Enantioselective synthesis of highly functionalized octahydro-6-oxo-1-phenylnaphthalene-2-carbaldehydes *via* organocatalytic domino reactions†‡

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Organocatalytic double Michael reaction and the subsequent aldol condensation of (*E*)-7-oxooct-5-enal and 3-arylpropenal (*e.g.*, cinnamaldehyde) provided octahydro-6-oxo-1-phenylnaphthalene-2-carbaldehyde in high diastereoselectivity and high enantioselectivity (>99% ee). Structures of the adducts **5a** and **5j** were confirmed unambiguously by X-ray analysis.

Introduction

The synthesis of decalin systems, bicyclo[4.4.0]decanes, has long been of key interest in organic synthesis.[1] Many chiral decalins serve as building blocks for the synthesis of naturally occurring compounds and pharmaceutical drugs.[2] Among the many approaches to decalins, the proline-catalyzed Hajos–Parrish–Eder–Sauer–Wiechert reaction represents an efficient protocol. However, following this pioneering discovery in the 1970s, research into organocatalytic synthesis remained virtually dormant until the turn of this century.[3] Recently, when the study of organocatalysis resumed, the synthetic applications evolved even beyond the decalin system, and soon became a blossoming subject and focal point in the synthetic community.[4] Modern studies into organocatalytic synthesis of the decalin system include the improved Hajos–Parrish–Eder–Sauer–Wiechert reaction,[5] the Diels–Alder reaction,[6] the Michael reaction,[7] and oxidative dearomatization.[8] Other recent successes into organocatalytic synthesis of decalins, by intramolecular Diels–Alder (IMDA) reactions for the total synthesis of solanapyrone D,[9] amaminol B,[10] and UCS1025A,[11] have further demonstrated the range of its synthetic applications.

Despite these impressive achievements, a general and efficient organocatalytic cascade reaction allowing the direct preparation of highly functionalized and enantio-enriched decalins remains elusive. In conjunction with our continuing efforts to explore new organocatalytic annulations, we embarked upon a domino strategy using the tandem Michael–Michael–aldol condensation to attain this objective.[12] Herein, we report the development of a new domino Michael–Michael–aldol condensation process of (*E*)-7-oxooct-5-enal (**1a**) and arylacrylaldehyde (**2**) which provides the highly functionalized decalins, hexahydronaphthalen-2(1*H*)-ones, with the control of four stereocenters in a one-pot, three-bond-formation reaction sequence.
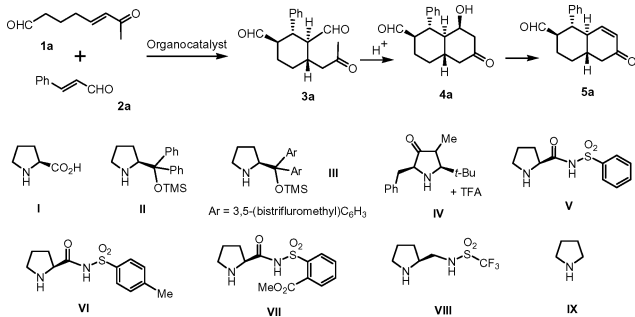
Results and discussion

At the outset of this study, reaction of (*E*)-7-oxooct-5-enal (**1a**)[13] and cinnamaldehyde (**2a**) with 0.2 equiv. of L-proline (**I**) in CH₃CN (4 mL, 0.25 M) at 28 °C for 72 h gave almost no reaction, with recovery of the starting materials (Table 1, entry 1). Conducting the reaction with Et₃N as an additive in an autonomous reaction remained fruitless (Table 1, entry 2). Encouragingly, the same reaction with catalyst **II**[14] and acetic acid (0.2 equiv) in CH₂Cl₂ for 24 h afforded 81% yield of the double Michael adduct **3a** (Table 1, entry 3). The yield increased when the reaction took place in CH₃CN (93% yield; Table 1, entry 4). However, further extension of the reaction time (72 h) did not provide the aldol cyclization product. Noteworthily, a suitable acid additive (*e.g.*, AcOH) was required for the formation of **3a** in CH₃CN or CH₂Cl₂; the reactions with catalyst **II** without an acid additive gave no reaction even after 3 days. Accordingly, a series of solvents was then screened for optimization of yields. However, reactions in polar aprotic solvents (*e.g.*, DMF and DMSO) gave no reaction, and low yields of **3a** were obtained when the reactions proceeded in other, less polar solvents (*e.g.*, 35% yield for the reaction in toluene; Table 1, entries 5–7). Interestingly, the reaction with catalyst **II** in EtOH (a polar protic solvent) without acid additive for 3 days provided a 61% yield of **3a** and a 22% yield of the consequent aldol product **4a** (Table 1, entry 8). We considered the attractive possibility that the synthesis of decalins, which requires three reactions, could be performed as a one-pot synthesis. Furthermore, acceleration of 6-enol*endo* aldolizations[15] by the addition of *p*-TsOH has been reported.[16] In an independent reaction, after the formation of **3a** in CH₂Cl₂ (12 h), *p*-TsOH (1 equiv.) was added to the reaction solution and the resulting mixture was stirred at the same temperature for a further 4 h, leading to the formation of **5a** in 68% yield (>99% ee; Table 1, entry 9). The yield was increased to 86% when reacted in CH₃CN (Table 1, entry 10). With a smaller amount of *p*-TsOH applied in the second-step reaction, the aldol condensation took a longer time for completion. For example, in the reaction with the addition of 0.5 equiv of *p*-TsOH, more than 10 h was required for the complete transformation of **3a** to **5a** (Table 1, entry 11). Unfortunately, replacement of HOAc by *p*-TsOH in the initial step of the reaction in CH₃CN gave no reaction for 16 h (Table 1, entry 12).[17]

Many other pyrrolidine derivatives thereof were tested as potential catalysts. The reactions with catalysts **III–VII** and AcOH

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† Dedicated to Professor Teh-Chang Chou on the occasion of his 65th Birthday.
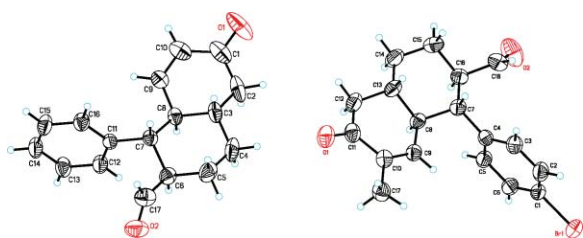
‡ Electronic supplementary information (ESI) available: ORTEP plots, NMR spectra, and HPLC analysis. CCDC reference numbers 716016 and 716017. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/b906205j

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Table 1 Screening of the conditions for the domino reaction[a]

Entry	Cat.[b]	Additive[b]	Solvent	t_1/h[c]	t_2/h[d]	Yield (%)[e]	Prod. (ratio)[f]	Ee (%)[g]
1	I	—	CH_3CN	72	—	~0[h]	—	n.a.
2	I	Et_3N	CH_3CN	72	—	~0[i]	—	n.a.
3	II	HOAc	CH_2Cl_2	24	—	81	3a	n.d.
4	II	HOAc	CH_3CN	12	—	93	3a	n.d.
5	II	HOAc	DMF	12	—	~0[h]	—	n.a.
6	II	HOAc	DMSO	12	—	~0[h]	—	n.a.
7	II	HOAc	toluene	12	—	35	3a	n.d.
8	II	—	EtOH	72	—	83	3a/4a (2.8 : 1)	n.d.
9	II	HOAc	CH_2Cl_2	12	4	68	5a	>99
10	II	HOAc	CH_3CN	12	4	86	5a	>99
11	II	HOAc	CH_3CN	12	10[j]	78	5a	>99
12	II	TsOH	CH_3CN	16	—	~0[h]	—	n.a.
13	III	HOAc	CH_3CN	72	—	~0[h]	—	n.a.
14	IV	TFA	CH_3CN	72	—	~0[h]	—	n.a.
15	V	HOAc	CH_3CN	72	—	~0[h]	—	n.a.
16	VI	HOAc	CH_3CN	36	—	~0[h]	—	n.a.
17	VII	HOAc	CH_3CN	36	—	~0[h]	—	n.a.
18	VIII	—	CH_3CN	16	4	72	5a	−54
19	IX	HOAc	CH_3CN	16	4	61	5a	0

[a] The reactions were performed in 0.25 M of **1** and 1.2 equiv. of cinnamaldehyde at 28 °C. [b] 0.2 equiv. of catalyst and additive, respectively, were applied. [c] First-step reaction time. [d] Unless otherwise specified, reaction time after the addition of p-TsOH (1.0 equiv.). [e] Isolated yield. [f] Determined by ¹H NMR prior to work up. [g] Enantiomeric excess (ee) of **5a** determined by HPLC with a chiral column (Chiralpak IA). n.d. = not determined; n.a. = not available. [h] No reaction and recovery of starting materials. [i] Complicated mixture with the decomposition of starting materials. [j] Reaction time after the addition of p-TsOH (0.5 equiv.).
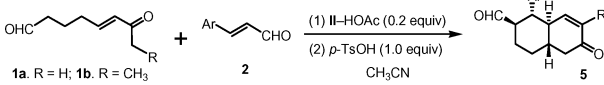
for 36–72 h gave no reaction in the first-step double Michael reaction. On the other hand, reaction with catalyst **VIII** at ambient temperature for 16 h afforded **3a**; the subsequent addition of p-TsOH (1 equiv.) with stirring at the same temperature for 4 h provided a 72% yield of **5a** and 54% ee, but with the inverse enantioselectivity (Table 1, entries 13–18). Reaction with pyrrolidine (**IX**)–AcOH followed by the addition of p-TsOH afforded lower yields of **5a** (61% yield; Table 1, entry 19); nevertheless, this racemic product was a suitable standard for HPLC analysis in determining the ee of **5a**, prepared by various catalysts and conditions in Table 1. The structure and relative stereochemistry of **5a** were assigned unambiguously by single-crystal X-ray analysis (Fig. 1).
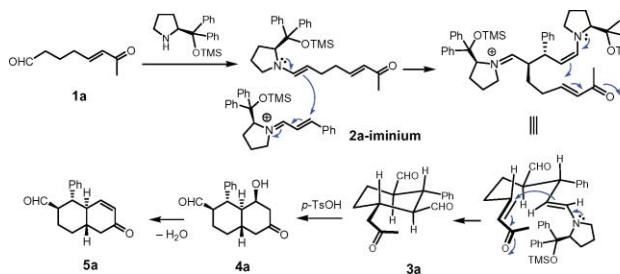

Fig. 1 ORTEP plots for the X-ray crystal structures of **5a** and **5j**.

Although this domino Michael–Michael–aldol condensation could theoretically generate 16 stereoisomers (producing four chiral centers in a three-bond-forming sequence), only one enantiomer was isolated in this reaction.[18] This high stereoselectivity is probably due to the first Michael addition of **1a** to cinnamaldehyde, as it is known that organocatalytic Michael reaction of an aldehyde to α,β-unsaturated aldehydes can proceed with high diastereo- and enantioselectivity,[19] and the resulting product presumably dictates the stereochemistry of the subsequent reactions, including the second Michael reaction and the aldol condensation. A plausible mechanism for the formation of **5a** is shown in Scheme 1. The initial Michael addition of **1a** to cinnamaldehyde is followed by the second Michael reaction in the cyclization to afford **3a**. After the addition of p-TsOH, aldol reaction of **3a** produced **4a**, followed by dehydration to provide the hexahydronaphthalenone **5a**.

Having established the optimal reaction conditions, a series of arylacrylaldehydes (**2**) were reacted with **1** at ambient temperature in the presence of **II**–AcOH for 11–24 h, followed by the addition of p-TsOH in CH_3CN and reacted for an additional 4 h at the same temperature (Table 2). Significantly, regardless of the electron-donating or -withdrawing substituents on **2**, all of the reactions gave **5** in excellent enantioselectivities (>99% ee)[20] and
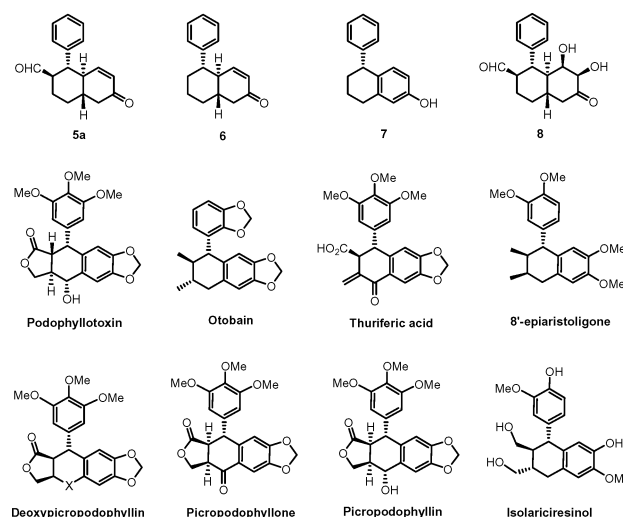
Representative procedure for the preparation of 3a and 4a (Table 1, entry 8)

To a solution of (*E*)-7-oxooct-5-enal (70 mg, 0.5 mmol) and *trans*-cinnamaldehyde (79 mg, 0.6 mmol) in EtOH (2 mL) was added dropwise a solution of catalyst **II** (32.5 mg, 0.1 mmol) in EtOH (1 mL). The resulting solution was stirred at ambient temperature for 72 h and diluted with EtOAc (10 mL). The solution was washed with brine (2 mL), dried over Na_2SO_4, and concentrated *in vacuo* to give the crude product. The residue was purified by flash column chromatography with 20% EtOAc–hexane (R_f = 0.25 for **3a**, R_f = 0.18 for **4a** in 40% EtOAc–hexane) to give **3a** (white solid, 83 mg, 61% yield, m.p. 92–94 °C) and **4a** (white solid, 30 mg, 22% yield, m.p. 118–120 °C).

(1*R*,2*S*,3*S*,4*S*)-4-(2-Oxopropyl)-2-phenylcyclohexane-1,3-dicarbaldehyde (3a). $[\alpha]_D^{25}$ −24 (c 4 $CHCl_3$); IR (neat): 2926, 2722, 1719, 1453, 1358, 1161, 1031, 761, 703 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 1.18–1.32 (m, 1 H), 1.53 (qd, J = 12.98, 3.05 Hz, 1 H), 1.93–2.04 (m, 2 H), 2.06 (s, 3 H), 2.25–2.33 (m, 2 H), 2.33–2.41 (m, 1 H), 2.45–2.53 (m, 1 H), 2.63 (t, J = 11.84 Hz, 1 H), 3.12 (t, J = 11.23 Hz, 1 H), 7.11–7.20 (m, 3 H), 7.23–7.29 (m, 2 H), 9.26 (d, J = 4.39 Hz, 1 H), 9.38 (d, J = 1.71 Hz, 1 H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 206.9 (C), 203.4 (CH), 202.7 (CH), 139.2 (C), 128.8 (two CH), 127.9 (two CH), 127.7 (CH), 60.5 (CH), 54.4 (CH), 47.5 (CH_2), 45.2 (CH), 32.3 (CH), 30.5 (CH_3) 30.4 (CH_2), 25.9 (CH_2); MS (*m/z*, relative intensity): 272 (M^+, 5), 255 (16), 226 (15),186 (26), 168 (68), 129 (39), 115 (43), 91 (100), 77 (26), 55 (14); exact mass calculated for $C_{17}H_{20}O_3$ (M^+): 272.1412; found 272.1415.

(1*R*,2*R*,4a*S*,8*S*,8a*S*)-Decahydro-8-hydroxy-6-oxo-1-phenyl-naphthalene-2-carbaldehyde (4a). $[\alpha]_D^{25}$ +22.5 (c 0.6 $CHCl_3$); IR (neat): 3406, 2923, 1708, 1451, 1309, 1154, 1022, 758, 701 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 1.32–1.43 (m, 1 H), 1.45–1.57 (m, 1 H), 1.72 (t, J = 10.74 Hz, 1 H), 1.96 (d, J = 12.45 Hz, 2 H), 2.06–2.26 (m, 3 H), 2.31–2.46 (m, 3 H), 2.69 (t, J = 11.96 Hz, 1 H), 3.01 (t, J = 11.47 Hz, 1 H), 3.76 (br. s, 1 H), 7.18–7.26 (m, 3 H), 7.28–7.34 (m, 2 H), 9.35 (d, J = 2.20 Hz, 1 H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 209.3 (C), 203.8 (CH), 140.7 (C), 129.0 (two CH), 128.1 (CH), 127.3 (two CH), 68.4 (CH), 55.8 (CH), 50.1 (CH), 49.8 (CH_2), 48.0 (CH_2), 45.2 (CH), 35.2 (CH), 32.6 (CH_2), 25.9 (CH_2).

Representative procedure for the preparation of 5a (Table 2, entry 10)

To a solution of (*E*)-7-oxooct-5-enal (70 mg, 0.5 mmol) and *trans*-cinnamaldehyde (79 mg, 0.6 mmol) in CH_3CN (2 mL) was added dropwise a solution of catalyst **II** (32.5 mg, 0.1 mmol) and acetic acid (6 mg, 0.1 mmol) in CH_3CN (1 mL). The resulting solution was stirred at ambient temperature for 12 h, followed by the addition of *p*-TsOH (80 mg, 0.5 mmol), and stirring for an additional 4 h. The solution was diluted with EtOAc (10 mL), washed with brine (2 mL), dried over Na_2SO_4, and concentrated *in vacuo* to give the crude product. The residue was purified by flash column chromatography with 15% EtOAc–hexane (R_f = 0.38 for **5a** in 40% EtOAc–hexane) to give **5a** as a white solid (109 mg, 86% yield), m.p. 161–163 °C.

(1*R*,2*R*,4a*S*,8a*R*)-1,2,3,4,4a,5,6,8a-Octahydro-6-oxo-1-phenyl-naphthalene-2-carbaldehyde (5a). $[\alpha]_D^{25}$ +38.8 (c 3 $CHCl_3$); IR (neat): 3030, 2927, 2857, 1722, 1678, 1453, 1389, 1258, 1105, 877, 754, 703 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 1.41–1.56 (m, 2 H), 1.87–1.97 (m, 2 H), 2.02 (d, J = 10.99 Hz, 1 H), 2.14–2.27 (m, 1 H), 2.39 (t, J = 10.86 Hz, 1 H), 2.50 (dd, J = 16.60, 2.93 Hz, 1 H), 2.63 (t, J = 11.47 Hz, 1 H), 2.76 (t, J = 11.11 Hz, 1 H), 5.86 (dd, J = 10.01, 1.22 Hz, 1 H), 6.43 (d, J = 10.25 Hz, 1 H), 7.21–7.30 (m, 3 H), 7.29–7.36 (m, 2 H), 9.37 (d, J = 2.5 Hz, 1 H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 202.9 (CH), 199.1 (C), 150.7 (CH), 139.8 (C), 129.9 (two CH), 129.1 (two CH), 128.4 (CH), 127.6 (CH), 56.3 (CH), 47.9 (CH), 46.6 (CH), 44.9 (CH_2), 40.9 (CH), 31.2 (CH_2), 25.8 (CH_2); MS (*m/z*, relative intensity): 254 (M^+, 90), 226 (10), 183 (15), 157 (15), 128 (48), 120 (84), 108 (82), 91 (100), 77 (42), 55 (26); exact mass calculated for $C_{17}H_{18}O_2$ (M^+): 254.1307; found 254.1305.

Representative one-pot procedure for the preparation of 5b (Table 2, entry 2)

To a solution of (*E*)-7-oxooct-5-enal (70 mg, 0.5 mmol) and (*E*)-3-(4-nitrophenyl)acrylaldehyde (106 mg, 0.6 mmol) in CH_3CN (2 mL) was added dropwise a solution of catalyst **II** (32.5 mg, 0.1 mmol) and acetic acid (6 mg, 0.1 mmol) in CH_3CN (1 mL). The resulting solution was stirred at ambient temperature for 11 h, followed by the addition of *p*-TsOH (80 mg, 0.5 mmol), and stirring for an additional 4 h. The solution was diluted with EtOAc (10 mL), washed with brine (2 mL), dried over Na_2SO_4, and concentrated *in vacuo* to give the crude product. The residue was purified by flash column chromatography with 30% EtOAc–hexane (R_f = 0.13 for **5b** in 40% EtOAc–hexane) to give **5b** as a yellow oil (124 mg, 83% yield).

(1*R*,2*R*,4a*S*,8a*R*)-1,2,3,4,4a,5,6,8a-Octahydro-1-(4-nitrophenyl)-6-oxonaphthalene-2-carbaldehyde (5b). $[\alpha]_D^{25}$ +54.3 (c 3.5 $CHCl_3$); IR (neat): 3030, 2928, 2858, 1723, 1680, 1598, 1519, 1346, 1259, 1102, 853, 751, 701 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 1.41–1.56 (m, 2 H), 1.92–2.00 (m, 2 H), 2.15 (d, J = 11.96 Hz, 1 H), 2.23 (t, J = 15.26 Hz, 1 H), 2.38–2.46 (m, 1 H), 2.53 (d, J = 16.36 Hz, 1 H), 2.81–2.88 (m, 2 H), 5.88 (d, J = 10.25 Hz, 1 H), 6.29 (d, J = 10.01 Hz, 1 H), 7.43 (d, J = 7.57 Hz, 2 H), 8.19 (d, J = 7.32 Hz, 2 H), 9.39 (s, 1 H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 201.5 (CH), 198.8 (C), 149.5 (CH), 148.5 (C), 147.5 (C), 130.8 (two CH), 129.7 (CH), 124.5 (two CH), 56.6 (CH), 47.4 (CH), 46.4 (CH), 45.0 (CH_2), 41.0 (CH), 34.5 (CH_2), 26.0 (CH_2); MS (*m/z*, relative intensity): 299 (M^+, 100), 270 (21), 228 (19), 202 (53), 152 (15), 128 (70), 115 (63), 91 (31), 77 (43), 55 (43); exact mass calculated for $C_{17}H_{17}NO_4$ (M^+): 299.1158; found 299.1156.

(1*R*,2*R*,4a*S*,8a*R*)-1,2,3,4,4a,5,6,8a-Octahydro-1-(4-methoxyphenyl)-6-oxonaphthalene-2-carbaldehyde (5c). R_f = 0.3 for **5c** in 40% EtOAc–hexane, yellow solid, m.p. 99–101 °C, 69% yield. Selected spectroscopic data for **5c**: $[\alpha]_D^{25}$ +43.7 (c 2.5 $CHCl_3$); IR (neat): 3030, 2928, 2860, 1719, 1682, 1610, 1513, 1249, 1180, 1032, 820, 772 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 1.40–1.56 (m, 2 H), 1.86–1.97 (m, 2 H), 2.01 (d, J = 12.21 Hz, 1 H), 2.16–2.27 (m, 1 H), 2.33 (t, J = 10.62 Hz, 1 H), 2.50 (d, J = 16.36 Hz, 1 H), 2.59 (t, J = 10.86 Hz, 1 H), 2.66–2.75 (m, 1 H), 3.77 (s, 3 H), 5.87 (d, J = 10.01 Hz, 1 H), 6.47 (d, J = 10.01 Hz, 1 H), 6.87 (d, J = 6.84 Hz, 2 H), 7.13 (d, J = 6.84 Hz, 2 H), 9.38 (br. s, 1 H);

^{13}C NMR (CDCl$_3$, 125 MHz): δ 203.3 (CH), 199.3 (C), 155.8 (C), 150.9 (CH), 131.7 (C), 129.9 (CH), 129.4 (two CH), 114.5 (two CH), 56.5 (CH), 55.2 (CH$_3$), 47.1 (CH), 46.8 (CH), 44.9 (CH$_2$), 41.0 (CH), 31.3 (CH$_2$), 25.9 (CH$_2$); MS (m/z, relative intensity): 284 (M$^+$, 20), 213 (3), 164 (9), 147 (6), 128 (4), 121 (100), 108 (13), 91 (8), 77 (7), 65 (4); exact mass calculated for C$_{18}$H$_{20}$O$_3$ (M$^+$): 284.1412; found 284.1414.

(1R,2R,4aS,8aR)-1-(4-Bromophenyl)-1,2,3,4,4a,5,6,8a-octahydro-6-oxonaphthalene-2-carbaldehyde (5d). R_f = 0.31 for **5d** in 40% EtOAc–hexane, white solid, m.p. 146–148 °C, 74% yield. Selected spectroscopic data for **5d**: [α]$_D^{25}$ +19.6 (c 7.5 CHCl$_3$); IR (neat): 3030, 2926, 2857, 1721, 1675, 1489, 1256, 1010, 881, 805, 766 cm^{-1}; ^{1}H NMR (CDCl$_3$, 500 MHz): δ 1.41–1.54 (m, 2 H), 1.87–1.97 (m, 2 H), 2.01–2.09 (m, 1 H), 2.17–2.26 (m, 1 H), 2.34 (t, J = 10.62 Hz, 1 H), 2.51 (d, J = 16.60 Hz, 1 H), 2.60–2.68 (m, 1 H), 2.70–2.78 (m, 1 H), 5.88 (d, J = 10.01 Hz, 1 H), 6.40 (d, J = 10.25 Hz, 1 H), 7.11 (d, J = 7.57 Hz, 2 H), 7.47 (d, J = 7.57 Hz, 2 H), 9.38 (s, 1 H); ^{13}C NMR (CDCl$_3$, 125 MHz): δ 202.3 (CH), 198.9 (C), 150.1 (CH), 147.0 (CH), 139.1 (C), 137.3 (CH), 131.7 (CH), 130.2 (CH), 130.0 (CH), 121.4 (C), 56.3 (CH), 47.1 (CH), 46.3 (CH), 44.8 (CH$_2$), 40.9 (CH), 31.7 (CH$_2$), 25.8 (CH$_2$); MS (m/z, relative intensity): 332 (M$^+$, 49), 261 (9), 235 (14), 182 (15), 171 (58), 128 (72), 120 (86), 108 (100), 95 (38), 91 (30), 77 (37), 55 (22); exact mass calculated for C$_{17}$H$_{17}$BrO$_2$ (M$^+$): 332.0412; found 332.0417.

(1R,2R,4aS,8aR)-1,2,3,4,4a,5,6,8a-Octahydro-6-oxo-1-p-tolylnaphthalene-2-carbaldehyde (5e). R_f = 0.53 for **5e** in 40% EtOAc–hexane, white solid, m.p. 106–108 °C, 72% yield. Selected spectroscopic data for **5e**: [α]$_D^{25}$ +39.0 (c 2 CHCl$_3$); IR (neat): 3030, 2925, 2857, 1721, 1683, 1515, 1259, 1103, 809, 771 cm^{-1}; ^{1}H NMR (CDCl$_3$, 500 MHz): δ 1.40–1.57 (m, 2 H), 1.86–1.97 (m, 2 H), 2.01 (d, J = 12.70 Hz, 1 H), 2.22 (t, J = 15.14 Hz, 1 H), 2.31 (s, 3 H), 2.36 (t, J = 10.74 Hz, 1 H), 2.51 (d, J = 16.36 Hz, 1 H), 2.60 (t, J = 11.48 Hz, 1 H), 2.73 (t, J = 10.99 Hz, 1 H), 5.86 (d, J = 10.01 Hz, 1 H), 6.47 (d, J = 10.25 Hz, 1 H), 7.06–7.12 (m, 2 H), 7.12–7.17 (m, 2 H), 9.37 (s, 1 H); ^{13}C NMR (CDCl$_3$, 125 MHz): δ 203.2 (CH), 199.2 (C), 150.9 (CH), 137.2 (C), 136.7 (C), 129.8 (CH), 129.7 (CH), 129.6 (CH), 128.2 (two CH), 56.4 (CH), 47.6 (CH), 46.6 (CH), 44.9 (CH$_2$), 41.0 (CH), 31.2 (CH$_2$), 25.8 (CH$_2$), 21.0 (CH$_3$); MS (m/z, relative intensity): 268 (M$^+$, 39), 197 (9), 148 (37), 128 (26), 115 (23), 105 (100), 91 (26), 77 (17), 55 (7); exact mass calculated for C$_{18}$H$_{20}$O$_2$ (M$^+$): 268.1463; found 268.1460.

(1R,2R,4aS,8aR)-1,2,3,4,4a,5,6,8a-Octahydro-1-(2-nitrophenyl)-6-oxonaphthalene-2-carbaldehyde (5f). R_f = 0.13 for **5f** in 40% EtOAc–hexane, yellow oil, 63% yield. Selected spectroscopic data for **5f**: [α]$_D^{25}$ +54.3 (c 5.5 CHCl$_3$); IR (neat): 2925, 2855, 1717, 1683, 1525, 1354, 1258, 853, 745 cm^{-1}; ^{1}H NMR (CDCl$_3$, 500 MHz): δ 1.43–1.55 (m, 2 H), 1.92–2.06 (m, 2 H), 2.14 (d, J = 8.30 Hz, 1 H), 2.18–2.27 (m, 1 H), 2.45 (t, J = 10.74 Hz, 1 H), 2.54 (d, J = 16.85 Hz, 1 H), 2.71–2.81 (m, 1 H), 3.39 (t, J = 11.35 Hz, 1 H), 5.92 (d, J = 10.01 Hz, 1 H), 6.39 (d, J = 10.25 Hz, 1 H), 7.35–7.43 (m, 1 H), 7.45 (d, J = 7.81 Hz, 1 H), 7.56–7.63 (m, 1 H), 7.77 (d, J = 8.06 Hz, 1 H), 9.37 (s, 1 H); ^{13}C NMR (CDCl$_3$, 125 MHz): δ 201.2 (CH), 198.6 (C), 151.6 (C), 149.9 (CH), 134.9 (C), 133.1 (CH), 130.3 (CH), 128.2 (CH), 128.15 (CH), 124.3 (CH), 57.0 (CH), 46.6 (CH), 44.8 (CH$_2$), 40.8 (CH), 40.4 (CH), 31.3 (CH$_2$), 25.7 (CH$_2$); MS (m/z, relative intensity):

299 (M$^+$, 26), 264 (45), 236 (71),180 (36), 146 (46), 130 (60), 120 (100), 115 (72), 91 (67), 77 (78), 55 (88); exact mass calculated for C$_{17}$H$_{17}$NO$_4$ (M$^+$): 299.1158; found 299.1162.

(1R,2R,4aS,8aR)-1,2,3,4,4a,5,6,8a-Octahydro-1-(naphthalen-1-yl)-6-oxonaphthalene-2-carbaldehyde (5g). R_f = 0.43 for **5g** in 40% EtOAc–hexane, pale yellow oil, 71% yield. Selected spectroscopic data for **5g**: [α]$_D^{25}$ +18.2 (c 3.5 CHCl$_3$); IR (neat): 2926, 2863, 1717, 1683, 1507, 1457, 1260, 1102, 818, 774, 750 cm^{-1}; ^{1}H NMR (CDCl$_3$, 500 MHz): δ 1.49–1.66 (m, 2 H), 1.91–2.04 (m, 2 H), 2.04–2.14 (m, 1 H), 2.20–2.31 (m, 1 H), 2.47–2.59 (m, 2 H), 2.78–2.86 (m, 1 H), 2.86–2.95 (m, 1 H), 5.85 (d, J = 9.77 Hz, 1 H), 6.46 (d, J = 10.01 Hz, 1 H), 7.37 (d, J = 8.30 Hz, 1 H), 7.42–7.52 (m, 2 H), 7.68 (br. s, 1 H), 7.74–7.89 (m, 3 H), 9.41 (d, J = 2.0 Hz, 1 H); ^{13}C NMR (CDCl$_3$, 125 MHz): δ 202.9 (CH), 199.2 (C), 150.7 (CH), 137.3 (C), 133.4 (C), 132.8 (C), 130.0 (CH), 129.2 (CH), 127.7 (CH), 127.6 (CH), 126.6 (two CH), 126.1 (two CH), 56.2 (CH), 48.1 (CH), 46.5 (CH), 45.0 (CH$_2$), 41.0 (CH), 31.3 (CH$_2$), 25.9 (CH$_2$); MS (m/z, relative intensity): 304 (M$^+$, 89), 276 (6), 233 (7), 184 (20), 165 (27), 141 (100), 128 (31), 115 (13), 95 (15), 69 (12), 55 (24); exact mass calculated for C$_{21}$H$_{20}$O$_2$ (M$^+$): 304.1463; found 304.1469.

(1R,2R,4aS,8aR)-1,2,3,4,4a,5,6,8a-Octahydro-7-methyl-6-oxo-1-phenylnaphthalene-2-carbaldehyde (5h). R_f = 0.6 for **5h** in 40% EtOAc–hexane, white solid, m.p. 107–109 °C, 84% yield. Selected spectroscopic data for **5h**: [α]$_D^{25}$ +57.4 (c 2 CHCl$_3$); IR (neat): 2925, 2895, 1718, 1671, 1541, 1455, 1259, 1070, 1011, 800, 760, 702 cm^{-1}; ^{1}H NMR (CDCl$_3$, 500 MHz): δ 1.36–1.53 (m, 2 H), 1.59 (br. s, 3 H), 1.81–1.92 (m, 2 H), 1.97 (d, J = 13.43 Hz, 1 H), 2.17 (t, J = 15.14 Hz, 1 H), 2.35 (t, J = 10.50 Hz, 1 H), 2.49 (d, J = 16.36 Hz, 1 H), 2.59 (t, J = 11.47 Hz, 1 H), 2.70 (t, J = 11.11 Hz, 1 H), 6.14 (br. s, 1 H), 7.17–7.23 (m, 3 H), 7.28–7.34 (m, 2 H), 9.33 (s, 1 H); ^{13}C NMR (CDCl$_3$, 125 MHz): δ 203.2 (CH), 199.2 (C), 145.6 (CH), 140.1 (C), 136.0 (C), 129.0 (two CH), 128.5 (CH), 127.4 (two CH), 56.4 (CH), 48.0 (CH), 46.6 (CH), 45.0 (CH$_2$), 41.2 (CH), 31.0 (CH$_2$), 25.8 (CH$_2$), 15.7 (CH$_3$); MS (m/z, relative intensity): 268 (M$^+$, 99), 240 (15), 197 (18), 162 (11), 134 (100), 122 (61), 115 (33), 91 (67), 77 (23), 55 (9); exact mass calculated for C$_{18}$H$_{20}$O$_2$ (M$^+$): 268.1463; found 268.1465.

(1R,2R,4aS,8aR)-1,2,3,4,4a,5,6,8a-Octahydro-7-methyl-1-(4-nitrophenyl)-6-oxonaphthalene-2-carbaldehyde (5i). R_f = 0.25 for **5i** in 40% EtOAc–hexane, white solid, m.p. 164–166 °C, 82% yield. Selected spectroscopic data for **5i**: [α]$_D^{25}$ +55.8 (c 2.5 CHCl$_3$); IR (neat): 2925, 2858, 1719, 1673, 1519, 1346, 1083, 855, 754, 700 cm^{-1}; ^{1}H NMR (CDCl$_3$, 500 MHz): δ 1.48 (br. s, 2 H), 1.63 (br. s, 3 H), 1.94 (br. s, 2 H), 2.14 (br. s, 1 H), 2.17–2.28 (m, 1 H), 2.41 (br. s, 1 H), 2.56 (d, J = 16.60 Hz, 1 H), 2.82 (d, J = 3.17 Hz, 2 H), 6.02 (br. s, 1 H), 7.44 (br. s, 2 H), 8.22 (br. s, 2 H), 9.40 (d, J = 3.66 Hz, 1 H); ^{13}C NMR (CDCl$_3$, 125 MHz): δ 201.4 (CH), 198.7 (C), 148.5 (C), 147.2 (C), 144.1 (CH), 136.9 (C), 129.4 (two CH), 124.2 (two CH), 56.5 (CH), 47.4 (CH), 46.2 (CH), 44.9 (CH$_2$), 41.1 (CH), 31.0 (CH$_2$), 25.7 (CH$_2$), 15.7 (CH$_3$); MS (m/z, relative intensity): 313 (M$^+$, 100), 271 (15), 242 (21), 216 (11), 165 (11), 141 (26), 134 (44), 115 (42), 91 (27), 69 (42), 55 (15); exact mass calculated for C$_{18}$H$_{19}$NO$_4$ (M$^+$): 313.1314; found 313.1318.

(1R,2R,4aS,8aR)-1-(4-Bromophenyl)-1,2,3,4,4a,5,6,8a-octahydro-7-methyl-6-oxonaphthalene-2-carbaldehyde (5j). R_f = 0.48 for **5j** in 40% EtOAc–hexane, white solid, m.p. 183–185 °C, 75%

yield. Selected spectroscopic data **5j**: $[\alpha]_D^{25}$ +38.8 (c 3 CHCl₃); IR (neat): 2931, 2856, 1716, 1673, 1490, 1258, 1078, 1010, 899, 807, 757 cm⁻¹; ¹H NMR (CDCl₃, 500 MHz): δ 1.38–1.54 (m, 2 H) 1.63 (br. s., 3 H) 1.90 (d, $J = 6.59$ Hz, 2 H) 2.03 (dd, $J = 9.28$, 1.95 Hz, 1 H) 2.14–2.25 (m, 1 H) 2.33 (br. s., 1 H) 2.53 (d, $J = 16.60$ Hz, 1 H) 2.58–2.66 (m, 1 H) 2.69 (d, $J = 9.28$ Hz, 1 H) 6.12 (br. s., 1 H) 7.11 (d, $J = 5.62$ Hz, 2 H) 7.48 (d, $J = 5.62$ Hz, 2 H) 9.37 (d, $J = 2.5$ Hz, 1 H); ¹³C NMR (CDCl₃, 125 MHz): δ 202.5 (CH), 199.0 (C), 145.0 (CH), 139.4 (C), 136.4 (C), 132.2 (two CH), 130.1 (two CH), 121.3 (C), 56.4 (CH), 47.4 (CH), 46.5 (CH), 45.0 (CH₂), 41.2 (CH), 31.0 (CH₂), 25.8 (CH₂), 15.7 (CH₃); MS (m/z, relative intensity): 346 (M⁺, 26), 277 (5), 196 (3), 169 (24), 134 (100), 122 (58), 115 (24), 91 (16), 77 (15), 55 (7); exact mass calculated for C₁₈H₁₉BrO₂ (M⁺): 346.0568; found 346.0563.

(4aR,5S,8aS)-4a,5,6,7,8,8a-Hexahydro-5-phenylnaphthalen-2(1H)-one (6). To a solution of **5a** (100 mg, 0.4 mmol) in toluene (5 mL) was added Wilkinson's catalyst (182 mg, 0.2 mmol), and the resulting solution was heated to reflux for 5 h. After cooling to room temperature, the solution was diluted with EtOAc (10 mL), filtered over celite, and concentrated in *vacuo* to afford the crude product. The residue was purified by flash column chromatography with 10% EtOAc–hexane ($R_f = 0.43$ for **6** in 20% EtOAc–hexane) to give **6** as a white solid (65 mg, 73%), m.p. 107–109 °C. Selected spectroscopic data for **6**: $[\alpha]_D^{25}$ +57.3 (c 0.7 CHCl₃); IR (neat): 3028, 2925, 2854, 1678, 1445, 1385, 1265, 1104, 843, 761, 702 cm⁻¹; ¹H NMR (CDCl₃, 500 MHz): δ 1.30–1.42 (m, 1 H), 1.50 (qd, $J = 12.86$, 2.93 Hz, 1 H), 1.56–1.67 (m, 1 H), 1.78 (d, $J = 12.70$ Hz, 1 H), 1.84–2.00 (m, 3 H), 2.17–2.28 (m, 1 H), 2.27–2.35 (m, 1 H), 2.35–2.43 (m, 1 H), 2.48 (d, $J = 16.60$ Hz, 1 H), 5.84 (d, $J = 10.01$ Hz, 1 H), 6.51 (d, $J = 9.52$ Hz, 1 H), 7.14–7.27 (m, 3 H), 7.28–7.38 (m, 2 H); ¹³C NMR (CDCl₃, 125 MHz): δ 200.1 (C), 152.8 (CH), 143.9 (C), 129.4 (CH), 128.7 (two CH), 127.8 (two CH), 126.7 (CH), 48.1 (CH), 46.9 (CH), 45.4 (CH₂), 41.7 (CH), 35.9 (CH₂), 32.8 (CH₂), 25.8 (CH₂); MS (m/z, relative intensity): 227 (M⁺+1, 16), 226 (M⁺, 91), 183 (8), 157 (11), 128 (24), 108 (100), 91 (61); exact mass calculated for C₁₆H₁₈O (M⁺): 226.1358; found 226.1359.

(R)-5,6,7,8-Tetrahydro-5-phenylnaphthalen-2-ol (7). To a solution of **6** (57 mg, 0.25 mmol) in *o*-dichlorobenzene (3 mL) was added DDQ (86 mg, 0.38 mmol) and catalytic amount of *p*-TsOH (4.5 mg, 0.026 mmol). The resulting solution was heated to 170 °C and stirred for 7 h. After cooling to room temperature, the reaction mixture was directly loaded on to a column and purified by silica gel chromatography with 15% EtOAc–hexane ($R_f = 0.3$ for **7** in 20% EtOAc–hexane) to give **7** as a brown oil (31 mg, 53%). Selected spectroscopic data for **7**: $[\alpha]_D^{25}$ −11.2 (c 0.5 CHCl₃); IR (neat): 3550–3100, 2929, 2857, 1607, 1497, 1448, 1254, 940, 822, 754, 701 cm⁻¹; ¹H NMR (CDCl₃, 500 MHz): δ 1.65–1.75 (m, 1 H), 1.77–1.89 (m, 2 H), 2.07–2.15 (m, 1 H), 2.72–2.80 (m, 1 H), 2.80–2.89 (m, 1 H), 4.02 (t, $J = 6.59$ Hz, 1 H), 4.67 (br. s., 1 H), 6.51 (d, $J = 8.30$ Hz, 1 H), 6.59 (br. s., 1 H), 6.68 (d, $J = 8.30$ Hz, 1 H), 7.08 (d, $J = 7.32$ Hz, 2 H), 7.14–7.21 (m, 1 H), 7.22–7.29 (m, 2 H); ¹³C NMR (CDCl₃, 125 MHz): δ 153.4 (C), 147.7 (C), 139.1 (C), 131.7 (C), 131.3 (CH), 128.7 (two CH), 128.2 (two CH), 125.9 (CH), 114.8 (CH), 113.1 (CH), 44.9 (CH), 33.4 (CH₂), 29.9 (CH₂), 20.8 (CH₂); MS (m/z, relative intensity): 224 (M⁺, 92), 196 (61), 147 (78), 134 (100), 91 (60), 73 (71); exact mass calculated for C₁₆H₁₆O (M⁺): 224.1201; found 224.1208.

(1R,2R,4aS,7R,8R,8aS)-Decahydro-7,8-dihydroxy-6-oxo-1-phenylnaphthalene-2-carbaldehyde (8). To a solution of **5a** (25 mg, 0.1 mmol) in THF/*t*-BuOH:H₂O (1 : 3 : 0.5 mL) was added *N*-methylmorpholine *N*-oxide (NMO, 35 mg, 0.3 mmol) and OsO₄ (20 μL, 2.5 wt% in *t*-BuOH), and the solution was stirred for 8 h at ambient temperature. The reaction was quenched by the addition of sodium sulfite (50 mg). The mixture was stirred for 30 min, and extracted with EtOAc (25 mL × 2). The combined organic layers were washed with brine (25 mL), dried over Na₂SO₄, and concentrated *in vacuo* to afford the crude product. The residue was purified by flash column chromatography with 50% EtOAc–hexane ($R_f = 0.20$ for **8** in 50% EtOAc–hexane) to give **8** as a white solid (22 mg, 79%), m.p. 197–199 °C. Selected spectroscopic data for **8**: $[\alpha]_D^{25}$ +65.1 (c 0.5 CHCl₃); IR (neat): 3458, 2918, 1639, 1438, 1325, 1258, 1126, 889, 758, 702 cm⁻¹; ¹H NMR (CDCl₃, 500 MHz): δ, 1.34–1.46 (m, 1 H) 1.46–1.57 (m, 1 H) 1.80 (t, $J = 10.01$ Hz, 1 H) 1.93–2.04 (m, 2 H) 2.12–2.23 (m, 2 H) 2.27 (s, 1 H) 2.50–2.61 (m, 1 H) 2.70 (t, $J = 11.96$ Hz, 1 H) 3.10 (t, $J = 11.48$ Hz, 1 H) 3.65–3.75 (m, 2 H) 3.96 (br. s., 1 H) 7.24 (br. s., 3 H) 7.27–7.35 (m, 2 H) 9.36 (d, $J = 1.95$ Hz, 1 H); ¹³C NMR (CDCl₃, 125 MHz): δ 208.6 (C), 203.7 (CH), 140.3 (C), 129.0 (three CH), 127.3 (two CH), 77.4 (CH), 71.8 (CH), 55.3 (CH), 48.5 (CH), 44.9 (CH₂), 44.8 (CH), 35.8 (CH), 32.2 (CH₂), 25.8 (CH₂); MS (m/z, relative intensity): 288 (M⁺, 60), 241 (12), 215 (38), 197 (21), 169 (42), 129 (24), 115 (30), 91 (100), 77 (18), 55 (20); exact mass calculate for C₁₇H₂₀O₄ (M⁺): 288.1362; found 288.1363.

Acknowledgements

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Org. Biomol. Chem., 2009, **7**, 3095–3101 | 3101