Synthesis of Aliphatic (*E*)-α,β-Unsaturated Amides with High Diastereoselectivity from α,β-Epoxyamides Promoted by SmI_2/HMPA

José M. Concellón*[a] and Eva Bardales[a]

Keywords: Amides / α,β-Epoxyamides / Samarium / Synthesis design

Synthesis of aliphatic (*E*)-α,β-unsaturated amides **2**, in which the C=C bond is di- or trisubstituted, is achieved by using samarium diiodide and HMPA. The starting compounds **1** were easily prepared by the reaction of the corresponding lithium or potassium enolates of α-chloroamides with aldehydes. A mechanism to explain this process is proposed.

Introduction

Samarium diiodide has been shown to be a useful reagent in reductive elimination reactions in recent years.[1] We have described the diastereoselective synthesis of (*Z*)-vinyl halides from *O*-acetylated 1,1-dihaloalkan-2-ols,[2] the preparation of (*E*)-α,β-unsaturated esters[3] or amides[4] from 2-halo-3-hydroxy esters or amides, respectively, and the formation of (*Z*)-vinylsilanes from 1-chloro-1-trialkylsilylalkan-2-ols. In addition, we have described the transformation of α,β-epoxy esters into (*E*)-α,β-unsaturated esters.[5] In this respect, samarium diiodide has been used to transform epoxides into alkenes, however, this reaction takes place with poor diastereoselectivity,[6] and to the best of our knowledge no general transformation of aliphatic α,β-epoxyamides into the synthetically interesting aliphatic α,β-unsaturated amides has been reported.

α,β-Unsaturated amides are an important class of compounds not only for their biological[7] and insecticidal[8] activities but also because of their presence in the structure of natural products.[9] However, the preparation of α,β-unsaturated amides has scarcely been reported. For these reasons, an easy and general transformation of aliphatic α,β-epoxyamides into aliphatic α,β-unsaturated amides would be desirable.

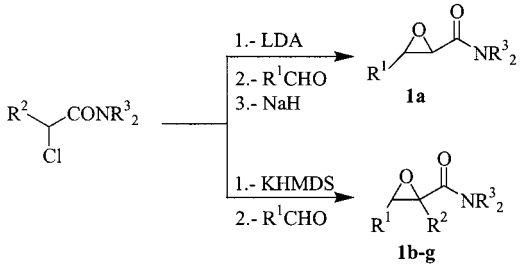
Recently, we described the transformation, with total or high diastereoselectivity, of aromatic α,β-epoxyamides, in which the oxirane ring is trisubstituted, into (*Z*)-α,β-unsaturated amides, promoted by SmI_2 in the presence of MeOH, and the synthesis of (*E*)-α,β-unsaturated amides from aromatic di- or tetrasubstituted α,β-epoxyamides by using SmI_2.[10]

[a] Departamento de Química Orgánica e Inorgánica, Universidad de Oviedo,
Julián Clavería, 8, 33071 Oviedo, Spain
Fax: (internat.) +34-98-5103446
E-mail: jmcg@sauron.quimica.uniovi.es

Here, we report a general synthesis of aliphatic α,β-unsaturated amides **2** from α,β-epoxyamides with high diastereoselectivity by using SmI_2 in the presence of HMPA.

Results and Discussion

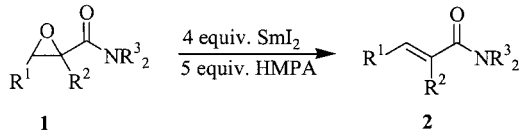
The disubstituted epoxyamide **1a** was prepared by reaction of the lithium enolate of chloroacetamide (generated by treatment of α-chloroacetamide with LDA at −78 °C) with cyclohexanecarbaldehyde and subsequent treatment with sodium hydride. Trisubstituted epoxyamides **1b−g** were obtained by reaction of the corresponding potassium enolates of α-chloroamides (generated by treatment of α-chloroamides with potassium hexamethyldisilazide at −78 °C) with different aldehydes at temperatures ranging from −78 to 25 °C (Scheme 1).



Scheme 1

When the reaction conditions used to obtain aromatic α,β-unsaturated amides from α,β-epoxyamides[10] were applied to aliphatic α,β-epoxyamides, no elimination reaction was observed. For this reason and because the reduction potential of SmI_2 is higher in a solution of HMPA and THF,[11] we carried out the β-elimination reaction of aliphatic α,β-epoxyamides by using SmI_2 in the presence of HMPA.

Thus, treatment of different α,β-epoxyamides **1** with a solution of SmI_2 (4 equiv.) in THF and HMPA (5 equiv.)[12] for 30 min at room temperature afforded, after hydrolysis, the corresponding α,β-unsaturated amides **2** with high diastereoselectivity and in good yields (Scheme 2, Table 1).

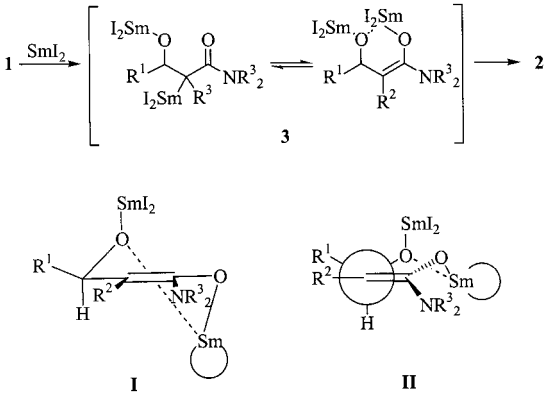


Scheme 2

Table 1. Synthesis of aliphatic (*E*)-α,β-unsaturated amides **2**

2[a]	R^1	R^2	R^3	*de* (%)[b]	Yield (%)[c]
2a	Cyclohexyl	H	*i*Pr	>98	40
2b	Bu	Me	Et	>98	70
2c	Bu	Ph	Et	83	82
2d	C_7H_{15}	Me	Et	95	64
2e	$Me_2C{=}CH(CH_2)_2CH(Me)CH_2$	Me	Et	94	85
2f	MeCH(Ph)	Me	Et	95	83
2g	Cyclohexyl	Me	Et	93	91

[a] All products were fully characterized by spectroscopic methods (IR, NMR, and MS). [b] Determined on crude reaction products by ^{1}H NMR spectroscopy and GC-MS. [c] Yield of isolated product after column chromatography based on compound **1**.



Scheme 3

This proposed methodology provides a general route to obtain α,β-unsaturated amides **2**, in which R^1, R^2 and R^3 can be varied widely. Thus linear, branched, cyclic or unsaturated aliphatic aldehydes may be used to introduce different R^1 groups; R^2 may also be varied using different α-chloroamides to prepare the starting compounds **1** (Scheme 1).

The *de* was calculated on the crude reaction products by ^{1}H NMR spectroscopy and GC-MS.

The (*E*) stereochemistry of the C−C double bond of the α,β-unsaturated amide **2a** was assigned from the value of the coupling constant between the olefinic protons in the ^{1}H NMR spectrum (J = 15.1 Hz). In the case of trisubstituted α,β-unsaturated amides the stereochemistry was established by comparison of the ^{1}H NMR and ^{13}C NMR spectra with those of authentic samples, as reported in the literature.[4]

It is noteworthy that although the starting α,β-epoxyamides were mixtures of *cis* and *trans* diastereoisomers, the corresponding α,β-unsaturated amides were obtained with total or very high (*E*)-selectivity.

Different behavior was observed when α,β-epoxyamides **1**, derived from ketones instead of aldehydes, and α-chloroamides were used. Instead of the α,β-unsaturated amides, β,δ-unsaturated α-hydroxyamides were obtained.[13]

The observed stereochemistry of products **2** may be explained by assuming a chelation-control model (Scheme 3). Thus, reduction of the C_α−O bond generates the enolate intermediate **3**, in which the chelation of the Sm^{III} center with the carbonyl oxygen atom of the amide group produces a six-membered ring. Tentatively we propose a transition state model **I** with the R^1 in the equatorial orientation (to avoid 1,3-diaxial interactions). As depicted in **II** (C2−C3 Newman projection of **I**) R^1 and R^2 show a *cis* relationship. Consequently, elimination from **I** affords (*E*)-α,β-unsaturated amides. This transition state could also explain the total or very high diastereoselectivity observed in the β-elimination reaction from a mixture of diastereoisomers of **1**.

The proposed reduction of the C_α−O bond, instead of the C_β−O bond, is supported by the fact that the treatment of aliphatic α,β-epoxyamides with SmI_2 in the presence of water affords β-hydroxyamides.[14]

Conclusion

In conclusion, we present an easy and general preparation of aliphatic α,β-unsaturated amides **2** with high diastereoselectivity by treating α,β-epoxyamides with samarium diiodide and HMPA. The reaction is general, and the C−C double bond of **2** can be di- or trisubstituted. A mechanism has been proposed to explain this reaction.

Experimental Section

General Remarks: Reactions requiring an inert atmosphere were conducted under dry nitrogen, and the glassware was oven dried (120 °C). THF was distilled from sodium/benzophenone ketyl immediately prior to use. All reagents were purchased in the highest quality available and were used without further purification. ^{1}H NMR spectra were recorded at 200 or 300 MHz. ^{13}C NMR spectra and DEPT experiments were determined at 50 or 75 MHz. GC-MS and HRMS were measured at 70 eV. Chemical shifts are given in δ (ppm) relative to TMS as internal standard in the case of ^{1}H NMR spectra and relative to $CDCl_3$ or [D_6]DMSO in the case of ^{13}C NMR spectra.

General Procedure for the Synthesis of Compound 1a: A solution of lithium diisopropylamide [prepared from MeLi (3.3 mL of a 1.5 M solution) in diethyl ether (5 mmol) and diisopropylamine (0.8 mL,

5 mmol) in THF (25 mL) at 0 °C] was added dropwise to a stirred solution of the *N*,*N*-diisopropyl chloroacetamide (0.8 g, 4.5 mmol) in dry THF (4 mL) at −78 °C. After stirring for 10 min, a solution of the cyclohexanecarbaldehyde (0.4 mL, 3.5 mmol) in dry THF (4.5 mL) was added dropwise at −78 °C and the mixture was stirred for 1 h. The reaction mixture was quenched with an aqueous saturated solution of NH_4Cl (20 mL) followed by extraction with diethyl ether which provided the corresponding 2-chloro-3-hydroxyamide, which was treated with sodium hydride (1 g, 45 mmol) at 25 °C. The mixture was stirred for 2.5 h at this temperature, quenched with H_2O (10 mL) and then extracted with diethyl ether (3 × 10 mL) to afford crude 2,3-epoxyamide **1a**, which was purified by flash column chromatography on silica gel (hexane/EtOAc), yielding pure compound **1a**.

3-Cyclohexyl-2,3-epoxy-*N*,*N*-diisopropylpropanamide (1a): Yield: 64%, 567 mg. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.23 (d, *J* = 6.7 Hz, 3 H), 1.25 (d, *J* = 6.7 Hz, 3 H), 1.42 (d, *J* = 6.7 Hz, 6 H), 2.06−1.57 (m, 11 H), 2.93−2.86 (m, 1 H), 3.53−3.37 (m, 1 H), 3.53 (d, *J* = 4.4 Hz, 1 H) 4.34−4.21 (m, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 18.8 (CH_3), 19.1 (CH_3), 19.4 (CH_3), 19.7 (CH_3), 24.1 (CH_2), 24.2 (CH_2), 25.0 (CH_2), 27.5 (CH_2), 29.1 (CH_2), 35.5 (CH), 44.6 (CH), 46.6 (CH), 53.5 (CH), 60.0 (CH), 164.2 (C) ppm. IR (film): $\tilde{\nu}$ = 2953, 1651, 1454, 1372, 1136 2953, 1651, 1454, 1372, 1136 cm^{-1}; R_f = 0.2 (hexane/EtOAc, 3:1)

General Procedure for the Synthesis of Compounds 1b−g: A solution of potassium hexamethyldisilazide (6.5 mL of a 0.5 M solution in toluene, 3.25 mmol) was added dropwise to a stirred solution of the appropriate 2-chloroamide (2.5 mmol) in dry THF (4 mL) at −78 °C. After stirring for 10 min, a solution of the corresponding aldehyde (2.5 mmol) in dry THF (4 mL) was added dropwise at −78 °C and the mixture was warmed to room temperature. The resulting solution was quenched with an aqueous saturated solution of NH_4Cl (10 mL) followed by extraction with diethyl ether (3 × 10 mL) provided crude 2,3-epoxyamides **1b−g**, which were purified by column flash chromatography over silica gel (hexane/EtOAc) affording pure compounds **1b−g**.

2,3-Epoxy-*N*,*N*-diethyl-2-methylheptanamide (1b): Yield: 55%, 294 mg. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 0.96−076 (m, 6 H), 1.07 (t, *J* = 7.1 Hz, 6 H), 1.15 (t, *J* = 7.1 Hz, 6 H), 1.43 (s, 6 H), 1.87−1.24 (m, 8 H), 3.02−2.96 (m, 4 H), 3.59−3.12 (m, 8 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 12.8 (CH_3), 13.4 (CH_3), 14.2 (CH_3), 14.4 (CH_3), 14.6 (CH_3), 15.8 (CH_3), 15.6 (CH_3), 15.9 (CH_3), 25.1 (CH_2), 27.9 (CH_2), 28.6 (CH_2), 39.5 (CH_2), 41.5 (CH_2), 60.6 (C), 61.0 (CH), 62.7 (C), 169.9 (C), 170.0 (C) ppm. IR (film): $\tilde{\nu}$ = 2959, 1639, 1467, 1382, 1073 cm^{-1}; R_f = 0.2 (hexane/EtOAc, 3:1)

2,3-Epoxy-*N*,*N*-diethyl-2-phenylheptanamide (1c): Yield: 74%, 509 mg. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.72 (t, *J* = 7.1 Hz, 3 H), 0.80 (t, *J* = 7.1 Hz, 3 H), 0.86 (t, *J* = 7.1 Hz, 3 H), 0.97 (t, *J* = 7.1 Hz, 3 H), 1.03 (t, *J* = 7.1 Hz, 3 H), 1.10 (t, *J* = 7.1 Hz, 3 H), 1.55−1.15 (m, 12 H), 3.46−2.88 (m, 10 H), 7.45−7.23 (m, 10 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 12.2 (CH_3), 12.4 (CH_3), 13.2 (CH_3), 13.6 (CH_3), 13.7 (CH_3), 13.9 (CH_3), 21.9 (CH_2), 22.3 (CH_2), 26.5 (CH_2), 27.8 (CH_2), 28.3 (CH_2), 30.7 (CH_2), 39.2 (CH_2), 39.3 (CH_2), 40.8 (CH_2), 41.4 (CH_2), 64.0 (C), 64.9 (CH), 65.9 (C), 68.2 (CH), 124.7 (CH), 126.0 (CH), 127.7 (CH), 127.8 (CH), 127.9 (CH) ppm. IR (film): $\tilde{\nu}$ = 2940, 1644, 1463, 1380, 1032 cm^{-1}; R_f = 0.4, 0.3 (hexane/EtOAc, 5:1)

2,3-Epoxy-*N*,*N*-diethyl-2-methyldecanamide (1d): Yield: 92%, 587 mg. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 0.89−0.79 (m, 6 H), 1.08 (t, *J* = 7.1 Hz, 6 H), 1.15 (t, *J* = 7.1 Hz, 6 H), 1.42−1.20 (m, 24 H), 1.45 (s, 3 H), 1.50 (s, 3 H), 3.56−2.96 (m, 10 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 12.3 (CH_3), 12.4 (CH_3), 13.9 (CH_3), 14.0 (CH_3), 14.1 (CH_3), 15.4 (CH_3), 20.5 (CH_2), 22.4 (CH_2), 26.1 (CH_2), 27.8 (CH_2), 29.0 (CH_2), 29.1 (CH_2), 30.0 (CH_2), 31.5 (CH_2), 39.1 (CH_2), 39.2 (CH_2), 41.0 (CH_2), 41.3 (CH_2), 60.8 (CH), 61.2 (CH), 61.9 (C), 63.9 (C), 168.5 (C), 169.9 (C) ppm. IR (film): $\tilde{\nu}$ = 2927, 1644, 1464, 1380, 1079 cm^{-1}; R_f = 0.1 (hexane/EtOAc, 5:1).

2,3-Epoxy-*N*,*N*-diethyl-2,5,9-trimethyldecan-8-enamide (1e): Yield: 90%, 632 mg. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.01 (d, *J* = 6.4 Hz, 6 H), 1.15 (t, *J* = 7.2 Hz, 6 H), 1.20 (t, *J* = 7.1 Hz, 6 H), 1.49 (s, 6 H), 1.60 (s, 6 H), 1.68 (s, 6 H), 2.10−1.31 (m, 14 H), 3.68−3.03 (m, 10 H), 5.13−5.05 (m, 2 H) ppm. ^{13} C NMR (75 MHz, $CDCl_3$): δ = 12.0 (CH_3) 13.7 (CH_3), 15.2 (CH_3), 15.3 (CH_3) 17.1 (CH_3), 18.8 (CH_3), 19.2 (CH_3), 20.1 (CH_3), 24.9 (CH_3), 25.2 (CH_2), 30.2 (CH), 30.6 (CH), 34.4 (CH_2), 34.5 (CH_2), 36.4 (CH_2), 36.6 (CH_2), 38.8 (CH_2), 39.1 (CH_2), 40.7 (CH_2), 41.1 (CH_2), 59.9 (C), 60.6 (CH), 60.7 (CH), 124.0 (CH), 124.1 (CH) ppm.. IR (film): $\tilde{\nu}$ = 2968, 1635, 1434, 1380, 1076 cm^{-1}; R_f = 0.3 (hexane/EtOAc, 5:1).

2,3-Epoxy-*N*,*N*-diethyl-2-methyl-4-phenylpentanamide (1f): Yield: 62%, 404 mg. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 0.95 (t, *J* = 7.2 Hz, 6 H), 1.08 (t, *J* = 7.2 Hz, 6 H), 1.40 (d, *J* = 6.9 Hz, 3 H), 1.50 (d, *J* = 6.9 Hz, 3 H), 1.54 (s, 3 H), 1.52 (s, 3 H), 3.57−2.48 (m, 12 H), 7.37−7.24 (m, 10 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 12.1 (CH_3), 12.3 (CH_3), 13.5 (CH_3), 13.9 (CH_3), 15.5 (CH_3), 17.4 (CH_3), 18.6 (CH_3), 20.6 (CH_3), 39.4 (CH), 40.5 (CH_2), 41.2 (CH_2), 41.5 (CH_2), 61.3 (C), 62.5 (C), 65.9 (CH), 67.7 (CH), 126.3 (CH), 126.5 (CH), 127.2 (CH), 127.9 (CH), 128.0 (CH), 128.1 (CH), 141.3 (C), 141.9 (C) ppm. IR (film): $\tilde{\nu}$ = 2972, 1637, 1452, 1381, 1086 cm^{-1}; R_f = 0.3, 0.2 (hexane/EtOAc, 3:1).

3-Cyclohexyl-2,3-epoxy-*N*,*N*-diethyl-2-methylpropanamide (1g): Yield: 85%, 508 mg. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.11 (t, *J* = 6.9 Hz, 6 H), 1.19 (t, *J* = 6.9 Hz, 6 H), 1.51 (s, 3 H), 1.53 (s, 3 H), 2.01−1.39 (m, 22 H), 2.57 (d, *J* = 8.2 Hz, 1 H), 2.75 (d, *J* = 7.4 Hz, 1 H), 3.69−3.20 (m, 8 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 12.3 (CH_3), 12.4 (CH_3), 14.0 (CH_3), 14.2 (CH_3), 15.5 (CH_3), 25.1 (CH_2), 25.2 (CH_2), 25.9 (CH_2), 26.0 (CH_2), 28.2 (CH_2), 28.3 (CH_2), 29.8 (CH_2), 30.0 (CH_2), 36.8 (CH), 38.6 (CH_2), 39.0 (CH_2), 40.9 (CH_2), 41.6 (CH_2), 60.9 (CH), 61.8 (CH), 65.8 (C), 67.6 (C), 169.8 (C) ppm. IR (film): $\tilde{\nu}$ = 2930, 1636, 1450, 1381, 1074 cm^{-1}. R_f = 0.3, 0.2 (hexane/EtOAc, 3:1).

General Procedure for the Synthesis of Compounds 2: A solution of SmI_2 (1.6 mmol) in THF (19 mL) and HMPA (2 mmol) was added, under nitrogen, to a stirred solution of the appropriate epoxyamide **1** (0.4 mmol) in THF (4 mL) at room temperature. After stirring for 30 min the reaction was quenched with aqueous HCl (20 mL of a 0.1 M solution) followed by extraction with diethyl ether (3 × 10 mL) affording crude α,β-unsaturated amide **2**, which was purified by column flash chromatography over silica gel (hexane/EtOAc, 10:1).

(*E*)-3-Cyclohexyl-*N*,*N*-diisopropylpropenamide (2a): Yield: 40%, 38 mg. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 2.22−1.08 (m, 23 H), 4.12−3.58 (m, 2 H), 6.14 (d, *J* = 15.1 Hz, 1 H), 6.74 (dd, *J* = 15.1, 7.4 Hz, 1 H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 20.3 (CH_3), 21.2 (CH_3), 25.8 (CH_2), 25.9 (CH_2), 32.1 (CH_2), 40.6 (CH), 45.5 (CH), 48.1 (CH), 120.5 (CH), 149.5 (CH), 166.7 (C) ppm. MS (70 eV): *m*/*z* (%) =237 $[M]^+$ (2), 222 (5), 194 (26), 124 (62), 55 (100). IR (film): $\tilde{\nu}$ = 2926, 1654, 1438, 1337 cm^{-1}. R_f = 0.2 (hexane/EtOAc, 3:1).

(*E*)-*N*,*N*-Diethyl-2-methylhep-2-enamide (2b): Yield: 70%, 55 mg. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 0.91 (t, *J* = 6.9 Hz, 3 H), 1.14

(t, J = 7.2 Hz, 6 H), 1.58−1.12 (m, 4 H), 1.83 (s, 3 H), 2.14−2.03 (m, 2 H), 3.33 (q, J = 7.2 Hz, 4 H), 5.48 (t, J = 7.2 Hz, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.8 (CH_3), 14.0 (CH_3), 14.3 (CH_3), 22.3 (CH_2), 22.6 (CH_3), 27.1 (CH_2), 31.1 (CH_2), 31.5 (CH_2), 129.6 (CH), 131.7 (C), 173.5 (C). MS (70 eV): *m/z* (%) =197 (4) $[M]^+$, 168 (6), 140 (72), 125 (49) ppm. IR (film): ṽ = 2938, 1624, 1458, 1431, 1380 cm^{-1}. R_f = 0.3 (hexane/EtOAc, 3:1)

(*E*)-*N*,*N*-Diethyl-2-phenylhep-2-enamide (2c): Yield: 82%, 85 mg. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.96−0.89 (m, 6 H), 1.23 (t, J = 7.1 Hz, 3 H), 1.54−1.33 (m, 4 H), 2.25−2.18 (m, 2 H), 3.24 (q, J = 7.1 Hz, 2 H), 3.54 (q, J = 7.1 Hz, 2 H), 6.04 (t, J = 7.6 Hz, 1 H), 7.39−7.21 (m, 5 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 12.5 (CH_3), 13.6 (CH_3), 13.7 (CH_3), 22.3 (CH_2), 29.5 (CH_2), 31.2 (CH_2), 38.2 (CH_2), 42.3 (CH_2), 125.1 (CH), 127.3 (CH), 128.4 (CH), 129.3 (CH), 136.4 (C), 137.5 (C), 169.1 (C) ppm. MS (70 eV): *m/z* (%) = 259 (86) $[M]^+$, 230 (71), 202 (100), 159 (4), 77 (9). IR (film): ṽ = 2960, 1627, 1430, 1435, 1387 cm^{-1}. R_f = 0.5 (hexane/EtOAc, 1:1)

(*E*)-*N*,*N*-Diethyl-2-methyldec-2-enamide (2d): Yield: 64%, 70 mg. ^{1}H NMR (300 MHz, [D$_6$]DMSO, 373 K): δ = 0.84 (t, J = 6.7 Hz, 3 H), 1.11 (t, J = 7.2 Hz, 6 H), 1.50−1.22 (m, 10 H), 1.78 (s, 3 H), 2.04 (q, J = 6.9 Hz, 2 H), 3.34 (q, J = 7.2 Hz, 4 H), 5.46 (dt, J = 7.4, 1.5 Hz, 1 H) ppm. ^{13}C NMR (75 MHz, [D$_6$]DMSO, 373 K): δ = 12.8 (CH_3), 13.9 (CH_3), 14.2 (CH_3), 22.4 (CH_2), 27.3 (CH_2), 28.8 (CH_2), 29.0 (CH_2), 29.1 (CH_2), 31.6 (CH_2), 41.5 (CH_2), 130.3 (CH), 130.8 (C), 173.7 (C) ppm. MS (70 eV): *m/z* (%) = 239 $[M]^+$ (2), 167 (27), 140 (100), 55 (40), 41 (40). IR (film): ṽ = 2928, 2856, 1624, 1460, 1379 cm^{-1}; R_f = 0.5 (hexane/EtOAc, 1:1)

(*E*)-*N*,*N*-Diethyl-2,5,9-trimethyldec-2,8-dienamide (2e): Yield: 85%, 90 mg. ^{1}H NMR (300 MHz, [D$_6$]DMSO, 373 K): δ = 0.99 (d, J = 6.7 Hz, 3 H), 1.17 (t, J = 7.3 Hz, 6 H), 1.68 (s, 3 H), 1.75 (s, 3 H), 1.83 (s, 3 H), 2.21−0.93 (m, 7 H), 3.41 (q, J = 7.3 Hz4 H,), 5.21−5.17 (m, 1 H), 5.53−5.48 (m, 1 H) ppm. ^{13}C NMR (75 MHz, [D$_6$]DMSO, 373 K): δ = 13.4 (CH_3), 14.2 (CH_3), 17.3 (CH_3), 19.3 (CH_3), 25.2 (CH_2), 32.5 (CH), 34.2 (CH_2), 36.4 (CH_2), 40.4 (CH_2), 124.6 (CH), 127.3 (CH), 130.5 (C), 132.9 (C), 172.4 (C) ppm. MS (70 eV): *m/z* (%) = 265 (6) $[M]^+$, 250 (10), 182 (67), 154 (12). IR (film): ṽ = 2966, 1624, 1459, 1379 cm^{-1}; R_f = 0.2 (hexane/EtOAc, 3:1).

(*E*)-*N*,*N*-Diethyl-2-methyl-4-phenylpent-2-enamide (2f): Yield: 83%, 81 mg. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.27−1.01 (m, 6 H), 1.39 (d, J = 6.9 Hz, 3 H), 1.91 (s, 3 H), 3.48−3.21 (m, 4 H), 3.80−3.70 (m, 1 H), 5.63 (d, J = 9.4 Hz, 1 H), 7.42−7.11 (m, 5 H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 14.2 (CH_3), 14.5 (CH_3), 21.4 (CH_3), 36.6 (CH_2), 36.7 (CH_2), 37.6 (CH), 126.0 (CH), 126.6 (CH), 128.4 (CH), 130.8 (C), 133.7 (CH), 145.3 (C), 172.9 (C) ppm. MS (70 eV): *m/z* (%) = 245 (33) $[M]^+$, 173 (37), 140 (100), 126 (100), 77 (19). IR (film): ṽ = 3008, 2945, 1647 cm^{-1}. R_f = 0.5 (hexane/EtOAc, 1:1)

(*E*)-3-Cyclohexyl-*N*,*N*-diethyl-2-methylpropenamide (2g): Yield: 91%, 81 mg. ^{1}H NMR (300 MHz, [D$_6$]DMSO, 373 K): δ = 1.17 (t, J = 7.0 Hz, 6 H), 1.50−1.21 (m, 5 H), 1.81−1.68 (m, 5 H), 1.84 (d, J = 1.7 Hz, 3 H), 2.43−2.30 (m, 1 H), 3.39 (q, J = 7.0 Hz, 4 H), 5.33 (dq, J = 8.9, 1.7 Hz, 1 H) ppm. ^{13}C NMR (75 MHz, [D$_6$]DMSO, 373 K): δ = 13.4 (CH_3), 14.0 (CH_3), 25.1 (CH_2), 25.6 (CH_2), 32.0 (CH_2), 36.0 (CH), 40.4 (CH_2), 130.4 (C), 134.0 (CH), 172.5 (C) ppm. MS (70 eV): *m/z* (%) = 223 $[M]^+$ (9), 208 (2), 151 (57), 140 (100). IR (film): ṽ = 2974, 1623, 1457, 1380 cm^{-1}. R_f = 0.2 (hexane/EtOAc, 3:1)

Acknowledgments

We thank the II Plan Regional de Investigación del Principado de Asturias (PB-EXP01−11) and the Ministerio de Ciencia y Tecnología (BQU2001−3807) for financial support. J. M. C. thanks Carmen Fernández-Flórez for her time and E. B thanks the Principado de Asturias for a predoctoral fellowship. We also thank Scott J. S. Hartman for correcting the English.

[1] [1a] J. Inanaga, J. Katsuki, M. Yamaguchi, *Chem. Lett.* **1991**, 1025−1026. [1b] S. Hanessian, C. Girard, J. L. Chiara, *Tetrahedron Lett.* **1992**, *33*, 573−576.
[2] J. M. Concellón, P. L. Bernad, J. A. Pérez-Andrés, *Angew. Chem. Int. Ed.* **1999**, *38*, 2384−2386.
[3] J. M. Concellón, J. A. Pérez-Andrés, H. Rodríguez-Solla, *Angew. Chem. Int. Ed.* **2000**, *39*, 2773−2775.
[4] J. M. Concellón, J. A. Pérez-Andrés, H. Rodríguez-Solla, *Chem. Eur. J.* **2001**, *7*, 3062−3068.
[5] J. M. Concellón, E. Bardales, *Org. Lett.* **2002**, *4*, 189−191.
[6] [6a] P. Girard, J. L. Namy, H. B. Kagan, *J. Am. Chem. Soc.* **1980**, *102*, 2693−2698. [6b] M. Matsukawa, T. Tabuchi, J. Inanaga, M. Yamaguchi, *Chem. Lett.* **1987**, 2101−2102.
[7] [7a] L. Crombie, A. H. Krasinski, M. Manzoor-I-Khuda, *J. Chem. Soc.* **1963**, 4970−4976. [7b] F. Bohlmann, R. Miethe, *Chem. Ber.* **1967**, 3861−3868. [7c] N. Hirayama, K. Shimizu, K. Shirahata, K. Ueno, G. Tamura, *Agric. Biol. Chem.* **1980**, *44*, 2083−2087. [7d] M. Onda, Y. Konda, K. Hinottozawa, S. Omura, *Chem. Pharm. Bull.* **1982**, *30*, 1210−1214. [7e] H. Cho, J. M. Beale, C. Graff, U. Mocek, A. Nakagawa, S. Omura, H. G. Floss, *J. Am. Chem. Soc.* **1993**, *115*, 12296−12304. [7f] M. Ojika, H. Niwa, Y. Shizuri, K. Yamada, *J. Chem. Soc., Chem. Commun.* **1982**, 628−629. [7g] R. Grote, A. Zeeck, H. Drautz, H. Zähner, *J. Antibiot.* **1988**, *41*, 1275−1276. [7h] G. Werner, H. Hagenmaier, H. Drautz, A. Baumgartner, H. Zähner, *J. Antibiot.* **1984**, *37*, 110−117. [7i] S. Omura, N. Imamura, K. Hinitizawa, K. Otoguro, G. Lukacs, R. Faghih, R. Tolmann, B. H. Arison, J. L. Smith, *J. Antibiot.* **1983**, *36*, 1783−1786.
[8] [8a] J. E. Baldwin, W. A. Dupont, *Tetrahedron Lett.* **1980**, *21*, 1881−1182. [8b] G. B. Mpango, K. K. Mahalanabis, Z. Mahdavi-Damghani, V. Snieckus, *Tetrahedron Lett.* **1980**, *21*, 4823−4826. [8c] H. Greger, M. Grentz, F. Bohlmann, *Phytochemistry* **1981**, *20*, 2579−2581. [8d] H. Greger, M. Grentz, F. Bohlmann, *Phytochemistry* **1982**, *21*, 1071−1074. [8e] F. Bohlmann, M. Gancer; M. Kruger, E. Nordhoff, *Tetrahedron* **1983**, *39*, 123−128.
[9] K. Takai; M. Tezuka, K. Utimoto, *J. Org. Chem.* **1991**, *56*, 5980−5982.
[10] J. M. Concellón, E. Bardales, *J. Org. Chem.* **2003**, *68*, 9492−9494.
[11] J. Inanaga, Y. Handa, T. Tabuchi, J. Otsubo, M. Yamaguchi, T. Hanamoto, *Tetrahedron Lett.* **1991**, *32*, 6557−6558.
[12] When the reactions were carried out with more HMPA (HMPA/SmI_2, 4:1) similar yields and diastereoselectivities were obtained.
[13] J. M. Concellón, P. L. Bernad, E. Bardales, *Chem. Eur. J.* , in press.
[14] J. M. Concellón, E. Bardales, C. Gómez, *Tetrahedron Lett.* **2003**, *44*, 5323−5326.

Received October 9, 2003

