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Study of the Asymmetric Diels-Alder Reaction of a Chiral Azlactone

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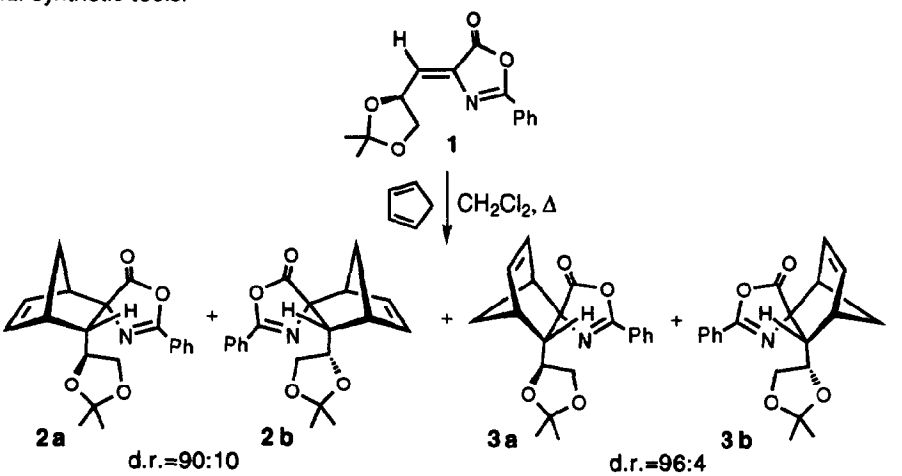
Abstract: *The chiral Z-azlactone derived from 1,2-O-isopropylidene-D-glyceraldehyde underwent diastereoselective Diels-Alder reaction with cyclopentadiene. Catalyst, temperature and solvent dependence of the product ratio is described.*

Cyclic non-metabolizable amino acids have useful biological properties, in particular α-amino acids with a norbornane skeleton have been used to study the transport of amino acids with hydrophobic side chains (i.e. leucine, isoleucine and valine).[1] Moreover, it has been shown that the incorporation of one or more conformationally-constrained amino acids (generally cyclic amino acids) into bioactive peptides often gives rise to analogues with enhanced biological activities.[2]

α,β-Didehydroamino acid derivatives are useful prochiral building blocks in synthetic organic chemistry. In particular azlactones unsaturated in C_4 have proved to be versatile intermediates in the synthesis of amino acids,[3] cycloaliphatic[4] and cyclopropylamino acids.[5] Moreover, these compounds are easily transformed into N-acyl-α,β-didehydroamino acid derivatives which are powerful synthetic tools.[6]



Scheme 1

In an previous communication[7] we reported the reaction as a dienophile of the chiral *Z*-azlactone derived from glyceraldehyde[8] with an excess of cyclopentadiene at room temperature to give a mixture of the four possible Diels-Alder adducts (Scheme 1). These compounds were easily isolated by medium-pressure chromatography and fully characterised on the basis of NOE difference ^{1}H NMR experiments and single crystal X-ray analysis.

The study of catalyst influence previously communicated showed that the use of some organometallic compounds, such as $EtAlCl_2$, Et_3Al and $TiCl_4$ involved the formation of cycloadducts from *E*-azlactone together with the four adducts from *Z*-azlactone and the amount of the by-products obtained depended on the catalyst used and was greater when $TiCl_4$ and $AlCl_3$ were used. Other catalysts, such as ZnI_2 or lithium perchlorate (5.0 M in diethyl ether) did not improve either *exo* selectivity or *exo* and *endo* diastereofacial selectivity (Table 1). We therefore decided to study some factors influencing uncatalysed Diels-Alder reactions.

Table 1. Catalyst influence on Diels-Alder reaction of **1** with cyclopentadiene at room temperature.

temp (°C)	catalyst (eq)	t	Conversion	*exo/endo*[a]	*exo* d.r.[a]	*endo* d.r.[a]
25	none	2 h	100	64/36	90/10	96/4
25	$LiClO_4$[b]	2 h	100	56/44	80/20	78/22
25	$EtAlCl_2$(0.2)[c]	1 h	100	72/28	95/5	97/3
25	$AlCl_3$(0.2)[c]	1 h	100	73/27	93/7	97/3
25	$TiCl_4$(0.2)[c]	0.5 h	100	75/25	93/7	>98/2
25	BF_3(1)	0.5 h	100	77/23	94/6	94/6
25	ZnI_2(0.2)	0.5 h	100	60/40	77/23	66/34

[a] The product ratio was determined by HPLC. Column radial pack silica (8 mp 10 mm). Eluent hexane-ethyl acetate 96/4. Flow rate 3.5 ml/min. Detection 254 nm. [b] The reaction was performed in a solution 5.0 M of lithium perchlorate in diethyl ether. [c] Cycloadducts from *E*-azlactone were observed

As it has been reported that the rate, *endo/exo* selectivity and diastereofacial selectivities of intermolecular Diels-Alder cycloadditions can be greatly influenced by the polarity of the reaction solvent,[9] we decided to study the influence of the solvent on the stereochemical course of this diastereoselective Diels-Alder reaction, as well as the influence of temperature.

When a solution of azlactone **1** in the chosen solvent containing an excess of cyclopentadiene (2.5 equiv.) was stirred at room temperature for 2 hours, the formation of four Diels-Alder adducts was observed. Examination of the crude reaction mixture by HPLC indicated total conversion, a slight preference for the compounds in which the carbonyl group had the *exo* stereochemistry, usual in α,β-didehydroamino acid derivatives,[6,10] as well as a high diastereofacial selectivity in the formation of both *exo* and *endo* adducts.

As can be seen in Table 2, at room temperature the *exo/endo* selectivity was not influenced by the solvent polarity, *exo* diastereofacial selectivity was usually better in non-polar solvents and

endo diastereofacial selectivity was, in all cases, excellent and better than *exo* diastereofacial selectivity.

When the reaction was carried out at low temperature (-40 °C) there was a decrease in the reaction rate and in some cases 4 days were not enough to reach total conversion at this temperature. Nevertheless, in all cases, the *exo* selectivity was slightly better and the formation of both *exo* and *endo* adducts was highly diastereoselective.

An additional decrease in the temperature reaction (-75 °C) did not improve *exo/endo* selectivity and considerably decreased the reaction rate so that two weeks were not enough to reach the total conversion in any case.

Table 2. Solvent influence on Diels-Alder reaction of **1** with cyclopentadiene

Solvent	temp (°C)	t	Conversion	exo/endo[a]	exo d.r.[a]	endo d.r.[a]
Benzene	20	2 h	100	66/34	93/7	97/3
Dioxane	20	2 h	100	66/34	> 98/2	> 98/2
Acetonitrile	20	2 h	100	66/34	80/20	91/9
Tetrahydrofurane	20	2 h	100	67/33	91/9	94/4
Dichloromethane	20	2 h	100	64/36	90/10	96/4
Acetone	20	2 h	100	67/33	85/15	94/6
n-hexane	20	2 h	100	67/33	96/4	> 98/2
Toluene	20	2 h	100	67/33	93/7	97/3
Ethyl acetate	20	2 h	100	66/34	90/10	96/4
Diethyl ether	20	2 h	100	66/34	95/5	97/3
Acetonitrile	- 40	4 d	83	69/31	80/20	93/7
Tetrahydrofurane	- 40	4 d	72	70/30	92/8	> 98/2
Dichloromethane	- 40	4 d	82	71/29	98/2	> 98/2
Acetone	- 40	4 d	89	71/29	86/14	96/4
n-hexane	- 40	4 d	13	67/33	95/5	97/3
Toluene	- 40	4 d	95	70/30	96/4	> 98/2
Ethyl acetate	- 40	4 d	72	70/30	92/8	> 98/2
Diethyl ether	- 40	4 d	55	67/33	96/4	> 98/2

[a] The product ratio was determined by HPLC. Column radial pack silica (8 mp 10 mm). Eluent hexane-ethyl acetate 96/4. Flow rate 3.5 ml/min. Detection 254 nm.

An X-ray structure determination of the absolute configuration of the major *exo* adduct[7] showed a *(1R, 2S, 3R, 4S)* stereochemistry for this compound and in order to rationalise the stereochemical course of this Diels-Alder reaction we have combined these experimental results with theoretical studies. AM1 semi-empirical calculations[11] were carried out to evaluate the conformational energy curve derived from rotation around the C_1-C_2 bond (Figure 1).

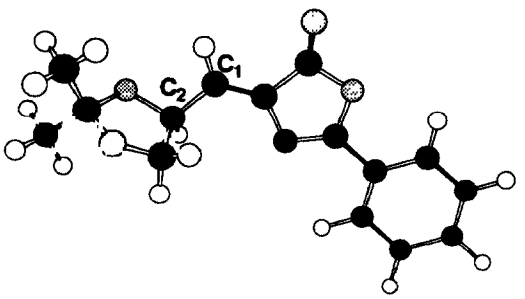


Figure 1

It is apparent from the curve in Figure 2 that there is only one deep minimum, and hence, only a single conformation can be expected for this compound. The exact location of the minimum was achieved by full optimisation of the molecular coordinates, leading to a dihedral angle between the hydrogen atoms linked to C_1 and C_2 of 131 degrees. This value is in excellent agreement with that estimated by applying the Karplus type of equation developed especially for Csp^2-Csp^3 rotamer by Garbish[12] (J = 7.4 Hz, dihedral angle 137 degrees).

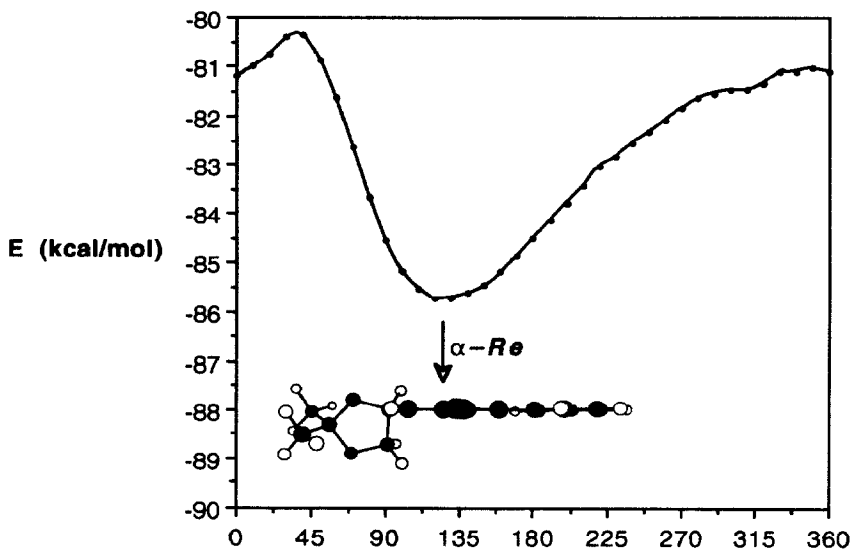


Figure 2

In this conformation, the hydrogen at the stereogenic centre occupied a *syn-clinal* position in the plane of the neighbouring π-system. This is responsible for the steric shielding of the $C_{\alpha\text{-}Si}$ side of the olefinic bond, as shown by the model in Figure 2, so that the attack of the reagent should come almost exclusively from the $C_{\alpha\text{-}Re}$ side. Admittedly, the conformational preference of the

dienophile cannot be directly related to the transition state through which most of the reaction takes place. However, in this case, the theoretical result is in accordance with the observed sense of diastereofacial selectivity on reacting azlactone **1** with cyclopentadiene in the *exo* approach as well as with the high values of diastereofacial selectivity obtained.

If we accept this theoretical interpretation, we can assume that the absolute configuration of the major *endo* adduct is *(1R, 2R, 3S, 4S)* as the *endo* approach of the diene to the olefinic bond must also come almost exclusively from the $C_{\alpha\text{-}Re}$ side, which is less sterically hindered.

To sum up, since *endo* and *exo* adducts are easily isolated by flash chromatography we can conclude that the best way to carry out the Diels-Alder reaction is to work at room temperature and use hexane (an innocuous solvent) as a solvent. In these conditions the rate and the *endo* and *exo* diastereofacial selectivity are excellent and allow us to obtain diastereomerically pure samples of both adducts.

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EXPERIMENTAL

Apparatus: ^{1}H-NMR and ^{13}C-NMR spectra were recorded on a Varian Unity 300 spectrometer in deuteriochloroform using the solvent signal as internal standard. Chemical shifts are expressed in ppm. IR spectra were recorded on a Perkin-Elmer 1600 FTIR infrared spectrophotometer. Optical rotations were measured on a Perkin-Elmer 241-C polarimeter at 25°C. Melting points were determined on a Büchi 510 capillary melting point apparatus and are uncorrected. HPLC analyses were carried out with a Waters 600-E chromatograph equipped with a photodiode array detector. Elemental analyses were made on a Perkin-Elmer 2400 C,H,N,S elemental analyser.

Chemicals: The reactions were carried out under Ar with magnetic stirring. Solvents were dried prior to use. Dicyclopentadiene, hippuric acid and 1,2:5,6-di-O-isopropylidene-*D*-mannitol were purchased from Aldrich Chemical Co. TLC was performed on Merck pre-coated silicagel plates, which were visualised using UV light. Medium pressure chromatography was performed using 230-400 mesh (Merck) silicagel.

Z-2-Phenyl-4-[*(S)*- 2,2-dimethyl-1,3-dioxolan-4-ylmethylen]-5(4H)-oxazolone **1:**

Lead tetraacetate (1.1 g, 2.52 mmol) was added to a solution of 1,2:5,6-di-O-isopropylidene-*D*-mannitol (0.6 g, 2.29 mmol) in dry THF (10 ml) at 0 °C and the mixture was stirred for 5 min. Hippuric acid (0.533 g, 2.98 mmol) and acetic anhydride (0.93 ml, 9.85 mmol) were then added and stirring was continued under reflux conditions for 15 h. The reaction mixture was evaporated in vacuo and the residue was then dissolved in chloroform, washed successively with a saturated aqueous sodium hydrogen carbonate solution and water, dried with magnesium sulphate and concentrated in vacuo. Purification of the residue by flash chromatography on a silicagel column (eluent hexane/ethyl acetate 85/15) afforded 0.49 g (60% yield) of pure *Z*-2-phenyl-4-[*(S)*- 2,2-dimethyl-1,3-dioxolan-4-ylmethylen]-5(4H)-oxazolone **1.**

Mp 62-64°C; $[\alpha]_D$ = + 22 (c = 1 in $CHCl_3$); IR 1804, 1681 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.42 (s, 3H), 1.46 (s, 3H), 3.80 (dd, 1H, J = 8.3 Hz, J = 6.7 Hz), 4.32 (dd, 1H, J = 8.3 Hz, J = 6.7 Hz), 5.36 (m, 1H, J = 7.5 Hz, J = 6.7 Hz, J = 6.7 Hz), 6.58 (d, 1H, J = 7.5 Hz), 7.42-7.50 (m, 2H), 7.54-7.62 (m, 1H), 8.00-8.08 (m, 2H). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 25.5, 26.5, 68.9, 72.2, 110.3, 125.0, 128.4, 128.9, 133.6, 133.9, 136.9, 163.9, 165.4. Anal. cal. for $C_{15}H_{15}NO_4$ C: 65.93, H: 5.53, N: 5.12; found C: 66.18, H: 5.40, N: 5.29.

General Procedure for uncatalysed Diels-Alder reactions at room temperature

A typical experiment was run as follows: Freshly distilled cyclopentadiene (10 μl, 0.125 mmol) was added to a stirred solution of azlactone **1** (14 mg, 0.05 mmol) in the chosen solvent (0.2 ml) and the mixture was stirred at the appropriate temperature for the time indicated in Table 2. For analysis the solvent was evaporated under vacuum to give a mixture, the composition of which was analysed by HPLC.

Isolation of Diels-Alder cycloadducts 2a, 2b, 3a and 3b for characterization

Freshly distilled cyclopentadiene (1 ml, 12.5 mmol) was added by means of a syringe to a stirred solution of azlactone **1** (1.10 g, 4 mmol) and zinc chloride (319 mg, 1 mmol) in dry methylene chloride (10 ml) under argon and the mixture was stirred at room temperature for 2 h. After completion the solution was treated with $Na_2CO_3.10H_2O$ (1g). The solution was filtered and washed with water (3 x 30 ml), the organic phase was dried ($MgSO_4$), and evaporated to dryness in vacuo to afford a mixture of cycloadducts **2a**, **2b**, **3a** and **3b** as a pale yellow oil ; yield: 1.28 g (95%). Medium pressure chromatography on silicagel using hexane-ethyl acetate 9/1 enabled us to isolate of the four Diels-Alder adducts in diastereomerically pure form.

(1R, 2S, 3R, 4S)- [*(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} **(2a).**

Mp 162 °C; $[\alpha]_D$ = + 142.8 (c = 1 in $CHCl_3$); IR 1806, 1648 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.27 (s, 3H), 1.36 (s, 3H), 1.79 (ddd, 1H, J_{7a-7s} = 9.3 Hz, J_{7a-1} = 1.8 Hz J_{7a-4} = 1.8 Hz, H_{7a}), 2.23 (d,1H, J_{7s-7a} = 9.3 Hz, H_{7s}), 2.64 (dd, 1H, J_{3x-A} = 10.2 Hz, J_{3x-4} = 3.3 Hz, H_{3x}), 3.00-3.03 (m, 1H, H_1), 3.10-3.15 (m, 1H, H_C), 3.27-3.31 (m, 1H, H_4), 3.71-3.84 (m, 2H, H_A, H_B), 6.31 (dd, 1H, J_{6-5} = 5.4 Hz, J_{6-1} = 2.7 Hz, H_6), 6.57 (dd, 1H, J_{5-6} = 5.4 Hz, J_{5-4} = 3 Hz, H_5), 7.42-7.48 (m, 2H, Arom), 7.52-7.58 (m, 1H, Arom), 7.90-7.94 (m, 2H, Arom). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 25.3, 26,8, 45.8, 55.3, 56.8, 68.3, 75.1, 76.1, 108.6, 125.6, 127.8, 128.8, 132.8, 135.8, 137.5, 160.8, 181.5. Anal. cal. for $C_{20}H_{21}NO_4$ C: 70.78, H: 6.24, N: 4.13; found C: 70.53, H: 6.14, N: 4.57.

(1S, 2R, 3S, 4R)- [*(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} **(2b).**

Mp 83 °C; $[\alpha]_D$ = - 103.4 (c = 1 in $CHCl_3$); IR 1807, 1657 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.07 (s, 3H), 1.19 (s, 3H), 1.58 (ddd, 1H, J_{7a-7s} = 9 Hz, J_{7a-1} = 1.8 Hz J_{7a-4} = 1.8 Hz, H_{7a}), 2.23 (d,1H, J_{7s-7a} = 9 Hz, H_{7s}), 2.64 (dd, 1H, J_{3x-A} = 10 Hz, J_{3x-4} = 3 Hz, H_{3x}), 2.85-2.91 (m, 1H, H_4), 3.02-3.07 (m, 1H, H_1), 3.59 (dd, 1H, J_{C-A} = 7.6 Hz, J_{C-B} = 7.6 Hz, H_C), 3.81 (ddd, 1H, J_{A-3x} = 10 Hz, J_{A-B} = 5.5 Hz, J_{A-C} = 7.6 Hz, H_A), 3.95 (dd, 1H, J_{B-A} = 5.5 Hz, J_{B-C} = 7.6 Hz, H_B), 6.30-6.38 (m, 2H, H_5, H_6), 7.40-7.46 (m, 2H, Arom), 7.48-7.56 (m, 1H, Arom), 7.90-7.96 (m, 2H, Arom).^{13}C NMR ($CDCl_3$, 75 MHz) δ 25.6, 26,8, 45.1, 47.1, 53.9, 57.1, 68.2, 75.3, 75.6, 108.8, 126.5, 127.8, 128.5, 132.2, 135.0, 137.1, 160.1, 182.5. Anal. cal. for $C_{20}H_{21}NO_4$ C: 70.78, H: 6.24, N: 4.13; found C: 70.59, H: 6.07, N: 4.24.

(1S, 2S, 3R, 4R)- [*(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} **(3a).**

Mp 145 °C; $[\alpha]_D$ = - 27.6 (c = 0.5 in $CHCl_3$); IR 1809, 1647 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.31 (s, 3H), 1.33 (s, 3H), 1.66-1.72 (m, 1H, H_{7a}), 1.99 (dd, 1H, J_{3n-A} = 10.2 Hz, J_{3n-4} = 1.8 Hz, H_{3n}), 2.37 (d,1H, J_{7s-7a} = 9 Hz, H_{7s}), 2.80-2.84 (m, 1H, H_1), 3.11 (dd, 1H, J_{C-A} = 6.9 Hz, J_{C-B} = 8.1 Hz, H_C), 3.26-3.31 (m, 1H, H_4), 3.87 (dd, 1H, J_{B-A} = 6.3 Hz, J_{B-C} = 8.1 Hz, H_B), 4.23 (ddd, 1H, J_{A-3n} = 10.2 Hz, J_{A-B} = 6.3 Hz, J_{A-C} = 6.9 Hz, H_A), 6.19 (dd, 1H, J_{6-5} = 5.7 Hz, J_{6-1} = 3 Hz, H_6), 6.60 (dd, 1H, J_{5-6} = 5.7 Hz, J_{5-4} = 3.3 Hz, H_5), 7.42-7.50 (m, 2H, Arom), 7.53-7.60 (m, 1H, Arom), 7.94-8.00 (m, 2H, Arom). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 25.4, 26,7, 46.7, 46.8, 56.0, 57.7, 68.6, 73.8, 76.4, 108.6, 125.7, 127.8, 128.8, 131.8, 132.8, 141.7, 160.2, 179.8. Anal. cal. for $C_{20}H_{21}NO_4$ C: 70.78, H: 6.24, N: 4.13; found C: 70.36, H: 5.98, N: 4.12.

(1R, 2R, 3S, 4S)- [*(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} **(3b).**

Mp 98 °C; $[\alpha]_D$ = + 34.5 (c = 1 in $CHCl_3$); IR 1807, 1651 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.11 (s, 3H), 1.20 (s, 3H), 1.65-1.72 (m, 1H, H_{7a}), 2.08 (dd, 1H, J_{3n-A} = 9.6 Hz, J_{3n-4} = 1.8 Hz, H_{3n}), 2.37 (d,1H, J_{7s-7a} = 8.7 Hz, H_{7s}), 2.70-2.74 (m, 1H, H_4), 2.86-2.90 (m, 1H, H_1), 3.63 (dd, 1H, J_{C-A} = 7.6 Hz, J_{C-B} = 7.6 Hz, H_C), 4.07 (dd, 1H, J_{B-A} = 5.4 Hz, J_{B-C} = 7.6 Hz, H_B), 4.21 (ddd, 1H, J_{A-3n} = 9.6 Hz, J_{A-B} = 5.5 Hz, J_{A-C} = 7.6 Hz, H_A), 6.23 (dd, 1H, J_{6-5} = 5.7 Hz, J_{6-1} = 3 Hz, H_6), 6.55 (dd, 1H, J_{5-6} = 5.7 Hz, J_{5-4} = 3.3 Hz, H_5), 7.42-7.48 (m, 2H, Arom), 7.50-7.58 (m, 1H, Arom), 7.94-8.00 (m, 2H, Arom). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 25.6, 26,8, 45.4, 47.7, 54.8, 57.7, 68.4, 73.8, 75.6, 108.7, 126.6, 127.8, 128.6, 132.1, 132.3, 141.5, 159.7, 180.6. Anal. cal. for $C_{20}H_{21}NO_4$ C: 70.78, H: 6.24, N: 4.13; found C: 70.92, H: 6.37, N: 4.02.

REFERENCES

1. a) Christensen, H. N.; Handlogten, M. I.; Lam, I.; Tager, H. S.; Zand, R. *J. Biol. Chem.*, **1969**, *244*, 1510-1520. b) Christensen, H. N.; Cullen, A. M. *J. Biol. Chem.*, **1969**, *244*, 1521-1526. c) Tager, H. S.; Christensen, H. N. *J. Am. Chem. Soc.*, **1972**, *94*, 968-972.
2. Gelbein, C. G.; Carraher, C. E.; Jr, 'Bioactive Polymer systems', Plenum, New York 1985.
3. (a) Badsashah, A.; Khan, N. H.; Kidwai, A. R.; *J. Org. Chem.*, **1972**, *37*, 2196. (b) Karpeiskaya, E. I.; Levitina, E. S.; Godunova, L. F.; Klavunovskii, E. I.; *J. Mol. Catal.*, **1986**, *34*, 129.
4. (a) Cativiela, C.; Mayoral, J. A.; Avenoza; Gonzalez, M.; *Synthesis*, **1990**, 1114. (b) Cativiela, C.; Diaz-de-Villegas, M. D.; Mayoral, J. A.; Avenoza; A.; Peregrina, J. M.; *Tetrahedron*, **1993**, *49*, 677. (c) Cativiela, C.; Diaz-de-Villegas, M. D.; Avenoza; A.; Peregrina, J. M.; *Tetrahedron*, **1993**, *49*, 10987.
5. (a) Pages, R. A.; Burger, A.; *J. Med. Chem.*, **1966**, *9*, 766. (b) Pages, R. A.; Burger, A.; *J. Med. Chem.*, **1967**, *10*, 435. (c) Bernabé, M.; Fernández-Alvarez, M.; Penadés-Ullate, S.; *An. Quim.*, **1972**, *68*, 501. (d) Hines, J. W. ; Breitholle, E. G. ; Sato, M.; Stammer, C. H.; *J. Org. Chem.*, **1976**, *41*, 1466. (e) King, S. W. ; Riordan, J. M. ; Holt, E M.; Stammer, C. H.; *J. Org. Chem.*, **1982**, *47*, 3270. (f) Arenal, I.; Bernabé, M.; Fernández-Alvarez, M.; Penadés-Ullate, S.; *Synthesis*, **1985**, 773. (g) Bland, J.; Shah, A.; Bortolusi, A.; Stammer, C. H.; *J. Org. Chem.*, **1988**, *53*, 992.

6. For a review see Schmidt, U.; Lieberknecht, A.; Wild, J.; *Synthesis*, **1988**, 159.
7. Buñuel, E.; Cativiela, C,; Diaz-de-Villegas, M. D.; *Tetrahedron: Asymmetry*, **1994**, *5*, 157
8. Combs, A. P.; Amstrong, R. W.; *Tetrahedron Lett.*, **1992**, *33*, 6419.
9. (a) Cativiela, C.; Garcia, J. I.; Mayoral, J. A.; Avenoza, A.; Peregrina, J. M.; Roy, M. A.; *J. Phys. Org. Chem.*, **1991**, *4*, 48. (b) Cativiela, C.; Garcia, J. I.; Mayoral, J. A.; Royo, A. J.; Salvatella, L.; Assfeld, X.; Ruiz-Lopez, M. F.; *J. Phys. Org. Chem.*, **1992**, *5*, 230.
10. (a) Crossley, M. J.; Hambley, T. W.; Stamford, A. W.; *Aust. J. Chem.*, **1990**, *43*, 1827. (b) Schmidt, U.; Lienerknecht, A.; Wil, J.; *Synthesis*, **1988**, 159.
11. Dewar, M. J. S.; Zoebisch, E. G.; Healy, E. F.; Stewart, J. J. P.; *J. Am. Chem. Soc.*, **1985**, *107*, 3902.
12. (a) Garbish, E. W.; *J. Am. Chem. Soc.*, **1964**, *86*, 5561. (b) Vorontsva, L.; Bochkov, F.; *Org. Magn. Reson.;* **1974**, *6*, 654. (c) Jankowski, K,; Berlanger, J.; Soler, F.; Zamojski, A.; *Org. Magn. Reson.;* **1979**, *12*, 544.

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