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Supporting Information

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Organocatalytic Highly Enantioselective a-Arylation of ß-Ketoesters

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Contents

General Methods. The ^{1}H and ^{13}C NMR spectra were recorded at 400 MHz and 100 MHz, respectively. The chemical shifts (*d*) for ^{1}H and ^{13}C are given in ppm relative to residual signals of the solvents ($CHCl_3$). Coupling constants are given in Hz. The following abbreviations are used to indicate the multiplicity: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; bs, broad signal. Chromatography was carried out by flash chromatography (FC) using Merck silica gel 60 (230-400 mesh). Optical rotations were measured on a Perkin-Elmer 241 polarimeter and they are reported as follows: $[a]_D^{20}$ (*c* in g per 100 mL, solvent).

The absolute configuration of the quinone ß-ketoester was established by single-crystal X-ray analysis of *ent*-**3g.** The same approach of the nucleophile to the corresponding α,β-unsaturated quinone was assumed for assigning the absolute configuration of the rest of the compounds.

Materials. The *tert*-butyl ß-ketoesters **1** were either prepared by Claisen-condensation,[1] or from the corresponding methyl esters[2] by Bu_2SnO catalyzed transesterification with *tert*-BuOH in refluxing toluene.[3] The quinones **2a**-**d** were purchased from Aldrich.

Experimental Procedures and Characterizations

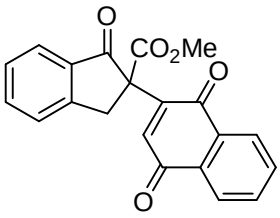
General Procedure. In an ordinary vial equipped with a magnetic stirring bar, **1a**-**g** (0.2 mmol), **2a**-**d** (0.2 mmol) in the indicated solvent (0.4 mL) was cooled at indicated temperature for 15 min. After this time, the corresponding catalyst (20 mol%) was added. The stirring was maintained at the indicated temperature until completion of the reaction. The crude reaction mixture was directly charged on silica gel and subjected to FC.

[1] Cyclopentanone-core (**1a**) and cyclohexanone-core (**1e**): M. E. Bunnage, S. G. Davies, R. M. Parkin, P. M. Roberts, A. D. Smith, J. M. Withey, *Org. Biomol. Chem.* **2004**, *2*, 3337.

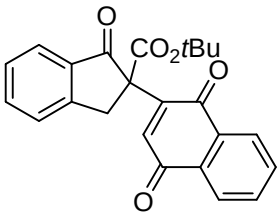
[2] 1-Indanone-core (**1a**) and 6-chloro-1-indanone-core (**1c**): a) H. O. House, C. B. Hudson, *J. Org. Chem.* **1970**, *35*, 674; 6,7-dimethoxy-1-indanone-core (**1b**): b) H. Fukushi, H. Mabuchi, K. Itoh, Z.-I. Terashita, K. Nishikawa, H. Sugihara, *Chem. Pharm. Bull.* **1994**, *42*, 541; 1-tetralone-core: c) F. Bennett, G. Fenton, D. W. Knight, *Tetrahedron*, **1994**, *50*, 5147.

[3] a) J. Otera, T. Yano, A. Kawabata, H. Nozaki, *Tetrahedron Lett.* **1986**, *27*, 2383; b) M. Nakajima, S. Yamamoto, Y. Yamaguchi, S. Nakamura, S. Hashimoto, *Tetrahedron*, **2003**, *59*, 7307.

Modified General Procedure. In an ordinary vial equipped with a magnetic stirring bar, **1a**-**g** (0.2 mmol), **2a**-**d** (0.2 mmol) in the suitable solvent (0.4 mL) was cooled at the indicated temperature for 15 min. After this time, the corresponding catalyst (20 mol%) was added. When the starting material was completed consumed, followed by TLC, the reaction was allowed to reach room temperature and 4 equiv. of Et_3N were added. After 15 min the crude reaction mixture was directly charged on silica gel and subjected to FC.

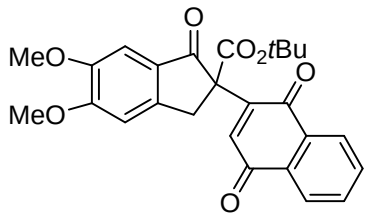


(-)-Methyl 2,3-dihydro-2-(1,4-dihydro-1,4-dioxonaphthalen-2-yl)-1-oxo-1H-indene-2-carboxylate (3a'). Following the general procedure **3a'** was isolated as orange oil after 5 h by FC (*n*-hexane/Et_2O: 2/1) with the solvents and catalyst indicated in Table 1. Yields are collected in Table 1 [for entry 5, $[a]^{20}_D$ = -122.9 (*c* = 1.5, CH_2Cl_2), 67% *ee*]. The *ee* was determined by HPLC analysis on Daicel Chiralpak AS column, Hex/*i*-PrOH: 98/2, flow rate = 1.0 mL/min, t = 29.6 min (minor) and t = 33.2 min (major). ^{1}H NMR (400 MHz, $CDCl_3$) *d* 8.11-8.05 (m, 2H), 7.87 (d, *J* = 7.6 Hz, 1H), 7.77-7.75 (m, 2H), 7.68 (t, *J* = 7.2 Hz, 1H), 7.49 (d, *J* = 8.0 Hz, 1H), 7.45 (t, *J* = 7.2 Hz, 1H), 6.86 (s, 1H), 4.40 (d, *J* = 17.6 Hz, 1H), 3.74 (s, 3H), 3.20 (d, *J* = 17.6 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) *d* 198.6, 184.5, 184.2, 168.2, 152.7, 148.7, 136.3, 135.3, 134.5, 134.3, 133.9, 131.8, 131.7, 128.2, 126.9, 126.5, 126.3, 125.1, 53.6, 39.8, 29.7. HRMS calc.: $C_{21}H_{14}NaO_5$: 369.0739; found: 369.0739.

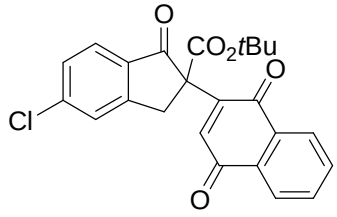


(-)-*t*-Butyl 2,3-dihydro-2-(1,4-dihydro-1,4-dioxonaphthalen-2-yl)-1-oxo-1H-indene-2-carboxylate (3a). Following the general procedure **3a** was isolated as orange oil after 6 h by FC (*n*-hexane/Et_2O: 2/1) using 20 mol% of (-)-quinine as catalyst. 76% yield. $[a]^{20}_D$ = -195.0 (*c* = 1.0, CH_2Cl_2), 94% *ee*. The *ee* was determined by HPLC analysis on Daicel Chiralcel OD column by transformation to compound **5** as was indicated in scheme 3, Chiralcel OD column, Hex/*i*-PrOH: 90/10, flow rate = 1.0 mL/min, t = 11.5 min (major) and t = 13.0 min (minor). ^{1}H NMR (400 MHz, $CDCl_3$) *d* 8.12-8.05 (m, 2H), 7.86 (d, *J* = 7.6 Hz, 1H), 7.77-7.76 (m,

2H), 7.66 (t, *J* = 7.2 Hz, 1H), 7.49-7.42 (m, 2H), 6.84 (s, 1H), 4.32 (d, *J* = 18.0 Hz, 1H), 3.17 (d, *J* = 18.0 Hz, 1H), 1.38 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) *d* 199.3, 184.9, 184.5, 167.0, 153.1, 149.5, 136.4, 136.3, 135.1, 134.4, 134.2, 132.2, 132.0, 128.3, 126.9, 126.6, 126.5, 125.2, 83.5, 64.2, 40.1, 27.9. HRMS calc.: $C_{24}H_{20}NaO_5$: 411.1208; found: 411.1226.

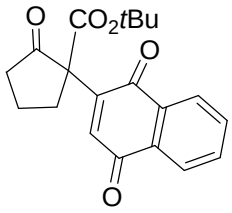


(-)-*tert*-Butyl 2,3-dihydro-2-(1,4-dihydro-1,4-dioxonaphthalen-2-yl)-5,6-dimethoxy-1-oxo-1H-indene-2-carboxylate (3b). Following the modified general procedure **3b** was isolated as yellow oil after 6 h by FC (*n*-hexane/Et_2O: 2/1) using 20 mol% of (-)-quinine as catalyst. 69% yield. $[a]^{20}_D$ =-163.0 (*c* = 0.5, CH_2Cl_2), 94% *ee*. The *ee* was determined by HPLC analysis on Daicel Chiralcel OD column, Hex/*i*-PrOH: 80/20, flow rate = 1.0 mL/min, t = 10.6 min (major) and t = 15.6 min (minor). ^{1}H NMR (400 MHz, $CDCl_3$) *d* 8.11-8.05 (m, 2H), 7.77-7.76 (m, 2H), 7.23 (s, 1H), 6.86 (s, 1H), 6.85 (s, 1H), 4.40 (d, *J* = 17.6 Hz, 1H), 3.96 (s, 3H), 3.93 (s, 3H), 3.20 (d, *J* = 17.6 Hz, 1H), 1.37 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) *d* 197.2, 184.8, 184.5, 167.1, 156.6, 149.9, 149.5, 148.6, 134.7, 134.1, 133.8, 131.9, 131.8, 127.5, 126.6, 126.2, 107.0, 104.9, 83.7, 64.2, 56.4, 56.1, 39.6, 27.6. HRMS calc.: $C_{26}H_{24}NaO_7$: 471.1420; found: 471.1423.

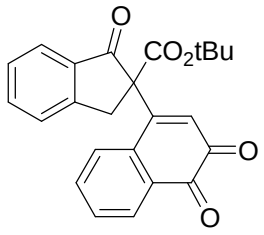


(-)-*tert*-Butyl 5-chloro-2,3-dihydro-2-(1,4-dihydro-1,4-dioxonaphthalen-2-yl)-1-oxo-1H-indene-2-carboxylate (3c). Following the modified general procedure **3c** was isolated as orange oil after 7 h by FC (*n*-hexane/Et_2O: 2/1) using 20 mol% of (-)-quinine as catalyst. 80% yield. $[a]^{20}_D$ = -188.4 (*c* = 0.3, CH_2Cl_2), 88% *ee*. The *ee* was determined by HPLC analysis on Daicel Chiralcel OD column, Hex/*i*-PrOH: 99/1, flow rate = 1.0 mL/min, t = 18.4 min (minor) and t = 19.8 min (major). ^{1}H NMR (400 MHz, $CDCl_3$) *d* 8.04-7.98 (m, 2H), 7.72-7.68 (m, 3H), 7.68 (s, 1H), 7.38 (d, *J* = 8.0 Hz, 1H), 6.78 (s, 1H), 4.23 (d, *J* = 17.6 Hz, 1H), 3.08 (d, *J* = 17.6 Hz, 1H), 1.30 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) *d* 197.8, 184.8, 184.5, 166.7, 154.5, 149.1, 142.9, 135.3,

134.5, 134.2, 133.5, 132.1, 131.9, 129.1, 127.0, 126.8, 126.5, 126.3, 83.8, 64.2, 39.7, 27.9. HRMS calc.: $C_{24}H_{19}ClNaO_5$: 445.08187; found: 445.0808.



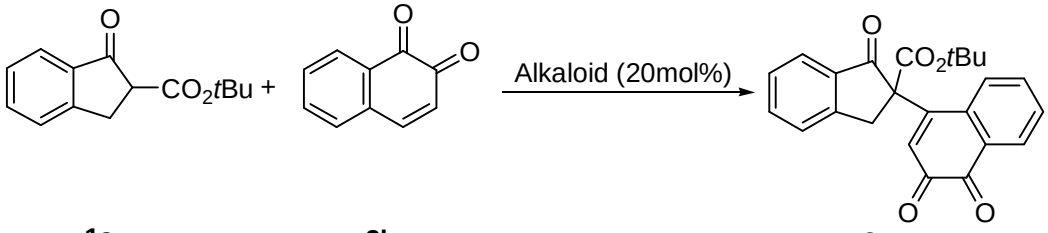
(-)-*tert*-Butyl 1-(1,4-dihydro-1,4-dioxonaphthalen-3-yl)-2-oxocyclopentanecarboxylate (3d). Following the general modified procedure **3d** was isolated as yellow oil after 12 h by FC using Iatrobeads 6RS-8060 (*n*-hexane/Et_2O: 4/1) using 20 mol% of (-)-quinine as catalyst. 59% yield. $[a]^{20}_D$ =-32.2 (*c* = 0.2, CH_2Cl_2), 96% *ee*. The *ee* was determined by HPLC analysis on Daicel Chiralcel OD column, Hex/*i*-PrOH: 95/5, flow rate = 1.0 mL/min, t = 10.6 min (major) and t = 19.2 min (minor). ^{1}H NMR (400 MHz, $CDCl_3$) *d* 8.06-8.05(m, 2H), 7.79-7.70 (m, 2H), 6.78 (s, 1H), 2.91-2.85 (m, 1H), 2.54 (t, *J* = 7.6 Hz,2H), 2.40-2.36 (m, 1H), 2.28-2.22 (m, 1H), 2.12-2.03 (m, 1H), 1.44 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) *d* 208.9, 190.7, 189.9, 167.9, 134.7, 134.3, 134.0, 133.9, 132.7, 131.3, 127.8, 126.6, 83.5, 58.2, 37.5, 31.2, 27.7, 18.8. HRMS calc.: $C_{20}H_{20}NaO_5$: 363.1208; found: 363.1191.



(-)-*tert*-Butyl 2,3-dihydro-2-(1,2-dihydro-1,2-dioxonaphthalen-4-yl)-1-oxo-1H-indene-2-carboxylate (3e). Following the general procedure **3e** was isolated as yellow solid (mp = 178-180 ^{o}C) after 4 h by FC (*n*-hexane/Et_2O: 2/1) using 20 mol% of (-)-quinine as catalyst (see below Table S-1). 58% yield $[a]^{20}_D$ =-121.8 (*c* = 1.0, CH_2Cl_2), 44% *ee*. The *ee* was determined by HPLC analysis on Daicel Chiralcel OJ column, Hex/*i*-PrOH: 90/10, flow rate = 1.0 mL/min, t = 45.0 min (minor) and t = 61.9 min (major). ^{1}H NMR (400 MHz, $CDCl_3$) *d* 8.19 (dd, *J* = 7.6 Hz, 1.2 Hz, 1H), 7.86 (d, *J* = 7.6 Hz, 1H), 7.68 (t, *J* = 7.6 Hz, 2H), 7.55 (t, *J* = 7.6 Hz, 1H), 7.48-7.44 (m, 2H), 7.39 (d, *J* = 8.0 Hz, 1H), 6.35 (s, 1H), 4.41 (d, *J* = 17.2 Hz, 1H), 3.42 (d, *J* = 17.2, 1H), 1.35 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) *d* 198.5, 180.7, 178.8, 167.6, 153.6, 152.1, 136.4, 135.0, 134.3(2C), 131.7, 130.7, 130.5,

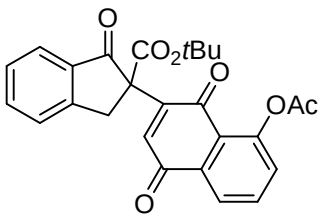
128.4, 126.8, 126.7, 126.3, 125.3, 84.1, 66.0, 39.5, 27.5. HRMS calc.: $C_{24}H_{20}NaO_5$: 411.1208; found: 411.1197.

Table S-1. Representative screening results for the enantioselective organocatalytic addition of the ß-ketoester **1a** to 1,2-quinone **2b** under various reaction conditions to give **3e**.



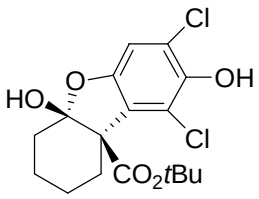
1a **2b** **3e**

Entry	Solvent	Catatalyst	T(°C)	Yield [%]	*Ee* [%]
1	CH_2Cl_2	Quinine	-20	55	40
2	CH_2Cl_2	Quinine	-40	58	44
3	DCE	Quinine	-20	69	0
4	DCE	Cinchonidine	-20	40	-10
5	CH_2Cl_2	Cinchonidine	-40	nd	4

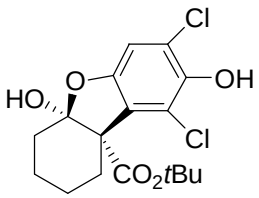


(-)-*tert*-Butyl 2,3-dihydro-2-(1,4-dihydro-5-acetoxy-1,4-dioxonaphthalen-2-yl)-1-oxo-1H-indene-2-carboxylate (3f). Following the modified general procedure **3f** was isolated as green oil after 6 h by FC (*n*-hexane/Et_2O: 1/1). 72% yield. $[a]^{20}_D$ =-205.0 (*c* = 0.2, CH_2Cl_2), 80% *ee*. The *ee* was determined by HPLC analysis on Daicel Chiralcel AS column, Hex/*i*-PrOH: 98/2, flow rate = 1.0 mL/min, t = 18.8 min (major) and t = 23.4 min (minor). ^{1}H NMR (400 MHz, $CDCl_3$) *d* 8.02 (d, *J* = 8.0 Hz, 1H), 7.83 (d, *J* = 7.6 Hz, 1H), 7.76 (t, *J* = 8.0 Hz, 1H), 7.65 (t, *J* = 7.6 Hz, 1H), 7.48-7.38 (m, 3H), 6.72 (s, 1H), 4.30 (d, *J* = 18.0 Hz, 1H), 3.10 (d, *J* = 18.0 Hz, 1H), 2.43 (s, 3H), 1.38 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) *d* 199.3, 184.2, 183.1, 169.7, 166.9, 153.3, 150.7, 150.0, 136.4, 135.3, 135.0, 133.7, 133.6, 133.5,

130.0, 128.3, 126.7, 125.2, 125.1, 83.6, 64.1, 40.3, 27.7, 21.3. HRMS calc.: $C_{26}H_{22}NaO_7$: 469.1263; found: 469.1255.

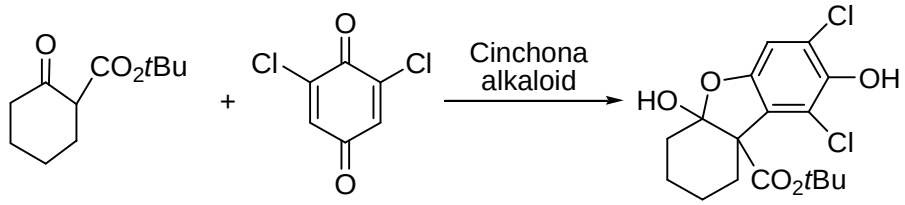


(+)-*tert*-Butyl 1-(2,4-dichloro-3,6-dihydroxyphenyl)-2-oxocyclohexanecarboxylate (3g). Following the general procedure **3g** was isolated as white solid (mp = 103-105 ^{o}C) after 5 h by FC (*n*-hexane/Et_2O: 2/1) using (-)-cinchonidine (20 mol%) and DCE at -32 ^{o}C. See Table S-2 for the screening of this reaction. 66% yield. $[a]^{20}_{D}$ = +40.3 (*c* = 0.35, CH_2Cl_2), 90% *ee*. The *ee* was determined by HPLC analysis on two Daicel Chiralpak AS columns, Hex/*i*-PrOH: 97/3, flow rate = 0.8 mL/min, t = 22.7 min (major) and t = 25.7 min (minor). ^{1}H NMR (400 MHz, $CDCl_3$) *d* 6.80 (s, 1H), 5.52 (s, 1H), 5.30 (s, 1H), 2.45-2.39 (m, 1H), 2.11 (dt, *J* = 14.4, 4.8 Hz, 1H), 1.88-1.63 (m, 4H), 1.59-1.50 (m, 2H), 1.48 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) *d* 170.0, 150.1, 142.0, 128.5, 119.8, 117.5, 109.8, 109.4, 83.0, 59.0, 31.9, 30.4, 27.2, 20.1, 19.6. HRMS calc.: $C_{17}H_{20}Cl_2NaO_5$: 397.0585; found: 397.0597.



(-)-***tert*-Butyl 1-(2,4-dichloro-3,6-dihydroxyphenyl)-2-oxocyclohexanecarboxylate (*ent*-3g).** The title compound was obtained according to the general procedure after 5 h reaction at -32 °C using the catalyst (+)-cinchonine in 1,2-dichloroethane as solvent (see Table S-2 for the screening), as a white solid (mp = 103-105 ^{o}C) after FC (*n*-hexane/Et_2O 2/1). 87% yield. $[a]_{D}^{20}$ = -34.9 (c 1.1, CH_2Cl_2), -92% *ee*. Spectral data were identical to compound **3g**. The *ee* was determined by HPLC analysis on two Daicel Chiralcel AS columns, Hex/*i*-PrOH: 97/3, flow rate = 0.8 mL/min, t = 22.7 min (minor) and t = 25.7 min (major).

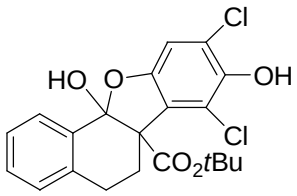
Table S-2. Representative screening results for the enantioselective organocatalytic addition of the ß-ketoester **1e** to 1,4-quinone **2d** under various reaction conditions to give **3g**.



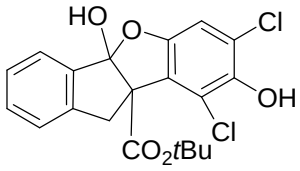
1e **2d** **3g (*ent*-3g)**

Entry	Solvent	Catalyst	T(°C)	Yield [%]	*Ee* [%]
1	CH_2Cl_2	Quinine (20 mol%)	-20	86	50
2	CH_2Cl_2	Quinine (20 mol%)	-40	81	60
3	CH_2Cl_2	Quinine (20 mol%)	-60	80	59
4	DCE	Quinine (20 mol%)	-20	70	55
5	CH_2Cl_2	Quinidine (20 mol%)	-20	84	-30
6	CH_2Cl_2	$(DHQD)_2PYR$ (20 mol%)	-40	85	0
7	CH_2Cl_2	Cinchonine (20 mol%)	-40	65	-84
8	DCE	Cinchonine (20 mol%)	-32	87	-92
9	DCE	Cinchonidine (20 mol%)	-32	66	90
10	DCE	Cinchonidine (1 mol%)	-32	67	82
11[a]	DCE	Cinchonidine (1 mol%)	-32	56	80

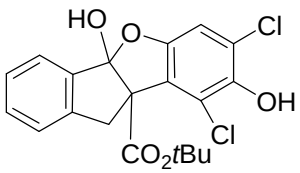
[a] This reaction was carried out in a 5 mmol scale, starting from 5 mmol of the ß-ketoester (1.0 gram), 5 mmol of the quinone (973 mg), and 1 mol% of the (-)-cinchonidine catalyst (15 mg) in 10 ml of DCE at -32 °C. After 66 hours the crude reaction was directly charged on silica gel and subjected to FC (2:1, hexane/Et_2O).



(-)- *tert*-Butyl 2-(2,4-dichloro-3,6-dihydroxyphenyl)-1,2,3,4-tetrahydro-1-oxonaphthalene-2-carboxylate (3h). Following the general procedure **3h** was isolated as yellow oil after 3 h by FC (*n*-hexane/Et_2O: 2/1). 88% yield. $[a]^{20}_D$ =-132.4 (*c* = 0.6, CH_2Cl_2), 84% *ee*. The *ee* was determined by HPLC analysis on Daicel Chiralpak AS column, Hex/*i*-PrOH: 90/10, flow rate = 1.0 mL/min, t = 8.3 min (major) and t = 13.4 min (minor). ^{1}H NMR (400 MHz, $CDCl_3$) *d* 7.84 (dd, *J* = 7.6 Hz, 1.6 Hz, 1H), 7.33-7.27 (m, 2H), 7.10 (dd, *J* = 6.8 Hz, 1.6 Hz, 1H), 6.73 (s, 1H), 5.53 (s, 1H), 5.50 (s, 1H), 2.91-2.83 (m, 1H), 2.61-2.51 (m, 3H), 1.48 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) *d* 170.5, 151.7, 142.9, 137.7, 135.0, 129.2, 127.8, 127.2, 127.1, 126.6, 121.1, 109.9, 109.8, 108.6, 84.5, 61.4, 28.8, 28.1, 26.2. HRMS calc.: $C_{21}H_{20}Cl_2NaO_5$: 445.0585; found: 445.0581.



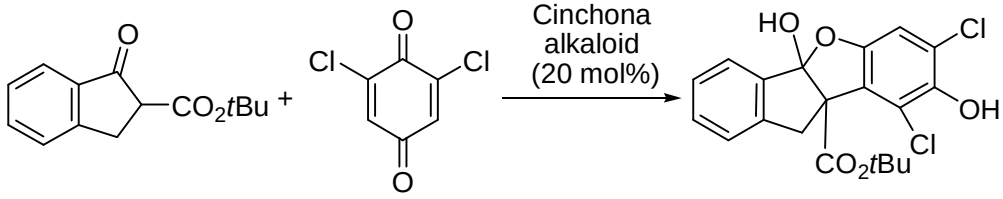
(-)-*tert*-Butyl 2-(2,4-dichloro-3,6-dihydroxyphenyl)-2,3-dihydro-1-oxo-1H-indene-2-carboxylate (3i). Following the general procedure **3i** was isolated as white solid (mp = 90-92 ^{o}C) after 3 h by FC (*n*-hexane/Et_2O: 4/1). 66% yield. $[a]^{20}_D$ =-137.0 (*c* = 0.8, CH_2Cl_2), 80% *ee*. The *ee* was determined by HPLC analysis on Chiralcel AD column, Hex/*i*-PrOH: 90/10, flow rate = 1.0 mL/min, t = 13.0 min (major) and t = 25.0 min (minor). ^{1}H NMR (400 MHz, $CDCl_3$) *d* 7.59 (dd, *J* = 6.4, 2.0 Hz, 1H), 7.40-7.31 (m, 2H), 7.23 (d, *J* = 6.8 Hz, 1H), 6.73 (s, 1H), 5.51 (s, 1H), 4.62 (s, 1H), 4.15 (d, *J* = 17.2 Hz, 1H), 3.48 (d, *J* = 17.2 Hz, 1H), 1.485 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) *d* 168.9, 151.3, 142.5, 140.5, 138.5, 130.7, 128.1, 127.9, 126.0, 123.7, 121.0, 120.7, 117.3, 109.6, 83.9, 65.3, 38.6, 27.9. HRMS calc.: $C_{20}H_{18}Cl_2NaO_5$: 431.0429; found: 431.0435.



(+)-*tert*-Butyl 2-(2,4-dichloro-3,6-dihydroxyphenyl)-2,3-dihydro-1-oxo-1H-indene-2-carboxylate (*ent*-3i). The title compound was obtained as white solid (mp = 90-92 ^{o}C) according to the general procedure after 40 h reaction at -60°C using the catalyst (+)-cinchonine using CH_2Cl_2 as solvent (see Table S-3), after FC (Et_2O/*n*-hexane 1/2). 92% yield. $[a]_D^{20}$

= +103.1 (*c* = 1.0, CH_2Cl_2), -72% *ee*. Spectral data were identical to compound **3i**. The *ee* was determined by HPLC analysis on Chiralcel AD column, Hex/*i*-PrOH: 90/10, flow rate = 1.0 mL/min, t = 13.0 min (minor) and t = 25.0 min (major).

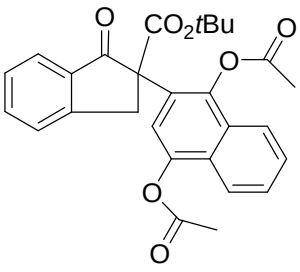
Table S-3. Representative screening results for the enantioselective organocatalytic addition of the ß-ketoester **1a** to 1,4-quinone **2d** under various reaction conditions to give **3i**.



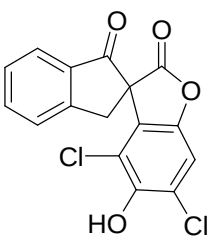
1a **2d** **3i**

Entry	Solvent	Catatyst	T(°C)	Yield [%]	*Ee* [%]
1	CH_2Cl_2	Quinine	-20	64	59
2	DCE	Cinchonidine	-32	66	80
3	CH_2Cl_2	Quinine	-60	78	74
4	CH_2Cl_2	Quinidine	-60	81	-65
5	CH_2Cl_2	Cinchonine	-60	92	-72
6	CH_2Cl_2	Cinchonidine	-60	66	74

Reactions for Scheme 3



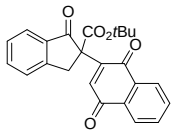
(-)-*tert*-Butyl-2,3-dihydro-2-(1,2-diacetoxynaphthalene -2-yl)-1-oxo-1H-indene-2-carboxylate (4). In an ordinary vial equipped with a magnetic stirring bar, **1a** (0.2 mmol), **2a** (0.2 mmol) in CH_2Cl_2 (0.4 mL) was cooled to –20 ^oC during 15 min under argon atmosphere. After this time, the corresponding (-)-quinine (20 mol%) was added. The stirring was maintained at -20 ^oC until completion of the reaction, usually 12 h. After this time the reaction was treated with 5 equiv. of Et_3N. After 15 min at room temperature, 5 equiv. of AcCl were added. When the reaction was finished the crude reaction was treated with some drops of sat. $NaHCO_3$ and the organic phase was directly charged on silica gel and subjected to FC, obtaining the compound as a white solid (mp = 96-98 ^oC). Yield = 51%. $[a]^{20}_D$ = -111.2 (*c* = 1.0, CH_2Cl_2), 91% *ee*. The *ee* was determined by HPLC analysis on Daicel Chiralcel OD column, Hex/*i*-PrOH: 90/10, flow rate = 1.0 mL/min, t = 11.5 min (major) and t = 13.0 min (minor). ^1H NMR (400 MHz,60 ^oC in $CDCl_3$) *d* 7.88-7.82 (m, 2H), 7.64-7.59 (m, 2H), 7.51-7.39 (m, 4H), 7.28 (s, 1H), 4.28 (d, *J* = 17.2 Hz, 1H), 3.27 (d, *J* = 17.2 Hz, 1H), 2.39 (s, 3H), 2.26 (s, 3H), 1.40 (s, 9H). (100 MHz, $CDCl_3$) *d* 199.6, 169.0 (2C), 167.7, 152.9, 144.4, 142.4, 135.9, 134.7, 130.1, 127.8, 127.7, 127.1, 126.8, 126.7, 126.4, 124.9, 121.8, 121.7, 117.7, 82.8, 64.9, 39.7, 29.7, 27.6. HRMS calc.: $C_{29}H_{26}NaO_7$: 497.1576; found: 497.1552.



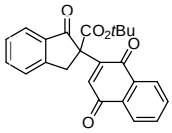
(+)-(4,6-Dichloro-5-hydroxy)-3*H*-benzofuran-2-one-3-spiro-2′-indan-1′-one (5). To a solution of the compound **3i** (0.1 mmol) in 0.3 mL of CH_2Cl_2 at 0 ^oC, TfOH (150 mol%) was added slowly. After 5 min the reaction was treated with some drops of $NaHCO_3$, and the organic phase was directly charged on silica gel and subjected to FC, obtaining the compound as a white solid (mp = 229-231^oC). Yield = 61%.$[a]^{20}_D$ = +47.0 (*c* = 1.1, CH_2Cl_2), 80% *ee*. The *ee* was determined by HPLC analysis on Daicel Chiralcel OJ column, Hex/*i*-PrOH: 85/15, flow rate = 1.0 mL/min,

t = 51.5 min (minor) and t = 57.5 min (major). ^{1}H NMR (400 MHz, $CDCl_3$) *d* 7.79 (d, *J* = 7.6 Hz, 1H), 7.69 (t, *J* = 6.8 Hz, 1H), 7.46 (d, *J* = 7.6 Hz, 1H), 7.43 (t, *J* = 6.8 Hz, 1H), 7.12 (s, 1H), 5.72 (bs, 1H), 3.78 (d, *J* = 17.2 Hz, 1H), 3.69 (d, *J* = 17.2 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) *d* 195.9, 172.7, 152.7, 147.4, 145.5, 136.5, 134.5, 128.6, 126.5, 125.6, 121.7, 119.2, 115.6 110.8, 61.5, 36.3. HRMS calc.: $C_{16}H_8Cl_2O_4$: 356.9697; found: 356.9695.

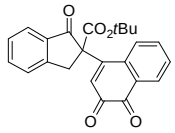
Representative spectra of Table 2 and Scheme 3



3a



3a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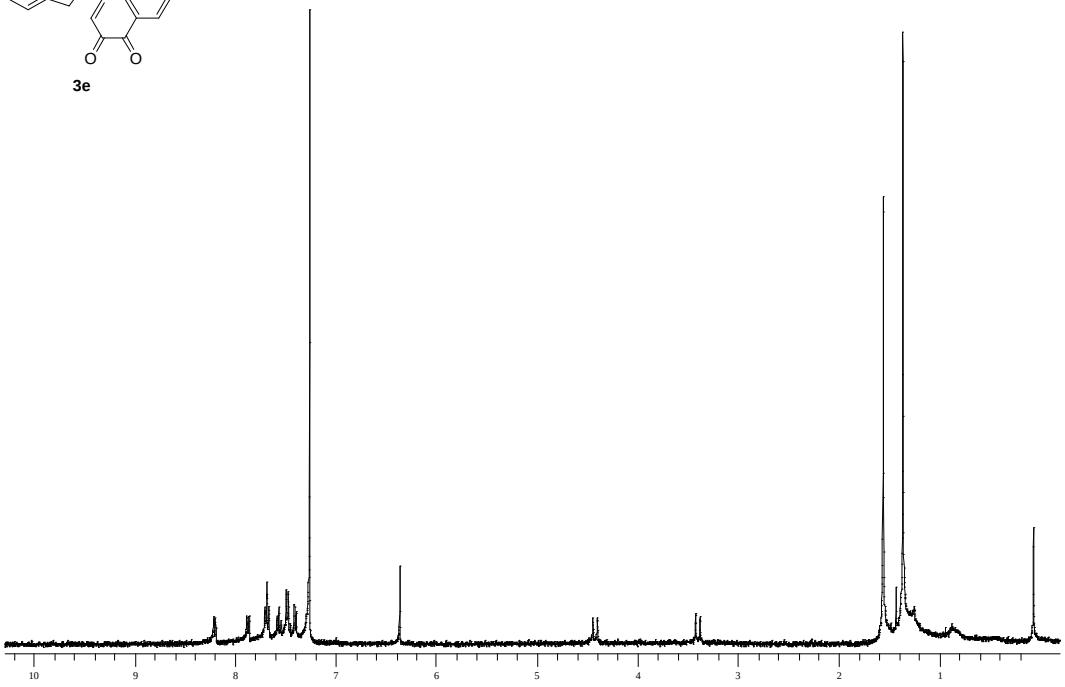
O

3e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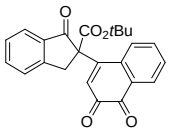
4
3
2
1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CO2tBu
O
O

3e

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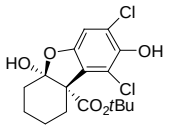
175
150
125
100
75
50
25
0



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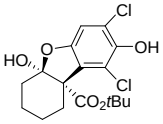

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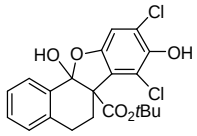
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OH
Cl
CO2tBu

3h

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7
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3
2
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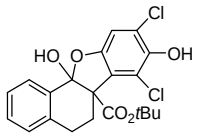
0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OH
Cl
CO2tBu

3h

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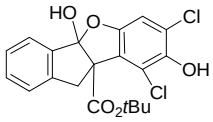
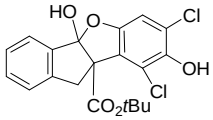
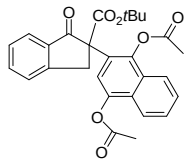


3i (*ent*-3i)



3i (*ent*-3i)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O
O

4

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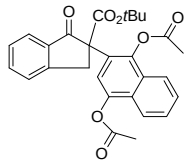
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CO2tBu
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O
O

4

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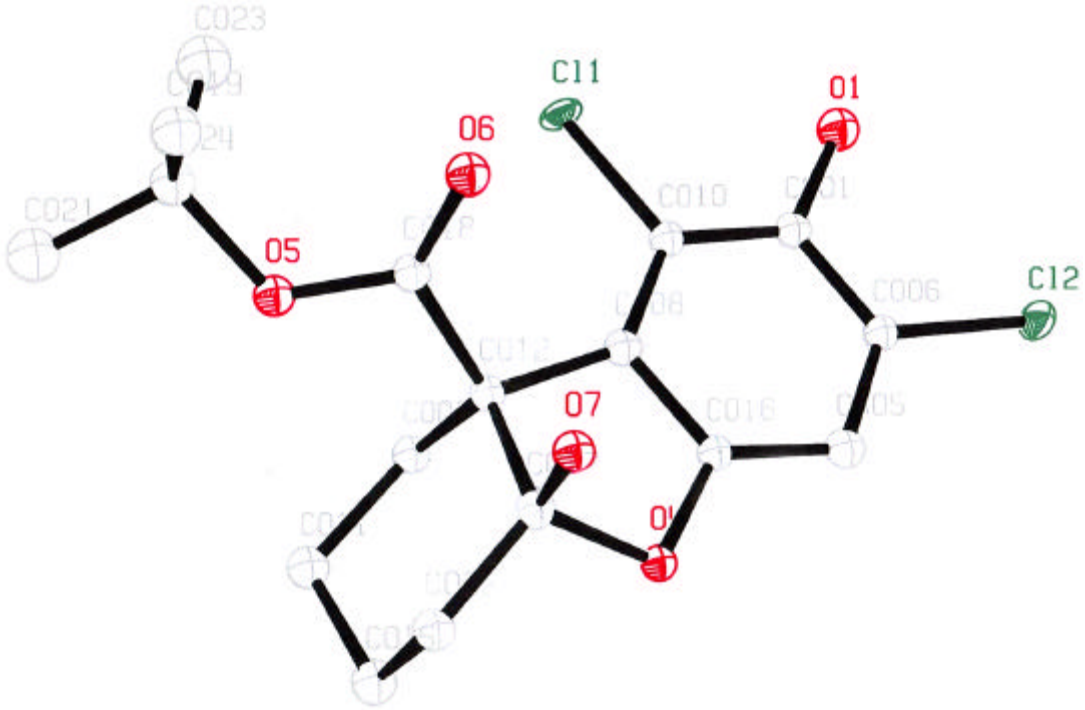
-25

ORTEP OF COMPOUND ENT-3g



ORTEP OF COMPOUND rac-5