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Enantioselective synthesis of 1-aryl-2-propenylamines: a new approach to a stereoselective synthesis of the Taxol® side chain

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Dedicated to Professor R. Nicoletti on the occasion of his 70th birthday

Abstract—A variety of substituted 1-aryl-2-propenylamines of high enantiomeric purity were prepared via lipase-catalysed resolution of the corresponding racemates. (*R*)-1-Phenyl-2-propenylamine was further synthesised into (2*R*,3*S*)-3-benzoylamino-2-hydroxy-3-phenylpropanoic acid methyl ester, the side chain of Taxol®.

1. Introduction

Chiral amines are important building blocks and auxiliaries for the stereoselective synthesis of biologically active compounds and natural products.[1] As a result, a number of methodologies have been developed for their preparation in enantiomerically pure form as well as to determine their absolute configurations.[2] Nevertheless, only two methodologies for obtaining 1-aryl-2-propenylamines in nonracemic form have been described so far. Recently, Pallavicini et al.[3a] reported the resolution of racemic allylamines by selective precipitation of their diastereomeric salts with isopropylideneglyceryl hydrogen phthalate. Kibayashi et al.[3b] reported the synthesis of the enantiopure (*R*)-allylamine by the reaction of benzaldehyde oxime ether with vinyl lithium and the subsequent cleavage using Zn–AcOH.

Following our previous work concerning the synthesis of chiral 1-aryl-2-propynylamines **1**[4] in high enantiomeric excess by stereoselective amidation via acyl tranfer reactions catalysed by *Candida antarctica* lipase (CAL),[5] we decided to explore the possibility of obtaining homochiral 1-aryl-2-propenylamines **2** via lipase-catalysed resolution of their corresponding racemates. Our interest in these compounds stemmed from our current synthetic and molecular modeling studies on taxoids.[6] In particular, we have identified 1-aryl-2-propenylamines as possible intermediates for developing a new enantioselective synthesis of α-hydroxy-β-amino acids. These are important components of biologically active compounds, such as angiotensin-converting enzyme (ACE) and HIV-1 protease inhibitors. Both the *syn*- and *anti*-stereoisomer of this class of compounds are found in drugs and natural products. Thus, phenylisoserine, the most important representative for *syn* aminoalcohols, is present as a side chain in Taxol® and Taxotere®, two of the most potent antitumour agents currently used in cancer chemotherapy. In contrast, the *anti*-isomers show biological activities when incorporated in structures such as sphingosine and phytosphingonsine, which are involved in various functions of the central nervous system.[7]

Herein we report the lipase-catalysed resolution of racemic 1-aryl-2-propenylamines **2** to give the corresponding (*R*)- and (*S*)-enantiomers with high enantiomeric excess as well as the further elaboration of (*R*)-1-phenyl-2-propenylamine into (2*R*,3*S*)-3-benzoylamino-2-hydroxy-3-phenylpropanoic acid methyl ester **3**, which has previously been used[8] as a synthon to insert the side chain of Taxol®.

2. Results and discussion

In an attempt to provide easy access to the required compounds and based on our experience in this field,[1,4] we synthesised the racemic starting materials **2a**–**h** (Scheme 1, Table 1) by hydrolysis of the corresponding acetamides **4a**–**h**, in turn obtained by catalytic hydrogenation of the triple bond of acetamides **5a**–**h** in the

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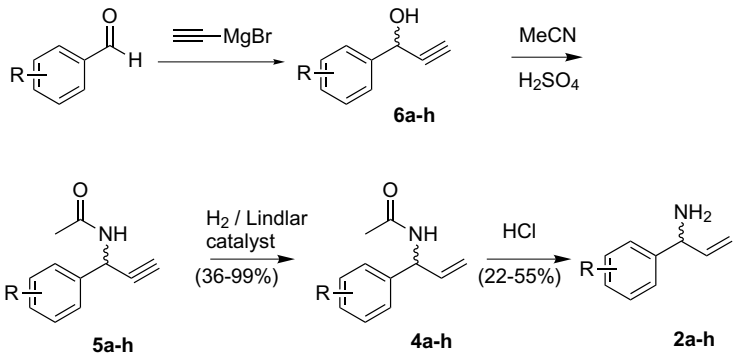


Scheme 1.

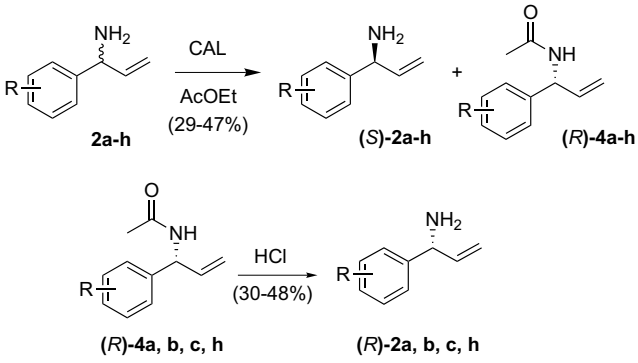
Table 1. Preparation of (±)-*N*-1-aryl-2-propenylacetamides **4a**–**h** and (±)-*N*-1-aryl-2-propenylamines **2a**–**h**

Compound	R	Time (h)	Yield (%)[a]	Mp (°C)
4a	H	3	99	Oil
4b	4-Cl	3	60	81–84
4c	4-F	2	63	Oil
4d	3-F	3	78	Oil
4e	3-Me	2	97	83–85
4f	2-Me	2	99	93–94
4g	4-Me	2	95	77–80
4h	4-Br	1.5	36	85–89
2a	H	12	38	Oil
2b	4-Cl	22	49	Oil
2c	4-F	16	35	Oil
2d	3-F	18	55	Oil
2e	3-Me	14	36	Oil
2f	2-Me	12	27	Oil
2g	4-Me	18	22	Oil
2h	4-Br	20	32	Oil

[a] Referred to isolated and purified materials.

presence of Lindlar's catalyst,[9] using DMF as a solvent and ethylenediamine as a poisoning agent to avoid the overreduction of the double bond.[10,11] The latter compounds were synthesised from aryl propargylic alcohols **6a**–**h**[12] via a Ritter reaction (acetonitrile/sulfuric acid).

We then investigated the enantioselective acetylation of (±)-**2** using CAL as a catalyst, ethyl acetate as an acyl donor, and diethyl ether as a solvent (Scheme 2, Table 2).



Scheme 2.

Monitoring of the reaction by GC on a chiral column allowed the simultaneous determination of conversion and enantiomeric excesses of both educt and product. The transformations were stopped as soon as the desired conversion (approximately 50%) was achieved. Following the usual workup, compounds (*S*)-**2** and (*R*)-**4** were purified by flash column chromatography and their ee's determined again by chiral GC. In no case was there a loss of ee due to work-up and silica gel chromatography. As can be seen from the data reported in Table 2, CAL

Table 2. CAL-catalysed resolution of (±)-*N*-1-aryl-2-propenylamines **2a**–**h**

(*R*,*S*)-2		Time (h)	Conv.[a] (%)	(*S*)-2			(*R*)-4			E
				Yield[b] (%)	Ee (%)	$[\alpha]_D^{20}$[c] $CHCl_3$	Yield[b] (%)	Ee (%)	$[\alpha]_D^{20}$ $CHCl_3$	
2a	H	66	49.4	43.4	98	−10.2	46.0	>98	+63.0	420
2b	4-Cl	72	49.5	38.6	98	−9.0	41.0	98	+71.3	390
2c	4-F	110	52.0	34.2	93	−4.9	44.5	87	+69.7	51.3
2d	3-F	168	55.5	N.D.[d]	61	N.D.[d]	N.D.[d]	48	N.D.[d]	5.0
2e	3-Me	168	N.D.[d]	N.D.[d]	34	N.D.[d]	N.D.[d]	N.D.[d]	N.D.[d]	N.D.[d]
2f	2-Me	168	47.5	N.D.[d]	37	N.D.[d]	N.D.[d]	42	N.D.[d]	3.5
2g	4-Me	120	N.D.[d]	29.0	91	−8.0	38.0	N.D.[d]	+75.0	N.D.[d]
2h	4-Br	118	50.0	32.0	95	−11.0	47.0	96	+12.0	195

[a] Determined by chiral GC (FS-CYCLODEX-BETA-I/P).
[b] Referred to isolated and purified materials.
[c] Measured in $CHCl_3$ solution.
[d] N.D. = not determined.

proved to be an effective catalyst ($E > 100$) for the resolution of substrates **2a**,**b** and **h**, leading to both (*S*)-**2a**,**b**,**h** and (*R*)-**4a**,**b**,**h** in good yields and high enantiomeric excesses (95–98%). Acceptable results were also obtained with substrates **2c** and **g**, whereas compounds **2d**–**f**, bearing an *ortho*/*meta*-substituted aromatic ring, proved to be resistant to enantioselective bioconversion, even after a prolonged reaction time (>160 h).

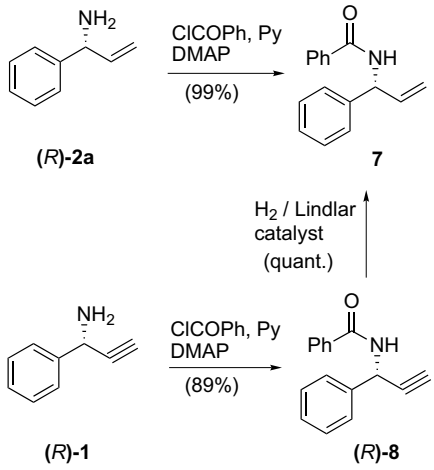
The absolute configuration of **2** and **4** was assigned based on the specific rotation of (−)-**2a**, which is described in the literature,[3] establishing an (*S*)-configuration for (*S*)-**2a** and hence an (*R*)-configuration for the amide (*R*)-**4a**. This result is in perfect agreement with the reported preference of CAL for the acylation of (*R*)-amines.[2,13]

Acidic hydrolysis of acetamides (*R*)-**4a**,**b**,**c** and **h**, under the same experimental conditions as described for their racemic counterparts, afforded amines (*R*)-**2a**,**b**,**c** and **h** without loss of enantiomeric excess (Table 3).

Table 3. Preparation of (*R*)-*N*-1-aryl-2-propenylamines (*R*)-**2a**, **b**, **c** and **h**

(*R*)-(**2**)		Yield[b] (%)	Ee[a] (%)	$[\alpha]_D^{20}$ $CHCl_3$
2a	H	32	98	+10.2
2b	4-Cl	48	98	+12.3
2c	4-F	30	87	+8.8
2h	4-Br	32	97	+12.0

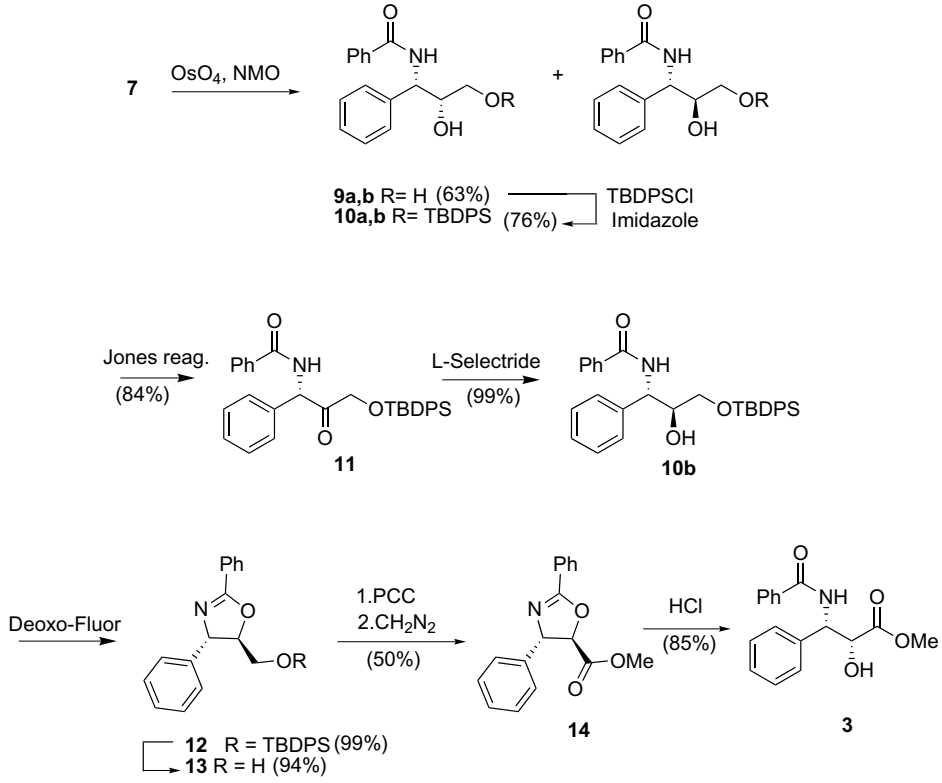
[a] Determined by chiral GC (FS-CYCLODEX-BETA-I/P).
[b] Referred to isolated and purified materials.



Scheme 3.

We then turned our attention to the development of a new stereoselective synthesis of (2*R*,3*S*)-3-benzoylamino-2-hydroxy-3-phenylpropanoic acid methyl ester **3**. The key intermediate for this synthesis was envisaged in the homochiral *N*-benzoylallylamine **7** (Scheme 3), obtained by benzoylation of (*R*)-1-phenyl-2-propenylamine **2a** or by partial hydrogenation[10,11] of enantiomerically pure *N*-benzoylpropargylamine (*R*)-**8**, in turn obtained from (*R*)-**1**.[4]

Our first approaches to *syn*-diol **9a** and **b** (Scheme 4), based on the asymmetric dihydroxylation of carbon–carbon double bond of **7** using chiral ligands, proved to



Scheme 4.

be unsuccessful, leading to a mixture of **9a** and **b** with low diasteromeric excess.

These results are in agreement with previous studies on asymmetric dihydroxylation of allylamines.[14] As a result, we preferred converting **7** into a 1:1 diastereomeric mixture (OsO_4, NMO)[15] of amino alcohols **9a** and **9b**, which, after selective protection at the primary hydroxyl as *tert*-butyldiphenylsilyl ether[16] **10a** and **10b**, were subjected to Jones' oxidation to the enantiomerically pure ketone **11** followed by stereoselective reduction using L-Selectride[17,18] to provide compound **10b** in 98% de.

The *anti*-diastereoisomer **10b** was transformed into the *trans*-oxazoline **12** through dehydrative cyclisation using bis(2-methoxyethyl)aminosulfur trifluoride (Deoxo-Fluor®)[19] entailing inversion of configuration at C-2. The *trans*-configuration of oxazoline **12** was assigned by ^{1}H NMR analysis by comparison of the coupling constant values of the deprotected compound **13** with those of already known compounds.[20] No trace of *cis*-oxazoline could be detected.

Oxidation of **13** with freshly prepared pyridinium chlorochromate (PCC) gave the corresponding carboxylic acid, which was directly treated with an ethereal solution of diazomethane to provide methyl ester **14**. Acid catalysed opening of the oxazoline **14** gave (2*R*,3*S*)-3-benzoylamino-2-hydroxy-3-phenylpropanoic acid methyl ester **3** in 85% yield; spectroscopic and analytical data for compound **3** were in agreement with those reported in the literature (see Experimental).[20,21,8]

3. Conclusions

Resolution of (±)-1-arylallylamines via acyl transfer catalysed by *C. antarctica* lipase proved to be a quite efficient route, both in terms of chemical yield and stereoselectivity, to (*R*)- and (*S*)-1-aryl-2-propenylamines substituted at the *para*-position of the aryl moiety. These compounds are versatile intermediates for the preparation of diasteromerically and enantiomerically pure forms of biologically relevant compounds, such as *syn*- and *anti*-α-hydroxy-β-amino acids. In particular, starting from (*R*)-*N*-benzoyl-1-phenyl-2-propenylamine **7**, a new synthesis of a paclitaxel side chain, namely (2*R*,3*S*)-3-benzoylamino-2-hydroxy-3-phenylpropanoic acid methyl ester **3**, can be performed with 16% overall yield.

4. Experimental

Reagents were obtained from commercial suppliers and used without further purification. Merck silica gel 60 was used for both column chromatography (70–230 mesh) and flash chromatography (230–400 mesh). Melting points are uncorrected. ^{1}H NMR spectra were measured at 200 MHz. Chemical shifts are reported relative to $CDCl_3$ at δ 7.24 ppm and tetramethylsilane at δ 0.00 ppm. EI low resolution mass spectra were recorded with an electron beam of 70 eV. Elemental analyses (C, H, N) were performed in-house.

4.1. General procedure for the preparation of (±)-*N*-1-acetyl-1-phenyl-2-propynylamines 5g and h

A solution of 96% H_2SO_4 (490 mg, 5 mmol) in dry acetonitrile (2 mL) was added to a stirred mixture of 1-aryl-2-propynyl-1-ol (1 mmol) and anhydrous Na_2SO_4 (142 mg, 1 mmol) in dry acetonitrile (3.1 mL) at −20 °C. The mixture was allowed to reach room temperature, and stirring then continued for the required time. The mixture was concentrated, poured on ice, and extracted with ether and dichloromethane. The combined organic layers were dried over Na_2SO_4, filtered and concentrated. Flash chromatography, using ethyl acetate/petroleum ether (1:1) as eluant, afforded pure (±)-*N*-1-acetyl-1-aryl-2-propynylamines **5g** and **h**.

4.1.1. (±)-*N*-1-Acetyl-1-(methylphenyl)-2-propynylamines 5g. Time 14 h, yield 51%, mp 94–97 °C. ^{1}H NMR ($CDCl_3$): δ 7.39–7.35 (2H, d, $J = 8.0$ Hz, Ph), 7.16–7.12 (2H, d, $J = 8.0$ Hz, Ph), 5.94 (1H, s, C*H*O), 2.44 (1H, s, CC*H*), 2.32 (3H, s, CH_3), 1.98 (3H, s, CH_3). IR (KBr): 1676, 1497 cm^{-1}. MS: 197 (M^+). Anal. Calcd for $C_{12}H_{13}NO$: C, 76.98; H, 7.00; N, 7.48. Found: C, 76.62; H, 6.87; N, 7.32.

4.1.2. (±)-*N*-1-Acetyl-1-(bromophenyl)-2-propynylamines 5h. Time 16 h, yield 89%, mp 119–123 °C. ^{1}H NMR ($CDCl_3$): δ 7.49–7.44 (2H, d, $J = 8.7$ Hz, Ph), 7.37–7.33 (2H, d, $J = 7.0$ Hz, Ph), 5.97 (1H, d, $J = 1.6$ Hz, C*H*O), 2.49 (1H, d, $J = 1.5$ Hz CC*H*), 2.00 (3H, s, CH_3). IR (KBr): 1669, 1486 cm^{-1}. MS: 251 $[M-H]^+$. Anal. Calcd for $C_{11}H_{10}BrNO$: C, 52.41; H, 4.00; N, 5.56. Found: C, 51.98; H, 3.78; N, 5.23.

4.2. General procedure for the preparation of (±)-*N*-1-acetyl-1-phenyl-2-propenylamines 4a–h

To a solution of (±)-*N*-1-acetyl-1-aryl-2-propynylamines[6] (1 mmol) in dry DMF, under magnetic stirring, ethylenediamine (66 μL) and Lindlar catalyst (8 mg) were added. The mixture was submitted to hydrogen atmosphere (1 atm) and stirred at room temperature for the required time. The mixture was filtered on Celite and washed with ethyl acetate. The organic layer was washed with NH_4Cl (3 mL) and water, dried over Na_2SO_4, filtered and concentrated. The crude product was purified with flash chromatography, using ethyl acetate/petroleum ether (1:1) as eluant (Table 1).

4.2.1. (±)-*N*-1-Acetyl-1-phenyl-2-propenylamine 4a. Time 3 h, yield 99%, oil. ^{1}H NMR ($CDCl_3$): δ 7.32–7.28 (5H, m, Ph), 6.07–5.91 (1H, ddd, $J = 5.1$ Hz, $J = 10.5$ Hz,

$J = 16.2$ Hz, CH_2CHC), 5.65–5.62 (1H, m, CHN), 5.25 (1H, m, CH_2CHC), 5.20–5.15 (1H, d, $J = 10.8$ Hz, CH_2CHC), 2.00 (3H, s, CH_3). IR (KBr): 3295, 1656, 1545 cm^{-1}. MS: 175 (M^+). Anal. Calcd for $C_{11}H_{13}NO$: C, 75.12; H, 7.31; N, 8.13. Found: C, 75.42; H, 7.42; N, 8.00.

4.2.2. (±)-*N*-1-Acetyl-1-(4-chlorophenyl)-2-propenylamine 4b. Time 3 h, yield 60%, mp 81–84 °C. ^1H NMR ($CDCl_3$): δ 7.25–7.18 (4H, m, Ph), 6.68 (1H, d, $J = 8.2$ Hz, N*H*), 5.95–5.84 (1H, m, CH_2CHC), 5.68–5.66 (1H, m, CHN), 5.50–5.24 (2H, m, CH_2CHC), 2.00 (3H, s, CH_3). MS: 211/209 $(M+H)^+$, 210/208 (M^+), 130 (100%). Anal. Calcd for $C_{11}H_{12}ClNO$: C, 63.01; H, 5.77; N, 6.68. Found: C, 63.05; H, 5.81; N, 6.69.

4.2.3. (±)-*N*-1-Acetyl-1-(4-fluorophenyl)-2-propenylamine 4c. Time 2 h, yield 63%, oil. ^1H NMR ($CDCl_3$): δ 7.22–7.15 (2H, dd, $J = 8.4$ Hz, $J = 5.6$ Hz, Ph), 6.97–6.98 (2H, m, Ph), 6.68–6.65 (1H, d, $J = 7.3$ Hz, N*H*), 5.93–5.82 (1H, ddd, $J = 5.6$ Hz, $J = 10.5$ Hz, $J = 16.4$ Hz, CH_2CHC), 5.55–5.48 (1H, m, CH N), 5.18–5.16 (1H, d, $J = 4.7$ Hz, CH_2CHC), 5.13–5.07 (1H, d, $J = 12.3$ Hz, CH_2CHC), 1.91 (3H, s, CH_3). MS: 193 (M^+). Anal. Calcd for $C_{11}H_{12}FNO$: C, 68.38; H, 6.26; N, 7.25. Found: C, 68.39; H, 6.23; N, 7.22.

4.2.4. (±)-*N*-1-Acetyl-1-(3-fluorophenyl)-2-propenylamine 4d. Time 3 h, yield 78%, oil. ^1H NMR ($CDCl_3$): δ 7.31–6.89 (4H, m, Ph), 5.92–5.76 (1H, m, CH_2CHC), 5.64–5.46 (1H, m,CHN), 5.14–5.05 (2H, m, CH_2CHC), 1.84 (3H, s, CH_3). MS: 194 ($M+H^+$), 150 (100%). Anal. Calcd for $C_{11}H_{12}FNO$: C, 68.38; H, 6.26; N, 7.25. Found: C, 68.31; H, 6.25; N, 7.23.

4.2.5. (±)-*N*-1-Acetyl-1-(3-methylphenyl)-2-propenylamine 4e. Time 2 h, yield 97%, mp 83–85 °C. ^1H NMR ($CDCl_3$): δ 7.18–7.04 (4H, m, Ph), 6.34–6.30 (1H, d, $J = 6.9$ Hz, N*H*), 6.04–5.87 (1H, m, CH_2CHC), 5.58–5.52 (1H, m, CHN), 5.20–5.13 (2H, m, CH_2CHC), 2.30 (3H, s, CH_3Ph), 1.95 (3H, s, CH_3). MS: 189 (M^+). Anal. Calcd for $C_{12}H_{15}NO$: C, 76.16; H, 7.99; N, 7.40. Found: C, 76.13; H, 7.93; N, 7.39.

4.2.6. (±)-*N*-1-Acetyl-1-(2-methylphenyl)-2-propenylamine 4f. Time 2 h, yield 99%, mp 93–94 °C ^1H NMR ($CDCl_3$): δ 7.37–7.33 (1H, d, $J = 8.09$, N*H*), 7.25–7.11 (4H, m, $PhCH_2CHC$), 6.03–5.80 (1H, m, CH_2CHC), 5.77–5.74 (1H, m, CHN), 5.18–5.05 (2H, m, CH_2CHC), 2.33 (3H, s, CH_3Ph), 1.88 (3H, s, CH_3). MS: 189 (M^+). Anal. Calcd for $C_{12}H_{15}NO$: C, 76.16; H, 7.99; N, 7.40. Found: C, 76.19; H, 7.97; N, 7.41.

4.2.7. (±)-*N*-1-Acetyl-1-(4-methylphenyl)-2-propenylamine 4g. Time 2 h, yield 95%, mp 76–80 °C. ^1H NMR ($CDCl_3$): δ 7.15 (4H, m), 6.06–5.90 (1H, ddd, $J = 4.64$ Hz, $J = 10.23$ Hz, $J = 16.45$ Hz, CH_2CHC), 5.61 (1H, m, CHN), 5.24 (1H, m, CH_2CHC), 5.19–5.14 (1H, d, J = 9.4 Hz, CH_2CHC), 2.32 (3H, s, CH_3) 2.00 (3H, s, CH_3). MS: 189 (M^+). IR (KBr): 1672, 1504 cm^{-1}. Anal. Calcd for $C_{12}H_{15}NO$: C, 76.16; H, 7.99; N, 7.40. Found: C, 76.15; H, 7.96; N, 7.39.

4.2.8. (±)-*N*-1-Acetyl-1-(4-bromophenyl)-2-propenylamine 4h. Time 1.5 h, yield 36%, mp 84–89 °C. ^1H NMR ($CDCl_3$): δ 7.42–7.34 (4H, m), 6.85–6.81 (1H, d, $J = 7.9$ Hz, N*H*), 5.94–5.77 (1H, ddd, $J = 5.4$ Hz, $J = 10.26$ Hz, $J = 16.2$ Hz, CH_2CHC), 5.45 (1H, m, CHN), 5.17–5.05 (2H, m, CH_2CHC), 1.87 (3H, s, CH_3). IR (KBr): 1664, 1507 cm^{-1}. MS: 253 $(M-H)^+$, 212 (100%). Anal. Calcd for $C_{11}H_{12}BrNO$: C, 51.99; H, 4.76; N, 5.51. Found: C, 51.96; H, 4.73; N, 5.49.

4.3. General procedure for the preparation of (±)-1-aryl-2-propenylamines 2a–h

A suspension of (±)-*N*-1-acetyl-1-aryl-2-propenylamines (1 mmol) and 1.2 M aqueous HCl (5.7 mL) was heated to 90 °C for the required time. The resulting solution was extracted with Et_2O (5 mL). The aqueous layer was alkalinised by the addition of solid $NaHCO_3$ to pH 8.5 and extracted with Et_2O (4 × 5 mL). The combined organic solution was dried over Na_2SO_4, filtered and concentrated in vacuo. The oil residue was subjected to flash chromatography, using ethyl acetate/petroleum ether 1:1 as eluant, affording pure (±)-1-aryl-2-propenylamines (Table 1).

4.3.1. (±)-1-Phenyl-2-propenylamine 2a. Time 12 h, yield 38%, oil. ^1H NMR ($CDCl_3$): δ 7.33–7.24 (5H, m, Ph), 6.10–5.93 (1H, ddd, $J = 17$ Hz, $J = 10$ Hz, $J = 6.1$ Hz, CH_2CHC), 5.26–5.18 (1H, d, $J = 17$ Hz, CH_2CHC), 5.12–5.07 (1H, d, $J = 10$ Hz, CH_2CHC), 4.52–4.49 (1H, d, $J = 5.9$ Hz, CHN), 1.76 (2H, br s, NH_2). IR (KBr): 3353, 3265, 2095, 1590 cm^{-1}. MS: 133 (M^+), 131[$(M-H)^+$, 100%], 117, 105. Anal. Calcd for $C_9H_{11}N$: C, 81.16; H, 8.32; N, 10.52. Found: C, 81.20; H, 8.27; N, 10.50.

4.3.2. (±)-1-(4-Chlorophenyl)-2-propenylamine 2b. Time 22 h, yield 49%, oil. ^1H NMR ($CDCl_3$): δ 7.14–7.28 (4H, m, Ph), 5.93–5.77 (1H, ddd, $J = 5.1$ Hz, $J = 10.0$ Hz, $J = 16.3$ Hz, CH_2CHC), 5.22–5.13 (1H, d, $J = 16.5$ Hz, CH_2CHC), 5.08–5.03 (1H, d, $J = 10$ Hz, CH_2CHC), 4.84–4.82 (1H, d, $J = 5.3$ Hz, CHN), 1.48 (2H, br s, NH_2). MS: 169/167 (M^+), 168/166 $(M-H)^+$, 132 (100%). Anal. Calcd for $C_9H_{10}ClN$: C, 64.60; H, 5.80; N, 7.13. Found: C, 64.58; H, 5.78; N, 7.10.

4.3.3. (±)-1-(4-Fluorophenyl)-2-propenylamine 2c. Time 16 h, yield 35%, oil. ^1H NMR ($CDCl_3$): δ 7.30–6.92 (4H, m, Ph), 6.12–5.93 (1H, m, CH_2CHC), 5.05–5.12 (2H, m, CH_2CHC), 4.92–4.94 (1H, d, $J = 6.5$ Hz, CHN), 1.88 (2H, br s, NH_2). MS: 150 [$(M-H)^+$, 100%]. Anal. Calcd

for $C_9H_{10}FN$: C, 71.29; H, 6.35; N, 9.24. Found: C, 71.22; H, 6.32; N, 9.27.

4.3.4. (±)-1-(3-Fluorophenyl)-2-propenylamine 2d. Time 18 h, yield 55%, oil. ^{1}H NMR ($CDCl_3$): δ 7.31–6.85 (4H, m, Ph), 6.00 (1H, ddd, $J = 6.4$ Hz, $J = 10.3$ Hz, $J = 16.7$ Hz, CH_2CHC), 5.21 (1H, d, $J = 17$ Hz, CH_2CHC), 5.09 (1H, d, $J = 10.3$ Hz, CH_2CHC), 4.49 (1H, d, $J = 6.2$ Hz, CHN), 1.74 (2H, br s, NH_2). MS: 151 (M^+), 150 [$(M-H)^+$, 100%]. Anal. Calcd for $C_9H_{10}FN$: C, 71.29; H, 6.35; N, 9.24. Found: C, 71.26; H, 6.34; N, 9.21.

4.3.5. (±)-1-(3-Methylphenyl)-2-propenylamine 2e. Time 14 h, yield 36%, oil. ^{1}H NMR ($CDCl_3$): δ 7.32–7.04 (4H, m, Ph), 6.06–5.94 (1H, m, CH_2CHC), 5.28–5.03 (2H, m, CH_2CHC), 4.39 (1H, d, $J = 6.5$ Hz, CHN), 2.31 (3H, s, CH_3), 1.88 (2H, br s, NH_2). MS: 146 $(M-H)^+$, 130 (100%). Anal. Calcd for $C_{10}H_{13}N$: C, 81.61; H, 8.65; N, 9.49. Found: C, 81.63; H, 8.64; N, 9.52.

4.3.6. (±)-1-(2-Methylphenyl)-2-propenylamine 2f. Time 12 h, yield 27%, oil. ^{1}H NMR ($CDCl_3$): δ 7.38–7.35 (1H, m, Ph), 7.24–7.13 (3H, m, Ph), 6.07–5.91 (1H, m, CH_2CHC), 5.27–5.22 (2H, m, CH_2CHC), 4.73 (1H, d, $J = 5.4$ Hz, CHN), 2.35 (3H, s, CH_3), 1.19 (2H, br s, NH_2). MS: 146 $(M-H)^+$, 130 (100%). Anal. Calcd for $C_{10}H_{13}N$: C, 81.61; H, 8.65; N, 9.49. Found: C, 81.60; H, 8.63; N, 9.47.

4.3.7. (±)-1-(4-Methylphenyl)-2-propenylamine 2g . Time 18 h, yield 22%, oil. ^{1}H NMR ($CDCl_3$): δ 7.13–7.09 (2H, d, $J = 7.8$ Hz, Ph), 7.03–6.99 (2H, d, $J = 7.8$ Hz, Ph), 5.89 (1H, ddd, $J = 18.0$ Hz, $J = 11.2$ Hz, $J = 6.1$ Hz, CH_2CHC), 5.15–5.06 (1H, d, $J = 18.06$ Hz, CH_2CHC), 4.99–4.93 (1H, d, $J = 11.16$ Hz, CH_2CHC), 4.35 (1H, d, $J = 6.04$ Hz, CHN), 2.21 (3H, s, CH_3), 1.74 (2H, br s, NH_2). IR (KBr): 1670, 1512 cm^{-1}. MS: 147 (100%). Anal. Calcd for $C_{10}H_{13}N$: C, 81.61; H, 8.65; N, 9.49. Found: C, 81.64; H, 8.66; N, 9.44.

4.3.8. (±)-1-(4-Bromophenyl)-2-propenylamine 2h. Time 20 h, yield 32%, oil. ^{1}H NMR ($CDCl_3$): δ 7.45–7.40 (2H, d, $J = 8.3$ Hz, Ph), 7.22–7.18 (2H, d, $J = 8.3$ Hz, Ph), 6.02–5.86 (1H, ddd, $J = 5.9$ Hz, $J = 10.3$ Hz, $J = 16.7$ Hz, CH_2CHC), 5.24–5.15 (1H, d, $J = 16.9$ Hz, CH_2CHC), 5.11–5.06 (1H, d, $J = 10.3$ Hz, CH_2CHC), 4.48–4.44 (1H, d, $J = 6.0$ Hz, CHN), 1.83 (2H, br s, NH_2). IR (KBr): 1665, 1507 cm^{-1}. MS: 212, 132 (100%). Anal. Calcd for $C_9H_{10}BrN$: C, 50.97; H, 4.75; N, 6.60. Found: C, 50.65; H, 4.69; N, 6.57.

4.4. General procedure for the CAL-catalysed resolution of (±)-1-aryl-2-propenylamines 2a–h

A mixture of racemic amines **2a**–**h** (2 mmol), ethyl acetate (0.78 mL, 8 mmol) and lipase B from *C. antarctica* (immobilised form NOVOZYM 435®) (100 mg) in Et_2O (5 mL) was stirred at room temperature, and the reaction monitored by GC with chiral column (FS-CYCLODEX-BETA-I/P). After the desired conversion was reached, the reaction mixture was diluted with Et_2O and filtered to remove the enzyme. The organic layer was washed twice with HCl (1.0 M), obtaining the hydrochloride of amines, and the two phases then separated. The organic layer, containing the amide was washed once with brine, dried over Na_2SO_4, filtered and evaporated to give crude (*R*)-**4**. The aqueous phase containing the (*S*)-**2** hydrochloride was alkalinised with solid $NaHCO_3$ to pH 7–8 and extracted three times with Et_2O. The combined organic layers was washed with brine, dried over Na_2SO_4, filtered and evaporated to give crude (*S*)-**2**. The crude products were purified by flash chromatography on silica gel, using ethyl acetate/petroleum ether 1:1 as eluant. The enantiomeric excesses of the purified products were determined by GC on the above mentioned chiral column (Table 2).

4.5. General procedure for synthesis of (*R*)-1-aryl-2-propenylamines (*R*)-2a,b,c and h

A suspension of (*R*)-*N*-1-acetyl-1-aryl-2-propenylamines (1 mmol) and 1.2 M aqueous HCl (5.7 mL) was heated to 90 °C for the required time. The resulting solution was extracted with Et_2O (5 mL). The aqueous layer was alkalinised by addition of solid $NaHCO_3$ to pH 8.5 and extracted with Et_2O (4×5 mL). The combined organic solution was dried over Na_2SO_4, filtered and concentrated in vacuo. The oily residue was subjected to flash chromatography, using ethyl acetate/petroleum ether (1:1) as eluant, affording pure (*R*)-1-aryl-2-propenylamines. The enantiomeric excesses of the products were determined by GC with chiral column (FS-CYCLODEX-BETA-I/P). In all cases the enantiomeric purity of starting materials was conserved (Table 3).

4.6. (*R*)-*N*-Benzoyl-1-phenyl-2-propenylamine 7

To a stirred solution of (*R*)-1-phenyl-2-propenylamine **2a** (1 mmol) in dry pyridine (2.7 mL), a solution of benzoyl chloride (1.2 mmol) in dry dichloromethane (2 mL) was added slowly at 0 °C. The reaction was stirred in inert atmosphere at room temperature for 3 h. The mixture was concentrated under reduced pressure, dissolved in chloroform, washed with a solution of $NaHCO_3$ (2×1 mL) and brine. The organic layer was dried over Na_2SO_4, filtered and concentrated. The residue was subjected to flash chromatography, using ethyl acetate/petroleum ether 1:4 as eluant, affording pure (*R*)-*N*-benzoyl-1-phenyl-2-propenylamine **7**. Time 4 h, yield 99%, mp 103–105 °C. ^{1}H NMR ($CDCl_3$): δ 7.79–7.28 (10H, m, Ph), 6.76–6.72 (1H, d, $J = 7.5$ Hz, NH), 6.16–6.00 (1H, ddd, $J = 5.5$ Hz, $J = 10.0$ Hz, $J = 15.7$ Hz, CH_2CHC), 5.85–5.78 (1H, m, CHN), 5.30 (1H, m, CH_2CHC), 5.25 (1H, d, $J = 11.5$ Hz, CH_2CHC). IR (KBr): 3290, 1670, 1530 cm^{-1}. MS: 237 (M^+). $[\alpha]_D^{20}$ +57.0 (*c* 1.0). Anal. Calcd for $C_{16}H_{15}NO$: C,

81.02; H, 6.31; N, 5.73. Found: C, 81.01; H, 6.32; N, 5.70.

4.7. (*R*)-*N*-Benzoyl-1-phenyl-2-propynylamine 8

To a stirred solution of (*R*)-1-phenyl-2-propynylamine **1** (1 mmol) in dry pyridine (2.7 mL), a solution of benzoyl chloride (1.2 mmol) in dry dichloromethane (2 mL) was added slowly at 0 °C. The reaction was stirred in an inert atmosphere at room temperature for 3 h. The mixture was concentrated under reduced pressure, dissolved with chloroform, washed with a solution of $NaHCO_3$ (2×1 mL) and brine. The organic layer was dried over Na_2SO_4, filtered and concentrated. The residue was subjected to flash chromatography, using ethyl acetate/petroleum ether (1:4) as eluant, affording pure (*R*)-*N*-benzoyl-1-phenyl-2-propynylamine **8**. Time 3 h, yield 89%, mp 135–137 °C. ^{1}H NMR ($CDCl_3$): δ 7.79–7.24 (10H, m, Ph), 6.80–6.56 (1H, d, $J = 7.8$ Hz, N*H*), 6.22 (1H, d, $J = 8.5$ Hz, C*H* N), 2.52 (1H, d, $J = 1.7$ Hz, C*H*). IR (KBr): 3290, 1665, 1535 cm^{-1}. MS: 235 (M^+). $[\alpha]_D^{20}$ +14.8 (*c* 2.0). Anal. Calcd for $C_{16}H_{13}NO$: C, 81.12; H, 5.31; N, 5.13. Found: C, 81.10; H, 5.33; N, 5.20.

4.8. (*R*)-*N*-Benzoyl-1-phenyl-2-propenylamine 7

To a solution of (*R*)-*N*-benzoyl-1-phenyl-2-propynylamine **8** (1 mmol) in dry DMF, under magnetic stirring, ethylenediamine (66 μL) and Lindlar catalyst (8 mg) were added. The mixture was submitted to a hydrogen atmosphere (1 atm) and stirred at room temperature for the 2 h. The mixture was filtered on Celite and washed with ethyl acetate. The organic layer was washed with NH_4Cl (3 mL) and water, dried over Na_2SO_4, filtered and concentrated. The crude product was purified by flash chromatography, using ethyl acetate/petroleum ether (1:1) as eluant.

4.9. (1*S*,2*R*)-*N*-1-(1-Phenyl-2,3-dihydroxypropyl)benzamide 9a; (1*S*,2*S*)-*N*-1-(1-phenyl-2,3-dihydroxypropyl)-benzamide 9b

To a stirred solution of (*R*)-*N*-benzoyl-1-phenyl-2-propenylamine **7** (3 mmol) in THF with 10% of water, 1.05 g (9 mmol) of 4-methylmorpholine *N*-oxide (NMO) were added. The solution was cooled to 0 °C, then OsO_4 (0.1 mmol) added and the reaction stirred at room temperature for 48 h. The mixture was concentrated under reduced pressure, diluted with ethyl acetate and extracted (2×3 mL). The combined organic layers were washed with brine, dried over Na_2SO_4, filtered and concentrated. The crude product was purified by flash chromatography, using ethyl acetate/petroleum ether (4:1) as eluant. Analytical and spectroscopic data of the mixture of diastereoisomers are reported. Time 48 h, yield 63%. ^{1}H NMR ($CDCl_3$) **9a**: δ 7.77–7.24 (10H, m, Ph), 7.13 (1H, d, $J = 7.9$ Hz, N*H*), 5.32–5.26 (1H, m, C*H*N), 4.10–3.93 (1H, m, C*H*O), 3.70–3.42 (2H, m, CH_2O). **9b**: δ 7.77–7.24 (10H, m, Ph), 5.32–5.26 (1H, m, C*H*N), 4.10–3.93 (1H, m, C*H*O), 3.70–3.42 (2H, m, CH_2O). IR (KBr): 3430, 3140, 2929, 1720, 1656 cm^{-1}. MS: 271 (M^+). Anal. Calcd for $C_{16}H_{17}NO_3$: C, 70.02; H, 6.21; N, 5.13. Found: C, 70.14; H, 6.27; N, 5.16.

4.10. (1*S*,2*R*)-*N*-1-(3-{[(1-*tert*-Butyl)-1,1-diphenylsilyl]-oxy}-2-hydroxy-1-phenylpropyl)benzamide 10a; (1*S*,2*S*)-*N*-1-(3-{[(1-*tert*-butyl)-1,1-diphenylsilyl]oxy}-2-hydroxy-1-phenylpropyl)benzamide 10b

Imidazole (1 mmol) and *tert*-butyldiphenylsilyl chloride (1.1 mmol) were added to the mixture of compounds **9a** and **9b** (1 mmol) dissolved in dry DMF (2.2 mL). The mixture was stirred under an inert atmosphere for 14 h. The mixture was diluted in CH_2Cl_2, washed with a 5% solution of $KHSO_4$ (1×2 mL), water (2×3 mL) and brine, dried over Na_2SO_4, filtered and concentrated. The crude product was purified by flash chromatography, using ethyl acetate/petroleum ether (4:1) as eluant. Analytical and spectroscopic data of the mixture of diastereoisomers are reported. Time 14 h, yield 76%, oil. ^{1}H NMR ($CDCl_3$) **10a**: δ 7.74–7.24 (20H, m, Ph), 7.08–7.04 (1H, d, $J = 7.8$ Hz, N*H*), 5.28–5.23 (1H, dd, $J = 7.9$ Hz, $J = 3.3$ Hz, C*H*N), 4.13–4.08 (1H, m, C*H*O), 3.82–3.45 (2H, m, CH_2O), 2.79 (1H, bs, O*H*), 1.06 (9H, s, (CH_3)$_3$C). **10b**: δ 7.74–7.23 (20H, m, Ph), 5.40–5.34 (1H, dd, $J = 8.2$ Hz, $J = 4.4$ Hz, C*H*N), 4.13–4.08 (1H, m, C*H*O), 3.68–3.45 (2H, m, CH_2O), 2.72 (1H, d, $J = 5.4$ Hz, O*H*), 1.03 (9H, s, (CH_3)$_3$C). IR (KBr): 3436, 2932, 1737, 1656, 1506 cm^{-1}. MS: 452, 298, 149 (100 %). Anal. Calcd for $C_{32}H_{35}NO_3$ Si: C, 75.42; H, 6.81; N, 2.71. Found: C, 75.44; H, 6.87; N, 2.75.

4.11. (*S*)-*N*-1-(3-[(1-*tert*-Butyl)-1,1-diphenylsilyl]oxy-2-oxo-1-phenylpropyl)benzamide 11

Freshly prepared Jones reactive (0.79 mL) [1 mL of CrO_3 (0.20 g) in H_2SO_4 (98%)/water, 3:7] was added to a stirred solution of the mixture of products **10a** and **10b** (0.11 mmol) in acetone (16 mL). The mixture was stirred for 30 min, then diluted with ethyl acetate and washed with a solution of $NaHCO_3$ and brine. The organic layer was dried over Na_2SO_4, filtered and concentrated. The crude product was purified by flash chromatography, using ethyl acetate/petroleum ether (1:1) as eluant. Time 30 min, yield 84%, oil. ^{1}H NMR ($CDCl_3$): δ 7.87–7.23 (20H, m, Ph), 6.16–6.12 (1H, d, $J = 6.8$ Hz, C*H*N), 4.28 (2H, s, CH_2O), 1.05 (9H, s, (CH_3)$_3$C). IR (KBr): 2929, 1659, 1509, 1481 cm^{-1}. MS: 147 (100%). $[\alpha]_D^{20}$ +79.3 (*c* 1.4). Anal. Calcd for $C_{32}H_{33}NO_3Si$: C, 75.62; H, 6.31; N, 2.73. Found: C, 75.73; H, 6.50; N, 2.76.

4.12. (1*S*,2*S*)-*N*-1-(3-{[(1-*tert*-Butyl)-1,1-diphenylsilyl]-oxy}-2-hydroxy-1- phenylpropyl)benzamide 10b

A 1 M solution of L-Selectride in THF (1.5 mL) was added to a solution of (*S*)-*N*-1-(3-[(1-*tert*-butyl)-1,1-diphenylsilyl]oxy-2-oxo-1-phenylpropyl)benzamide **11** in dry THF that had been cooled to 0 °C for a few minutes under magnetic stirring. After 4 h at the same temperature 1 mL of NaOH (3.0 M) and 1 mL of H_2O_2

(30%) were added and the solution stirred for 30 min. The mixture was extracted with ethyl acetate (2×2 mL), washed with brine and dried over Na_2SO_4. After filtering, the solvent was removed under reduced pressure and the crude product purified by flash chromatography (diethyl ether/petroleum ether 2:3).

Time 4 h, yield 99%, oil. ^{1}H NMR ($CDCl_3$): δ 7.74–7.23 (20H, m, Ph), 5.40–5.34 (1H, dd, $J = 8.2$ Hz, $J = 4.4$ Hz, C*H*N), 4.13–4.08 (1H, m, C*H*O), 3.68–3.45 (2H, m, CH_2O), 2.72 (1H, d, $J = 5.4$ Hz, O*H*), 1.03 (9H, s, (CH_3)$_3$C). IR (KBr): 3436, 2932, 1737, 1656, 1506 cm^{-1}. MS: 452, 298, 149 (100%). $[\alpha]_D^{20}$ −16.0 (*c* 1.0). Anal. Calcd for $C_{32}H_{35}NO_3Si$: C, 75.42; H, 6.81; N, 2.71. Found: C, 75.44; H, 6.87; N, 2.75. de > 98%.

4.13. (4*S*,5*R*)-5-({[1-(*tert*-Butyl)-1,1-diphenylsilyl]-oxy}-methyl)-2,4-diphenyl-1,3-oxazoline 12

A stirred solution of (1*S*, 2*S*)-*N*-1-(3-{[(1-*tert*-butyl)-1,1-diphenylsilyl]oxy}-2-hydroxy-1-phenylpropyl)benzamide **10b** (1 mmol) in dry CH_2Cl_2 (1 mL) under an inert atmosphere was cooled at −20 °C and 20 μL of Deoxo-Fluor® (1.1 mmol) were added. The mixture was stirred for 30 min at the same temperature. A saturated solution of $NaHCO_3$ (0.1 mL) was added and the mixture warmed to room temperature. The solution was diluted with $CHCl_3$, extracted and washed with brine. The organic layer was dried over Na_2SO_4, filtered and concentrated. The crude product was purified by flash chromatography, using diethyl ether/petroleum ether 2:3 as eluant. Time 30 min, yield 99%, oil. ^{1}H NMR ($CDCl_3$): δ 8.07–8.03 (2H, m, Ph), 7.71–7.25 (18H, m, Ph), 5.24 (1H, d, $J = 6.8$ Hz, C*H*N), 4.60 (1H, ddd, $J = 4.3$ Hz, $J = 6.8$ Hz, $J = 4.8$ Hz, C*H*O), 3.99 (1H, dd, $J = 4.3$ Hz, $J = 11.2$ Hz, CH_2O), 3.90 (1H, dd, $J = 4.8$ Hz, $J = 11.2$ Hz, CH_2O), 1.05 (9H, s, (CH_3)$_3$C). IR (KBr): 1649 cm^{-1}. $[\alpha]_D^{20}$ −29.2 (*c* 1.9). MS: 491 (M^+). Anal. Calcd for $C_{32}H_{33}NO_2$ Si: C, 78.12; H, 6.71; N, 2.81. Found: C, 78.20; H, 6.72; N, 2.85.

4.14. (4*S*,5*R*)-[2,4-Diphenyl-(5-Hydroxymethyl)]-1,3-oxazoline 13

A 1 M solution in THF in tetrabutylammonium fluoride (1.1 mL) was added dropwise to a solution of (4*S*,5*R*)-5-([1-(*tert*-butyl)-1,1-diphenylsilyl]-oxy-methyl)-2,4-diphenyl-1,3-oxazoline **12** (1 mmol) in dry THF (21 mL). The mixture was stirred for 1 h, then treated with a saturated solution of $NaHCO_3$ (2 mL), diluted with ethyl acetate and extracted. The organic layer was dried over Na_2SO_4, filtered and concentrated. The crude product was purified by flash chromatography, using diethyl ether/petroleum ether (3:1) as eluant. Time 1 h, yield 94%, foam. ^{1}H NMR ($CDCl_3$): δ 8.03–7.20 (10H, m, Ph), 5.02 (1H, d, $J = 7.4$ Hz, C*H*N), 4.49 (1H, ddd, $J = 7.4$ Hz, $J = 5.4$ Hz, $J = 3.8$ Hz, C*H*O), 3.78 (1H, dd, $J = 3.8$ Hz, $J = 12.2$ Hz, CH_2O), 3.66 (1H, dd, $J = 5.4$ Hz, $J = 12.2$ Hz, CH_2O). IR (KBr): 3248, 1649 cm^{-1}. $[\alpha]_D^{20}$ −26.6 (*c* 1.4). MS: 253 (M^+), 193 (100%). Anal. Calcd for $C_{16}H_{15}NO_2$: C, 72.12; H, 6.01; N, 5.11. Found: C, 72.45; H, 6.03; N, 5.28.

4.15. (4*S*,5*R*)-Methyl-2,4-Diphenyl-1,3-oxazoline-5-carboxylate 14

To a stirred solution of (4*S*,5*R*)-[2,4-diphenyl-(5-hydroxymethyl)]-1,3-oxazoline **13**(1 mmol) in dry DMF (20 mL), freshly prepared PCC (3.5 mmol) was added. The reaction was stirred for 2 h under an inert atmosphere, then treated with an excess of a freshly prepared ethereal solution of diazomethane. After a few minutes, the mixture was concentrated under reduced pressure and extracted with ethyl acetate (2×3 mL). The combined organic layers were dried over Na_2SO_4, filtered and concentrated. The crude product was purified by flash chromatography, using diethyl ether/petroleum ether (3:1) as eluant. Time 2 h, yield 50%, oil. ^{1}H NMR ($CDCl_3$): δ 8.21–7.07 (10H, m, Ph), 5.43 (1H, d, $J = 6.6$ Hz, C*H*N), 4.89 (1H, d, $J = 6.7$ Hz, C*H*O), 3.85 (3H, s, CH_3). IR (KBr): 1760, 1650 cm^{-1}. $[\alpha]_D^{20}$ +14.0 (*c* 1.0). MS: 281 (M^+), 222 (100%), 193. Anal. Calcd for $C_{17}H_{15}NO_3$: C, 72.42, H, 5.31; N, 4.91. Found: C, 72.59; H, 5.33; N, 4.98.

4.16. (2*R*,3*S*)-3-Benzoylamino-2-hydroxy-3-phenylpropanoic acid methyl ester 3

A solution of (4*S*,5*R*)-methyl-2,4-diphenyl-1,3-oxazoline-5-carboxylate **14** in methanol (6.5 mL) and HCl (1 M, 2.2 mL) was refluxed under magnetic stirring for 5 h. The solvents were removed under reduced pressure. The product was dissolved with CH_2Cl_2 and washed twice with water. The organic layer was dried over Na_2SO_4, filtered and concentrated; the crude product was purified by flash chromatography, using ethyl acetate/petroleum ether (1:4) as eluant. Time 5 h, yield 85%, mp 185–186 °C. ^{1}H NMR ($CDCl_3$): δ 7.77–7.42 (10H, m, Ph), 6.94 (1H, d, $J = 9.1$ Hz, N*H*), 5.73 (1H, dd, $J = 2.0$ Hz, 9.1 Hz, C*H*N), 4.62 (1H, d, $J = 2.0$ Hz, C*H*O), 3.83 (3H, s, CH_3), 2.48 (1H, br s, O*H*). IR (KBr): 1730, 1638 cm^{-1}. $[\alpha]_D^{20}$ −49.0 (*c* 0.4, CH_3OH). MS: 299 (M^+). Anal. Calcd for $C_{17}H_{17}NO_4$: C, 68.22; H, 5.68; N, 4.68. Found: C, 68.20; H, 5.56; N, 4.78. Spectroscopic data reported for **3** in the literature:[21b] mp: 184–185 °C. ^{1}H NMR ($CDCl_3$): δ 7.59–7.18 (10H, m, Ph), 6.98 (1H, d, $J = 9.0$ Hz, N*H*), 5.74 (1H, dd, $J = 2.0$ Hz, 9.0 Hz, C*H*N), 4.63 (1H, d, $J = 2.0$ Hz, C*H*O), 3.84 (3H, s, CH_3), 3.26 (1H, br s, O*H*). IR (KBr): 1740, 1640 cm^{-1}. $[\alpha]_D^{26}$ −48 (*c* 0.92, CH_3OH). MS: 300 (M^++1).

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