Pergamon

SCIENCE DIRECT®

Tetrahedron 59 (2003) 6937–6945

TETRAHEDRON

Toward the enantioselective total synthesis of lyngbyatoxin A: on the stereocontrolled introduction of the quaternary stereogenic centre

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Received 2 April 2003; revised 23 April 2003; accepted 12 May 2003

Dedicated to Professor K. C. Nicolaou, upon his receipt of the Tetrahedron Prize for 2002

Abstract—This paper deals with an approach to the enantioselective total synthesis of Lyngbyatoxin A, with focus on the stereocontrolled introduction of the quaternary stereogenic centre. The key step in the synthesis involves an enantiospecific Lewis-acid mediated rearrangement of chiral vinyl epoxides carrying a 7-substituted indole moiety.

1. Introduction

Lyngbyatoxin A (**1**, also known as teleocidin A-1) is a marine natural product isolated from the Hawaiian variant of *Lyngbya Majuscula Gomont*.[1] Alkaloids of this indolactam family, which also includes indolactam-V (**2**) and teleocidin B-3 (**3**), have attracted much biological interest because they are potent activators of protein kinase C (PKC)[2] which is implicated in the regulation of various cellular responses. Malfunction of PKC can lead *inter alia* to tumor development and diabetic complications, and members of the PKC family are thus promising targets for medicinal chemistry; selective activators and inhibitors of PKC are therefore perceived as useful tools for drug development (Fig. 1).[3–14]

The structurally more elaborate teleocidins also present a substantial challenge to chemical synthesis, and while several syntheses of **2** have been documented[15,16] we are aware of only one total synthesis[17] of **1** and two completed routes[18,19] to **3**. A common feature of these approaches is the lack of stereochemical control of the quaternary stereogenic centre(s)[20–23] of the targets. More recently, Sames[24] has reported a very intriguing approach to the racemic form of teleocidin B-4 (which is the epimer of **3** at both quaternary centres). We are currently engaged in research into the chemical biology of structures which activate PKC, and as part of that program we have undertaken the total synthesis of **1**. The present paper describes a method for stereocontrolled introduction of the quaternary centre of Lyngbyatoxin A.

Our overall retrosynthetic analysis is shown in Scheme 1(a), application of the indicated disconnections leading back to trisubstituted indole **6**, which was envisioned to derive from 7-bromoindole, **7**. The synthetic sequence which takes **7** to **6**

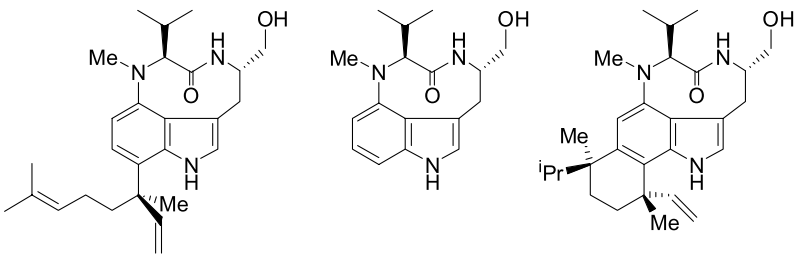

Figure 1.

Keywords: lyngbyatoxin A; teleocidins; vinyl epoxide rearrangement.
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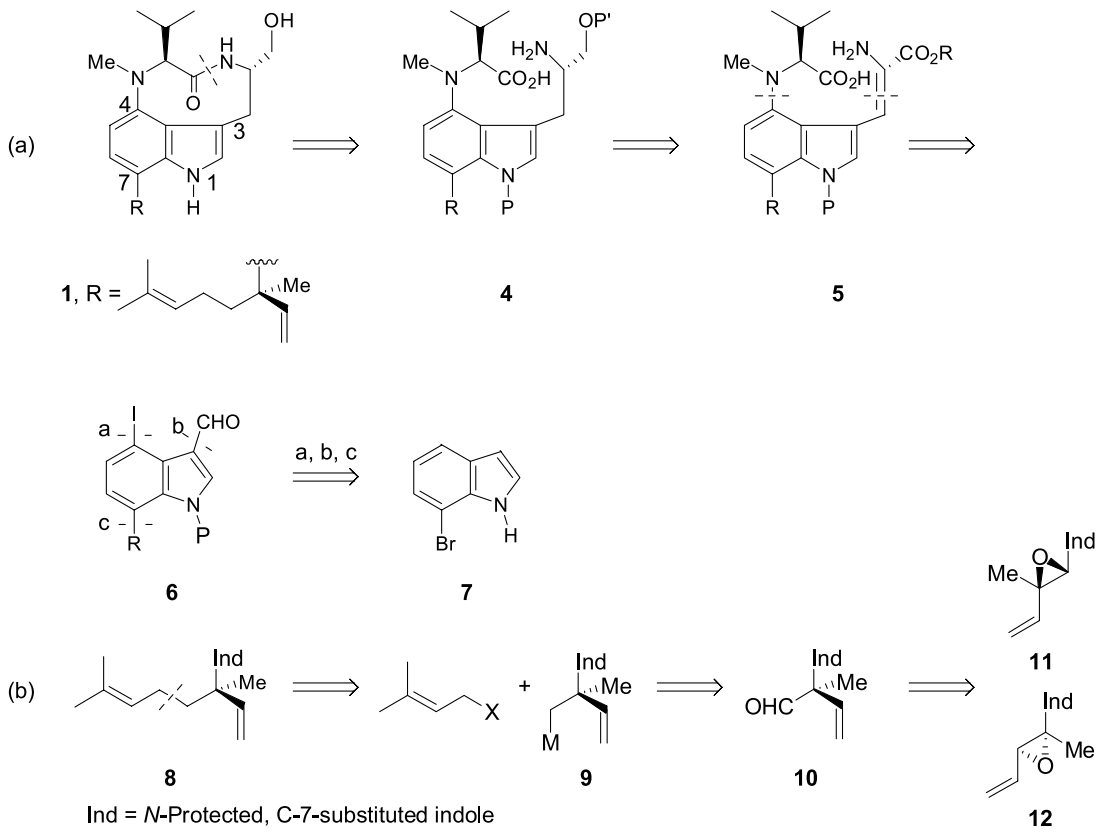
0040–4020/$ - see front matter © 2003 Elsevier Ltd. All rights reserved.
doi:10.1016/S0040-4020(03)00822-6



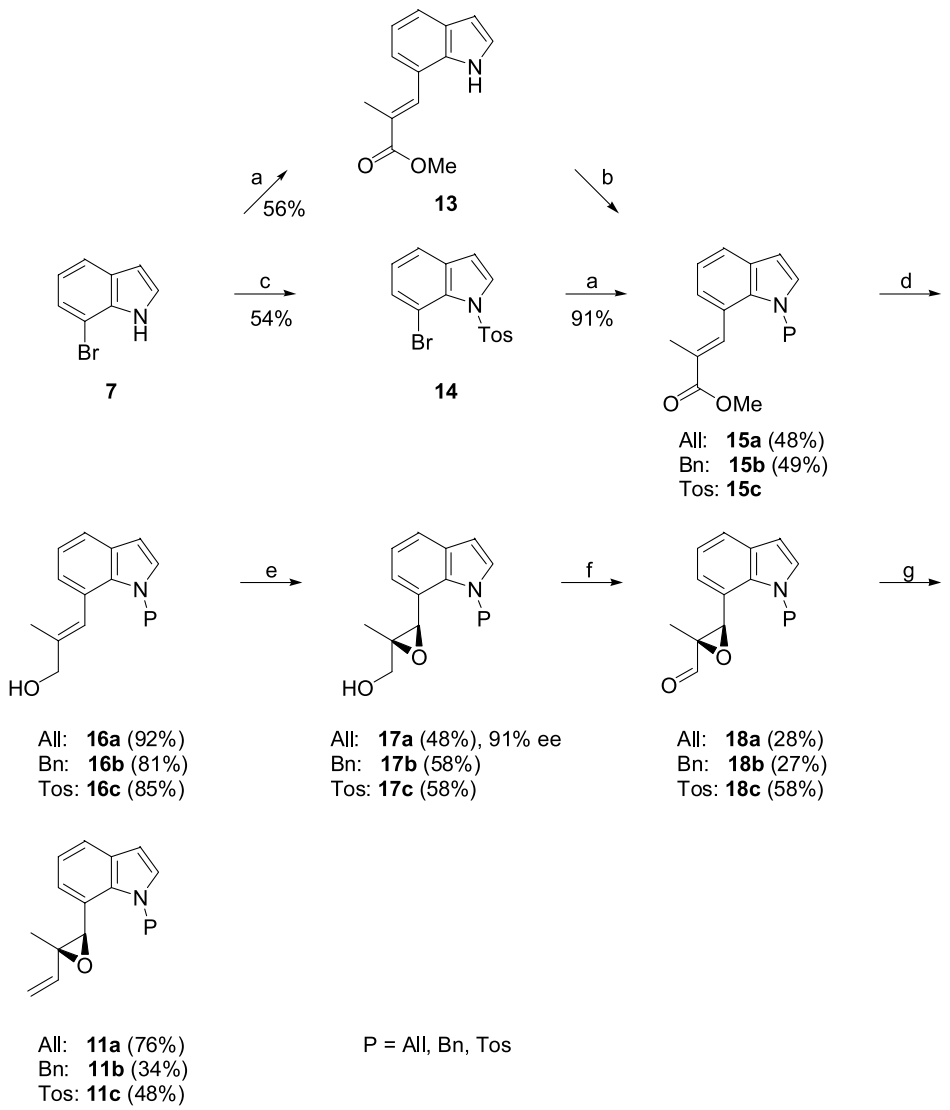
Scheme 1. (a) Retrosynthetic analysis of Lyngbyatoxin A, **1**. (b) Scheme for control of stereochemistry at the 4° stereogenic centre.

is thus (i) introduction of functionality at C-7; (ii) Vilsmeier formylation[25] at C-3 and (iii) regioselective iodination[25] at C-4. Scheme 1(b) shows our plan for elaboration of, and control over, the stereogenic centre in the C-7 side-chain. The key step involves methodology developed by Jung[26,27] and relies on the enantiospecific Lewis-acid mediated rearrangement of chiral vinyl epoxides,[28] which are themselves available via the Sharpless asymmetric epoxidation[29] reaction. Jung[27] has made studies of migratory aptitudes[30] and the relative stability of cationic intermediates involved in this type of rearrangement, and on that basis we surmised that two regioisomeric vinyl epoxides could serve our purpose: rearrangement of **11** via migration of the indole moiety, or rearrangement of **12** via vinyl migration. At the outset, we had no information regarding the migratory aptitude of the indole nucleus, so **11** was chosen as the first target, to allow direct comparison with the work of Jung[27] which involved a phenyl group instead of the indole system.

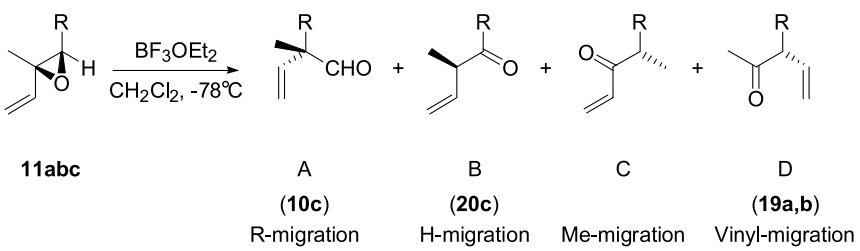
2. Results and discussion

The synthesis of three differently *N*-protected variants of **11** is shown in Scheme 2, the Heck reaction being used for introduction of the embryonic C-7 side-chain.[31] Apart from **15c** all the *cis*/*trans* isomeric mixtures resulting from the Heck reaction could be separated by flash chromatography. In fact, the *N*-tosyl products proved impossible to separate at any stage of the sequence, and were thus carried through as a 1:2 *cis*/*trans* mixture. The stereochemistry of the Heck products was assigned by NMR spectroscopy.[32,33] The epoxides shown in Scheme 2 (and Scheme 5) were rather unstable, and were used as soon as possible. This was particularly true for the *N*-benzyl series leading to **11b**, and these intermediates could not be fully characterized. The results of the rearrangement reactions (Scheme 3) are collected in Table 1.

The rearrangement reactions were carried out according to the published procedure[26] and proved to be both rapid and highly efficient processes, requiring only very short reaction times at −78°C. We began by repeating earlier work[27] with **11d** (Table 1, entry 4) and could easily reproduce the exclusive phenyl migration to the tertiary and allylic carbocation. However, subjection of the *N*-allyl or *N*-benzyl indole substrates (**11a** or **11b**) to the same reaction conditions gave exclusively the products of vinyl migration, implying that the secondary indole-stabilized carbocation is preferred to the tertiary allylic species (Table 1, entries 1 and 2). In order to attenuate the cation-stabilizing effect of the indole nitrogen, the *N*-tosyl derivative **11c** was chosen, and rearrangement of this substrate did indeed deliver the desired product, but as the minor component (Table 1, entry 3). The tertiary carbocation is now favoured, but hydride migration is faster than migration of the indole moiety. This quite surprising result can be explained on the basis of the mechanistic rationale introduced and refined by Coxon[34] and also invoked by Jung.[26] Formation of the tertiary allylic carbocation is followed by rotation of the O–BF_3 unit toward the sterically less demanding group on the adjacent carbocation centre, which aligns the C–H bond with the vacant p-orbital (Scheme 4). However, there is obviously little energetic difference between this pathway and the



Scheme 2. The Tosyl-protected compounds (**15c**–**18c** and **11c**) were obtained as a mixture of (*Z*/*E*)-isomers. (a) 2-Methyl methacrylate, $PdCl_2(P(o\text{-}Tol)_3)_2$, Bu_4NBr, NEt_3, DMF, 90°C; (b) AllBr, NaH, DMF, 20°C; (c) TosCl, NaH, DMF; (d) Dibal-H, toluene; (e) *tert*-BuOOH, D-(−)-DIPT, $Ti(O^iPr)_4$; (f) TPAP, NMO, 4 Å molecular sieves, CH_2Cl_2, 20°C; (g) KHMDS, Ph_3PCH_3Br, THF, 20°C.



Scheme 3. Rearrangement of vinyl epoxides.

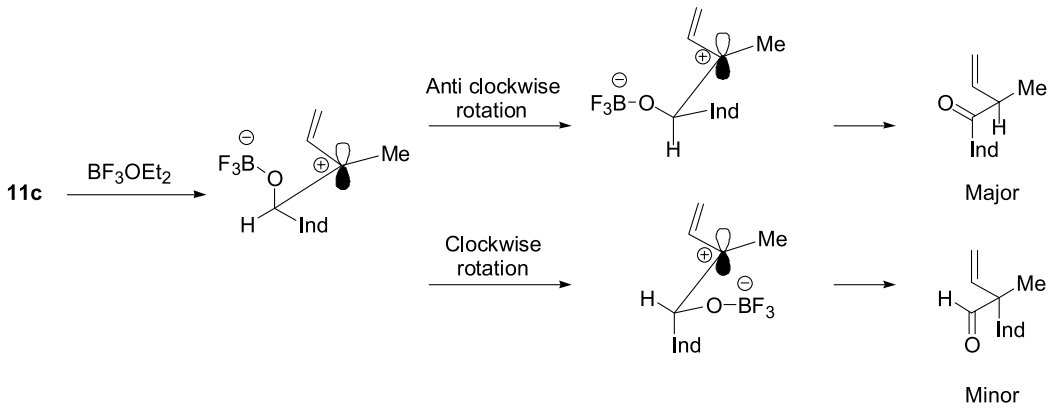
Table 1. Lewis acid catalysed rearrangement of vinyl epoxides

Compound	R	A	B	C	D
11a	All-indole	0	0	0	>99% (19a)
11b	Bn-indole	0	0	0	>99% (19b)
11c	Tos-indole	40% (**10c**)	60% (**20c**)	0	0
11d[27]	Ph	>99%	0	0	0

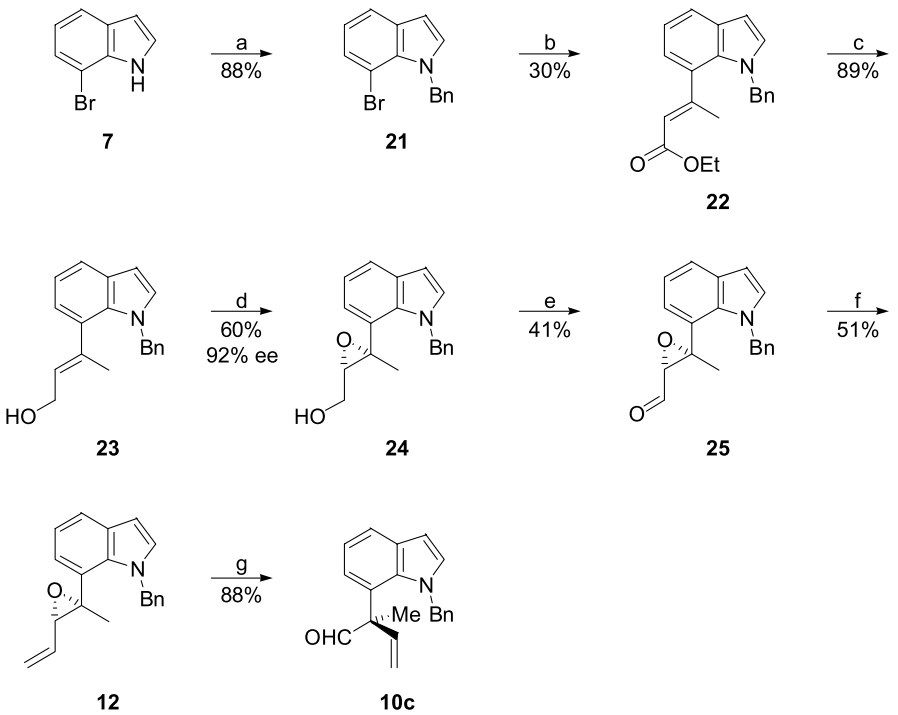
The product distribution was measured by ^1H NMR spectroscopy.

alternative clockwise rotation which correctly aligns the indole moiety for migration. It should be noted that the experiment with the *N*-tosyl species was carried out on the inseparable *cis*/*trans* mixture of vinyl epoxides, and the *cis* compound (not shown in Scheme 4) gives rise to the enantiomer of each type of rearrangement product. Products of type B and D (Table 1) quite rapidly isomerized to the conjugated ketones.

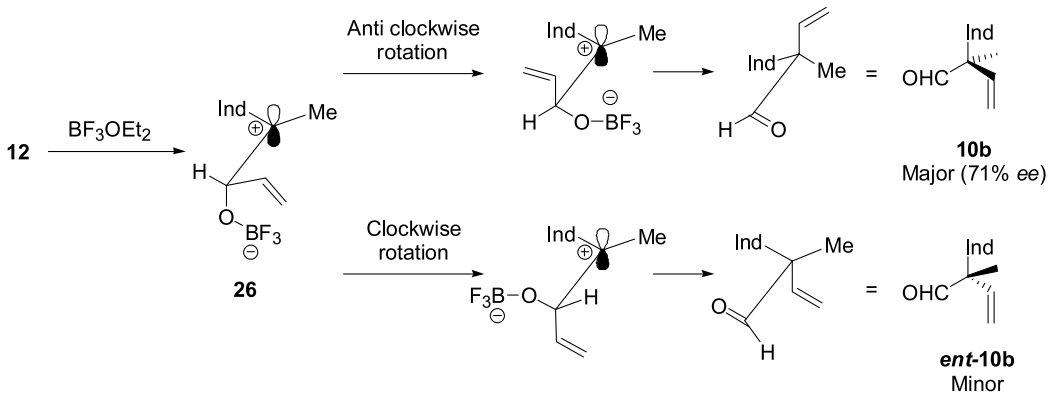
A simple solution to the problem was found by switching to



Scheme 4. Ind=*N*-tosyl, C-7-substituted indole.



Scheme 5. (a) BnBr, KOH, DMF, 20°C; (b) ethyl crotonate, $PdCl_2(P(o\text{-}Tol)_3)_2$, Bu_4NBr, NEt_3, DMF, 90°C; (c) Dibal-H, toluene, −50→5°C; (d) *tert*-BuOOH, L-(+)-DET, $Ti(O^iPr)_4$, CH_2Cl_2, −20°C; (e) TPAP, NMO, 4 Å molecular sieves, CH_2Cl_2, 20°C; (f) KHMDS, Ph_3PCH_3Br, THF, 20°C; (g) $BF_3{\cdot}OEt_2$, CH_2Cl_2, −78°C, 2.5 min.



Scheme 6. Ind=*N*-benzyl, C-7-substituted indole.

rearrangement of the regioisomeric vinyl epoxide **12**, the synthesis of which is shown in Scheme 5. In this rearrangement a tertiary, indole-stabilized carbocation is pitted against a secondary allylic centre. This process requires the opposite sense of absolute configuration of the epoxide, and relies on the assumption that vinyl migration should be considerably faster[30] than hydride migration. Fortunately, this turned out to be the case and the desired chiral aldehyde was obtained in 88% yield.

However, the enantiomeric purity of the starting vinyl epoxide (92% ee) was not reflected in that of the product (71% ee), indicating that the rate of vinyl migration is only slightly higher than the rate of conformer equilibration in the complex formed after C–O bond cleavage. The absolute configuration of the major enantiomer of the product (Scheme 6) is assigned on the basis of the type of argument presented earlier: anti-clockwise rotation in complex **26** places the OBF_3 and indole moieties as far apart as possible, and correctly aligns the vinyl group for migration, leading to the desired absolute stereochemistry (**10b**).

In conclusion, we have developed the first enantioselective method for stereocontrolled introduction of the quaternary stereogenic centre of Lyngbyatoxin A. We are currently exploring 'second generation' enantioselective approaches, and results will be reported elsewhere.

3. Experimental

3.1. General remarks

Tetrahydrofuran and toluene were distilled under nitrogen from sodium/benzophenone prior to use. Triethylamine and dichloromethane were distilled under nitrogen from calcium hydride prior to use. Methyl methacrylate, ethyl crotonate and $Ti(O^iPr)_4$, were vacuum distilled before use. All other commercially available compounds were used as received. *N*-Benzyl-7-bromoindole (**21**)[35] and dichlorobis(tri-*o*-tolylphosphine)palladium(II)[36] were synthesised following literature procedures. All air- and moisture-sensitive reactions were carried out under nitrogen in oven-dried glassware. ^1H (300 or 500 MHz) and ^{13}C (75 or 125 MHz) NMR spectra were recorded on a Varian Mercury 300 or a Varian Inova 500, respectively. High resolution mass spectra were provided by the Department of Chemistry, University of Copenhagen. Enantiomeric excess (ee) was determined by chiral HPLC analysis using a Daicel OD column with heptane/isopropanol 90:10 as eluent. Compounds **11b** and **15b–19b** were characterized only by ^1H NMR due to instability problems.

3.1.1. 7-Bromo-1-*p*-toluenesulfonylindole (14). Sodium hydride (306 mg, 3.27 mmol) was added to a 0°C solution of 7-bromoindole (493 mg, 2.51 mmol) in THF (20 mL). This greyish mixture was stirred at 20°C for 15 min, before addition of *p*-toluenesulfonyl chloride (575 mg, 3.02 mmol). Stirring was continued at 20°C overnight. Water (5 mL) was added and the mixture was concentrated in vacuo. To the residue was added water (25 mL), and the mixture was extracted with dichlorormethane. The combined organic phases were dried ($MgSO_4$), and evaporated to give 819 mg (93%) of an orange oil. Column chromatography (ethyl acetate/heptane 1:7) gave 474 mg (54%) of the desired product as a violet oil, which solidified on standing. 182 mg (37%) starting material was recovered. ^1H NMR ($CDCl_3$) δ 7.92 (d, J=3.9 Hz, 1H), 7.69 (d, J=8.4 Hz, 2H), 7.53 (dd, J=7.8, 1.2 Hz, 1H), 7.46 (dd, J=7.8, 1.2 Hz, 1H), 7.27 (d, J=8.7 Hz, 2H), 7.06 (t, J=7.8 Hz, 1H), 6.72 (d, J=3.9 Hz, 1H), 2.40 (s, 3H). ^{13}C NMR ($CDCl_3$) δ 144.7, 137.5, 135.0, 133.7, 130.8, 130.7, 129.8, 127.2, 124.6, 120.8, 107.7, 106.2, 21.8. MS (EI): 351, 204, 196, 155, 115, 91. HRMS (EI) *m/z* calcd for $C_{15}H_{12}BrNO_2S$ 348.9772, found 348.9776.

3.2. General procedure for the Heck reaction

3.2.1. (*E*)-Methyl 3-(7-indolyl)-2-methacrylate (13). A mixture of 7-bromoindole (2.77 g, 14.1 mmol), methyl methacrylate (7.56 mL, 70.6 mmol), dichlorobis(tri-*o*-tolylphosphine)palladium(II) (0.42 g, 0.53 mmol), triethylamine (29 mL, 212 mmol), and tetrabutylammonium bromide (0.909 g, 2.82 mmol) in DMF (75 mL) was stirred at 90°C under nitrogen for 2 h. Ethyl acetate (250 mL) was added and the mixture was washed with brine (2×100 mL) and water (100 mL), dried ($MgSO_4$) and evaporated to give 4.05 g of a brown oil. ^1H NMR showed the desired product as a mixture of isomers in a *Z*/*E* relationship of 1:2. The assignment was based on literature data.[32] Column chromatography (ethyl acetate/heptane 1:5) gave 1.22 g (40%) of the desired product as a yellow oil.

^1H NMR ($CDCl_3$) (*E*-isomer): δ 8.29 (bs, 1H), 7.95 (s, 1H), 7.66 (dd, J=8.0, 1.0 Hz, 1H), 7.25–7.22 (m, 1H), 7.22–7.21 (m, 1H), 7.17 (td, J=8.0, 2.5 Hz, 1H), 6.62–6.60 (m, 1H), 3.87 (s, 3H), 2.13 (s, 3H). ^{13}C NMR ($CDCl_3$) (*E*-isomer): δ 168.4, 134.5, 124.5, 122.7, 121.8, 121.6, 120.7, 119.8, 119.5, 103.3, 103.2, 52.3, 14.8. MS (EI): 215, 184, 154, 129, 77. HRMS (EI) *m/z* calcd for $C_{13}H_{13}NO_2$ 215.0946, found 215.0951.

3.2.2. (*Z*/*E*)-Methyl 3-(*N*-*p*-toluenesulfonylindol-7-yl)-2-methacrylate (15c). Prepared from 7-bromo-1-*p*-toluenesulfonylindole (**14**) (1.10 g, 3.14 mmol), methyl methacrylate (3.36 mL, 31.4 mmol), $PdCl_2(P(o\text{-tolyl})_3)_2$ (0.123 g, 0.157 mmol), triethylamine (6.56 mL, 47.1 mmol), and tetrabutylammonium bromide (0.202 g, 0.63 mmol) by the general procedure for the Heck reaction. There was obtained 1.06 g (91%) of the desired product as a mixture of isomers in a *Z*/*E* relationship of 1:2 (Assignment was based on comparison with **15a** and **22**). ^1H NMR ($CDCl_3$) δ (*E*) 8.14–8.13 (m, 1H), 7.84 (d, J=3.9 Hz, 1H), 7.54 (d, J=7.8 Hz, 1H), 7.47 (d, J=8.7 Hz, 1H), 7.22 (t, J=7.8 Hz, 1H), 7.16 (dd, J=8.7, 1.2 Hz, 2H), 6.98 (d, J=7.8 Hz, 1H), 6.75 (d, J=3.9 Hz, 1H), 3.90 (s, 3H), 2.35 (s, 3H), 1.60 (d, J=1.2 Hz, 3H). (*Z*) 7.79 (d, 3.9 Hz, 1H), 7.54 (d, J=7.8 Hz, 1H), 7.51 (d, J=8.7 Hz, 1H), 7.18 (t, J=7.8 Hz, 1H), 7.16 (dd, J=8.7, 1.2 Hz, 2H), 6.98 (d, J=7.8 Hz, 1H), 6.71 (d, J=3.9 Hz, 1H), 3.75 (s, 3H), 2.36 (s, 3H), 1.60 (d, J=1.2 Hz, 3H). MS (EI): 369, 214, 198, 182, 155, 154, 91. HRMS (EI) *m/z* calcd for $C_{20}H_{19}NO_4S$ 369.1035, found 369.1026.

3.2.3. (*E*)-Ethyl 3-(*N*-benzylindol-7-yl)-crotonate (22). Prepared from 7-bromo-*N*-benzylindole (**21**) (3.00 g,

10.5 mmol), ethyl crotonate (26.0 mL, 210 mmol), $PdCl_2$-($P(o\text{-tolyl})_3)_2$ (0.413 g, 0.525 mmol), triethylamine (22.0 mL, 158 mmol), and tetrabutylammonium bromide (0.677 g, 2.10 mmol) by the general procedure for the Heck reaction. 947 mg (30%) of the pure desired product isomer (**22**) was obtained as well as 599 mg (19%) of a (*Z*/*E*)-mixture. The overall (*Z*/*E*)-ratio is 1:8. The assignment was based on literature data.[33] (*E*)-isomer: ^{1}H NMR ($CDCl_3$) δ 7.63 (dd, *J*=8.0, 1.5 Hz, 1H), 7.26–7.21 (m, 3H), 7.12 (d, *J*=3.0 Hz, 1H), 7.10 (d, *J*=8.0 Hz, 1H), 6.90 (dd, *J*=7.5, 1.0 Hz, 1H), 6.83 (d, *J*=8.0 Hz, 2H), 6.63 (d, *J*=2.5 Hz, 1H), 5.73 (q, *J*=1.5 Hz, 1H), 5.38 (bs, 2H), 4.20 (q, *J*=7.5 Hz, 2H), 2.29 (d, *J*=1.0 Hz, 3H), 1.30 (t, *J*=7.5 Hz, 3H). ^{13}C NMR ($CDCl_3$) δ 167.0, 156.3, 139.0, 132.5, 131.5, 131.2, 129.3, 129.3, 128.0, 126.9, 122.3, 121.5, 121.1, 120.1, 103.2, 60.5, 52.8, 22.4, 15.0. MS (EI): 319, 246, 230, 168, 154, 91. HRMS (EI) *m*/*z* calcd for $C_{21}H_{21}NO_2$ 319.1572, found 319.1564.

3.2.4. (*E*)-Methyl 3-(*N*-allylindol-7-yl)-2-methacrylate (15a). A solution of (*E*)-methyl 3-(7-indolyl)-2-methacrylate (**13**) (500 mg, 2.3 mmol) in DMF (10 mL) was added to a 0°C suspension of sodium hydride in DMF (5 mL). This mixture was stirred at 0°C for 15 min, before addition of allyl bromide (0.24 mL, 2.8 mmol). Stirring was continued at 0°C for 30 min and then the reaction was allowed to warm to 20°C. Water (200 mL) and NaCl (200 mg) were added and the mixture was extracted with diethyl ether (4×100 mL). The combined organic phases were washed with water (2×50 mL), dried ($MgSO_4$), and evaporated. Column chromatography (ethyl acetate/heptane 1:5) afforded 282 mg (48%) of the desired product as a yellow oil. ^{1}H NMR ($CDCl_3$) δ 8.16 (s, 1H), 7.62 (d, *J*=7.8 Hz, 1H), 7.11 (t, *J*=7.8 Hz, 1H), 7.07 (d, *J*=3 Hz, 1H), 6.99 (d, *J*=7.8 Hz, 1H), 6.57 (d, *J*=3 Hz, 1H), 6.09–5.94 (m, 1H), 5.19 (d, *J*=10.5 Hz, 1H), 4.88 (d, *J*=16.2 Hz, 1H), 4.83 (m, 2H), 3.87 (s, 3H), 2.03 (s, 3H). ^{13}C NMR ($CDCl_3$) δ 204.7, 169.0, 142.2, 137.7, 135.1, 129.8, 129.6, 123.4, 121.6, 120.2, 119.3, 116.6, 102.2, 52.2, 50.9, 14.2. MS (EI): 255, 196, 180, 168, 167, 154. HRMS (EI) *m*/*z* calcd for $C_{16}H_{17}NO_2$ 255.1259, found 255.1259.

3.2.5. (*E*)-Methyl 3-(*N*-Benzylindol-7-yl)-2-methacrylate (15b). Prepared from (*E*)-methyl 3-(7-indolyl)-2-methacrylate (500 mg, 2.30 mmol) (**13**) and benzyl bromide (0.33 mL, 2.8 mmol) in 49% yield as described above for **15a**. ^{1}H NMR ($CDCl_3$) δ 7.92 (s, 1H), 7.66 (d, *J*=8.1 Hz, 1H), 7.41–7.36 (m, 1H), 7.29–7.25 (m, 2H), 7.15 (d, *J*=3.0 Hz, 1H), 7.12 (d, *J*=7.5 Hz, 1H), 6.96–6.90 (m, 3H), 6.63 (d, *J*=3.3 Hz, 1H), 5.48 (s, 2H), 3.79 (s, 3H), 1.84 (d, *J*=1.5 Hz, 3H).

3.3. General procedure for the Dibal reduction

3.3.1. (*E*)-3-(*N*-Allylindol-7-yl)-2-methyl-2-propenol (16a). Dibal-H (1.2 M in toluene, 2.9 mL, 3.5 mmol) was added to a −50°C solution of **15a** (219 mg, 0.86 mmol) in toluene (20 mL) over a period of 2 min. Stirring for 30 min at −40°C led to completion of the reaction, and the reaction was quenched with methanol (5 mL). Then water (25 mL) and dichloromethane (50 mL) were added, the layers were separated, and the aqueous layer was extracted with dichloromethane (4×25 mL). Drying ($MgSO_4$) and concentration of the combined organic layers gave 286 mg of a yellowish oil which turned red on standing. Column chromatography (ethyl acetate/heptane 1:3) gave 179 mg (92%) of the desired alcohol as a colourless oil.

^{1}H NMR ($CDCl_3$) δ 7.57 (d, *J*=7.8 Hz, 1H), 7.10 (dt, *J*=7.8, 1.2 Hz, 1H), 7.05 (d, *J*=3.0 Hz, 1H), 6.95–6.93 (m, 2H), 6.56 (dd, *J*=3.3, 1.2 Hz, 1H) 6.05–5.94 (m, 1H), 5.17–5.12 (m, 1H), 4.92–4.82 (m, 3H), 4.28 (s, 2H), 1.82 (bs, 1H), 1.79 (s, 3H) ^{13}C NMR ($CDCl_3$) δ 138.7, 135.4, 134.0, 129.6, 129.4, 123.9, 122.7, 121.8, 120.0, 119.4, 116.1, 101.9, 68.3, 50.6, 15.3. MS (EI): 227, 168, 154, 130, 117. HRMS (EI) *m*/*z* calcd for $C_{15}H_{17}NO$ 227.1310, found 227.1311.

3.3.2. (*E*)-3-(*N*-Benzylindol-7-yl)-2-methyl-2-propenol (16b). Prepared from Dibal-H (1.2 M in toluene, 3.2 mL, 3.8 mmol) and **15b** (0.286 g, 0.94 mmol) by the general procedure. There was obtained 210 mg (81%) of the desired alcohol as a colourless oil. ^{1}H NMR ($CDCl_3$) δ 7.57 (d, *J*=7.8 Hz, 1H), 7.30–7.25 (m, 1H), 7.25–7.19 (m, 2H), 7.09 (d, *J*=3.6 Hz, 1H), 7.06 (d, *J*=7.5 Hz, 1H), 6.90–6.82 (m, 3H), 6.66 (s, 1H) 6.58 (d, *J*=3.3 Hz, 1H), 5.51 (s, 2H), 4.04 (s, 2H), 1.50 (d, *J*=1.5 Hz, 1H), 1.19 (bs, 1H).

3.3.3. (*Z*/*E*)-3-(*N*-*p*-Toluenesulfonylindol-7-yl)-2-methyl-2-propenol (16c). Prepared from Dibal-H (1.2 M in toluene, 9.3 mL, 11 mmol) and **15c** (1.0 g, 2.7 mmol) by the general procedure. There was obtained 782 mg (85%) of the desired alcohol as a colourless oil. ^{1}H NMR ($CDCl_3$) (*E*) δ 7.79 (d, *J*=3.9 Hz, 1H), 7.50 (d, *J*=8.4 Hz, 1H), 7.46–7.40 (m, 2H), 7.23–7.14 (m, 3H), 7.00 (d, *J*=7.2 Hz, 1H), 6.92 (s, 1H), 6.72 (d, *J*=2.1 Hz, 1H), 4.15 (d, *J*=1.5 Hz, 2H), 2.34 (s, 3H), 1.80 (bs, 1H), 1.46 (d, *J*=1.5 Hz, 3H). MS (EI): 341, 323, 186, 168, 154, 130, 117, 91. HRMS (EI) *m*/*z* calcd for $C_{19}H_{19}NO_3S$ 341.1086, found 341.1081.

3.3.4. (*E*)-3-(*N*-Benzylindol-7-yl)-but-2-en-1-ol (23). Prepared from Dibal-H (1.2 M in toluene, 9.9 mL, 11 mmol) and **22** (885 mg, 2.90 mmol) by the general procedure, with the exception that the reaction mixture was allowed to slowly reach 5°C during 2.5 h, where upon extra Dibal-H (1.2 mL, 1.45 mmol) was added. There was obtained 0.716 g (89%) of the desired product as a colourless oil. ^{1}H NMR ($CDCl_3$) δ 7.76 (dd, *J*=8.0, 1.0 Hz, 1H), 7.45–7.36 (m, 3H), 7.26–7.24 (m, 2H), 7.05 (dd, *J*=7.0, 0.5 Hz, 1H), 7.01 (d, *J*=6.5 Hz, 2H), 6.79 (d, *J*=3.0 Hz, 1H), 5.65–5.58 (m, 3H), 4.35 (d, *J*=7 Hz, 2H), 2.01 (d, *J*=0.5 Hz, 3H), 1.17 (bs, 1H). ^{13}C 140.0, 137.7, 133.3, 131.0, 130.9, 130.0, 130.0, 129.4, 127.9, 126.5, 123.2, 120.6, 120.2, 103.1, 78.0, 77.7, 77.5, 60.2, 52.3, 20.3. MS (EI): 277, 259, 244, 207, 168, 91. HRMS (EI) *m*/*z* calcd for $C_{19}H_{19}NO$ 277.1467, found 277.1468.

3.4. General procedure for the Sharpless asymmetric epoxidation

3.4.1. 2-Methyl-3-(*N*-allylindol-7-yl)-2(*R*),3(*R*)-epoxypropanol (17a). A mixture of diisopropyl D-tartrate (0.011 mL, 0.050 mmol) and 4 Å molecular sieves (40 mg) in dichloromethane (8 mL) was cooled to −30°C before addition of titanium(IV) isopropoxide (0.010 mL, 0.033 mmol) and *tert*-butyl hydroperoxide (3.88 M in toluene, 0.37 mL, 1.45 mmol). The solution was left stirring

at −20°C for 60 min. A solution of **16a** (150 mg, 0.66 mmol) in dichloromethane (2 mL) was then added over a period of 1 min at a temperature of −30°C. Stirring was continued at −20°C for 2.5 h when NaOH (10% in brine, 0.05 mL) and diethyl ether (2 mL) was added and the cooling bath removed, allowing the mixture to warm to 10°C. The mixture was stirred at 10°C for 10 min, whereupon $MgSO_4$ (0.05 g) and Celite (7 mg) were added. The mixture was stirred at 10°C for 15 min and the inorganic precipitate allowed to settle. The reaction mixture was filtered through celite and concentrated in vacuo. Then toluene (2×10 mL) was added and the solutions reconcentrated in vacuo. This afforded 174 mg of the crude product. Column chromatography (ethyl acetate/heptane 1:2→1:1) gave 77 mg (48%) of the desired product as a pale yellow oil which crystallised and darkened on standing.

^{1}H NMR ($CDCl_3$) δ 7.58 (d, J=7.8 Hz, 1H), 7.18 (dd, J=7.5, 0.9 Hz, 1H), 7.10 (t, J=7.5 Hz, 1H), 7.05 (d, J=3.0 Hz, 1H), 6.56 (dd, J=3.0, 0.9 Hz, 1H), 6.10–5.98 (m, 1H), 5.17 (d, J=10.5 Hz, 1H), 4.99–4.83 (m, 2H), 4.78 (d, J=17.1 Hz, 1H), 4.68 (s, 1H), 3.95–3.80 (m, 2H), 1.87–1.83 (m, 1H), 1.09 (s, 3H). ^{13}C NMR ($CDCl_3$) δ 134.9, 134.8, 129.7, 120.8, 120.8, 119.4, 118.9, 116.4, 102.5, 64.7, 64.2, 58.4, 51.0, 14.1. MS (CI): 244, 226, 214, 159, 130. HRMS (EI) m/z calcd for $C_{15}H_{17}NO_2$ 243.1259, found 243.1255, $[\alpha]_D^{28}$=−97.1° (c=2.26, CH_2Cl_2) ee=91.0%.

3.4.2. 2-Methyl-3-(*N*-benzylindol-7-yl)-2(*R*),3(*R*)-epoxypropanol (17b). Prepared from diethyl L-tartrate (11.0 μL, 0.051 mmol), 4 Å molecular sieves (40 mg), Ti(O^{i}Pr)$_4$ (10 μL, 0.034 mmol), *tert*-butyl hydroperoxide (3.88 M in toluene, 0.39 mL, 1.51 mmol), and **16b** (190 mg, 0.685 mmol) by the general procedure. There was obtained 117 mg (58%) of the desired product as a colourless oil. ^{1}H NMR ($CDCl_3$) δ 7.62 (dd, J=8.1, 2.1 Hz, 1H), 7.30–7.22 (m, 3H), 7.13 (d, J=1.8 Hz, 1H), 7.11–7.08 (m, 2H), 6.87–6.83 (m, 2H), 6.62 (d, J=3.3 Hz, 1H), 5.65 (d, J=17.4 Hz, 1H), 5.51 (d, J=17.4 Hz, 1H), 4.44 (s, 1H), 3.66 (dd, J=12.6, 3.6 Hz, 1H), 3, 48 (dd, J=12.6, 8.7 Hz, 1H), 1.66 (dd, J=8.4, 3.6 Hz, 1H), 0.85 (s, 3H).

3.4.3. 2-Methyl-3-(*N*-*p*-toluenesulfonylindol-7-yl)-2,3-epoxypropanol (17c). Prepared from diisopropyl D-tartrate (0.033 mL, 0.15 mmol), 4 Å molecular sieves (120 mg), Ti(O^{i}Pr)$_4$ (0.030 mL, 0.10 mmol), *tert*-butyl hydroperoxide (3.88 M in toluene, 1.16 mL, 4.51 mmol), and **16c** (700 mg, 2.05 mmol) by the general procedure. There was obtained 426 mg (58%) of the desired product as a colourless oil. ^{1}H NMR ($CDCl_3$) δ 7.69 (d, J=3.6 Hz, 1H), 7.53–7.49 (m, 3H), 7.39 (d, J=7.8 Hz, 1H), 7.28 (t, J=8.1 Hz, 1H), 7.21 (d, J=8.1 Hz, 2H), 6.75 (d, J=2.4 Hz, 1H), 4.40 (s, 1H), 3.98 (dd, J=12.0, 9.3 Hz, 1H), 3.81 (dd, J=12.0, 4.2 Hz, 1H), 2.36 (s, 3H), 2.28–2.23 (m, 1H), 1.13 (s, 3H). MS (EI): 339, 184, 168, 142, 141, 91. HRMS (EI) m/z calcd for $C_{19}H_{19}NO_4S$ 357.1035, found 357.1023.

3.4.4. 3-(*N*-Benzylindol-7-yl)-2(*S*),3(*S*)-epoxybutanol (24). Prepared from diethyl L-tartrate (29.0 μL, 0.167 mmol), 4 Å molecular sieves (130 mg), Ti(O^{i}Pr)$_4$ (33 μL, 0.11 mmol), *tert*-butyl hydroperoxide (3.88 M in toluene, 1.26 mL, 4.89 mmol), and **23** (616 mg, 2.22 mmol) by the general procedure. There was obtained 394 mg (60%) of the desired product as a colourless oil. The compound turned out to be highly unstable even if kept under vacuum and away from sunlight. ^{1}H NMR ($CDCl_3$), two rotamers, δ 7.60 (bm, 1H), 7.36–7.18 (m, 4H), 7.12 (t, J=7.5 Hz, 1H), 7.07–6.96 (m, 2H), 6.80 (d, J=6.6 Hz, 1H), 6.63–6.56 (bm, 1H), 5.88 (d, J=16.2 Hz, 0.5H), 5.67 (d, J=16.8 Hz, 0.5H), 5.62 (d, J=16.8 Hz, 0.5H), 5.54 (d, J=16.8 Hz, 0.5H), 4.06–3.63 (m, 2H), 3.55 (bm, 0.5H), 3.05 (bm, 0.5H), 1.72 (bs, 1H), 1.58 (bs, 1.5H), 1.48 (bs, 1.5H). MS (EI): 293, 277, 263, 232, 218, 202, 91. HRMS (EI) m/z calcd for $C_{19}H_{19}NO_2$ 293.1416, found 293.1415.

3.5. General procedure for the TPAP oxidation

3.5.1. 2-Methyl-3-(*N*-allylindol-7-yl)-2(*S*),3(*R*)-epoxypropanal (18a). TPAP (2.2 mg, 0.006 mmol) was added to a stirred mixture of **17a** (30 mg, 0.12 mmol), 4-methylmorpholine *N*-oxide monohydrate (25 mg, 0.18 mmol), and 4 Å molecular sieves (powdered, 60 mg) in dichloromethane (3 mL) at 20°C under N_2. When reaction was complete (TLC) the reaction mixture was filtered through silica and eluted with dichloromethane and ethyl acetate. The filtrate was evaporated to give 28 mg of an orange oil. Column chromatography (ethyl acetate/heptane 1:2) gave 8 mg (28%) of an oil which contained the desired product. This material was carried on to the Wittig reaction without further purification.

^{1}H NMR ($CDCl_3$) δ 9.22 (s, 1H), 7.63 (dd, J=7.8, 1.5 Hz, 1H), 7.19 (d, J=7.5 Hz, 1H), 7.12 (t, J=7.5 Hz, 1H), 7.04 (d, J=3.3 Hz, 1H), 6.57 (d, J=3.0 Hz, 1H), 6.00–5.91 (m, 1H), 5.19 (d, J=10.5 Hz, 1H), 4.81 (dm, J=18 Hz, 1H), 4.76 (s, 1H), 4.73 (dm, J=17 Hz, 1H), 4.66 (dm, J=18 Hz, 1H), 1.23 (s, 3H). HRMS (EI) m/z calcd for $C_{15}H_{15}NO_2$ 241.1103, found 241.1071.

3.5.2. 2-Methyl-3-(*N*-benzylindol-7-yl)-2(*S*),3(*R*)-epoxypropanal (18b). Prepared from TPAP (10 mg, 0.028 mmol), **17b** (45 mg, 0.15 mmol), 4 Å molecular sieves (100 mg), and 4-methylmorpholine *N*-oxide monohydrate (23 mg, 0.17 mmol) by the general procedure. There was obtained 12 mg (27%) of the desired product as a colourless oil. ^{1}H NMR ($CDCl_3$), two rotamers, δ 8.92 (s, 1H), 7.63 (d, J=7.8 Hz, 1H) 7.30–7.04 (m, 6H), 6.87–6.83 (m, 1H), 6.79 (d, J=7.5 Hz, 2H), 6.64 (d, J=3.3 Hz, 1H), 5.51 (d, J=17.4 Hz, 1H), 5.29 (d, J=17.4 Hz, 1H), 4.30 (s, 0.6H), 3.79 (s, 0.4 H), 2.24 (s, 0.4H), 2.03 (s, 0.6H) 1.12 (s, 3H).

3.5.3. 2-Methyl-3-(*N*-*p*-toluenesulfonylindol-7-yl)-2,3-epoxypropanal (18c). Prepared from TPAP (79 mg, 0.22 mmol), **17c** (400 mg, 1.12 mmol), 4 Å molecular sieves (560 mg), and 4-methylmorpholine *N*-oxide monohydrate (166 mg, 1.23 mmol) by the general procedure. There was obtained 231 mg (58%) of the desired product as a colourless oil. ^{1}H NMR ($CDCl_3$) δ 9.20 (s, 1H), 7.70 (d, J=4.0 Hz, 1H), 7.58 (dd, J=7.2, 3.0 Hz, 1H), 7.41–7.13 (m, 5H), 6.78 (d, J=4.0 Hz, 1H), 4.73 (s, 1H), 2.37 (s, 3H), 1.10 (s, 3H). MS (EI): 327, 220, 205, 172, 155, 130. HRMS (EI) m/z calcd for $C_{19}H_{17}NO_4S$ 355.0878, found 355.0881.

3.5.4. 3-(1-Benzylindol-7-yl)-2(*S*),3(*S*)-epoxybutanal (25). Prepared from TPAP (88 mg, 0.25 mmol), **24**

(367 mg, 1.25 mmol), 4 Å molecular sieves (700 mg), and *N*-methyl morpholine oxide monohydrate (186 mg, 1.38 mmol) by the general procedure. There was obtained 150 mg (41%) of the desired product as a yellow oil, which contained the desired product. This material was carried on to the Wittig reaction without further purification.

^{1}H NMR ($CDCl_3$) δ 9.46 (s, 1H), 7.65 (d, J=7.2 Hz, 1H), 7.31–7.19 (m, 4H), 7.10–7.03 (m, 2H), 6.79 (d, J=6.9 Hz, 1H), 6.66–6.60 (m, 1H), 5.60 (d, J=16.8 Hz, 1H), 5.44 (d, J=16.8 Hz, 1H), 3.44 (s, 1H), 1.19 (s, 3H). MS (EI): 291, 275, 200, 172, 91. HRMS (EI) m/z calcd for $C_{19}H_{17}NO_2$ 219.1259, found 219.1259.

3.6. General procedure for the Wittig reaction

3.6.1. (2*R*,3*R*)-2-Methyl-3-(*N*-allylindol-7-yl)-2-vinyl oxirane (11a). KHMDS (8.6 mg, 0.043 mmol) was added to a suspension of methyltriphenylphosphonium bromide (14 mg, 0.040 mmol) in THF (1 mL) at 25°C under N_2. Stirring was continued at 25°C for 30 min, whereupon **18a** (8.0 mg, 0.033 mmol) was added as a solution in THF (1 mL). Stirring was continued at 25°C for 90 min. Dichlorormethane (5 mL) was added and the resulting suspension was filtered through Hyflo Super-Cel. The filtrate was concentrated in vacuo to give 21 mg of a colourless oil. Column chromatography (ethyl acetate/heptane 1:5) gave 6.0 mg (76%) of the desired product as a colourless oil.

^{1}H NMR ($CDCl_3$) δ 7.58 (ddd, J=7.8, 1.5, 0.9 Hz, 1H), 7.21 (dt, J=7.2, 1.2 Hz, 1H), 7.10 (t, J=7.8 Hz, 1H), 7.04 (d, J=3 Hz, 1H), 6.57 (d, J=3.3 Hz, 1H), 5.98 (ddt, J=17.1, 10.5, 4.5 Hz, 1H), 5.89 (dd, J=17.4, 10.5 Hz, 1H), 5.50 (dd, J=17.4, 0.9 Hz, 1H), 5.38 (dd, J=10.8, 0.9 Hz, 1H), 5.16 (td, J=10.5, 0.9 Hz, 1H), 4.83–4.81 (m, 2H), 4.76 (ddt, J=17.1, 2.1, 0.9 Hz, 1H), 4.35 (s, 1H), 1.55 (s, 2H), 1.20 (s, 3H). ^{13}C NMR ($CDCl_3$) δ 140.0, 135.0, 134.0, 129.6, 129.6, 120.9, 120.8, 119.5, 119.1, 117.5, 116.4, 102.5, 63.8, 62.9, 50.7, 14.7. MS (EI): 239, 196, 181, 168, 154. HRMS (EI) m/z calcd for $C_{16}H_{17}NO$ 239.1310, found 239.1306. $[\alpha]_D^{21}=-171°$ (c=0.350, CH_2Cl_2).

3.6.2. (2*R*,3*R*)-2-Methyl-3-(*N*-benzylindol-7-yl)-2-vinyl oxirane (11b). Prepared from KHMDS (11 mg, 0.054 mmol), methyltriphenylphosphonium bromide (18 mg, 0.049 mmol), and **18b** (12 mg, 0.041 mmol) by the general procedure. There was obtained 4.0 mg (34%) of the desired product as a colourless oil. ^{1}H NMR ($CDCl_3$), two rotamers, δ 7.62 (ddd, J=7.2, 1.5, 0.6 Hz, 1H), 7.31–7.21 (m, 3H), 7.18–7.14 (m, 1H), 7.13 (d, J=7.5 Hz, 1H), 7.09 (d, J=3.0 Hz, 1H), 6.83–6.79 (m, 2H), 6.62 (d, J=3.0 Hz, 1H), 5.68 (dd, J=17.4, 10.5 Hz, 1H), 5.46 (d, J=5.4 Hz, 2H), 5.41 (d, J=2.4 Hz, 0.5H), 5.35 (dd, J=1.8, 0.9 Hz, 1H), 5.31 (d, J=1.2 Hz, 0.5H), 4.03 (s, 1H), 1.55 (s, 2H), 1.07 (s, 3H). ^{13}C NMR ($CDCl_3$), two rotamers, δ 139.9, 139.0, 134.1, 130.3, 130.0, 129.0, 127.7, 125.6, 121.1, 121.0, 119.7, 119.5, 117.6, 102.8, 63.7, 62.9, 52.5, 52.1, 14.6.

3.6.3. 2-Methyl-3-(*N*-*p*-toluenesulfonylindol-7-yl)-2-vinyl oxirane (11c). Prepared from KHMDS (156 mg, 0.78 mmol), methyltriphenylphosphonium bromide (258 mg, 0.72 mmol), and **18c** (214 mg, 0.60 mmol) by the general procedure. There was obtained 101 mg (48%) of the desired product as a colourless oil as well as 34 mg (16%) of unconverted starting material. ^{1}H NMR ($CDCl_3$) δ 7.72 (d, J=3.6 Hz, 1H), 7.52 (d, J=7.8 Hz, 1H), 7.45 (d, J=8.1 Hz, 2H), 7.39 (d, J=7.2 Hz, 1H), 7.26 (t, J=7.8 Hz, 1H), 7.19 (d, J=8.4 Hz, 2H), 6.74 (d, J=3.9 Hz), 6.03 (dd, J=17.4, 10.8 Hz, 1H), 5.43 (dd, J=17.1, 0.9 Hz, 1H), 5.32 (dd, J=10.5, 0.9 Hz, 1H), 4.22 (s, 1H), 2.35 (s, 3H), 1.12 (s, 3H). MS (EI): 353, 342, 310, 198, 155, 91. HRMS (EI) m/z calcd for $C_{20}H_{19}NO_3S$ 353.1086, found 353.1089.

3.6.4. 4-(*N*-Benzylindol-7-yl)-(3*R*,4*S*)-epoxypropene (12). Prepared from KHMDS (127 mg, 0.63 mmol), methyltriphenylphosphonium bromide (210 mg, 0.58 mmol), and **25** (143 mg, 0.49 mmol) by the general procedure. There was obtained 72 mg (51%) of the desired product as a colourless oil.

^{1}H NMR ($CDCl_3$), two rotamers, δ 7.64 (d, J=9.0 Hz, 1H), 7.40 (bm, 1H), 7.34–7.25 (m, 3H), 7.17 (bm, 1H), 7.10 (bm, 1H), 7.02 (bm, 1H), 6.84 (bm, 1H), 6.65 (bm, 1H), 5.95 (bm, 1H), 5.84–5.60 (m, 2H), 5.52 (s, 2H), 5.37 (d, J=6.0 Hz, 1H), 5.15 (d, J=9.9 Hz, 1H), 3.84 (bm, 0.3H), 3.45 (bm, 0.7H), 1.60 (s, 3H). ^{13}C NMR ($CDCl_3$), two rotamers, δ 132.3, 129.8, 128.9, 128.8, 127.6, 127.1, 126.2, 121.9, 121.3, 121.2, 121.1, 120.0, 119.8, 119.9, 103.7, 64.9, 51.3, 44.9, 20.4. MS (EI): 289, 232, 218, 198, 156, 154, 91. HRMS (EI) m/z calcd for $C_{20}H_{19}NO$ 289.1467, found 289.1472, $[\alpha]_D^{20}=+67.2°$ (c=1.95, CH_2Cl_2) ee=92.1%.

3.7. General procedure for the vinyl epoxide rearrangement reaction

3.7.1. (*S*)-3-(*N*-Allylindol-7-yl)-4-penten-2-one (19a). Boron trifluoride etherate (3.5 μL, 0.028 mmol) was added to a solution of **11a** (6.0 mg, 0.025 mmol) in dichloromethane at −78°C. After 2.0 min at −78°C the reaction mixture was poured into diethylether and shaken with $NaHCO_3$ (5% solution in water). The layers were separated and the aqueous layer was extracted with diethylether. The combined organic extracts were then dried ($MgSO_4$) and concentred in vacuo. Column chromatography (ethyl acetate/heptane 1:4) gave 6.0 mg (>99%) of the product resulting from vinyl-migration.

^{1}H NMR ($CDCl_3$) δ 7.59 (dd, J=7.5, 1.5 Hz, 1H), 7.10 (t, J=7.5 Hz, 1H), 7.04 (d, J=3.0 Hz, 1H), 6.90 (dd, J=7.5, 1.2 Hz, 1H), 6.57 (d, J=3.3 Hz, 1H), 6.34 (ddd, J=17.1, 10.2, 6.0 Hz, 1H), 1H), 6.11 (ddt, J=17.1, 10.2, 3.9 Hz, 1H), 5.29 (dt, J=10.5, 1.5 Hz, 1H), 5.24 (ddt, J=10.5, 1.8, 0.9 Hz, 1H), 4.97–4.80 (m, 5H), 2.06 (s, 3H). MS (EI): 239, 196, 181, 167, 154. HRMS (EI) m/z calcd for $C_{16}H_{17}NO$ 239.1310, found 239.1382.

3.7.2. (*S*)-3-(*N*-Benzylindol-7-yl)-4-penten-2-one (19b). Prepared from the **11b** and boron trifluoride etherate by the general procedure. ^{1}H NMR ($CDCl_3$) δ 7.62 (dd, J=7.0, 1.0 Hz, 1H), 7.34–7.29 (m, 3H), 7.16 (d, J=3.5 Hz, 1H), 7.10 (t, J=7.5 Hz, 1H), 6.97 (d, J=7.5 Hz, 2H), 6.82 (dd, J=7.5, 1.0 Hz, 1H), 6.64 (d, J=3.5 Hz, 1H), 6.20 (ddd, J=16.5, 10.0, 6.5 Hz, 1H), 5.54 (s, 2H), 5.19 (ddd, J=10.0,

1.0, 1.0 Hz, 1H), 4.76 (d, *J*=6.0 Hz, 1H), 4.68 (ddd, *J*=17.0, 1.0, 1.0 Hz, 1H), 1.64 (s, 3H).

3.7.3. 2-Methyl-2-(*N*-*p*-toluenesulfonylindol-7-yl)-but-3-enal (10c) and 1-(*N*-*p*-toluenesulfonylindol-7-yl)-2-methyl-3-butenone (20c). Prepared from **11c** (90 mg, 0.25 mmol) and boron trifluoride etherate (35 μL, 0.28 mmol) by the general procedure. There was obtained 44 mg (50%) of a colourless oil which was a 2:3 mixture of **10c** and **20c** as well as 10 mg (11%) of unconverted starting material.

^{1}H NMR ($CDCl_3$) **10c** δ 9.74 (s, 1H), 7.58–7.16 (m, 7H), 7.03 (d, *J*=8.4 Hz, 2H), 6.58 (d, *J*=3.9 Hz, 1H), 6.28 (dd, *J*=16.8, 12 Hz, 1H), 5.33 (d, *J*=12 Hz, 1H), 5.02 (d, *J*=16.8 Hz, 1H), 2.28 (s, 3H), 1.88 (s, 3H). **20c** δ 7.58–7.16 (m, 7H), 7.09 (d, *J*=8.4 Hz, 2H), 6.71 (d, *J*=3.9 Hz, 1H), 5.92–5.72 (m, 1H), 5.01–4.86 (m, 2H), 4.07 (dq, *J*=8 Hz, 1H), 2.28 (s, 3H), 1.37 (d, *J*=8 Hz, 3H). MS (EI) (mixture of **10c** and **20c**): 353, 298, 198, 170, 168, 154, 143. HRMS (EI) *m*/*z* calcd for $C_{20}H_{19}NO_3S$ 353.1086, found 353.1089.

3.7.4. (*R*)-2-Methyl-2-(*N*-benzylindol-7-yl)-but-3-enal (10b). Prepared from **12** (25 mg, 0.086 mmol) by the general procedure. There was obtained 22 mg (88%) of the desired product as a colourless oil.

^{1}H NMR ($CDCl_3$) δ 9.64 (s, 1H), 7.79–7.74 (m, 1H), 7.35–7.29 (m, 3H), 7.28–7.25 (m, 2H), 6.96 (dd, *J*=3.0, 2.5 Hz, 1H), 6.84 (d, *J*=8.0 Hz, 2H), 6.70 (dd, *J*=3.0, 2.5 Hz, 1H), 6.56 (ddd, *J*=17.5, 10.5, 2.5 Hz, 1H), 5.46 (d, *J*=16.5 Hz, 1H), 5.28 (d, *J*=16 Hz, 1H), 5.23 (dd, *J*=10.5, 2.0 Hz, 1H), 4.91 (dd, *J*=17.5, 1.5 Hz, 1H), 1.74 (s, 3H). ^{13}C ($CDCl_3$) δ 169.0, 132.1, 131.2, 129.2, 128.0, 127.2, 123.9, 122.4, 120.4, 118.3, 104.4, 58.7, 53.8, 24.4. MS (EI): 289, 260, 168, 154, 130, 91. HRMS (EI) *m*/*z* calcd for $C_{20}H_{19}NO$ 289.1467, found 289.1472, $[\alpha]_D^{20}=+137°$ (*c*=0.500, CH_2Cl_2) ee=70.7%.

Acknowledgements

We thank the Danish Research Agency and Novo Nordisk A/S for financial support, and Professor Tobias Rein for valuable discussions.

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