Chart I for numeration), and fixing the relative position of the ester group respect to the double C-C_3 bond to be s-cis. All calculations were carried out with the AMPAC program.[32]

Methyl (1S,2R)-2-[(4S)-4-(2,2-dimethyl-1,3-dioxolo)]-4-cyclohexen-1-ylcarboxylate (10). Yield: 0.94 g (58%); ot 75 °C (0.1 Torr); $(\alpha)_D$ +33.1 ° (c=4.25, $CHCl_3$); IR (film) 1736 cm^{-1}; MS, m/e (%) 241 (M +1, 1.7), 183 (22.8), 151 (17.3), 105 (39.8), 91 (21.4), 79 (51.4), 43 (100); 400-MHz ^1H NMR ($CDCl_3$) δ 1.36 (3 H, s), 1.39 (3 H, s), 2.00-2.50 (5 H, complex absorption), 2.70 (1 H, m), 3.58 (1 H, m), 3.68 (3 H, s), 4.10 (2 H, m), 5.70 (2 H, m); 20-MHz ^{13}C NMR ($CDCl_3$) δ 25.73, 26.52, 26.60, 26.76, 39.22, 39.89, 51.31, 68.02, 77.09, 108.48, 124.10, 126.02, 174.06. Anal. Calcd for $C_{13}H_{20}O_4$: C, 65.05; H, 8.33. Found: C, 65.20; H, 8.46.

Mixture of methyl (1R,2R)- and methyl (1S,2S)-2-[(4S)-4-(2,2-dimethyl-1,3-dioxolo)]-4-cyclohexen-1-ylcarboxylate (12) and (13). Yield: 1.34 g (92%); ot 75 °C (0.1 Torr); MS, m/e (%) 241 (M+1, 0.6), 225 (10.1), 182 (11.1), 105 (30.1), 79 (59.5), 43 (100); 80-MHz ^1H NMR ($CDCl_3$) δ 1.3 (3H, s), 1.4 (3 H, s), 1.8-2.7 (6 H, complex absorption), 3.5-4.2 (6 H, complex absorption), 5.7 (2 H, m). Anal. Calcd for $C_{13}H_{20}O_4$: C, 65.05; H, 8.33. Found: C, 65.17; H, 8.37.

Methyl (1R*,2S*)-2-acetyl-4-cyclohexen-1-ylcarboxylate (14).[19] Yield: 0.36 g (50%). Previously undescribed spectra follow. 400-MHz ^1H NMR ($CDCl_3$) δ 1.90-2.01 (1 H, m), 2.05-2.14 (1 H, m), 2.21 (3 H, s), 2.33-2.45 (2 H, complex absorption), 2.83 (1 H, ddd, J=J'=11 Hz, J''=5 Hz), 2.97 (1 H, ddd, J=J'=11 Hz, J''=5 Hz), 3.64 (3 H, s), 5.68 (complex absorption, 2 H); 100-MHz ^{13}C NMR ($CDCl_3$) δ 27.30, 27.84, 28.65, 40.53, 47.81, 51.45, 124.57, 124.95, 175.35, 210.53.

Methyl (1R*,2R*)-2-acetyl-4-cyclohexen-1-ylcarboxylate (15).[19] Yield: 0.02 g (7%). Previously undescribed spectra follow. 400-MHz ^1H NMR ($CDCl_3$) δ 2.11 (3 H, s), 2.33-2.64 (4 H, complex absorption), 2.89 (1 H, m), 3.07 (1 H, m), 3.65 (3 H, s), 5.67 (2 H, complex absorption); 100-MHz ^{13}C NMR ($CDCl_3$) δ 25.30, 26.20, 27.64, 39.34, 47.21, 51.69, 124.60, 125.62, 174.46, 208.71.

Methyl (1R,2R,6S)-2-[(4S)-4-(2,2-dimethyl-1,3-dioxolo)]-6-trimethylsilyloxy-4-cyclohexen-1-ylcarboxylate (16). Yield: 0.86 g (98%); ot 140 °C (0.3 Torr); mp 58-60 °C; $(\alpha)_D$ -64.5 ° (c=0.93, $CHCl_3$); IR (KBr) 1735 cm^{-1}; MS, m/e (%) 329 (M+1, 0.5), 313 (1.2), 101 (36.4), 59 (30.4), 43 (100); 400-MHz ^1H NMR ($CDCl_3$) δ 0.15 (9 H, m), 1.28 (3 H, s), 1.37 (3 H, s), 2.00-2.40 (3 H, complex absorption), 4.77 (1 H, dd, J=6.4 Hz, J'=3.6 Hz), 3.50-3.70 (4 H, complex absorption), 4.87 (1 H, m), 4.07 (1 H, dd, J=7.6 Hz, J'=6.0 Hz), 4.48 (1 H, m), 5.50 (1 H, m), 5.80 (1 H, m); 20-MHz ^{13}C NMR ($CDCl_3$) δ 25.74, 25.82, 26.81, 38.74, 47.47, 51.06, 67.85, 67.94, 78.05, 108.91, 127.89, 128.45, 171.17. Anal. Calcd. for $C_{16}H_{28}O_5Si$: C, 58.71; H, 8,31. Found: C, 58.71; H, 8.42.

Methyl (1R,2S,3R,4S)-3-[(4S)-4-(2,2-dimethyl-1,3-dioxolo)]bicyclo-(2.2.1)-5-hepten-2-ylcarboxylate (21).[14] Yield: 8.71 g (73%); ot 90 °C (0.2 Torr); $(\alpha)_D$ +28.3 ° (c=10.85, $CHCl_3$) (Lit.[14] $(\alpha)_D$ +20.4 ° (c=6.66, $CHCl_3$)); 400-MHz ^1H NMR ($CDCl_3$) δ 1.50-1.20 (2 H, complex absorption), 1.28 (3 H, s), 1.43 (3 H, s), 2.49 (1 H, ddd, J=10 Hz, J'=J''=3.1 Hz), 3.02 (1 H, dd, J=10.0 Hz, J'=3.0 Hz), 3.10 (1 H, br s), 3.13 (1 H, br s), 3.59 (3 H, s), 3.80 (1 H, m), 3.63 (1 H, dd, J=8.0 Hz, J'=4.9 Hz), 3.92 (1 H, dd, J=8.0 Hz, J'=5.9 Hz), 6.22 (1 H, dd, J=5.5 Hz, J'=2.8 Hz), 6.26 (1 H, dd, J=5.5 Hz, J'=2.8 Hz). IR, MS and ^{13}C NMR spectra are in good agreement with those

previously described for this compound.[14] Anal. Calcd. for $C_{14}H_{20}O_4$: C, 66.65; H, 7.99. Found: C, 66.21; H, 8.19.

Methyl (1S,2S,3R,4R)-3-[(4S)-4-(2,2-dimethyl-1,3-dioxolo)]bicyclo-(2.2.1)-5-hepten-2-ylcarboxylate (22).[14] Yield: 1.78 g (14%); ot 90 °C (0.2 Torr); $(\alpha)_D$ +65.84 ° (c=12.1, $CHCl_3$) (Lit.[14] $(\alpha)_D$ +65.90 (c=6.66, $CHCl_3$); MS, m/e (%) 253 (M+1, 2.2), 237 (11.1), 194 (17.7), 186 (6.8), 11 (21.6), 97 (18.3), 66 (78), 43 (100); 400-MHz ^1H NMR ($CDCl_3$) δ 1.20-1.60 (2 H, complex absorption), 1.32 (3 H, s), 1.40 (3 H, s), 1.81 (1 H, ddd, J=J'=9.0 Hz, J''=1.6 Hz), 2.02 (1 H, d, J=8.8 Hz), 2.30 (1 H, dd, J=8.8 Hz, J'=1.7 Hz), 2.95 (1 H, br s), 3.06 (1 H, br s), 3.66 (3 H, s), 3.56 (1 H, dd, J=7.9 Hz, J'=6.0 Hz), 3.87 (1 H, dd, J=7.9, J' 6.0 Hz), 4.10 (1 H, ddd, J=10 Hz, J'=J''=6.4 Hz), 6.12 (1 H, dd, J=5.5 Hz, J'=3.1 Hz), 6.26 (1 H, dd, J=5.5 Hz, J'=3.0 Hz). IR and ^{13}C NMR spectra are in good agreement with those previously described for this compound.[14] Anal. Calcd. for $C_{14}H_{20}O_4$: C, 66.65; H, 7.99. Found: C, 66.21; H, 8.19.

Methyl (1S,2R,3S,4R)-3-[(4S)-4-(2,2-dimethyl-1,3-dioxolo)]bicyclo-(2.2.1)-5-hepten-2-ylcarboxylate (23). Yield: 0.75 g (6%); ot 90 °C (0.2 Torr); $(\alpha)_D$ -55.9 ° (c=12.9, $CHCl_3$); IR (film) 1738 cm^{-1}; MS, m/e (%) 253 (M+1, 2.2), 237 (11.1), 194 (17.7), 186 (6.8), 11 (21.6), 97 (18.3), 66 (78.0), 43 (100); 400-MHz ^1H NMR ($CDCl_3$) δ 1.23 (3 H, s), 1.36 (3 H, s), 1.10-1.50 (2 H, complex absorption), 2.55 (1 H, ddd, J=10.0 Hz, J'=J''=3.0 Hz), 2.70 (1 H, broad s), 3.07 (1 H, br s), 3.14 (1 H, dd, J=10.0 Hz, J'=3.0 Hz), 3.54 (1 H, dd, J=J'=6.0 Hz), 3.60 (3 H, s), 3.76 (1 H, m), 3.95 (1 H, dd, J=6.0 Hz, J'=5.0 Hz), 6.06 (1 H, dd, J=5.6 Hz, J'=3.0 Hz), 6.32 (1 H, dd, J=5.6 Hz, J'=3.0 Hz); 20-MHz ^{13}C NMR ($CDCl_3$) δ 25.55, 26.93, 45.39, 45.58, 46.48, 48.69, 49.91, 50.95, 68.60, 76.54, 108.37, 132.57, 136.44, 173.58. Anal. Calcd. for $C_{14}H_{20}O_4$: C, 66.65; H, 7.99. Found: C, 66.72; H, 8.11.

Methyl (1S,2R,3R,4R)-3-[(4S)-4-(2,2-dimethyl-1,3-dioxolo)]bicyclo-(2.2.1)-5-hepten-2-ylcarboxylate (24).[14] Yield: 0.34 g (27%); some contamination with isomer 25 did not allow $(\alpha)_D$ determination; previously undescribed spectrum follows. MS, m/e (%) 253 (M+1, 2), 237 (17), 187 (12), 117 (33), 66 (100), 59 (16), 43 (43); 80-MHz ^1H NMR ($CDCl_3$) δ 1.3 (3 H, s), 1.4 (3 H, s), 1.5-2.0 (3 H, complex absorption), 2.4 (1 H, dd, J=J'=4.5 Hz), 3.0 (1 H, m), 3.2 (1 H, m), 3.7 (3 H, s), 3.7-4.2 (3 H, complex absorption), 6.1 (dd, J=6 Hz, J'=3 Hz), 6.3 (dd, J=6 Hz, J'=3 Hz).

Methyl (1R,2R,3R,4S)-3-[(4S)-4-(2,2-dimethyl-1,3-dioxolo)]bicyclo-(2.2.1)-5-hepten-2-ylcarboxylate (25). Yield: 1.16 g (58%); ot 65 °C (0.8 Torr); $(\alpha)_D$ -70.4 ° (c=3.6, $CHCl_3$); IR (film) 1733 cm^{-1}; MS, m/e (%) 252 (M, 1), 237 (32), 117 (78), 66 (100), 43 (76); 400-MHz ^1H NMR ($CDCl_3$) δ 1.30 (3 H, s), 1.40 (3 H, s), 1.46 (1 H, dd, J= 8.72 Hz, J'=1.60 Hz), 1.61 (1 H, d, J=8.72 Hz), 1.64 (1 H, dd, J=5.02 Hz, J'=1.62 Hz), 2.39 (1 H, ddd, J=8.50 Hz, J'=5.02 Hz, J''=3.44 Hz), 3.00 (1 H, m), 3.06 (1 H, m), 3.48 (1 H, ddd, J=8.50 Hz, J'=6.88 Hz, J''=5.84 Hz), 3.64 (1 H, dd, J=8.04 Hz, J'=7.04 Hz), 3.68 (3 H, s), 3.91 (1 H, dd, J=8.04, J'= 5.84 Hz), 6.18 (2 H, m); 20-MHz ^{13}C NMR ($CDCl_3$) δ 25.73, 26,91, 44.49, 46.30, 47.06, 48.18, 51.75, 68.47, 79.15, 108.81, 135.92, 136.39, 175.36. Anal. Calcd. for $C_{14}H_{20}O_4$: C, 66.65; H, 7.99. Found: C, 66.75; H, 7.96.

(1R*,2S*,5R*,6S*,7S*)-5-Methyl-5-methoxy-4-oxatricyclo(5.2.1.$0^{2,6}$)-8-decen-3-one (30). Yield: 0.11 g (26%); ot 55 °C (0.1 Torr); IR (film) 1766 cm^{-1}; MS (CI, NH_3) m/e (%) 195 (M+1, 41), 212 (M+18, 100), 229 (M+35, 11); 400-MHz ^1H NMR (acetone-d_6) δ 1.39-1.67 (2 H, complex absorption), 1.57 (3 H, s), 3.02-3.11 (2 H, complex absorption), 3.16 (1 H, m), 3.36 (3 H, s), 3.51 (1 H, dd, J=8.42 Hz, J'=4.98 Hz), 6.00 (1 H, dd, J=5.72 Hz, J'=2.81 Hz), 6.22 (1 H, dd, J=5.72 Hz, J'=1.94 Hz); 100-MHz ^{13}C NMR (acetone-d_6) δ 25.60, 45.70, 46.03, 50.27, 51.27, 51.80, 52.48, 108.42, 133.32, 137.57,

174.90. Anal. Calcd. for $C_{11}H_{14}O_3$: C, 68.02; H, 7.26. Found: C, 68.03; H, 7.19.

(1R*,2S*,5R*,6S*,7R*)-5-Methyl-5-methoxy-4-oxatricyclo(5.2.1.$0^{2,6}$)-8-decen-3-one (31). Yield: 0.05 g (15%); mp 56–57 °C (hexane-ethyl acetate); IR (KBr) 1771 cm^{-1}; MS (CI, NH_3), m/e (%) 195 (M+1, 18), 212 (M+18, 100), 229 (M+35, 1); 400-MHz ^1H NMR (acetone-d_6) δ 1.42 (3 H, s), 1.48 (1 H, ddd, J=J'=8.32 Hz, J''=1.54 Hz), 1.55 (1H, ddd, J=J'=8.32 Hz, J''=1.74 Hz), 2.94 (1 H, dd, J=8.56 Hz, J'=3.89 Hz), 3.10–3.17 (2 H, complex absorption), 3.23 (3H, s), 3.40 (1 H, dd, J=8.57 Hz, J'=5.04 Hz), 6.12 (1 H, dd, J=5.78 Hz, J'=3.03 Hz), 6.25 (1 H, ddd, J=5.78, J'=2.81, J''=0.80 Hz); 100-MHz ^{13}C NMR (acetone-d_6) δ 19.25, 45.35, 45.85, 48.74, 49.28, 52.03, 53.16, 108.66, 135.14, 136.79, 176.97. Anal. Calcd. for $C_{11}H_{14}O_3$: C, 68.02; H, 7.26. Found: C, 68.11; H, 7.39.

(1R*,2R*,5S*,6S*7R*)-5-Methyl-5-methoxy-4-oxatricyclo(5.2.1.$0^{2,6}$)-8-decen-3-one (32). Yield: 0.03 g (8%); ot 100 °C (0.8 Torr); IR (CCl_4) 1729 cm^{-1}; MS (CI, NH_3), m/e (%) 195 (M+1, 47), 212 (M+18, 100), 229 (M+35, 9); 400-MHz ^1H NMR (acetone-d_6) δ 1.35–1.47 (2 H, complex absorption), 2.31 (1 H, d, J=7.66 Hz), 2.81 (1 H, d, J=7.14 Hz), 3.12 (1 H, m), 3.16 (1 H, m), 3.33 (3 H, s), 6.25–6.36 (2 H, complex absorption); 100-MHz ^{13}C NMR (acetone-d_6) δ 18.8, 44.0, 44.8, 46.9, 49.5, 49.6, 52.4, 109.2, 138.4, 130.5, 176.7. Anal. Calcd. for $C_{11}H_{14}O_3$: C, 68.02; H, 7.26. Found: C, 68.07; H, 7.30.

(1R*,2R*,5S*,6S*,7S*)-5-Methyl-5-methoxy-4-oxatricyclo(5.2.1.$0^{2,6}$)-8-decen-3-one (33). Yield: 0.06 g (16%); ot 100 °C (0.8 Torr); IR (CCl_4) 1773 cm^{-1}; EM (CI, NH_3) 195 (M+1, 41), 212 (M+18, 100), 229 (M+35, 10); 400-MHz ^1H NMR (acetone-d_6) δ 1.32–1.50 (2 H, complex absorption), 2.32 (1 H, d, J=8.25 Hz), 2.81 (1 H, d, J=8.15 Hz), 3.12 (1 H, m), 3.18 (1 H, m), 3.41 (3 H, s), 6.19–6.25 (2 H, complex absorption); 100-MHz ^{13}C NMR (acetone-d_6) δ 25.27, 44.50, 45.60, 46.51, 50.92, 51.46, 53.01, 108.33, 138.79, 139.75, 175.15. Anal. Calcd. for $C_{11}H_{14}O_3$: C, 68.02; H, 7.26. Found: C, 68.07; H, 7.30.

(1S,6R,7S)-7-Hydroxymethyl-8-oxabicyclo(4.3.0)-3-nonen-9-one (34). Yield: 0.17 g (99%); mp 66–67 °C (hexane-ethyl acetate); $(\alpha)_D$ -75.21 ° (c=1.63, $CHCl_3$); IR (KBr) 3650–3100 (br), 1765 cm^{-1}; MS, m/e (%) 169 (M+1, 2.6), 168 (M, 1.3), 91 (29.3), 80 (19.2), 79 (100.0), 51 (22.6); 400-MHz ^1H NMR ($CDCl_3$) δ 1.55 (1 H, br s), 1.70–2.09 (2 H, complex absorption), 2.38 (1 H, m), 2.50–2.62 (2 H, complex absorption), 2.89 (1 H, m), 3.80 (1 H, d, J=10.8 Hz), 3.95 (1 H, dd, J=12 Hz, J'=7.6 Hz), 4.54 (1 H, dt, J=8.0 Hz, J'=4.4 Hz), 5.70 (2 H, br s); 20-MHz ($CDCl_3$) δ 19.69, 21.81, 34.17, 39.37, 61.31, 82.45, 124.27, 125.27, 178.16. Anal. Calcd. for $C_9H_{12}O_3$: C, 64.27; H, 7.19. Found: C, 64.28; H, 7.08.

(1S,2S,5S,6R,7R)-5-Hydroxymethyl-4-oxatricyclo(5.2.1.$0^{2,6}$)-8-decen-3-one (35). Yield: 0.31 g (85%); mp 164–165 °C; $(\alpha)_D$ +116.5 ° (c=1.03, MeOH); IR (KBr) 3700–3100 (br), 1730 cm^{-1}; MS, m/e (%) 181 (M+1, 1.8), 180 (M, 1.1), 149 (14.8), 115 (43.1), 91 (50.1), 66 (100); 400-MHz ^1H NMR (acetone-d_6) δ 1.32 (1 H, d, J=8.0 Hz), 1.43 (1 H, d, J=8.0 Hz), 2.48 (1 H, ddd, J=J'=9.0 Hz, J''=1.0 Hz), 2.70 (1 H, d, J=7.5 Hz), 3.04 (1 H, m), 3.12 (1 H, m), 3.76 (1 H, dd, J=11.0 Hz, J'=6.0 Hz), 3.82 (1 H, dd, J=11.0 Hz, J'=7.0 Hz), 4.60 (1 H, m), 6.18 (2 H, m); ^{13}C NMR (acetone-d_6) δ 43.87, 44.29, 45.27, 47.00, 49.44, 61.55, 81.32, 138.28, 140.05, 177.24. Anal. Calcd. for $C_{10}H_{12}O_3$: C, 66.66; H, 6.66. Found: C, 66.74; H, 6.71.

(1R,2S,5S,6R,7S)-5-Hydroxymethyl-4-oxatricyclo(5.2.1.$0^{2,6}$)-8-decen-3-one (36). Yield: 1.32 g (77%); ot 180 °C (0.4 Torr); $(\alpha)_D$ +157 ° (c=3.32, $CHCl_3$); IR (film) 3700–3000 (br), 1754 cm^{-1}; MS, m/e (%) 181 (M+1, 1.31), 91 (34.4), 66 (100.0), 65 (34.3); 400-MHz ^1H NMR ($CDCl_3$) δ 1.46 (1 H, d,

J=8.5 Hz), 1.68 (1 H, dt, J=8.5 Hz, J'=1.6 Hz), 1.80 (1 H, broad s), 3.05-3.15 (2 H, complex absorption), 3.30 (1 H, m), 3.45 (1 H, dd, J=8.9 Hz, J'=4.9 Hz), 3.75 (1 H, dd, J=11.7 Hz, J'=4.1 Hz), 3.87 (1 H, dd, J=11.7 Hz, J'=8.0 Hz), 4.65 (1 H, m), 6.15 (1 H, dd, J=5.7 Hz, J'=2.0 Hz), 6.25 (1 H, dd, J=5.7 Hz, J'=2.9 Hz); 20-MHz ^{13}C NMR ($CDCl_3$) δ 42.42, 44.41, 44.64, 47.90, 53.03, 62.14, 82.14, 134.96, 135.69, 177.63. Anal. Calcd. for $C_{10}H_{12}O_3$: C, 66.66; H, 6.66. Found: C, 66.63; H, 6.70.

(1R,2S,5S,6R,7S)-5-p-Toluenesulfonyloxymethyl-4-oxatricyclo-(5.2.1.0^{2,6})-8-decen-3-one (37). Yield: 0.67 mg, (80%); m.p. 109-110 °C (hexane-chloroform); $(\alpha)_D$ +87.01° (c=1.65, $CHCl_3$); IR (KBr) 1773, 1755 cm^{-1}; MS, m/e (%) 335 (M+1, 1), 97 (71), 91 (39), 66 (100); 400-MHz ^{1}H NMR ($CDCl_3$) δ 1.43 (1 H, d, J=8.6 Hz), 1.64 (1 H, dt, J=8.6 Hz, J'=1.6 Hz), 3.09-3.15 (2 H, complex absorption), 3.29 (1 H, m), 3.40 (1 H, dd, J=9.0 Hz, J'=4.9 Hz), 4.11 (1 H, dd, J=10.5 Hz, J'=7.2 Hz), 4.18 (1 H, dd, J=10.5 Hz, J'=5.5 Hz), 4.66 (1 H, m), 5.98 (1 H, dd, J=5.9 Hz, J'=2.8 Hz), 6.20 (1 H, dd, J=5.7 Hz, J'=3.0 Hz), 7.38 (2 H, d, J=8.3 Hz), 7.81 (2 H, d, J=8.3 Hz); 100-MHz ^{13}C NMR ($CDCl_3$) δ 21.65, 42.71, 44.58, 44.99, 47.75, 53.26, 67.90, 127.96, 130.00, 132.30, 136.83, 145.38, 176.26. Anal. Calcd. for $C_{17}H_{18}O_5S$: C, 61.08; H, 5.39; S, 9.58. Found: C, 60.97; H, 5.47; S, 9.65.

(1R,2S,6S,7R,8S)-6-Hydroxy-4-oxatricyclo(6.2.1.0^{2,7})-9-decen-3-one (38). Yield: 0.39 g (23%); mp 128-130 °C (hexane-chloroform); $(\alpha)_D$ +103.2° (c=1.57, $CHCl_3$); IR (KBr) 3600-3100 (br), 1705 cm^{-1}; MS, m/e (%) 181 (M+1, 2.9), 115 (35.5), 77 (12.6), 66 (100.0), 55 (12.1); 400-MHz ^{1}H NMR ($CDCl_3$) δ 1.38 (1 H, d, J= 8.7 Hz), 1.60 (1 H, dt, J=8.7 Hz, J'=1.9 Hz), 2.2 (1 H, br s), 2.54 (1 H, ddd, J=10.7 Hz, J'=9.3 Hz, J''=3.4 Hz), 3.12 (1 H, dd, J=10.7 Hz, J'=3.9 Hz), 3.18 (1 H, m), 3.35-3.42 (2 H, complex absorption), 3.96 (1 H, dd, J=J'=10.3 Hz), 4.10 (1 H, dd, J=10.4 Hz, J'=4.2 Hz), 6.18 (1 H, dd, J=5.7 Hz, J'=3.0 Hz), 6.33 (1 H, dd, J=5.7 Hz, J'=2.9 Hz); 20-MHz ^{13}C NMR ($CDCl_3$) δ 43.06, 43.61, 45.53, 46.96, 48.20, 67.26, 70.42, 135.48, 137.82, 173.90. Anal. Calcd. for $C_{10}H_{12}O_3$: C, 66.66; H, 6.66. Found: C, 66.59; H, 6.62.

(1R,2S,6R,7S)-2-Hydroxy-7-hydroxymethyl-8-oxabicyclo(4.3.0)-3-nonen-9-one (39). Yield: 0.12 g (80%); mp 97-99 °C; $(\alpha)_D$ +15.8 ° (c=0.93, MeOH); IR (KBr) 3340, 3249 (br), 1765 cm^{-1}; MS, m/e (%) 167 ((M+1)-18, 10), 115 (24), 81 (39), 79 (100), 77 (44), 69 (77), 43 (40), 41 (74); 400-MHz ^{1}H NMR (acetone-d_6) δ 2.00-2.20 (2 H, complex absorption), 3.02 (1 H, m), 3.27 (1 H, t, J=J'=6.9 Hz), 3.77 (1 H, ddd, J=11.8 Hz, J'=6.1 Hz, J''=5.1 Hz), 3.85 (1 H, ddd, J= 11.8 Hz, J'=6.9 Hz, J''=5.2 Hz), 4.16 (1 H, dd, J=6.0 Hz, J'=5.2 Hz), 4.33 (1 H, d, J=10.1 Hz), 4.38 (1 H, m), 4.59 (1 H, ddd, J=6.9 Hz, J'=J''=5.1 Hz), 5.70-5.80 (2 H, complex absorption); 100-MHz ^{13}C NMR (acetone-d_6) δ 20.47, 35.93, 45.14, 61.29, 64.88, 84.11, 122.41, 132.34, 178.80. Anal. Calcd. for $C_9H_{12}O_4$: C, 58.69; H, 6.57. Found: C, 58.77; H, 6.67.

Acknowledgements. We are indebted to Prof. F. Fariña, Instituto de Química Orgánica, CSIC, Madrid, for a generous gift of pseudoester 3. R. C. and T. P. thank grants from MEC and UAB, respectively. Financial support from DGICYT, through the project PB88-0241 and "Acción Integrada Hispano-Francesa" (nº 21, 1990), is gratefully acknowledged.

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& This work was presented at the "Seventh European Symposium on Organic Chemistry, ESOC 7" held in Namur, Belgium, on July 15-19, 1991.

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