Electronic Supplementary Material (ESI) for Chemical Communications.

Experimental Procedures and Characterization Data for

Chiral squaramide catalyzed asymmetric synthesis of pyranones and pyranonaphthoquinones via cascade reactions of 1,3-dicarbonyls with Morita-Baylis-Hillman acetates of nitroalkenes

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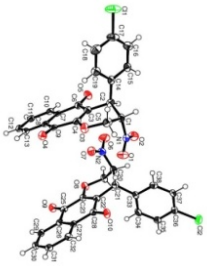
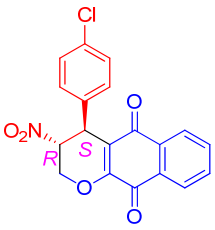
1. Table S1 Crystal data and structure refinement for **5j**





5j

Identification code	inn008
Empirical formula	C38 H24 N2 O10 Cl2
Formula weight	739.49
Temperature	150(2) K
Wavelength	0.71073 A
Crystal system, space group	Orthorhombic, P 21 21 21
Unit cell dimensions	a = 8.0662 (3) A α = 90 deg.
	b = 12.7774 (4) A β = 90 deg
	c = 31.4054 (11) A γ = 90 deg.
Volume	3236.80 (19) A^3

Z, Calculated density	4, 1.517 Mg/m^3
Absorption coefficient	0.268 mm^1
F(000)	1520
Crystal size	0.23 x 0.17 x 0.13 mm
Theta range for data collection	2.9805 to 32.2090 deg.
Limiting indices	-9<=h<=9, -15<=k<=15, -37<=l<=37
Reflections collected / unique	13214 / 2550 [R(int) = 0.0373]
Completeness to theta	= 25, 99.7%
refine_ls_abs_structure_Flack	0.05(9)

2. Experimental section

3. General experimental details

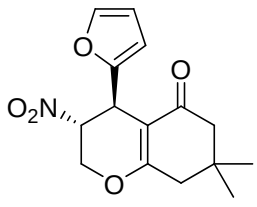
The melting points recorded are uncorrected. NMR spectra (^{1}H, ^{1}H decoupled ^{13}C and ^{13}C-APT) were recorded with TMS as the internal standard. The coupling constants (*J* values) are given in Hz. High resolution mass spectra were recorded under ESI Q-TOF conditions. The optical rotations were recorded on a digital polarimeter. X-ray data were collected on a diffractometer equipped with graphite monochromated Mo Kα radiation. The structure was solved by direct methods shelxs97 and refined by full-matrix least squares against F^2 using shelxl97 software. Catalyst **C1** was commercially available (Aldrich) and **C2-C10** were prepared following reported procedures.[1-6] The MBH acetates[7] were prepared from corresponding alcohols.[8]

4. General procedure for the synthesis of pyrans 4 and 5

To a stirred solution of MBH acetate **2** (0.5 mmol) in 1,4-dioxane (2.5 mL) under N_2, was added catalyst **C9** (32 mg, 0.05 mmol) and the reaction mixture was stirred at rt. After 5 minutes, 1,3-dicarbonyl compound **1** (0.5 mmol) was added and continued the stirring till the completion of the reaction. The solvent was evaporated in *vacuo* and the crude residue was directly purified by silica gel column chromatography by eluting with 20-30% EtOAc-pet ether (gradient elution) to afford pyran **4** or **5**.

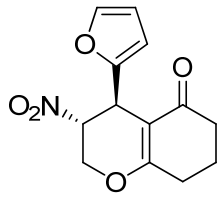
5. Experimental data for compounds 4a-c and 5a-l

(3*R*,4*S*)-4-(Furan-2-yl)-7,7-dimethyl-3-nitro-3,4,7,8-tetrahydro-2H-chromen-5(6H)-one (4a)



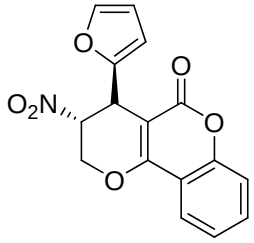
Yellow sticky liquid; Yield 134 mg, 92% (dr 91:09); υ_{max}(film)/cm^{-1} 2962m, 2931m, 1630s, 1556s, 1455m, 1401m, 1374m, 1358m, 1266m, 1128m, 1098 m, 738vs, δ_H(400 MHz: $CDCl_3$, major) 7.33 (1H, d, *J* 1.2), 6.29 (1H, dd, *J* 3.2, 1.2), 6.09 (1H, d, *J* 3.2 Hz,), 4.91 (1H, ddd collapsed to q, *J* 2.4), 4.87 (1H, dt, *J* 12.4, 2.4), 4.85 (1H, t, *J* 2.4), 4.31 (1H, dd, *J* 12.4, 2.4), 2.28-2.43 (4H, m), 1.11 (3H, s), 1.05 (3H, s); δ_C (100 MHz: $CDCl_3$, major) 196.2, 169.4, 152.0, 142.6, 110.9, 108.7, 107.3, 79.5, 64.0, 50.7, 42.2, 32.6, 30.9, 29.2, 27.5; MS (ES^+, Ar) m/z (rel intensity) 292 (MH^+, 100), 245 (25); HRMS (ES^+, Ar) calcd for $C_{15}H_{18}NO_5$ (MH^+) 292.1185, found 292.1177; $[\alpha]^{20}_D$ -85.20 (c 1.0, $CHCl_3$); HPLC: Chiralcel AD-H (pet ether/*i*-PrOH = 90/10, flow rate 0.5 mL/min, λ = 230 nm), t_R (major) = 23.11 min, t_R (minor) = 50.59 min; 95% ee.

(3*R*,4*S*)-4-(Furan-2-yl)-3-nitro-3,4,7,8-tetrahydro-2H-chromen-5(6H)-one (4b)



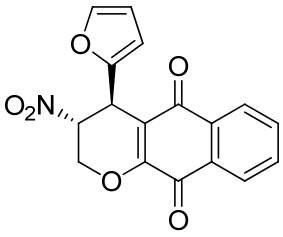
Yellow sticky liquid; Yield 108 mg, 81% (dr 88:12); υ_{max}(film)/cm^{-1} 2953m, 2929m, 1660m, 1627s, 1552s, 1456m, 1400m, 1375m, 1361m, 1268m, 1101m, 1015m, 740vs; δ_H(500 MHz: $CDCl_3$, major) 7.33 (1H, d, *J* 1.1), 6.28 (1H, dd, *J* 3.2, 1.5), 6.07 (1H, d, *J* 3.2 Hz,), 4.82-4.89 (3H, unresolved m), 4.28 (1H, dd, *J* 11.6, 1.9), 2.46-2.52 (2H, m), 2.36-2.42 (2H, m), 1.95-2.04 (2H, m); δ_C(125 MHz: $CDCl_3$, major) 196.2, 171.1, 152.2, 142.6, 110.9, 108.6, 108.3, 79.5, 63.6, 36.8, 30.9, 28.5, 20.7; MS (ES$^+$, Ar) m/z (rel intensity) 265 ([MH+1]$^+$, 25), 264 (MH$^+$, 100), 218 (10), 217 (25), 189 (5), 150 (10); HRMS (ES$^+$, Ar) calcd for $C_{13}H_{14}NO_5$ (MH$^+$) 264.0872, found 264.0871; $[\alpha]^{20}_D$ -154.84 (c 1.0, $CHCl_3$); HPLC: Chiralcel AD-H (pet ether/*i*-PrOH = 90/10, flow rate 0.5 mL/min, λ = 230 nm), t_R (major) = 18.39 min, t_R (minor) = 24.93 min; 92% ee.

(3*R*,4*R*)-4-(Furan-2-yl)-3-nitro-3,4-dihydropyrano[3,2-c]chromen-5(2H)-one (4c)



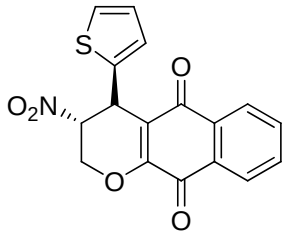
Yellow viscous liquid; Yield 147 mg, 93% (dr 99:1); υ_{max}(film)/cm^{-1} 2932w, 1717vs, 1634vs, 1556vs, 1612s, 1578m, 1456m, 1410m, 1376m, 1357m, 1315m, 1276m, 1206m, 1177m, 1119s, 1053m, 1017w, 989m, 739m; δ_H(400 MHz: $CDCl_3$, major) 7.78 (1H, d, *J* 7.3), 7.56 (1H, t, *J* = 7.3), 7.28-7.34 (3H, m), 6.31 (1H, d, *J* 4.7), 6.23 (1H, d, *J* 3.0), 5.19 (1H, d, *J* = 12.9), 5.08 (1H, unresolved), 5.02 (1H unresolved), 4.59 (1H d, *J* 12.9); δ_C (100 MHz: $CDCl_3$, major) 161.3, 159.7, 152.6, 150.5, 143.0, 132.8, 124.4, 123.0, 116.8, 114.5, 111.0, 109.4, 97.8, 79.1, 64.2, 32.4; MS (ES$^+$, Ar) m/z (rel intensity) 315 ([MH+1]$^+$, 25), 314 (MH$^+$, 100), 297 (15), 267 (16), 200 (25); HRMS (ES$^+$, Ar) calcd for $C_{13}H_{12}NO_6$ (MH$^+$) 314.0665, found 314.0649; $[\alpha]^{20}_D$ -69.48 (c 1.0, $CHCl_3$); HPLC: Chiralcel AD-H (pet ether/*i*-PrOH = 90/10, flow rate 0.5 mL/min, λ = 230 nm), t_R (major) = 36.04 min, t_R (minor) = 45.21 min; 49% ee.

(3*R*,4*S*)-4-(Furan-2-yl)-3-nitro-3,4-dihydro-2H-benzo[g]chromene-5,10-dione (5a)



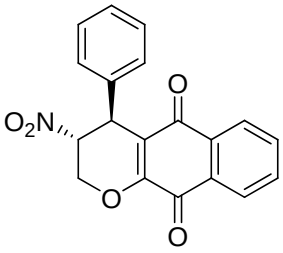
Yellow solid; mp 164 ^oC; Yield 132 mg, 81% (dr 98:2); υ_{max}(film)/cm^{-1} 2933w, 1677s, 1654s, 1629vs, 1597m, 1580m, 1556s, 1455m, 1393m, 1370m, 1353m, 1335m, 1302m, 1268m, 1254m, 1201vs, 1155w, 1088m, 1011m, 948m, 727s; δ_H(500 MHz: $CDCl_3$, major) 8.12-8.16 (1H, m), 8.06-8.09 (1H, m), 7.71-7.77 (2H, m), 7.38 (1H, dd, *J* 1.9, 0.7), 6.35 (2H, dd, *J* 3.3, 1.9), 5.18-5.20 (1H, unresolved), 5.18 (1H, dt, *J* 14.4, 1.7), 5.02 (1H, ddd collapsed to q, *J* 1.7), 4.56 (1H, dt, *J* 14.4, 1.7); δ_C(125 MHz: $CDCl_3$, major) 182.5, 178.6, 154.1, 150.4, 143.3, 134.7, 133.9, 131.9, 130.9, 126.9, 126.8, 117.2, 111.2, 109.6, 79.1, 64.6, 31.6; MS (ES$^+$, Ar) m/z (rel intensity) 327 ([MH+1]$^+$, 25), 326 (MH$^+$, 100), 279 (58), 251 (20), 212 (15); HRMS (ES$^+$, Ar) calcd for $C_{17}H_{12}NO_6$ (MH$^+$) 326.0665, found 326.0679; $[\alpha]^{20}_D$ -91.24 (c 1.0, $CHCl_3$); HPLC: Chiralcel OD-H (pet ether/*i*-PrOH = 80/20, flow rate 1.0 mL/min, λ = 230 nm), t_R (major) = 29.01 min, t_R (minor) = 35.10 min; >99% ee.

(3*R*,4*R*)-3-Nitro-4-(thiophen-2-yl)-3,4-dihydro-2H-benzo[g]chromene-5,10-dione (5b)



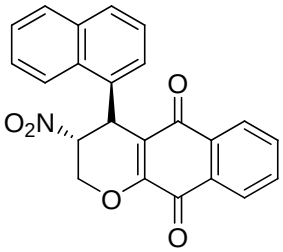
Yellow solid; mp 155 ^{o}C; Yield 136 mg, 80% (dr 71:29); υ_{max}(film)/cm^{-1} 2939w, 1677m, 1654m, 1597w, 1580w, 1629s, 1555m, 1456w, 1394w, 1370w, 1335m, 1302w, 1270w, 1254m, 1201vs, 1088m, 1011m, 948m, 727s; δ_H(400 MHz: $CDCl_3$, major) δ 8.13-8.16 (1H, m), 8.01-8.06 (1H, m), 7.71-7.76 (2H, m), 7.21-7.28 (1H, m), 6.92-6.99 (2H, m), 5.33 (1H, unresolved), 5.15 (1H, dd, *J* 13.2, 1.8), 4.91 (1H, ddd collapsed to q, *J* 1.8), 4.54 (1.8, dd, *J* 13.2); δ_C(100 MHz: $CDCl_3$, major) 182.5, 178.6, 153.6, 141.7, 134.8, 133.9, 131.8, 130.9, 127.9, 127.0, 126.9, 126.8, 126.2, 119.2, 81.4, 63.7, 32.5; MS (ES$^+$, Ar) m/z (rel intensity) 343 ([MH+1]$^+$, 28), 342 (MH$^+$, 100), 295 (19), 214 (11), 158 (12); HRMS (ES$^+$, Ar) calcd for $C_{17}H_{12}NO_5S$ (MH$^+$) 342.0436, found 342.0450; $[\alpha]^{20}_D$ -117.96 (c 1.0, $CHCl_3$); HPLC: Chiralcel AD-H (pet ether/*i*-PrOH = 80/20, flow rate 1.0 mL/min, λ = 230 nm), t_R (major) = 9.85 min, t_R (minor) = 42.97 min; 97% ee.

(3*R*,4*S*)-3-Nitro-4-phenyl-3,4-dihydro-2H-benzo[g]chromene-5,10-dione (5c)

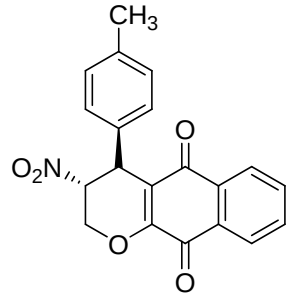


Yellow solid; mp 220 ^{o}C; Yield 141 mg, 84% (dr 93:7); υ_{max}(film)/cm^{-1} 2927s, 1683s, 1626s, 1552s, 1454v, 1374vw, 1333w, 1302m, 1255s, 1201vs, 1093s, 744m; δ_H(400 MHz: $CDCl_3$, major) δ 8.16 (1H, dd, *J* 5.7, 3.2), 8.02 (1H, dd, *J* 5.7, 3.2), 7.73 (2H, dd, *J* 5.7, 3.3), 7.26-7.40 (5H, m), 5.10 (1H, unresolved), 5.08 (1H, dt, *J* = 13.1, 2.1), 4.82 (1H, ddd collapsed to q, *J* 2.1), 4.36 (1H, dd, *J* 13.1, 2.1); δ_C(100 MHz: $CDCl_3$, major) 182.6, 178.6, 154.4, 139.0, 134.7, 133.8, 131.9, 131.0, 129.7, 128.5, 128.1, 126.9, 126.8, 118.9, 82.0, 63.3, 37.6; MS (ES$^+$, Ar) m/z (rel intensity) 337 ([MH+1]$^+$, 25), 336 (MH$^+$, 100), 289 (20), 214 (18), 158 (17); HRMS (ES$^+$, Ar) calcd for $C_{19}H_{14}NO_5$ (MH$^+$) 336.0872, found 336.0881; $[\alpha]^{20}_D$ -139.44 (c 1.0, $CHCl_3$); HPLC: Chiralcel AD-H (pet ether/*i*-PrOH = 80/20, flow rate 1.0 mL/min, λ = 230 nm), t_R (major) = 8.96 min, t_R (minor) = 50.64 min; 99% ee.

(3*R*,4*R*)-4-(Naphthalen-1-yl)-3-nitro-3,4-dihydro-2H-benzo[g]chromene-5,10-dione (5d)



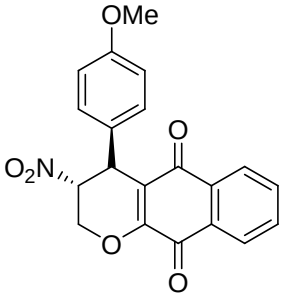
Yellow solid; mp 227 ^{o}C; Yield 165 mg, 86% (dr >99:1); υ_{max}(film)/cm^{-1} 2920m, 1680m, 1659m, 1628s, 1553vs, 1333w, 1271s, 1200s, 1157m, 1090 s, 1019m, 805m, 740s; δ_H(400 MHz: $CDCl_3$,) 8.32 (1H, d, *J* 8.6), 8.17-8.21 (1H, m), 7.98-8.02 (1H, m), 7.93 (1H, d, *J* 7.9), 7.82 (1H, d, *J* 7.9), 7.68-7.77 (2H, m), 7.70 (1H, d, *J* 8.6), 7.60 (1H, t, *J* 7.9), 7.36 (1H, t, *J* 7.9), 7.15 (1H, d, *J* 7.9), 5.92 (1H, unresolved), 5.06 (1H, d, *J* 13.1), 4.91 (1H, unresolved), 4.29 (1H, d, *J* 13.1); δ_C(100 MHz: $CDCl_3$,) 182.5, 178.6, 155.1, 134.7, 134.6, 134.5, 133.8, 131.9, 131.0, 130.2, 129.7, 129.5, 128.0, 126.9, 126.8 (× 2), 126.2, 125.4, 122.0, 118.8, 80.2, 63.2, 34.2; MS (ES$^+$, Ar) m/z (rel intensity) 387 ([MH+1]$^+$, 25), 386 (MH$^+$, 100), 340 (22), 339 (90), 321 (35), 311 (37); HRMS (ES$^+$, Ar) calcd for $C_{23}H_{16}NO_5$ (MH$^+$) 386.1028, found 386.1020; $[\alpha]^{20}_D$ -171.36 (c 1.0, $CHCl_3$); HPLC: Chiralcel AD-H (pet ether/*i*-PrOH = 80/20, flow rate 1.0 mL/min, λ = 230 nm), t_R (major) = 9.42 min, t_R (minor) = 74.68 min; >99% ee.



(3*R*,4*R*)-3-Nitro-4-p-tolyl-3,4-dihydro-2H-benzo[g]chromene-5,10-dione (5e)

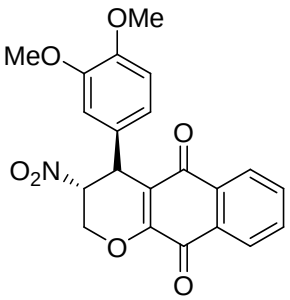
Yellow solid; mp 165-168 ^{o}C; Yield 144 mg, 83% (dr 89:11); υ_{max}(film)/cm^{-1} 2929w, 1680s, 1652m, 1625s, 1547s, 1461m, 1373m, 1334m, 1301m, 1252s, 1198vs, 1092m, 766m; δ_H (400 MHz: $CDCl_3$, major) 8.16 (1H, dd, *J* 9.0, 2.4), 8.02 (1H, dd, *J* 9.0, 2.4), 7.75 (2H, dd, *J* 9.0, 2.4), 7.16, 7.17 (4H, ABq, *J* 1.7), 5.07 (1H, dt, *J* 13.6, 1.9), 5.05 (1H, unresolved), 4.80 (1H, ddd collapsed to q, *J* 1.9), 4.37 (1H, dt, *J* 13.6, 1.9), 2.32 (3H, s); δ_C(100 MHz: $CDCl_3$, major) 182.7, 178.7, 154.4, 138.5, 136.0, 134.7, 133.8, 131.9, 131.0, 130.4, 127.9, 126.8, 126.7, 119.1, 82.1, 63.3, 37.3, 21.2; MS (ES$^+$, Ar) m/z (rel intensity) 351 ([MH+1]$^+$, 25), 350 (MH$^+$, 100), 303 (30), 212 (5); HRMS (ES$^+$, Ar) calcd for $C_{20}H_{16}NO_5$ (MH$^+$) 350.1028, found 350.1033; $[\alpha]^{20}_D$ -87.64 (c 1.0, $CHCl_3$); HPLC: Chiralcel AD-H (pet ether/*i*-PrOH = 80/20, flow rate 1.0 mL/min, λ = 230 nm), t_R (major) = 8.74 min, t_R (minor) = 41.83 min; 98% ee.

(3*R*,4*R*)-4-(Methoxyphenyl)-3-nitro-3,4-dihydro-2H-benzo[g]chromene-5,10-dione (5f)



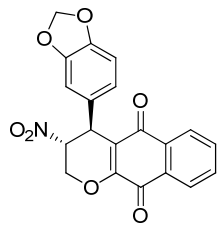
Yellow solid; mp 120 ^{o}C; Yield 164 mg, 90% (dr 89:11); υ_{max}(film)/cm^{-1} 2933m, 1682s, 1652m, 1626s, 1593m, 1551s, 1515s, 1455m, 1334m, 1301m, 1265s, 1244s, 1200s, 1157m, 1146s, 1093m, 1025s, 736s, 725s; δ_H(400 MHz: $CDCl_3$, major) 8.17 (1H, dd, *J* 9.1, 2.4), 8.03 (1H, dd, *J* 9.1, 2.4), 7.74 (2H, dd, *J* 9.1, 2.4), 7.20 (2H, d, *J* 6.8), 6.90 (2H, d, *J* 6.8), 5.07 (1H, dt, *J* 12.7, 2.6), 5.04 (1H, d, *J* 2.6), 4.78 (1H, ddd collapsed to q, *J* 2.6), 4.37 (1H, dd, *J* 12.7, 2.6), 3.78 (3H, s); δ_C(100 MHz: $CDCl_3$, major) 182.6, 178.6, 159.6, 154.2, 134.6, 133.7, 131.8, 130.9, 130.0, 129.2, 126.7, 126.6, 119.2, 115.0, 82.0, 63.2, 55.5, 36.8; MS (ES$^+$, Ar) m/z (rel intensity) 367 ([MH+1]$^+$, 28), 366 (MH$^+$, 100), 338 (80), 319 (15), 244 (15), 214 (18), 158 (18); HRMS (ES$^+$, Ar) calcd for $C_{20}H_{16}NO_6$ (MH$^+$) 366.0978, found 366.0991; $[\alpha]^{20}_D$ -86.12 (c 1.0, $CHCl_3$); HPLC: Chiralcel AD-H (pet ether/*i*-PrOH = 80/20, flow rate 1.0 mL/min, λ = 230 nm), t_R (major) = 12.18 min, t_R (minor) = 87.19 min; 98% ee.

(3*R*,4*R*)-4-(3,4-Dimethoxyphenyl)-3-nitro-3,4-dihydro-2H-benzo[g]chromene-5,10-dione (5g)



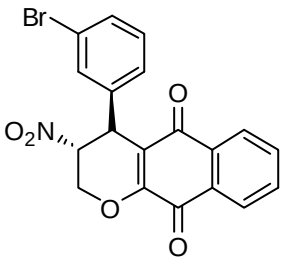
Yellow solid; mp 223 ^{o}C; Yield 174 mg, 88% (dr >99:1); υ_{max}(film)/cm^{-1} 2931m, 1681s, 1653m, 1625m, 1550s, 1454m, 1373w, 1356w, 1333m, 1301m, 1264s, 1244s, 1157m, 1145m, 1093m, 1025s, 985m, 724 s; δ_H(400 MHz: $CDCl_3$) 8.18 (1H, dd, *J* 9.0, 3.3), 8.04 (1H, dd, *J* 9.0, 3.3), 7.74 (2H, dd, *J* 9.0, 3.3), 6.87 (1H, d, *J* 2.1), 6.81 (1H, d, *J* 8.3), 6.69 (1H, dd, *J* 8.3, 2.1), 5.08 (1H, dt, *J* 13.1, 2.2), 5.02 (1H, unresolved), 4.81 (1H, ddd collapsed to q, *J* 2.2), 4.41 (1H, dd, *J* 13.1, 2.2), 3.89 (3H, s), 3.84 (3H, s); δ_C(125 MHz: $CDCl_3$) 182.7, 178.7, 154.3, 150.0, 149.3, 134.7, 133.8, 131.9, 131.4, 130.9, 126.9, 126.8, 120.1, 119.1, 111.7, 111.2, 82.0, 63.4, 56.3, 56.1, 37.3; MS (ES$^+$, Ar) m/z (rel intensity) 397 ([MH+1]$^+$, 25), 396 (MH$^+$, 100), 349 (20), 212 (25); HRMS (ES$^+$, Ar) calcd for $C_{21}H_{18}NO_7$ (MH$^+$) 396.1083, found 396.1094; $[\alpha]^{20}_D$ -89.40 (c 1.0, $CHCl_3$); HPLC: Chiralcel AD-H (pet ether/*i*-PrOH = 80/20, flow rate 1.0 mL/min, λ = 230 nm), t_R (major) = 13.42 min, t_R (minor) = 63.51 min; 89% ee.

(3*R*,4*S*)-4-(Benzo[d][1,3]dioxol-4-yl)-3-nitro-3,4-dihydro-2H-benzo[g]chromene-5,10-dione (5h)



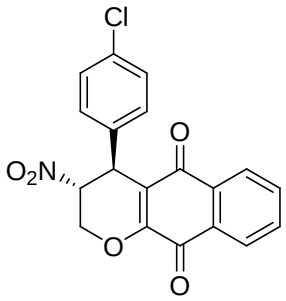
Orange solid; mp 211-213 ^{o}C; Yield 161 mg, 85% (dr 93:7); υ_{max}(film)/cm^{-1} 2927w, 1682m, 1657m, 1652s, 1627vs, 1552s, 1515s, 1463m, 1452m, 1334m, 1302m, 1264s, 1200s, 1145m, 1092m, 1023s, 725s; δ_H(400 MHz: $CDCl_3$, major) 8.12 (1H, dd, *J* 9.0, 2.4), 7.99 (1H, dd, *J* 9.0, 2.4), 7.72 (2H, dd, *J* 9.0, 2.4), 6.67-6.76 (3H, m), 5.89, 5.91 (2H, ABq, *J* 6.1), 5.07 (1H, dt, *J* 13.2, 1.9), 5.02 (1H, unresolved d), 4.79 (1H, d, *J* 1.9), 4.37 (1H, dd, *J* 13.2, 1.9); δ_C(125 MHz: $CDCl_3$, major) 182.7, 178.6, 154.4, 148.9, 148.0, 134.8, 133.9, 132.8, 131.9, 131.0, 126.9, 126.8, 121.5, 119.0, 109.2, 108.4, 101.8, 82.1, 63.0, 37.3; MS (ES$^+$, Ar) m/z (rel intensity) 381 ([MH+1]$^+$, 25), 380 (MH$^+$, 100), 333 (40), 212 (60); HRMS (ES$^+$, Ar) calcd for $C_{20}H_{14}NO_7$ (MH$^+$) 380.0770, found 380.0787; $[\alpha]^{20}_D$ -78.56 (c 1.0, $CHCl_3$); HPLC: Chiralcel AD-H (pet ether/*i*-PrOH = 80/20, flow rate 1.0 mL/min, λ = 230 nm), t_R (major) = 15.73 min, t_R (minor) = 80.44 min; 98% ee.

(3*R*,4*R*)-4-(3-bromophenyl)-3-nitro-3,4-dihydro-2H-benzo[g]chromene-5,10-dione (5i)



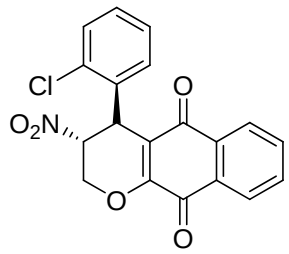
Yellow solid; mp 130 ^{o}C; Yield 166 mg, 80% (dr >99:1); υ_{max}(film)/cm^{-1} 2926w, 1683s, 1654m, 1627s, 1553s, 1301m, 1254s, 1201vs, 1092s, 734vs; δ_H(400 MHz: $CDCl_3$) 8.14-8.18 (1H, m), 8.01-8.05 (m, 1H), 7.73 (2H, dd, *J* 9.0, 2.1), 7.47 (1H, dt, *J* 7.4, 1.6), 7.42 (1H, t, *J* 1.6), 7.21-7.30 (2H, m), 5.11 (1H, dt, *J* 12.3, 2.2), 5.08 (1H, d, *J* 2.2), 4.81 (1H, ddd collapsed to q, *J* 2.2), 4.35 (1H, dd, *J* 12.3, 2.2), δ_C(100 MHz: $CDCl_3$) 182.5, 178.4, 154.6, 141.2, 134.7, 133.9, 131.7, 131.1, 130.8, 126.8, 126.7, 123.7, 118.2, 81.6, 63.2, 37.2; MS (ES$^+$, Ar) m/z (rel intensity) 438 ([M+2]$^+$, 98), 436 (M$^+$, 100); HRMS (ES$^+$, Ar) calcd for $C_{19}H_{12}BrNO_5Na$ (MNa$^+$) 435.9791, found 435.9791; $[\alpha]^{20}_D$ -101.20 (c 1.0, $CHCl_3$); HPLC: Chiralcel AD-H (pet ether/*i*-PrOH = 80/20, flow rate 1.0 mL/min, λ = 230 nm), t_R (major) = 7.29 min, t_R (minor) = 47.83 min; 97% ee.

(3*R*,4*S*)-4-(4-Chlorophenyl)-3-nitro-3,4-dihydro-2H-benzo[g]chromene-5,10-dione (5j)



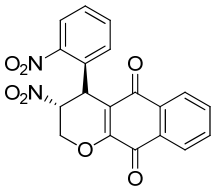
Yellow solid; mp 178 ^{o}C; Yield 153 mg, 83% (dr 92:8); υ_{max}(film)/cm^{-1} 2932w, 1684s, 1655m, 1627s, 1553s, 1492m, 1453w, 1372w, 1355w, 1333m, 1301m, 1255m, 1201s, 1157w, 1092s, 725s; δ_H(400 MHz: $CDCl_3$, major) 8.15 (1H, dd, *J* 9.0, 2.3), 8.03 (1H, dd, *J* 9.0, 2.3), 7.77 (2H, dd, *J* 9.0, 2.3), 7.25, 7.37 (4H, ABqt, *J* 7.0, 2.6), 5.09 (1H, dt, *J* 14.3, 2.0), 5.08 (1H, d, *J* 2.0), 4.79 (1H, ddd collapsed to q, *J* 2.0), 4.35 (1H, dt, *J* 14.3, 2.0); δ_C(100 MHz: $CDCl_3$, major) 182.5, 178.3, 154.4, 137.4, 134.7, 134.4, 133.8, 131.6, 130.7, 129.7, 129.4, 126.7, 126.6, 118.4, 81.6, 63.1, 37.0; MS (ES$^+$, Ar) m/z (rel intensity) 371 ([MH+1]$^+$, 35), 370 (MH$^+$, 100), 338 (30), 323 (32), 278 (10), 228 (15), 214 (35), 164 (10), 158 (50), 141 (15); HRMS (ES$^+$, Ar) calcd for $C_{19}H_{13}NO_5Cl$ (MH$^+$) 370.0482, found 370.0493; $[\alpha]^{20}_D$ -163.40 (c 1.0, $CHCl_3$); HPLC: Chiralcel AD-H (pet ether/*i*-PrOH = 80/20, flow rate 1.0 mL/min, λ = 230 nm), t_R (major) = 10.12 min, t_R (minor) = 56.70 min; >99% ee.

(3*R*,4*S*)-4-(2-Chlorophenyl)-3-nitro-3,4-dihydro-2H-benzo[g]chromene-5,10-dione (5k)



Yellow solid; mp 214 °C; Yield 146 mg, 80% (dr >99:1); υ_{max}(film)/cm^{-1} 3056w, 2987vw, 2933vw, 2987s, 1686s, 1631s, 1558s, 1455w, 1332m, 1302m, 1266vs, 1203s, 1094m, 704m; δ_H(400 MHz: $CDCl_3$,) 8.18 (1H, dd, *J* 9.0, 2.4), 8.05 (1H, dd, *J* 9.0, 2.4), 7.76 (2H, dd, *J* 9.0, 2.4); 7.52 (1H, dd, *J* 7.6, 1.4), 7.29 (1H, td, *J* 7.6, 1.4), 7.24 (1H, td, *J* 7.6, 1.4), 7.05 (1H, dd, *J* 7.6, 1.4), 5.47 (1H, unresolved), 5.12 (1H, dt, *J* 13.1, 2.0), 4.90 (1H, ddd collapsed to q, *J* 2.0), 4.27 (1H, dd, *J* 13.1, 2.0); δ_C(100 MHz: $CDCl_3$,) 182.4, 178.4, 155.2, 136.0, 134.8, 133.9, 133.8, 131.8, 130.9, 130.8, 129.9, 129.5, 127.8, 126.9, 126.8, 118.6, 79.6, 63.6, 35.1; MS (ES$^+$, Ar) m/z (rel intensity) 371 ([MH+1]$^+$, 30), 370 (MH$^+$, 100), 339 (20), 338 (65), 323 (40), 214 (15), 158 (20); HRMS (ES$^+$, Ar) calcd for $C_{19}H_{13}NO_5Cl$ (MH$^+$) 370.0482, found 370.0496; $[\alpha]^{20}_D$ -127.80 (c 1.0, $CHCl_3$); HPLC: Chiralcel AD-H (pet ether/*i*-PrOH = 80/20, flow rate 1.0 mL/min, λ = 230 nm), t_R (major) = 8.81 min, t_R (minor) = 46.24 min; >99% ee.

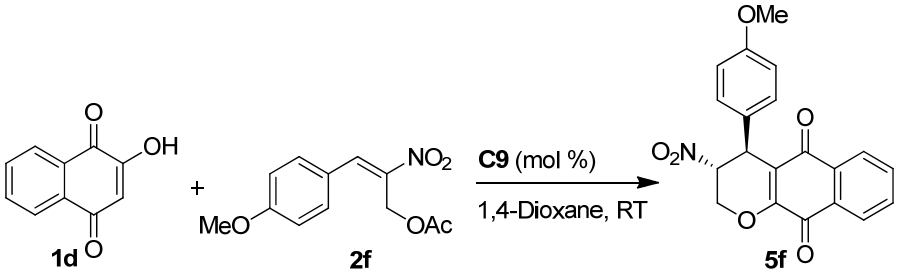
(3*R*,4*R*)-3-Nitro-4-(2-nitrophenyl)-3,4-dihydro-2H-benzo[g]chromene-5,10-dione (5l)



Yellow solid; mp 237 °C; Yield 146 mg, 77% (dr >99:1); υ_{max}(film)/cm^{-1} 2920s, 1685s, 1655m, 1626s, 1553s, 1492m, 1372m, 1355m, 1333m, 1301m, 1255m, 1201vs, 1092s, 725 s; δ_H(400 MHz: $CDCl_3$) 8.15-8.20 (2H, m), 7.96-8.00 (1H, m), 7.73-7.78 (2H, m), 7.60 (1H, td, *J* 7.6, 1.3), 7.55 (1H, td, *J* 7.6, 1.3), (1H, dd, *J* 7.7, 1.3), 5.53 (1H, unresolved), 5.18 (1H, dt, *J* 13.5, 2.0), 5.16 (1H, unresolved), 4.42 (1H, dd, *J* 13.5, 2.0); δ_C(100 MHz: $CDCl_3$,) 182.4, 178.3, 155.4, 148.7, 134.9, 134.2, 134.1, 133.9, 131.7, 131.0, 130.5, 129.7, 127.0, 126.8, 126.5, 118.8, 80.8, 64.1, 34.1; MS (ES$^+$, Ar) m/z (rel intensity) 382 ([MH+1]$^+$, 25), 381 (MH$^+$, 100), 288 (35), 260 (8), 205 (5); HRMS (ES$^+$, Ar) calcd for $C_{19}H_{13}N_2O_7$ (MH$^+$) 381.0723, found 381.0705; $[\alpha]^{20}_D$ -394.48 (c 0.5, $CHCl_3$); HPLC: Chiralcel AD-H (pet ether/*i*-PrOH = 80/20, flow rate 1.0 mL/min, λ = 230 nm), t_R (major) = 19.06 min, t_R (minor) = 62.03 min; 99% ee.

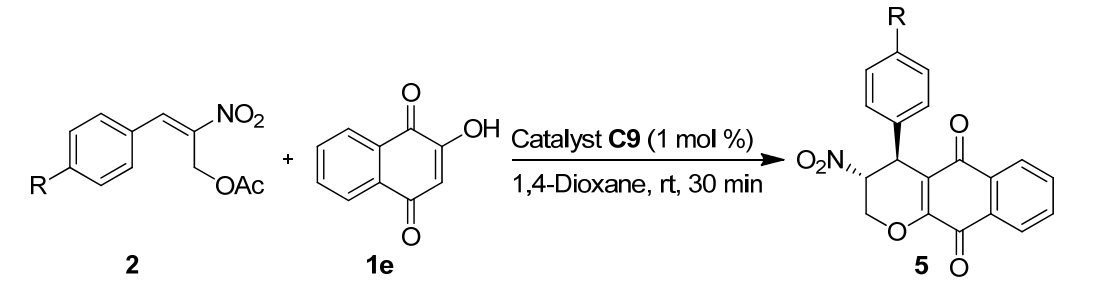
6. Scale up of the synthesis of 5c and 5f

7. Table S2 Optimization of the amount of catalyst **C9**



Cat (mol %)	Time (min)	% Yield[a]	dr[b]	% ee[c]
10	20	84	90:10	97
5	25	84	89:11	97
2.5	30	82	88:12	97
1	40	80	88:12	97

[a] After purification by silica gel column chromatography. [b] Determined by ^{1}H NMR and further confirmed by chiral HPLC using AD-H column. [c] Determined by chiral HPLC using AD-H column for the major diastereomer.

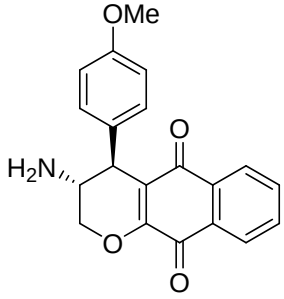


To a stirred solution of MBH acetate **2** (4 mmol) in 1,4-dioxane (10 mL), was added catalyst **C9** (30 mg, 0.04 mmol, 1 mol %) and the reaction mixture was stirred at rt. After 5 minutes, 1,3-dicarbonyl compound **1** (696 mg, 4 mmol) was added and continued the stirring till the completion of the reaction. The solvent was evaporated in *vacuo* and the crude residue was directly purified by silica gel column chromatography by eluting with 20-30% EtOAc-pet ether (gradient elution) to afford pyran **5c** or **5f** as a yellow solid (for experimental data, see *vide supra*).

8. General procedure for the reduction of the nitro group in 5c and 5f

To a stirred solution of pyranonaphthaquinone **5c** or **5f** (0.5 mmol) in ethanol (10 mL) was added $NiCl_2.6H_2O$ (238 mg, 1.0 mmol) and the reaction mixture was cooled to 0 ^oC. Sodium borohydride (95 mg, 2.5 mmol) was added portionwise over a period of 1 h and the stirring continued for 2 h at the same temperature. The reaction mixture was concentrated in vacuo and quenched with saturated aqueous NH_4Cl solution (15 mL). The aqueous layer was then extracted with ethyl acetate (4 × 20 mL). The combined organic layer was dried over Na_2SO_4 and concentrated in *vacuo*. Attempted purification of crude residue of **6c** (brown sticky liquid, 131 mg, 85%) by silicagel column chromatography led to decomposition. Therefore, crude amine **6c** was used as such for the next step. The crude residue of **6f** was successfully purified by silicagel column chromatography (gradient elution 80% EA/pet ether) to afford the pure amine **6f**.

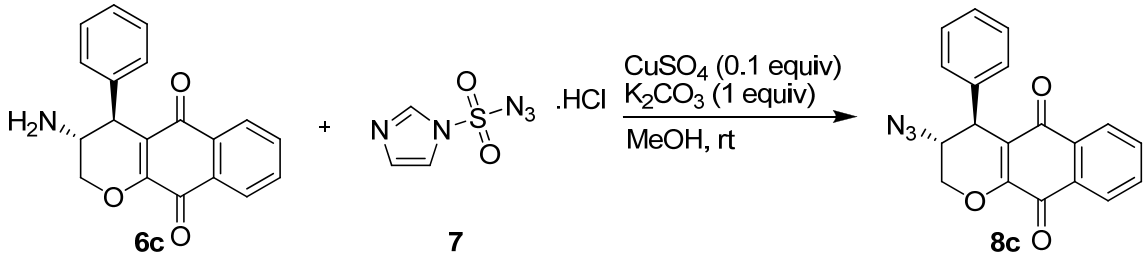
(3*R*,4*S*)-3-Amino-4-(4-methoxyphenyl)-3,4-dihydro-2H-benzo[g]chromene-5,10-dione (6f)



Yellow solid; Yield 154 mg, 92% (dr 92:8); mp 136 ^oC, υ_{max}(film)/cm^{-1} 3354m, 2926m, 1674m, 1649m, 1618s, 1511s, 1463m, 1303m, 1256vs, 1201s, 1180m, 1028m, 981m, 723s; δ_H(400 MHz: $CDCl_3$, major) 8.15 (1H, dd, *J* 9.0, 3.3), 8.00 (1H, dd, *J* 9.0,

3.3), 7.71 (2H, td, *J* 9.0, 3.3), 7.14 (2H, d, *J* 8.6), 6.85 (2H, d, *J* 8.6), 4.17 (2H, br q, *J* 11.6), 4.06 (1H, unresolved), 3.74 (3H, s), 3.28 (1H, unresolved), the NH_2 protons are not observed; δ_C(100 MHz: $CDCl_3$ major) 183.8, 179.6, 158.7, 155.1, 134.4, 134.3, 133.3, 132.2, 131.1, 128.9, 126.5, 120.8, 114.4, 68.2, 55.4, 50.6, 43.3; MS (ES^+, Ar) m/z (rel intensity) 358 (MNa^+, 100); HRMS (ES^+, Ar) calcd for $C_{20}H_{17}NO_4Na$ (MNa^+) 358.1050, found 358.1047; $[\alpha]^{20}_D$ -5.2 (c 1.0, $CHCl_3$); HPLC: Chiralcel AD-H (pet ether/*i*-PrOH = 80/20, flow rate 1.0 mL/min, λ = 230 nm), t_R (major) = 11.72 min, t_R (minor) = 57.19 min; 97% ee.

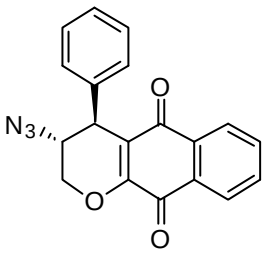
(3*R*,4*S*)-3-Azido-4-phenyl-3,4-dihydro-2H-benzo[g]chromene-5,10-dione (8c)



To a stirred solution of crude amine **6c** (100.5 mg, 0.33 mmol), $CuSO_4$ (8.2 mg, 0.033 mmol) and K_2CO_3 (45.5 mg, 0.33 mmol) in MeOH (6 mL) was added imidazole-1-sulfonyl azide hydrochloride[9] (83 mg, 0.396 mmol) at room temperature. The reaction mixture was stirred till complete consumption of **6c** (3-4 h, monitored by TLC). It was then concentrated *in vacuo*, the residue was treated with water (5 mL), acidified by conc HCl and the aqueous layer was extracted with EtOAc (3 × 10 mL). The combined organic layer was dried over Na_2SO_4, concentrated *in vacuo* and purified by silica gel column chromatography (20-25% EA/pet ether) to give the azide **8c**.

9. Synthesis of azide 8c

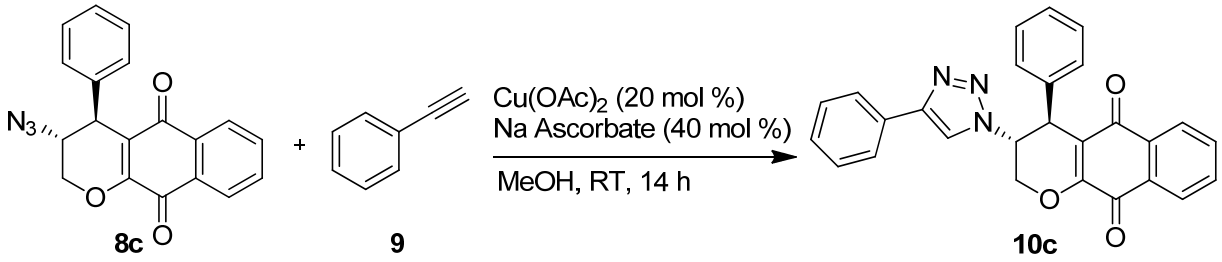
(3*R*,*4S*)-3-Azido-4-phenyl-3,4-dihydro-2H-benzo[g]chromene-5,10-dione (8c)



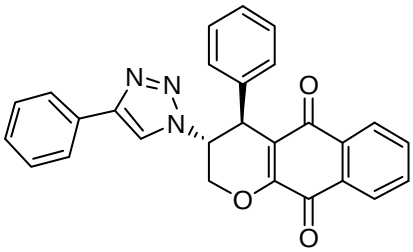
Yellow solid; Yield 81 mg, 81% (dr 88:12, after recrystallization from $CHCl_3$ >99:1); mp 168 °C; υ_{max}(film)/cm^{-1} 2918w, 2111s, 1683s, 1649s, 1622s, 1333m, 1297m, 1251m, 1201m, 1087m, 762vs; δ_H(500 MHz: $CDCl_3$,) 8.18 (1H, dd, *J* 5.6, 2.2), 8.03 (1H, dd, *J* 5.6, 3.4), 7.74 (2H, ddd, *J* 5.6, 3.4, 2.2), 7.33-7.36 (2H, m), 7.18-7.29 (3H, m), 4.46 (1H, dt, *J* 14.5, 2.2), 4.38 (1H, s), 4.17 (1H, d, *J* 12.2), 3.99 (1H, d, *J* 1.8); δ_C(125 MHz: $CDCl_3$,) 183.2, 179.1, 155.2, 140.3, 134.5, 133.6, 132.1, 131.1, 129.4, 128.2, 128.0, 126.8, 126.7, 119.3, 64.3, 58.8, 40.0; MS (ES^+, Ar) m/z (rel intensity) 354 (MNa^+, 100); HRMS (ES^+, Ar) calcd for $C_{19}H_{13}N_3O_3Na$ (MNa^+) 354.0849, found 354.0846; $[\alpha]^{20}_D$ -47.80 (c 1.0, $CHCl_3$); HPLC: Chiralcel AD-H (pet ether/*i*-PrOH = 80/20, flow rate 1.0 mL/min, λ = 230 nm), t_R (major) = 8.173 min, t_R (minor) = 26.05 min; 97% ee.

10. Synthesis of triazole 10c

(3*R*,4*S*)-4-Phenyl-3-(4-phenyl-1H-triazol-1-yl)-3,4-dihydro-2H-benzo[g]chromene-5,10-dione (10c)



To a stirred solution of azidoquinone **8c** (99.3 mg, 0.3 mmol), $Cu(OAc)_2$ (12 mg, 0.06 mmol, 20 mol %), and sodium ascorbate (24 mg, 0.12 mmol) in MeOH (3 mL), was added phenyl acetylene **9** (33.7 mg, 0.33 mmol) and the reaction mixture was stirred at rt till complete consumption of **8c** (14 h, monitored by TLC). It was then concentrated *in vacuo*, the residue was treated with water (5 mL) and the aqueous layer was extracted with EtOAc (3 × 10 ml). The combined organic layer was dried over Na_2SO_4, concentrated *in vacuo* and purified by silica gel column chromatography (45-50% EA/pet ether) to give pure **10c**.



Pale yellow solid; mp 255 ^{o}C; Yield 88 mg, 81% (dr 92:8); υ_{max}(film)/cm^{-1} 2925w, 2306w, 1682s, 1649s, 1626s, 1265s, 1198m, 740vs, 703s; δ_H(500 MHz: $CDCl_3$, major) 8.19 (1H, dd, *J* 5.1, 2.1), 8.00 (1H, dd, *J* 5.1, 2.1), 7.71-7.79 (5H, m), 7.30-7.47 (8H, m), 5.15, 5.09 (1H, ABq, *J* 2.4), 4.91 (1H, d, *J* 2.4), 4.88 (1H, t, *J* 2.4), 4.63 (1H, dd, *J* 12.2, 2.4); δ_C(125 MHz: $CDCl_3$, major) 182.8, 179.0, 155.0, 148.3, 140.3, 134.8, 133.8, 132.1, 131.0, 130.2, 129.6, 129.0, 128.6, 128.4, 128.1, 126.9, 126.0, 120.2, 118.5, 64.9, 58.9, 41.3; MS (ES^+, Ar) m/z (rel intensity) 456 (MNa^+, 100); HRMS (ES^+, Ar) calcd for $C_{27}H_{19}N_3O_3Na$ (MNa^+) 456.1319, found 456.1312; $[\alpha]^{20}_D$ -38.64 (c 0.5, $CHCl_3$); HPLC: Chiralcel AD-H (pet ether/*i*-PrOH = 80/20, flow rate 1.0 mL/min, λ = 230 nm), t_R (major) = 24.4 min, t_R (minor) = 46.5 min; 97% ee.

11. Biological: trypanocidal Assay

For trypanocidal assay, stock solutions of the compounds were prepared in dimethyl sulfoxide (DMSO); final DMSO concentrations used in the experiments never exceeded 0.1%. Y strain bloodstream trypomastigotes[10] were obtained at the peak of parasitemia from infected albino mice, isolated by differential centrifugation and resuspended in Dulbecco's modified Eagle's medium (DMEM) to a concentration of 10^7 parasites per mL in the presence of 10% mouse blood. This suspension (100 mL) was added to an equal volume of each compound at twice the desired final concentration. Cell counts were performed in a Neubauer chamber, and the trypanocidal activity was expressed as IC_{50}, corresponding to the concentration that leads to lysis of 50% of the parasites.

Table S3. IC_{50} Values for the trypanocidal activity of selected compounds **5**

Sample Code	Structure Number	IC_{50}/ 24 h (μM)
INN-DKN 488	**5a**	>4000.0
INN-DKN 491	**5b**	>4000.0
INN-DKN 496	**5c**	>2000.0
INN-DKN 509	**5d**	>1000.0
INN-DKN 490	**5e**	>1000.0
INN-DKN 511	**5f**	>4000.0
INN-DKN 512	**5g**	>1000.0
INN-DKN 633	**5i**	>3000.0
INN-DKN 498	**5j**	>2000.0
INN-DKN 522	**5l**	>2000.0
Benznidazole[10]		103.6 ± 0.6

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