Pergamon

Tetrahedron: Asymmetry, Vol. 7, No. 8, pp. 2391-2398, 1996

0957-4166/96 $15.00 + 0.00

PII: S0957-4166(96)00295-9

Diels–Alder Reactions of (*E*)-2-Phenyl-4-[(*S*)-2,2-dimethyl-1,3-dioxolan-4-ylmethylen]-5(4*H*)-oxazolone with Heterogeneous Catalysts

Carlos Cativiela*, José M. Fraile, José I. García, Mª Pilar López, José A. Mayoral*, Elisabet Pires

Instituto de Ciencia de Materiales de Aragón. Departamento de Química Orgánica. Universidad de Zaragoza–C.S.I.C. E-50009 Zaragoza. España. E-mail: jose.mayoral@msf.unizar.es.

Abstract: Diels–Alder reactions of (*E*)-2-Phenyl-4-[(*S*)-2,2-dimethyl-1,3-dioxolan-4-ylmethylen]-5(4*H*)-oxazolone with 2,3-dimethylbutadiene, cyclopentadiene, and 2-methyl-1,3-butadiene (isoprene) are catalysed by silica gel and aluminium, titanium, and zinc catalyst supported on silica gel. Overall conversion and asymmetric induction are obtained with very low percentages of *E/Z* isomerisation. The best results are obtained with $ZnCl_2$ supported on silica gel, and by carrying out the reaction without a solvent. The stereochemistry of the major cycloadducts has been determined by single crystal X-ray structure determination and AM1 calculations of the corresponding transition structures.

INTRODUCTION

Cycloaliphatic α-amino acids, a particular kind of conformationally restricted amino acid, have interesting biological properties,[1] and some asymmetric syntheses of this kind of amino acid have already been described.[2] Az-lactones are among the most important precursors of α-amino acids,[3] and they have also been used in the synthesis of cyclic compounds. Thus, (*Z*)-2-phenyl-4-benzylidene-5(4*H*)-oxazolone has been used as a dienophile with different dienes.[2d,4,5] A very interesting asymmetric version of these reactions has been described using (*Z*)-2-phenyl-4-[(*S*)-2,2-dimethyl-1,3-dioxolan-4-ylmethylen]-5(4*H*)oxazolone as a chiral dienophile.[6]

In order to increase the number of compounds accessible by means of this methodology, the use of *E*-azlactones has been proposed. This strategy has been tested with the (*E*)-2-phenyl-4-benzylidene-5(4*H*)-oxazolone, but the less stable *E*-isomer easily isomerises to the *Z*-isomer,[5] and a complex mixture of both dienophiles and the corresponding Diels–Alder cycloadducts is obtained upon reaction. Although it has not been described, the situation must be similar, or even worse, in the case of the (*E*)-2-phenyl-4-[(*S*)-2,2-dimethyl-1,3-dioxolan-4-ylmethylen]-5(4*H*)oxazolone **1** (Scheme 1). In fact, when the *Z*-isomer of **1**, **2**, is made to react with not very reactive dienes, products coming from **1** are also detected[6c] in spite of the higher stability of **2**.

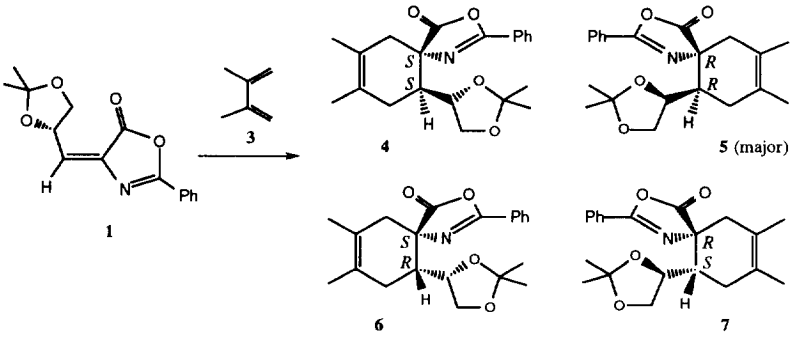
Several solids with Lewis acid properties have proven to be efficient catalysts in Diels–Alder reactions of dienophiles which are α -amino acid precursors, such as *N*-acetyl-α,β-dehydroalaninates,[7] (*E*)-2-cyano-cinnamates,[8] and (*Z*)- and (*E*)-2-phenyl-4-benzylidene-5(4*H*)-oxazolones.[9] In particular, it has been described that silica gel and several aluminium-,[10] titanium-,[10], and zinc-supported[11] catalysts promote the reaction between (*E*)-2-phenyl-4-benzylidene-5(4*H*)-oxazolone and cyclopentadiene, and the *E/Z* isomerisation is reduced to less than 5%.[9]

In view of these results we considered it interesting to test if the same methodology can be used in the Diels–Alder reactions of the chiral *E*-azlactone **1** with several dienes (Scheme 1).

RESULTS AND DISCUSSION

Reaction of 1 with 2,3-dimethylbutadiene 3

The reaction of **1** with 2,3-dimethylbutadiene **3** (Scheme 1) was carried out in the presence of silica gel and several silica-supported catalysts. The results obtained (Table 1) show that the percentage of *E/Z* isomerization depends on the nature of the catalysts and whether solvent is used or not.



Scheme 1

In general it may be expected that the presence of a catalyst increases the extent to which the isomerisation takes place, with regard to the non-catalysed reaction, but this behaviour is only observed with the silica gel and with the titanium-supported catalysts (SiO_2–Ti). The use of aluminium-supported catalysts (SiO_2–Al) leads to the same overall amount of *Z* compounds as the non-catalysed reaction (19%), and this proportion is noticeably reduced with the zinc-supported catalyst (SiO_2–Zn).

The major diastereomer resulting from the reactions can be easily isolated from the reactions catalysed by SiO_2–Zn, purified by column chromatography on silica gel using toluene/ethyl acetate 9:1 as an eluent, and recrystallysed from $CHCl_3$. The structure of this product was confirmed by single crystal structure determination (Figure 1), showing that this product comes from the attack of the diene on the less-hindered $C_{\alpha\text{-}si}$ face of the double bond.

Semiempirical AM1[12] calculations agree with this result, showing that the *endo* transition structure (TS) leading to the major cycloadduct **5** is 2.4 kcal·mol^{-1} more stable than the corresponding *endo* TS leading to **4**. For the *exo* approach, the TS leading to **5** is also more stable than that leading to **4** by 2.9 kcal·mol^{-1} (Figure 2). These energy differences, although they must be interpreted at a semi-quantitative level, account for the high asymmetric induction experimentally observed.

Table 1. Results obtained in the reaction of **1** with 2,3-dimethylbutadiene (**3**) at 20°C during 24 h.[a]

Catalyst	Solvent	**1** (%)	**2** (%)	**4** (%)	**5** (%)	**6** (%)	**7** (%)
none	CH_2Cl_2	1.5	7	1.5	78	9	3
SiO_2[b]	CH_2Cl_2	0	0	0	48	52	0
	—	0	0	4	91	5	0
SiO_2–Al[c]	CH_2Cl_2	1	5	1	80	13	1
	—	1.5	1.5	0	83	13	0.5
SiO_2–Ti[d]	CH_2Cl_2	0	4	2.5	45.5	43.5	5
	—	0	24	0	67	6.5	2.5
SiO_2–Zn[e]	CH_2Cl_2	0	0	1	91.5	6.5	1
		0	0	0	94	5.5	1

[a] Determined by hplc. [b] Merck silica gel 60, 63–200 nm. [c] Merck silica gel treated with $AlClEt_2$. [d] Merck silica gel treated with $TiCl_4$. [e] $ZnCl_2$ supported on silica EP11 from Crossfield.

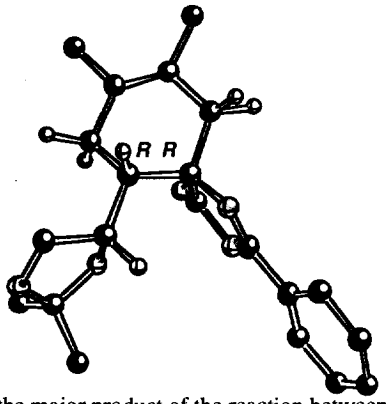


Figure 1. X-Ray structure of the major product of the reaction between the chiral azlactone **1** and 2,3-dimethylbutadiene **3** (most of hydrogen atoms have been omitted for clarity).

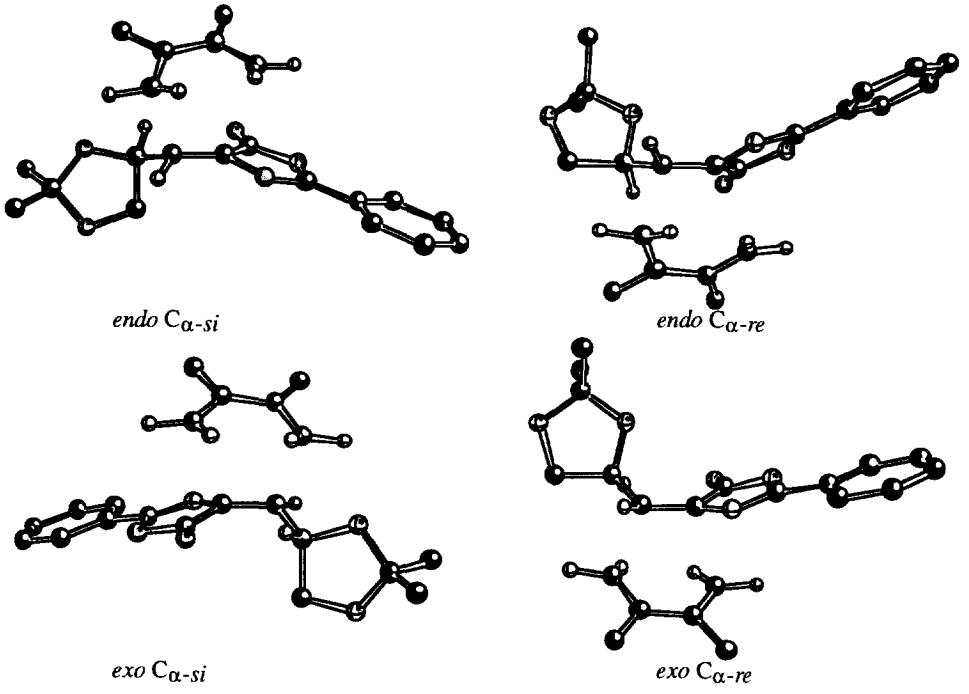
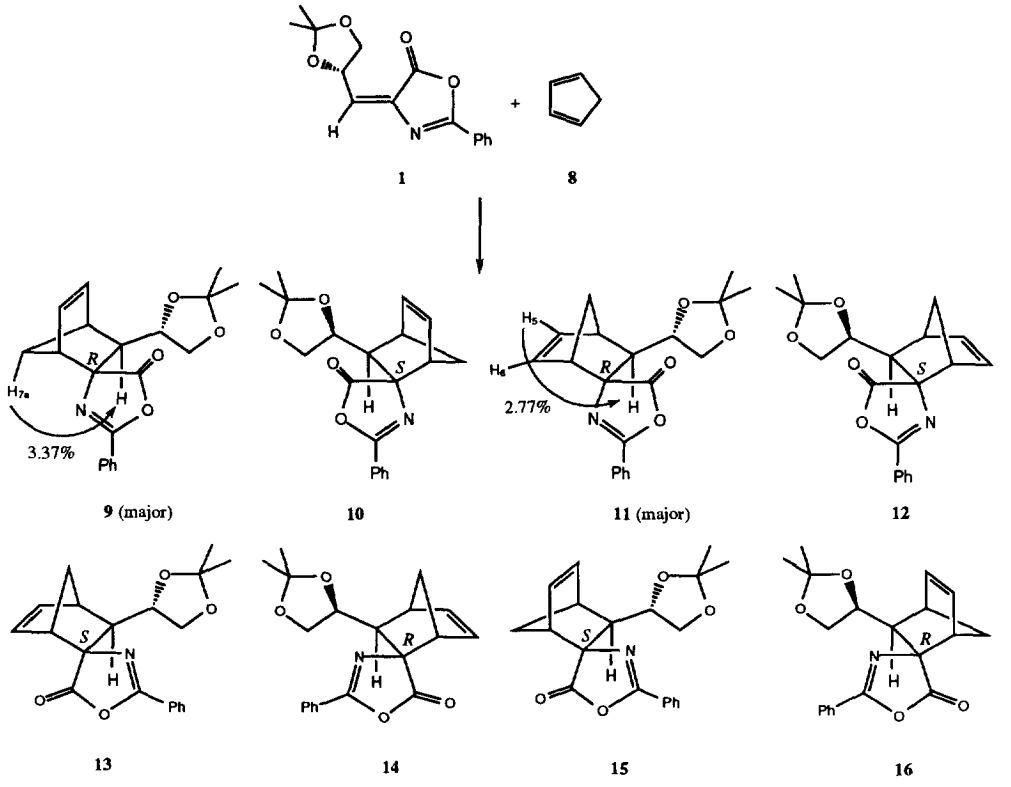


Figure 2. Calculated (AM1) transition structures for the reaction between the chiral azlactone **1** and 2,3-dimethylbutadiene **3** (most of hydrogen atoms have been omitted for clarity).

Reaction of 1 with cyclopentadiene 8

The reaction of **1** with cyclopentadiene is quite fast, so therefore it was carried out at a lower temperature and with a shorter reaction time. The use of low temperatures in the absence of a solvent makes the reproducibility of the results difficult, due to diffussional problems, among others, so therefore all the reactions were carried out in methylene chloride (Scheme 2). The results obtained (Table 2) show that all the solids catalyse the reaction and, with the only exception of the unmodified silica gel, the percentage of isomerisation decreases with regard to the non-catalysed reaction. SiO_2–Zn is again the most favourable in this respect. The use of supported Lewis acids

increases the asymmetric induction, but decreases the *endo/exo* selectivity. This fact is particularly observed with the titanium- and zinc-supported catalysts, for which only one *endo* and one *exo* cycloadducts are obtained, but in the same proportion.



Scheme 2

The major *endo* **9** and *exo* **11** cycloadducts were purified by column chromatography on silica gel, using hexane/ethyl acetate 9:1 as an eluent. The relative *endo* and *exo* configuration was unequivocally assigned by means of Nuclear Overhauser effect (NOe) difference ^{1}H-NMR experiments. Thus, in **11** the signal of the vinylic proton H_5 shows a significant NOe enhancement when the H_{3n} proton was selectively irradiated. On the other hand, in **9**, the irradiation of H_{3x} leads to an enhancement of the signal corresponding to H_{7a} (Scheme 2).

Table 2. Results obtained in the reaction of **1** with cyclopentadiene **8** in CH_2Cl_2 at –20°C during 1 h.[a]

Catalyst	**1** (%)	**2** (%)	**9** (%)	**10** (%)	**11** (%)	**12** (%)	**13+14+15+16** (%)
none	11	22	48.5	9.5	9	1	0
SiO_2	0	0	20	8.5	9.5	0	62
SiO_2–Al	0	0	52	9	27	2	10
SiO_2–Ti	0	0	42	0	42	0	16
SiO_2–Zn	0	0	47.5	0	47.5	0	5

[a] Determined by hplc.

The absolute configurations were assigned on the basis of the preferred approach of the diene on the C_{α}-*si* face of the double bond. The theoretical calculations also support this assignment. Thus, the AM1 results show that the most stable *endo* and *exo* TS are those leading to **9** and **11**, respectively (Figure 3). The energy differences between the *si* and the *re* attacks both for the *endo* (2.4 kcal·mol^{-1}) and the *exo* (3.0 kcal·mol^{-1}) TS also agree with the high asymmetric inductions experimentally observed.

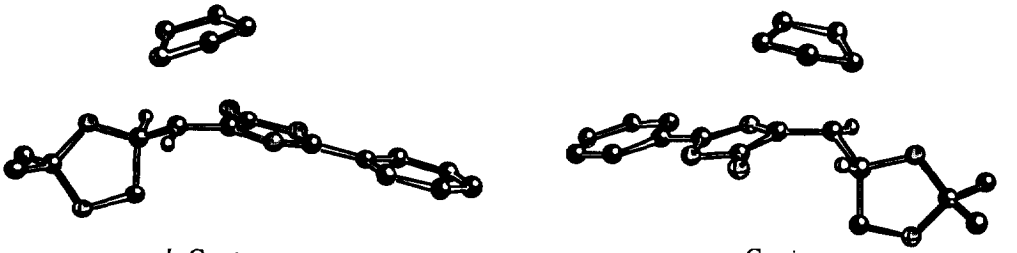
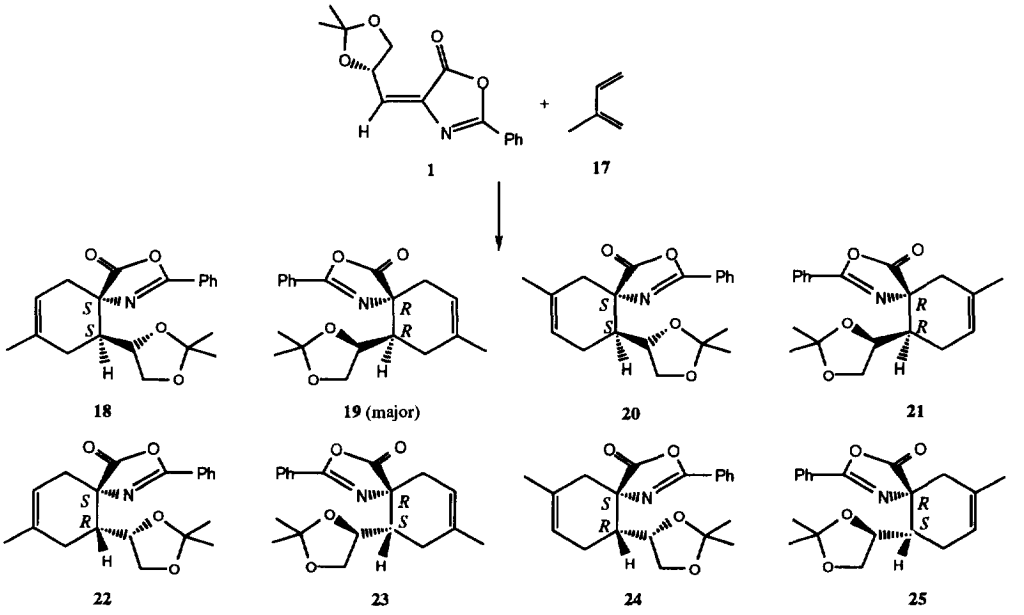


Figure 3. Most stable calculated (AM1) *endo* and *exo* transition structures for the reaction between the chiral azlactone **1** and cyclopentadiene **8** (most of hydrogen atoms have been omitted for clarity).

Reaction of 1 with isoprene 17

The reactions of the chiral dienophile **1** with isoprene **17** (Scheme 3) were carried out in the same experimental conditions used for the reactions of 2,3-dimethylbutadiene **3** .



Scheme 3

With this less-reactive diene the differences between the different catalyts and conditions are clearly highlighted (Table 3). The silica gel treated with $TiCl_4$ (SiO_2–Ti) as well as the reactions carried out in

methylene chloride in the presence of silica gel or those without a catalyst, lead to an extensive *E/Z* isomerisation. This problem is reduced using silica treated with $AlClEt_2$ (SiO_2–Al) and almost suppressed using silica gel in the absence of a solvent or $ZnCl_2$ supported on silica gel (SiO_2–Zn). The use of SiO_2–Zn, with or without a solvent, leads to an increase in the conversion and the regioselectivity, and to a decrease in the *E/Z* isomerisation. In this way, the major cycloadduct is obtained in a proportion of *ca.* 80%.

Table 3. Results obtained in the reaction of **1** with isoprene (**17**) at 20°C during 24 h.[a]

Catalyst	Solvent	**1** (%)	**2** (%)	**18** (%)	**19** (%)	**20** (%)	**21** (%)	**22+23+24+25** (%)
none	CH_2Cl_2	19	42.5	0	27	0	9.5	2
SiO_2	CH_2Cl_2	17.5	45	1	29.5	0	5.5	2.5
	—	0	0	4	60.5	0	24	11.5
SiO_2–Al	CH_2Cl_2	21	17	0.5	53.5	0	4	4
	—	29.5	16	0.5	40	0	10.5	3.5
SiO_2–Ti	CH_2Cl_2	8.5	46	0	44.5	0	1	0
	—	0	74.5	0	25	0	0.5	0
SiO_2–Zn	CH_2Cl_2	2.5	4	0	79.5	0	6	8
	—	0	0	0	81	0	11.5	7.5

[a] Determined by hplc, except the ratio **19/21**, which could not be separated, and was determined by ^{1}H-NMR.

The *para/meta* regiochemistry of the major cycloadducts (**19** and **21**) was assigned by ^{1}H-NMR of the mixture. The spectrum of the minor product displays a doublet centred at 2.05 ppm (J=18 Hz), corresponding to a proton bonded to the C_2 carbon atom. This signal corresponds to an AB system, consistent with the *meta* regiochemistry of this cycloadduct. Both products also show different chemical shifts for the vinylic proton (5.30 ppm for **19** and 5.63 ppm for **21**), which allows the determination of their relative proportions.

The absolute configurations were again assigned assuming the attack of the diene on the $C_{\alpha\text{-}si}$ face of the double bond, and this assigment was corroborated by the theoretical calculations.

It can be concluded that the use of some heterogeneous catalysts allows the improvement of the selectivity of the Diels–Alder reactions of the chiral azlactone **1**, by reducing the percentage of *E/Z* isomerisation. The best results are obtained with $ZnCl_2$ supported on silica gel, which is easily removed from the reaction medium and can be recovered, and also by carrying out the reactions in the absence of a solvent when possible.

EXPERIMENTAL

Preparation of the heterogeneous catalysts: Before its use as a catalyst, silica gel (Merck silica gel 60, 63–200 nm) was activated by heating under vacuum at 140°C for 12 h. This solid was also used to support aluminium and titanium derivatives by treatment with 1M solutions of $AlClEt_2$ and $TiCl_4$, respectively, following a previously described method.[10] $ZnCl_2$ was supported on silica gel (EP11 from Crossfield, 415 $m^2 \cdot g^{-1}$) as previously described.[11]

Preparation of the (E)-2-phenyl-4-[(S)-2,2-dimethyl-1,3-dioxolan-4-ylmethylen]-5(4H)-oxazolone **1**: A mixture of **1** and **2** was obtained as previously described.[13] From this mixture **1** is purified by column chromatography on silica gel, using hexane/ethyl acetate 85:15 as an eluent.

Diels–Alder reactions in CH_2Cl_2: Under argon, 382 mg (1.4 mmol) of **1** and 14 mmol of the corresponding diene were added to a suspension of the catalyst (1g) in dry methylene chloride (8 ml). The mixture was stirred at 20°C or –20°C, after the corresponding time the catalyst was removed by filtration, repeatedly washed with methylene chloride, and the solution analysed by HPLC using the following conditions:

• Reactions with 2,3-dimethylbutadiene. Column: Radial Pack from Waters, silica 4 μm. Eluent: *n*-hexane/ethyl acetate 97:3 at a flow rate of 2.5 $ml \cdot min^{-1}$. Detection at λ=254 nm. Retention times: 5.8 min (**2**), 6.1 min (**6**), 8.1 min **1**, 8.9 min **7**, 13.0 min **4**, 20.7 min **5**.

• Reactions with cyclopentadiene. Column: Radial Pack from Waters, silica 4 μm. Eluent: *n*-hexane/ethyl acetate 97:3 at a flow rate of 3.5 ml·min^{-1}. Detection at λ=254 nm. Retention times: 4.3 min **2**, 4.3 min **13**, 4.4 min **9**, 5.5 min **15**, 6.2min **11**, 7.0 min **1**, 8.0 min **16**, 12.9 min **10**, 18.3 min **12**.

• Reactions with isoprene. Column: Radial Pack from Waters, silica 4 μm. Eluent: *n*-hexane/ethyl acetate 97:3 at a flow rate of 2.0 ml·min^{-1}. Detection at λ=254 nm. Retention times: 6.4 min (**2**), 8.1 min (**22**), 8.9 min (**1**), 13.0 min (**24**), 17.6 min (**19+21**), 25.9 min (**18**).

Quantitative determinations were made by using correction factors determined from calibration curves. The reactions without a catalyst were carried out with the same proportion of reagents.

Diels–Alder reactions in the absence of a solvent: A solution of the dienophile **1** (393 mg, 1.44 mmol) was mixed with the corresponding catalyst (3 g), and the solvent was removed under reduced pressure. Then, 14.4 mmol of the corresponding diene were added and the mixture was shaken at 20°C for 24 h. After this time, methylene chloride was added, the catalyst removed by filtration and repeatedly washed with methylene chloride. The solutions were analysed by HPLC as described above.

Major cycloadducts obtained from the Diels–Alder reactions

• (1*R*,6*R*)-6-[(*S*)-2,2-Dimethyl-1,3-dioxolan-4-yl]-3,4-dimethylcyclohex-3-en-1-spiro{4'[2'-phenyl-5'(4'*H*)-oxazolone]} **5**. ^{1}H-NMR ($CDCl_3$, 300 MHz): δ 1.14 (s, 3H), 1.34 (s, 3H), 1.62 (s, 3H), 1.73 (s, 3H), 2.05 (m, 1H), 2.15 (m, 1H), 2.35 (m, 1H), 2.58 (d, 1H; J=15.6 Hz), 2.68 (d, 1H; J=15.6 Hz), 3.7 (dd, 1H; J=8.4 Hz, J=6.6Hz), 3.82 (dd, 1H; J=8.4 Hz, J=6.6 Hz), 4.02 (ddd, 1H; J=6.6 Hz, J=6.6 Hz, J=11.4 Hz), 7.42–7.58 (m, 3H), 7.94–7.99 (m, 2H). ^{13}C-NMR ($CDCl_3$, 75 MHz): δ 18.4, 18.9, 25.1, 25.9, 28.5, 40.9, 43.6, 67.2, 68.8, 74.5, 108.7, 119.4, 126.0, 126.2, 127.8, 128..8, 132.6, 160.8, 177.2. Elem. Anal. calc. for $C_{21}H_{25}NO_4$: C=70.96%, H=7.09%, N=3.94%; found: C=71.10%, H=6.91%, N=3.90%. $[\alpha]_D$ = –33.82 (c=0.89 in $CHCl_3$).

• (1*R*,2*R*,3*R*,4*S*)-3-[(*S*)-2,2-Dimethyl-1,3-dioxolan-4-yl]-bicyclo[2.2.1]-hept-5-en-2-spiro{4'[2'-phenyl-5'(4'*H*)-oxazolone]} **9**. ^{1}H-NMR ($CDCl_3$, 300 MHz): δ 1.20 (s, 3H), 1.40 (s, 3H), 1.73 (ddd, 1H; J=1.5 Hz, J=8.7 Hz), 2.24 (d, 1H; J=8.7 Hz), 2.68 (dd, 1H; J=10.8 Hz, J=3.3 Hz), 2.9 (m, 1H), 3.22 (dd, 1H; J=8.1 Hz, J=5.4 Hz), 3.28 (m, 1H), 3.84 (dd, 1H; J=6.0 Hz, J=8.1 Hz), 3.95 (ddd, 1H; J=6.0 Hz, J=5.4 Hz, J=10.8 Hz), 6.30 (dd, 1H; J=5.4 Hz, J=3.0 Hz), 6.60 (dd, 1H; J=5.4 Hz, J=3.0 Hz), 7.42–7.49 (m, 2H), 7.50–7.80 (m, 1H), 7.80–7.95 (m, 2H). ^{13}C-NMR ($CDCl_3$, 75 MHz): δ 25.0, 27.0, 46.5, 48.6, 55.9, 58.4, 67.8, 75.9, 76.6, 109.0, 125.8, 127.8, 132.6, 133.0, 139.5, 159.5, 178.3. Elem. Anal. calc. for $C_{20}H_{21}NO_4$: C=70.78%, H=6.24%, N=4.13%; found: C=70.55%, H=6.22%, N=4.20%. $[\alpha]_D$ = +41.75 (c=0.91 in $CHCl_3$).

• (1*S*,2*R*,3*R*,4*R*)-3-[(*S*)-2,2-Dimethyl-1,3-dioxolan-4-yl]-bicyclo[2.2.1]-hept-5-en-2-spiro{4'[2'-phenyl-5'(4'*H*)-oxazolone]} **11**. ^{1}H-NMR ($CDCl_3$, 300 MHz): δ 1.30 (s, 3H), 1.38 (s, 3H), 1.58 (m, 1H), 1.98 (dd, 1H; J=10.8 Hz, J=2.7 Hz), 2.45 (d, 1H; J=9.6 Hz), 3.03 (m, 1H), 3.20 (m, 1H), 3.25 (dd, 1H; J=6.0 Hz, J=8.1 Hz), 3.97 (dd, 1H; J=6.0 Hz, J=8.1 Hz), 4.33 (ddd, 1H; J=6.0 Hz, J=6.0 Hz, J=10.8), 6.25 (dd, 1H; J=5.7 Hz, J=3.0 Hz), 6.62 (dd, 1H; J=5.7 Hz, J=3.0 Hz), 7.42–7.49 (m, 2H), 7.50–7.58 (m, qH), 7.95–8.00 (m, 2H). ^{13}C-NMR ($CDCl_3$, 75 MHz): δ 25.4, 26.9, 44.1, 45.2, 55.1, 56.1, 67.7, 76.3, 76.6, 109.1, 125.6, 127.9, 128.8, 132.7, 134.4, 140.1, 160.2, 180.2. Elem. Anal. calc. for $C_{20}H_{21}NO_4$: C=70.78%, H=6.24%, N=4.13%; found: C=70.71%, H=6.38%, N=4.12%. $[\alpha]_D$ = –63.33 (c=0.75 in $CHCl_3$).

• (1*R*,6*R*)-6-[(*S*)-2,2-Dimethyl-1,3-dioxolan-4-yl]-4-methylcyclohex-3-en-1-spiro{4'[2'-phenyl-5'(4'*H*)-oxazolone]} **19**. ^{1}H-NMR ($CDCl_3$, 300 MHz): δ 1.12 (s, 3H), 1.35 (s, 3H), 1.75 (s, 3H), 2.10–2.25 (m, 2H), 2.36–2.45 (ddd, 1H; J=4.9 Hz, J=4.9 Hz, J=11.4 Hz), 2.50–2.70 (m, 2H), 3.65 (dd, 1H; J=7.2 Hz, J=6.0 Hz), 3.82 (dd, 1H; J=7.2 Hz, J=6.0 Hz), 4.05 (ddd, 1H; J=6.0 Hz, J=6.0 Hz, J=11.4 Hz), 5.30 (m, 1H), 7.42–7.50 (m, 2H), 7.50–7.58 (m, 1H), 7.94–7.99 (m, 2H). ^{13}C-NMR ($CDCl_3$, 75 MHz): δ 23.3, 25.0, 25.9, 27.0, 35.2, 43.6, 67.0, 68.4, 74.4, 108.8, 114.6, 125.9, 127.8, 132.6, 134.9, 160.9, 177.2. These spectra were determined from a mixture of **19+21**. Elem. Anal. calc. for $C_{20}H_{23}NO_4$: C=70.36%, H=6.79%, N=4.10%; found: C=70.42%, H=6.87%, N=4.00%.

X-Ray structure determination:: The room temperature single crystal X-ray determination is derivative of a unique diffreactometer data set (w/2θ scan mode; monochromatic MoKα radiation, λ=0.71073 Å) yielding 2449 independent reflections, none of these with F≥4.0s(F) were considered. The structure was solved by direct methods, using the SIR92 program, and refined using the SHEXL93 program.

Absorption corection was not applied in any case. Anisotropic thermal parametres were refined for C, N, O; (x, y, z, U_{iso}) H were also refined. Derivative conectivities, conformation and stereochemistry is shown pictorially in Figure 1; the geometry is esentially as expected. Atomic coordinates, bond lenghts, angles, and thermal parameters have been deposited in the Cambridge Crystallographic Data Centre.

Theoretical calculations: All the theoretical calculations were carried out using the AM1 Hamiltonian[12] as implemented in the MOPAC 6.0 program.[14]

Transition structures for all the reactions studied were located by means of the Eigenvector-following algorithm,[15] through the use of the "TS" keyword. Gradient norms were always below 0.1 kcal·mol^{-1}, and the existence of only one imaginary frequence, corresponding to the formation of the new C–C bonds, was checked in all cases by means of "FORCE" single point calculations.

Acknowledgements: This work was made possible by the generous financial support of the Comisión Interministerial de Ciencia y Tecnología (Project MAT96-1053-C02-01) and of the European Union (Contract CHRX CT93-0276). One of us (E.P.) thanks the Diputación General de Aragón for a grant.

REFERENCES

1. (a) Christensen, H. N.; Handlogten, M. E.; Lam, I.; Tager, H. S.; Zandl, R *J. Biol. Chem.* **1969**, *244*, 1510. (b) Christensen, H. N.; Cullen, A. M. *J. Biol. Chem.* **1969**, *244*, 1521. (c) Tager, H. S.; Christensen, H. N. *J. Am. Chem. Soc.* **1972**, *94*, 968.
2. (a) Cativiela, C.; López, P.; Mayoral, J. A. *Tetrahedron:Asymmetry* **1991**, *2*, 1295. (b) Cativiela, C.; Mayoral, J. A.; Avenoza, A.; Peregrina, J. M.; Lahoz, F. J.; Gimeno, S. *J. Org. Chem.* **1992**, *57*, 4664 . (c) Cativiela, C.; Díaz de Villegas, M. D.; Mayoral, J. A.; Avenoza, A.; Peregrina, J. M. *Tetrahedron:Asymmetry* **1993**, *4*, 677. (d) Cativiela, C.; Díaz de Villegas, M. D.; Avenoza, A.; Peregrina, J. M. *Tetrahedron* **1993**, *47*, 10987. (e) Pyne, S. G.; Safei, G. J.; Hockless, D. C. R.; Skelton, B. W.; Sobolev, A. N.; White, A. H. *Tetrahedron* **1994**, *48*, 941. (f) Cativiela, C.; Avenoza, A.; París, M.; Peregrina, J. M. *J. Org. Chem.* **1994**, *59*, 7774 . (g) Avenoza, A.; Cativiela, C.; Fernández-Recio, M. A.; Peregrina, J. M. *Tetrahedron:Asymmetry* **1996**, *7*, 721.
3. See for instance: (a) Rao, V. S.; Filler, R., in "Chemistry of Heterocyclic Compounds", vol. 45; Turchi, I. J., Ed.; John Wiley and Sons, Inc.; New York, 1986. (b) Mukerjee, A. K. *Heterocycles* **1987**, *26*, 1077.
4. Cativiela, C.; Mayoral, J. A.; Avenoza, A.; González, M.; Roy, M. A. *Synthesis* **1990**, 1114.
5. Avenoza, A.; Busto, J. H.; Cativiela, C.; Peregrina, J. M. *Tetrahedron* **1994**, *50*, 12989.
6. (a) Buñuel, E.; Cativiela, C.; Díaz de Villegas, M. D. *Tetrahedron:Asymmetry* **1994**, *5*, 157. (b) Buñuel, E.; Cativiela, C.; Díaz de Villegas, M. D.; García, J. I. *Tetrahedron:Asymmetry* **1994**, *5*, 759. (c) Buñuel, E.; Cativiela, C.; Díaz de Villegas, M. D. *Tetrahedron* **1995**, *51*, 8923.
7. (a) Cativiela, C.; García, J. I.; Mayoral, J. A.; Pires, E.; Royo, A. J.; Figueras, F. *Tetrahedron* **1995**, *51*, 1295. (b) Cativiela, C.; García, J. I.; Mayoral, J. A.; Pires, E.; Royo, A. J.; Figueras, F. *Appl. Catal. A* **1995**, *131*, 159.
8. Fraile, J. M.; García, J. I.; Mayoral, J. A.; Pires, E.; Tarnai, T.; Figueras, F. *Appl. Catal. A* **1996**, *136*, 113.
9. Cativiela, C.; García, J. I.; Mayoral, J. A.; Pires, E.; Brown, R. *Tetrahedron* **1995**, *51*, 9217.
10. (a) Cativiela, C.; Fraile, J. M.; García, J. I.; Mayoral, J. A.; Pires, E.; Royo, A. J.; Figueras, F.; de Mènorval, L. C. *Tetrahedron* **1993**, *49*, 4073. (b) Cativiela, C.; García, J. I.; Mayoral, J. A.; Pires, E.; Royo, A. J.; Figueras, F. *Tetrahedron:Asymmetry* **1993**, *4*, 621.
11. (a) Rhodes, C. N.; Brown, D. R. *J. Chem. Soc., Faraday Trans.* **1992**, *88*, 2269 (b) Rhodes, C.; Brown, D. R. *J. Chem. Soc., Faraday Trans.* **1993**, *89*, 1387. (c) García, J. I.; Mayoral, J. A.; Pires. E.; Brown, D. R.; Massam, J. *Catal. Lett.* **1996**, *37*, 261.
12. Dewar, M. J. S.; Zoebisch, E. G.; Healy, E. F.; Stewart, J. J. P. *J. Am. Chem. Soc.* **1985**, *107*, 3902.
13. Comds, A. P.; Armstrong, R. J. *Tetrahedron Lett.* **1992**, *43*, 6419.
14. Stewart, J. J. P. MOPAC 6.0, QCPE 455.
15. Baker, J. *J. Comput. Chem.* **1986**, *7*, 385.

(*Received in UK* 24 *May* 1996)