A New Rapid and Specific Iodination Reagent for Phenolic Compounds

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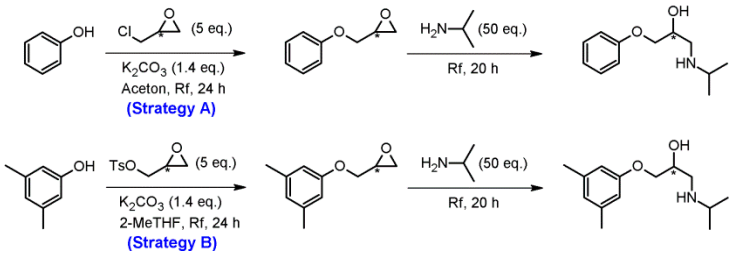
- Supplementary Materials -

Synthetic strategies of the ß-sympatholytic agents. *Synthesis of (2R,2S)-1-(isopropylamino)-3-phenoxypropan-2-ol (Strategy A).*[S1-] 15 mmol (1 eq.) of phenol were dissolved in ~ 80 ml acetone at RT [S19] under inert gas conditions under constant stirring. The resulting homogeneous solution was mixed with 2.9 g (21 mmol, 1.4 eq.) of anhydrous K_2CO_3. After stirring for 20 min at RT, 5.9 ml (75 mmol, 5 eq.) (R,S)-epichlorhydrin was added and the obtained reaction mixture was refluxed for 24 h. The solvent was removed on a rotary evaporator under reduced pressure, and the resulting residue was dissolved in a mixture of a 5% sodium hydroxide solution and diethylether (DEE) (1:1) under constant stirring. The organic layer was separated and the aqueous basic solution was extracted twice with ~ 80 ml DEE. Then the combined organic layer was extracted with ~ 80 ml of a 10% sodium hydroxide solution, washed neutral with cold H_2O_{dd}, pre-dried twice with 80 ml of a saturated sodium chloride solution, dried over anhydrous $MgSO_4$, filtered. The resulting filtrate was concentrated to dryness on a rotary evaporator. Subsequently, 1 eq. of the isolated epoxide (2.03 g, 13.5 mmol, 90%) was refluxed with 50 eq. of isopropylamine for 16 h. After removing the excess of isopropylamine under slightly reduced pressure, purification of the crude product using preparative TLC, dissolving of the product spot in THF, filtration and removal of the solvent again, the resulting product was dissolved once more in anhydrous acetonitrile to remove the precipitated silica gel by filtration using 0.2 µm PTFE syringe filter. The resulting filtrate was stored at - 20°C over night. The resulting recrystallized product was isolated using Buchner funnel and freeze-drying for 24 h to yield (2R,2S)-1-(isopropylamino)-3-phenoxypropan-2-ol (2.64 g, 12.6 mmol, 93%) as colorless crystalline solid.



Scheme S1. Synthetic strategies of the two ß-sympatholytic agents, (2R,2S)-1-(isopropylamino)-3-phenoxypropan-2-ol (see strategy A) and (2R,2S)-1-(3,5-dimethylphenoxy)-3-(isopropylamino)propan-2-ol (see strategy B).

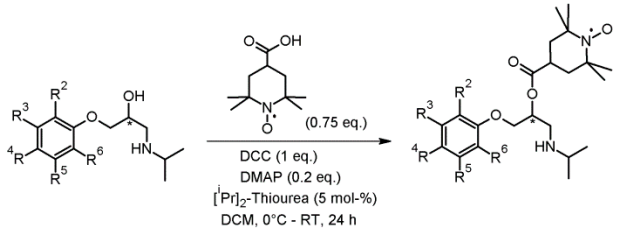
Synthesis of (2R,2S)-1-(3,5-dimethylphenoxy)-3-(isopropylamino)propan-2-ol (Strategy B).[S20-S24] The synthesis/purification of (2R,2S)-1-(3,5-dimethylphenoxy)-3-(isopropylamino)propan-2-ol was carried out in the same manner as indicated in strategy

A, synthesis of (2R,2S)-1-(isopropylamino)-3-phenoxypropan-2-ol. The starting point for all calculations based on 15 mmol (1 eq.) of 3,5-dimethylphenol. Instead of (R,S)-epichlorhydrin, (R,S)-glycidyl tosylate was used. The yield of the isolated epoxide (2.48 g, 13.9 mmol) was 93%. After recrystallization of the purified product using preparative TLC once from acetonitrile and freeze-drying for 24 h, (2R,2S)-1-(3,5-dimethylphenoxy)-3-(isopropylamino)propan-2-ol (3.04 g, 12.8 mmol, 92%) presented itself as colorless crystalline solid.

Characterizations of the ß-sympatholytic agents. *(2R,2S)-1-(isopropylamino)-3-phenoxypropan-2-ol*: TLC: R_f (Diethyl ether/Acetone (6:1)) = 0.22, R_f (n-Hexane/Ethyl acetate (1:1)) = 0.14; Recryst.: Acetonitrile; Colorless crystalline solid; Mp. 88.0°C; EA calcd. (%) for $C_{12}H_{19}NO_2$: C 68.87, H 9.15, N 6.69; found: C 68.88, H 9.14, N 6.69; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30-7.24 (m, 2H, 2ArH, *2H**7***), 6.97-6.91 (m, 2H, 2ArH, *2H**6***), 6.91-6.88 (m, 1H, ArH, *H**8***), 4.10-4.02 (m, 1H, CH, *H**4***), 4.02-3.92 (m, 2H, CH_2, *2H**5***), 3.08 (s, 1H, OH, *H**10***), 2.92-2.77 (m, 2H, CH ovlp. with C$\underline{H}_2$, *H**2*** ovlp. with *H**3***), 2.72 (dd, $^2J_{H3H3}$ = 12.0 Hz, $^3J_{H3H4}$ = 8.1 Hz, 1H, C$\underline{H}_2$, *H**3***), 1.10 (d, $^3J_{H1H2}$ = 6.3 Hz, 6H, $2CH_3$, *6H**1***); ^{13}C (APT) NMR (101 MHz, $CDCl_3$) δ 158.78 (*C**9***), 129.55 (*2C**7***), 121.07 (*C**8***), 114.64 (*2C**6***), 70.63 (*C**5***), 68.47 (*C**4***), 49.51 (*C**3***), 49.08 (*C**2***), 23.00 (*C**1***), 22.96 (*C**1***); IR (KBr) $\tilde{\nu}_{max}$ 3422 (-OH, m), 3315 (-N-H, m), 3060, 3047, 3027 (=C-H, m-w), 2970 (-C-H, s), 2957 (-CH_3, m), 2926 (-CH_2, m), 2869 (-CH_3, m), 2837 (-C-H, m), 2758, 2738, 2707, 2625, 2547, 1978, 1952, 1927, 1881, 1856, 1795, 1726, 1599, 1585 (ring vibrations and N-H-def., s), 1492 (ring vibration, s), 1469, 1448 (CH_3- and CH_2-def., s-m), 1382 (CH_3-def., m), 1355, 1341, 1334, 1321, 1297, 1271, 1242, 1173, 1147, 1110, 1085, 1035 (-C-O-C, OH-def. and -C-O, s-m), 1019, 991, 977, 965, 950, 927, 895, 855, 814, 762, 697 (=C-H-def. and -C-C, s-w), 622, 550, 531, 514, 490, 469, 445, 416 (-C-C, m-w); MS (FD, 8 kV) *m/z* (%) 208.3 (62.4) [M^+-H^+] with ^{14}N, 209.3 (100) [M^+] with ^{14}N, 210.4 (15.7) [M^+] with ^{15}N, 417.7 (25.5) [$2M^+$-H^+] with ^{14}N, 418.6 (38.2) [$2M^+$] with ^{14}N, 420.8 (3.4) [$2M^+$] with ^{15}N (calcd. for $C_{12}H_{19}NO_2$: *m/z* 209.3 [M^+]).

(2R,2S)-1-(3,5-dimethylphenoxy)-3-(isopropylamino)propan-2-ol: TLC: R_f (Dichloromethane) = 0.19, R_f (Diethyl ether) = 0.17; Recryst.: Acetonitrile; Colorless crystalline solid; Mp. 108.6°C; EA calcd. (%) for $C_{14}H_{23}NO_2$: C 70.85, H 9.77, N 5.90; found: C 70.84, H 9.78, N 5.90; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.61 (s, 1H, 1ArH, *2H**8***), 6.55 (d, $^3J_{H6H8}$ = 1.4 Hz, 2H, 2ArH, *2H**6***), 4.05-3.99 (m, 1H, CH, *H**4***), 3.98-3.90 (m, 2H, CH_2, *2H**5***), 2.89-2.78 (m, 2H, CH ovlp. with C$\underline{H}_2$, *H**2*** ovlp. with *H**3***), 2.71 (dd ovlp. with s, $^2J_{H3H3}$ = 12.0 Hz, $^3J_{H3H4}$ = 8.0 Hz, 2H, C$\underline{H}_2$ ovlp. with OH, *H**3*** ovlp. with *H**11***), 2.28 (s, 6H, $2CH_3$, *6H**10***), 1.09 (dd, $^3J_{H1H2}$ = 6.3 Hz, $^4J_{H1H1}$ = 1.0 Hz, 6H, $2CH_3$, *6H**1***); ^{13}C (APT) NMR (126 MHz, $CDCl_3$) δ 158.85 (*C**9***), 139.26 (*2C**7***), 122.82 (*C**8***), 112.43 (*2C**6***), 70.63 (*C**5***), 68.60 (*C**4***), 49.62 (*C**3***), 49.01 (*C**2***), 23.11 (*C**1***), 23.09 (*C**1***), 21.49 (*2C**10***); IR (KBr) $\tilde{\nu}_{max}$ 3420 (-OH, m), 3302 (-N-H, s), 3059, 3035, 3012 (=C-H, m-w), 2973 (-C-H, s), 2964 (-CH_3, s), 2918 (-C-H, m), 2875 (-CH_3, m), 2850 (-CH_2, w), 2773, 2727, 2694, 2629, 1732, 1710, 1671 (-C=C, m), 1611, 1596 (ring vibrations and N-H-def., s), 1513 (N-H-def., w), 1471, 1447, 1402 (CH_3- and CH_2-def., s-m), 1382 (CH_3-def., m), 1359, 1348, 1340, 1323, 1295, 1263, 1226, 1174, 1154, 1115, 1098, 1087, 1075, 1054 (-C-O-C, OH-def. and -C-O, s-m), 1001, 983, 956, 935, 896, 868 (=C-H-def. and -C-C, m-m), 845, 826, 687, 658, 581, 562, 554, 532, 507, 496, 463 (=C-H-def. and -C-C, s-w); MS (FD, 8 kV) *m/z* (%) 236.4 (64.0) [M^+-H^+] with ^{14}N, 237.3 (100) [M^+] with ^{14}N, 238.4 (15.3) [M^+] with ^{15}N, 473.7 (26.1) [$2M^+$-H^+] with ^{14}N, 474.6 (33.7) [$2M^+$] with ^{14}N, 476.8 (4.9) [$2M^+$] with ^{15}N (calcd. for $C_{14}H_{23}NO_2$: *m/z* 237.3 [M^+]).

Synthetic strategies of the TEMPO spin-labeled ß-sympatholytic agents. *Syntheses of (2R,2S)-1-(isopropylamino)-3-phenoxypropan-2-yl 2,2,6,6-tetramethylpiperidine-1-oxyl-4-carboxylate, and (2R,2S)-1-(3,5-dimethylphenoxy)-3-(isopropylamino)propan-2-yl 2,2,6,6-tetramethylpiperidine-1-oxyl-4-carboxylate.* The syntheses of both TEMPO spin-labelled ß-sympatholytic agents were carried out in the same manner as described below and summarized in Scheme 2.



Scheme S2. Synthetic strategies of the two TEMPO spin-labeled ß-sympatholytic agents, (2R,2S)-1-(isopropylamino)-3-phenoxypropan-2-yl 2,2,6,6-tetramethylpiperidine-1-oxyl-4-carboxylate (R^{2-6} = H) and (2R,2S)-1-(3,5-dimethylphenoxy)-3-(isopropylamino)propan-2-yl 2,2,6,6-tetramethylpiperidine-1-oxyl-4-carboxylate ($R^{2,4,6}$ = H, $R^{3,5}$ = CH_3).

0.20 mmol (1 eq.) of the respective ß-sympatholytic agent, (2R,2S)-1-(isopropylamino)-3-phenoxypropan-2-ol or (2R,2S)-1-(3,5-dimethyl-phenoxy)-3-(isopropylamino)propan-2-ol, 30.0 mg (0.15 mmol, 0.75 eq.) 4-carboxy-TEMPO and 4.9 mg (0.04 mmol, 0.2 eq.) DMAP were dissolved in 15 ml of dry DCM at RT under inert gas conditions and under continuous stirring. The resulting orange solution was cooled down to 0°C and 1.6 mg (5 mol-%, 0.01 mmol) of N,N'-diisopropylthiourea ($[^iPr]_2$-thiourea) was added. After stirring the reaction mixture for 5 minutes at 0°C, a solution of DCC (41.3 mg, 0.20 mmol, 1 eq.) in ~ 1 ml of dry DCM was slowly added dropwise. Subsequently, the mixture was stirred for 2 h at 0°C and further 24 h at RT. After appropriate reaction monitoring (TLC), the precipitated DCU was removed from the reaction solution by filtration and the obtained filtrate was concentrated on a rotary evaporator to approximately 4 ml. After the purification of each crude product by column chromatography, recrystallization of each isolated product once from n-hexane and freeze-drying for 24 h was done to yield (2R,2S)-1-(isopropylamino)-3-phenoxypropan-2-yl 2,2,6,6-tetramethylpiperidine-1-oxyl-4-carboxylate (71.3 mg, 0.182 mmol, 91%) as a dark orange shiny, and (2R,2S)-1-(3,5-dimethylphenoxy)-3-(isopropylamino)propan-2-yl 2,2,6,6-tetramethylpiperidine-1-oxyl-4-carboxylate (75.5 mg, 0.180 mmol, 90%) as a red, crystalline solid.

Characterizations of the spin-labeled ß-sympatholytic agents. *(2R,2S)-1-(isopropylamino)-3-phenoxypropan-2-yl 2,2,6,6-tetramethylpiperidine-1-oxyl-4-carboxylate*: TLC: R_f (n-Hexane/Ethyl acetate (6:1)) = 0.31, R_f (Dichloromethane) = 0.42; Recryst.: n-Hexane; Dark orange shiny crystalline solid; Mp. 100.7°C; EA calcd. (%) for $C_{22}H_{35}N_2O_4$: C 67.49, H 9.01, N 7.15; found: C 67.49, H 8.99, N 7.16; IR (KBr) $\tilde{\nu}_{max}$ 3315 (-N-H, m), 3124, 3092, 3059, 3049, 3028 (=C-H, m-w), 2992, 2972 (-C-H, s-m), 2957 (-CH_3, s), 2937 (-C-H, w), 2928 (-CH_2, m), 2870 (-CH_3, m), 2838 (-C-H, m), 2755, 2738, 2705, 2670, 2625, 2541, 2067, 2025, 1979, 1953, 1927, 1881, 1856, 1733 (-C=O, s), 1692, 1682, 1642, 1631 (-C=C and N-H-def., w), 1599, 1585 (ring vibrations and N-H-def., s-m), 1556, 1537 (-N-O and N-H-def., w), 1493 (ring vibration, s), 1468, 1449, 1433 (CH_3- and CH_2-def., s-m), 1381 (CH_3-def., m), 1367, 1341, 1332, 1314 (-N-O, s-m), 1297, 1271, 1244, 1223, 1198, 1164, 1109, 1085, 1035 (-C-O-C, s-m), 1016, 990, 966, 948, 924, 894, 843, 814, 761, 724, 697 (=C-H-def. and -C-C, s-w), 664, 649, 621, 561, 549, 531, 490, 468, 445 (=C-H-def. and -C-C, m-w); MS (FD, 8 kV) *m/z* (%) 390.6 (100) [$M^{+\cdot}$-H^+] with $^{14}N/^{14}N$, 391.5 (76.1) [$M^{+\cdot}$] with $^{14}N/^{14}N$, 392.4 (9.2) [$M^{+\cdot}$] with $^{14}N/^{15}N$, 781.2 (23.7) [$2M^{+\cdot}$-$2H^+$] with $^{14}N/^{14}N$, 782.1 (27.9) [$2M^{+\cdot}$-H^+] with $^{14}N/^{14}N$, 783.0 (21.2) [$2M^{+\cdot}$] with $^{14}N/^{14}N$, 784.9 (4.6) [$2M^{+\cdot}$] with $^{14}N/^{15}N$ (calcd. for $C_{22}H_{35}N_2O_4$: *m/z* 391.5 [$M^{+\cdot}$]).

(2R,2S)-1-(3,5-dimethylphenoxy)-3-(isopropylamino)propan-2-yl 2,2,6,6-tetramethylpiperidine-1-oxyl-4-carboxylate: TLC: R_f (Diethyl ether) = 0.58, R_f (Dichloromethane) = 0.55; Recryst.: n-Hexane; Red crystalline solid; Mp. 117.2°C; EA calcd. (%) for $C_{24}H_{39}N_2O_4$: C 68.70, H 9.37, N 6.68; found: C 68.70, H 9.38, N 6.67; IR (KBr) $\tilde{\nu}_{max}$ 3302 (-N-H, m), 3060, 3035, 3030, 3010 (=C-H, m-w), 2998, 2992, 2975 (-C-H, s-w), 2962 (-CH_3, s), 2937, 2920 (-C-H, w), 2874 (-CH_3, m), 2771, 2728, 2696, 2629, 1797, 1733 (-C=O, s), 1693, 1681, 1643 (-C=C and N-H-def., w), 1612, 1596 (ring vibrations and N-H-def., s-m), 1556, 1537, 1513 (-N-O and N-H-def., w), 1470, 1456, 1433, 1402 (CH_3- and CH_2-def., s-m), 1382 (CH_3-def., m), 1366, 1348, 1339, 1321 (-N-O, s-w), 1296, 1262, 1246, 1225, 1197, 1169, 1155, 1115, 1087, 1075, 1054 (-C-O-C, s-w), 1013, 1001, 985, 966, 957, 935, 921, 896, 868 (=C-H-def. and -C-C, m-w), 844, 826, 760, 719, 687, 657, 580, 561, 531, 507, 496, 462 (=C-H-def. and -C-C, s-w); MS (FD, 8 kV) *m/z* (%) 209.4 (3.1) [$M^{2+\cdot}$-H^+] with $^{14}N/^{14}N$, 209.8 (3.7) [$M^{2+\cdot}$] with $^{14}N/^{14}N$, 418.7 (100) [$M^{+\cdot}$-H^+] with $^{14}N/^{14}N$, 419.6 (75.5) [$M^{+\cdot}$] with $^{14}N/^{14}N$, 420.6 (9.9) [$M^{+\cdot}$] with $^{14}N/^{15}N$, 837.1 (25.2) [$2M^{+\cdot}$-$2H^+$] with $^{14}N/^{14}N$, 838.2 (31.0) [$2M^{+\cdot}$-H^+] with $^{14}N/^{14}N$, 839.2 (22.9) [$2M^{+\cdot}$] with $^{14}N/^{14}N$, 841.0 (3.4) [$2M^{+\cdot}$] with $^{14}N/^{15}N$ (calcd. for $C_{24}H_{39}N_2O_4$: *m/z* 419.6 [$M^{+\cdot}$]).

Post-modifications by triple iodination of selected aromatic substrates using 1. *Syntheses of 2,4,6-triiodophenol, 2,4,6-triiodo-3,5-dimethylphenol, (2R,2S)-1-(isopropylamino)-3-(2,4,6-triiodophenoxy)propan-2-ol, (2R,2S)-1-(isopropylamino)-3-(2,4,6-triiodo-3,5-dimethyl-phenoxy)propan-2-ol, (2R,2S)-3-(isopropylamino)-1-(2,4,6-triiodophenoxy)propan-2-yl 2,2,6,6-tetramethylpiperidine-1-oxyl-4-carboxylate and (2R,2S)-3-(isopropylamino)-1-(2,4,6-triiodo-3,5-dimethylphenoxy)propan-2-yl 2,2,6, 6-tetramethylpiperidine-1-oxyl-4-carboxylate.* The syntheses of all above-mentioned triple iodinated products were performed in the same manner as described below and summarized in Tab. 1, entries 1-6. 0.1 mmol (1 eq.) of each aromatic

EPR active substrate (see Tab. 1, entries 5 and 6) or 2 mmol (1 eq.) of each aromatic non EPR-active substrate (see Tab. 1, entries 1-4) were dissolved in 10 ml (substrates of entries 5 and 6), 20 ml (substrates of entries 1 and 2) or 30 ml (substrates of entries 3 and 4) of dry DCM Under inert gas conditions at RT. To each continuously stirred solution, 2 mmol (1 eq.), or 0.1 mmol (1 eq.), of **1** was added in portions. After stirring for 5-10 minutes (see Tab. 1, reaction conditions) at RT, each reactive mixture was quenched with ~ 2.5 ml (relating to entries 5 and 6), ~ 5 ml (relating to entries 1 and 2) or ~ 10 ml (relating to entries 3 and 4) of a saturated sodium thiosulfate solution. Each organic layer was separated from the aqueous layer, diluted with ~ 30 ml DCM, extracted three times with 25 ml H_2O_{dd}, pre-dried once with 50 ml of a saturated sodium chloride solution, dried over anhydrous $MgSO_4$, filtered and the resulting filtrate concentrated to ~ 4 ml on rotary evaporator. After purification of each crude product using preparative TLC, dissolving of each product spot in THF, removal of the solvent, and dissolving the obtained solids in acetonitrile again in order to remove the precipitated silica gel by filtration, the resulting filtrates were concentrated to dryness on a rotary evaporator under reduced pressure. En suite, all products were recrystallized once from the respective solvent (see characterization of each isolated compound) and freeze-dried overnight (24 h) to yield 2,4,6-triiodophenol (924.7 mg, 1.96 mmol, 98%) as a yellowish solid, 2,4,6-triiodo-3,5-dimethylphenol (989.8 mg, 1.98 mmol, 99%) as a slightly yellowish crystalline solid, (2R,2S)-1-(Isopropylamino)-3-(2,4,6-triiodophenoxy)propan-2-ol (1.11 g, 1.89 mmol, 95%) as a colorless crystalline solid, (2R,2S)-1-(Isopropylamino)-3-(2,4,6-triiodo-3,5-dimethylphenoxy)propan-2-ol (1.18 g, 1.92 mmol, 96%) as a colorless to slightly yellowish crystalline solid, (2R,2S)-3-(Isopropylamino)-1-(2,4,6-triiodophenoxy)propan-2-yl 2,2,6,6-tetramethylpiperidine-1-oxyl-4-carboxylate (73.1 mg, 0.095 mmol, 95%) as an orange to slightly reddish shiny crystalline solid, and (2R,2S)-3-(Isopropylamino)-1-(2,4,6-triiodo-3,5-dimethylphenoxy)propan-2-yl 2,2,6,6-tetramethylpiperidine-1-oxyl-4-carboxylate (75.7 mg, 0.095 mmol, 95%) as an orange crystalline solid.

Characterizations of all triple iodinated aromatic substrates using 1. *2,4,6-triiodophenol*: The stated characterization data, such melting point (mp.), NMR shifts in DMSO-*d6*, IR bands using KBr etc. (see below), correspond with 2,4,6-triiodophenol as mentioned in previous literature (lit.).[25-27]

TLC: R_f (n-Hexane/Dichloromethane (1:1)) = 0.81, R_f (Petroleum ether/Dichloromethane (2:1)) = 0.64; Slightly yellowish crystalline solid; Mp. 158.7°C (lit.,[S25] mp. 158.5-159.0); EA calcd. (%) for $C_6H_4I_2O$: C 15.27, H 0.64; found: C 15.26, H 0.66; ^{1}H NMR (500 MHz, DMSO-*d6*) δ 9.74 (s, 1H, OH), 7.98 (s, 2H, 2CH);[S26,S27] ^{13}C NMR (126 MHz, DMSO-*d6*) δ 155.63 (*C-OH*), 145.71 (*2C-H*), 88.70 (*2C-I*), 84.80 (*C-I*);[S26] IR (KBr) $\tilde{\nu}_{max}$ 3445 (-OH, s), 3077, 3055 (-CH, w), 1627, 1543, 1524 (-C=C, m), 1462, 1436, 1400, 1369, 1324, 1296, 1268, 1232 (OH-def., s-m), 1204, 1173, 1138 (-C-O, m), 860 (=C-H-def., m), 701, 632, 542, 533 (=C-H-def. and -C-I, s-m);[S26] MS (FD, 8 kV) *m/z* (%) 236.1 (4.9) [M^{2+}], 471.8 (100) [M^+], 943.8 (42.2) [$2M^+$] (calcd. for $C_8H_7I_3O$: *m/z* 471.8 [M^+]).

2,4,6-triiodo-3,5-dimethylphenol: TLC: R_f (n-Hexane/Dichloromethane (1:1)) = 0.72, R_f (Dichloromethane) = 0.91; Slightly yellowish crystalline solid; Mp. 175.6°C; EA calcd. (%) for $C_8H_7I_3O$: C 19.22, H 1.41; found: C 19.21, H 1.42; ^{1}H NMR (500 MHz, DMSO-*d6*) δ 9.53 (s, 1H, OH, ***H1***), 2.83 (s, 6H, $2CH_3$, ***6H2***); ^{13}C (APT) NMR (126 MHz, DMSO-*d6*) δ 155.39 (***C1***), 143.36 (***2C5***), 94.49 (***C4***), 89.86 (***2C3***), 37.21 (***2C2***); IR (KBr) $\tilde{\nu}_{max}$ 3456 (-OH, m), 2956 (-CH_3, m), 2870 (-CH_3, m), 1438, 1374 (CH_3-def., s-m), 1355, 1301, 1262 (OH-def., s-m), 1190, 1120, 1069, 1054, 1038 (-C-O, m), 965, 937, 851 (=C-H-def., m), 703, 618, 594, 577 (=C-H-def. and -C-I, s-m); MS (FD, 8 kV) *m/z* (%) 249.8 (7.1) [M^{2+}], 499.8 (100) [M^+], 999.7 (42.2) [$2M^+$] (calcd. for $C_8H_7I_3O$: *m/z* 499.9 [M^+]).

(2R,2S)-1-(isopropylamino)-3-(2,4,6-triiodophenoxy)propan-2-ol: TLC: R_f (Diethyl ether/Acetone (6:1)) = 0.23; Recryst.: Acetonitrile; Colorless crystalline solid; Mp. 126.2°C; EA calcd. (%) for $C_{12}H_{16}I_3NO_2$: C 24.55, H 2.75, N 2.39; found: C 24.55, H 2.74, N 2.40; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05 (s, 2H, 2ArH, ***2H7***), 4.18-4.12 (m, 1H, CH, ***H4***), 4.03-3.96 (m, 2H, CH_2, ***2H5***), 2.93 (dd, $^2J_{H3H3}$ = 12.1 Hz, $^3J_{H3H4}$ = 4.2 Hz, 1H, C$\underline{H}_2$, ***H3***), 2.90-2.79 (m, 2H, CH ovlp. with C$\underline{H}_2$, ***H2*** ovlp. with ***H3***), 2.34 (s, 1H, OH, ***H10***), 1.10 (dd, $^3J_{H1H2}$ = 6.3 Hz, $^4J_{H1H1}$ = 2.2 Hz, 6H, $2CH_3$, ***6H1***); ^{13}C (APT) NMR (101 MHz, $CDCl_3$) δ 157.47 (***C9***), 147.58 (***C7***), 91.97 (***2C6***), 89.60 (***C8***), 75.33 (***C5***), 69.01 (***C4***), 49.32 (***C3***), 49.11 (***C2***), 23.33 (***C1***), 23.31 (***C1***); IR (KBr) $\tilde{\nu}_{max}$ 3416 (-OH, m), 3289 (-N-H, s), 3076, 3052 (=C-H, m-w), 2962 (-CH_3, s), 2918 (-C-H, m), 2872 (-CH_3, m), 2846 (-CH_2, m), 2764, 2688, 2620, 2572, 2484, 1748, 1727, 1633 (-C=C and N-H-def., w), 1574, 1541, 1519 (N-H-def., m-w), 1468, 1428, 1417 (CH_3- and CH_2-def., s-m), 1383 (CH_3-def., m), 1361, 1335, 1314, 1247, 1206, 1194, 1177, 1135, 1116, 1097, 1084, 1077, 1047, 1022 (-C-O-C, OH-def. and -C-O, s-w), 989, 948, 914, 896, 855 (=C-H-def. and -C-C, s-m), 822, 804, 732, 703,

661, 564, 535, 525, 512, 461, 404 (=C-H-def., -C-I and -C-C, m-w); MS (FD, 8 kV) *m/z* (%) 586.0 (52.4) [M^+-H^+] with ^{14}N, 586.9 (100) [M^+] with ^{14}N, 588.0 (11.9) [M^+] with ^{15}N, 1172.6 (25.3) [$2M^+$-H^+] with ^{14}N, 1173.8 (38.5) [$2M^+$] with ^{14}N, 1759.1 (7.1) [$3M^+$-$2H^+$] with ^{14}N, 1761.0 (16.3) [$3M^+$] with ^{14}N, 1763.8 (2.6) [$3M^+$] with ^{15}N (calcd. for $C_{12}H_{16}I_3NO_2$: *m/z* 587.0 [M^+]).

(2R,2S)-1-(isopropylamino)-3-(2,4,6-triiodo-3,5-dimethylphenoxy)propan-2-ol: TLC: R_f (Dichloromethane) = 0.21; Recryst.: Acetonitrile; Colorless to slightly yellowish crystalline solid; Mp. 139.8°C; EA calcd. (%) for $C_{14}H_{20}I_3NO_2$: C 27.34, H 3.28, N 2.28; found: C 27.34, H 3.29, N 2.27; ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.32-4.23 (m, 1H, CH, ***H4***), 4.05-3.97 (m, 2H, CH_2, ***2H5***), 3.02 (dd, $^2J_{H3H3}$ = 12.1 Hz, $^3J_{H3H4}$ = 4.1 Hz, 1H, C<u>H</u>$_2$, ***H3***), 2.98-2.91 (s ovlp. with m, 8H, $2CH_3$ ovlp. with CH and C<u>H</u>$_2$, ***2H10*** ovlp. with ***H2*** and ***H3***), 2.40 (s, 1H, OH, ***H11***), 1.15 (dd, $^3J_{H1H2}$ = 6.3 Hz, $^4J_{H1H1}$ = 1.6 Hz, 6H, $2CH_3$, ***6H1***); ^{13}C (APT) NMR (126 MHz, $CDCl_3$) δ 157.04 (***C9***), 145.61 (***2C7***), 99.91 (***C8***), 92.81 (***2C6***), 74.34 (***C5***), 68.73 (***C4***), 49.39 (***C3***), 49.36 (***C2***), 37.83 (***2C10***), 22.81 (***C1***), 22.79 (***C1***); IR (KBr) $\tilde{\nu}_{max}$ 3418 (-OH, m), 3288 (-N-H, m), 2975 (-C-H, s), 2963 (-CH_3, s), 2949 (-C-H, s), 2929 (-CH_2, s), 2912 (-C-H, m), 2872 (-CH_3, m), 2826 (-C-H, s), 2779, 2761, 2739, 2696, 2670, 2609, 2589, 2569, 2553, 1643, 1632 (-C=C and N-H-def., w), 1601 (ring vibration and N-H-def., w), 1572 (N-H-def., m), 1469, 1459, 1447 (CH_3- and CH_2-def., s-m), 1382 (CH_3-def., s), 1359, 1340, 1314, 1295, 1231, 1207, 1182, 1142, 1122, 1099, 1084, 1066, 1036 (-C-O-C, OH-def. and -C-O, s-m), 990, 964, 951, 924, 915, 901, 854 (=C-H-def. and -C-C, s-w), 824, 737, 658, 634, 619, 539, 463 (=C-H-def., -C-I and -C-C, s-w); MS (FD, 8 kV) *m/z* (%) 614.1 (41.6) [M^+-H^+] with ^{14}N, 615.0 (100) [M^+] with ^{14}N, 615.9 (7.7) [M^+] with ^{15}N, 1228.2 (14.7) [$2M^+$-$2H^+$] with ^{14}N, 1229.0 (31.5) [$2M^+$-H^+] with ^{14}N, 1230.1 (39.1) [$2M^+$] with ^{14}N (calcd. for $C_{14}H_{20}I_3NO_2$: *m/z* 615.0 [M^+]).

(2R,2S)-3-(isopropylamino)-1-(2,4,6-triiodophenoxy)propan-2-yl 2,2,6,6-tetramethylpiperidine-1-oxyl-4-carboxylate: TLC: R_f (Diethyl ether/Acetone (10:1)) = 0.83; Recryst.: n-Hexane; Orange to slightly reddish shiny crystalline solid; Mp. 149.6°C; EA calcd. (%) for $C_{22}H_{32}I_3N_2O_4$: C 34.35, H 4.19, N 3.64; found: C 34.35, H 4.20, N 3.63; IR (KBr) $\tilde{\nu}_{max}$ 3289 (-N-H, m), 3122, 3072, 3038 (=C-H, w), 2999, 2993, 2977 (-C-H, m), 2959 (-CH_3, s), 2941, 2878 (-C-H, m-w), 2871 (-CH_3, m), 2846 (-CH_2, m), 2785, 2760, 2739, 2698, 2619, 2598, 2570, 2482, 1733 (-C=O, s), 1693, 1682, 1644, 1633 (-C=C and N-H-def., w), 1574, 1556, 1540, 1518 (-N-O and N-H-def., m-w), 1504 (-N-O and ring vibration, w), 1494 (ring vibration, w), 1467, 1457, 1429, 1416 (CH_3- and CH_2-def., s-m), 1382 (CH_3-def., m), 1366, 1333, 1313 (-N-O, s-m), 1298, 1246, 1198, 1175, 1163, 1135, 1115, 1098, 1083, 1076, 1046 (-C-O-C, s-m), 1014, 988, 966, 947, 922, 914, 895, 855 (=C-H-def. and -C-C, s-m), 847, 820, 760, 731, 702, 660, 649, 562, 535, 524, 511, 500, 461, 403 (=C-H-def., -C-I and -C-C, m-w); MS (FD, 8 kV) *m/z* (%) 768.1 (100) [$M^{+\cdot}$-H^+] with $^{14}N/^{14}N$, 769.2 (71.2) [$M^{+\cdot}$] with $^{14}N/^{14}N$, 770.2 (7.4) [$M^{+\cdot}$] with $^{14}N/^{15}N$, 1536.3 (21.2) [$2M^{+\cdot}$-$2H^+$] with $^{14}N/^{14}N$, 1537.3 (26.8) [$2M^{+\cdot}$-H^+] with $^{14}N/^{14}N$, 1538.4 (16.7) [$2M^{+\cdot}$] with $^{14}N/^{14}N$, 1540.2 (3.1) [$2M^{+\cdot}$] with $^{14}N/^{15}N$ (calcd. for $C_{22}H_{32}I_3N_2O_4$: *m/z* 769.2 [$M^{+\cdot}$]).

(2R,2S)-3-(isopropylamino)-1-(2,4,6-triiodo-3,5-dimethylphenoxy)propan-2-yl 2,2,6,6-tetramethylpiperidine-1-oxyl-4-carboxylate: TLC: R_f (Dichloromethane) = 0.48, R_f (Dichloromethane/Ethyl acetate (10:1)) = 0.68; Recryst.: n-Hexane; Orange crystalline solid; Mp. 163.7°C; EA calcd. (%) for $C_{24}H_{36}I_3N_2O_4$: C 36.16, H 4.55, N 3.51; found: C 36.16, H 4.56, N 3.50; IR (KBr) $\tilde{\nu}_{max}$ 3288 (-N-H, m-w), 2993, 2977 (-C-H, s-m), 2956 (-CH_3, s), 2942 (-C-H, m), 2931 (-CH_2, w), 2872 (-CH_3, m), 2826 (-C-H, m), 2778, 2741, 2667, 2608, 2548, 1733 (-C=O, s), 1692, 1643, 1633 (-C=C and N-H-def., w), 1573, 1556, 1537, 1513 (-N-O and N-H-def., w), 1504 (-N-O and ring vibration, m), 1466, 1455, 1432 (CH_3- and CH_2-def., s-m), 1381 (CH_3-def., m), 1367, 1340, 1314 (-N-O, s-w), 1297, 1245, 1198, 1163, 1123, 1106, 1086, 1066, 1043 (-C-O-C, s-w), 1013, 988, 966, 950, 922, 900, 886, 867, 853 (=C-H-def. and -C-C, s-w), 841, 823, 813, 760, 736, 719, 658, 649, 634, 619, 561, 499, 465 (=C-H-def., -C-I and -C-C, m-w); MS (FD, 8 kV) *m/z* (%) 796.2 (100) [$M^{+\cdot}$-H^+] with $^{14}N/^{14}N$, 797.3 (73.7) [$M^{+\cdot}$] with $^{14}N/^{14}N$, 798.3 (10.3) [$M^{+\cdot}$] with $^{14}N/^{15}N$, 1592.6 (22.3) [$2M^{+\cdot}$-$2H^+$] with $^{14}N/^{14}N$, 1593.5 (27.4) [$2M^{+\cdot}$-H^+] with $^{14}N/^{14}N$, 1594.5 (21.9) [$2M^{+\cdot}$] with $^{14}N/^{14}N$, 1596.6 (3.9) [$2M^{+\cdot}$] with $^{14}N/^{15}N$ (calcd. for $C_{24}H_{36}I_3N_2O_4$: *m/z* 797.3 [$M^{+\cdot}$]).

Final remark: All measured FTIR- and NMR-spectra of all characterized compounds (see above) are additionally summarized in Figs. S1-S22, if not already shown in previously literature using the same measurement conditions (e.g. deuterated solvents, temperature, standards, etc.).

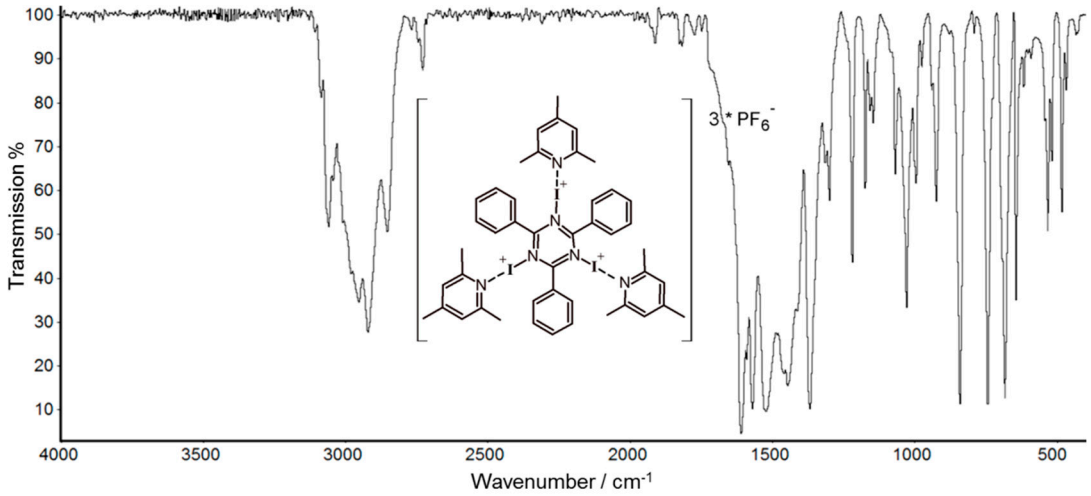


Fig. S1. Baseline-corrected FTIR transmission spectrum of **1**, recorded at RT.

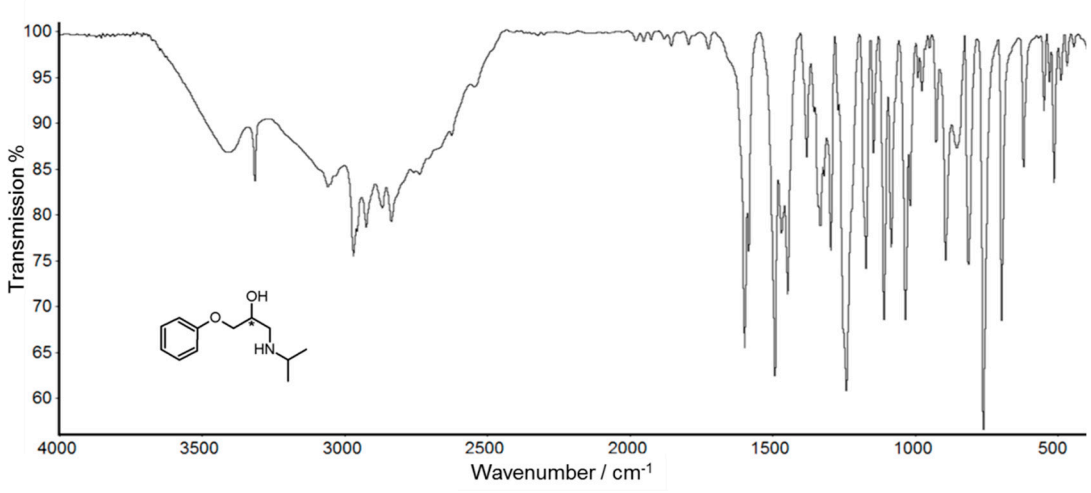


Fig. S2. Baseline-corrected FTIR transmission spectrum of (2R,2S)-1-(isopropylamino)-3-phenoxypropan-2-ol, recorded at RT.

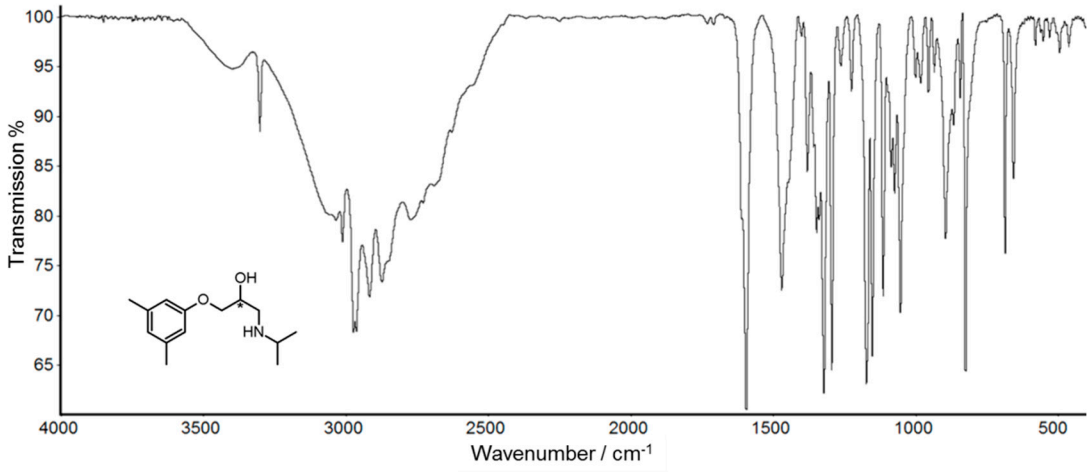


Fig. S3. Baseline-corrected FTIR transmission spectrum of (2R,2S)-1-(3,5-dimethylphenoxy)-3-(isopropylamino)propan-2-ol, recorded at RT.

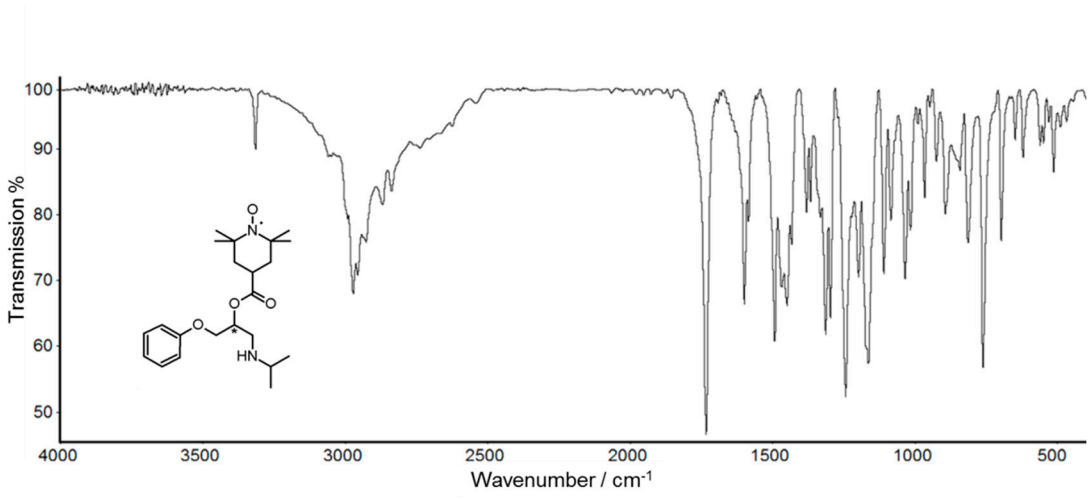


Fig. S4. Baseline-corrected FTIR transmission spectrum of (2R,2S)-1-(isopropylamino)-3-phenoxypropan-2-yl 2,2,6,6-tetramethylpiperidine-1-oxyl-4-carboxylate, recorded at RT.

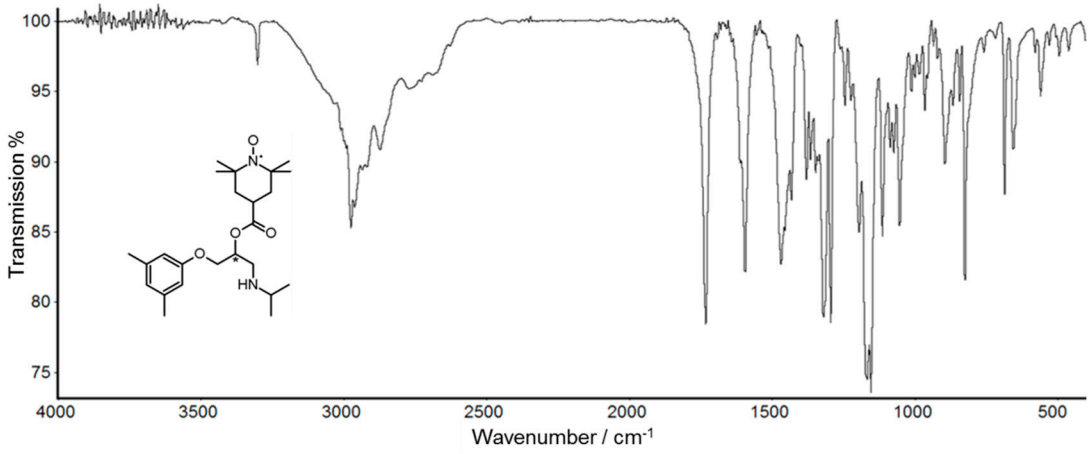


Fig. S5. Baseline-corrected FTIR transmission spectrum of (2R,2S)-1-(3,5-dimethylphenoxy)-3-(isopropylamino)propan-2-yl 2,2,6,6-tetramethylpiperidine-1-oxyl-4-carboxylate, recorded at RT.

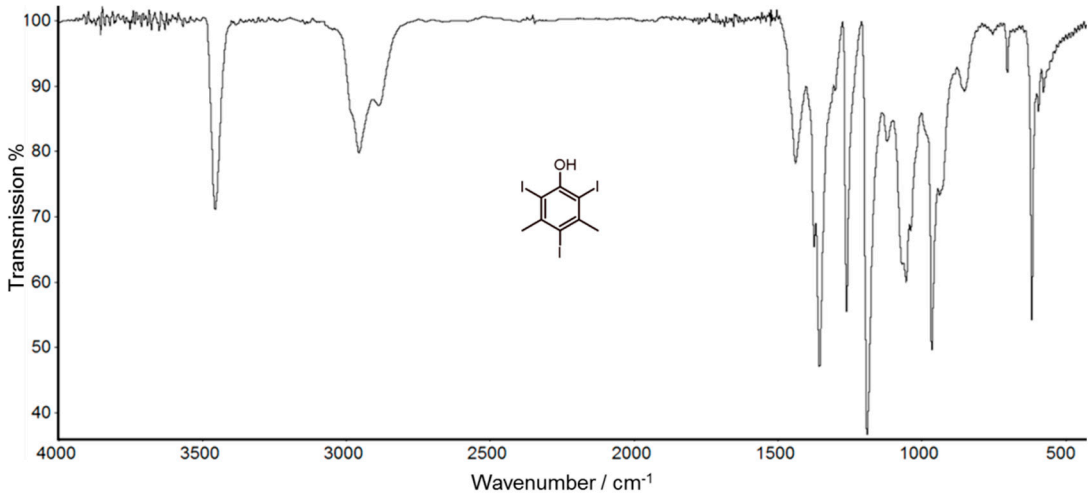


Fig. S6. Baseline-corrected FTIR transmission spectrum of 2,4,6-triiodo-3,5-dimethylphenol, recorded at RT.

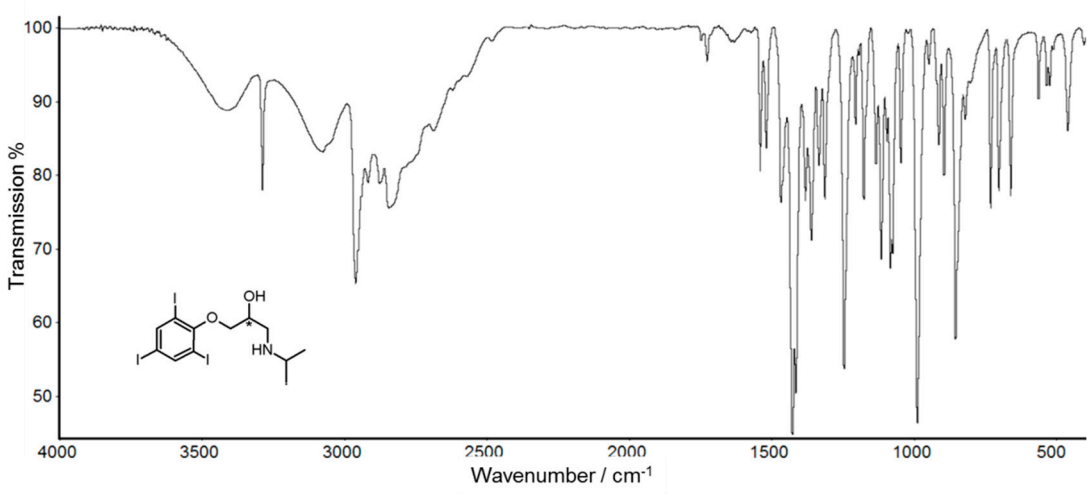


Fig. S7. Baseline-corrected FTIR transmission spectrum of (2R,2S)-1-(isopropylamino)-3-(2,4,6-triiodophenoxy)propan-2-ol, recorded at RT.

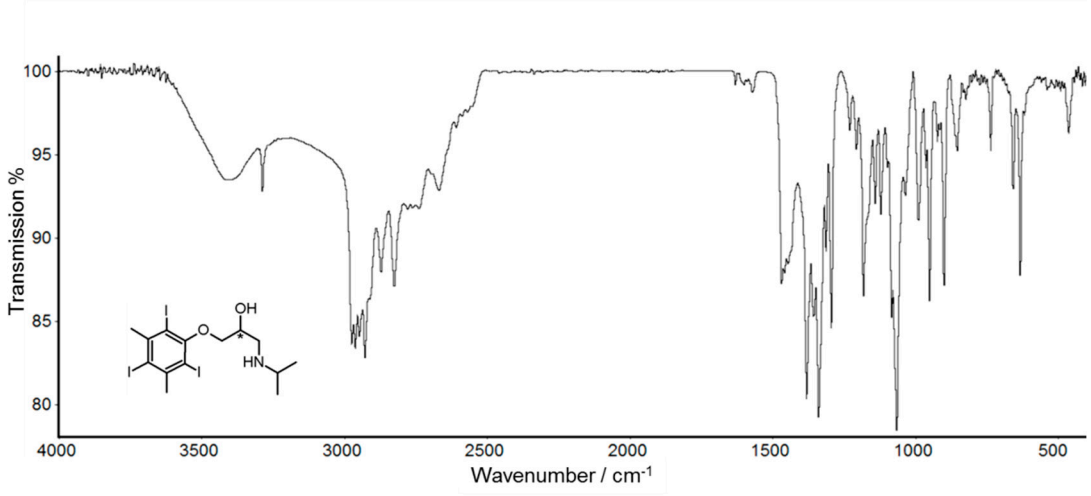


Fig. S8. Baseline-corrected FTIR transmission spectrum of (2R,2S)-1-(isopropylamino)-3-(2,4,6-triiodo-3,5-dimethylphenoxy)propan-2-ol, recorded at RT.

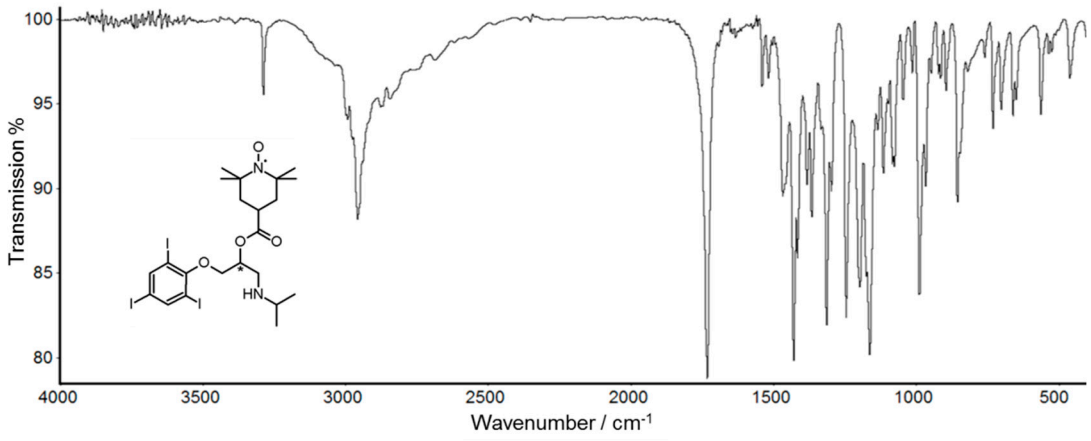


Fig. S9. Baseline-corrected FTIR transmission spectrum of (2R,2S)-3-(isopropylamino)-1-(2,4,6-triiodophenoxy)propan-2-yl 2,2,6,6-tetramethylpiperidine-1-oxyl-4-carboxylate, recorded at RT.

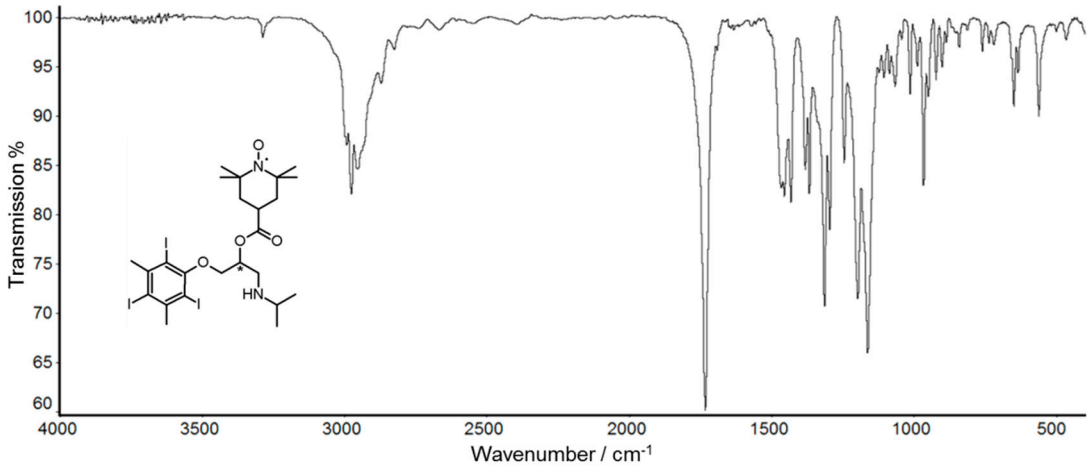


Fig. S10. Baseline-corrected FTIR transmission spectrum of (2R,2S)-3-(isopropylamino)-1-(2,4,6-triiodo-3,5-dimethylphenoxy)propan-2-yl 2,2,6,6-tetramethyl-piperidine-1-oxyl-4-carboxylate, recorded at RT.

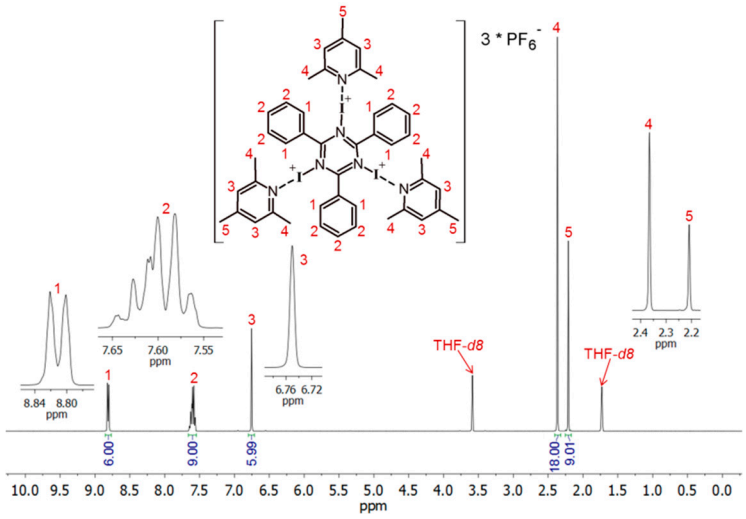


Fig. S11. ^{1}H NMR spectrum of **1** in THF-*d8*, recorded at 27°C and 400 MHz.

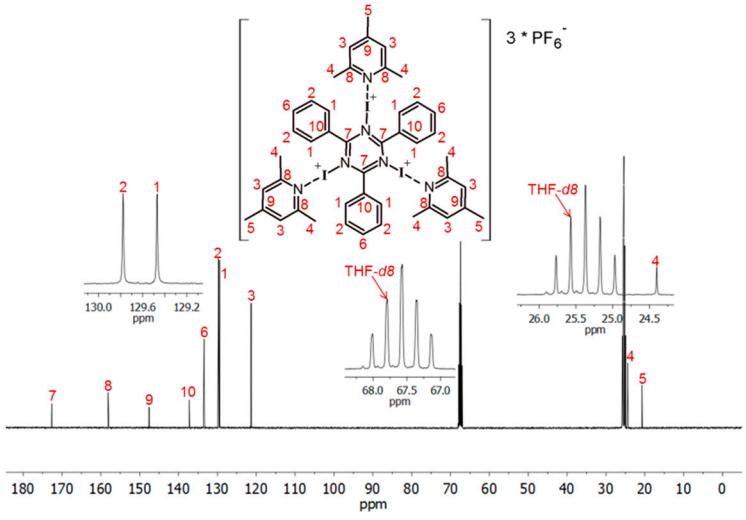


Fig. S12. ^{13}C NMR spectrum of **1** in THF-*d8*, recorded at 27°C and 101 MHz.

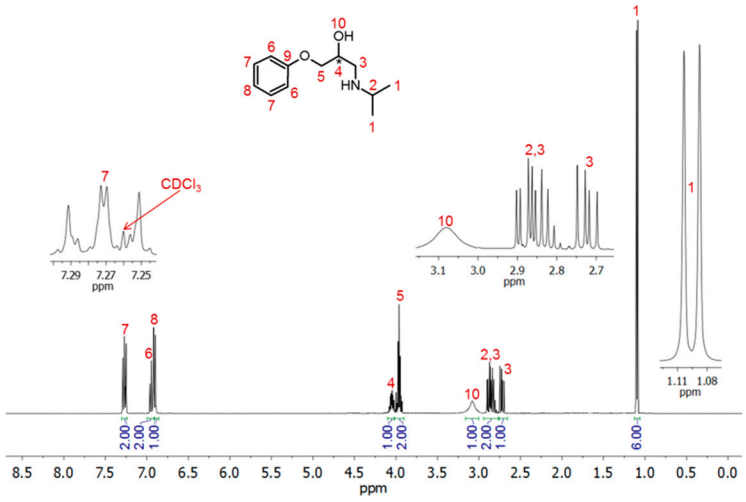


Fig. S13. ^{1}H NMR spectrum of (2R,2S)-1-(isopropylamino)-3-phenoxypropan-2-ol in $CDCl_3$, recorded at 27°C and 400 MHz.

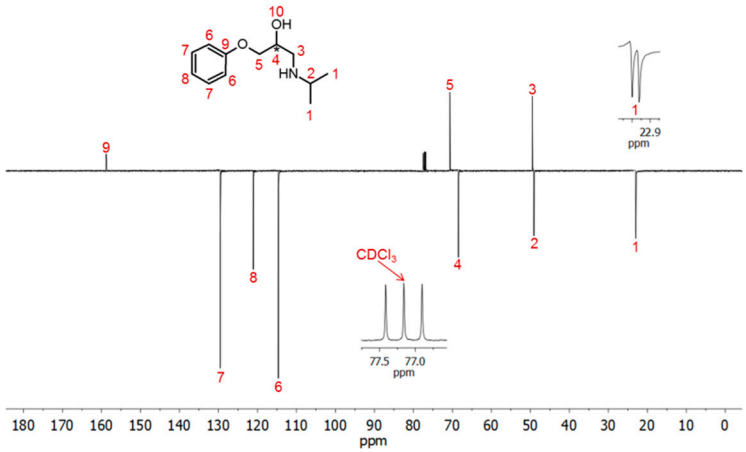


Fig. S14. ^{13}C (APT)-NMR spectrum of (2R,2S)-1-(isopropylamino)-3-phenoxypropan-2-ol in $CDCl_3$, recorded at 27°C and 101 MHz.

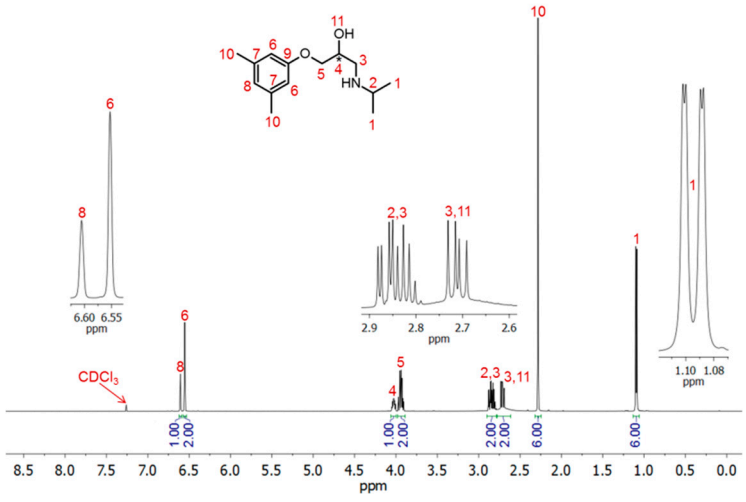


Fig. S15. ^{1}H NMR spectrum of (2R,2S)-1-(3,5-dimethylphenoxy)-3-(isopropylamino)propan-2-ol in $CDCl_3$, recorded at 27°C and 500 MHz.

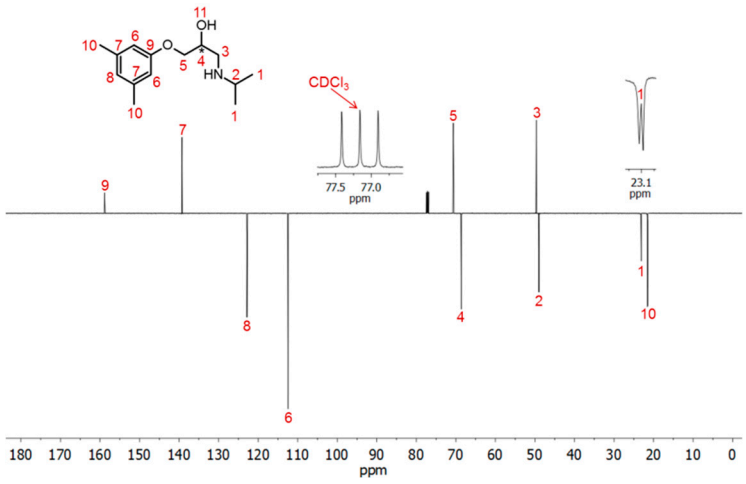


Fig. S16. ^{13}C (APT)-NMR spectrum of (2R,2S)-1-(3,5-dimethylphenoxy)-3-(isopropylamino)propan-2-ol in $CDCl_3$, recorded at 27°C and 126 MHz.

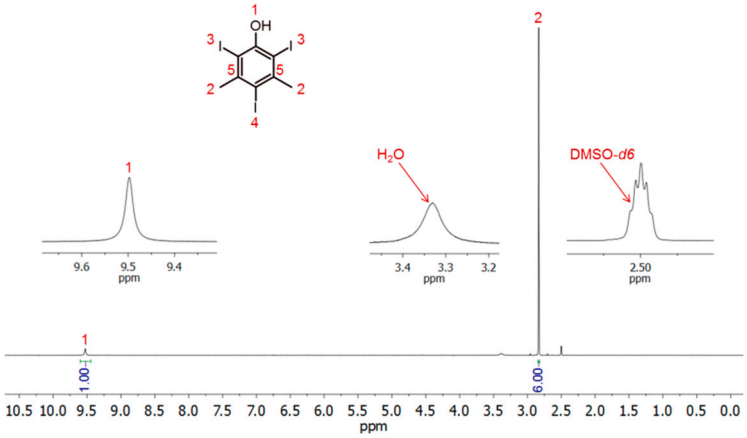


Fig. S17. ^{1}H NMR spectrum of 2,4,6-triiodo-3,5-dimethylphenol in DMSO-*d6*, recorded at 27°C and 500 MHz.

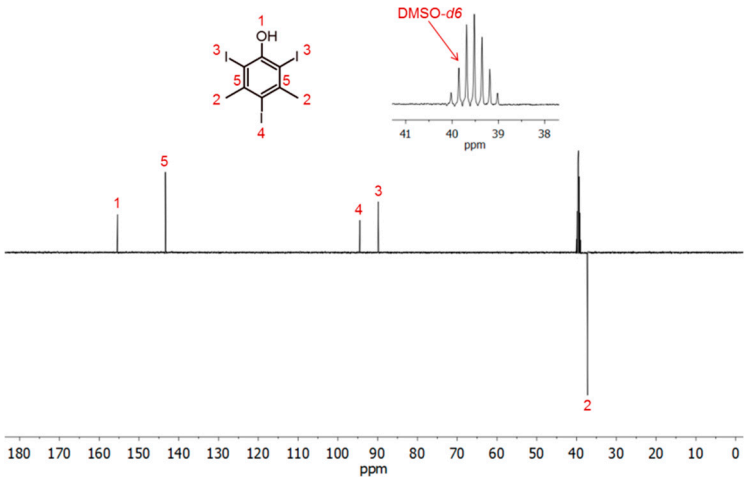


Fig. S18. ^{13}C (APT)-NMR spectrum of 2,4,6-triiodo-3,5-dimethylphenol in DMSO-*d6*, recorded at 27°C and 126 MHz.

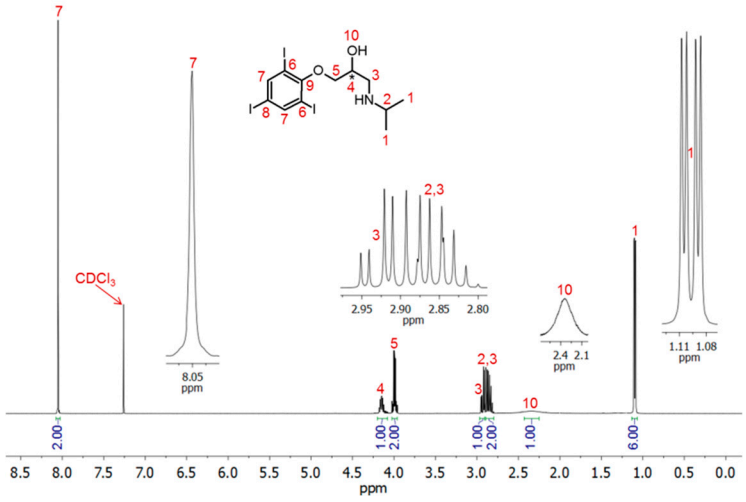


Fig. S19. ^{1}H NMR spectrum of (2R,2S)-1-(isopropylamino)-3-(2,4,6-triiodophenoxy)propan-2-ol in $CDCl_3$, recorded at 27°C and 400 MHz.

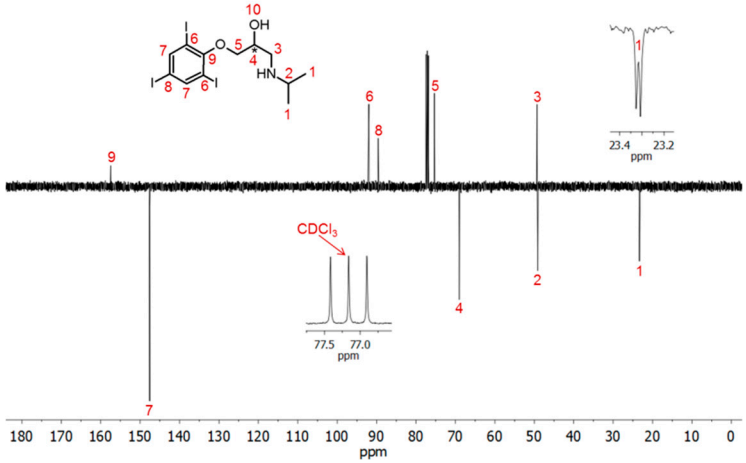


Fig. S20. ^{13}C (APT)-NMR spectrum of (2R,2S)-1-(isopropylamino)-3-(2,4,6-triiodophenoxy)propan-2-ol in $CDCl_3$, recorded at 27°C and 101 MHz.

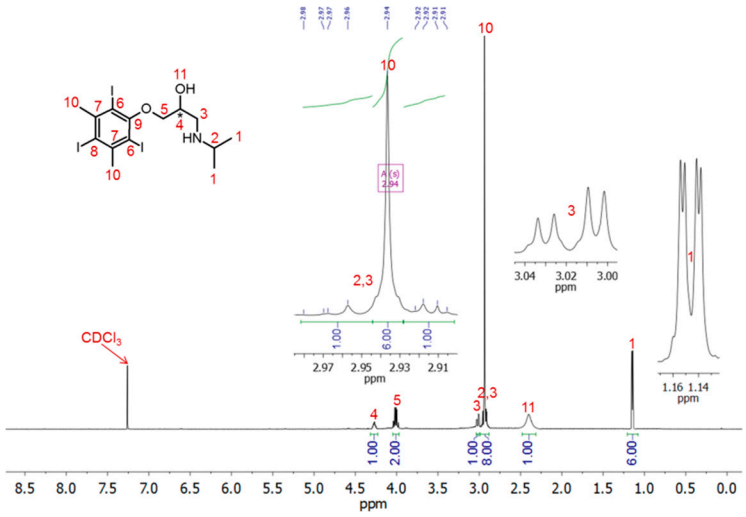


Fig. S21. ^{1}H NMR spectrum of (2R,2S)-1-(isopropylamino)-3-(2,4,6-triiodo-3,5-dimethylphenoxy)propan-2-ol in $CDCl_3$, recorded at 27°C and 500 MHz.

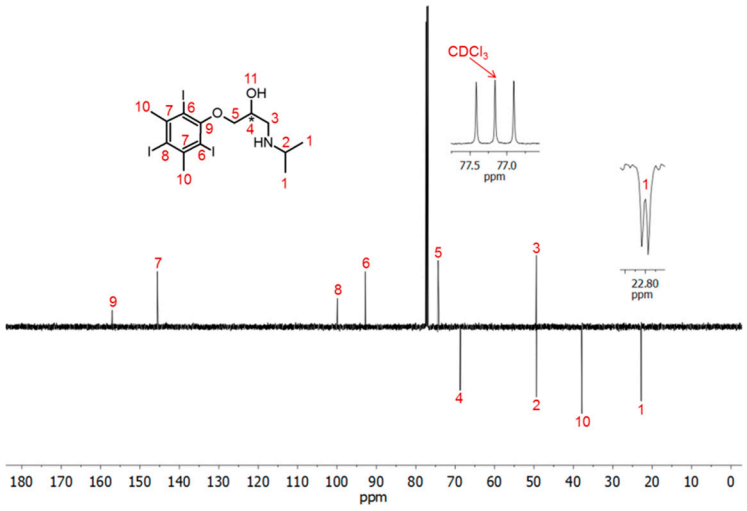


Fig. S22. ^{13}C (APT)-NMR spectrum of (2R,2S)-1-(isopropylamino)-3-(2,4,6-triiodo-3,5-dimethylphenoxy)propan-2-ol in $CDCl_3$, recorded at 27°C and 126 MHz.

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