Catalytic Asymmetric Total Synthesis of the Muscarinic Receptor Antagonist (*R*)-Tolterodine

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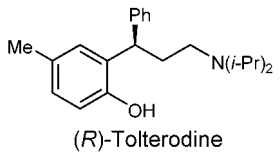
Abstract: A convenient and high yielding method for the preparation of (*R*)-tolterodine, utilizing a catalytic asymmetric Me-CBS reduction was developed. Highly enantioenriched (*R*)-6-methyl-4-phenyl-3,4-dihydrochromen-2-one (94% ee) was recrystallized to yield practically enantiopure material (ee >99%) and converted to (*R*)-tolterodine in a four-step procedure. The configuration of the crucial stereocenter was preserved during the synthesis and the obtained product was identified by chiral HPLC to be the (*R*)-tolterodine enantiomer.

Keywords: asymmetric synthesis; Me-CBS catalyst; sigmatropic rearrangement; tolterodine; total synthesis

Introduction

(*R*)-Tolterodine (Figure 1) is the first muscarinic receptor antagonist that has been specifically developed for treatment of an overactive bladder.[1] Tolterodine is non-selective with respect to the muscarinic M1-M5 receptor subtypes, but has a greater effect on the bladder than on the salivary glands *in vivo*, in both animal and humans.[2] (*R*)-Tolterodine (Detrol®) is equipotent to oxybutynin, but shows less impact on saliva output than the latter, suggesting that tolterodine may give rise to fewer side effects related to decreased saliva production compared to oxybutynin.[3] (*R*)-Tolterodine can today be regarded as the drug of choice to treat overactive bladders in most patient groups.[4]

An earlier reported asymmetric total synthesis of tolterodine was carried out using an oxazolidinone as a chiral auxiliary.[5] This approach led directly to the desired β,β′-diaryl-substituted propionic acid. Attempts to design a catalytic asymmetric synthesis of (*R*)-tolterodine have been reported recently in the literature, utilizing an asymmetric hydroformylation as a key step.[6] However, despite good yields, low enantioselectivity was reported.



(*R*)-Tolterodine

Figure 1.

Results and Discussion

We were interested in developing a catalytic asymmetric route to (*R*)-tolterodine. Retrosynthetic analysis of tolterodine suggests that the corresponding dihydrocoumarin is a suitable key intermediate for a catalytic asymmetric synthesis. The most interesting approach would be an asymmetric hydrogenation of coumarin **12**, directly leading to the desired dihydrochromen-2-one **7**.[7] However, this pathway to tolterodine was abandoned because of difficulties of preparing coumarin **12** from simple starting materials by Pechmann condensation.[8] Some years ago, Clark et al. reported a novel enantioselective synthesis of highly enantioenriched 3-arylindanones *via* three consecutive, base-induced [1,5]-suprafacial sigmatropic rearrangements of the corresponding 3-arylindenol, easily available by catalytic asymmetric methyloxazaborolidine (Me-CBS) reduction of the indenone.[9] By adopting this approach, we would be able to access the dihydrochromen-2-one **7** *via* a Baeyer–Villiger oxidation (Scheme 1).

The synthesis of **7** starts with the condensation of 2′-bromo-4′-methylacetophenone with benzaldehyde to give the suitable brominated chalcone in high yield. Palladium-catalyzed Heck cyclization gives the corresponding indenone in good yield.[10] Enantioselective reduction of the indenone was performed by slow addition (1.5 h) of **4** to a solution of the (*S*)-Me-CBS catalyst (5 mol %) and $BH_3 \cdot THF$ (1.05 equivs.) in THF at −20 °C. Fast quenching of the reaction mixture at complete conversion was crucial to achieve high enantioselectivity. Because the indenone **4** is bright yellow, and the indenol **5** colorless, the progress of the reaction could

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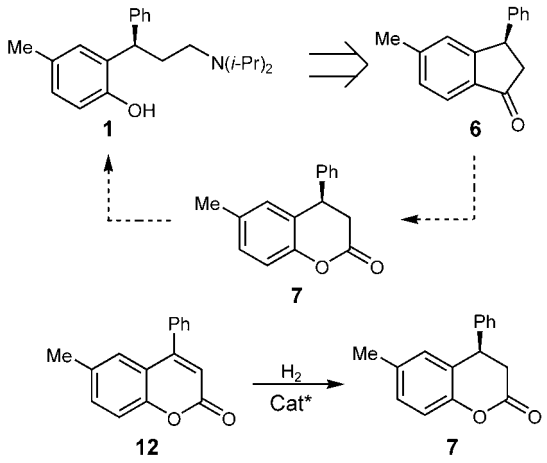
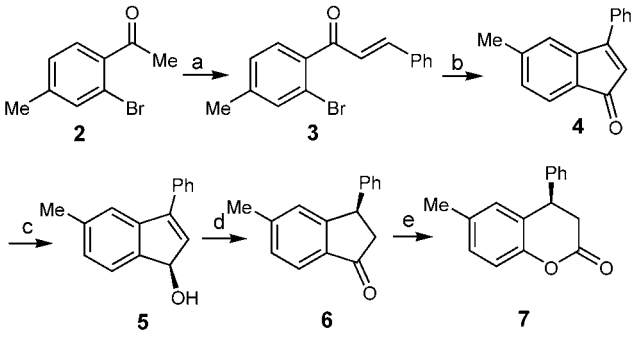


Scheme 1.



(a) PhCHO, MeOH, MeONa, 0 °C to rt, 16 h (95%)

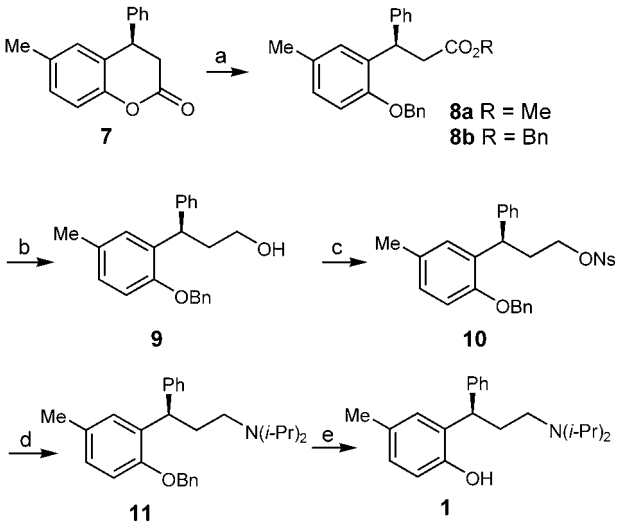
(b) $PdCl_2$ (5 mol %), PPh_3 (15 mol %), K_2CO_3 (2.2 equivs.), DMF, 130 °C, 1 h (73%)

(c) (*S*)-Me-CBS (5 mol %), BH_3·THF, THF, –20 °C, 2 h (91%, 97% ee)

(d) Et_3N, DABCO (20 mol %), THF, 60 °C, 4 h (90%, 94% ee)

(e) *m*-CPBA, TsOH·H_2O, MS 4 Å, CH_2Cl_2, 4 °C (92%, 94% ee, recryst. 99% ee)

Scheme 2.



(a) *i*: MeOH, K_2CO_3, reflux, 1 h; *ii*: BnBr, NaI, Me_2CO, reflux, 16 h

(b) $LiAlH_4$, THF, rt (87% over two steps)

(c) 4-Nitrophenylsulfonyl chloride, Et_3N, DMAP, 0 °C (83%)

(d) $(i\text{-Pr})_2NH$, K_2CO_3, MeCN, reflux, 48 h (81%)

(e) Pd/C (10%) MeOH, 1 atm H_2, rt, 12 h (97%, 99% ee)

Scheme 3.

easily be monitored. Prolonged reaction times, even at low temperature, led to partial racemization of the product. In the next step the resulting indenol (97% ee) was treated with base (Et_3N/DABCO) in THF at reflux for 3 h, which furnished the desired indanone with almost complete retention of chirality (94% ee) in 90% yield. Baeyer–Villiger oxidations of 3-arylindanones have been reported in the literature previously.[11] To our surprise, commercial 60% *m*-CPBA did not transform indanone **6** to the corresponding dihydrochromen-2-one **7**. By changing to pure *m*-CPBA,[12] a catalytic amount of $TsOH \cdot H_2O$ (20 mol %) and 4 Å molecular sieves a quantitative conversion and a high yield were obtained after 38 h at 4 °C. Only a trace amount of the other oxidation regioisomer could be observed by LC-MS. Recrystallization of **7** gave, in principle, enantiopure material in 86% isolated yield (Scheme 2).

To complete the synthesis of (*R*)-tolterodine, dihydrochromen-2-one **7** was treated with MeOH/K_2CO_3 followed by BnBr in acetone to give the corresponding 2′-*O*-benzylated methyl ester **8a**, together with the benzyl ester **8b** as an inseparable mixture. Direct reduction of the mixture gave alcohol **9**, which was converted to the *p*-nitrophenylsulfonyl ester **10**, which in turn was treated with $(i\text{-Pr})_2NH$ to give **11**.[13] Debenzylation by hydrogenolysis of the benzyl ether gave (*R*)-tolterodine **1** in 30% overall yield starting from acetophenone **2**.

Conclusion

In conclusion, we have developed an efficient catalytic asymmetric total synthesis of (*R*)-tolterodine in high overall yield from commercially available starting materials. The desired compound is produced in 10 steps with an overall yield of 30% and ee of 99%.[14]

Experimental Section

(*E*)-1-(2-Bromo-4-methylphenyl)-3-phenylprop-2-en-1-one (3)

To a solution of 2′-bromo-4′-methylacetophenone[15] (7.20 g, 34.0 mmol) and benzaldehyde (3.65 g, 34.0 mmol) in dry

MeOH (50 mL), freshly prepared CH_3ONa (35.7 mmol) in dry MeOH (30 mL) was added at 0 °C. The resulting mixture was stirred at 0 °C for 5 h and warmed to room temperature overnight. HCl (10%, 10 mL) was added slowly and the mixture was evaporated to near dryness under reduced pressure. The residue was suspended in saturated $NaHCO_3$ (50 mL) and extracted with Et_2O (3 × 150 mL). The organic layer was washed with brine and dried over $MgSO_4$. Purification was done by flash chromatography eluting with Et_2O:pentane (5:95) gave **3** as a yellow oil; yield: 10.1 g (95%). R_f = 0.66 (Et_2O:pentane, 20:80); IR (neat): ν = 2359, 2341, 1649, 1603, 1268, 766 cm^{-1}; ^1H NMR: δ = 2.25 (s, 3H), 6.96 (d, J = 10.2 Hz, 1H), 7.15 (d, J = 10.2 Hz, 1H), 7.05 (dd, J_1 = 7.6 Hz, J_2 = 2.6 Hz, 1H), 7.24 (m, 3H), 7.34 (m, 2H), 7.40 (m, 3H); ^{13}C NMR: δ = 21.4, 112.5, 117.3, 122.5, 122.8, 123.7, 124.9, 128.4, 132.2, 133.6, 133.9, 143.6, 145.3, 186.6; MS (EI 70 eV): *m/z* (rel. intensity) = 301(100) [M^+], 221 (50), 193 (62), 178 (84), 77 (44); anal. calcd. for $C_{16}H_{19}BrO$: C 63.81, H 4.35; found: C 63.85, H 4.20.

5-Methyl-3-phenyl-1*H*-inden-1-one (4)

To a suspension of anhydrous K_2CO_3 (9.76 g, 70.6 mmol) in dry DMF (100 mL), **3** (8.40 g, 28.3 mmol) was added and the mixture was de-aerated by five freeze-thaw pump cycles. PPh_3 (0.73 g, 2.83 mmol) was added followed by $PdCl_2$ (0.20 g, 1.13 mmol). The mixture was heated at 120 °C until an NMR sample indicated the disappearance of the starting material (5 h). The mixture was reduced to half its volume under reduced pressure and poured on ice/water (200 mL). Extractive work-up with CH_2Cl_2 (3 × 100 mL) was followed by flash chromatography eluting with Et_2O:pentane (5:95) to afford **4** as a yellow oil that solidifies upon standing; yield: 4.2 g (72%). R_f = 0.62 (Et_2O:pentane, 20:80); IR (neat): ν = 1704, 1606, 1355, 1101, 815, 743 cm^{-1}; ^1H NMR: δ = 2.40 (s, 3H), 5.99 (s, 1H), 7.11 (d, J = 7.2 Hz, 1H), 7.18 (s, 1H), 7.43 (d, J = 7.6 Hz, 1H), 7.53 (m, 3H), 7.66 (m, 2H); ^{13}C NMR: δ = 22.1, 122.7, 122.9, 123.5, 127.4, 128.6, 128.9, 129.2, 129.9, 130.3, 133.2, 143.7, 144.4, 162.4; MS (direct inlet EI 70 eV): *m/z* (rel. intensity) = 220 (100) [M^+], 205 (75), 191 (51), 177 (10), 165 (15); anal. calcd. for $C_{16}H_{12}O$: C 87.25, H 5.49; found: C 87.30, H 5.30.

(*R*)-5-Methyl-3-phenyl-1*H*-inden-1-ol (5)

Commercial (S)-Me CBS catalyst (0.22 mL, 1 M in toluene, 0.22 mmol) was mixed under argon in dry THF (5 mL). After cooling to −20 °C, 2 M BH_3·THF (5.0 mmol, 2.5 mL) in THF was added and the mixture stirred for 10 min. Indenone **4** (1.00 g, 4.54 mmol) was added as a solution in THF (2 mL) over 2 h *via* a syringe pump. The reaction was followed by TLC. Then, MeOH (17 mmol, 0.6 mL) was added at 0 °C and the mixture was evaporated to dryness. Flash chromatography eluting with EtOAc:pentane (10:90) gave **5** as a white solid; yield: 0.96 g (95%). An analytical sample, recrystallized from hexanes/TBME (5:1) had mp. 76–78 °C. R_f = 0.35 (EtOAc:pentane, 20:80); ChiralCel OD-H, 0.5 mL min^{-1}, hexane/*i*-PrOH, 95/5: (*R*)-isomer 24.53 min, (*S*)-isomer 27.22 min, 97% ee; IR (neat): ν = 3300, 1605, 1446, 949, 813 cm^{-1}; ^1H NMR: δ = 1.40 (s, 1H), 2.40 (s, 3H), 5.27 (d, J = 8 Hz, 1H), 6.43 (d J = 2 Hz, 1H), 7.18 (d, J = 8 Hz, 1H), 7.27 (s, 1H), 7.47 (m, 4H), 7.59 (m, 2H); ^{13}C NMR: δ = 21.6, 76.2, 121.6, 123.6, 126.9, 127.6, 128.2, 128.6, 134.1, 134.9, 138.2, 142.1, 143.7, 145.6; MS (EI 70 eV): *m/z* (rel. intensity) = 222 (100) [M^+], 207 (71), 178 (66), 144 (42), 116 (23); anal. calcd. for $C_{16}H_{14}O$: C 86.45, H 6.35; found: C 86.36, H 6.29.

(*R*)-5-Methyl-3-phenyl-2,3-dihydroinden-1-one (6)

Indenol **5** (0.75 g, 3.41 mmol) and DABCO (0.19 g, 1.71 mmol) were dissolved in dry THF:Et_3N (20:1 by volume, 15 mL) and refluxed until TLC indicated complete disappearance of **5** (3 h). The reaction mixture was evaporated to dryness. Flash chromatography (EtOAc:pentane, 5:95) gave **6**; yield: 0.690 g (92%); mp 92–94 °C. R_f = 0.62 (EtOAc:pentane, 20:80); ChiralCel OD-H, 0.5 mL min^{-1}, hexane/*i*-PrOH, 95/5: (*R*)-isomer 19.12 min, (*S*)-isomer 22.33 min, 94% ee; IR (neat): ν = 3027, 2361, 1710, 1605, 1280, 1238, 1040 cm^{-1}; ^1H NMR: δ = 2.39 (s, 3H), 2.69 (dd, J_1 = 3.0 Hz, J_2 = 19.2 Hz, 1H), 3.23 (dd, J_1 = 8.0 Hz, J_2 = 19.2 Hz, 1H), 4.53 (q, J = 4 Hz, 1H), 7.07 (s, 1H), 7.14 (d, J = 8.4 Hz, 1H), 7.15 (s, 1H), 7.26 (m, 2H), 7.33 (m, 2H), 7.72 (d, J = 7.6 Hz, 1H); ^{13}C NMR: δ = 22.1, 44.3, 46.9, 123.2, 126.9, 127.0, 127.6, 128.9, 134.5, 143.8, 146.3, 158.4, 205.5; MS (EI 70 eV): *m/z* (rel intensity) = 222 (100) [M^+], 207 (55), 194 (19), 178 (60), 144 (10); calcd. for $C_{16}H_{14}O$: C 86.45, H 6.35; found: C 86.22, H 6.18.

(*R*)-6-Methyl-4-phenyl-3,4-dihydrochromen-2-one (7)

Indanone **6** (0.400 g, 1.8 mmol) and 98% *m*CPBA (0.485 g, 2.8 mmol) were suspended in dry CH_2Cl_2 (6 mL) at 0 °C followed by addition of $TsOH \cdot H_2O$ (0.034 g, 0.18 mmol). The reaction mixture was kept at 4 °C for 48 h, then diluted with CH_2Cl_2 (10 mL), filtered and washed with saturated Na_2SO_3 (2 × 10 mL), saturated $NaHCO_3$ and brine. Flash chromatography eluting with EtOAc:pentane (10:90) gave **7**; yield: 0.390 g (92%). R_f = 0.83 (EtOAc:pentane, 20:80); ChiralCel OD-H, 0.5 mL min^{-1} hexane/*i*-PrOH, 95/5: minor (*S*)-isomer 15.18 min, major (*R*)-isomer 17.42 min, 94% ee. Recrystallization from TBME/hexane gave **7** in 89% recovery and 99% ee; mp 84–86 °C, $[\alpha]_D^{25}$: +36° (*c* 1.0, CH_2Cl_2); IR (neat): ν = 2900, 2360, 1769, 1495, 1208, 1145 cm^{-1}; ^1H NMR: δ = 2.28 (s, 3H), 3.05 (m, 1H), 4.32 (t, J = 6.8 Hz, 1H), 6.98 (s, 1H), 7.04 (d, J = 8.4 Hz, 1H), 7.11 (dd, J_1 = 2.0 Hz, J_2 = 8.4 Hz, 1H), 7.18 (d, J = 8.4 Hz, 1H), 7.19 (s, 1H), 7.33 (m, 3H); ^{13}C NMR: δ = 20.7, 37.1, 40.7, 116.8, 125.3, 127.5, 127.6, 128.6, 129.1, 129.3, 134.3, 140.5, 149.6, 167.8; MS (EI 70 eV): *m/z* (rel. intensity) = 238 (55) [M^+], 220 (57), 195 (100), 181(10), 165 (12), 152 (9); anal. calcd. for $C_{16}H_{14}O_2$: C 80.65, H 5.92; found: C 80.60, H 5.81.

(*R*)-3-[2-(Benzyloxy)-5-methylphenyl]-3-phenylpropan-1-ol (9)

Compound **7** (0.35 g, 1.46 mmol) was dissolved in dry MeOH (10 mL) and anhydrous K_2CO_3 (1.01 g, 7.4 mmol) added. The mixture was refluxed until a TLC sample showed disappearance of **7**. The reaction mixture was evaporated to near dryness and the residue suspended in dry acetone (10 mL), benzyl bromide (0.75 g, 4.38 mmol) was added, followed by NaI (0.233 g,

1.46 mmol). The mixture was heated at 40 °C for 36 h and evaporated to dryness under reduced pressure. The residue was then portioned between CH_2Cl_2 (20 mL) and H_2O (20 mL). The organic layer was separated and the aqueous phase was extracted CH_2Cl_2 (2 × 20 mL). The combined organic extracts were washed with brine and dried ($MgSO_4$) and evaporated under reduced pressure to give a 3:1 mixture of *(*R*)-methyl 3-(2-(benzyloxy)-5-methylphenyl)-3-phenylpropanoate* (**8a**) and *(*R*)-benzyl 3-(2-(benzyloxy)-5-methylphenyl)-3-phenylpropanoate* (**8b**) as a colourless oil.

The crude ester mixture was dissolved in dry THF (10 mL) and added dropwise to a slurry of $LiAlH_4$ (0.074 g, 2.0 mmol) in dry THF (10 mL) at 0 °C. After stirring for 4 h at 0 °C, quenching, filtration and evaporation followed by flash chromatography (EtOAc:pentane, 20:80) afforded **9** as a colorless oil; yield: 0.422 (87% over two steps). $[\alpha]_D^{25}$: +44° (*c* 2.0, CH_2Cl_2); IR (neat): ν = 3368, 3061, 3028, 2937, 1499, 1453, 1239, 1025 cm^{-1}; ^1H NMR: δ = 2.26 (s, 3H), 2.20–2.36 (m 2H), 3.58 (m, 2H), 4.64 (t, *J* = 9 Hz, 1H), 5.04 (q, *J* = 11.7 Hz, 2H), 6.83 (d, *J* = 8.2 Hz, 1H), 6.96 (dd, J_1 = 8.2 Hz, J_2 = 2.2 Hz 1H), 7.00 (d, *J* = 2.2 Hz, 1H), 7.16–7.40 (m, 10H); ^{13}C NMR: δ = 20.67, 37.58, 39.26, 60.98, 64.99, 70.47, 112.11, 125.79, 126.81, 127.37, 127.45, 127.76, 128.08, 128.10, 128.36, 128.39,128.71, 130.18, 132.86, 136.99, 140.86, 144.46, 153.82; MS (EI 70 eV): *m/z* (rel. intensity) = 331(100) [M^+], 299 (12), 285 (21), 223 (11), 165 (28); anal. calcd. for $C_{23}H_{24}O_2$: C 83.10, H 7.28; found: C 83.22, H 7.26.

(*R*)-3-[2-(Benzyloxy)-5-methylphenyl]-3-phenylpropyl 4-Nitrobenzenesulfonate (10)

To a solution of **9** (0.380 g, 1.1 mmol) in dry CH_2Cl_2 (5 mL), Et_3N (0.35 g, 3.3 mmol) and DMAP (0.013 g, 0.11 mmol) were added. The resulting mixture was cooled to 0 °C and *p*-nitrophenylsulfonyl chloride (0.266 g, 1.2 mmol) was added portionwise under vigorous stirring. The reaction was stirred 30 min at 0 °C then left at room temperature until TLC indicated complete conversion (6 h). The reaction mixture was diluted with CH_2Cl_2 (10 mL) and washed with brine, dried ($MgSO_4$) and evaporated. Flash chromatography (pentane:EtOAc, 80:20) afforded **10** as a light yellow oil; yield: 0.490 g (83%). $[\alpha]_D^{25}$: +44.2° (*c* 2.05, CH_2Cl_2); IR (neat): ν = 3400, 2924, 1532, 1350, 1185, 920, 736 cm^{-1}; ^1H NMR: δ = 2.41 (s, 3H), 2.47 (m, 2H), 4.16 (m, 2H) 4.52 (t, *J* = 8 Hz, 1H), 4.99 (app. q, *J* = 11.7 Hz, 2H), 6.82 (d, *J* = 9 Hz, 1H), 6.98 (s, 1H), 7.01 (s, 1H), 7.13–7.45 (m, 10H), 7.93 (m, 2H), 8.21 (m, 2H); ^{13}C NMR: δ = 20.52, 29.54, 33.31, 39.33, 70.00, 70.10, 111.92, 124.04, 126.11, 127.24, 127.71, 127.80, 128.04, 128.11, 128.15, 128.33, 128.81, 128.85, 129.85, 131.13, 136.90, 141.34, 142.65, 150.26, 153.65; MS (EI 70 eV): *m/z* (rel. intensity) = 517 (5) [M^+], 404 (11), 314 (25), 224 (100), 91 (28); anal. calcd. for $C_{29}H_{27}NO_6S$: C 67.29, H 5.26, N 2.71; found: C 67.35, H 5.31, N 2.79.

(*R*)-3-[2-(Benzyloxy)-5-methylphenyl]-*N*,*N*-diisopropyl-3-phenylpropan-1-amine (11)

To a solution of **10** (0.41 g, 0.79 mmol) in dry MeCN (5 mL), anhydrous K_2CO_3 (0.53 g, 3.9 mmol) was added followed by $(i\text{-Pr})_2NH$ (0.240 g, 2.4 mmol). The resulting mixture was stirred at 60 °C under argon until the TLC indicated complete consumption of 7 (*ca.* 48 h). The reaction mixture was evaporated to dryness and the residue portioned between CH_2Cl_2 (20 mL) and 2 N NaOH (10 mL). The organic phase was washed with brine and dried over anhydrous K_2CO_3. Flash chromatography afforded **11** as a colorless oil; yield: 0.265 g (81%). $[\alpha]_D^{25}$: +52° (*c* 1.04, CH_2Cl_2); IR (neat): ν = 3028, 2964, 2928, 2868, 1499, 1238, 1026 cm^{-1}; ^1H NMR: δ = 0.97 (d, *J* = 6.6 Hz 12H), 2.22 (m, 2H), 2.32 (s, 3H), 2.41 (m, 2H), 3.02 (sept, *J* = 6.6 Hz, 2H), 4.46 (t, *J* = 7.7 Hz, 1H), 5.01 (m, 2H), 6.79 (d, *J* = 8.2 Hz, 1H), 6.96 (dd, J_1 = 1.7 Hz, J_2 = 8.2 Hz, 1H), 7.17–7.40 (m, 11H); ^{13}C NMR: δ = 20.47, 20.54, 20.73, 36.83, 41.54, 44.12, 48.88, 70.12, 111.79, 125.58, 127.14, 127.29, 127.57, 127.95, 128.26, 128.30, 128.34,128.45, 129.77, 133.55, 137.46, 145.04, 153.91; MS (EI 70 eV): *m/z* (rel. intensity) = 416 (18) [M^+], 223 (19), 167 (41), 91 (100); anal. calcd. for $C_{29}H_{37}NO$: C 83.81, H 8.97, N 3.85; found: C 83.92, H 9.07, N 3.80.

(*R*)-2-[3-(Diisopropylamino)-1-phenylpropyl]-4-methylphenol, (*R*)-Tolterodine (1)

A solution of **11** (0.215 g, 0.52 mmol) in dry methanol (2 mL) was added to a slurry of Pd/C (10%; 0.050 g) in dry methanol (5 mL). The resulting mixture was debenzylated overnight at room temperature and 1 atm of H_2. Filtration and evaporation gave **1**; yield: 0.164 g (97%). The absolute configuration was determined by HPLC on a chiral column by comparing retention times with a sample of enantiopure (*R*)-tolterodine reference standard. By the same method the ee was determined to be 99%; ChiralCel OD-H, 0.5 mL min^{-1}, hexane/*i*-PrOH, 95/5: minor (*S*)-isomer 21.33 min, major (*R*)-isomer 24.12 min. $[\alpha]_D^{25}$: +72° (*c* 1.0, CH_2Cl_2); ^1H NMR: δ = 7.35–7.15 (m, 5 H), 6.84 (dd, *J* = 8, 2 Hz, 1H), 6.79 (d, *J* = 8 Hz, 1H), 6.54 (d, *J* = 2 Hz, 1H), 4.47 (dd, *J* = 10, 3.5 Hz, 1H), 3.21 (m, 2H), 2.70 (m, 1H), 2.35 (m, 2H), 2.10 (s and m, 4 H), 1.10 (m, 12 H, 4 × Me); ^{13}C NMR: δ = 153.18, 144.77, 132.40, 129.35, 128.62, 128.49, 128.25, 127.70, 126.09, 118.12, 47.88, 42.13, 39.37, 33.38, 20.72, 19.94, 19.59.

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