Available online at www.sciencedirect.com
SCIENCE DIRECT®
Tetrahedron: Asymmetry
Tetrahedron: *Asymmetry* 16 (2005) 875–881

Asymmetric synthesis of 3-hetero-substituted 2,3-dihydro-1*H*-isoindol-1-ones

Eric Deniau,[a,*] Dieter Enders,[b] Axel Couture[a] and Pierre Grandclaudon[a]

[a]*Laboratoire de Chimie Organique Physique, UMR 8009, Université des Sciences et Technologies de Lille, Bâtiment C3(2), F-59655 Villeneuve d'Ascq Cédex, France*

[b]*Institut für Organische Chemie, Rheinisch-Westfälische Technische Hochschule, Professor-Pirlet-Straße 1, 52074 Aachen, Germany*

Received 18 November 2004; revised 18 December 2004; accepted 10 January 2005

Abstract—An efficient asymmetric synthesis of highly enantioenriched 3-hetero-substituted 2,3-dihydro-1*H*-isoindolinones is reported. The key step is a diastereoselective nucleophilic addition on *N*-acylhydrazonium intermediates generated by acidic treatment of hemiaminal precursors bearing an (*S*)-2-alkoxymethyl-pyrrolidin-1-yl type auxiliary. The auxiliary is removed by an oxidative *N*,*N*-bond cleavage with magnesium monoperoxyphthalate.

1. Introduction

2,3-Dihydro-1*H*-isoindol-1-ones (isoindolinones) and many derivatives containing this heterobicyclic unit embedded in their skeleton have attracted a great deal of interest, since they represent the common building block of a wide range of naturally occurring and/or bioactive substances.[1]

Within this family, 3-hetero-substituted isoindolinones occupy a special place as witnessed by a great number of papers emphasizing their pharmaceutical and medicinal bioactivities. For example, biologically active compounds (Fig. 1) such as tricyclic isoindolones **1** (non-nucleosidic HIV-reverse transcriptase inhibitor),[2] 3-pyrazolyl derivatives **2** (antifungic and antibacterial),[3] the benzoimidazo isoindolone **3** (cytotoxic)[4] or the bisquaternary bisphthalimidine **4** (ligand of the allosteric binding site of muscarinic M_2 receptor)[5] have recently been studied. Accordingly, the synthesis of 3-hetero-substituted isoindolinones has developed extensively over recent years and this is linked to their synthetic potential. Indeed, such *N*,*X*-acetals have been involved in the elaboration of architecturally sophisticated compounds via α-aminoalkylation,[6] olefination,[7] S_N[8] or S_EAr[9] reactions. Surprisingly, little effort has been devoted to the stereoselective synthesis of enantioenriched 3-hetero-substituted models even though it has been well established that the control of the stereogenic centre at C-3 plays a crucial role for the biological activity.[2a,10] To the best of our knowledge, the only way to build up these bicyclic lactams relies on the condensation of chiral amino alcohols, thiols or amines with an *ortho*-acyl benzoic acid.[11] Moreover, to the best of our knowledge, no report dealing with the synthesis of N–H free models has appeared.

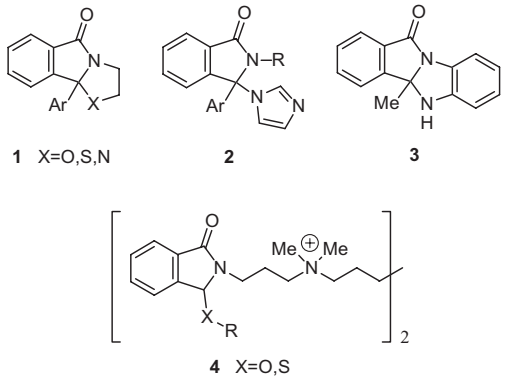


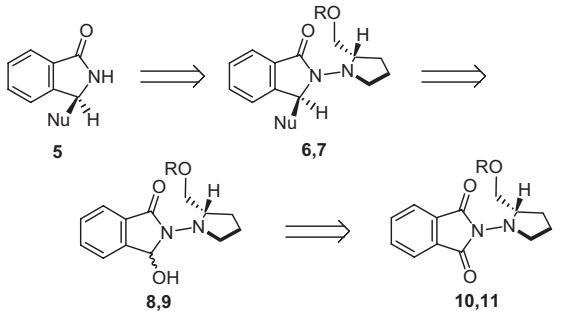
Figure 1. Examples of synthetic pharmacologically active 3-hetero-substituted isoindolinones.

2. Results and discussion

Herein we report a new and efficient asymmetric synthesis of a variety of 3-hetero-substituted 2,3-dihydro-1*H*-isoindol-1-ones **5**. The new synthetic approach, which

* Corresponding author. Tel.: +33 03 20 43 49 40; fax: +33 03 20 33 63 09; e-mail: eric.deniau@univ-lille1.fr

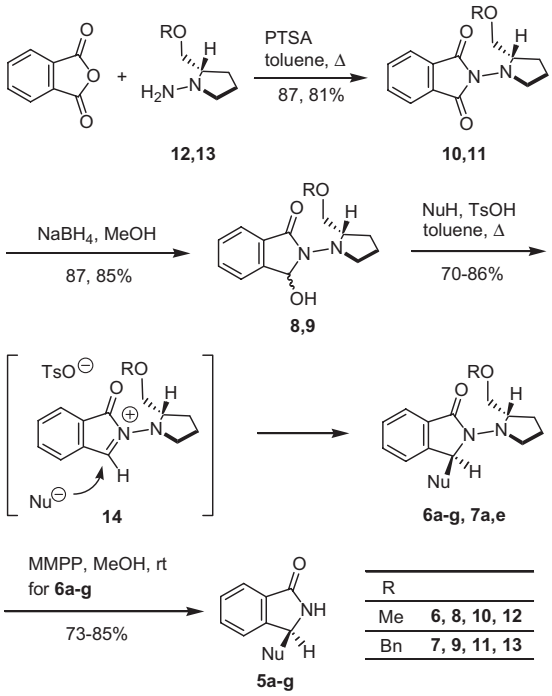
0957-4166/$ - see front matter © 2005 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tetasy.2005.01.012



Scheme 1. Retrosynthetic analysis of chiral 3-hetero-substituted isoindolinones.

is depicted in the retrosynthetic Scheme 1, hinges on the key step, a diastereoselective S_N1 type reaction between an appropriate hetero-nucleophile and the chiral hemiaminals **8** and **9** to afford the adducts **6** and **7**. The 3-hydroxy isoindolinones should be obtained by the reduction of the corresponding imides **10** and **11** equipped with a (*S*)-2-alkoxymethyl-pyrrolidin-1-yl type auxiliary[12] connected to the lactam nitrogen atom. The ultimate cleavage of the chiral auxiliary should then complete the synthesis of the target enantioenriched isoindolinones.

The new synthetic route is depicted in Scheme 2 and requires the preliminary elaboration of the enantiopure phthalhydrazides **10** and **11**. These parent compounds were readily obtained[13] by condensation between phthalic anhydride and (*S*)-1-amino-2-methoxy and 2-benzyloxymethylpyrrolidine[14] **12** and **13**, respectively. The imides **10** and **11** were then reduced with sodium borohydride to provide the hemiaminals **8** and **9** with fairly good yields as a mixture of diastereomers. The resulting 3-hydroxy isoindolinones **8** and **9** were then allowed to react with an array of hetero-nucleophiles (N, S, P) under acidic conditions to afford the 3-hetero-substituted compounds **6** and **7** (Table 1). As it can be seen from Table 1, the formation of the *N*-aminolactams **6** and **7** occurs with a good to high level of diastereoselection and the virtually diastereomerically pure compounds (de >96%) were obtained after the purification steps. According to Kibayashi's assumptions,[15] the facial selectivity might be ascribed to the nucleophilic addition onto the less hindered face of the preferred conformer of the transient *N*-acylhydrazonium ions **14**, thus leading to (3*S*)-isomers. The absolute configuration of the 3-hetero-substituted isoindolinones obtained was confirmed by the single crystal X-ray analysis of compound **6e** (Fig. 2). It is noteworthy that a slight enhancement in terms of diastereoselectivity was observed by using the more hindered (*S*)-2-benzyloxymethylpyrrolidine auxiliary instead of its corresponding *O*-methylated analogue. Moreover, the same phenomenon was observed when increasing the size of the nucleophile. This clearly demonstrates that the face differentiation associated with the diastereoselective nucleophilic addition process is mainly governed by steric repulsion between the nucleophile and the alkoxymethyl chain present in the chiral appendage. Finally, removal of the chiral auxiliary was cleanly achieved under oxidation conditions by treatment of the diastereoenriched adducts **6a**–**g** with magnesium monoperoxyphthalate hexahydrate (MMPP).[16] This operation afforded the target non-racemic 3-hetero-substituted isoindolinones **5a**–**g** (Table 1).



Scheme 2. Asymmetric synthesis of 3-hetero-substituted isoindolinones **5**.

3. Conclusion

In summary, a concise and efficient synthesis of highly enantioenriched 3-hetero-substituted isoindolinones based on a diastereoselective nucleophilic addition to hydrazonium salts bearing a (*S*)-2-alkoxymethylpyrrolidin-1-yl type of auxiliary has been developed. The protocol described opens an efficient and general entry to the title compounds and should be widely applicable to the asymmetric synthesis of biologically active compounds of this type.

4. Experimental

4.1. General

Melting points were determined on a Reichert-Thermopan apparatus and are uncorrected. NMR spectra were recorded on Bruker AM 300 and Bruker AMX 400 spectrometers. They were referenced against internal tetramethylsilane. Coupling constants (*J*) are given in Hz and rounded to the nearest 0.1 Hz. IR absorption spectra were run on a Perkin–Elmer 881. Mass spectral analyses were performed on a Thermo-finnigan mass spectrometer. Optical rotations were measured on a Perkin–Elmer P 343 polarimeter. Elemental analyses

Table 1. Isoindolinones **5a–g**, **6a–g**, **7a,e** prepared

Entry	5–7	NuH	6 (R = Me)		7 (R = Bn)		5	
			Yield[a] (%)	De[b] (%)	Yield[a] (%)	De[b] (%)	Yield[a] (%)	Ee[c] (%)
1	a	Benzotriazole	83	75 (>96)[d]	81	90 (>96)[d]	73	>96
2	b	$PhSO_2H$[e]	73	90 (>96)[d]			85	>96
3	c	4-$TolSO_2H$[e]	70	90 (>96)[d]			82	>96
4	d	4-$ClC_6H_4SO_2H$[e]	72	90 (>96)[d]			80	>96
5	e	$Ph_2P(O)H$[17]	86	80 (>96)[d]	84	90 (>96)[d]	81	>96
6	f	$(4\text{-}MeOC_6H_4)_2P(O)H$[18]	81	80 (>96)[d]			83	>96
7	g	$(Naphth\text{-}2\text{-}yl)_2P(O)H$[18]	74	90 (>96)[d]			78	>96

[a] After purification.
[b] Determined by ^1H NMR spectroscopy.
[c] In correlation to the de value of the corresponding hydrazides **6a–g** assuming that the deprotection step takes place without racemization.[16]
[d] After recrystallization from hexane/toluene.
[e] PTSA (1 equiv) was added to the corresponding sulfinates in order to generate arylsulfinic acids in situ.

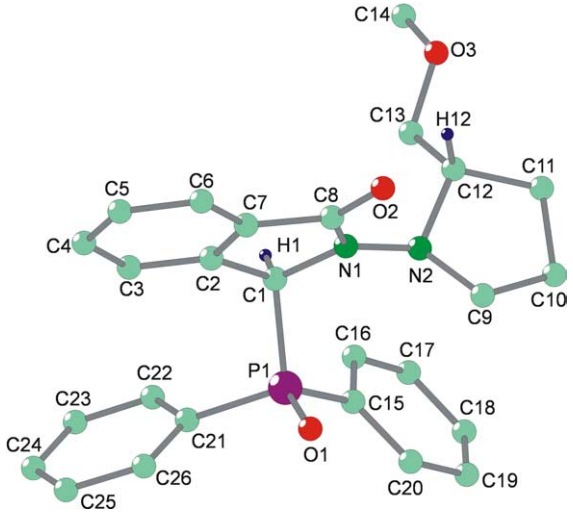


Figure 2. ORTEP view of the crystal structure of (2*S*,3*S*)-3-diphenylphosphinoyl-2-(2-methoxymethylpyrrolidin-1-yl)-2,3-dihydro-1*H*-isoindol-1-one **6e** with atom numbering.

were determined by the CNRS microanalysis centre. TLC was performed with plates coated with Kieselgel G (Merck). The silica gel used for flash column chromatography was Merck Kieselgel of 0.040–0.063 mm particle size. Dry glassware was obtained by oven drying and assembly under Ar. Ar was used as the inert atmosphere and passed through a drying tube to remove moisture. The glassware was equipped with rubber septa and reagent transfer performed by syringe techniques. Tetrahydrofuran (THF) was distilled from sodium benzophenone ketyl immediately before use. Methanol was distilled from magnesium turnings.

4.2. Preparation of phthalhydrazides 10 and 11

Phthalhydrazides **10** and **11** were prepared according to a precedently reported procedure.[13]

4.2.1. (2*S*)-2-(2-Benzyloxymethylpyrrolidin-1-yl)phthalimide 11. Mp 88–89 °C; $[\alpha]_D^{25} = +5.70$ (*c* 2.60, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$): 1.58–1.70 (m, 1H), 1.88–2.14 (m, 3H), 3.29–3.37 (m, 1H), 3.51 (d, $J = 5.8$ Hz, 2H), 3.59 (q, $J = 8.2$ Hz, 1H), 3.90–4.00 (m, 1H), 4.30 (d, $J = 11.5$ Hz, 1H), 4.34 (d, $J = 11.5$ Hz, 1H), 7.00–7.11 (m, 5H, H_{arom}), 7.58–7.64 (m, 2H, H_{arom}), 7.68–7.73 (m, 2H, H_{arom}); ^{13}C NMR ($CDCl_3$): C 167.7 (CO), 138.3, 130.6, CH 134.1, 128.2, 127.6, 127.4, 123.3, 61.1, CH_2 74.5, 73.5, 52.9, 27.1, 22.4. MS (EI) *m*/*z* (%): 336 (M^+, 6), 215 (100), 216 (17), 130 (16). IR (KBr) *v* 2853, 1724, 1385, 1204, 1124, 887. Anal. Calcd for $C_{20}H_{20}N_2O_3$: C, 71.41; H, 5.99; N, 8.33. Found: C, 71.48; H, 6.03; N, 8.56.

4.3. General procedure for the preparation of hydrazides 6 and 7

Phthalhydrazide **10** or **11** (100 mmol), was dissolved in absolute MeOH (500 mL) and carefully treated with $NaBH_4$ (4.2 g, 110 mmol) under N_2 in an ice-cooled flask. The mixture was stirred for an additional 30 min. Saturated aqueous NH_4Cl solution was added and the MeOH removed under vacuum. The crude product was extracted with CH_2Cl_2 (3 × 100 mL), which was then dried over Na_2SO_4. Evaporation of the solvent furnished oily products, which were then subjected to chromatography on SiO_2 column using acetone/hexanes as eluent (30/70) to furnish the alcohols **8** and **9** as a mixture of diastereomers. Hydroxyphthalimidines **8** and **9** (10 mmol), the appropriate hetero-nucleophile (11 mmol) and *p*-toluenesulfonic acid (19 mg, 1 mmol) were dissolved in toluene (50 mL) and the mixture refluxed for 3 h while removing the reaction water via a Dean–Stark apparatus. The solution was then cooled, washed with a saturated aqueous solution of $NaHCO_3$ (10 mL) and dried over $MgSO_4$. After removal of the solvent, the crude compounds were subjected to chromatography on SiO_2 column using $CHCl_3$/diethyl ether/hexanes as eluent (50/20/30) and recrystallized from hexane/toluene to afford the hydrazides **6**, **7**.

4.3.1. (2*S*,3*S*)-3-(1*H*-Benzotriazol-1-yl)-2-(2-methoxymethylpyrrolidin-1-yl)-2,3-dihydro-1*H*-isoindol-1-one 6a. Mp 175–176 °C; $[\alpha]_D^{25} = +26.6$ (*c* 1.60, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$): 1.26–1.37 (m, 1H), 1.39–1.51 (m, 1H), 1.72–1.84 (m, 1H), 1.99–2.19 (m, 2H), 3.28–3.41 (m, 6H), 4.02 (s, 1H), 6.77 (s, 1H, H_{arom}), 7.21–7.34 (m, 4H, H_{arom}), 7.52–7.64 (m, 2H, H_{arom}), 7.95 (d, $J = 7.4$ Hz, 1H, H_{arom}), 8.06 (d, $J = 8.3$ Hz, 1H, H_{arom});

^{13}C NMR ($CDCl_3$): C 165.6 (CO), 146.9, 138.2, 131.6, 131.5, CH 132.9, 130.4, 127.6, 124.2, 123.6, 123.4, 120.2, 110.0, 74.3, 60.1, CH_2 77.5, 53.0, 26.8, 22.7, CH_3 59.0. MS (EI) *m*/*z* (%): 363 (M^+, 4), 318 (100), 221 (14), 132 (12). IR (KBr) *v* 2900, 1713, 1370, 1278, 1091. Anal. Calcd for $C_{20}H_{21}N_5O_2$: C, 66.10; H, 5.82; N, 19.27. Found: C, 66.26; H, 6.01; N, 19.38.

4.3.2. (2*S*,3*S*)-3-Benzenesulfonyl-2-(2-methoxymethylpyrrolidin-1-yl)-2,3-dihydro-1*H*-isoindol-1-one 6b. Mp 131–132 °C; $[\alpha]_D^{22} = -89.1$ (*c* 1.69, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): 1.19–1.33 (m, 1H), 1.53–1.70 (m, 1H), 1.92–2.11 (m, 2H), 3.02 (t, *J* = 9.5 Hz, 1H), 3.11 (s, 3H), 3.18 (dd, *J* = 2.9, 9.3 Hz, 1H), 3.43–3.54 (m, 1H), 3.69–3.80 (m, 2H), 5.96 (s, 1H), 7.38 (t, *J* = 7.8 Hz, 1H, H_{arom}), 7.42–7.65 (m, 6H, H_{arom}), 7.69 (d, *J* = 7.6 Hz, 1H, H_{arom}), 7.93 (d, *J* = 7.9 Hz, 1H, H_{arom}); ^{13}C NMR (75 MHz, $CDCl_3$): C 167.2 (CO), 136.2, 134.6, 132.1, CH 133.8, 132.3, 130.0, 129.1, 128.4, 125.3, 123.4, 80.9, 60.5, CH_2 77.3, 53.6, 26.9, 22.9, CH_3 58.5. MS (EI) *m*/*z* (%): 386 (M^+, 1), 341 (5), 245 (91), 213 (100). IR (KBr) *v* 1687, 1453, 1363, 1318, 1139. Anal. Calcd for $C_{20}H_{22}N_2O_4S$: C, 62.16; H, 5.74; N, 7.25. Found: C, 62.29; H, 5.59; N, 7.29.

4.3.3. (2*S*,3*S*)-2-(2-Methoxymethylpyrrolidin-1-yl)-3-(toluene-4-sulfonyl)-2,3-dihydro-1*H*-isoindol-1-one 6c. Mp 126–127 °C; $[\alpha]_D^{20} = -57.6$ (*c* 1.30, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): 1.24–1.41 (m, 1H), 1.62–1.78 (m, 1H), 1.95–2.17 (m, 2H), 2.36 (s, 3H), 3.07–3.18 (m, 4H), 3.23 (dd, *J* = 3.1, 9.4 Hz, 1H), 3.52–3.63 (m, 1H), 3.69–3.86 (m, 2H), 5.92 (s, 1H), 7.14 (d, *J* = 8.0 Hz, 1H, H_{arom}), 7.44–7.54 (m, 3H, H_{arom}), 7.55–7.66 (m, 2H, H_{arom}), 7.92 (d, *J* = 7.8 Hz, 1H, H_{arom}); ^{13}C NMR (75 MHz, $CDCl_3$): C 167.3 (CO), 144.9, 135.0, 132.7, 132.1, CH 132.2, 129.9, 129.2, 129.0, 125.3, 123.3, 81.1, 60.4, CH_2 76.7, 53.7, 27.0, 22.9, CH_3 58.6, 21.6. MS (EI) *m*/*z* (%): 400 (M^+, 1), 355 (6), 245 (100), 213 (100). Anal. Calcd for $C_{21}H_{24}N_2O_4S$: C, 62.98; H, 6.04; N, 6.99. Found: C, 63.08; H, 6.15; N, 6.78.

4.3.4. (2*S*,3*S*)-3-(4-Chlorobenzenesulfonyl)-2-(2-methoxymethylpyrrolidin-1-yl)-2,3-dihydro-1*H*-isoindol-1-one 6d. Mp 86–87 °C; $[\alpha]_D^{20} = -121.2$ (*c* 2.09, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): 1.12–1.28 (m, 1H), 1.46–1.64 (m, 1H), 1.75–2.05 (m, 2H), 2.94 (t, *J* = 9.4 Hz, 1H), 3.01 (s, 3H), 3.11 (dd, *J* = 2.2, 9.2 Hz, 1H), 3.33–3.44 (m, 1H), 3.62–3.77 (m, 2H), 5.94 (s, 1H), 7.29 (d, *J* = 8.5 Hz, 2H, H_{arom}), 7.41 (t, *J* = 7.4 Hz, 1H, H_{arom}), 7.48–7.61 (m, 4H, H_{arom}), 7.85 (d, *J* = 7.5 Hz, 1H, H_{arom}), 8.06 (d, *J* = 8.3 Hz, 1H, H_{arom}); ^{13}C NMR ($CDCl_3$): C 167.1 (CO), 140.5, 134.7, 134.4, 132.1, CH 132.4, 130.5, 130.2, 128.7, 125.3, 123.4, 80.9, 60.6, CH_2 77.2, 53.6, 26.9, 22.9, CH_3 58.5. MS (EI) *m*/*z* (%): 420 (M^+, 1), 375 (4), 245 (100), 213 (85). Anal. Calcd for $C_{20}H_{21}ClN_2O_4S$: C, 57.07; H, 5.03; N, 6.66. Found: C, 57.10; H, 5.23; N, 6.72.

4.3.5. (2*S*,3*S*)-3-Diphenylphosphinoyl-2-(2-methoxymethylpyrrolidin-1-yl)-2,3-dihydro-1*H*-isoindol-1-one 6e. Mp 214–215 °C; $[\alpha]_D^{28} = +35.0$ (*c* 1.05, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): 1.07–1.27 (m, 2H), 1.68–1.83 (m, 1H), 1.94–2.09 (m, 1H), 2.32–2.43 (m, 1H), 3.22 (d, *J* = 6.1 Hz, 2H), 3.29 (s, 3H, OMe), 3.51–3.63 (m, 1H), 3.75–3.88 (m, 1H), 5.92 (d, *J* = 5.9 Hz, 1H), 7.20 (d, *J* = 6.6 Hz, 1H, H_{arom}), 7.26–7.38 (m, 4H, H_{arom}), 7.39–7.52 (m, 3H, H_{arom}), 7.54–7.65 (m, 2H, H_{arom}), 7.75 (dd, *J* = 7.5, 10.9 Hz, 2H, H_{arom}), 7.89 (dd, *J* = 7.5, 11.8 Hz, 2H, H_{arom}); ^{13}C NMR (75 MHz, $CDCl_3$): C 167.9 (d, *J* = 2 Hz, CO), 138.3 (d, *J* = 4 Hz), 132.1 (d, *J* = 3 Hz), 131.5 (d, *J* = 89 Hz), 128.5 (d, *J* = 98 Hz), CH 132.4, 132.3 (d, *J* = 13 Hz), 132.0 (d, *J* = 2 Hz), 131.7 (d, *J* = 8 Hz), 131.4 (d, *J* = 2 Hz), 128.3, 124.1 (d, *J* = 2 Hz), 123.2, 62.6 (d, *J* = 74 Hz), 60.8, CH_2 76.8, 52.7, 27.0, 23.1, CH_3 58.6; ^{31}P NMR (121 MHz, $CDCl_3$): 28.8. MS (EI) *m*/*z* (%): 446 (M^+, 4), 401 (48), 203 (63), 201 (41), 132 (38), 114 (100). IR (KBr) *v* 1672, 1469, 1441, 1364, 1199, 1160. Anal. Calcd for $C_{26}H_{27}N_2O_3P$: C, 69.94; H, 6.10; N, 6.27. Found: C, 69.75; H, 6.23; N, 6.42.

4.3.6. (2*S*,3*S*)-2-(2-Methoxymethylpyrrolidin-1-yl)-3-(di-(4-methoxyphenyl)phosphinoyl)-2,3-dihydro-1*H*-isoindol-1-one 6f. Mp 207–208 °C; $[\alpha]_D^{20} = +246.7$ (*c* 1.05, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): 1.21–1.49 (m, 2H), 1.73–1.87 (m, 1H), 1.90–2.08 (m, 1H), 2.85–2.95 (m, 1H), 3.13–3.21 (m, 4H), 3.26 (t, *J* = 8.8 Hz, 1H), 3.44 (q, *J* = 7.7 Hz, 1H), 3.64 (s, 3H), 3.69 (s, 3H), 3.81–3.92 (m, 1H), 5.50 (d, *J* = 8.5 Hz, 1H), 6.30 (d, *J* = 7.6 Hz, 1H, H_{arom}), 6.66 (d, *J* = 8.6 Hz, 2H, H_{arom}), 6.81 (d, *J* = 8.5 Hz, 2H, H_{arom}), 7.06–7.17 (m, 3H, H_{arom}), 7.21 (t, *J* = 7.2 Hz, 1H, H_{arom}), 7.41 (t, *J* = 7.6 Hz, 1H, H_{arom}), 7.59 (d, *J* = 7.5 Hz, 1H, H_{arom}); ^{13}C NMR (75 MHz, $CDCl_3$): C 166.3, 161.1, 160.1, 142.0 (d, *J* = 3 Hz), 132.1, 125.4 (d, *J* = 179 Hz), 125.2 (d, *J* = 181 Hz), CH 136.7 (d, *J* = 23 Hz), 134.1 (d, *J* = 19 Hz), 130.7, 127.5, 123.1, 123.0, 113.9 (d, *J* = 7 Hz), 113.8 (d, *J* = 7 Hz), 64.1 (d, *J* = 21 Hz), 60.7, CH_2 76.8, 53.3, 27.5, 23.3, CH_3 58.6, 55.2, 55.1; ^{31}P NMR (121 MHz, $CDCl_3$): 29.6. MS (EI) *m*/*z* (%): 506 (M^+, 3), 461 (50), 263 (48), 261 (35), 132 (42), 114 (100). Anal. Calcd for $C_{28}H_{31}N_2O_5P$: C, 66.39; H, 6.17; N, 5.53. Found: C, 66.45; H, 6.25; N, 5.40.

4.3.7. (2*S*,3*S*)-2-(2-Methoxymethylpyrrolidin-1-yl)-3-(di-(naphth-2-yl)phosphinoyl)-2,3-dihydro-1*H*-isoindol-1-one 6g. Mp 203–204 °C; $[\alpha]_D^{20} = +118.5$ (*c* 0.89, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): 0.74–1.00 (m, 2H), 1.57–1.70 (m, 1H), 1.72–1.78 (m, 1H), 2.32–2.43 (m, 1H), 2.49–2.67 (m, 1H), 2.70–2.86 (m, 1H), 3.10 (s, 3H), 3.41–3.58 (m, 1H), 3.72–3.83 (m, 1H), 6.30 (d, *J* = 8.8 Hz, 1H), 7.20–7.65 (m, 10H, H_{arom}), 7.73 (d, *J* = 7.5 Hz, 1H, H_{arom}), 7.77–7.88 (m, 2H, H_{arom}), 7.96 (d, *J* = 8.0 Hz, 2H, H_{arom}), 8.03 (d, *J* = 8.2 Hz, 1H, H_{arom}), 8.70 (d, *J* = 8.5 Hz, 1H, H_{arom}), 9.23 (d, *J* = 7.8 Hz, 1H, H_{arom}); ^{13}C NMR (75 MHz, $CDCl_3$): C 168.0, 139.3 (d, *J* = 4 Hz), 134.7 (d, *J* = 8 Hz), 134.2 (d, *J* = 7 Hz), 133.9, 133.7, 131.8 (d, *J* = 2 Hz), 129.1 (d, *J* = 96 Hz), 126.3 (d, *J* = 96 Hz), CH 133.4 (d, *J* = 3 Hz), 132.9 (d, *J* = 13 Hz), 131.7, 128.9 (d, *J* = 12 Hz), 128.3, 127.6, 127.4 (d, *J* = 5 Hz), 127.3, 126.5 (d, *J* = 6 Hz), 124.7 (d, *J* = 2 Hz), 124.2 (d, *J* = 15 Hz), 123.9 (*J* = 14 Hz), 123.2, 64.9 (d, *J* = 75 Hz), 59.6, CH_2 76.4, 52.6, 26.6, 22.2, CH_3 58.6; ^{31}P NMR (121 MHz, $CDCl_3$): 35.3. MS (EI) *m*/*z* (%): 546 (M^+, 2), 501 (43), 303 (52), 301 (38), 132 (57), 114

(100). Anal. Calcd for $C_{34}H_{31}N_2O_3P$: C, 74.71; H, 5.72; N, 5.12. Found: C, 74.55; H, 5.70; N, 5.21.

4.3.8. (2*S*,3*S*)-3-(1*H*-Benzotriazol-1-yl)-2-(2-benzyloxymethylpyrrolidin-1-yl)-2,3-dihydro-1*H*-isoindol-1-one 7a. Mp 136–137 °C; $[\alpha]_D^{25} = +15.0$ (*c* 1.60, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$): 1.27–1.55 (m, 2H), 1.71–1.87 (m, 1H), 1.97–2.22 (m, 2H), 3.36 (q, *J* = 8.2 Hz, 1H), 3.56 (d, *J* = 6.0 Hz, 2H), 4.02–4.28 (m, 1H), 4.50 (d, *J* = 11.5 Hz, 1H), 4.57 (d, *J* = 11.5 Hz, 1H), 6.74 (d, *J* = 7.7 Hz, 1H, H_{arom}), 7.06–7.36 (m, 8H, H_{arom}), 7.40 (s, 1H), 7.50 (t, *J* = 7.6 Hz, 1H, H_{arom}), 7.60 (t, *J* = 7.4 Hz, 1H, H_{arom}), 7.96 (d, *J* = 7.2 Hz, 1H, H_{arom}), 8.07 (d, *J* = 8.2 Hz, 1H, H_{arom}); ^{13}C NMR ($CDCl_3$): C 165.8 (CO), 146.6, 138.2, 137.9, 131.6, 131.5, CH 132.9, 130.4, 128.2, 127.6, 127.5, 127.4, 124.2, 123.5, 123.4, 120.2, 110.1, 74.5, 59.8, CH_2 75.4, 73.3, 53.1, 26.7, 22.6. MS (EI) *m*/*z* (%): 439 (M^+, 2), 318 (100), 221 (10), 91 (14). IR (KBr) *v* 1707, 1366, 1097, 1066, 736. Anal. Calcd for $C_{26}H_{25}N_5O_2$: C, 71.05; H, 5.73; N, 15.93. Found: C, 70.98; H, 5.81; N, 15.88.

4.3.9. (2*S*,3*S*)-2-(2-Benzyloxymethylpyrrolidin-1-yl)-3-diphenylphosphinoyl-2,3-dihydro-1*H*-isoindol-1-one 7e. Mp 167–168 °C; $[\alpha]_D^{25} = +55.0$ (*c* 1.35, CH_2Cl_2); ^1H NMR (400 MHz, $CDCl_3$): 1.04–1.24 (m, 2H), 1.69–1.81 (m, 1H), 1.96–2.07 (m, 1H), 2.40–2.48 (m, 1H), 3.33 (t, *J* = 9.2 Hz, 1H), 3.39 (dd, *J* = 3.4, 9.5 Hz, 3H, OMe), 3.59 (q, *J* = 7.8 Hz, 1H), 3.90–3.98 (m, 1H), 4.42 (d, *J* = 11.5 Hz, 1H), 4.47 (d, *J* = 11.5 Hz, 1H), 5.86 (d, *J* = 3.6 Hz, 1H), 6.69 (d, *J* = 7.5 Hz, 1H, H_{arom}), 7.15 (dd, *J* = 1.8, 7.8 Hz, 2H, H_{arom}), 7.20–7.28 (m, 4H, H_{arom}), 7.29–7.47 (m, 6H, H_{arom}), 7.50–7.57 (m, 1H, H_{arom}), 7.61–7.69 (m, 3H, H_{arom}), 7.71–7.79 (m, 2H, H_{arom}); ^{13}C NMR (100 MHz, $CDCl_3$): C 167.7 (CO), 138.0 (d, *J* = 4 Hz), 137.9, 132.4 (d, *J* = 3 Hz), 131.5 (d, *J* = 97 Hz), 129.7 (d, *J* = 98 Hz), CH 132.2 (d, *J* = 3 Hz), 131.9 (d, *J* = 9 Hz), 131.8 (d, *J* = 3 Hz), 131.6 (d, *J* = 9 Hz), 131.2 (d, *J* = 2 Hz), 128.4, 128.3 (d, *J* = 12 Hz), 128.2 (d, *J* = 2 Hz), 127.9 (d, *J* = 12 Hz), 127.7, 127.6, 123.8 (d, *J* = 2 Hz), 123.2, 62.6 (d, *J* = 55 Hz), 60.5, CH_2 74.6, 73.1, 52.6, 26.9, 22.9; ^{31}P NMR (162 MHz, $CDCl_3$): 28.8. MS (EI) *m*/*z* (%): 522 (M^+, 1), 414 (10), 401 (43), 203 (36), 201 (28), 190 (100), 132 (27), 91 (38). IR (KBr) *v* 2867, 1674, 1439, 1363, 1204, 1116. Anal. Calcd for $C_{32}H_{31}N_2O_3P$: C, 73.55; H, 5.98; N, 5.36. Found: C, 73.62; H, 6.12; N, 5.38.

4.4. Preparation of isoindolinones 5

Deprotection of isoindolinones **6** was achieved according to a precedently reported procedure.[13]

4.4.1. (3*S*)-3-(1*H*-Benzotriazol-1-yl)-2,3-dihydro-1*H*-isoindol-1-one 5a. Mp 197–198 °C; $[\alpha]_D^{20} = -112.1$ (*c* 1.08, DMSO); ^1H NMR (300 MHz, DMSO-d_6): 6.99 (d, *J* = 7.1 Hz, 1H, H_{arom}), 7.35–7.50 (m, 3H, H_{arom}), 7.61–7.73 (m, 2H, H_{arom}), 7.82 (s, 1H, H_{arom}), 7.92 (d, *J* = 6.8 Hz, 1H, H_{arom}), 8.11 (d, *J* = 7.1 Hz, 1H, H_{arom}), 9.67 (br s, 1H, NH); ^{13}C NMR (75 MHz, DMSO-d_6): C 168.8 (CO), 145.9, 141.7, 132.0, 131.1, CH 133.0, 130.6, 128.0, 124.5, 124.1, 123.4, 119.8, 68.5. MS (EI) *m*/*z* (%): 250 (M^+, 65), 222 (19), 132 (100), 119 (35), 104 (25), 91 (42), 77 (22). IR (KBr) *v* 3227, 1678, 1444, 1276, 1077, 773. Anal. Calcd for $C_{14}H_{10}N_4O$: C, 67.19; H, 4.03; N, 22.39. Found: C, 67.10; H, 4.00; N, 22.48.

4.4.2. (3*S*)-3-Benzenesulfonyl-2,3-dihydro-1*H*-isoindol-1-one 5b. Mp 182–183 °C; $[\alpha]_D^{20} = -42.0$ (*c* 1.62, $CHCl_3$); ^1H NMR (300 MHz, DMSO-d_6): 6.36 (s, 1H), 7.35–7.73 (m, 8H, H_{arom}), 7.77 (d, *J* = 7.6 Hz, 1H, H_{arom}), 9.81 (br s, 1H, NH); ^{13}C NMR (75 MHz, DMSO-d_6): C 169.3 (CO), 137.1, 133.5, 132.2, CH 134.5, 133.3, 130.2, 129.3, 128.8, 125.1, 123.0, 75.2. MS (EI) *m*/*z* (%): 273 (M^+, 1), 132 (100), 104 (22). IR (KBr) *v* 3233, 1699, 1301, 1127, 1081. Anal. Calcd for $C_{14}H_{11}NO_3S$: C, 61.53; H, 4.06; N, 5.12. Found: C, 61.66; H, 4.12; N, 5.21.

4.4.3. (3*S*)-3-(Toluene-4-sulfonyl)-2,3-dihydro-1*H*-isoindol-1-one 5c. Mp 248–249 °C; $[\alpha]_D^{20} = -11.5$ (*c* 1.03, DMSO); ^1H NMR (300 MHz, DMSO-d_6): 2.27 (s, 3H), 6.30 (s, 1H), 6.91–8.12 (m, 8H, H_{arom}), 9.78 (br s, 1H, NH); ^{13}C NMR (75 MHz, DMSO-d_6): C 169.3 (CO), 145.1, 137.2, 130.7, 130.6, CH 132.2, 130.1, 129.3, 129.2, 124.9, 123.0, 75.1, CH_3 21.0. MS (EI) *m*/*z* (%): 287 (M^+, 1), 132 (100), 104 (25). Anal. Calcd for $C_{15}H_{13}NO_3S$: C, 62.70; H, 4.56; N, 4.87. Found: C, 62.59; H, 4.43; N, 4.92.

4.4.4. (3*S*)-3-(4-Chlorobenzenesulfonyl)-2,3-dihydro-1*H*-isoindol-1-one 5d. Mp 198–199 °C; $[\alpha]_D^{20} = -4.0$ (*c* 0.76, DMSO); ^1H NMR (300 MHz, DMSO-d_6): 6.42 (s, 1H), 7.18–7.99 (m, 8H, H_{arom}), 9.82 (br s, 1H, NH); ^{13}C NMR (75 MHz, DMSO-d_6): C 169.5 (CO), 140.0, 137.1, 132.8, 132.5, CH 132.7, 131.3, 130.6, 129.3, 125.3, 123.4, 75.3. MS (EI) *m*/*z* (%): 307 (M^+, 1), 132 (100), 104 (18). Anal. Calcd for $C_{14}H_{10}ClNO_3S$: C, 54.64; H, 3.28; N, 4.55. Found: C, 54.68; H, 3.10; N, 4.49.

4.4.5. (3*S*)-3-Diphenylphosphinoyl-2,3-dihydro-1*H*-isoindol-1-one 5e. Mp 284–285 °C; $[\alpha]_D^{20} = -16.4$ (*c* 1.30, DMSO); ^1H NMR (300 MHz, DMSO-d_6): 6.20 (d, *J* = 4 Hz, 1H), 6.98 (d, *J* = 6.0 Hz, 1H, H_{arom}), 7.38–8.12 (m, 13H, H_{arom}), 9.17 (br s, 1H, NH); ^{13}C NMR (75 MHz, DMSO-d_6): C 169.9 (CO), 140.8 (d, *J* = 5 Hz), 132.7 (d, *J* = 3 Hz), 130.9 (d, *J* = 91 Hz), 129.6 (d, *J* = 92 Hz), CH 132.4 (d, *J* = 3 Hz), 132.2 (d, *J* = 2 Hz), 131.4 (d, *J* = 9 Hz), 131.2 (d, *J* = 3 Hz), 128.8 (d, *J* = 10 Hz), 128.4 (d, *J* = 12 Hz), 128.3, 123.7 (d, *J* = 2 Hz), 123.0, 55.6 (d, *J* = 72 Hz); ^{31}P NMR (121 MHz, DMSO-d_6): 28.4. MS (EI) *m*/*z* (%): 333 (M^+, 65), 201 (100), 132 (26). IR (KBr) *v* 3008, 2824, 1684, 1433, 1164. Anal. Calcd for $C_{20}H_{16}NO_2P$: C, 72.07; H, 4.84; N, 4.20. Found: C, 71.97; H, 4.82; N, 4.34.

4.4.6. (3*S*)-3-(Di-(4-methoxyphenyl)phosphinoyl)-2,3-dihydro-1*H*-isoindol-1-one 5f. Mp 255–256 °C; $[\alpha]_D^{20} = -30.0$ (*c* 1.46, DMSO); ^1H NMR (300 MHz, DMSO-d_6): 3.60 (s, 6H), 5.78 (d, *J* = 6.5 Hz, 1H), 6.80 (d, *J* = 8.5 Hz, 2H, H_{arom}), 6.95 (d, *J* = 6.1 Hz, 1H, H_{arom}), 7.05 (d, *J* = 8.6 Hz, 2H, H_{arom}), 7.35–8.00 (m, 7H, H_{arom}); ^{13}C NMR (75 MHz, DMSO-d_6): C 168.7, 161.5, 140.9 (d, *J* = 5 Hz), 132.5, 125.2 (d, *J* = 174 Hz),

125.0 (d, J = 176 Hz), CH 136.9 (d, J = 20 Hz), 135.2 (d, J = 18 Hz), 132.5, 127.6, 123.5, 123.1, 114.0 (d, J = 7 Hz), 56.1 (d, J = 25 Hz), CH_3 55.3; ^{31}P NMR (121 MHz, DMSO-d_6): 27.0. MS (EI) m/z (%): 393 (M^+, 53), 261 (100), 132 (44). Anal. Calcd for $C_{22}H_{20}NO_4P$: C, 67.17; H, 5.12; N, 3.56. Found: C, 67.03; H, 4.95; N, 3.73.

4.4.7. (3*S*)-3-(Di-(naphth-2-yl)phosphinoyl)-2,3-dihydro-1*H*-isoindol-1-one 5g. Mp 293–294 °C; $[\alpha]_D^{20} = -26.8$ (c 1.17, DMSO); ^1H NMR (300 MHz, DMSO-d_6): 6.51 (d, J = 4 Hz, 1H), 7.12–7.58 (m, 9H, H_{arom}), 7.64–7.92 (m, 3H, H_{arom}), 8.01 (t, J = 6.5 Hz, 2H, H_{arom}), 8.25 (d, J = 8.8 Hz, 2H, H_{arom}), 8.42 (d, J = 8.5 Hz, 1H, H_{arom}), 8.60 (d, J = 8.5 Hz, 1H, H_{arom}), 9.47 (br s, 1H, NH); ^{13}C NMR (75 MHz, DMSO-d_6): C 169.9 (CO), 140.7 (d, J = 4 Hz), 133.5, 133.1, 132.8, 132.7 (d, J = 10 Hz), 126.3 (d, J = 150 Hz), CH 133.4 (d, J = 4 Hz), 133.1 (d, J = 10 Hz), 133.0, 132.4 (d, J = 11 Hz), 131.0, 129.1, 128.6, 128.3, 127.1, 126.5 (d, J = 12 Hz), 126.1, 126.0, 125.0 (d, J = 6 Hz), 124.9 (d, J = 7 Hz), 124.4 (d, J = 14 Hz), 122.8, 55.8 (d, J = 73 Hz); ^{31}P NMR (121 MHz, DMSO-d_6): 36.0. MS (EI) m/z (%): 433 (M^+, 43), 301 (100), 132 (32). Anal. Calcd for $C_{28}H_{20}NO_2P$: C, 77.59; H, 4.65; N, 3.23. Found: C, 77.62; H, 4.54; N, 3.34.

4.5. X-ray crystallographic analysis

Cell dimensions and intensities were measured at 100 K on a Bruker AXS SMART three-circle diffractometer with graphite-monochromated Mo[Kα] radiation (λ = 0.71073 Å) and equipped with CCD two-dimensional detector. Collection with ω and φ scans. The structure was solved by direct methods and expanded using Fourier maps. All non-hydrogen atoms were refined anisotropically. Hydrogen atom positions were refined but their temperature coefficients were fixed to 1.2 times the U_{eq} of the atoms they are bound to. The SHELXTL[19] crystallographic software package was used for all calculations. Compound **6e**: $C_{26}H_{27}N_2O_3P$, M = 446.47, $F(000)$ = 472, colourless crystal, D_c = 1.305 g cm^{-3}, μ (Mo Kα) = 0.152 cm^{-1} monoclinic, $P2_1$, Z = 2, a = 9.1013(14), b = 11.8299(18), c = 10.7967(16) Å, β = 102.116(3)°, U = 1136.6(3) Å^3; 9277 independent reflections were used $-12 < h < 11$, $-15 < k < 15$, $-14 < l < 14$, θ_{max} = 28.58°, $R1$ = 0.0459, $Rw2$ = 0.0924; the estimated standard deviations for non-hydrogen atoms were in the range 0.002–0.004 Å for the bond lengths and 0.1–0.3° for the bond angles. Further details of the X-ray structure data are available free on request from the Cambridge Crystallographic Data Centre (deposition number CCDC 245173).

Acknowledgements

This work was supported by the Deutsche Forschungsgemeinschaft (Leibniz-Preis) and the Fonds der Chemischen Industrie. We thank Degussa AG, BASF AG, the former Hoechst AG and Bayer AG for the donation of chemicals.

References

1. (a) Valencia, E.; Weiss, I.; Firdous, S.; Freyer, A. J.; Shamma, M.; Urzua, A.; Fayardo, V. *Tetrahedron* **1984**, *40*, 3957–3962; (b) Fang, F. G.; Danishefsky, S. J. *Tetrahedron Lett.* **1989**, *30*, 2747–2750; (c) Couture, A.; Deniau, E.; Grandclaudon, P.; Hoarau, C. *Tetrahedron* **2000**, *56*, 1491–1499; (d) Rys, V.; Couture, A.; Deniau, E.; Grandclaudon, P. *Eur. J. Org. Chem.* **2003**, 1231–1237; (e) Moreau, A.; Couture, A.; Deniau, E.; Grandclaudon, P. *Tetrahedron* **2004**, *60*, 6169–6176; (f) Moreau, A.; Couture, A.; Deniau, E.; Grandclaudon, P. *J. Org. Chem.* **2004**, *69*, 4527–4530.
2. (a) Mertens, A.; Zilch, H.; Koenig, B.; Schaefer, W.; Poll, T.; Kampe, W.; Seidel, H.; Leser, U.; Leinert, H. *J. Med. Chem.* **1993**, *36*, 2526–2535; (b) Maass, G.; Immendoerfer, U.; Koenig, B.; Leser, U.; Mueller, B.; Goody, R.; Pfaff, E. *Antimicrob. Agents Chemother.* **1993**, *37*, 2612–2617; (c) Jingshan, R.; Esnouf, R. M.; Hopkins, A. L.; Stuart, D. I.; Stammers, D. K. *J. Med. Chem.* **1999**, *42*, 3845–3851.
3. Ogata, M.; Matsumoto, H.; Tawara, K. *Eur. J. Med. Chem. Chim. Ther.* **1981**, *16*, 373–378.
4. Hadfield, J. A.; Pavlidis, V. H.; Roffey, J. R. A. *Synth. Commun.* **1995**, *25*, 1319–1330.
5. (a) Holzgrabe, U.; Bender, W.; Botero Cid, H. M.; Staudt, M.; Pick, R.; Pfletschinger, C.; Balatkova, E.; Traenkle, C.; Mohr, K. *Pharm. Acta Helv.* **2000**, *74*, 149–155; (b) Botero Cid, H. M.; Traenkle, C.; Baumann, K.; Pick, R.; Mies-Klomfass, E.; Kostenis, E.; Mohr, K.; Holzgrabe, U. *J. Med. Chem.* **2000**, *43*, 2155–2164.
6. (a) Luzzio, F. A.; Zacherl, D. P. *Tetrahedron Lett.* **1998**, *39*, 2285–2288; (b) Hoarau, C.; Couture, A.; Deniau, E.; Grandclaudon, P. *Synthesis* **2000**, 655–660; (c) Deniau, E.; Enders, D. *Tetrahedron* **2001**, *57*, 2581–2588; (d) Hunter, R.; Richards, P. *Org. Biomol. Chem.* **2003**, *1*, 2348–2356.
7. (a) Couture, A.; Deniau, E.; Grandclaudon, P. *Tetrahedron* **1997**, *53*, 10313–10330; (b) Deniau, E.; Enders, D. *Tetrahedron Lett.* **2002**, *43*, 8055–8058.
8. (a) Ukaji, Y.; Tsukamoto, K.; Nasada, Y.; Shimizu, M.; Fujisawa, T. *Chem. Lett.* **1993**, 221–224; (b) Allin, S. M.; Northfield, C. J.; Page, M. I.; Slawin, A. M. Z. *J. Chem. Soc., Perkin Trans. 1* **2000**, 1715–1721.
9. (a) Alonso, R.; Castedo, L.; Dominguez, D. *Tetrahedron* **1985**, *26*, 2925–2928; (b) Bahajaj, A. A.; Vernon, J. M. *J. Chem. Soc., Perkin Trans. 1* **1996**, 1041–1046; (c) Katritzky, A. R.; Maimait, R.; Xu, Y.-J.; Akhmedova, R. G. *Synthesis* **2002**, 601–604.
10. (a) Belliotti, T. R.; Brink, W. A.; Kesten, S. R.; Rubin, J. R.; Wustrow, D. J.; Zoski, K. T.; Whetzel, S. Z.; Corbin, A. E.; Pugsley, T. A.; Heffner, T. G.; Wise, L. D. *Bioorg. Med. Chem. Lett.* **1998**, *8*, 1499–1502; (b) Wood, J. L.; Petsch, D. T.; Stoltz, B. M.; Hawkins, E. M.; Elbaum, D.; Stover, D. R. *Synthesis* **1999**, 1529–1533; (c) Bishop, A. C.; Ubersax, J. A.; Petsch, D. T.; Matheos, D. P.; Gray, N. S.; Blethrow, J.; Shimizu, E.; Tsien, J. Z.; Schultz, P. G.; Rose, M. D.; Wood, J. L.; Morgan, D. O.; Shokat, K. M. *Nature (London)* **2000**, *407*, 395–401.
11. (a) Allin, S. M.; Vaidya, D. G.; Page, M. I.; Slawin, A. M. Z.; Smith, T. *Tetrahedron Lett.* **2000**, *41*, 2219–2222; (b) Katritzky, A. R.; He, H.-Y.; Verma, A. K. *Tetrahedron: Asymmetry* **2002**, *13*, 933–938.
12. Review: Enders, D.; Klatt, M. *Synthesis* **1996**, 1403–1418.
13. Deniau, E.; Enders, D.; Couture, A.; Grandclaudon, P. *Tetrahedron: Asymmetry* **2003**, *14*, 2253–2258.

14. Review: Job, A.; Janeck, C. F.; Bettray, W.; Peters, R.; Enders, D.. *Tetrahedron* **2002**, *58*, 2253–2329.
15. (a) Suzuki, H.; Aoyagi, S.; Kibayashi, C. *Tetrahedron Lett.* **1994**, *35*, 6119–6122; (b) Suzuki, H.; Aoyagi, S.; Kibayashi, C. *J. Org. Chem.* **1995**, *60*, 6114–6122.
16. (a) Fernandez, R.; Ferrete, A.; Lassaletta, J. M.; Llera, J. M.; Monge, A. *Angew. Chem., Int. Ed.* **2000**, *39*, 2893–2897; (b) Enders, D.; Braig, V.; Raabe, G. *Can. J. Chem.* **2001**, *79*, 1528–1535; (c) Fernandez, R.; Ferrete, A.; Lassaletta, J. M.; Llera, J. M.; Martin-Zamora, E. *Angew. Chem., Int. Ed.* **2002**, *41*, 831–833.
17. Kabat, M. M.; Garofalo, L. M.; Daniewski, A. R.; Hutchings, S. D.; Liu, W.; Okabe, M.; Radinov, R.; Zhou, Y. *J. Org. Chem.* **2001**, *66*, 6141–6150.
18. Hobbs, C. F.; Knowless, W. S. *J. Org. Chem.* **1981**, *46*, 4422–4427.
19. Sheldrick, G. M. SHELXTL, *Program for Crystal Structure Solution and Refinement*; Bruker AXS Inc.: Madison, WI, 1997.