HETEROCYCLES, Vol. 65, No. 4, 2005, pp. 823 - 841
Received, 14th January, 2005, Accepted, 21st February, 2005, Published online, 22nd February, 2005

$Yb(OTf)_3$-CATALYZED VINYLOGOUS MANNICH REACTION OF TRIALKYLSILYLOXYFURAN

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Abstract – The one-pot three-component vinylogous Mannich reaction of trialkylsilyloxyfurans with anilines and aldehydes in the presence of catalytic amounts of $Yb(OTf)_3$ gave the substituted aminoalkyl-butenolides in good yields (> 90 %) and diastereoselectivities (d.e. > 60 %). The configuration of the major product is *erythro* (*anti*) and was confirmed by chemical transformation into piperidinone derivatives and ^1H NMR spectral studies of the latter compounds. The vinylogous Mannich reaction performed with preformed imines proceeded similarly with a preferred *erythro* selectivity while the condensation of 3-methyl-2-trialkylsilyloxyfurans was *threo* selective.

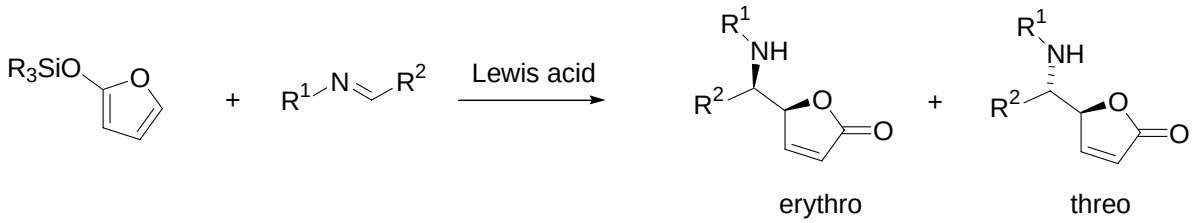
INTRODUCTION

Ytterbium triflate was proposed by Kobayashi[1] as a very convenient catalyst for various addition reactions to imines. It is very efficient, easy to handle and since some years broadly used.[1] We showed that this compound is quite useful to catalyse the reaction of silyloxypyrrole with imines.[2] As ytterbium triflate was known to be much less reactive with aldehydes, we also developed a similar strategy in the three-component Mannich-type reaction.[3] An *erythro*-selectivity was observed in both cases, the three-component reaction allowing reactions with aliphatic enolisable aldehydes while the corresponding imines do not react.

In the present paper we want to present the application of the same three-component strategy to silyloxyfuran and a careful study of the diastereoselectivity of this reaction.

Indeed, the reaction of silyloxyfurans with imines,[4] iminiums or acyliminiums[5] and nitrones[6] has already

been reported by several groups in racemic and enantioselective forms.[7] Such reaction is interesting and was applied to total syntheses.[8] The condensation of silyloxyfuran with imines was found to be catalyzed with various Lewis acids (mainly $BF_3.OEt_2$, $Ti(OPr\text{-}i)_4$) giving mixture of *threo* (*syn*) and *erythro* (*anti*) isomers (Scheme 1). Despites some contradictory reports,[4b-e] the *erythro* adduct was usually observed as the major product[7] with imines while *threo* adducts predominate in the condensation of cyclic acyliminiums.[5]

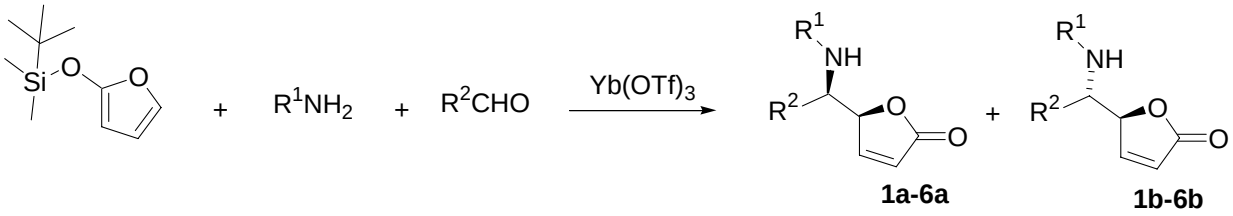


Scheme 1

RESULTS AND DISCUSSION

1- Three-component Mannich type reaction:

Our investigation was concerned with the condensation of *t*-butyldimethylsilyloxyfuran with simple aromatic or aliphatic aldehydes and anilines (Scheme 2). A clean and rapid reaction was observed by just mixing the three components in CH_2Cl_2 at -78°C in the presence of 5-10% of $Yb(OTf)_3$. The results are reported in Table 1.



Scheme 2

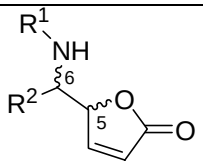
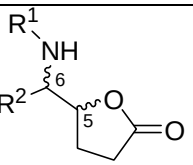
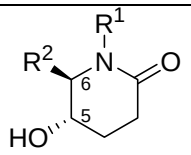
Table 1: Three-component Mannich type reaction of *t*-butyldimethylsilyloxyfuran with some anilines and aldehydes

R^1	R^2	compound (yield %)	*erythro* / *threo* **a** : **b**
Ph	Ph	**1** (95)	83 : 17
p-MeO-C_6H_4	Ph	**2** *	79 : 21
Ph	Me	**3** (99)	83 : 17
p-MeO-C_6H_4	Me	**4** (95)	80 : 20
Ph	Et	**5** (90)	90 : 10
Ph	*n*-C_6H_{13}	**6** (99)	92 : 8

*not isolated

The yields are very high (90 to 99%) in all cases and refer to isolated products. The diastereoselectivities are good and ranging between 80:20 to 90:10 depending upon the structures. Aware of a possible equilibration (*via* a retro-Mannich reaction for example) leading to erratic diastereoselectivities,[7] a very careful protocol was followed and applied to all experiments. As a matter of fact, the crude reaction mixture was analyzed by ^{1}H NMR spectrum to determine the diastereomeric ratio before any purification by chromatography on silica gel.

Table 2: Comparison of ^3J H5-H6 coupling constants of major and minor Mannich adducts, the corresponding reduced lactones and the rearranged δ-lactams.

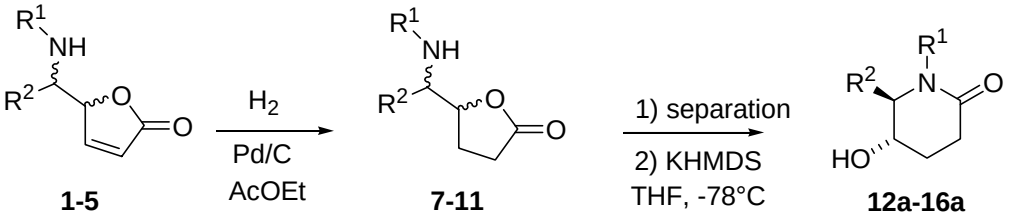
R^1	R^2		^3J H5-H6 (Hz) major	^3J H5-H6 (Hz) minor		^3J H5-H6 (Hz) major	^3J H5-H6 (Hz) minor		^3J H5-H6 (Hz)
Ph	Ph	**1**	4.2	6.8	**7**	3.1	5.5	**12a**	2.9
p-MeO-C_6H_4	Ph	**2**	4.0	7.0	**8**	3.1	6.1	**13a**	2.4
Ph	Me	**3**	-	3.0	**9**	4.1	-	**14a**	2.6
p-MeO-C_6H_4	Me	**4**	4.7	3.4	**10**	4.2	2.8	**15a**	3.0
Ph	Et	**5**	6.0	-	**11**	5.2	1.1	**16a**	2.4
Ph	*n*-C_6H_{13}	**6**	5.6	3.8	-	-	-	-	-

The assignement of the relative configuration is a very difficult problem to solve. The examination of ^{1}H NMR spectra for each diastereoisomers and namely the H5-H6 coupling constants do not seem to be a valuable proof to assign the relative configuration of the major isomer. We report in Table 2, the observed H5-H6 coupling constants for both diastereoisomers. The major Mannich adduct exhibits the smaller coupling constant value for reactions using benzaldehyde (R^2=Ph, compounds **(1)** and **(2)**). At the opposite, when R^2 is aliphatic (from aliphatic aldehydes) the major adduct exhibits larger coupling constant or could not be observed due to overlapping. The same trend was observed for the corresponding reduced products **(7-11)** (Table 2) obtained by hydrogenation (see Scheme 3).

The reversal of the larger coupling constant from the minor to the major isomer could be explained as an inversion of the diastereoselectivities between the aliphatic and aromatic aldehydes, but a conformational change in the same *erythro* (or *threo*) adduct arising from the aliphatic or aromatic R^2 group could also

lead to a change in the coupling constant. Thus, the ^{1}H NMR spectral analysis of the Mannich adducts could not provide an unambiguous configuration assignment.

The relative configuration of the major diastereomer was determined after chemical transformation. Casiraghi,[4c] first reported the transformation of such furanones to δ–lactam derivatives by DBU treatment allowing a convenient assignment of the relative configuration. In our hands, the DBU or acidic[4g] treatment did not undergo the desired cyclization due to the nature of the secondary amine. The sequence described in Scheme 3 was applied to compounds **(1a,b-5a,b)**. The double bond was first reduced and the diastereomeric saturated lactones were then separated permitting the isolation of the major isomers **(7a-11a)**. The latter were treated with KHMDS in THF at low temperature to furnish in good yield the δ-lactams **(12a-16a)** which were subjected to ^{1}H NMR spectral analyses. A pure sample of minor lactam **(15b)** was also obtained. The coupling constants between H5 and H6 for **12a-16a** are low values around 3 Hz (Table 2) suggesting a *trans*-diaxal relationship of the two substituents born at the δ-lactam ring and thus an *erythro* relative configuration of the major Mannich products. This was confirmed, by the pattern of H5 in the ^{1}H NMR spectrum of compound **(12a-16a)** which is characteristic of a pseudo-equatorial position (two small and a medium coupling constants, see EXPERIMENTAL) and by the observation of a ^{4}J coupling constant between H6 and H4. All these features are consistent with a *trans*-diequatorial arrangement of the diagnostic protons H5 and H6. Furthermore, analysis of isomeric δ–lactam **(15b)** arising from the minor isomer exhibits a H5-H6 coupling constant value of 4.3 Hz characteristic of a *cis*-axial-equatorial configuration. The *trans*-diaxial arrangement of both substituents at C5 and C6 resulted from the presence of a large group on nitrogen which is sp^2 hybridized. An important allylic interaction exists forcing substituents at C5 and C6 to be both placed in an axial position. The same behaviour was already reported for similar products.[4g, 9]



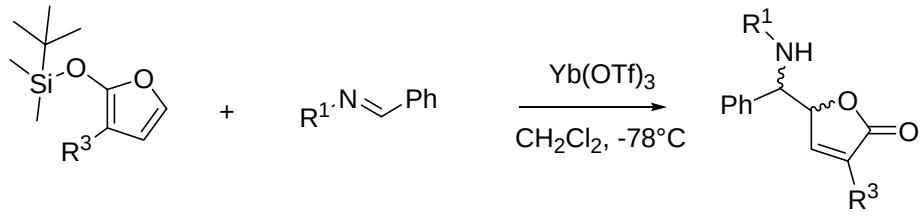
Scheme 3

As shown in this study, the Mannich reaction we reported herein is highly *erythro* selective independently of the nature of R^1 or R^2. This is consistent with the usually observed diastereoselectivity of silyloxyfuran condensation with imines.[7]

2- $Yb(OTf)_3$ catalyzed condensation of imines:

The *threo* configuration reported by Martin[4f] for the condensation of some 2-trimethylsilyloxyfurans with

imines derived from various benzaldehydes and anilines and catalyzed by Ti(OPr-*i*)$_4$/(*S*)-BINOL was still puzzling. Is the discrepancy in the diastereoselectivity due to the presence of a methyl group on the silyloxyfuran ? to the presence of a substituent on the aromatic group ? or to the use of Ti(OPr-*i*)$_4$/(*S*)-BINOL as a catalytic system ? We studied some condensations of 2-*t*-butyldimethylsilyloxyfuran and 3-methyl-2-*t*-butyldimethylsilyloxyfuran with preformed imines derived from benzaldehyde in the presence of Yb(OTf)$_3$ as a catalyst (Scheme 4).



1, 2, 17-20

Scheme 4

Table 3: Condensation of *t*-butyldimethylsilyloxyfuran with preformed imines

R^1	R^3	compound (yield %)	^{3}J H5-H6 major	minor	*erythro* / *threo*	
Ph	H	**1** (99)	4.2	6.8	72 / 28	(83/17)[a]
p-MeO-C_6H_4	H	**2** (95)	4.0	7.0	79 / 21	(79/21)[a]
o-MeO- C_6H_4	H	**17** (92)	3.6	6.4	73 / 27	
o-HO- C_6H_4	H	**18** (82)	3.8	5.0	70 / 30	(66/34)[b]
o-HO- C_6H_4	Me	**19** (90)	5.0	3.8	12 / 88	(09/91)[b]
Ph	Me	**20** (99)	7.0	3.8	21 / 79	

[a] one-pot procedure (cf. Table 2). [b] values reported by Martin[4f]

The results are reported in Table 3. A clean and rapid reaction was observed, very similar in all aspects to the reaction conducted in the three-component method: very similar yields and diastereoselectivities were observed in the reactions leading to **1** and **2**. Two condensations of imines derived from *o*-aminophenol and reported by Martin were reproduced in the conditions described by this author or using Yb(OTf)$_3$. Once again, very similar results were obtained in both conditions (Table 3, **18** and **19**).

Looking at the relative configuration of the major isomer, we again examined the coupling constants between H5 and H6. It appears that the major Mannich adducts all showed smaller ^{3}J values when R^3 = H consistent with the *erythro* configuration demonstrated for **1** and **2** (see above). At the opposite, for reactions conducted with 3-methyl-2-*t*-butyldimethylsilyloxyfuran (R^3= CH_3, **19** and **20**), the major

adducts exhibit the larger ^{3}J constant which could correspond to a *threo* configuration. The same *threo* configuration was obtained and proved in the work of Martin.[4f]

It thus appears that a reversal of stereoselectivity is occurring by the simple presence or absence of the methyl group on the silyloxyfuran ring. It is difficult to explain this phenomenon by application of "Diels-Alder" or "open" form approach mechanism both invoked in vinylogous Mannich reactions.[10]

In conclusion, we showed along this study, the efficiency of $Yb(OTf)_3$ as a catalyst for the three-component Mannich-type condensation of silyloxyfuran. This procedure gave very similar yields and diastereoselectivities compared to the condensation using preformed imines and the same catalyst or other Lewis acids described in the literature. The diastereoselectivity is mainly in favor of the *erythro* adduct except for condensation using 3-methyl-2-trialkylsilyloxyfuran.

EXPERIMENTAL

General conditions

All the solvents were dried according to the common methods and distilled before use. IR spectra were recorded on a Nicolet 205-FT infrared spectrophotometer. Melting points were determinated with a Leica VMHB Koffler type apparatus. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker AC 250, AC 300 or 400 Avance. Chemical shifts are reported in δ (ppm). In the case of *erythro/threo* mixture, NMR spectral data of the *threo* isomer were given in square brackets. CIMS spectra were recorded on AEI MS-9, ESMS on a Micromass ZQ 2000 with an Z-spray source, EIMS on a AEI MS-50 and HRMS on Micromass Q-Tof 1 with an ESI Z-spray source by the Mass Spectrometry Laboratory at the Faculty of Pharmacy (Paris). Elementary analyses were performed at the Microanalysis Laboratory (Pierre and Marie Curie University, Paris). All reactions were carried out under argon atmosphere and were monitored by thin-layer chromatography with Merck 60F-254 precoated silica (0.2 mm) on aluminium. Flash chromatographies were performed with SDS Silicagel 60ACC (35-70 μm); preparative layer chromatographies were performed with Merck 60 HF-254 precoated silica (1 mm) on glass. The solvent systems were given v/v.

General procedure for the one-pot three-component $Yb(OTf)_3$-catalyzed Mannich-type reaction of silyloxyfuran with amines and aldehydes:

10% mol of $Yb(OTf)_3$ was added to a 0.16M CH_2Cl_2 solution of silyloxyfuran (1 equiv.) and of aldehyde (1.2 to 2 equiv.) containing molecular sieves (4Å) at -78°C, followed by the dropwise addition of amine (1.2 to 2 equiv.). When the complete consumption of the starting materials was observed (about 45 min), the reaction mixture was filtered and the solvent was evaporated under reduced pressure. The crude mixture was dissolved in CH_2Cl_2 and washed with water. The layers were separated. The aqueous

solution was extracted with CH_2Cl_2 (2x15 mL). The collected organic fractions were dried over $MgSO_4$, filtered and evaporated under reduced pressure. The crude reaction mixtures were examined by ^{1}H NMR spectrum in order to determine the diastereoisomeric ratios. Products were isolated by flash chromatography on silica gel using AcOEt-cyclohexane or AcOEt-heptane as solvent.

5-[(Phenylamino)phenylmethyl]furan-2(5*H*)-one (1).

The general one-pot three-component procedure was applied to *t*-butyldimethylsilyloxyfuran (63 mg, 0.32 mmol), benzaldehyde (38 μL, 0.38 mmol) and aniline (35 μL, 0.38 mmol) to give **1** (58 mg, 95%) as a *83/17 erythro/threo* mixture and as a glassy solid after purification by flash chromatography (AcOEt/heptane 50/50); R_f *erythro/threo* mixture: 0.25 (AcOEt/heptane 30/70). ^{1}H-NMR (300 MHz, $CDCl_3$) δ *erythro,* [*threo*]: 7.50-6.60 (m, 11H, H-4, H-Ph, [H-4] and [H-Ph]); [6.20 (dd, *J*=5.8, 2.0 Hz, 0.17H, H-3)]; 6.10 (dd, *J*=5.8, 1.8 Hz, 0.83H, H-3); 5.45 (ddd, *J*=4.2, 2.0, 2.0 Hz, 0.83H, H-5); [5.15 (ddd, *J*=6.8, 1.8, 1.8 Hz, 0.17H, H-5)]; 4.70 (d, *J*=4.2 Hz, 0.83H, H-6); [4.50 (d, *J*=6.8 Hz, 0.17H, H-6)]. ^{13}C-NMR (75 MHz, $CDCl_3$) δ *erythro,* [*threo*]: 172.4, [172.4] (CO); [154.0], 153.2 (C-4); [146.6], 146.1 (C-q Ar); [138.3], 136.9 (C-q Ph); 129.3, 129.1, 128.9, 128.5, 128.4, 127.2 (C-Ph and [C-Ph]); 123.2, [122.8] (C-3); 118.7, [118.7] (C-p Ar); [114.2], 114.0 (C-o Ar); [85.8], 85.3 (C-5); [61.1], 59.4 (C-6). CIMS (isobutane 180°C) *m/z* 266 $(M+H)^+$, 182 $((M\text{-furanone})^+$, base peak).

5-[[(4-Methoxyphenyl)amino]phenylmethyl]furan-2(5*H*)-one (2).

Characterized by ^{1}H NMR spectrum (*erythro/threo* mixture: 79/21) but not isolated; R_f *erythro/threo* mixture: 0.50 (AcOEt/heptane 50/50). Described below in the imine condensation procedure section.

5-[1-(Phenylamino)ethyl]furan-2(*5H*)-one (3).

The general one-pot three-component procedure was applied to *t*-butyldimethylsilyloxyfuran (63 mg, 0.32 mmol), acetaldehyde (66 μL, 0.64 mmol) and aniline (58 μL, 0.64 mmol) to give **3** (66 mg, 99%) as a 83/17 *erythro/threo* mixture and as a glassy solid after purification by flash chromatography (AcOEt/heptane 30/70); R_f *erythro/threo* mixture: 0.25 (AcOEt/heptane 30/70). ^{1}H-NMR (250 MHz, $CDCl_3$) δ *erythro,* [*threo*]: 7.45 (2dd app., *J*=5.8, 1.2 Hz, 1H, H-4 and [H-4]); 7.20 (2dd app., *J*=7.4 Hz, 2H, H-*m* and [H-*m*]); 6.75 (2t app., *J*=7.4 Hz, 1H, H-*p* and [H-*p*]); 6.60 (2d, *J*=7.4 Hz, 2H, H-*o* and [H-*o*]); 6.15 (dd, *J*=5.8, 2.0 Hz, 0.83H, H-3); [6.10 (dd, *J*=5.8, 2.0 Hz, 0.17H, H-3)]; [5.20 (td app., *J*=3.0, 1.5 Hz, 0.17H, H-5)]; 5.10-5.00 (m, 0.83H, H-5); [4.00 (qd, *J*=6.6, 3.0 Hz, 0.17H, H-6)]; 3.80 (m, 1.83H, H-6, NH and [NH]); [1.25 (d, *J*=6.6 Hz, 0.51H, CH_3)]; 1.20 (d, *J*=6.6 Hz, 2.49H, CH_3). ^{13}C-NMR (50 MHz, $CDCl_3$) δ *erythro,* [*threo*]: 173.0, [172.9] (CO); 154.7, [154.3] (C-4); 146.2, [146.2] (C-q); 129.5, [129.5] (C-*m*); 122.6, [122.2] (C-*p*); 118.4, [118.1] (C-3); 113.7, [113.2] (C-*o*); 85.6, [85.1] (C-5); [50.9],

49.6 (C-6); [17.2], 16.0 (CH_3). CIMS (isobutane 180°C) *m/z* 204 $(M+H)^+$, 120 ((M-furanone)$^+$, base peak).

5-[1-[(4-Methoxyphenyl)amino]ethyl]furan-2(*5H*)-one (4).

The general one-pot three-component procedure was applied to *t*-butyldimethylsilyloxyfuran (531 mg, 2.70 mmol), acetaldehyde (0.30 mL, 5.40 mmol) and *p*-anisidine (660 mg, 5.40 mmol) to give **4** (593 mg, 95%) as a 80/20 *erythro/threo* mixture. Separation of diastereoisomers by flash chromatography (AcOEt/cyclohexane 30/70) furnished pure *erythro* **4a** and *threo*-enriched **4b**.

4a (*erythro*): pale yellow oil; R_f: 0.16 (AcOEt/cyclohexane 30/70). ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.44 (dd, *J*=5.7, 1.4 Hz, 1H, H-4); 6.75 (d, *J*=8.9 Hz, 2H, H-*m*); 6.60 (d, *J*=8.9 Hz, 2H, H-*o*); 6.12 (dd, *J*=5.7, 2.0 Hz, 1H, H-3); 5.05 (ddd, *J*=4.7, 1.9, 1.4 Hz, 1H, H-5); 3.72 (s, 3H, OCH_3); 3.67-3.64 (m, 1H, H-6); 3.50 (br s, 1H, NH); 1.10 (d, *J*=6.6 Hz, 3H, CH_3). ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 173.0 (CO); 154.8 (C-4); 153.0, 140.4 (C-q); 122.2 (C-3); 115.9, 115.2 (C-*m* and C-*o*); 85.6 (C-5); 55.8 (OCH_3); 52.4 (C-6); 15.9 (CH_3). ESMS *m/z* 272 $(M+K)^+$, 257 $(M+H+Na)^+$, 256 ($(M+Na)^+$, base peak), 234 $(M+H)^+$, 150 (M-furanone)$^+$. IR ν (cm^{-1}) (neat) 3390, 3370, 3089, 3034, 2974, 2934, 2833, 1759, 1620, 1597, 1538, 1514, 1504, 1454. Anal. Calcd for $C_{13}H_{15}NO_3$: C, 66.84; H, 6.48, N, 6.00. Found: C,66.82; H, 6.97; N, 6.07.

4b (*threo*-enriched): pale yellow oil; R_f: 0.25 (AcOEt/cyclohexane 30/70). ^{1}H-NMR (400 MHz, $CDCl_3$) δ (*erythro/threo* mixture: *14/86*): 7.40 (dd, *J*=5.7, 1.4 Hz, 1H, H-4); 6.75 (d, *J*=8.9 Hz, 2H, H-*m*); 6.60 (d, *J*=8.9 Hz, 2H, H-*o*); 6.05 (dd, *J*=5.7, 2.0 Hz, 1H, H-3); 5.15 (ddd, *J*=3.4, 1.7, 1.6 Hz, 1H, H-5); 3.70 (s, 3H, OCH_3); 3.70-3.60 (m, 1H, H-6); 3.5 (br s, 1H, NH); 1.20 (d, *J*=6.6 Hz, 3H, CH_3). ^{13}C-NMR (100 MHz, $CDCl_3$) δ (*erythro/threo* mixture: *14/86*): 173.0 (CO); 154.5 (C-4); 152.2, 140.3 (C-q); 122.6 (C-3); 116.5, 115.0 (C-*m* and C-*o*); 85.5 (C-5); 55.8 (OCH_3); 51.0 (C-6); 17.3 (CH_3).

5-[1-(Phenylamino)propyl]furan-2(*5H*)-one (5).

The general one-pot three-component procedure was applied to *t*-butyldimethylsilyloxyfuran (159 mg, 0.80 mmol), propionaldehyde (0.12 mL, 1.60 mol) and aniline (0.16 mL, 1.60 mmol) to give **5** (156 mg, 90%) as a 90/10 *erythro/threo* mixture. Separation of diastereoisomers by flash chromatography (AcOEt/cyclohexane 20/80) furnished pure *erythro* **5a** and *threo*-enriched **5b**.

5a (*erythro*): mp: 57-60°C (pale yellow solid, AcOEt/cyclohexane); R_f: 0.53 (AcOEt/cyclohexane 30/70). ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.48 (dd, *J*=4.4, 1.3 Hz, 1H, H-4); 7.20 (t app., *J*=7.4 Hz, 2H, H-*m*); 6.75 (t app., *J*=7.6 Hz, 1H, H-*p*); 6.60 (d app., *J*=7.8 Hz, 2H, H-*o*); 6.15 (dd, *J*=5.7, 2.0 Hz, 1H, H-3); 5.03 (d app., *J*=6.0 Hz, 1H, H-5); 3.61 (br s, 1H, NH); 3.51-3.57 (m, 1H, H-6); 1.83 (qdd, *J*=14.8, 7.5, 3.5 Hz, 1H,

H-7); 1.60-1.45 (m, 1H, H-7'); 1.02 (t, *J*=7.4 Hz, 3H, CH_3). ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 173.0 (CO); 155.1 (C-4); 147.1 (C-q); 129.6 (C-*m*); 122.2 (C-*p*); 118.3 (C-3); 113.6 (C-*o*); 85.5 (C-5); 57.4 (C-6); 25.0 (C-7); 10.5 (CH_3). ESMS *m/z* 257 $(M+H+K)^+$, 256 $(M+K)^+$, 241 $(M+H+Na)^+$, 240 ($(M+Na)^+$, base peak), 218 $(M+H)^+$. IR ν (cm^{-1}) (KBr) 3388, 2966, 2931, 2874, 1737, 1601, 1498, 1458. HR-ESMS Calcd for $C_{13}H_{15}NO_2Na$ $(M+Na)^+$ *m/z* 240.1000, found 240.1000.

5b (*threo*-enriched): pale yellow oil; R_f: 0.46 (AcOEt/cyclohexane 30/70). ^{1}H-NMR (400 MHz, $CDCl_3$) δ (*erythro/threo* mixture: *83/17*): 7.50 (dd, *J*=4.4, 1.3 Hz, 1H, H-4); 7.20 (t app., *J*=7.4 Hz, 2H, H-*m*); 6.75 (t app., *J*=7.6 Hz, 1H, H-*p*); 6.60 (d app., *J*=7.8 Hz, 2H, H-*o*); 6.05 (dd, *J*=5.7, 2.0 Hz, 1H, H-3); 5.25-5.20 (m, 1H, H-5); 3.80-3.70 (m, 1H, H-6); 3.60 (br s, 1H, NH); 1.85-1.75 (m, 1H, H-7); 1.05 (t, *J*=7.6 Hz, 3H, CH_3). ^{13}C-NMR (100 MHz, $CDCl_3$) δ (*erythro/threo* mixture: *83/17*): 173.0 (CO); 154.4 (C-4); 146.7 (C-q); 129.6 (C-*m*); 122.5 (C-*p*); 118.1 (C-3); 113.1 (C-*o*); 84.5 (C-5); 57.7 (C-6); 25.7 (C-7); 11.0 (CH_3).

5-[1-(Phenylamino)heptyl]furan-2(5*H*)-one (6).

The general one-pot three-component procedure was applied to *t*-butyldimethylsilyloxyfuran (63 mg, 0.32 mmol), heptaldehyde (68 μL, 0.48 mmol) and aniline (46 μL, 0.48 mmol) to give **6** (86 mg, 99%) as a 92/8 *erythro/threo* mixture and as a glassy solid after purification by flash-chromatography (AcOEt/heptane 30/70); R_f *erythro/threo* mixture: 0.65 (AcOEt/heptane 50/50). ^{1}H-NMR (250 MHz, $CDCl_3$) δ *erythro,* [*threo*]: 7.60-7.40 (m, 1H, H-4 and [H-4]); 7.20-6.50 (m, 5H, H-Ph and [H-Ph]); 6.15 (dd, *J*=6.0, 1.8 Hz, 0.92H, H-3); [6.05 (dd, *J*=5.6, 1.4 Hz, 0.08H, H-3)]; [5.20 (ddd, *J*=3.8, 1.6, 1.6 Hz, 0.08H, H-5)]; 5.05 (ddd, *J*=5.6, 1.8, 1.8 Hz, 0.92H, H-5); [3.85 (m, 0.08H, H-6)]; 3.60 (m, 0.92H, H-6); 1.85-1.20 (m, 10H, H-7 to H-11 and [H-7 to H-11]); 0.90 (2t, *J*=7.0 Hz, 3H, CH_3). ^{13}C-NMR (50 MHz, $CDCl_3$) δ *erythro*, [*threo*]: 172.8, [172.8] (CO); 154.9, [154.3] (C-4); [147.0], 146.8 (C-q); 129.4, [129.4] (C-*m*); [122.2], 121.9 (C-3); 118.1, [117.8] (C-*p*); 113.3, [112.8] (C-*o*); 85.5, [84.5] (C-5); 55.7, [53.9] (C-6); 32.2, 32.1, 31.7, 31.5, 29.1, 29.0, 26.2, 25.7, 22.4 (C-7 to C-11); 13.9, [13.9] (CH_3). EIMS (isobutane 180°C) *m/z* 273 (M^+), 190 ((M-furanone)$^+$, base peak).

Hydrogenation of furan-2(*5H*)-one derivatives:

A solution of pure furan-2(*5H*)-one derivative (1 equiv.) in AcOEt (10 mL) was hydrogenated for 4 h at atmospheric pressure in the presence of 10 wt. % palladium on charcoal (Acros, 10% Pd on activated carbon). The catalyst was removed by filtration through celite, the filter pad was washed with AcOEt (30 mL) then with MeOH (30 mL). The combined filtrate and washings were evaporated under reduced

pressure to afford the expected product which was used without further purification for the following step starting from pure *erythro* or *threo*-enriched derivatives or purified (and separated) by chromatography on silica gel starting from crude *erythro*/*threo* mixtures.

5-[(Phenylamino)phenylmethyl]dihydrofuran-2(3*H*)-one (7).

The hydrogenation procedure was applied to a crude 83/17 diastereoisomeric mixture of **1** (1.10 g) to give **7** (427 mg, 70% from 2-*t*-butyldimethylsilyloxyfuran) as a 82/18 *erythro/threo* mixture. Separation of diastereoisomers by flash chromatography (AcOEt/cyclohexane 30/70) furnished pure *erythro* **7a** and *threo*-enriched **7b**.

7a (*erythro*): mp: 152-154°C (white solid, AcOEt/cyclohexane); R_f: 0.32 (AcOEt/cyclohexane 30/70). ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.39-7.31 (m, 5H, H-Ph); 7.10 (t app., *J*=7.5 Hz, 2H, H-*m* Ar); 6.68 (t app., *J*=7.3 Hz, 1H, H-*p* Ar); 6.56 (d app., *J*=7.7 Hz, 2H, H-*o* Ar); 5.00 (dddd, *J*=9.7, 6.1, 3.5, 1.3 Hz, 1H, H-5); 4.63 (d, *J*=7.5 Hz, 1H, NH); 4.54 (dd, *J*=7.5, 3.1 Hz, 1H, H-6); 2.34-2.21 (m, 2H, H-4); 2.12-2.05 (m, 1H, H-3); 1.82-1.73 (m, 1H, H-3'). ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 177.0 (CO); 146.4, 137.1 (C-q); 129.3, 129.0, 128.3, 128.2 (C-Ph and C-*m* Ar); 118.3, 114.0 (C-Ar); 82.1 (C-5); 60.6 (C-6); 27.8 (C-3); 23.8 (C-4). ESMS *m/z* 307 $(M+H+K)^+$, 306 $(M+K)^+$, 291 $(M+H+Na)^+$, 290 $(M+Na)^+$, 268 $((M+H)^+$, base peak). IR ν (cm^{-1}) (KBr) 3362, 3026, 2989, 2916, 1774, 1602, 1498, 1454. HR-ESMS Calcd for $C_{17}H_{18}NO_2$ $(M+H)^+$ *m/z* 268.1338, found 268.1332.

7b (*threo*-enriched): pale yellow solid; R_f: 0.37 (AcOEt/cyclohexane 30/70). ^{1}H-NMR (400 MHz, $CDCl_3$) δ (*erythro/threo* mixture: *45/55*): 7.45-7.31 (m, 5H, H-Ph); 7.20 (t app., *J*=7.5 Hz, 2H, H-*m* Ar); 6.80 (t app., *J*=7.4 Hz, 1H, H-*p* Ar); 6.75-6.65 (m, 2H, H-*o* Ar); 4.75-4.65 (m, 2H, H-5 and NH); 4.44 (d, *J*=5.5 Hz, 1H, H-6); 2.51-2.47 (m, 2H, H-3); 2.35-2.15 (m, 1H, H-4); 2.15-2.00 (m, 1H, H-4'). ^{13}C-NMR (100 MHz, $CDCl_3$) δ (*erythro/threo* mixture *45/55*): 177.2 (CO); 147.1, 139.2 (C-q); 129.3, 129.1, 128.2, 127.4 (C-Ph and C-*m* Ar); 118.6, 114.3 (C-Ar); 83.2 (C-5); 61.7 (C-6); 28.7 (C-3); 25.1 (C-4).

5-[[(4-Methoxyphenyl)amino]phenylmethyl]dihydrofuran-2(3*H*)-one (8).

The hydrogenation procedure was applied to a crude 79/21 diastereoisomeric mixture of **2** (1.72 g, 5.80 mmol) to give **8** (902 mg, 90% from 2-*t*-butyldimethylsilyloxyfuran) as a 71/29 *erythro/threo* mixture. Separation of diastereoisomers by flash chromatography (AcOEt/cyclohexane 30/70) furnished pure *erythro* **8a** and *threo*-enriched **8b**.

8a (*erythro*): mp: 148-150°C (pale brown solid, AcOEt/cyclohexane); R_f: 0.54 (AcOEt/cyclohexane 50/50). ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.36-7.25 (m, 5H, H-Ph); 6.75 (dd, *J*=6.5, 2.3 Hz, 2H, H-*m* Ar); 6.53 (dd, *J*=6.7, 2.3 Hz, 2H, H-*o* Ar); 4.97 (ddd, *J*=9.9, 6.2, 3.4 Hz, 1H, H-5); 4.49 (d, *J*=3.1 Hz, 1H,

H-6); 3.69 (s, 3H, OCH_3); 2.34-2.18 (m, 2H, H-3); 2.14-2.05 (m, 1H, H-4); 1.90-1.80 (m, 1H, H-4'). ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 177.0 (CO); 152.9, 147.9, 137.3 (C-q); 128.9, 128.2 (C-Ph); 116.6, 114.9 (C-Ar); 82.2 (C-5); 61.5 (C-6); 55.8 (OCH_3); 27.8 (C-3); 23.8 (C-4). ESMS *m/z* 321 $(M+H+Na)^+$, 320 $(M+Na)^+$, base peak). IR ν (cm^{-1}) (KBr) 3384, 3222, 3004, 2915, 2835, 1775, 1654, 1635, 1514, 1495, 1451. HR-ESMS Calcd for $C_{18}H_{19}NO_3Na$ $(M+Na)^+$ *m/z* 320.1263, found 320.1270.

8b (*threo*-enriched): brown solid; R_f: 0.60 (AcOEt/cyclohexane 50/50). ^{1}H-NMR (400 MHz, $CDCl_3$) δ (*erythro/threo* mixture: *30/70*): 7.40-7.20 (m, 5H, H-Ph); 6.70 (dd, *J*=6.6, 2.1 Hz, 2H, H-*m* Ar); 6.55-6.51 (m, 2H, H-*o* Ar); 4.78-4.66 (m, 1H, H-5); 4.34 (d, *J*=6.1 Hz, 1H, H-6); 3.76 (s, 3H, OCH_3); 2.53-2.39 (m, 2H, H-3); 2.27-2.19 (m, 1H, H-4); 2.01-1.92 (m, 1H, H-4'). ^{13}C-NMR (100 MHz, $CDCl_3$) δ (*erythro/threo* mixture: *30/70*): 177.0 (CO); 152.9, 140.1, 137.3 (C-q); 129.0, 128.3, 127.5 (C-Ph); 116.6, 114.9 (C-Ar); 83.2 (C-5); 62.9 (C-6); 55.8 (OCH_3); 28.7 (C-3); 25.1 (C-4).

5-[1-(Phenylamino)ethyl]dihydrofuran-2(3*H*)-one (9).

The hydrogenation procedure was applied to a crude 83/17 diastereoisomeric mixture of **3** (521 mg) to give **9** (178 mg, 65% from 2-*t*-butyldimethylsilyloxyfuran) as a 90/10 *erythro/threo* mixture. Separation of distereoisomers by flash chromatography (AcOEt/cyclohexane 30/70) furnished pure *erythro* **9a** and *threo*-enriched **9b**.

9a (*erythro*): pale yellow oil, R_f: 0.26 (AcOEt/cyclohexane 30/70). ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.19 (dd, *J*=8.2, 7.5 Hz, 2H, H-*m*); 6.74 (t, *J*=7.3 Hz, 1H, H-*p*); 6.64 (d app., *J*=7.7 Hz, 2H, H-*o*); 4.58 (td app., *J*=7.4, 4.1 Hz, 1H, H-5); 3.77-3.66 (m, 2H, H-6 and NH); 2.60-2.53 (m, 2H, H-3); 2.39-2.27 (m, 1H, H-4); 2.11-2.02 (m, 1H, H-4'); 1.23 (d, *J*=6.5 Hz, 3H, CH_3). ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 177.1 (CO); 146.8 (C-q); 129.5 (C-*m*); 118.2 (C-*p*); 113.8 (C-*o*); 82.8 (C-5); 51.9 (C-6); 28.5 (C-3); 24.2 (C-4); 15.5 (CH_3). ESMS *m/z* 228 $(M+Na)^+$, 206 ($(M+H)^+$, base peak). IR ν (cm^{-1}) (neat) 3366, 3051, 3021, 2975, 2934, 2875, 1789, 1600, 1514, 1504, 1455. HR-ESMS Calcd for $C_{12}H_{15}NO_2Na$ $(M+Na)^+$ *m/z* 228.1000, found 228.0990.

9b (*threo*-enriched): pale yellow oil; R_f: 0.33 (AcOEt/cyclohexane 30/70). ^{1}H-NMR (400 MHz, $CDCl_3$) δ (*erythro/threo* mixture: *66/34*): 7.19 (t app., *J*=7.6 Hz, 2H, H-*m*); 6.74 (t, *J*=7.3 Hz, 1H, H-*p*); 6.64 (dd, *J*=7.7, 2.4 Hz, 2H, H-*o*); 4.64-4.58 (m, 1H, H-5); 3.80-3.53 (m, 2H, H-6 and NH); 2.60-2.52 (m, 2H, H-3); 2.26-2.21 (m, 2H, H-4); 1.31 (d, *J*=6.6 Hz, 3H, CH_3). ^{13}C-NMR (100 MHz, $CDCl_3$) δ (*erythro/threo* mixture: *66/34*): 177.4 (CO); 147.2 (C-q); 129.6 (C-*m*); 118.3 (C-*p*); 113.6 (C-*o*); 83.3 (C-5); 51.2 (C-6); 28.8 (C-3); 24.2 (C-4); 18.0 (CH_3).

5-[1-[4-Methoxyphenyl)amino]ethyl]dihydrofuran-2(3*H*)-one (10).

The hydrogenation procedure was applied to a crude 80/20 diastereoisomeric mixture of **4** (1.58 g) to give

10 (365 mg, 75% from 2-*t*-butyldimethylsilyloxyfuran) as a 80/20 *erythro/threo* mixture. Separation of diastereoisomers by flash chromatography (AcOEt/cyclohexane 50/50) furnished pure *erythro* **10a** and *threo*-enriched **10b**. Pure **10a** (117 mg, 70%) was also obtained from pure **4a** (167 mg, 0.72 mmol).

10a (e*rythro*): pale yellow oil; R_f: 0.49 (AcOEt/cyclohexane 50/50). ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 6.75 (dd, *J*=8.9, 2.1 Hz, 2H, H-*m*); 6.60 (dd, *J*=8.9, 2.1 Hz, 2H, H-*o*); 4.55 (td app., *J*=7.4, 4.2 Hz, 1H, H-5); 3.75 (s, 3H, OCH_3); 3.55 (qd, *J*=6.7, 4.2 Hz, 1H, H-6); 3.25 (br s, 1H, NH); 2.60-2.45 (m, 2H, H-3); 2.35-2.25 (m, 1H, H-4); 2.10-2.00 (m, 1H, H-4'); 1.20 (d, *J*=6.7 Hz, 3H, CH_3). ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 176.9 (CO); 152.5, 140.7 (C-q); 115.5, 114.8 (C-*m* and C-*o*); 87.5 (C-5); 55.6 (C-6); 53.0 (OCH_3); 28.3 (C-3); 23.9 (C-4); 15.3 (CH_3). ESMS *m/z* 275 $(M+H+K)^+$, 275 $(M+K)^+$, 259 $(M+H+Na)^+$, 258 ($(M+Na)^+$, base peak), 174 (M-furanone+Na)$^+$. IR ν (cm^{-1}) (neat) 3520, 3272, 3033, 2935, 2833, 1789, 1620, 1504, 1454. Anal. Calcd for $C_{13}H_{17}NO_3$: C, 66.36; H, 7.28, N, 5.95. Found: C,66.43; H, 7.81; N, 5.78.

10b (*threo*-enriched): pale yellow oil; R_f: 0.47 (AcOEt/cyclohexane 50/50). ^{1}H-NMR (400 MHz, $CDCl_3$) δ (*erythro/threo* mixture: *21/79*): 6.79 (dd, *J*=8.9, 2.1 Hz, 2H, H-*m*); 6.67-6.60 (m, 2H, H-*o*); 4.59 (td app., *J*=7.5, 2.8 Hz, 1H, H-5); 3.76 (s, 3H, OCH_3); 3.55 (qd, *J*=6.6, 2.8 Hz, 1H, H-6); 3.25 (br s, 1H, NH); 2.62-2.48 (m, 2H, H-3); 2.30-2.20 (m, 2H, H-4); 1.27 (d, *J*=6.6 Hz, 3H, CH_3). ^{13}C-NMR (100 MHz, $CDCl_3$) δ (*erythro/threo* mixture: *21/79*): 177.5 (CO); 152.7, 141.1 (C-q); 115.8, 115.1 (C-*m* and C-*o*); 83.4 (C-5); 55.9 (C-6); 52.6 (OCH_3); 28.9 (C-3); 24.3 (C-4); 17.8 (CH_3).

5-[1-(Phenylamino)propyl]dihydrofuran-2(3*H*)-one (11).

The hydrogenation procedure was applied to a crude 90/10 diastereoisomeric mixture of **5** (1.34 g) to give **11** (368 mg, 55% from 2-*t*-butyldimethylsilyloxyfuran) as a 90/10 *erythro/threo* mixture. Separation of diastereoisomers by flash chromatography (AcOEt/cyclohexane 20/80) furnished pure *erythro* **11a** and *threo*-enriched **11b**.

11a (*erythro*): mp: 87-89°C (white solid, AcOEt/cyclohexane); R_f: 0.28 (AcOEt/cyclohexane 30/70). ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.17 (t app., *J*=7.5 Hz, 2H, H-*m*); 6.73 (t, *J*=7.3 Hz, 1H, H-*p*); 6.71 (dd, *J*=7.7, 0.8 Hz, 2H, H-*o*); 4.54 (td app., *J*=7.2, 5.2 Hz, 1H, H-5); 3.55-3.45 (m, 1H, H-6); 3.40 (br s, 1H, NH); 2.60-2.50 (m, 2H, H-3); 2.35-2.25 (m, 1H, H-4); 2.15-2.05 (m, 1H, H-4'); 1.79 (qdd, *J*=14.8, 7.7, 3.6 Hz, 1H, H-7); 1.53-1.41 (m, 1H, H-7'); 1.01 (t, *J*=7.4 Hz, 3H, CH_3). ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 177.0 (CO); 147.9 (C-q); 129.5 (C-*m*); 118.1 (C-*p*); 113.6 (C-*o*); 82.3 (C-5); 58.1 (C-6); 28.6 (C-3); 24.5 (C-7); 24.2 (C-4); 10.6 (CH_3). ESMS *m/z* 258 $(M+K)^+$, 243 $(M+H+Na)^+$, 242 ($(M+Na)^+$, base peak), 220 $(M+H)^+$. IR ν (cm^{-1}) (KBr) 3360, 3057, 3021, 2967, 2935, 2877, 1759, 1601, 1518, 1495, 1458. HR-ESMS Calcd for $C_{13}H_{17}NO_2Na$ $(M+Na)^+$ *m/z* 242.1157, found 242.1158.

11b (*threo*-enriched): pale yellow glassy solid; R_f: 0.37(AcOEt/cyclohexane 30/70). ^{1}H-NMR (400 MHz, $CDCl_3$) δ (*erythro/threo* mixture: *48/52*): 7.20-7.12 (m, 2H, H-*m*); 6.75-6.70 (m, 1H, H-*p*); 6.67-6.61 (m, 2H, H-*o*); 4.72 (td app., *J*=7.5, 1.1 Hz, 1H, H-5); 3.50-3.45 (m, 1H, H-6); 3.25 (br s, 1H, NH); 2.61-2.51 (m, 2H, H-3); 2.55-2.15 (m, 2H, H-4); 1.80-1.60 (m, 1H, H-7); 1.60-1.40 (m, 1H, H-7'); 0.98 (t, *J*=7.4 Hz, 3H, CH_3). ^{13}C-NMR (100 MHz, $CDCl_3$) δ (*erythro/threo* mixture: *48/52*): 177.7 (CO); 147.9 (C-q); 129.6 (C-*m*); 117.8 (C-*p*); 113.1 (C-*o*); 81.8 (C-5); 57.1 (C-6); 28.9 (C-3); 26.2 (C-7); 24.1 (C-4); 11.0 (CH_3).

5-Hydroxy-1-arylpiperidin-2-one derivatives formation by base-promoted cyclization of various dihydrofuran-2(3*H*)-ones:

A solution of KHMDS (0.5M in toluene, 1.3 equiv.) was slowly added over a 0.07M cooled (-20°C) solution of the dihydrofuran-2(3*H*)-one (1 equiv.) in dry THF. The mixture was stirred for 30 min at this temperature and quenched with a saturated solution of ammonium chloride (10 mL). The mixture was extracted with CH_2Cl_2 (3x15 mL), the collected organic fractions were dried over Na_2SO_4, and the solvent was removed in vacuo yielding 5-hydroxy-1-arylpiperidin-2-one derivative after flash chromatography.

***trans*-5-Hydroxy-1,6-diphenylpiperidin-2-one (12a).**

The general base-promoted cyclization procedure was applied to **7a** (100 mg, 0.37 mmol) to give **12a** (62 mg, 62%) as a *trans* diastereoisomer and as a white solid (mp: 160-162°C, AcOEt) after purification by flash chromatography (AcOEt/cyclohexane 70/30); R_f: 0.12 (AcOEt/cyclohexane 70/30). ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.38-7.12 (m, 10H, H-Ph and H-Ar); 4.90 (d, *J*=2.9 Hz, 1H, H-6); 4.10 (td, *J*=4.8, 2.9 Hz, 1H, H-5); 2.86 (ddd, *J*=18.2, 10.0, 2.3 Hz, 1H, H-3); 2.64 (ddd, *J*=18.4, 7.4, 3.2 Hz, 1H, H-3'); 2.05-1.95 (m, 1H, H-4), 1.85-1.75 (m, 1H, H-4'). ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 171.0 (CO); 142.6, 139.1 (C-q); 129.1, 128.8, 127.8, 127.5, 127.1 (C-Ph and C-Ar); 72.1 (C-6); 69.7 (C-5); 27.7 (C-3); 23.4 (C-4). ESMS m/z 332 $(M+H+K)^+$, 331 $(M+K)^+$, 291 $(M+H+Na)^+$, 290 ($(M+Na)^+$, base peak), 268 $(M+H)^+$. IR ν (cm^{-1}) (KBr) 3345, 3059, 2952, 1636, 1591, 1493, 1457, 1441, 1421. HR-ESMS Calcd for $C_{17}H_{18}NO_2$ $(M+H)^+$ *m/z* 268.1338, found 268.1350.

***trans*-5-Hydroxy-1-(4-methoxyphenyl)-6-phenylpiperidin-2-one (13a).**

The general base-promoted cyclization procedure was applied to **8a** (201 mg, 0.68 mmol) to give **13a** (66 mg, 35%) as a *trans* diastereoisomer and as a pale yellow solid (mp: 172-174°C, AcOEt) after purification by flash chromatography (AcOEt 100); R_f: 0.15 (AcOEt 100). ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.36-7.26 (m, 5H, H-Ph); 7.05 (dd, *J*=8.8, 1.8 Hz, 2H, H-*m* Ar); 6.77 (dd, *J*=8.8, 1.9 Hz, 2H, H-*o* Ar); 4.83 (d, *J*=2.4 Hz, 1H, H-6); 4.20-4.10 (m, 1H, H-5); 3.73 (s, 3H, OCH_3); 2.85 (ddd, *J*=18.2, 9.7, 7.3 Hz,

1H, H-3); 2.69 (ddd, *J*=18.3, 7.3, 4.2 Hz, 1H, H-3'); 2.02-1.95 (m, 1H, H-4); 1.81-1.76 (m, 1H, H-4'). ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 171.3 (CO); 158.2, 139.2, 135.4 (C-q); 128.8, 128.6, 127.9, 127.1 (C-Ph and C-*m* Ar); 114.3 (C-*o* Ar); 72.4 (C-6); 69.6 (C-5); 55.4 (OCH_3); 27.6 (C-3); 23.3 (C-4). ESMS m/z 337 $(M+H+K)^+$, 336 $(M+K)^+$, 321 $(M+H+Na)^+$, 320 ($(M+Na)^+$, base peak). IR ν (cm^{-1}) (KBr) 3413, 3010, 2961, 2914, 2838, 1631, 1604, 1510, 1458, 1439, 1406, 1348. HR-ESMS Calcd for $C_{18}H_{19}NO_3Na$ $(M+Na)^+$ *m/z* 320.1263, found 320.1259.

***trans*-5-Hydroxy-6-methyl-1-phenyllpiperidin-2-one (14a).**

The general base-promoted cyclization procedure was applied to **9a** (78 mg, 0.38 mmol) to give **14a** (42 mg, 54%) as a *trans* diastereoisomer and as a colorless oil after purification by flash chromatography (AcOEt/MeOH 95/5); R_f: 0.34 (AcOEt/MeOH 95/5). ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.37 (t app., *J*=7.4 Hz, 2H, H-*m*); 7.27 (t app., *J*=7.4 Hz, 1H, H-*p*); 7.16 (d app., *J*=7.2 Hz, 2H, H-*o*); 3.80 (dt, *J*=5.0, 2.6 Hz, 1H, H-5); 3.72 (qdd, *J*=6.6, 3.1 (2.6 Hz after homodec. at 1.05 ppm), 0.7 Hz, 1H, H-6); 2.70 (ddd, *J*=18.0, 10.4, 7.2 Hz, 1H, H-3ax); 2.44 (ddd, *J*=18.2, 6.8, 3.6 Hz, 1H, H-3eq); 2.03 (dddd, *J*=16.6, 9.7, 6.9, 2.4 Hz, 1H, H-4ax), 1.91-1.83 (m, 1H, H-4eq), 1.05 (d, *J*=6.7 Hz, 3H, CH_3). ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 170.3 (CO); 141.8 (C-q); 129.3 (C-*m*); 128.2 (C-*o*); 127.4 (C-*p*); 68.0 (C-5); 62.9 (C-6); 27.6 (C-3); 24.3 (C-4); 18.9 (CH_3). ESMS m/z 244 $(M+K)^+$, 228 ($(M+Na)^+$, base peak), 206 $(M+H)^+$, 198 $(M+H-H_2O)^+$. IR ν (cm^{-1}) (neat) 3379, 3098, 2940, 2973, 2926, 1633, 1591, 1495, 1470, 1443, 1409. HR-ESMS Calcd for $C_{12}H_{16}NO_2$ $(M+H)^+$ *m/z* 206.1181, found 206.1137.

***trans*-5-Hydroxy-1-(4-methoxyphenyl)-6-methylpiperidin-2-one (15a).**

The general base-promoted cyclization procedure was applied to **10a** (77 mg, 0.33 mmol) to give **15a** (42 mg, 55%) as a *trans* diastereoisomer and as a pale yellow oil after purification by flash chromatography (AcOEt/MeOH 90/10); R_f: 0.41 (AcOEt/MeOH 90/10). ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.10 (dd, *J*=8.8, 2.1 Hz, 2H, H-*m*); 6.90 (dd, *J*=8.8, 2.1 Hz, 2H, H-*o*); 3.90 (dt app., *J*=5.6, 3.0 Hz, 1H, H-5); 3.80 (s, 3H, OCH_3); 3.70 (qdd, *J*=6.6, 3.4 (2.7 Hz after homodec. at 1.15 ppm), 0.7 Hz, 1H, H-6); 2.70 (ddd, *J*=17.8, 10.1, 7.1 Hz, 1H, H-3ax); 2.50 (ddd, *J*=18.1, 6.9, 4.2 Hz, 1H, H-3eq); 2.15 (dddd, *J*=16.7, 9.8, 6.9, 2.5 Hz, 1H, H-4ax), 2.00-1.90 (m, 1H, H-4eq), 1.15 (d, *J*=6.6 Hz, 3H, CH_3). ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 170.3 (CO); 158.5, 134.5 (C-q); 129.2 (C-*m*); 114.5 (C-*o*); 68.4 (C-5); 63.4 (C-6); 55.5 (OCH_3); 27.6 (C-3); 24.6 (C-4); 19.0 (CH_3). ESMS m/z 274 $(M+K)^+$, 259 $(M+H+Na)^+$, 258 ($(M+Na)^+$, base peak). IR ν (cm^{-1}) (neat) 3380, 3075, 2940, 2837, 1600, 1530, 1455. HR-ESMS calcd for $C_{13}H_{18}NO_3$ $(M+H)^+$ *m/z* 236.1287, found 236.1281.

***cis*-5-Hydroxy-1-(4-methoxyphenyl)-6-methylpiperidin-2-one (15b).**

The general base-promoted cyclization procedure was applied to **10b** (66 mg, 0.28 mmol) to give **15b** (30 mg, 45%) as a *cis* diastereoisomer and as a pale yellow oil after purification by flash chromatography (AcOEt/MeOH 100/0 to 90/10); R_f: 0.41 (AcOEt/MeOH 50/50). ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.10 (dd, *J*=8.9, 2.3 Hz, 2H, H-*m*); 6.90 (dd, *J*=8.9, 2.2 Hz, 2H, H-*o*); 4.20 (td app., *J*=8.4, 4.3 Hz, 1H, H-5); 3.85 (qd, *J*=6.7, 4.3 Hz, 1H, H-6); 3.80 (s, 3H, OCH_3); 2.70 (td app., *J*=18.1, 6.6 Hz, 1H, H-3); 2.50 (td app., *J*=18.1, 7.4 Hz, 1H, H-3'); 2.20-1.90 (m, 2H, H-4), 1.10 (d, *J*=6.6 Hz, 3H, CH_3). ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 170.2 (CO); 158.5, 134.0 (C-q); 129.0 (C-*m*); 114.5 (C-*o*); 67.3 (C-5); 59.9 (C-6); 55.5 (OCH_3); 28.9 (C-3); 25.7 (C-4); 14.9 (CH_3). ESMS m/z 258 $(M+Na)^+$, 236 ($(M+H)^+$, base peak), 218 $(M+H-H_2O)^+$. IR ν (cm^{-1}) (neat) 3331, 3045, 2970, 1623, 1600, 1522, 1458, 1408. HR-ESMS calcd for $C_{13}H_{17}NO_3Na$ $(M+Na)^+$ *m/z* 258.1106, found 258.1099.

***trans*-6-Ethyl-5-hydroxy-1-phenylpiperidin-2-one (16a).**

The general base-promoted cyclization procedure was applied to **11a** (150 mg, 0.68 mmol) to give **16a** (47 mg, 32%) as a *trans* diastereoisomer and as a colorless oil after purification by flash chromatography (AcOEt/MeOH 95/5); R_f: 0.37 (AcOEt/MeOH 95/5). ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.41-7.14 (m, 5H, H-Ph); 4.10 (td app., *J*=4.5, 2.4 Hz, 1H, H-5); 3.63-3.61 (m, 1H, H-6); 2.68 (ddd, *J*=18.0, 10.3, 7.5 Hz, 1H, H-3ax); 2.48 (ddd, *J*=18.2, 7.2, 3.4 Hz, 1H, H-3eq); 2.11-2.03 (m, 1H, H-4); 1.94-1.89 (m, 1H, H-4'); 1.78-1.63 (m, 1H, H-7); 1.46-1.32 (m, 1H, H-7'), 0.79 (t, *J*=7.5 Hz, 3H, CH_3). ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 170.1 (CO); 142.1 (C-q); 129.2, 128.1 (C-*m* and C-*o*); 127.2 (C-*p*); 68.7 (C-6); 65.0 (C-5); 27.4 (C-3); 25.3 (C-7); 24.6 (C-4); 10.3 (CH_3). ESMS m/z 259 $(M+H+K)^+$, 258 $(M+K)^+$, 243 $(M+H+Na)^+$, 242 ($(M+Na)^+$, base peak). IR ν (cm^{-1}) (neat) 3382, 3063, 2964, 2937, 2878, 1632, 1592, 1495, 1461, 1411, 1355. HR-ESMS calcd for $C_{13}H_{18}NO_2$ $(M+H)^+$ *m/z* 220.1338, found 220.1333.

General procedure for the $Yb(OTf)_3$-catalyzed Mannich-type reaction of silyloxyfuran with imines derived from aniline:

10% mol of $Yb(OTf)_3$ was added to a solution of imine (1.5 to 2 equiv.) in CH_2Cl_2 (2 mL) at -78°C, followed by the dropwise addition of silyloxyfuran (1 equiv.). When the complete consumption of the starting materials was observed (about 15 min), the reaction mixture was warmed to rt and washed with water. The layers were separated. The aqueous solution was extracted with CH_2Cl_2 (2x15 mL). The collected organic fraction was dried over $MgSO_4$, filtered and evaporated under reduced pressure. The crude reaction mixtures were examined by ^{1}H NMR spectrum in order to determine the diastereoisomeric ratios. Products were isolated by preparative layer chromatography using AcOEt-heptane as solvent.

5-[(Phenylamino)phenylmethyl]furan-2(5*H*)-one (1).

The general $Yb(OTf)_3$-catalyzed condensation of preformed imines procedure was applied to *t*-butyldimethylsilyloxyfuran (63 mg, 0.32 mmol) and *N*-benzylideneaniline (89 mg, 0.48 mmol) to give **1** (85 mg, 99%) as a 72/28 *erythro/threo* mixture and as a glassy solid after purification by preparative layer chromatography (AcOEt/heptane 50/50); R_f *erythro/threo* mixture: 0.25 (AcOEt/heptane 30/70).

5-[[(4-Methoxyphenyl)amino]phenylmethyl]furan-2(5*H*)-one (2).

The general $Yb(OTf)_3$-catalyzed condensation of preformed imines procedure was applied to *t*-butyldimethylsilyloxyfuran (63 mg, 0.32 mmol) and *N*-benzylidene-*p*-anisidine (96 mg, 0.49 mmol) to give **2** (91 mg, 95%) as a 79/21 *erythro/threo* mixture and as a glassy solid after purification by preparative layer chromatography AcOEt/heptane (50/50); R_f *erythro/threo* mixture: 0.50 (AcOEt/heptane 50/50). ^{1}H-NMR (300 MHz, $CDCl_3$) δ *erythro*, [*threo*]: 7.35-7.25 (m, 5H+0.79H, H-4, H-Ph and [H-Ph]); [7.20 (dd, *J*=6.0, 2.0 Hz, 0.21H, H-4)]; 6.60 (2d, *J*=9.0 Hz, 2H, H-*m* Ar and [H-*m* Ar]); 6.45 (2d, *J*=9.0 Hz, 2H, H-*o* Ar and [H-*o* Ar]); [6.05 (H-3, 0.21H, dd, *J*=6.0, 2.0 Hz)]; 5.95 (H-3, 0.79H, dd, *J*=6.0, 2.0 Hz); 5.55 (ddd, *J*=3.8, 1.6, 1.6 Hz, 0.79H, H-5); [5.15 (ddd, *J*=7.0, 1.6, 1.6 Hz, 0.21H, H-5)]; 4.70 (d, *J*=4.0 Hz, 0.79H, H-6); [4.35 (d, *J*=7.0 Hz, 0.21H, H-6)]; 3.60 (2s, 3H, OCH_3 and [OCH_3]). ^{13}C-NMR (75 MHz, $CDCl_3$) δ *erythro*, [*threo*]: 172.4, [172.4] (CO); 154.0, [153.4] (C-4); 152.9, [152.9], 140.5, [140.1] (C-q Ar); [138.5], 137.1 (C-q Ph); 129.1, 128.9, 128.5, 128.3, 127.3, 127.2 (C-Ph and [C-Ph]); 123.0, [122.6] (C-3); [115.8], 115.6 (C-*m* Ar); [114.7], 114.7 (C-*o* Ar); [85.9], 85.4 (C-5); 62.2, [60.4] (C-6); 60.4 (OCH_3 and [OCH_3]). ESMS *m/z* 318 $(M+Na)^+$, 296 ($(M+H)^+$, base peak). IR ν (cm^{-1}) (KBr) 3368, 1755.

5-[[(2-Methoxyphenyl)amino]phenylmethyl]furan-2(5*H*)-one (17).

The general $Yb(OTf)_3$-catalyzed condensation of preformed imines procedure was applied to *t*-butyldimethylsilyloxyfuran (63 mg, 0.32 mmol) and *N*-benzylidene-*o*-anisidine (96 mg, 0.49 mmol) to give **17** (88 mg, 92%) as a 73/27 *erythro/threo* mixture and as a glassy solid after purification by preparative layer chromatography (AcOEt/heptane 50/50); R_f *erythro/threo* mixture: 0.40 (AcOEt/heptane 50/50). ^{1}H-NMR (300 MHz, $CDCl_3$) δ *erythro*, [*threo*]: 7.50-7.20 (m, 6H, H-4, H-Ph, [H-4] and [H-Ph]); 7.00-6.10 (m, 4H+0.27H, H-Ar, [H-Ar] and [H-3]); 6.05 (dd, *J*=6.0, 2.0 Hz, 0.73H, H-3); 5.45 (ddd, *J*=3.6, 1.8, 1.8 Hz, 0.73H, H-5); [5.20 (ddd, *J*=6.4, 1.6, 1.6 Hz, 0.27H, H-5)]; 4.80 (d, *J*=3.6 Hz, 0.73H, H-6); [4.50 (d, *J*=6.4 Hz, 0.27H, H-6)]; 3.70 (s, 2.19H, OCH_3); [3.60 (s, 0.81H, OCH_3)]. ^{13}C-NMR (75 MHz, $CDCl_3$) δ *erythro*, [*threo*]: 172.3, [172.3] (CO); 160.6, [160.6] (C-q Ar); [153.9], 153.2 (C-4); [147.9], 147.5 (C-q Ar); [138.3], 136.8 (C-q Ph); 130.0, 129.9, 129.1, 128.8, 128.4, 128.3, 127.3 (C-Ph, C-Ar, [C-Ph] and [C-Ar]); 123.1, [122.7] (C-3); [107.1], 106.9, [103.8], 103.6, [100.2],

100.1 (other C-Ar); [85.7], 85.1 (C-5); [60.9], 59.3 (C-6); 55.0 (OCH_3 and [OCH_3]). ESMS *m/z* 318 $(M+Na)^+$, 296 ($(M+H)^+$, base peak). IR ν (cm^{-1}) (KBr) 3377, 1759.

5-[[(2-Hydroxyphenyl)amino]phenylmethyl]furan-2(5*H*)-one (18). CAS RN *threo* [258335-89-6].

The general $Yb(OTf)_3$-catalyzed condensation of preformed imines procedure was applied to *t*-butyldimethylsilyloxyfuran (52 mg, 0.26 mmol) and *o*-benzylideneaminophenol (81 mg, 0.42 mmol) to give **18** (65 mg, 82%) as a 70/30 *erythro/threo* mixture and as a glassy solid after purification by preparative layer chromatography (AcOEt/heptane 50/50); R_f *erythro/threo* mixture: 0.35 (AcOEt/heptane 50/50). ^{1}H-NMR (300 MHz, CD_3OD) δ *erythro*, [*threo*]: 7.65 (dd, *J*=5.8, 1.8 Hz, 0.70H, H-4); [7.55 (dd, *J*=5.8, 1.8 Hz, 0.30H, H-4)]; 7.50-7.20 (m, 5H, H-Ph and [H-Ph]); 6.70-6.40 (m, 4H, H-Ar and [H-Ar]); [6.15 (dd, *J*=5.8, 2.0 Hz, 0.30H, H-3)]; 6.05 (dd, *J*=5.8, 2.0 Hz, 0.70H, H-3)]; 5.55 (ddd, *J*=3.6, 1.8, 1.8 Hz, 0.70H, H-5); [5.45 (ddd, *J*=5.0, 1.8, 1.8 Hz, 0.30H, H-5)]; 4.95 (d, *J*=3.8 Hz, 0.70H, H-6); [4.80 (d, *J*=5.0 Hz, 0.30H, H-6)]. ^{13}C-NMR (50 MHz, CD_3OD) δ *erythro*, [*threo*]: 173.8, [173.8] (CO); [155.4], 155.0 (C-4); [148.7], 146.2 (C-q NH); [138.8], 137.4 (C-q Ph); [135.6], 135.2 (C-q OH); 128.6, 128.4, 128.3, 127.7, 127.3, 127.2 (C-Ph and [C-Ph]); 122.0, 121.7 (C-Ar and [C-Ar]); 119.9, [119.9] (C-3); 118.0, 117.4, 116.3, 113.7, 114.4, 112.5 (other C-Ar); [86.5], 86.1 (C-5); [60.0], 59.3 (C-6).

5-[[(2-Hydroxyphenyl)amino]phenylmethyl]-3-methylfuran-2(5*H*)-one (19). CAS RN *threo* [258335-80-7].

The general $Yb(OTf)_3$-catalyzed condensation of preformed imines procedure was applied to 3-methyl-2-*t*-butyldimethylsilyloxyfuran (20 mg, 0.09 mmol) and *o*-benzylideneaminophenol (28 mg, 0.18 mmol) to give **19** (24 mg, 90%) as a 12/88 *erythro/threo* mixture and as a glassy solid after purification by preparative layer chromatography (AcOEt/heptane 40/60); R_f *erythro/threo* mixture: 0.40 (AcOEt/heptane 50/50). ^{1}H-NMR (300 MHz, CD_3OD) δ *erythro*, [*threo*]: 7.50-7.20 (m, 5H, H-Ph and [H-Ph]); 7.10-7.00 (m, 1H, H-4 and [H-4]); 6.65-6.40 (m, 4H, H-Ar and [H-Ar]); 5.35 (ddd, *J*=3.8, 1.8, 1.8 Hz, 0.12H, H-5); [5.25 (ddd, *J*=5.0, 1.8, 1.8 Hz, 0.88H, H-5)]; 4.75 (d, *J*=3.8 Hz, 0.12H, H-6); [4.70 (d, *J*=5.0 Hz, 0.88H, H-6)]; [1.78 (dd, *J*=1.6, 1.6 Hz, 2.64H, CH_3)]; 1.73 (dd, *J*=1.6, 1.6 Hz, 0.36H, CH_3). ^{13}C-NMR (50 MHz, CD_3OD) δ *threo*: 168.2 (CO); 149.0 (C-4); 146.1, 140.7, 137.1, 131.6 (C-q and C-3); 129.5, 128.8, 128.5 (C-Ph and C-Ar); 121.0 (C-m Ar); 114.7 (C-p Ar); 114.0 (C-o Ar); 85.7 (C-5); 61.5 (C-6); 10.5 (CH_3).

5-[(Phenylamino)phenylmethyl]-3-methylfuran-2(5*H*)-one (20).

The general $Yb(OTf)_3$-catalyzed condensation of preformed imines procedure was applied to

3-methyl-2-*t*-butyldimethylsilyloxyfuran (20 mg, 0.09 mmol) and *N*-benzylideneaniline (34 mg, 0.18 mmol) to give **20** (26 mg, 99%) as a 21/79 *erythro/threo* mixture and as a glassy solid after purification by preparative layer chromatography (AcOEt/heptane 35/65); R_f *erythro/threo* mixture: 0.60 (AcOEt/heptane 50/50). ^{1}H-NMR (300 MHz, CD_3OD) δ *erythro,* [*threo*]: 7.50-7.30 (m, 6H, H-Ph, H-4, [H-Ph] and [H-4]); 7.10-6.45 (m, 5H, H-Ar and [H-Ar]); [5.35 (ddd, *J*=3.8, 1.8, 1.8 Hz, 0.79H, H-5)]; 5.25 (ddd, *J*=7.0, 1.8, 1.8 Hz, 0.21H, H-5); [4.75 (d, *J*=3.8 Hz, 0.79H, H-6)]; 4.35 (d, *J*=7.0 Hz, 0.21H, H-6); 1.95 (dd, *J*=1.6, 1.6 Hz, 0.63H, CH_3); [1.90 (dd, *J*=1.6, 1.6 Hz, 2.37H, CH_3)].

REFERENCES

1. a) S. Kobayashi and S. Nagayawa, *J. Am. Chem. Soc*., 1997, **119**, 10049. b) H. Oyamada and S. Kobayashi, *Synlett*, 1998, 249.
2. B. Dudot, J. Royer, M. Sevrin, and P. George, *Tetrahedron Lett*., 2000, **41**, 4367.
3. B. Dudot, A. Chiaroni, and J. Royer, *Tetrahedron Lett.*, 2000, **41**, 6355.
4. a). T. Tsukamoto and T. Kitazume, *Chem. Lett*., 1992, 1377. b) G. Rassu, L. Pinna, P. Spanu, N. Cudellu, and G. Casiraghi, *Tetrahedron*, 1992, **48**, 727. c) G. Casiraghi, G. Rassu, P. Spanu, L. Pinna, and F. Ilgheri, *J. Org. Chem*., 1993, **58**, 3397. d) L. Battistini, F. Zanardi, G. Rassu, P. Spanu, G. Pelosi, G. Gaspari Fava, M. Belicchi Ferrari, and G. Casiraghi, *Tetrahedron : Asymmetry*, 1997, **8**, 2975. e) L. Battistini, G. Rassu, L. Pinna, F. Zanardi, and G. Casiraghi, *Tetrahedron : Asymmetry*, 1999, **10**, 765. f) S. F. Martin and O. D. Lopez, *Tetrahedron Lett.*, 1999, **40**, 8949. g) M. V. Spanedda, M. Ourévitch, B. Crousse, J.-P. Bégué, and D. Bonnet-Delpont, *Tetrahedron Lett*., 2004, **45**, 5023
5. a) K. E. Harding, M. T. Coleman, and L. T. Liu, *Tetrahedron Lett*., 1991, **32**, 3795. b) S. F. Martin and J. W. Corbett, *Synthesis*, 1992, 55. c) M. Pichon, B. Figadere, and A. Cavé, *Tetrahedron Lett*., 1996, **37**, 7963. d) S. Hanessian and G. McNaughton-Smith, *Bioorg. Med. Chem. Lett*., 1996, **6**, 1567. e) M. Pichon, R. Hocquemiller, and B. Figadere, *Tetrahedron Lett*., 1999, **40**, 8567. f) S. Hanessian and B. Reddy, *Tetrahedron*, 1999, **55**, 3427. g) M. G. M. D'Oca, R. A. Pilli, and I. Vencato, *Tetrahedron Lett*., 2000, **41**, 9709. h) R. Razet, U. Thomet, R. Furtmüller, F. Jursky, E. Sigel, W. Sieghart, and R. H. Dodd, *Bioorg. Med. Chem. Lett*., 2000, **10**, 2579. i) R. Razet, U. Thomet, R. Furtmüller, A. Chiaroni, E. Sigel, W. Sieghart, and R. H. Dodd, *J. Med. Chem*., 2000, **43**, 4363. j) A. Boto, R. Hernandez, and E. Suarez, *Tetrahedron Lett*., 2000, **41**, 2899. k) S. K. Bur and S. F. Martin, *Org. Lett*., 2000, **2**, 3445. l) M. C. F. de Oliveira, L. S. Santos, and R. A. Pilli, *Tetrahedron Lett*., 2001, **42**, 6995. m) L. Di Bari, S. Guillarme, S. Hermitage, J. A. K. Howard, D. A.

Jay, G. Pescitelli, A. Whiting, and D. S. Yufit, *Synlett*, 2004, 708.

6. a) C. Camiletti, L. Poletti, and C. Trombini, *J. Org. Chem*., 1994, **59**, 6843. b) M. Lombardo and C. Trombini, *Tetrahedron*, 2000, **56**, 323. c) N. Mita, O. Tamura, H. Ishibashi, and M. Sakamoto, *Org. Lett*., 2002, **4**, 1111.
7. for a review see: S. K. Bur and S. F. Martin, *Tetrahedron*, 2001, **57**, 3221.
8. a) S. F. Martin and S. Liras, *J. Am. Chem. Soc.*, 1993, **115**, 10450. b) F. Zanardi, L. Battistini, G. Rassu, L. Pinna, M. Mor, N. Culeddu, and G. Casiraghi, *J. Org. Chem*., 1998, **63**, 1368. c) S. F. Martin, K. J. Barr, D. W. Smith, and S. K. Bur, *J. Am. Chem. Soc.*, 1999, **121**, 6990. d) S. F. Martin, *Acc. Chem. Res.*, 2002, **35**, 895.
9. a) M. Cushman and N. Castagnoli Jr., *J. Org. Chem.*, 1973, **38**, 440. b) M. Cushman and N. Castagnoli Jr., *J. Org. Chem.*, 1974, **39**, 1546. c) K. Paulvannan and J. R. Stille, *J. Org. Chem.*, 1994, **59**, 1613. d) G. R. Cook, L. G. Beholz, and J. R. Stille, *J. Org. Chem.*, 1994, **59**, 3575.
10. S. K. Bur and S. F. Martin, *Org. Lett.*, 2000, **2**, 3445 and references cited therein.