Supplementary Material (ESI) for Chemical Communications

Organocatalytic Asymmetric Vinylogous Addition to Quinones – Formation of Optically Active α-Aryl Ketones

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Supporting Information

Contents

General methods:

NMR spectra were acquired on a Varian AS 400 spectrometer, running at 400 and 100 MHz for ^{1}H and ^{13}C, respectively. Chemical shifts (δ) are reported in ppm relative to residual solvent signals ($CHCl_3$, 7.26 ppm for ^{1}H NMR, $CDCl_3$, 77.0 ppm for ^{13}C NMR). ^{13}C NMR spectra were acquired on a broad band decoupled mode. Mass spectra were recorded on a Micromass LCT spectrometer using electrospray (ES^+) ionization techniques. Analytical thin layer chromatography (TLC) was performed using pre-coated aluminum-backed plates (Merck Kieselgel 60 F254) and visualized by ultraviolet irradiation or $KMnO_4$ dip. Melting points are uncorrected. Optical rotations were measured on a Perkin-Elmer 241 polarimeter. The enantiomeric excess (ee) of the products was determined by chiral stationary phase HPLC (Daicel Chiralpak AS/AD or Daicel Chiralcel OD columns) or by GC analysis using chiral column (Astec G-TA).

Materials:

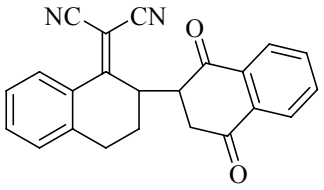
Analytical grade solvents and commercially available reagents were used as received. For flash chromatography (FC) silica gel (Silica gel 60, 230-400 mesh, Fluka) and Iatrobeads (Iatron Laboratories Inc. 6RS-8060) were used. The alkylidine derivatives **1a-g** was synthesized as described in literature.[1] Racemic samples were prepared using Et_3N as the catalyst.

General methodology for the addition of alkylidines derivatives 1a-g to quinones 2a-e. Synthesis of 4a-j:

To a sample vial equipped with a magnetic stirring bar was added **1a-g** (0.20 mmol), 1 mL of solvent (1/7 acetone/$CHCl_3$) and **2a-c** (0.22 mmol). The mixture was stirred at -20 ºC. When the mixture was cooled, the catalyst **3j** (20 mol%) was added and the mixture was vigorously stirred for the time stated below. After the reaction was judged to be complete by TLC analysis, the reaction was loaded onto a chromatographic column and the product **4** was obtained by FC (eluent indicated in each case).

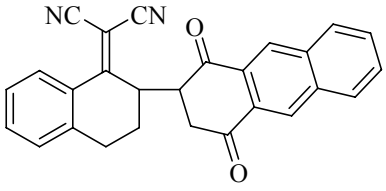
[1] (a) T. B. Poulsen, M. Bell and K. A. Jørgensen, *Org. Biomol. Chem*., **2006**, *4*, 63. (b) Xue, D., Chen, Y.-C., Wang, Q.W, Cun, L.-F., Zhu, J. , Deng, J.-G. *Org. Lett.* **2005**, *7*, 5293.

(-)-2-(2,3-Dihydro-3-(1,2,3,4-tetrahydro-1,4-dioxonaphthalen-3-yl)naphthalen-4(1H)-ylidene)malononitrile (4a)



The title compound (84% yield) was synthesized according to the general procedure as major diastereoisomer (14:1) after 24 h at -20 ^{o}C employing **1a** (0.20 mmol), **2a** (0.22 mmol) in the presence of the catalyst **3j** (0.04 mmol), in $CHCl_3$/acetone 7:1 (1.0 mL) as a mixture of solvents. For the purification of the title compound was used Et_2O/hexane 1/3 as the eluent. ^{1}H NMR ($CDCl_3$): δ 8.00-7.99 (m, 2H), 7.94 (dd, *J* = 8.0, 0.8 Hz, 1H), 7.75-7.73 (m, 2H), 7.47 (td, *J* = 7.6, 1.2 Hz, 1H), 7.33 (t, *J* = 7.2 Hz, 1H), 7.26-7.23 (m, 1H), 3.72 (dt, *J* = 8.8, 4.0 Hz, 1H), 3.23-3.11 (m, 2H), 3.01-3.29 (m, 3H), 2.25-2.21 (m, 2H). ^{13}C NMR ($CDCl_3$): δ 195.5, 194.2, 176.6, 138.6, 134.8, 134.7, 134.5, 133.4 (2C), 129.4, 129.2, 128.7, 127.3, 127.1, 126.5, 113.6, 112.9, 81.2, 47.7, 42.2, 40.5, 24.6, 20.1. HRMS: Calculated for $[C_{22}H_{16}N_2O_2Na]^+$: 375.1109; found: 375.1111. The ee was determined by HPLC using Chiralpak AD column [hexane/*i*-PrOH (75:25)]; flow rate 1.0 mL/min; τ_{major} = 13.6 min, τ_{minor} = 17.0 min (75% ee). $[\alpha]_D^{rt}$: -114.5 (c = 0.1, CH_2Cl_2).

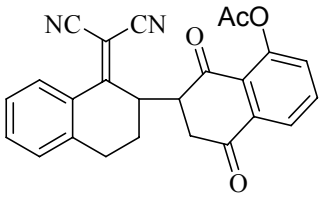
(-)-2-(2,3-Dihydro-3-(1,2,3,4-tetrahydro-1,4-dioxoanthracen-3-yl)naphthalen-4(1H)-ylidene)malononitrile (4b)



The title compound (39% yield) was synthesized according to the general procedure as single diastereoisomer after 48 h at -20 ^{o}C employing **1a** (0.20 mmol), **2b** (0.22 mmol) in the presence of the catalyst **3j** (0.04 mmol), in $CHCl_3$/acetone 7:1 (1.0 mL) as a mixture of solvents. For the purification of the title compound was used Iatrobeads (Et_2O/hexane 1/1 as eluent). ^{1}H NMR ($CDCl_3$): δ 8.47 (d, *J* = 3.6 Hz, 1H), 7.99-7.96 (m, 2H), 7.68-7.65 (m, 2H), 7.46 (td, *J* = 7.6, 0.8 Hz, 1H) 7.33 (t, *J* = 7.6 Hz, 1H), 7.26-7.24 (m, 3H), 3.78 (dt, *J* = 8.8, 4.0 Hz, 1H), 3.29-3.16 (m, 2H), 3.08-2.98 (m, 3H), 2.28-2.26 (m, 2H). ^{13}C NMR ($CDCl_3$): δ 195.5, 194.3, 176.9, 138.7, 135.2, 135.0, 133.4, 130.2, 130.1, 130.0 (2C), 129.7 (2C), 129.4 (2C), 129.2, 128.7, 128.6, 127.1 113.6, 113.0, 81.2, 47.7, 42.2, 40.7, 24.7, 24.6. HRMS: Calculated for $[C_{27}H_{16}N_2O_2Na]^+$: 425.1266; found: 425.1272. The ee was

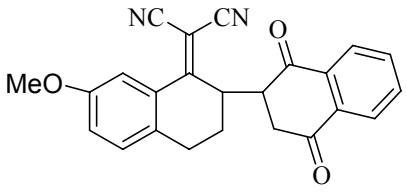
determined by HPLC using Chiralpak AS column [hexane/*i*-PrOH (75:25)]; flow rate 1.0 mL/min; τ_{minor} = 35.5 min, τ_{major} = 51.3 min (99% ee). $[\alpha]_D^{rt}$: -339.0 (c = 0.1, CH_2Cl_2).

2-(2,3-Dihydro-3-(1,2,3,4-tetrahydro-5-acetoxy-1,4-dioxonaphthalen-2-yl)naphthalen-4(1H)-ylidene)malononitrile (4c)



The title compound (80% yield) was synthesized according to the general procedure as major diastereoisomer (8:1) after 48 h employing **1a** (0.20 mmol), **2c** (0.22 mmol) in the presence of the catalyst **3j** (0.04 mmol), in $CHCl_3$/acetone 7:1 (1.0 mL) as a mixture of solvents at -20 ºC. For the purification of the title compound silica gel was used (AcOEt/hexane 1/4 as eluent). ^{1}H NMR ($CDCl_3$): δ 7.93-7.87 (m, 2H), 7.72-7.70 (m, 1H), 7.48 (t, *J* = 7.6 Hz, 1H), 7.37-7.34 (m, 2H), 7.24 (d, *J* = 8.0 Hz, 1H), 3.71 (dt, *J* = 8.4, 4.0 Hz, 1H), 3.20-3.09 (m, 2H), 2.98-2.92 (m, 3H), 2.40 (s, 3H), 2.24-2.20 (m, 2H). ^{13}C NMR ($CDCl_3$): δ 194.5, 193.2, 175.7, 169.3, 148.8, 138.6, 135.6, 134.9, 133.4, 129.8, 129.2, 129.1, 128.7, 127.0, 126.9, 124.8, 113.6, 112.7, 81.5, 48.7, 41.6, 40.2, 24.6, 24.3, 21.0. HRMS: Calculated for $[C_{25}H_{18}N_2O_4Na]^+$: 433.1164; found: 435.1154. The ee was determined by HPLC using Chiralcel OD column [hexane/*i*-PrOH (80:20)]; flow rate 1.0 mL/min; τ_{major} = 34.2 min, τ_{minor} = 39.6 min (60% ee). $[\alpha]_D^{rt}$: -204 (c = 0.1, CH_2Cl_2).

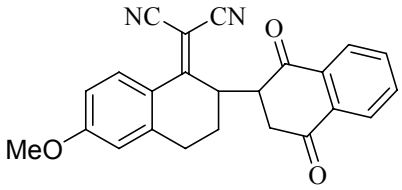
(-)-2-(2,3-Dihydro-3-(1,2,3,4-tetrahydro-1,4-dioxonaphthalen-3-yl)-6-methoxynaphthalen-4(1H)-ylidene)malononitrile (4d)



The title compound (81% yield) was synthesized according to the general procedure as major diastereoisomer (5:1) after 40 h employing **1b** (0.2 mmol), **2a** (0.22 mmol) in the presence of the catalyst **3j** (0.04 mmol), in $CHCl_3$/acetone 7:1 (1.0 mL) as a mixture of solvents at -20 ºC. For the purification of the title compound was used silica gel (AcOEt/hexane 1/3 as eluent). ^{1}H NMR ($CDCl_3$): δ 8.03-8.00 (m, 2H), 7.77-7.74 (m, 2H), 7.40 (d, *J* = 2.8 Hz, 1H), 7.14 (d, *J* = 8.4 Hz, 1H), 7.03 (dd, *J* = 8.4, 2.8 Hz, 1H), 3.84 (s, 3H), 3.69 (dt, *J* = 6.0, 2.0 Hz, 1H), 3.24-3.15 (m, 2H), 3.04-2.87 (m, 3H), 2.25-2.19 (m, 2H). ^{13}C NMR ($CDCl_3$): δ

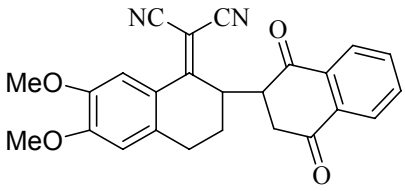
195.7, 194.3, 176.7, 158.0, 134.8, 134.7, 134.5 (2C), 130.5, 130.3, 129.8, 127.3, 126.5, 121.4, 113.7, 112.9, 111.8, 81.1, 55.7, 47.7, 42.2, 40.7, 25.1, 23.7. HRMS: Calculated for $[C_{24}H_{18}N_2O_3Na]^+$: 405.1215; found: 405.1218. The ee was determined by HPLC using Chiralcel OD column [hexane/*i*-PrOH (80:20)]; flow rate 1.0 mL/min; τ_{major} = 29.1 min, τ_{minor} = 44.6 min (63% ee). $[\alpha]_D^{rt}$: -278.0 (c = 0.1, CH_2Cl_2).

(-)-2-(2,3-Dihydro-3-(1,2,3,4-tetrahydro-1,4-dioxonaphthalen-3-yl)-5-methoxynaphthalen-4(1H)-ylidene)malononitrile (4e)



The title compound (76% yield) was synthesized according to the general procedure as major diastereoisomer (14:1) after 48 h employing **1c** (0.20 mmol), **2a** (0.22 mmol) in the presence of the catalyst **3j** (0.04 mmol), in $CHCl_3$/acetone 7:1 (1.0 mL) as a mixture of solvents at -20 ºC. For the purification of the title compound was used silica gel (AcOEt/hexane 1/3 as eluent). ^{1}H NMR ($CDCl_3$): δ 8.18-7.98 (m, 2H), 7.94 (d, *J* = 8.8 Hz, 1H), 7.75-7.77 (m, 2H), 6.86 (dd, *J* = 8.8, 2.8 Hz, 1H), 6.72 (d, *J* = 2.8 Hz, 1H), 3.83 (s, 3H), 3.67 (dt, *J* = 8.8, 4.0 Hz, 1H), 3.22-3.13 (m, 3H), 3.01-2.90 (m, 2H), 2.21-2.19 (m, 2H). ^{13}C NMR ($CDCl_3$): δ 195.6, 194.3, 175.3, 163.6, 141.1, 134.8, 134.6, 134.4 (2C), 130.8, 127.3, 126.5, 122.1, 114.2, 114.1, 113.3, 113.0, 78.7, 55.5, 47.9, 42.0, 40.4, 24.9, 24.3. HRMS: Calculated for $[C_{24}H_{18}N_2O_3Na]^+$: 405.1215; found: 405.1226. The ee was determined by HPLC using Chiralpak AS column [hexane/*i*-PrOH (80:20)]; flow rate 1.0 mL/min; τ_{major} = 52.8 min, τ_{minor} = 65.7 min (99% ee). $[\alpha]_D^{rt}$: -406.0 (c = 0.1, CH_2Cl_2).

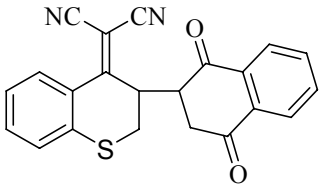
(-)-2-(2,3-Dihydro-3-(1,2,3,4-tetrahydro-1,4-dioxonaphthalen-3-yl)-6,7-dimethoxynaphthalen-4(1H)-ylidene)malononitrile (4f)



The title compound (69% yield) was synthesized according to the general procedure as single diastereoisomer (>98%) after 40 h employing **1d** (0.20 mmol), **2a** (0.22 mmol) in the presence of the catalyst **3j** (0.04 mmol), in $CHCl_3$/acetone 7:1 (1.0 mL) as a mixture of solvents at -20 ºC. For the purification of the title compound was used Iatrobeads (Et_2O/hexane 3/1 as

eluent). ^{1}H NMR ($CDCl_3$): δ 8.01-8.01 (m, 2H), 7.76-7.74 (m, 2H), 7.44 (s, 1H), 6.66 (s, 1H), 3.93 (s, 3H), 3.90 (s, 3H), 3.63 (dt, *J* = 8.4, 4.0 Hz, 1H), 3.25-3.15 (m, 3H), 3.06-2.89 (m, 2H), 2.26-2.21 (m, 2H). ^{13}C NMR ($CDCl_3$): δ 195.8, 194.4, 175.2, 153.6, 147.6, 134.8, 134.7, 134.4, 133.0, 127.4, 126.5, 121.4, 114.4, 113.4, 110.9, 110.6, 78.6, 56.2, 56.1, 42.0, 40.7, 30.2, 24.8, 24.4. HRMS: Calculated for $[C_{25}H_{20}N_2O_4Na]^+$: 435.1320; found: 435.1323. The ee was determined by HPLC using Chiralcel OD column [hexane/*i*-PrOH (75:25)]; flow rate 1.0 mL/min; τ_{minor} = 26.1 min, τ_{major} = 38.6 min (96% ee). $[\alpha]_D^{rt}$: -107.0 (c = 0.5, CH_2Cl_2).

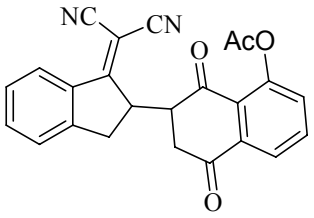
(-)-2-(2,3-Dihydro-3-(1,2,3,4-tetrahydro-1,4-dioxonaphthalen-3-yl)thiochromen-4-ylidene)malononitrile (4g)



The title compound (81% yield) was synthesized according to the general procedure as major diastereoisomer (4:1)[2] after 44 h employing **1e** (0.20 mmol), **2a** (0.22 mmol) in the presence of the catalyst **3j** (0.04 mmol), in $CHCl_3$/acetone 7:1 (1.0 mL) as a mixture of solvents at -20 ºC. For the purification of the title compound was used silica gel (AcOEt/hexane 1/4 as eluent). ^{1}H NMR ($CDCl_3$): δ 8.04-8.00 (m, 1H), 7.95-7.91 (m, 1H), 7.80 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.76-7.72 (m, 2H), 7.37-7.33 (m, 1H), 7.18-7.14 (m, 2H), 3.85-3.81 (m, 1H), 3.56 (dd, *J* = 14.4, 2.8 Hz, 1H), 3.51-3.44 (m, 1H), 3.35 (dd, *J* = 16.0, 6.0 Hz, 1H), 3.18 (dd, *J* = 14.4, 4.0, 1H), 3.02 (dd, *J* = 15.6. 12.0 Hz, 1H). ^{13}C NMR ($CDCl_3$): δ 195.6, 193.6, 173.8, 136.1, 134.8, 134.7, 134.6, 134.5, 133.4, 130.9, 127.2, 126.7, 126.6, 125.9, 125.1, 113.3, 112.7, 82.6, 46.6, 40.8, 39.1, 28.8. HRMS: Calculated for $[C_{22}H_{14}N_2O_2SNa]^+$: 393.0673; found: 393,0674. The ee was determined by HPLC using Chiralcel OD column [hexane/*i*-PrOH (85:15)]; flow rate 1.0 mL/min; τ_{major} = 51.2 min, τ_{minor} = 57.7 min (65% ee). $[\alpha]_D^{rt}$: -338.0 (c = 0.1, CH_2Cl_2).

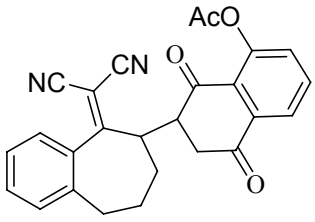
[2] Diastereomeric ratio determined by weight of the isolated products.

(-)-2-(1,2-Dihydro-2-(1,2,3,4-tetrahydro-2-acetoxy-1,4-dioxonaphthalen-2-yl)inden-3-ylidene)malononitrile (4h)



The title compound (67% yield) was synthesized according to the general procedure as major diastereoisomer (11:1) after 18 h employing **1f** (0.20 mmol), **2c** (0.22 mmol) in the presence of the catalyst **3j** (0.04 mmol), in $CHCl_3$/acetone 7:1 (1.0 mL) as a mixture of solvents at -20 ºC. For the purification of the title compound was used Iatrobeads (Et_2O/hexane 1/1 as eluent). ^{1}H NMR ($CDCl_3$): δ 8.40 (d, *J* = 8.0 Hz, 1H), 7.96 (d, *J* = 7.6 Hz, 1H), 7.75 (t, *J* = 7.6 Hz, 1H), 7.62 (t, *J* = 7.6 Hz, 1H), 7.50-7.40 (m, 3H), 4.38 (d, *J* = 6.8 Hz, 1H), 3.93 (d, *J* = 12.0 Hz, 1H), 3.54 (dd, *J* = 18.0, 6.8 Hz, 1H), 2.88 (d, *J* = 19.2 Hz, 1H), 2.55-2.35 (m, 2H), 2.44 (s, 3H). ^{13}C NMR ($CDCl_3$): δ 193.2, 192.9, 179.6, 169.6, 152.2, 149.2, 136.0, 135.9, 135.8, 135.2, 130.4, 128.6, 126.6, 125.9, 125.8, 125.1, 112.9, 112.5, 75.6, 50.3, 44.8, 37.1, 34.0, 20.9. HRMS: Calculated for $[C_{24}H_{16}N_2O_4Na]^+$: 419.1007; found: 419.0999. The ee was determined by HPLC using Chiralpak OD column [hexane/*i*-PrOH (75:25)]; flow rate 1.0 mL/min; τ_{minor} = 24.1 min, τ_{major} = 32.5 min (68% ee). $[\alpha]_D^{rt}$: -30.0 (c = 0.1, CH_2Cl_2).

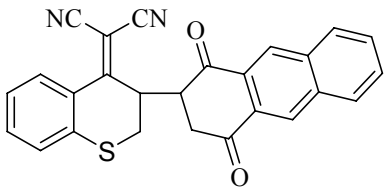
(-)-2-(5,6,7,8-Tetrahydro-8-(1,2,3,4-tetrahydro-5-acetoxy-1,4-dioxonaphthalen-3-yl)benzo[7]annulen-9-ylidene)malononitrile (4i)



The title compound (83% yield) was synthesized according to the general procedure as single diastereoisomer (>98%) after 24 h employing **1g** (0.20 mmol), **2c** (0.22 mmol) in the presence of the catalyst **3j** (0.04 mmol), in $CHCl_3$/acetone 7:1 (1.0 mL) as a mixture of solvents at -20 ºC. For the purification of the title compound was used silica gel (AcOEt/hexane 1/1 as eluent). ^{1}H NMR ($CDCl_3$): δ 7.91 (d, *J* = 7.6 Hz, 1H), 7.68 (d, *J* = 8.0 Hz, 1H), 7.35-7.16 (m, 4H), 6.97 (d, *J* = 7.2 Hz, 1H), 3.67-3.63 (m, 1H), 3.08 (dd, *J* = 16.0, 5.2 Hz, 1H), 3.01-2.95 (m, 1H), 2.80-2.60 (m, 4H), 2.49 (s, 3H), 2.35-2.20 (m, 1H), 2.04-1.92 (m, 2H). ^{13}C NMR ($CDCl_3$): δ 195.1, 193.0, 185.9, 169.3, 148.8, 137.4, 135.8, 134.8, 134.3, 131.0, 130.3, 129.9, 128.7, 128.6, 126.9, 125.0, 112.1, 111.9, 85.9, 48.4, 43.8, 40.1, 35.7, 32.4, 22.0,

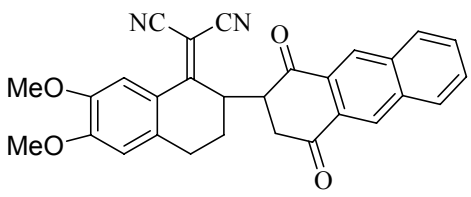
21.0. HRMS: Calculated for $[C_{26}H_{20}N_2O_4Na]^+$: 447.1320; found: 447.1312. The ee was determined by HPLC using Chiralpak AS column [hexane/*i*-PrOH (80:20)]; flow rate 1.0 mL/min; τ_{major} = 27.0 min, τ_{minor} = 34.5 min (80% ee). $[\alpha]_D^{rt}$: -48.0 (c = 0.1, CH_2Cl_2).

(-)-(2,3-Dihydro-3-(1,2,3,4-tetrahydro-1,4-dioxoanthracen-3-yl)thiochromen-4-ylidene)malononitrile (4j)



The title compound (50% yield) was synthesized according to the general procedure as major diastereoisomer (12:1) after 48 h employing **1e** (0.20 mmol), **2b** (0.22 mmol) in the presence of the catalyst **3j** (0.02 mmol), in $CHCl_3$/acetone 7:1 (1.0 mL) as a mixture of solvents at -20 ºC. For the purification of the title compound was used Iatrobeads (Et_2O/hexane 1/1 as eluent). ^{1}H NMR ($CDCl_3$): δ 8.50 (d, *J* = 2.0 Hz, 1H), 8.43 (d, *J* = 4.4 Hz, 1H), 7.97-7-96 (m, 2H), 7.82 (d, *J* = 8.0 Hz, 1H), 7.67-7.64 (m, 2H), 7.34-7.30 (m, 1H), 7.16-7.14 (m, 2H), 3.89 (dt, *J* = 5.6, 2.4 Hz, 1H), 3.57 (dd, *J* = 14.4, 2.8 Hz, 1H), 3.35-3.45 (m, 1H), 3.48 (dd, *J* = 15.8, 5.6 Hz,1H), 3.22 (dd, *J* = 14.4, 4.0 Hz, 1H), 3.09 (dd, *J* = 15.6, 12.0 Hz, 1H). ^{13}C NMR ($CDCl_3$): δ 195.6, 193.7, 174.1, 140.0, 136.2, 135.1, 135.0, 133.3, 131.1, 130.8, 130.3, 130.2, 130.0, 129.9, 129.7, 129.2 (2C), 128.8, 128.7, 126.5, 125.1, 82.5, 46.6, 40.8, 39.1, 28.9. HRMS: Calculated for $[C_{26}H_{16}N_2O_2Na]^+$: 443.0830; found: 443.0821. The ee was determined by HPLC using Chiralpak AS column [hexane/*i*-PrOH (70:30)]; flow rate 1.0 mL/min; τ_{minor} = 29.5 min, τ_{major} = 70.9 min (93% ee). $[\alpha]_D^{rt}$: -88.2 (c = 0.1, CH_2Cl_2).

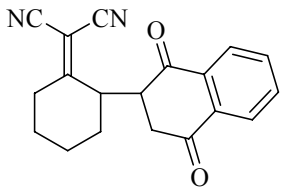
(-)-2-(2,3-Dihydro-3-(1,2,3,4-tetrahydro-1,4-dioxoanthracen-3-yl)-6,7-dimethoxythiochromen-4-ylidene)malononitrile (4k)



The title compound (51% yield) was synthesized according to the general procedure as a single diastereoisomer (>98%) after 48 h employing **1d** (0.20 mmol), **2b** (0.22 mmol) in the presence of the catalyst **3j** (0.02 mmol), in $CHCl_3$/acetone 7:1 (1.0 mL) as a mixture of solvents at -20 ºC. For the purification of the title compound was used Iatrobeads (Et_2O/hexane 3/1 as

eluent). ^{1}H NMR ($CDCl_3$): δ 8.53 (d, *J* = 5.2 Hz, 2H), 8.00-7.98 (m, 2H), 7.68-7.66 (m, 2H), 7.55 (s, 1H), 6.66 (s, 1H), 3.91 (s, 3H), 3.89 (s, 3H), 3.68 (dt, *J* = 8.0, 3.6 Hz, 1H), 3.30-3.22 (m, 3H), 2.93-2.91 (m, 2H), 2.33-2.17 (m, 2H). ^{13}C NMR ($CDCl_3$): δ 195.8, 194.4, 175.4, 153.5, 147.6, 135.3, 135.1, 133.1, 130.2, 130.2, 130.1, 130.0, 129.9, 129.7, 129.5, 128.5, 121.4, 114.5, 113.4, 110.9, 110.5, 78.6, 56.2, 56.1, 48.1, 42.0, 40.9, 24.9, 24.4. HRMS: Calculated for $[C_{29}H_{22}N_2O_4Na]^+$: 485.1477; found: 485.1477. The ee was determined by HPLC using Chiralpak AS column [hexane/*i*-PrOH (75:25)]; flow rate 1.0 mL/min; τ_{major} = 34.3 min, τ_{minor} = 75.3 min (92% ee). $[\alpha]_D^{rt}$: -30.0 (c = 0.1, CH_2Cl_2).

(-)-2-(2-(1,2,3,4-Tetrahydro-1,4-dioxonaphthalen-3-yl)cyclohexylidene)malononitrile (4l)



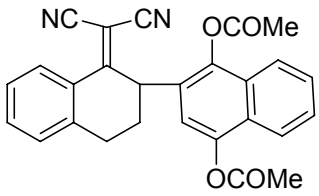
The title compound (57% yield) was synthesized according to the general procedure as single diastereoisomer (>98%) after 64 h employing **1e** (0.2 mmol), **2a** (0.22 mmol) in the presence of the catalyst **3j** (0.04 mmol), in $CHCl_3$/acetone 7:1 (1.0 mL) as a mixture of solvents at -20 ºC. For the purification of the title compound was used silica gel (AcOEt/hexane 1/3 as eluent). ^{1}H NMR ($CDCl_3$): δ 8.07-8.05 (m, 1H), 7.99-7.97 (m, 1H), 7.80-7.78 (m, 2H), 3.56-3.50 (m, 1H), 3.29 (dd, *J* = 16.4, 5.2 Hz, 1H), 3.31-3.26 (m, 1H), 3.05 (dd, *J* = 16.4, 6.8 Hz, 1H), 2.96 (d, *J* = 14.4 Hz, 1H), 2.53 (td, *J* = 13.6, 6.0 Hz, 1H), 2.23-2.12 (m, 2H), 1.72-1.52 (m, 4H). ^{13}C NMR ($CDCl_3$): δ 196.3, 194.1, 185.1, 135.1(2C), 135.0, 134.4, 127.3, 111.5, 110.9, 83.7, 48.0, 44.1, 40.5, 31.2, 29.7, 28.7, 19.6. HRMS: Calculated for $[C_{19}H_{16}N_2O_2Na]^+$: 327.1109; found: 327.1105. The ee was determined by HPLC using Chiralpak AD column [hexane/*i*-PrOH (90:10)]; flow rate 1.0 mL/min; τ_{minor} = 28.3 min, τ_{major} = 31.7 min (10% ee). $[\alpha]_D^{rt}$: -132.0 (c = 0.1, CH_2Cl_2).

Compounds in Table 3

General procedure for the aromatization acid catalyzed reaction

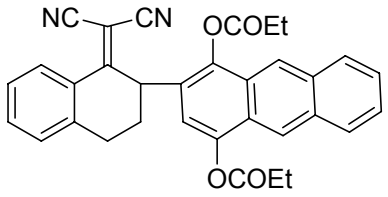
A flask equipped with a magnetic stirring bar was charged with compound **4** (0.1 mmol), and the corresponding anhydride (0.5 mmol). Then 5 μL of concentrated H_2SO_4 (0.05 mmol) was added. After 2 min the mixture was diluted with 1 mL of CH_2Cl_2 and directly charged and purified by FC (eluent indicated in each case).

(-)-2-(2,3-Dihydro-3-(1,4-diacetoxynaphthalen-3-yl)naphthalen-4(1H)-ylidene)malononitrile (5a)



The title compound (74% yield) was synthesized according to the general procedure after 1 min employing **4a** (0.1 mmol) and Ac_2O (0.5 mmol) (Et_2O/hexane 1/1 as eluent). This reaction could be done in 6.0 mmol scale (69% yield) ^{1}H NMR ($CDCl_3$): δ 8.15 (d, *J* = 8.0 Hz, 1H), 7.85-7.83 (m, 1H), 7.69-7.67 (m, 1H), 7.57-7.52 (m, 3H), 7.49 (t, *J* = 8.0 Hz, 1H), 7.47 (d, *J* = 7.6 Hz, 1H), 6.79 (s, 1H), 4.69 (dd, *J* = 8.4, 6.4 Hz, 1H), 2.95-2.89 (m, 1H), 2.75-2.67 (m, 1H), 2.49-2.43 (m, 1H), 2.37 (s, 3H), 2.36 (s, 3H), 1.91-1.82 (m, 1H). ^{13}C NMR ($CDCl_3$): δ 172.8, 169.3, 168.5, 144.9, 142.3, 141.9, 133.6, 131.1, 129.1, 128.8, 128.3, 127.9, 127.6, 127.4, 127.1, 127.1 122.1, 121.7, 117.5, 113.7, 112.5, 84.1, 43.2, 38.3, 31.3, 29.1, 28.2. HRMS: Calculated for $[C_{27}H_{20}N_2O_4Na]^+$: 459.1320; found: 459.1320. The ee was determined by HPLC using Chiralpak OD column [hexane/*i*-PrOH (80:20)]; flow rate 1.0 mL/min; τ_{major} = 15.2 min, τ_{minor} = 18.7 min (75% ee). $[\alpha]_D^{rt}$: -98.0 (c = 0.1, CH_2Cl_2).

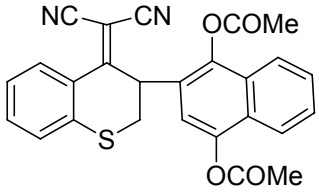
(-)-2-(1-(Dicyanomethylene)-1,2,3,4-tetrahydronaphthalen-2-yl)anthracene-1,4-diyl dipropionate (5b)



The title compound (71% yield) was synthesized according to the general procedure after 1 min employing **4b** (0.10 mmol) and propionic anhydride (0.50 mmol) (EtOAc/hexane 1/4 as eluent). ^{1}H NMR (60 ºC, $CDCl_3$): δ 8.40 (s, 1H), 8.26 (s, 1H), 8.18 (d, *J* = 7.6 Hz, 1H), 7.99-7.96 (m, 2H), 7.58 (dd, *J* = 7.2, 0.8 Hz, 1H), 7.52-7.48 (m, 3H), 7.38 (d, *J* = 7.6, 1H), 6.72 (s, 1H), 4.73 (t, *J* = 8.4 Hz,

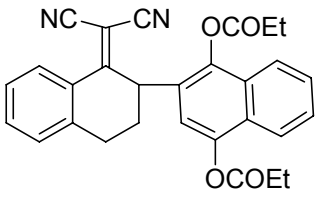
1H), 2.97-2.68 (m, 6H), 2.53-2.46 (m, 1H), 1.94-1.86 (m, 1H), 1.42 (t, *J* = 7.6 Hz, 3H), 1.35 (t, *J* = 7.6 Hz, 3H). ^{13}C NMR ($CDCl_3$): δ 173.5 (2C), 172.6, 145.3, 142.7, 141.7, 133.9, 132.5, 132.1, 131.3, 129.1, 129.0, 128.7, 128.6, 128.4, 127.9, 127.6, 126.9, 126.8, 126.2, 125.6, 121.5, 121.1, 114.1, 112.6, 84.4, 43.4, 29.1, 28.7, 28.1, 27.9, 9.7, 9.4. HRMS: Calculated for $[C_{33}H_{26}N_2O_4Na]^+$: 537.1785; found: 537.1779. The ee was determined by HPLC using Chiralcel OD column [hexane/*i*-PrOH (90:10)]; flow rate 1.0 mL/min; τ_{minor} = 22.0 min, τ_{major} = 28.7 min (90% ee). [α]: -127.0 (c = 0.1, CH_2Cl_2).

(-)-2-(4-(Dicyanomethylene)thiochroman-3-yl)naphthalene-1,4-diyl diacetate (5c)



The title compound (71% yield) was synthesized according to the general procedure after 1 min employing **4b** (0.1 mmol) and Ac_2O (0.5 mmol) (EtOAc/hexane 1/4 as eluent). ^{1}H NMR (60 ºC, $CDCl_3$): δ 7.88-7.84 (m, 2H), 7.736 (dd, *J* = 6.4, 2.4 Hz, 1H), 7.60-7.53 (m, 2H), 7.48 (d, *J* = 4.0 Hz, 2H), 7.38-7.33 (m, 1H), 7.06 (s, 1H), 5.01 (dd, *J* = 8.8, 6.0 Hz, 1H), 3.44 (dd, *J* = 13.6, 6.4 Hz, 1H), 3.09 (dd, *J* = 13.6, 9.2 Hz, 1H), 2.50 (s, 3H), 2.39 (s, 3H). ^{13}C NMR ($CDCl_3$): δ 172.5, 169.9, 168.9, 145.2, 142.1, 139.3, 133.2, 131.4, 130.0, 129.7, 128.1, 127.8 (2C), 127.4, 127.1, 126.9, 122.2, 121.9, 116.9, 113.1, 112.1, 86.2, 48.6, 32.8, 21.2, 21.1. HRMS: Calculated for $[C_{26}H_{18}N_2O_4SNa]^+$: 477.0879; found: 477.0880. The separation of enantiomers at HPLC was not possible. [α]: -320.0 (c = 0.1, CH_2Cl_2).

(-)-2-(2,3-Dihydro-3-(1,4-dipropionatoxynaphthalen-3-yl)naphthalen-4(1H)-ylidene)malononitrile (5d)



The title compound (93% yield) was synthesized according to the general procedure after 1 min employing **4a** (0.1 mmol) and propionic anhydride (0.5 mmol) (Et_2O/hexane 1/1 as eluent). ^{1}H NMR (60 ^{O}C, $CDCl_3$): δ 8.16 (d, *J* = 7.6 Hz, 1H), 7.82-7.80 (m, 1H), 7.67-7.65 (m, 1H), 7.55-7.48 (m, 3H), 7.44 (d, *J* = 7.6 Hz, 1H), 7.33 (d, *J* = 7.2 Hz, 1H), 6.73 (s, 1H), 4.69 (t, *J* = 7.6 Hz, 1H), 2.90 (dt, *J* = 10.8, 4.8 Hz, 1H), 2.75-2.60 (m, 6H), 2.45-2.41 (m, 1H), 1.95-1.84 (m, 1H), 1.33 (t, *J* = 7.2 Hz, 3H), 1.28 (t, *J* = 7.6 Hz, 3H).^{13}C NMR ($CDCl_3$): δ 172.9, 172.8, 172.0, 144.9, 142.3,

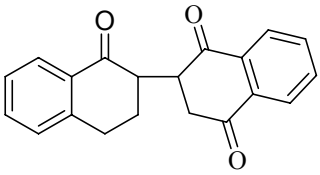
141.9, 133.5, 131.1, 129.1, 128.8, 128.8, 128.3, 128.3, 128.1, 127.5, 127.3, 127.1, 127.0, 122.1, 121.6, 113.7, 112.5, 94.5, 43.1, 29.2, 28.1, 27.7, 27.5, 9.2, 9.0. HRMS: Calculated for $[C_{29}H_{24}O_4N_2Na]^+$: 487.1633; found: 487.1643. The ee was determined by HPLC using Chiralpak OD column [hexane/*i*-PrOH (80:20)]; flow rate 1.0 mL/min; τ_{major} = 10.5 min, τ_{minor} = 13.4 min (70% ee). $[\alpha]_D^{rt}$: -90.3 (c = 0.6, CH_2Cl_2).

Compounds in Scheme 3

General procedure for the oxidative cleavage of 4a and 5a to 6 and 7 respectively.

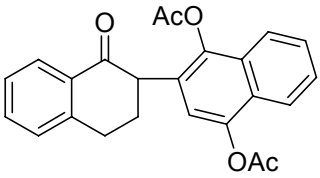
A flask equipped with a magnetic stirring bar was charged with **4a** or **5a** (0.1 mmol), $KMnO_4$ (0.25 mmol) and anhydrous $MgSO_4$ (0.2 mmol). Then acetone (1 mL) and water (one drop) was added and the mixture was stirred at room temperature for 15 min. The mixture was directly charged on FC (silica gel) (eluent indicated in each case).

(*R*)-2,3-dihydro-2-((*R*)-1,2,3,4-tetrahydro-1-oxonaphthalen-2-yl)naphthalene-1,4-dione (6)



The title compound (71% yield) was synthesized according to the general procedure as single diastereoisomer employing **4a** (0.1 mmol) (Et_2O/hexane 1/1 as eluent). ^{1}H NMR ($CDCl_3$): δ 8.10-8.05 (m, 2H), 7.77-7.74 (m, 2H), 7.50 (td, *J* = 7.5, 1.2 Hz, 1H), 7.33 (t, *J* = 7.4 Hz, 1H), 7.28-7.25 (m, 2H), 4.06 (ddd, *J* = 8.4 6.4, 2.4 Hz, 1H), 3.44 (ddd, *J* = 7.2, 4.8, 2.4 Hz, 1H), 3.21-3.00 (m, 4H), 2.22-2.12 (m, 2H). ^{13}C NMR ($CDCl_3$): δ 197.6, 197.1, 195.8, 143.9, 135.4, 135.2, 134.3, 134.2, 133.6, 132.3, 128.7, 127.5, 126.9, 126.7, 126.6, 47.9, 46.8, 40.5, 29.5, 26.2. HRMS: Calculated for $[C_{20}H_{16}O_3Na]^+$: 327.0997; found: 327.0991. The ee was determined by HPLC using Chiralpak OD column [hexane/*i*-PrOH (80:20)]; flow rate 1.0 mL/min; τ_{major} = 20.3 min, τ_{minor} = 25.0 min (68% ee). $[\alpha]_D^{rt}$: -69.2 (c = 0.2, CH_2Cl_2).

(+)-3,4-dihydro-2-(1,4-diacetoxynaphthalen-3-yl)naphthalen-1(2H)-one (7)



The title compound (82% yield) was synthesized according to the general procedure as single diastereoisomer employing **5a**

(0.1 mmol) (Et_2O/hexane 1/1 as eluent). ^1H NMR ($CDCl_3$): δ 8.04 (d, *J* = 8.0 Hz, 1H), 7.80-7.78 (m, 1H), 7.66-7.64 (m, 1H), 7.47-7.45 (m, 3H), 7.30-7.23 (m, 2H), 7.05 (s, 1H), 3.93 (dd, *J* = 8.0, 9.0 Hz, 1H), 3.10-3.03 (m, 2H), 2.40-2.30 (m, 2H), 2.35 (s, 3H), 2.30 (s, 3H).^{13}C NMR ($CDCl_3$): δ 196.6, 169.3, 169.1, 144.6, 143.9, 142.3, 133.6, 132.6, 128.8, 127.8, 127.1, 126.8, 126.6, 121.7, 121.6, 118.5, 49.7, 30.6, 303, 29.5, 21.0, 20.6. HRMS: Calculated for $[C_{24}H_{20}O_5Na]^+$: 411.1208; found: 411.1217. The ee was determined by HPLC using Chiralpak AD column [hexane/*i*-PrOH (80:20)]; flow rate 1.0 mL/min; τ_{major} = 24.0 min, τ_{minor} = 29.0 min (72% ee). $[\alpha]_D^{rt}$: +5 (c = 0.8, CH_2Cl_2).

NMR spectra of compounds 4e, 4l and 5d.

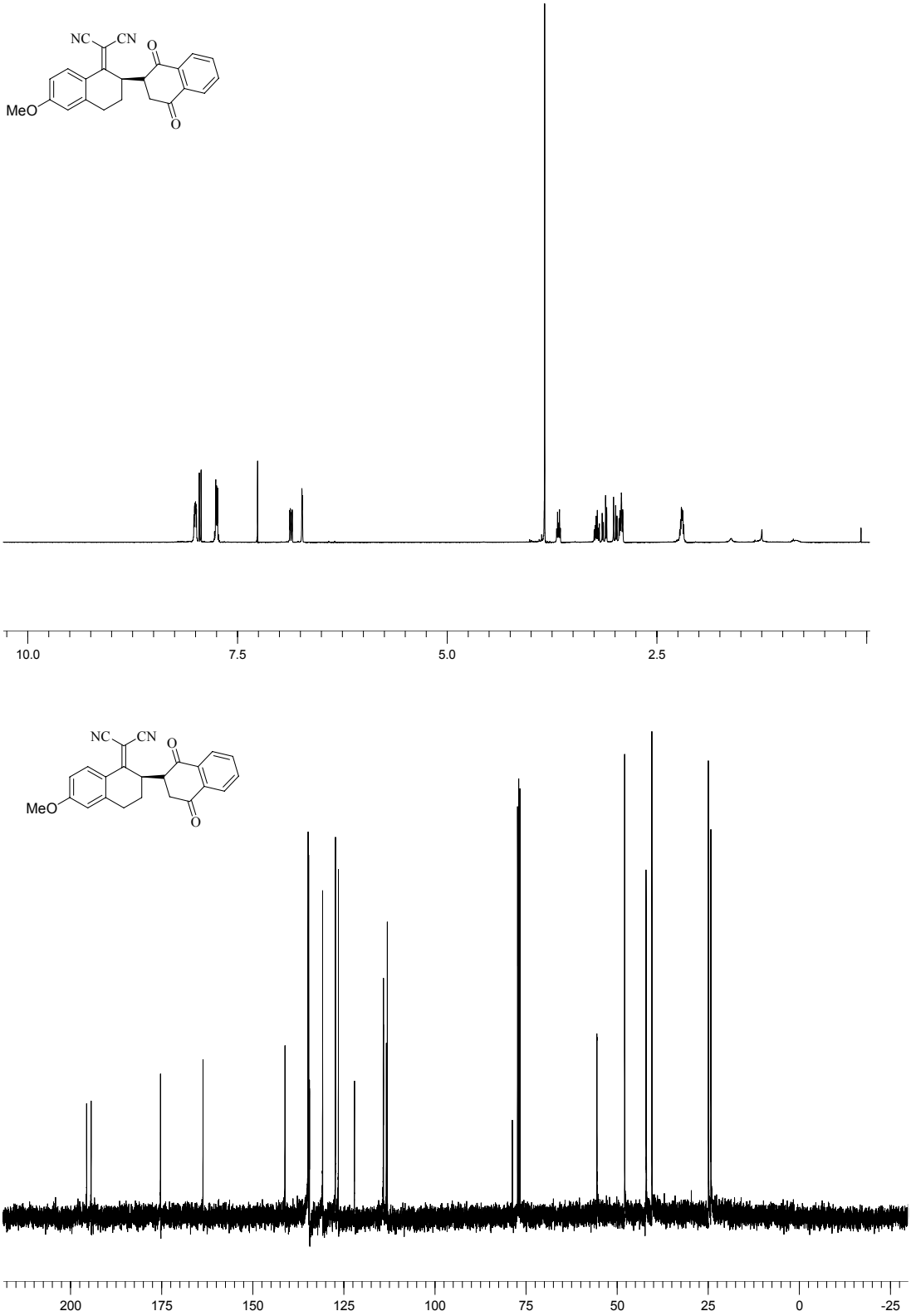


Figure S1: ^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) of **4e.**

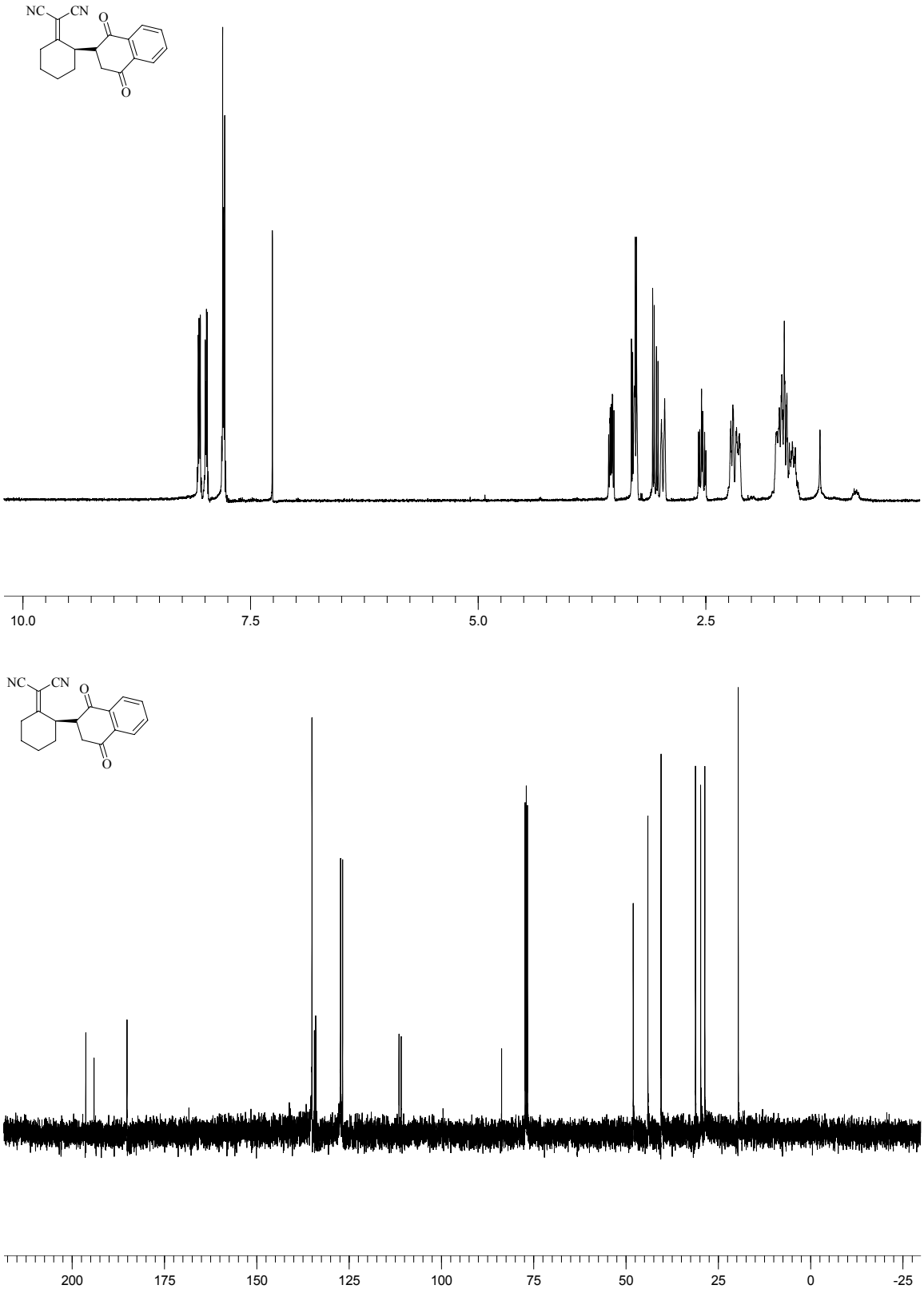


Figure S2: ^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) of **4l.**

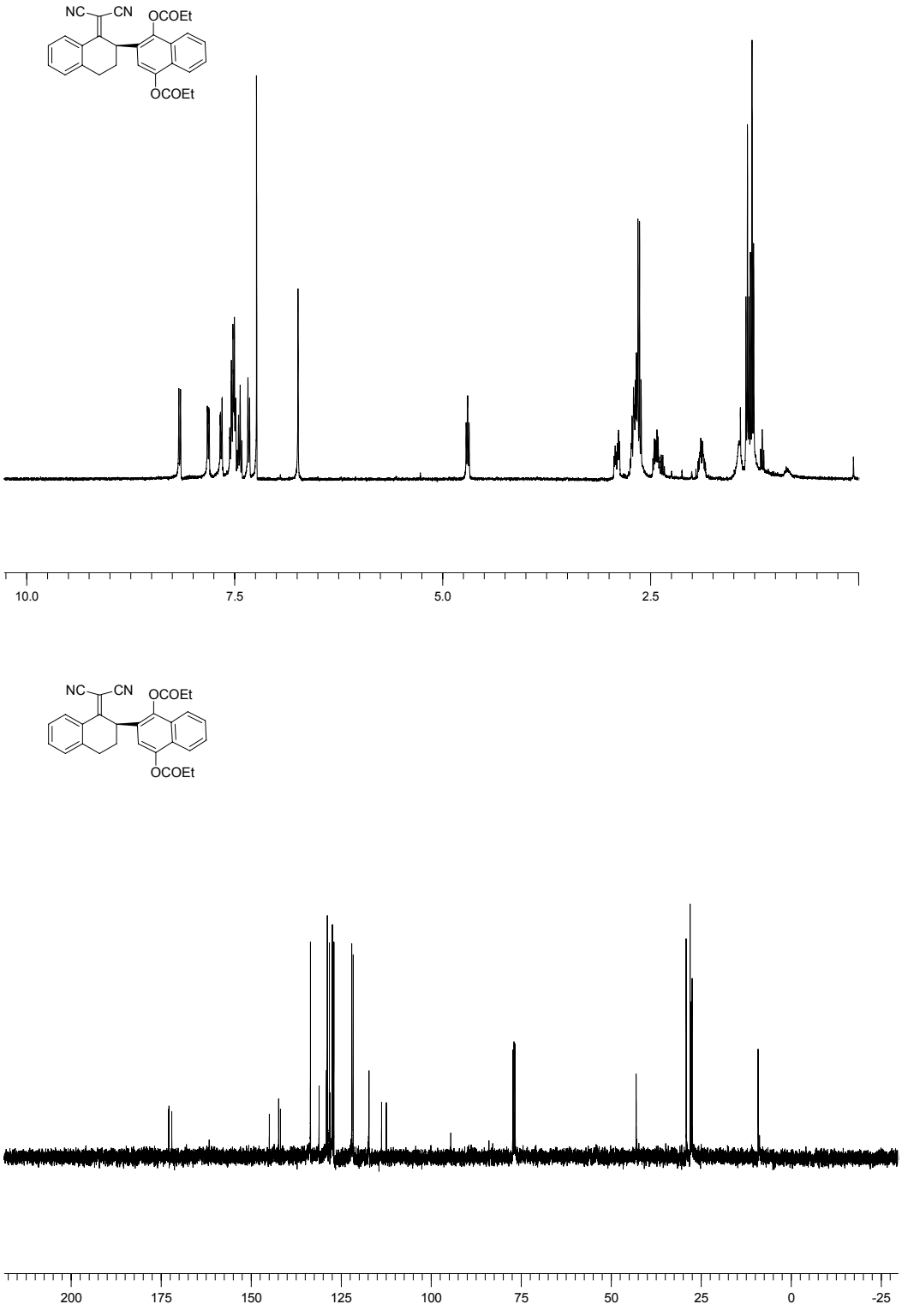
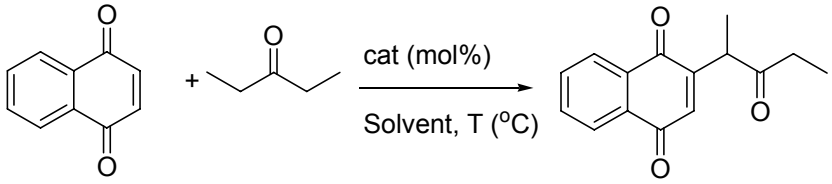
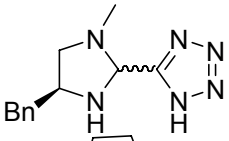
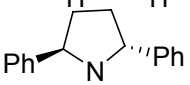
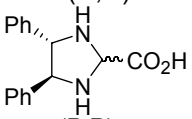
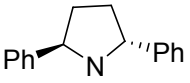
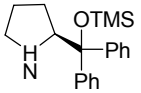


Figure S3: ^{1}H NMR (60 ^{o}C, 400 MHz) and ^{13}C NMR (60 ^{o}C, 100 MHz) of **5d**

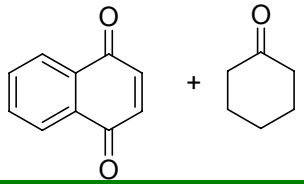
Table S-1. Addition of 2-pentanone to quinone **2a** in different conditions and catalyst.

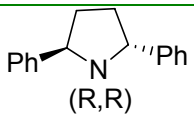
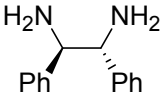
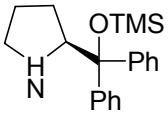


Ent	Catalyst[a]	Solvent (mL)	T (°C)	Time (h)	conv (%)	ee (%)
1	Proline	DMSO (0.2)/H_2O (0.05)	rt	72	no conv.	-
2	Proline	EtOH (0.2)/H_2O (0.05)	rt	72	no conv.	-
3	Proline	DMF (0.2)/H_2O (0.05)	rt	72	no conv.	-
4	Proline	CH_3CN (0.2)/H_2O (0.05)	rt	72	no conv.	-
5	Proline	CH_2Cl_2 (0,2)/H_2O (0,05)	rt	72	no conv.	-
7	Prolinamide	EtOH (0.2)/H_2O (0.05)	rt	48	no conv.	-
8	Prolinamide	DMF (0.2)/H_2O (0.05)	rt	48	no conv.	-
9	Prolinamide	EtOH (0.2)/H_2O (0.05)	rt	120	no conv.	-
10	Prolinamide	EtOH (0.15)/H_2O (0.1)	rt	120	no conv.	-
11	Prolinamide	DMF (0.2)/H_2O (0.05)	rt	120	no conv.	-
12	Prolinamide	DMF (0.15)/H_2O (0.1)	rt	120	no conv.	-
13	Prolinamide	EtOH (0.2)/H_2O (0.05)	40	120	-[b]	-
14	Prolinamide	DMF (0.2)/H_2O (0.05)	40	120	-[b]	-
15	Prolinamide	DMF (0.2)/H_2O (0.02)	rt	120	no conv.	-
16	Prolinamide	EtOH (0.2)/H_2O (0.02)	rt	120	no conv.	-
17	(*S*,*S*)-1,2-diphenylethyl diamine	DMF (0.2)/H_2O (0.025)	rt	240	no conv.	-
18	(*S*,*S*)-1,2-diphenylethyl diamine	THF (0.2)/H_2O (0.025)	rt	240	no conv.	-
19		DMF (0.2)/H_2O (0.025)	rt	240	no conv.	-
20	 (R,R)	DMF (0.2)/H_2O (0.025)	rt	240	no conv.	-
21	 (R,R)	DMF (0.2)/H_2O (0.025)	rt	240	no conv.	-
22	(*S*,*S*)-1,2-diphenylethyl diamine	DMF (0.2)/H_2O (0.025) + AcOH (1 mL, 5eq)	rt	240	no conv.	-
23	 (R,R)	THF (0.2)/H_2O (0.025)	rt	240	no conv.	-
24		EtOH (0.2)/H_2O (0.02)	rt	120	no conv.	-

[a] The reaction were carried out with 10-20 mol% of catalyst. [b] The 1,4-naphthoquinone was converted into the corresponding hydroquinone.

Table. S-2. Addition of cyclohexanone to quinone **2a** using different conditions and catalyst.



Ent	Catalyst	mol% cat	solvent (mL)	T	time (h)	conv (%)	ee (%)
1	 (R,R)	10	DMF (0.2)/H_2O (0.025)	rt	240	no conv.	-
2	 (R,R)	20	DMF (0.2)/H_2O (0.025)	rt	240	no conv.	-
3	Proline	20	EtOH (0.2)/H_2O (0.02)	rt	24	no conv.	-
4		20	EtOH (0.2)/H_2O (0.02)	rt	24	no conv.	-

Absolute structure determination

The relative configuration of compounds in Table 1,2 was *anti* according to the X-ray crystal analysis of the compound *rac*-**4j** (Figure S4).[3] The absolute configuration of the product was established by assuming an identical stereochemical reaction course with the same nucleophile and catalyst **3j**, used by us and others.[1] Therefore the configuration of these compounds is 2*R*,3*R*.

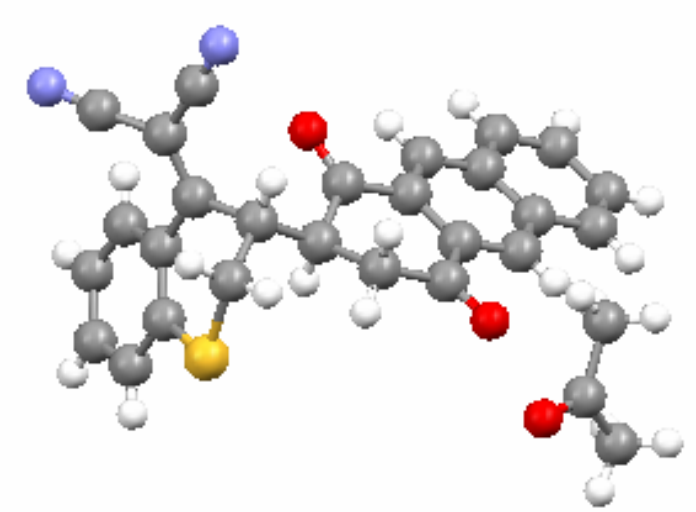


Figure S4: X-ray crystal structure of *rac*-**4j** including in the cell crystal structure one molecule of acetone.

[3] CCDC 666377 (rac-**4j**) contains the supplementary crystallographic data. These data can be obtained free of charge at www.ccdc.cam.ac.uk/conts/retrieving.html [or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: (internat.) +44(1223)336-033, e-mail: deposit@ccdc.cam.ac.uk].

[1] (a) T. B. Poulsen, M. Bell and K. A. Jørgensen, *Org. Biomol. Chem*., **2006**, *4*, 63. (b) D. Xue, Y.-C. Chen, Q. W. Wang, L.-F. Cun, J. Zhu, J.-G. Deng, *Org. Lett.* **2005**, *7*, 5293.