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DIELS-ALDER REACTION OF 4-BROMO-6-SPIROEPOXYCYCLOHEXA-2,4-DIENONE WITH ELECTRON-RICH AND NEUTRAL DIENOPHILES.

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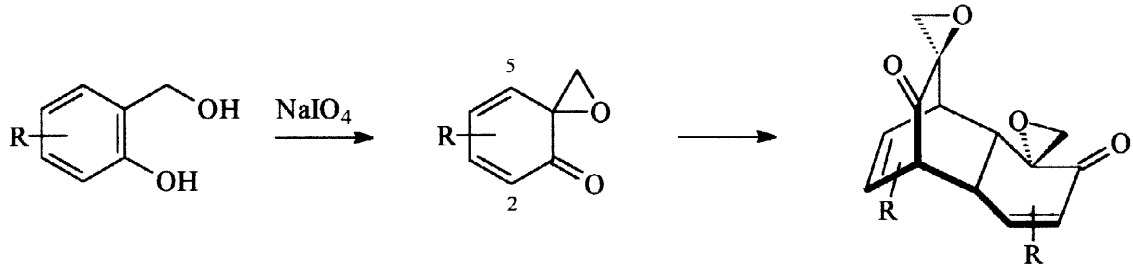
Abstract: Spirodienone **1**, prepared by Adler-Becker oxidation of 4-bromo-2-hydroxymethylphenol, undergoes [4+2] cycloaddition with various dienophiles (enol ethers, enol esters, styrenes, N-methylvinylacetamide) under thermal conditions (20-160°C). Three sets of experiments have been carried out, either with CH_2Cl_2 as solvent or neat with **1**, or under tandem oxidation-cycloaddition conditions with phase-transfer catalysis. Complete regio- and *syn* diastereofacial selectivities were obtained but a switch in *endo/exo* selectivity has been observed between enol ethers and styrenes (*endo* addition), enol esters (low selectivity) and an enamide (*exo* addition). The FMO analysis confirms that theses reactions are under $LUMO_{diene}$ control and that the observed regioselectivity is in agreement with orbital coefficients. Except for vinyl acetate, the formation of the major isomer is qualitatively confirmed at the AM1 level.

Introduction

6-Spiroepoxycyclohexadienones are easily obtained by Adler-Becker oxidation ($NaIO_4$) of salicyl alcohols[1]. However, dimerization usually occurs at room temperature, through a selective *syn-endo* Diels-Alder reaction which may be suppressed by bulky substituents such as *t*-Bu at C-2 and C-4[2] or methoxy at C-3[3] (Scheme 1).



Scheme 1

Some examples of cycloaddition of these dienones have previously been reported and only *syn-endo* adducts have been observed with maleic anhydride and some dienes (cyclopentadiene, dimethylfulvene,...)[4] as

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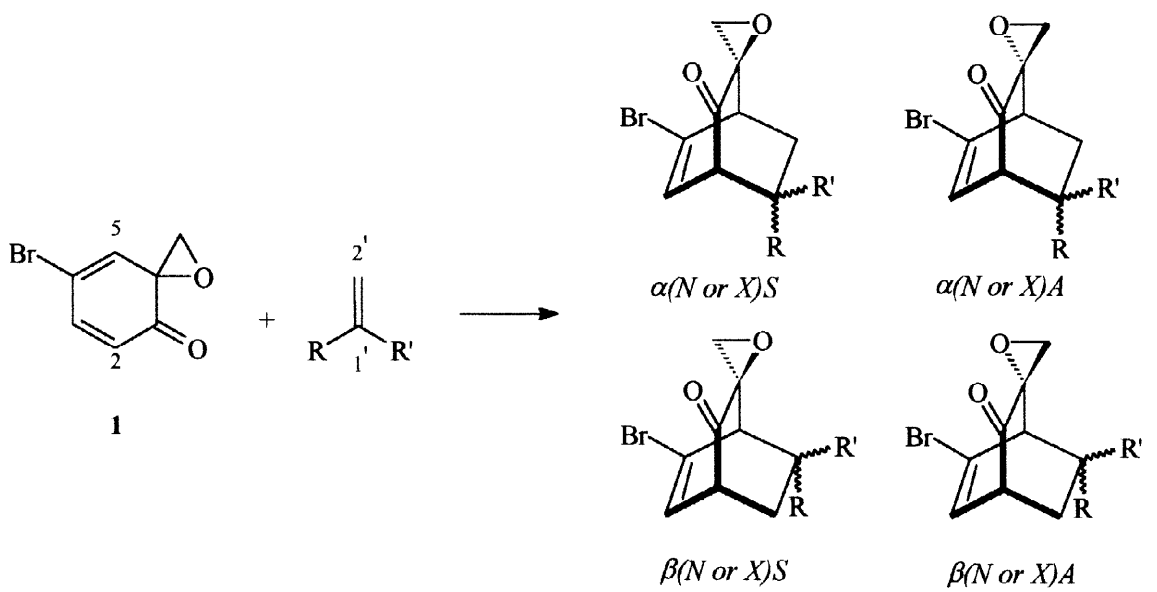
well as with methyl acetylenedicarboxylate (except in the case of a 4-*t*-Bu dienone leading to a mixture of *syn* and *anti* addition).[5] It is also worthy to note that related compounds such as quinols and quinol acetates exhibit the same selectivity with dienophiles,[6] including simple alkenes in intra[7] or intermolecular[8] processes.

The bicyclo[2,2,2] adducts thus obtained are potentially useful intermediates, after photochemically induced oxa-di-π methane rearrangement, toward cyclic natural products such as tricyclopentanoids.[9] Furthermore, cleavage of the α,β epoxyketone moiety should implement a short route to highly functionalized cyclohexane derivatives.[10]

It thus seems worthwhile to study the reactivity of such dienones toward electron rich (enol ethers, enol esters, enamides) and neutral (styrenes) dienophiles. The 4-bromo derivative **1** was selected because dimerization of this material is only observed above 60°C and for possible further transformation of the bromide substituent (reduction, Pd catalyzed alkylation). The eight possible adducts as well as the corresponding transition structures (TS's) will be subsequently referred to as *α* or *β* (depending on the regiochemistry), *N* or *X* (*endo* or *exo*) and *S* or *A* (*syn* or *anti*) (Scheme 2).



Scheme 2

Results and Discussion

Chemistry. Dienone **1** was obtained in 65% isolated yield by $NaIO_4$ oxidation of the corresponding phenol in MeOH at room temperature. Three sets of reaction conditions (A-C) have been studied: the dienone is used either neat (A) or in CH_2Cl_2 (B), or, according to the method introduced by Singh for the parent compound,[8b,c,9] generated *in situ* (tandem oxidation-cycloaddition) under phase-transfer conditions (C) (which consistently afforded better yields than the use of aqueous methanol). Selected results corresponding to the best

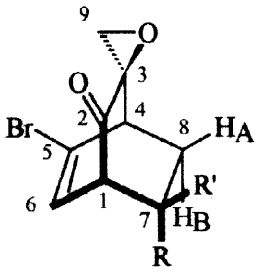
conditions for each dienophile are reported in Table 1. Cycloadditions were found to proceed with 5 equiv of dienophile under thermal conditions (20-160°C) in 54 to 88% yield depending on the dienophile. The phase transfer catalyzed tandem oxidation-cycloaddition (C) was preferred for enol ethers and styrenes. However, reactions with trimethylsilyl vinyl ether, 2,3-dihydrofuran and N-methyl vinyl acetamide gave higher yields under homogeneous conditions at room temperature (A), while enol ester cycloadditions were better carried out neat (B).

Table 1. Reaction of dienone 1 with selected dienophiles

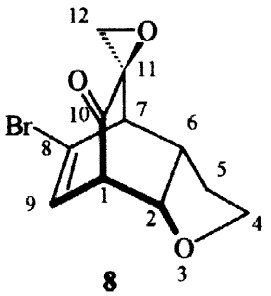
Dienophile	Conditions[a]	*αNS*	*αXS*	Ratio[b]	%[c]
X= OEt, Y= H	B, 120°C, 3 h	**2**	**3**	19:1	80[d]
	C, rt, 24 h	**2**	-	-	76
X=OMe, Y= Me	B, 120°C, 3 h	**4**	**5**	18:1	59[d]
	C, 60°C, 48 h	**4**	-	-	52
X= OTMS, Y= H	A, rt, 96 h	**6**	**7**	4.9:1	82
	B, 120°C, 5 h	**6**	**7**	2.2:1	64
2,3-dihydrofuran	A, 20°C, 72 h	**8**	**9**	3.9:1	68
	B, 160°C, 4 h	**8**	**9**	2.9:1	59
X= Ph, Y= H	B, 160°C, 1 h	**10**	**11**	5.4:1	63[d]
	C, rt, 24 h	**10**	**11**	8.8:1	88
X= Ph, Y= Me	B, 120°C, 0.3 h	**12**	**13**	24:1	76
	C, rt, 24 h	**12**	-	-	54
X= OAc, Y= H	B, 160°C, 1 h	**14**	**15**	1:2	54
	C, rt, 24 h	**14**	**15**	1:4	32
X=OCOPh, Y= H	B, 160°C, 1 h	**16**	**17**	1:1	60
X= N(Me)Ac, Y= H	A, rt, 48 h	-	**18**	-	80[e]
	B, 120°C, 0.3 h	-	**18**	-	73[e]

[a] (5 equiv of dienophile): A: 0.25 M **1**, CH_2Cl_2; B: neat; C: 4-bromo-2-hydroxymethyl phenol, 1.1 equiv $NaIO_4$, 0.2 equiv BTEAC, $CHCl_3/H_2O$ (3/1). [b] *αNS/αXS* ratio. [c] overall isolated yield. [d] 1-3 % of a third isomer is also observed. [e] an unseparable mixture (1-4%) of 2 other adducts is also observed.

Examination of the spectral data of adducts **2-18** revealed that only α regioisomers were obtained. Similar chemical shift (^1H and ^{13}C) or coupling constant (^1H-^1H) variations could be pointed out (Table 2). However an unambiguous structure determination appeared necessary and this was done for adducts **2**, **4**, **16**, **17** and **18** by X-Ray crystallography analysis (see experimental section).



2: R= OEt, R'= H
3: R= H, R'= OEt
4: R= OMe, R'= Me
5: R= Me, R'= OMe
6: R= OTMS, R'= H
7: R= H, R'= OTMS
10: R= Ph, R'= H
11: R= H, R'= Ph
12: R= Ph, R'= Me
13: R= Me, R'= Ph
14: R= OAc, R'= H
15: R= H, R'= OAc
16: R= OBz, R'= H
17: R= H, R'= OBz
18: R= H, R'= NMeAc



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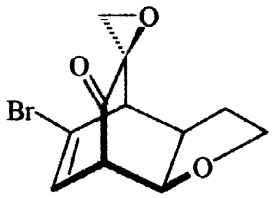

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Table 2. Characteristic ^{1}H and ^{13}C NMR data of *endo* and *exo* adducts

Adduct	δ H-8_A	δ H-8_B	Δδ[b]	^{3}J $H_{7,8}$ *syn*	δ ^{13}C-8	Δδ[c]
2[a]	2.50	1.80	-0.16	8.0	32.1	
3	1.96	2.34	-0.16	9.2	30.6	-1.5
4	2.08	2.08	-0.24	/	38.4	
5	2.32	1.80	-0.28	/	36.9	-1.5
6	2.47	1.72	-0.12	8.1	34.5	
7	1.84	2.30	-0.17	9.0	32.7	-1.8
8[d]	3.10	/	/	7.8	41.7	
9[d]	/	2.94	-0.16	8.6	41.9	+0.2
10[a]	2.67	2.10	-0.18	9.8	31.0	
11	2.29	2.49	-0.18	11.4	29.4	-1.6
12	2.30	2.58	-0.19	/	37.8	
13	2.77	2.07	-0.23	/	36.9	-0.9
14	2.65	1.88	-0.11	8.5	31.6	
15	1.99	2.50	-0.15	9.7	29.6	-2.0
16[a]	2.80	2.03	-0.10	8.3	31.8	
17[a]	2.13	2.60	-0.20	9.5	30.3	-1.5
18	2.31	2.01	/	11.5	23.1	

[a] Structure determined by X-Ray. [b] Δδ between H-8_A and H-8_B located in the same position with respect to C7 substituent(s). [c] Δδ between C-8_{exo} and C-8_{endo}. [d] In this case H-6, J $H_{2,6}$ and C-6 are considered (see numbering).

Then, from examination of the ^{1}H and ^{13}C NMR spectra of *αNS* and *αXS* compounds **16** and **17**, three main features were found. C-8 is more shielded ($\Delta\delta$: -1.5 ppm) and ^{3}J *syn* between H-7 and H-8 is slightly larger for **17** (J = 9.5 Hz) compared to **16** (J = 8.3 Hz) At position **8**, proton which is *syn* with respect to the substituent at C-7 is more deshielded in **16** than the corresponding proton in **17**. This is in agreement with an anisotropic shielding of the *endo* protons by the C(5),C(6) double bond.[11] These trends were also observed for the other pairs of isomers including adducts bearing a methyl group at C-7 (Table 2).

The above results establish that cycloaddition of dienone **1** with all tested dienophiles is fully regioselective and occurs almost exclusively *syn* to the oxygen epoxide (trace amounts (<3%) of a third isomer which may result from *anti* cycloaddition have been detected in some cases). Interestingly, whereas *endo* selectivity is observed for enol ethers and styrenes, as shown earlier for dienes,[4,8,9] the *exo* pathway is favored with enol esters and an enamide. These results are similar to those recently reported by Afarinkia for bromopyrone cycloadditions.[12] In order to explain the observed selectivities and possibly to provide a rationale for it, a theoretical study was then carried out.

Computations. Calculations have been performed on four model reactions using styrene, methyl vinyl ether (MVE), vinyl acetate (VA) and N-methyl vinyl formamide (NMVF) as dienophiles. These models were chosen to account for the high *αNS* selectivity observed for styrenes and enol ethers, the low *αNS/αXS* selectivity of enol esters and the high *αXS* selectivity of N-methyl vinyl acetamide. The semi-empirical AM1 method as implemented in the AMPAC program[13,14] has been used. This method has been parameterized to provide acceptable results in systems with non-bonding atom interactions and it has been shown to provide interesting results in Diels-Alder reactions.[15-17]

The regioselectivity was first studied since only α-regioisomers (bond formation between the dienophile C-2' and the dienone C-5 atoms) were obtained in our experiments in agreement with all other reported cases.[4,5] The simplest approach is probably within the context of frontier molecular orbital (FMO) theory.[18] The AM1 frontier orbital energies and coefficients for model dienophiles and dienone **1** are reported in Table 3. From these values, it appears that these reactions are under $LUMO_{diene}$ control and that the largest C5 coefficients for the LUMO of **1** together with the largest HOMO C-2' coefficient for each dienophile are indeed consistent with the observed α-regioselectivity.[19]

With styrene as dienophile, the eight TS's have been located (Table 4). The barrier heights (29-33 kcal/mol) are probably slightly overevaluated compared to typical values for the Diels-Alder reaction,[20] however, AM1 correctly predicts the formation of the major adduct (*αNS*).

Table 3. AM1 frontier orbital energies and coefficients for **dienone 1** and model dienophiles.

Reactant	Frontier orbital	ε(eV)	C''[b]	C''[c]
Dienone **1**	HOMO	−9.9	0.44	−0.52
	LUMO	−1.2	0.42	0.49
Styrene	HOMO	−9.1	0.31	0.42
	LUMO	+0.1	0.27	−0.39
MVE[a]	HOMO	−9.5	0.48	0.69
	LUMO	+1.4	0.72	−0.66
VA[a]	HOMO	−9.9	0.56	0.69
	LUMO	+0.7	0.38	−0.42
NMVF[a]	HOMO	−9.1	0.34	0.60
	LUMO	+0.7	0.49	−0.51

[a] The values given are for the more stable conformer. [b] C2 of dienone **1** or C1' of the dienophile. [c] C5 of dienone **1** or C2' of the dienophile.

Table 4. Energetics, percentages of adducts and selected geometrical parameters deduced from AM1 TS's for reaction of **1** with styrene as dienophile.

TS	E_0[a]	$\Delta S^{\neq}$[b]	%[c]	C_2–C[d]	C_5–C[d]	Q[e]
αNS	29.0 (0)	−48.3	88.7	2.283	2.021	+0.116
βNS	30.4 (1.4)	−49.2	5.4	2.183	2.087	+0.095
αXS	30.8 (1.9)	−49.5	2.4	2.275	2.036	+0.117
βXS	33.2 (4.2)	−48.7	0.1	2.175	2.107	+0.100
αNA	31.0 (2.0)	−48.3	3.1	2.287	2.023	+0.092
βNA	32.6 (3.6)	−48.8	0.2	2.180	2.093	+0.070
αXA	33.4 (4.4)	−47.5	0.1	2.282	2.033	+0.088
βXA	33.5 (4.5)	−48.5	0.0	2.174	2.104	+0.072

[a] barrier heights in kcal/mol (relative values in parentheses). [b] activation entropies (cal/K.mol) at 300 K. [c] percentage of adducts.[14c] [d] forming bond lengths (Å). [e] net charges in e units for styrene (positive values mean electron donation from styrene to **1** ($LUMO_{diene}$ control).

From the comparison of barrier heights for each *syn* TS and the corresponding *anti* one (for example the *αNS* and *αNA* pair may be considered) it appears that the *syn* value is always lower by about 2 kcal/mol, except in the case of the *βXS* TS which is lower in energy, compared to the *βXA* one, by only 0.3 kcal/mol (in this case, the phenyl ring is close to the epoxide group). Since an ethylenic hydrogen is close to the epoxide group

in the three other cases, it seems reasonable to consider that some attractive interaction between this atom and the epoxide oxygen atom occurs during the *syn* approach. The distances between these H and O atoms are 2.482, 2.522 and 2.422 Å for *αNS*, *αXS* and *βNS* TS's respectively. This interaction is probably to some extent electrostatic since in these three cases, the net charges on this hydrogen is between +0.13 e and +0.15 e whereas the charge on the epoxide oxygen is about −0.23 e. All the dienophiles considered here are of the $XYC{=}CH_2$ type (except one, 2,3-dihydrofuran) and for each of them, the major adduct corresponds to the *syn* approach. Thus, an attractive interaction between one ethylenic hydrogen and the epoxide oxygen is again likely to occur. For this reason, only *syn* approaches have been considered with the other model reactions. Similarly, only α TS's were searched for these model reactions.

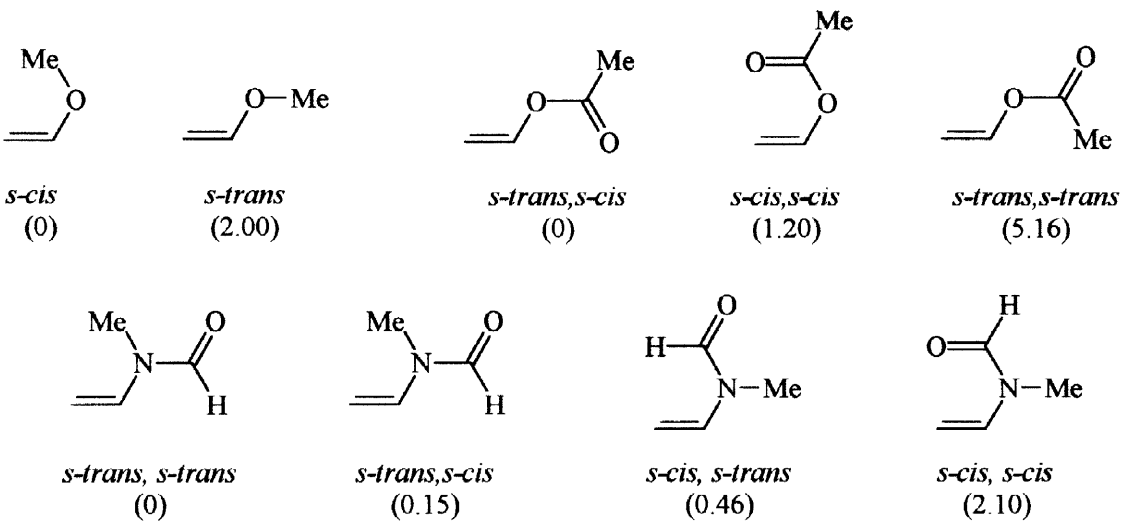

Figure 1. AM1 relative energies (kcal/mol) for the most stable conformers of MVE, VA and NMVF.

From AM1 calculations, two stable conformations are found for MVE (Figure 1). From experimental data, it has been reported that the lowest conformer is *s-cis*[21a] and that a gauche one lies 1.7 kcal/mol above.[21b] The four TS's ($\alpha NS_{s\text{-}cis}$, $\alpha NS_{s\text{-}trans}$, $\alpha XS_{s\text{-}cis}$ and $\alpha XS_{s\text{-}trans}$) have been located (Table 5). The $\alpha NS_{s\text{-}cis}$ TS is the lowest in agreement with the experimental data but the next TS ($\alpha XS_{s\text{-}cis}$) is only 0.6 kcal/mol above. This does not explain the high *endo* selectivity observed with ethyl vinyl ether and methyl isopropenyl ether as dienophiles (nearly 100% of *αNS* adduct). However, these gas-phase calculations do not take into account the polarity of the reaction medium which has been shown to influence the *endo/exo* orientation.[22] Given the calculated dipole moments, it is expected that the *s-trans*-MVE (μ = 1.75 D) would be more stabilized than the *s-cis*-MVE (μ = 0.87 D) in a polar medium (this may also hold if the reaction is carried out neat with excess MVE). Houk *et al.*[23] have recently published density functional Becke3LYP calculations on conformational effects in Diels-Alder reactions. With MVE as dienophile, conformational switches in transition states have been predicted, the *s-trans* TS being lower than the corresponding *s-cis* one. Since the $\alpha NS_{s\text{-}trans}$ TS is lower than the $\alpha XS_{s\text{-}trans}$ one

by about 1.8 kcal/mol, this may explain the experimental data for these two dienophiles. In contrast, the reaction with 2,3-dihydrofuran is obviously better described by the *s-cis*-MVE. The small difference between the $\alpha XS_{s\text{-}cis}$ and $\alpha NS_{s\text{-}cis}$ TS's (0.6 kcal/mol) could be an explanation to the lower selectivity observed in these experiments (about 80% of αNS adduct). However, this lower selectivity could also originate from the structure of 2,3-dihydrofuran (XHC=CHY dienophile): different interactions between the epoxide O atom and an ethylenic H (*endo* approach) or an allylic one (*exo* approach) may influence the balance between these two approaches.

Table 5. AM1 results for reaction of dienone 1 with MVE, VA and NMVF.

Dienophile	TS	E_0[a]	C2–C1'[b]	C5–C2'[b]	Q[c]
MVE	$\alpha NS_{s\text{-}cis}$	27.8 (0)	2.344	1.999	+0.194
	$\alpha NS_{s\text{-}trans}$	28.5 (0.7)	2.381	1.996	+0.200
	$\alpha XS_{s\text{-}cis}$	28.4 (0.6)	2.391	1.986	+0.209
	$\alpha XS_{s\text{-}trans}$	30.3 (2.5)	2.410	1.988	+0.213
VA	$\alpha NS_{s\text{-}trans,\ s\text{-}cis}$	28.4 (0)	2.266	2.041	+0.129
	$\alpha NS_{s\text{-}cis,\ s\text{-}cis}$	30.2 (1.8)	2.249	2.038	+0.102
	$\alpha NS_{s\text{-}trans,\ s\text{-}trans}$	33.4 (5.0)	2.300	2.020	+0.133
	$\alpha XS_{s\text{-}trans,\ s\text{-}cis}$	28.8 (0.4)	2.288	2.032	+0.142
	$\alpha XS_{s\text{-}cis,\ s\text{-}cis}$	31.1 (2.7)	2.271	2.028	+0.117
	$\alpha XS_{s\text{-}trans,\ s\text{-}trans}$	36.9 (8.5)	2.292	2.034	+0.129
NMVF	$\alpha NS_{s\text{-}trans,s\text{-}cis}$	28.4 (1.7)	2.410	1.977	+0.208
	$\alpha NS_{s\text{-}trans,s\text{-}trans}$	27.4 (0.7)	2.503	1.949	+0.238
	$\alpha XS_{s\text{-}trans,s\text{-}cis}$	26.7 (0)	2.496	1.957	+0.235
	$\alpha XS_{s\text{-}trans,s\text{-}trans}$	28.1 (1.4)	2.617	1.931	+0.273

[a] barrier heights in kcal/mol (relative values in parentheses). [b] forming bond lengths (Å).
[c] net charges in e units for the dienophile.

Three stable conformations were found for VA (Figure 1).[24] The calculated energy difference between the *s-trans,s-cis* and the *s-trans,s-trans* conformers is large but similar to those already reported between ester conformers.[25] The six αS TS's have been located (Table 5) and the two lowest TS's correspond to the most stable *s-trans,s-cis* conformer of VA. The *endo s-trans,s-cis* TS is more favorable by 0.4 kcal/mol in contrast to experimental data since the major isolated adduct is *exo*. The next two TS's correspond to the *s-cis,s-cis* VA, i.e., the next VA conformer. Again, the *endo* approach is more favorable by about 1 kcal/mol. The TS's corresponding to the less stable *s-trans,s-trans* conformer are significantly less favorable.

Four stable conformations were obtained for NMVF (Figure 1). The eight possible *αS* TS's have been searched. Our results for this model reaction contrast with those obtained for the former reactions since only four TS's have been located (Table 5). These TS's correspond to the two energetically lowest NMVF conformers (*s-trans,s-cis* and *s-trans,s-trans*) and are characterized by a high degree of asynchronicity. All attempts to locate concerted TS's with the two other conformers failed. We have not tried to search for the TS's corresponding to the two-step pathway since the AM1 method does not afford reliable relative energies of closed-shell (concerted mechanism) and open-shell (two-step mechanism) systems. Recently, Houk *et al.* carried out high level density-functional calculations on the butadiene + ethylene reaction.[26] They found that the free energy of activation for the concerted pathway is lower than the value for the two-step pathway by 2.3 to 7.7 kcal/mol, in excellent agreement with experimental data. From such a study it can be expected that in a cycloaddition involving asymmetrical reactants (diene and/or dienophile) the two-step mechanism is likely to become competitive. Thus, although AM1 correctly predicts the major adduct (*αXS*), it is clear that more sophisticated calculations are required not only to find more reliable relative barrier heights but also to confirm the cycloaddition mechanism.

Conclusion. Cycloaddition of dienone **1** with the dienophiles tested here occurs with complete regio- and diastereofacial selectivity. This is in agreement with all reported examples of similar cyclohexadienone (quinols, quinol acetates,...) as well as substituted cyclopentadiene cycloadditions.[27] The regioselectivity has been successfully analysed within the context of FMO theory. Furthermore, a good understanding of the facial selectivity was obtained and we suggest that this probably originates in an interaction with the epoxide group. Paquette *et al.* highlighted the role of such interactions in a recent study devoted to π-facial selectivity on dispiro[4.0.4.4]tetradeca-11,13-dienes.[28] Moreover, this electrostatic interaction may be the reason why, despite $LUMO_{diene}$ control of the reaction, the preferred approach occurs on the more nucleophilic π-surface in contradiction to Hehre's rule.[29] Concerning the *endo/exo* selectivity, our results are much less conclusive except for styrene. AM1 qualitatively predicts the major formation of an *endo* adduct with MVE and of an *exo* one with NMVF but the calculated relative barrier heights (0.6 to 0.7 kcal/mol) between the two processes are not consistent with the very high selectivity observed in theses cases. The slight preference for *exo* addition with VA is also not confirmed with these calculations.

Overall, an analysis based on secondary interactions provides a good understanding of the π-facial selectivity. The change in *endo/exo* selectivity observed with this dienone, which seems to parallel the one observed by Afarinkia in pyrone cycloaddition,[12] is more difficult to analyze at this point. Further experiments and higher level calculations are underway to explore this interesting selectivity change in such inverse electron demand Diels-Alder cycloadditions.

Experimental section

Melting points are uncorrected. ^{1}H NMR and ^{13}C NMR were recorded on a 300 MHz spectrometer, using $CDCl_3$ as solvent with TMS as internal standard. Assignment of ^{1}H NMR and ^{13}C NMR spectra were achieved using DEPT (Multiplicity by DEPT: s = C, d =CH, t =CH_2 q = CH_3) and 2D (HETCOR) methods. IR spectra were recorded on a FT-IR spectrophotometer. Elemental analyses and high resolution MS were performed by the "Centre de Recherche Pierre Fabre" (Castres, France) and by the "Service Central de Microanalyse" (CNRS, Lyon). All reactions were run under an inert atmosphere. THF was dried over and distilled from sodium/benzophenone and CH_2Cl_2 was distilled from P_2O_5. Organic extract mixtures were dried over anhydrous Na_2SO_4 and filtered and the solvent was then removed under reduced pressure. All separations were done under flash chromatography (MPLC) conditions on silica gel (25-40 mμ) completed, if necessary, by preparative thin-layer chromatography (TLC) performed on silica gel plates ($60GF_{254}$).

X-Ray analyses (**2**, **4**, **16**, **17** and **18**) were performed by means of a Enraf-Nonius CAD4 diffractometer with graphite monochromated MoKα radiation. The structures were solved by direct methods[30] and refined using least square calculations.[31] Positional and anisotropic thermal parameters of all atoms except hydrogen were refined. Hydrogen atom positions were calculated, an equivalent isotropic thermal parameter was given for hydrogen atom groups. A Chebychev polynomial with five coefficients was used in the weighting scheme. The crytallograpic data have been deposited at the Cambridge Crystallographic Data Centre.

Preparation of 7-bromo-1-oxaspiro[2.5]octa-5,7-dien-4-one (1). To a stirred solution of 4-bromo-2-hydroxymethyl phenol (9 g, 44.3 mmol) in MeOH (200 mL)-obtained from reduction of 5-bromo-2-hydroxy benzaldehyde ($NaBH_4$, THF, H_2O, 0°)-was added a solution of sodium periodate (10.5 g, 49 mmol) in water (100 mL), at 0°C. The mixture was stirred for 2 h at room temperature and was then filtered and extracted with CH_2Cl_2. Flash column chromatography (hexane/EtOAc, 75:25) afforded **1** as yellow needles (5.9 g, 65%): mp 73-74 °C; IR (CCl_4, cm^{-1}) 1687, 1624, 1610; ^{1}H NMR δ 3.23 and 3.32 (2H, ABq, J = 8 Hz), 6.20 (1H, d, J = 10.2 Hz), 6.37 (1H, d, J = 2 Hz), 7.20 (1H, dd, J = 10.2 and 2 Hz); ^{13}C NMR δ 57.9, 59.1, 118.6, 127.2, 138.2, 145.5, 192.6. A satisfactory elemental analysis could not be obtained.

General procedures for the Diels-Alder reactions:

Procedure A: A solution of spiroepoxydienone **1** and dienophile (5 equiv) in CH_2Cl_2 (4 mL/mmol **1**) was stirred at room temperature (20-72 h). Removal of the solvent and excess dienophile *in vacuo*, was followed by separation by MPLC, using hexane and ethyl acetate (EtOAc) as eluent.

Procedure B: A mixture of spiroepoxydienone **1** and dienophile (3 equiv), was heated in a sealed tube, at 120-160 °C, for a given period (15 min to 5 hours). Variable trace amounts (≤ 3%) of the insoluble dimer, formed from **1**, were filtered. Excess dienophile was then removed *in vacuo* and the crude residue was chromatographed by MPLC.

Procedure C: To a suspension of 4-bromo-2-hydroxymethyl phenol and dienophile (5 equiv) in chloroform (4 mL/mmol **1**) containing benzyltriethylammonium chloride (BTEAC, 0.2 equiv) as a phase transfer catalyst (PTC), was added a solution of $NaIO_4$ (1.1 equiv) in H_2O (1.2 mL/mmol). The reaction mixture was stirred at a temperature (rt to 80 °C) and for a given period (24 h to 2 days) after which the organic phase was separated

and the aqueous layer extracted with CH_2Cl_2. The combined organic extracts were washed with H_2O and dried over sodium sulfate. After removal of the solvent *in vacuo*, the residue was purified by flash chromatography.

Reaction conditions and results for the Diels-Alder reactions are presented below in the following abbreviated format: reactants; experimental conditions; purification; yield of adducts in order of elution; physical state and spectra data of adducts.

5-bromo-*endo*-7-ethoxy-*exo*-3-spiroepoxybicyclo[2.2.2]oct-5-en-2-one (2) and 5-bromo-*exo*-7-ethoxy-*exo*-3-spiroepoxybicyclo[2.2.2]oct-5-en-2-one (3). Procedure B: from **1** (400 mg, 1.98 mmol) and ethyl vinyl ether; 120 °C, 3 h, neat; MPLC (hexane/EtOAc, 95:5) and TLC; **2** (410 mg, 76%), **3** (23 mg, 4%). **Procedure C:** from 4-bromo-2-hydroxymethyl phenol (500 mg, 2.46 mmol); rt, 24 h, PTC ; MPLC; **2** (512 mg, 76%).

2 (white solid) : mp 58 °C; IR (CCl_4, cm^{-1}) 1745, 1607; ^1H NMR δ 1.19 (3H, t, J = 7 Hz), 1.80 (1H, dt, J = 14 and 2.7 Hz), 2.50 (1H, ddd, J = 14, 8 and 2.7 Hz), 2.67 (1H, app q, J = 2.5 Hz), 3.05 and 3.15 (2H, ABq, J = 6 Hz), 3.48 (2H, m), 3.77 (1H, dd, J = 6.5 and 2.7 Hz), 4.05 (1H, dtd, J = 8, 2.7, 0.8 Hz), 6.32 (1H, ddd, J = 6.5, 2.2, 0.8 Hz). ^{13}C δ 15.2 q, 32.1 t, 48.3 d, 52.7 t, 56.0 d, 57.2 s, 64.4 t, 75.0 d, 123.3 s, 125.5 d, 202.3 s. Anal. Calcd for $C_{11}H_{13}O_3Br$: C, 48.37; H, 4.80; Found: C, 48.38; H, 4.75. Crystal data: $C_{22}H_{26}Br_2O_6$, colourless prism, a = 14.311(2), b = 6.628(1), c = 24.320(5)Å, α = 90, β = 98.81(1),γ = 90°, V = 2279.68Å^3, space group P 2_1/c, Z = 4, D_c = 1.59 gcm^{-3}, F(000) = 1101.23. R = 4.79%, R_w = 3.89% and S = 1.14 for 273 refined parameters and 1568 refined reflexions (such as I≥3σ(I).

3 (oil): ^1H NMR δ 1.17 (3H, t, J = 7 Hz, Me), 1.96 (1H, dt, J = 14 and 3 Hz), 2.34 (1H, ddd, J = 14, 9.2 and 3 Hz), 2.67 (1H, app q, J = 2.5 Hz), 3.02 and 3.25 (2H, ABq, J = 6 Hz), 3.43 (1H, m), 3.60 (1H, m), 3.69 (1H, dd, J = 7.2 and 3.5 Hz), 3.99 (1H, dt, J = 9.2, 3.5 Hz), 6.28 (1H, dd, J = 7.2, 2.5, 0.8 Hz). ^{13}C: δ 15.2 q, 30.6 t, 48.8 d, 52.3 t, 54.8 d, 57.3 s, 64.3 t, 76.1 d, 125.3 s, 126.3s, 201.1 s.

5-bromo-*endo*-7-methoxy-*exo*-7-methyl-*exo*-3-spiroepoxybicyclo[2.2.2]oct-5-en-2-one (4) and 5-bromo-*exo*-7-methoxy-*endo*-7-methyl-*exo*-3-spiroepoxybicyclo[2.2.2]oct-5-en-2-one (5). Procedure B: from **1** (1g, 4.98 mmol), isopropenyl methyl ether; 120 °C, 3 h, neat; MPLC (hexane/EtOAc, 95:5) and TLC; **4** (700 mg, 50%), mixture of **4** and **5** in a 2:1 ratio (^1H NMR analysis) ((120 mg, 9%). **Procedure C**: from 4-bromo-2-hydroxymethyl phenol (500 mg, 2.46 mmol); rt, 3 h, then 60 °C, 2 days, PTC; MPLC; **4** (318 mg, 52%). In this case, isopropenyl methyl ether was added after 3 h at rt.

4 (white solid): mp 67 °C; IR (CCl_4, cm^{-1}) 1746,1610; ^1H NMR δ 1.35 (3H, s), 2.08 (2H, d, J = 2 Hz), 2.66 (1H, q, J = 2.5 Hz), 3.05 and 3.23 (2H, ABq, J = 6 Hz), 3.19 (3H, s), 3.53 (1H, d, J = 6.7 Hz), 6.34 (1H, dd, J = 6.7 and 2.5 Hz); ^{13}C NMR δ 23.9 q, 38.4 t, 47.8 d, 49.6 q, 52.3 t, 56.7 s, 60.1 d, 78.1 s, 123.3 s, 126.4 d, 202.5 s. Anal. Calcd for $C_{11}H_{13}O_3Br$: C, 48.37; H, 4.80. Found: C, 48.46; H, 4.79. Crystal data: $C_{11}H_{13}BrO_3$, colourless prism, a = 11.816(1), b = 7.746(1), c = 12.316(3)Å, α = 90, β = 96.22(1),γ = 90°, V = 1120.68Å^3, space group P 2_1/c, Z = 4, D_c = 1.62 gcm^{-3}, F(000) = 550.62. R = 6.64%, R_w = 5.84% and S = 0.83 for 138 refined parameters and 1970 refined reflexions such as I≥3σ(I).

5 (mixture with **4**): IR (CCl_4, cm^{-1}) 1746,1610; ^1H NMR δ 1.33 (3H, s), 1.80 (1H, dd, J = 13.6 and 2.7 Hz), 2.32 (1H, dd, J = 13.6 and 2.7 Hz), 2.69 (1H, q, J = 2.7 Hz), 3.00 and 3.24 (2H, ABq, J = 6), 3.24 (3H, s), 3.47 (1H, d, J = 7 Hz), 6.32 (1H, dd, J = 7 and 2.7 Hz); ^{13}C NMR δ 23.6 q, 36.9 t, 49.1 d, 49.8 q, 52.0 t, 55.6 s, 60.1 d, 79.9 s, 125.8 s, 125.9 d, 200.9 s.

5-bromo-*endo*-7-trimethylsilyloxy-*exo*-3-spiroepoxybicyclo[2.2.2]oct-5-en-2-one (6) and 5-bromo-*exo*-7-trimethylsilyloxy-*exo*-3-spiroepoxybicyclo[2.2.2]oct-5-en-2-one (7). Procedure A: from **1** (508 mg, 2.52 mmol) and trimethylsilylvinyl ether (obtained from ABCR); rt, 4 days (after 2 days, addition of 1 equiv of trimethylsilylvinyl ether); MPLC (hexane/EtOAc, 95:5) and TLC; **6** (542 mg, 68%) and **7** (112 mg, 14%). **Procedure B**: from **1** (730 mg, 3.61 mmol); 120 °C, 5 h, neat;.MPLC and TLC; **6** (502 mg, 44%) and **7** (222 mg, 20%).

6 (white solid): mp 99-100 °C (from ether); IR (CCl_4, cm^{-1}) 1745, 1608; ^1H NMR δ 0.1 (9H), 1.72 (1H, dt, J = 13.8 and 2.9 Hz), 2.47 (1H, ddd, J = 13.8, 8.1, 2.9 Hz), 2.64 (1H, app q, J = 2.7 Hz), 3.01 and 3.14 (2H, ABq, J = 6 Hz), 3.48 (1H, dd, J = 6.6 and 2.9 Hz), 4.37 (1H, dtd, J = 8.1, 2.9 and 0.7 Hz), 6.31 (1H, ddd, J = 6.6, 2.2 and 0.7 Hz); ^{13}C NMR δ -0.01, 34.5 t, 48.1 d, 52.6 t, 56.7 s, 59.6 d, 67.7 d, 122.9 s, 125.6 d, 202.5 s. Anal. Calcd for $C_{12}H_{17}BrSiO_3$: C, 45.43; H, 5.40. Found: C, 45.33 ; H, 5.38.

7 (oil): ^1H NMR δ 0.08 (9H), 1.84 (1H, dt, J = 13.6 and 2.9 Hz), 2.30 (1H, ddd, J = 13.6, 9 and 2.9 Hz), 2.65(1H,app q, J = 2.7 Hz), 2.99 and 3.20 (2H, ABq, J = 6 Hz), 3.35 (1H, dd, J = 7 and 3.9 Hz,), 4.30 (1H, dt, J = 9 and 3.4 Hz), 6.26 (1H, dd, J = 7 and 2.4 Hz); ^{13}C NMR δ -0.01, 32.7 t, 48.7 d, 52.4 t, 57.3 s, 58.6 d, 69.3 d, 125.9 s, 125.7 d, 201.1 s. Anal. Calcd for $C_{12}H_{17}BrSiO_3$: C, 45.43; H, 5.40. Found: C, 45.30 ; H, 5.37.

8-bromo-3-oxa-*exo*-11-spiroepoxy *endo* tricyclo[5,2,2,$0^{2,6}$]undec-8-en-10-one (8) and 8-bromo-3-oxa-*exo*-11-spiroepoxy *exo* tricyclo[5,2,2,$0^{2,6}$]undec-8-en-10-one (9). Procedure A: from **1** (195 mg, 0.97 mmol) and 2,3-dihydrofuran; rt, 72 h, CH_2Cl_2 (2 mL); MPLC (hexane/EtOAc, 95:5); **8** (142 mg, 54%) and **9** (37 mg, 14%). **Procedure B**: from **1** (150 mg, 0.74 mmol); 160 °C, 4 h, neat; MPLC; **8** (89 mg, 44%) and **9** (30 mg, 15%).

8: mp 110-111 °C; IR (CCl_4, cm^{-1}) 1750, 1607; ^1H NMR δ 1.85 (1H, m), 2.22 (1H, m), 2.81 (1H, t, J = 2.6 Hz), 3.04 (1H, d, J = 6 Hz), 3.11 (1H, m), 3.17 (1H, d, J = 6 Hz), 3.68 (1H, td, J = 8.9 and 6.5 Hz), 3.80 (1H, dd, J=6.6 and 3.4 Hz), 4.01 (1H, td, J = 8.2 and 3.4 Hz), 4.43 (1H, dd, J = 7.8 and 3.4 Hz), 6.36 (1H, dd, J = 6.6 and 2.6 Hz); ^{13}C NMR δ 29.8 t, 41.7 t, 52.0 d, 52.3 t, 56.5 d, 56.7 s, 69.5 t, 78.7 d, 121.7 s, 126.7 d, 201.7 s. Anal. Calcd for $C_{11}H_{11}O_3Br$: C, 48.73; H, 4.09. Found: C, 48.83; H, 4.09.

9: mp 108-109 °C; IR (CCl_4, cm^{-1}) 1751, 1601; ^1H NMR δ 2.10 (2H, m), 2.76 (1H, t, J = 2.3 Hz), 2.88 (1H, d, J = 6 Hz), 2.94 (1H, m), 3.04 (1H, d, J = 6 Hz), 3.67 (1H, dd, J = 6.9 and 4.5 Hz), 3.78 (1H, ddd, J = 8.9, 7.9 and 7.3 Hz), 4.08 (1H, ddd, J = 8.9, 7.2, and 4.8 Hz), 4.48 (1H, dd, J = 8.6 and 4.5 Hz), 6.30 (1H, dd, J = 6.9 and 2.3 Hz); ^{13}C NMR δ 28.0 t, 41.9 d, 49.8 t, 52.6 d, 55.4 d, 56.6 s, 70.7 t, 81.2 s, 125.8 d, 127.3 s 200.8 s.

5-bromo-*endo*-7-phenyl-*exo*-3-spiroepoxybicyclo[2.2.2]oct-5-en-2-one (10) and 5-bromo-*exo*-7-phenyl-*exo*-3-spiroepoxybicyclo[2.2.2]oct-5-en-2-one (11). Procedure A: from **1** (218 mg, 1.08 mmol); styrene; rt, 72 h, CH_2Cl_2; MPLC mixture of **10** and **11** in a 7:1 ratio (142 mg, 43 %). **Procedure B**: from **1** (500 mg, 2.46 mmol); 160°C, 1 h; MPLC (hexane/EtOAc, 95:5); mixture of **10** and **11** in a 5:1 ratio (^1H NMR analysis), (476 mg, 63%). **Procedure C**: from 4-bromo-2-hydroxymethyl phenol (500 mg, 2.47 mmol); rt, 24 h, PTC; MPLC; mixture of **10** and **11** in a 9:1 ratio (660 mg, 88%).

10 (white solid): mp 86 °C; IR (CCl_4, cm^{-1}) 1740, 1604; ^1H NMR δ 2.10 (1H, ddd, J = 13.7, 5.7 and 2.5 Hz), 2.67 (1H, ddd, J = 13.7, 9.8 and 2.5 Hz), 2.87 (1H, q, J = 2.5 Hz), 3.08 and 3.24 (2H, ABq, J = 6 Hz), 3.44 (1H, dd, J = 6.8 and 2 Hz), 3.50 (1H, ddd, J = 9.8, 5.7 and 2 Hz), 6.34 (1H, dd, J = 6.8 and 2.5 Hz), 7.23 (5H, m). ^{13}C NMR δ 31 t, 41.1 d, 49.9 d, 52.4 t, 56.9 s, 57.5 d, 124.2 s, 126.7 d, 127.2 d, 127.6 d, 128.8 d, 142.6 s,

202.3 s. HRMS (EI) *m/z* (M+) calcd 304.0099, obsd 304.0103. Anal. Calcd for $C_{15}H_{13}O_2Br$: C, 59.04; H, 4.31; Found: C, 59.09; H, 4.28.

11 (mixture with **10**): ^{1}H NMR δ 2.29 (1H, ddd, *J* = 13.7, 6.2 and 2.5 Hz), 2.49 (1H, ddd, *J* = 13.7, 11.4 and 3.2 Hz), 2.85 (1H, app q, *J* = 2.5 Hz), 3.14 and 3.30 (2H, ABq, *J* = 6 Hz), 3,32 (1H, dd, *J* = 6.9 and 2.5 Hz), 3.37 (1H, m), 6.55 (1H, dd, *J* = 6.9 and 2.5 Hz), 7.2 (5H, m). ^{13}C NMR δ 29.4 t, 44.5 d, 49.4 d, 52.9 t, 57.9 d, 58.4 s, 124.5 s, 127.2 d, 127.8 d, 128.8 d, 129.2 d, 141.3 s, 202.3 s.

5-bromo-*exo*-7-methyl-*endo*-7-phenyl-*exo*-3-spiroepoxybicyclo[2.2.2]oct-5-en-2-one (12) and 5-bromo-*endo*-7-methyl-*exo*-7-phenyl-*exo*-3-spiroepoxybicyclo[2.2.2]oct-5-en-2-one (13). Procedure B: from **1** (500 mg, 2.46 mmol); 120 °C, 20 min; MPLC (hexane/EtOAc, 95:5) completed by TLC; **12** (585 mg, 73%) and **13**, contaminated by **12** (24 mg, 3%). **Procedure C :** from 4-bromo-2-hydroxymethyl phenol (203 mg, 1 mmol); rt, 24 h; **12** (170 mg, 54%).

12 (oil): IR (CCl_4, cm^{-1}) 1745, 1607; ^{1}H NMR δ 1.46 (3H, s), 2.30 (1H, dd, *J* = 13.5 and 2.5 Hz), 2.58 (1H, dd, *J* = 13.5 and 2.5 Hz), 2.77 (1H, q, *J* = 2.5 Hz), 3.07 and 3.31 (2H, ABq, *J* = 6 Hz), 3.55 (1H, d, *J* = 7 Hz), 6.31 (1H, dd, *J* = 7 and 2.5 Hz), 7.28 (5H, m). ^{13}C NMR δ 31.0 q, 37.8 t, 43.3 s, 49.2 d, 52.3 t, 56.7 s, 61.3 d, 123.9 s, 126.1 d, 126.4 d, 128.4 d, 128.5 d, 147.7 s, 202.7 s. HRMS (EI) *m/z* (M+) calcd 318.0255, obsd 318.0253.

13 (oil): ^{1}H NMR δ 1.46 (3H, s), 2.07 (1H, dd, *J* = 13.5 and 2.5 Hz), 2.77 (1H, q, *J* = 2.5 Hz), 2.82 (1H, dd, *J* = 13.5 and 2.5 Hz), 3.02 and 3.19 (2H, ABq, *J* = 6 Hz), 3.57 (1H, d, *J* = 7 Hz), 6.51 (1H, dd, *J* = 7 and 2.5 Hz), 7.28 (5H, m).^{13}C NMR δ 31.6 q, 36.9 t, 44.7 s, 49.8 d, 52.3 t, 56.7 s, 61.8 d, 124.3 s, 126.7 d, 126.2 d, 128.2 d, 128.6 d, 146.3 s, 202.5 s.

5-bromo-*endo*-7-acetoxy-*exo*-3-spiroepoxybicyclo[2.2.2]oct-5-en-2-one (14) and 5-bromo-*exo*-7-acetoxy-*exo*-3-spiroepoxy-bicyclo[2.2.2]oct-5-en-2-one (15). Procedure B: from **1** (520 mg, 2.57 mmol); 160 °C, 1 h; MPLC (hexane/EtOAc, 90:10 to 80:20) and TLC; 1:2 mixture of **14** and **15** according to ^{1}H NMR analysis (54%). **Procedure C**: from 4-bromo-2-hydroxymethyl phenol (1 g, 4.92 mmol); rt, 24 h; MPLC gave a 1:4 mixture of **14** and **15** (32%). Careful chromatography allowed isolation of **14** and **15.**

14 (white solid): mp 111-112° C; IR (CCl_4, cm^{-1}) 1754, 1608; ^{1}H NMR δ 1.88 (1H, dt, *J* = 14.4 and 3 Hz), 2.06 (3H, s,), 2.65 (1H, ddd, *J* = 14.4, 8.5 and 2.6 Hz), 2.73 (1H, q, *J* = 2.6 Hz), 3.08 and 3.19 (2H, ABq, *J* = 6 Hz), 3.71 (1H, dd, *J* = 6.5 and 3 Hz), 5.30 (1H, dt, *J* = 8.5 and 3 Hz), 6.36 (1H, dd, *J* = 7 and 3 Hz). ^{13}C NMR δ 21 q , 31.8 t, 47.9 d, 52.7 t, 55.7 d, 56.8 s, 69.1 d, 124.1 s, 125.3 d, 170.0 s, 200.5 s.

15 (oil): IR (CCl_4, cm^{-1}) 1751, 1607; ^{1}H NMR δ 1.99 (1H, dt, *J* = 14 and 2.5 Hz), 2.07 (3H, s), 2.50 (1H, ddd, *J* = 14, 9.7 and 2.5 Hz), 2.75 (1H, q, *J* = 2.5 Hz), 3.08 and 3.24 (2H, ABq, *J* = 6 Hz), 3.63 (1H, dd, *J* = 6.5 and 4 Hz), 5.21 (1H, dt, *J* = 9.7 and 4 Hz), 6.34 (1H, dd, *J* = 6.5 and 2.5 Hz); ^{13}C NMR δ 20.9 q, 29.6 t, 48.5 d, 52.5 t, 54.4 d, 57.1 s, 70.0 d, 124.9 d, 126.6 s, 170.2 s, 200.0 s. MS (FABHR) *m/z* (MH^+) calcd 286.9918, obsd 286.9907. Anal. Calcd for $C_{11}H_{11}O_4Br$: C, 46.02; H, 3.86. Found: C, 45.91; H, 3.88.

5-bromo-*endo*-7-benzoyloxy-*exo*-3-spiroepoxybicyclo[2.2.2]oct-5-en-2-one (16) and 5-bromo-*exo*-7-benzoyloxy-*exo*-3-spiroepoxybicyclo[2.2.2]oct-5-en-2-one (17). Procedure B : from **1** (152 mg, 0.75 mmol) and vinyl benzoate; 160° C, 1 h; MPLC (hexane/EtOAc, 95:5 to 90:10); mixture of **16** and **17** (60%, in a 1:1 ratio by ^{1}H NMR analysis).

16 (white solid): mp 133-134 °C; IR (CCl_4, cm^{-1}) 1752, 1726,1605; ^1H NMR δ 2.03 (1H, dt, J = 14.4, 3 Hz), 2.80 (2H, m), 3.09 and 3.23 (2H, ABq, J = 6 Hz), 3,86 (1H, dd, J = 6.5 and 3 Hz), 5.57 (1H, dt, 8.3 and 3 Hz), 6.45 (1H, dd, J = 6.5 and 2 Hz) ,7.46 (2H, t, J = 7.5 Hz), 7.58 (1H, t, J = 7.5 Hz), 8.0 (2H, d, J = 7.5 Hz.); ^{13}C NMR δ 31.8 t, 47.8 d, 52.6 t, 55.5 d, 56.8 s, 69.6 d, 124.1 s, 125.2 d, 128.4 d, 129.3 d, 129.6 d, 133.3 d, 165.3 s, 200.4 s. Anal. Calcd for $C_{16}H_{13}O_4Br$: C, 55:04; H, 3.75. Found: C, 55.07; H, 3.78. Crystal data: $C_{16}H_{13}BrO_4$, colourless prism, a = 6.419(2), b = 7.506, c = 14.888(2)Å, α = 84.57(1), β = 81.11(2),γ = 83.31(2)°, V = 701.71Å^3, space group P -1, Z = 2, D_c = 1.65 gcm^{-3}, F(000) = 351.33. R = 3.54%, R_w = 3.35% and S = 1.12 for 192 refined parameters and 2575 refined reflexions (such as I≥3σ(I).

17 (white solid): mp 158 °C; IR (CCl_4, cm^{-1}) 1752, 1726; ^{1}HNMR δ 2.13 (1H, dt, J = 14.3, 2.8 Hz), 2.60 (1H, ddd, J = 14.3, 9.5 and 2.8 Hz), 2.80 (1H, q, J = 2.8 Hz), 3.10 and 3.30 (2H, ABq, J = 6 Hz), 3.74 (1H, dd, J = 7 and 4 Hz), 5.49 (1H, ddd, J = 9.5, 4 and 2.8 Hz), 6.38 (1H, dd, J = 7 and 2.8 Hz) ,7.42 (2H, bt, J = 7.5 Hz), 7.54 (1H, bt, J = 7.5 Hz), 7.95 (2H, bd, J = 7.5 Hz). ^{13}C NMR δ 30.3 t, 48.6 d, 52.5 t, 54.6 d, 57.1 s, 70.3 d, 124.7 d, 126.8 s, 128.4 d, 129.2 d, 129.7 d, 133.4 d, 165.6 s, 200.2 s. MS (FABHR) *m/z* (MH^+) calcd 349.0075, obsd 349.0064. Anal. Calcd for $C_{16}H_{13}O_4Br$: C, 55.04; H, 3.75. Found: C, 54.98; H, 3.76. Crystal data: $C_{32}H_{26}Br_2O_8$, colourless prism, a = 8.361(2), b = 30.734(6), c = 11.171(8)Å, α = 90(3), β = 90.25(3),γ = 90(2)°, V = 2870.33Å^3, space group P 2_1/c, Z = 4, D_c = 1.62 gcm^{-3}, F(000) = 1405.34. R = 7.25%, R_w = 5.87% and S = 1.23 for 381 refined parameters and 2047 refined reflexions (such as I≥3σ(I).

5-bromo-*exo*-7-(N-methyl-N-acetamido)-*exo*-3-spiroepoxy-bicyclo[2.2.2]oct-5-en-2-one (18). Procedure A: from **1** (240 mg, 1.19 mmol); N-methyl-N-vinyl acetamide; rt, 2 days, CH_2Cl_2 (5 mL); MPLC (hexane/EtOAc, 85:15 to 50:50); **18** (284 mg, 80%). **Procedure B**: from **1** (535 mg, 2.64 mmol); 120 °C, 20 min; MPLC; **18** (578 mg 73%).

18: mp 49°C; IR (CCl_4, cm^{-1}) 1742,1659,1397; ^1H NMR δ 1.55 (3H, s), 2.01 (1H, ddd, J = 14, 6, 2.7 Hz), 2.10 (3H, s), 2.31 (1H, ddd, J = 14, 11.5, 2.7 Hz), 2.85 (1H, q, J = 2.7 Hz), 3.14 and 3.32 (2H, ABq, J = 6 Hz), 3.36 (1H, dd, J = 7 and 3 Hz), 5.19 (1H, ddd, J = 11.5,6 and 3 Hz), 6.44 (1H, dd, J = 7 and 2.7 Hz); ^{13}C NMR δ 22.4 q, 23.1 t, 32.3 q, 48.7 d, 52.2 d, 52.9 t 55.5 d, 58.0 s, 124.4 s, 127.8 d, 171.0 s, 203.0 s. HRMS (EI) *m/z* (M^+) calcd 299.0157, obsd 299.0158. Anal. Calcd for $C_{12}H_{14}BrNO_3$: C, 48.02; H, 4.70; N, 4.67. Found: C, 48.02; H, 4.68; N, 4.65. Crystal data: $C_{12}H_{14}BrNO_3$, colourless prism, a = 20.41(2), b = 6.587(1), c = 19.55(4)Å, α = 90(5), β = 106.89(2),γ = 90(6)°, V = 2514.50Å^3, space group C 2_1/c, Z = 8, D_c = 1.59 gcm^{-3}, F(000) = 1213.23. R = 7.17%, R_w = 7.14% and S = 1.17 for 156 refined parameters and 934 refined reflexions (such as I≥3σ(I).

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