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Facile Construction of Vicinal Quaternary and Tertiary Stereocenters *via* Regio- and Stereoselective Organocatalytic Michael Addition to Nitrodienes

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Abstract: A highly regio- and stereoselective protocol for the synthesis of vicinal quaternary and tertiary stereocenters has been developed. The 6′-OH *Cinchona* alkaloids (**BnCPN** or **BnCPD**) at low catalyst loading (0.5–5 mol%) catalyze the Michael addition of trisubstituted carbon nucleophiles to nitrodienes in good to excellent yield (up to >99), high enantioselectivity (up to 99% *ee*) and high diastereoselectivity (up to >99:1 *dr*) under mild reaction conditions.

Keywords: *Cinchona* alkaloids; Michael addition; nitrodienes; organocatalysis; quaternary stereocenter

Introduction

The asymmetric Michael addition to nitroalkenes has emerged as one of the most important carbon-carbon bond-forming reactions for the synthesis of valuable chiral entities.[1] Nitro-olefins are considered as excellent electrophiles for the catalytic asymmetric Michael reaction, due to their high reactivity and the hydrogen bond accepting ability of the nitro functionality.[2] The corresponding nitroalkanes are synthetically useful molecules, since the nitro group can be transformed into other valuable functional groups. The synthetic utility of nitro-olefins can be enhanced by the introduction of a carbon-carbon double bond in conjugation with the nitro-olefinic double bond. The nitrodienes have an additional reactive site, i.e., a double bond, that can be exploited widely for the construction of synthetically valuable and potentially bioactive targets. Furthermore, in nitrodienes, there exists the additional possibilty of δ-attack rather than β-attack due to the two conjugate double bonds. So far, only a little progress has been made for the development of asymmetric Michael reactions employing nitrodienes as acceptors.[3,4] Although the nitrodienes have emerged as effective electrophiles in asymmetric enamine catalysis,[3] there are limited examples of their use as Michael acceptor in non-covalent bifunctional hydrogen bond catalysis[4]. Recently, Feng and co-workers have successfully extended the catalytic application of chiral bifunctional guanidine catalysts for the addition of tri-substituted β-keto esters to nitrodienes in order to obtain adjacent quaternary and tertiary stereocenters.[4c]

The vicinal quaternary and tertiary stereocenters are present in many natural products and biologically important molecules. Significant progress have been made towards the asymmetric synthesis of adjacent quaternary and tertiary stereocenters.[5] Owing to steric encumbrance, the stereoselective construction of quaternary stereocenters is considered to be a synthetic challenge for organic chemists, requiring relatively harsh reaction conditions.[6]

On the other hand, for the synthesis of potentially bioactive chiral molecules and their precursors, it is imperative to synthesize both enantiomers of the target molecules. In this regard *Cinchona* alkaloids have emerged as valuable organocatalysts since by using the pseudoenantiomeric catalysts, both enantiomers of the product can be synthesized.[7,8]

During our current investigations on bifunctional *Cinchona* alkaloids-catalyzed carbon-cabon bond formation,[9] we envisaged that the quinuclidine nitrogen of the *Cinchona* alkaloids activates the prochiral nucleophile and the hydroxy group (9-OH/or 6′-OH group) of the catalyst activates and orients the nitrodiene through hydrogen bonding with the nitro group.

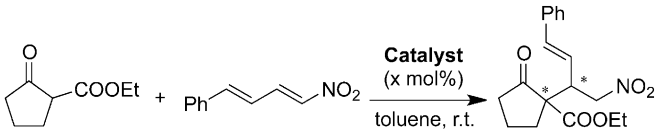
Herein, we disclose the catalytic potential of bifunctional *Cinchona*-derived organocatalysts for the highly regio- and stereoselective conjugate addition of trisubstituted carbon nucleophiles to nitrodienes for the construction of vicinal quaternary and tertiary stereocenters.

Results and Discussion

Our initial experiments involved the screening of different *Cinchona* alkaloid catalysts (10 mol%) for addition of the trisubstituted β-keto ester (**6a**) to nitrodiene **7a** in toluene at room temperature (Table 1). All *Cinchona* alkaloids (Figure 1) provided very high yields of **8a** in short reaction times, although the stereoselectivity varied from catalyst to catalyst. The natural (**QN**, **CD**, **CN** and **QD**) and 9-OH protected *Cinchona* alkaloids (**BnQN** and **AcQN**) provided moderate *ee* and high *dr* (Table 1, entries1–6). In order to achieve better results in terms of enantioselectivity, the 6′-OH *Cinchona* alkaloids were employed, as these catalysts have shown great potential as bifunctional organocatalysts for asymmetric conjugate addition reactions.[10,11] Cupreine (**CPN**) affords **8a** with 91% *ee* and *dr* of 91:9 (Table 1, entry 7). **BnCPN** provide the 1,4-adduct **8a** with 97% *ee* and 91:9 *dr* (Table 1, entry 8). The other 9-OH alkylated 6′-OH *Cinchona* catalysts such as **1g** and **1h** provide similar levels of stereoselectivity (Table 1, entries 9 and 10). The esterified catalysts **BzCPN** and **AcCPN** also provide **8a** in high enantioselectivity but with lower diastereoselectivity (Table 1, entries 11 and 12). The pseudoenantiomeric 6′-OH *Cinchona* alkaloid catalysts derived from quinidine such as cupreidine (**CPD**), **BnCPD** and **β-ICPD** provide the desired product **8a** with high enantioselectivity of opposite enantiomer (Table 1, entries 13–15). The thiourea derivatives of *Cinchona* alkaloids (**CDT** and **QDT**) resulted in moderate *ee* and high *dr* of up to 95:5 (Table 1, entries 16 and 17).

The effect of additives such as molecular sieves, benzoic acid and thiouredic acid (**5**) on the stereose-

Table 1. Catalyst screening and optimization.[a]



6a 7a 8a

Entry	Catalyst [x mol%]	Time [h]	Yield [%][b]	*dr*[c]	*ee* [%][d]
1	**QN** (10)	6	98	90:10	−45
2	**CD** (10)	6	99	90:10	−61
3	**CN** (10)	6	98	90:10	60
4	**QD** (10)	6	99	90:10	40
5	**BnQN**(10)	10	96	91:9	46
6	**AcQN** (10)	10	97	91:9	44
7	**CPN** (10)	5	99	91:9	91
8	**BnCPN** (10)	5	98	91:9	97
9	**NpCPN** (10)	5	99	91:9	95
10	**$C_{14}H_{29}$CPN** (10)	5	98	91:9	97
11	**BzCPN** (10)	5	97	82:18	97
12	**AcCPN** (10)	5	97	83:17	96
13	**CPD** (10)	5	98	91:9	−89
14	**BnCPD** (10)	5	99	91:9	−94
15	**β-ICPD** (10)	5	98	91:9	−82
16	**CDT** (10)	5	98	95:5	70
17	**QNT** (10)	5	99	95:5	81
18[e]	**BnCPN** (10)	6	97	91:9	96
19[f]	**BnCPN**(10)	10	96	91:9	96
20[g]	**BnCPN** (10)	10	97	91:9	97
21	**BnCPN** (5)	6	98	91:9	96
22	**BnCPN** (2)	10	99	91:9	97
23	**BnCPN** (1)	15	97	91:9	97
24	**BnCPN** (0.5)	24	97	91:9	97
25	**BnCPN** (0.25)	81	72	91:9	97
26	**BnCPN** (0.1)	120	38	91:9	97

[a] Unless otherwise noted, reactions were carried out with 0.3 mmol of **6a** and 0.2 mmol of **7a** in 0.2 mL of toluene with x mol% of catalyst at room temperature.
[b] Yield refers to isolated yield after column chromatography.
[c] *dr* refers to diastereomeric ratio after short column chromatography.
[d] *ee* refers to enantiomeric excess of major diastereomer.
[e] 4 Å molecular sieves (4 Å MS) were added.
[f] 10 mol% of PhCOOH was added.
[g] 10 mol% of **5** was used as additive .

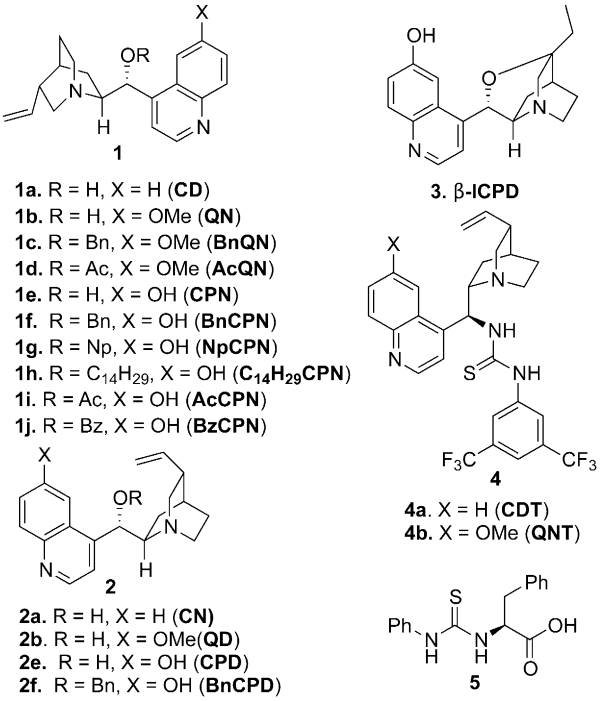


Figure 1. Structures of organocatalysts and additive used.

Table 2. Solvent screening.[a]

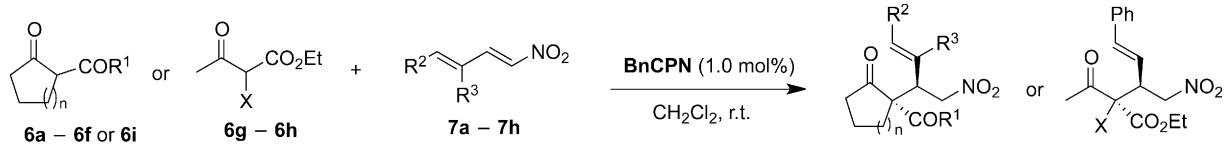
Entry	Solvent	Time [h]	Yield [%][b]	*dr*[c]	*ee* [%][d]
1	toluene	15	98	91:9	97
2	xylene	15	99	91.9	97
3	$CHCl_3$	15	98	90:10	96
4	CH_2Cl_2	15	>99	94:6	97
5	$ClCH_2CH_2Cl$	18	97	94:6	96
6	THF	18	99	93.7	96
7	MTBE	16	98	93:7	97
8	diethyl ether	12	99	92:8	90
9	DMF	36	26	91:9	84
10	MeOH	36	66	89:11	66

[a] Reactions were carried out with 0.3 mmol of **6a** and 0.2 mmol of **7a** in 0.2 mL of solvent with 1 mol% of **BnCPN** at room temperature.
[b] Yield refers to isolated yield after column chromatography.
[c] *dr* refers to *diastereomeric ratio* after short column chromatography.
[d] *ee* refers to *enantiomeric excess* of major diastereomer.

lectivity of the **BnCPN**-catalyzed reaction of **6a** with **7a** was evaluated. The additives slowed down the reaction and did not show any improvement in the *ee* and *dr* of the **8a** (entries 18–20). On reducing the catalyst loading from 10 mol% to 1 mol% stereoselectivity of **8a** remained nearly the same (entries 21–23). The 1 mol% of **BnCPN** provides 97% of **8a** with 97% *ee* and 91:9 *dr* in 15 h (Table 1, entry 23). Further lowering of the catalyst loading did not effect the stereochemical outcome of the reaction although a decrease in the reaction rate was observed (Table 1, entries 24–26).

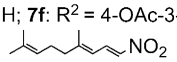
A very small effect on the yield and stereoselectivity of adduct **8a** was observed on screening different solvents with 1 mol% of **BnCPN** (Table 2). Dichloromethane turns out to be the solvent of choice that provides the product **8a** in quantitative yield, 97% *ee* and 94:6 *dr* after 15 h (Table 2, entry 4).

Table 3. BnCPN-catalyzed asymmetric Michael reaction of prochiral trisubstituted nucleophiles with nitrodienes.[a]



6a – **6f** or **6i** | **6g** – **6h** | **7a** – **7h** | **8a** – **8o** or **8r** | **8p** – **8q**

6a: R^1 = OEt, n =1; **6b:** R^1 = OMe, n = 1;
6c: R^1 = O-*i*-Pr, n = 1; **6d:** R^1 = O-*t*-Bu, n = 1;
6e: R^1 = OBn, n = 1; **6f:** R^1 = OEt, n = 2;
6g: X = Me, **6h.** X = Cl:
6i: R^1 = Me, n =1

7a: R^2 = Ph, R^3 = H; **7b:** R^2 = 2-$NO_2C_6H_4$, R^3 = H;
7c: R^2 = 4-$NO_2C_6H_4$, R^3 = H; **7d:** R^2 = 2-$MeOC_6H_4$, R^3 = H;
7e: R^2 = 4-$MeOC_6H_4$, R^3 = H; **7f**: R^2 = 4-OAc-3-$MeOC_6H_3$, R^3 = H;
7g: R^2 = Ph, R^3 = Me; **7h:** 

Entry	Nucleophile	Nitrodiene	Time [h]	Product	Yield [%][b]	*dr*[c]	*ee* [%][d]
1	**6a**	**7a**	15	**8a**	>99	94:6	97
2[e]	**6a**	**7b**	24	**8b**	98	96:4	96
3[e]	**6a**	**7c**	24	**8c**	99	93:7	95
4	**6a**	**7d**	48	**8d**	92	90: 10	91
5	**6a**	**7e**	48	**8e**	91	89:11	93
6	**6a**	**7f**	36	**8f**	97	93:7	97
7[f]	**6a**	**7g**	96	**8g**	74	>99:1	88
8	**6a**	**7h**	36	**8h**	77	65:35	91, 95[g]
9	**6b**	**7a**	18	**8i**	99	89:11	90
10	**6c**	**7a**	60	**8j**	88	96:4	93
11	**6d**	**7a**	72	**8k**	92	97:3	97
12	**6d**	**7e**	96	**8l**	80	98:2	98
13	**6e**	**7a**	48	**8m**	94	88:12	95
14	**6f**	**7a**	72	**8n**	82	99:1	99
15	**6f**	**7e**	96	**8o**	73	99:1	98
16[f]	**6g**	**7a**	96	**8p**	63	65:35	96, 75[g]
17[f]	**6h**	**7a**	15	**8q**	93	56:44	93, 89[g]
18	**6i**	**7a**	60	**8r**	93	79:21	90

[a] Unless noted, reactions were carried out with 0.3 mmol of **6** and 0.2 mmol of **7** in 0.2 mL of CH_2Cl_2 with 1 mol% of **1f**.
[b] Yield refers to isolated yield after column chromatography.
[c] *dr* refers to diastereomeric ratio after short column chromatography.
[d] *ee* refers to enantiomeric excess of major diastereomer.
[e] 0.5 mol% of catalyst was used.
[f] 5 mol% of catalyst was used.
[g] *ee* of minor diastereomer.

After optimization, the substrate scope was evaluated by screening different nitrodienes (**7**) and trisubstituted carbon nucleophiles (**6**) using **BnCPN** as catalyst in dichloromethane at room temperature (Table 3). Initially, the screening was carried out with **6a** as nucleophile with nitrodienes (**7b** and **7c**) substituted with electron-withdrawing groups in the aromatic ring. The products (**8b** and **8c**) were isolated in excellent yield and high stereo-induction with 0.5 mol% of catalysts (Table 3, entries 2 and 3). The nitrodienes substituted with electron-releasing groups (**7d**, **7e** and **7f**) also provide good yield and high *ee* and *dr* of 1,4-adducts (Table 3, entries 4–6). The nitrodiene bearing an α-methyl group **7g** also resulted in the formation of the desired adduct **8g** in good yield and *ee* with >99:1 *dr* in the presence of 5 mol% of the catalyst (Table 3, entry 7). Not only aromatic but also an aliphatic nitrodiene **7h** resulted in the formation of Michael adduct **8h** in good yield and enantioselectivity although the diastereoselectivity was low (Table 3, entry 8).

After successful screening of various nitrodiene derivatives, different cyclic β-keto esters were screened. The five-membered β-keto esters such as Me, *i*-Pr, *t*-Bu and Bn esters react with nitrodiene to provide the respective adducts **8i**–**8m** in good to high yield and stereoselectivity (Table 3, entries 9–13). The absolute configuration of the Michael adducts obtained with **BnCPN** can be assigned as 1*S*,2′*R* on comparision of the specific rotation and HPLC chromatogram of the adduct **8k** with that reported in the literature.[4c]

The six-membered cyclic β-keto ester (**6f**) also reacts with nitrodienes (**7a** and **7e**) providing the desired adducts (**8n** and **8o**) in good yield and excellent stereoselectivity (Table 3, entries 14 and 15). 5 mol% of **BnCPN** also catalyzes the Michael addition of acyclic trisubstituted β-keto ester **6g** with **7a** to provide the adduct **8p** in 63% yield and 96% *ee* of the major diastereomer, but the diastereoselectivity was poor (Table 3, entry 16).

The chlorinated quaternary stereocenter was obtained in high yield and low *dr* with a good level of *ee* for both the diastereomers in the presence of 5 mol% of **BnCPN** (Table 3, entry 17). Not only β-keto esters but cyclic diketones (e.g., **6i**) also resulted in the formation of Michael adduct **8r** with moderate *dr* and good *ee* (Table 3, entry 18).

The substrate scope was also evaluated with **BnCPD** as catalyst, which provides access to vicinal quaternary and tertiary stereocenters in comparable yield and stereoselectivity to that of **BnCPN**. The opposite enantiomers with good to excellent yield and *ee* were obtained with 0.5–5 mol% of **BnCPD** (Table 4).

Remarkably, on the lowering of catalyst loading of **BnCPN** (1–0.05 mol%), the Michael adduct **7a** was isolated without the loss of *ee* and *dr*, these results indicates a high turnover number for this transformation (Table 5). Generally, the turnover numbers of organocatalytic reactions are lower than those of transition metal-mediated processes. A high catalyst turnover renders this transformation ideal for industrial applications. To demonstrate this, a gram scale reaction was performed between **6a** and **7a** in the presence of 0.5 mol% of **BnCPN**. The product **8a** was isolated in 98% yield and with same level of stereoselectivity (Scheme 1). The enantiopure catalyst was recovered in 96% yield by simply washing the column with methanol.

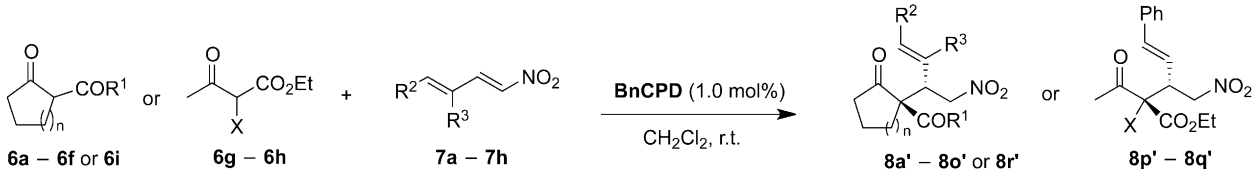
The proposed mechanism for this transformation can be elucidated as shown in Figure 2. **BnCPN** (or **BnCPD**) acts as bifunctional organocatalyst, which provides the synergic activation to both the reactants.[5a] The proposed transition state involves a ternary complex of prochiral nucleophile, nitrodiene and catalyst. The tertiary amine activates the nucleophile by stabilizing the enol through hydrogen bonding and the aromatic OH of the catalyst activate the nitrodiene and also orients the keto ester with the hydrogen bonding network.

The synthetic utility of this transformation was demonstrated for the synthesis of chiral octahydroindole derivative (**10**) (Scheme 2), since this octahydroindole is a common core in bioactive natural products such as aeruginosin 298 A, dysinosin A 1, oscillarin, etc.[12] The process involves the Zn/HCl-mediated reductive cyclization of adduct **8n** obtained with **BnCPN** to imine **9**. Reduction of imine (**9**) with $NaCNBH_3$ followed by Boc protection results in octahydroindole **9** in good overall yield and without racemization.

Conclusions

In conclusion, we have established a highly stereoselective approach for the construction of vicinal quaternary and tertiary stereocenters *via* 6′-OH *Cinchona* alkaloids-catalyzed Michael addition of trisubstituted carbon nucleophiles to nitrodienes. This reaction is applicable not only to a wide variety of carbon nucleophiles but also to a substantial range of nitrodienes as well. This asymmetric protocol expands the range of optically active molecules bearing adjacent tertiary and quaternary stereocenters that can be directly generated from readily available prochiral precursors. The present method has several advantages such as use of easily available pseudoenantiomeric organocatalysts, low catalyst loading, room temperature reaction, in combination with a high regio- and stereoselectivity that is insensitive to reactant concentration and catalyst loading as well as to air and moisture. The present methodology has a high turnover number that enables the scaling up of the reaction. The prod-

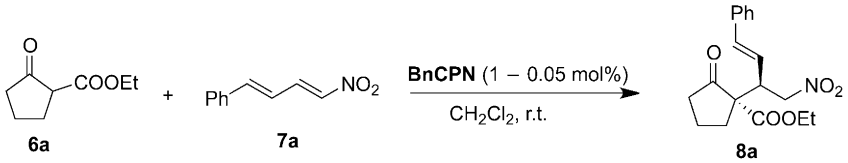
Table 4. BnCPD-catalyzed asymmetric Michael reaction of trisubstituted carbon nucleophiles with nitrodienes.[a]



Entry	Nucleophile	Nitrodiene	Time [h]	Product	Yield [%][b]	*dr*[c]	*ee* [%][d]
1	**6a**	**7a**	15	**8a′**	99	94:6	97
2[e]	**6a**	**7b**	24	**8b′**	97	95:5	97
3[e]	**6a**	**7c**	24	**8c′**	97	92:8	88
4	**6a**	**7d**	48	**8d′**	91	90:10	90
5	**6a**	**7e**	48	**8e′**	92	88:12	94
6	**6a**	**7f**	36	**8f′**	96	93:7	95
7[f]	**6a**	**7g**	96	**8g′**	71	>99:1	88
8	**6a**	**7h**	36	**8h′**	73	65:35	90, 90[g]
9	**6b**	**7a**	18	**8i′**	99	90:10	89
10	**6c**	**7a**	60	**8j′**	85	96:4	96
11	**6d**	**7a**	72	**8k′**	91	97:3	96
12	**6d**	**7e**	96	**8l′**	78	97:3	97
13	**6e**	**7a**	48	**8m′**	92	89:11	93
14	**6f**	**7a**	72	**8n′**	84	98:2	97
15	**6f**	**7e**	96	**8o′**	76	99:1	99
16[f]	**6g**	**7a**	96	**8p′**	57	67:33	88, 69[g]
17[f]	**6h**	**7a**	15	**8q′**	89	57:43	94, 87[g]
18	**6i**	**7a**	60	**8r′**	94	78:22	89

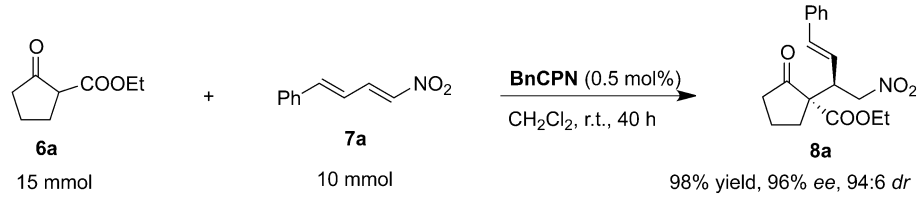
[a] Unless noted, reactions were carried out with 0.3 mmol of **6** and 0.2 mmol of **7** in 0.2 mL of CH_2Cl_2 with 1 mol% of **2f**.
[b] Yield refers to isolated yield after column chromatography.
[c] *dr* refers to diastereomeric ratio after short column chromatography.
[d] *ee* refers to enantiomeric excess of major diastereomer.
[e] 0.5 mol% of catalyst was used.
[f] 5 mol% of catalyst was used.
[g] *ee* of minor diastereomer.

Table 5. Effect of catalyst loading.[a]

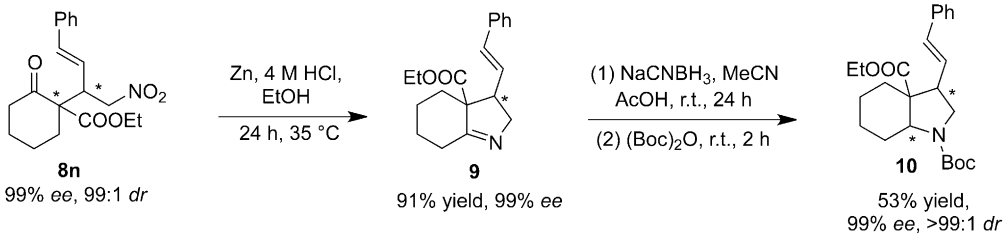


Entry	**BnCPN** [mol%]	Time [h]	Yield [%][b]	*dr*[c]	*ee* [%][d]	TON[e]
1	1	15	99	94:6	97	9,900
2	0.75	24	99	94:6	97	13,200
3	0.50	36	99	94:6	97	19,800
4	0.25	96	81	94:6	97	32,400
5	0.10	120	35	94:6	96	35,000
6	0.05	144	18	94:6	96	36,000

[a] Reactions were carried out with 0.3 mmol of **6a** and 0.2 mmol of **7a** in 0.2 mL of CH_2Cl_2 with **BnCPN** as catalyst at room temperature.
[b] Yield refers to isolated yield after column chromatography.
[c] *dr* refers to diastereomeric ratio after short column chromatography.
[d] *ee* refers to enantiomeric excess of major diastereomer.
[e] Turnover number (TON) was calculated as follows: TON = yield [%] × mmol of **7a**/mmol of **BnCPN**.



Scheme 1. Gram-scale prepration of **8a** having vicinal quaternary and tertiary stereocenters.



Scheme 2. Derivatization of Michael adducts **8n** to octahydroindole-carboxylate analogue **10**.

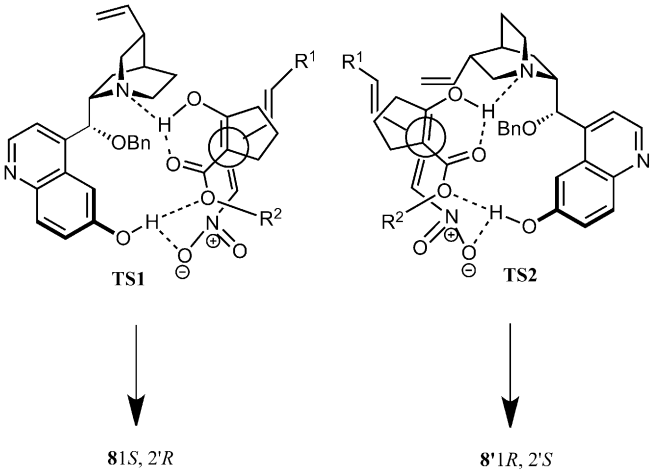


Figure 2. Plausible transition states: **TS1** with **BnCPN** and **TS2** with **BnCPD** catalyst

uct can be readily converted into a chiral octahydroindole analogue that, further enhances the utility of this transformation for the synthesis of potentially valuable chiral molecules.

Experimental Section

General Procedure for BnCPN-Catalyzed Michael Addition Reaction

To a stirred solution of nitrodienes **7** (0.2 mmol) and catalyst **BnCPN** (0.5–5 mol%) in 0.2 mL of CH_2Cl_2, β-keto ester **6** (0.3 mmol) was added. The reaction mixture was stirred at room temperature and monitored with thin layer chromatography. After the completion of the reaction the crude reaction mixture was purified by column chromatography (silica gel 60–120 mesh) using hexane:ethyl acetate (8.5:1.5) as eluent.

(*E*)-(*S*)-Ethyl 1-[(*R*)-1′-nitro-4′-phenylbut-3′-en-2′-yl]-2-oxocyclopentanecarboxylate (8a): Colorless oil; yield: >99%; *dr* 94:6; $[\alpha]_D^{20}$: +62.5 (*c* 1.0, $CHCl_3$); *ee* 97%; HPLC [Chiralpak AD-H, hexane/*i*-PrOH (95:5), 1 mL min^{-1}, 210 nm]: t_R = 15.5 min (major) and t_R = 20.5 min (minor); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.34–7.24 (m, 5H, ArH), 6.51 (d, *J* = 15.6 Hz, 1H, CH), 6.13 (dd, *J* = 14.1 and 9.5 Hz, 1H, CH), 5.00 (dd, *J* = 12.6 and 3.6 Hz, 1H, CH_2), 4.63 (dd, *J* = 12.6 and 10.5 Hz, 1H, CH_2), 4.21 (q, *J* = 6.9 Hz, 2H, OCH_2), 3.54–3.46 (m, 1H, CH), 2.50–2.42 (m, 2H, CH_2) 2.37–2.31 (m, 1H, CH_2), 2.13–2.00 (m, 3H, CH_2), 1.28 (t, *J* = 7.0 Hz, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.0, 19.4, 32.2, 38.0, 45.0, 61.1, 62.0, 76.2, 122.8, 126.6, 128.2, 128.3, 128.5, 128.6, 135.9, 136.5, 169.6, 212.9; MS (Q-TOF): *m/z* = 354.0989 $(M+Na)^+$.

(*E*)-(*S*)-Ethyl 1-[(*R*)-1′-nitro-4′-(2″-nitrophenyl)but-3′-en-2′-yl]-2-oxocyclopentanecarboxylate (8b): Yellow oil; yield: 98%; *dr* 96:4; $[\alpha]_D^{20}$: +63.0 (*c* 1.0, $CHCl_3$); *ee* 96%; HPLC [Chiralpak AD-H, hexane/*i*-PrOH (97/3), 0.3 mL min^{-1}, 235 nm]: t_R = 40.3 min (major) and t_R = 57.1 min (minor); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.99–7.97 (m, 1H, ArH), 7.70–7.32 (m, 3H, ArH), 6.99 (d, *J* = 15.6 Hz, 1H, CH), 6.14 (dd, *J* = 15.6 and 9.3 Hz, 1H, CH), 5.10 (dd, *J* = 12.6 and 3.3 Hz, 1H, CH_2), 4.75 (dd, *J* = 12.7 and 10.0 Hz, 1H, CH_2), 4.20 (q, *J* = 7.2 Hz, 2H, OCH_2), 3.49–3.41 (m, 1H, CH), 2.56–1.97 (m, 6H, CH_2), 1.27 (t, *J* = 7.2 Hz, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.0, 19.4, 33.2, 38.0, 38.6, 44.9, 60.7, 75.8, 124.5, 128.6, 128.8, 129.6, 132.3, 132.6, 133.5, 147.3, 169.8, 213.1; MS (Q-TOF): *m/z* = 399.0722 $(M+Na)^+$.

(*E*)-(*S*)-Ethyl 1-[(*R*)-1′-nitro-4′-(4″-nitrophenyl)but-3′-en-2′-yl]-2-oxocyclopentanecarboxylate (8c): Yellow oil; yield: 99%; *dr* 93:7; $[\alpha]_D^{20}$: +67.0 (*c* 0.5, $CHCl_3$); *ee* 95%; HPLC [Chiralpak AD-H, hexane/i-PrOH (90:10), 1.0 mL min^{-1}, 286 nm]: t_R = 34.8 min (major) and t_R = 43.8 min (minor); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.24–8.15 (m, 2H, ArH), 7.49–7.44 (m, 2H, ArH), 6.80–6.55 (m, 1H, CH), 6.42–5.84 (m, 1H, CH), 5.09–4.93(m, 1H, CH_2), 4.70–4.52 (m, 1H, CH_2), 4.26–4.18 (m, 2H, OCH_2), 3.92–3.46 (m, 1H, CH),

2.53–2.17 (m, 3H, CH_2), 2.15–1.95 (m, 3H, CH_2), 1.31–1.24 (m, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.0, 19.4, 33.7, 38.0, 38.7, 45.1, 62.2, 75.8, 123.8, 124.0, 127.2, 128.0, 128.7, 129.2, 133.8, 134.4, 169.6, 212.8; MS (Q-TOF): 399.0734 (M + Na).

(*E*)-(*S*)-Ethyl 1-[(*R*)-4′-(2″-methoxyphenyl)-1′-nitrobut-3′-en-2′-yl]-2-oxocyclopentanecarboxylate (8d): Yellow oil; yield: 92%; *dr* 90:10; $[\alpha]_D^{20}$: +62.0 (*c* 0.5, $CHCl_3$); *ee* 91%; HPLC [Chiralpak AD-H, hexane/*i*-PrOH (85:15), 0.5 mL min^{-1}, 210 nm]: t_R = 18.3 min (major) and t_R = 24.5 min (minor)]; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.36–7.34 (d, *J* = 7.5 Hz, 1H, ArH), 7.26–7.20 (m, 1H, ArH), 6.91–6.78 (m, 3H, ArH and CH), 6.14 (dd, *J* = 15.9 and 9.6 Hz, 1H, CH), 5.00 (dd, *J* = 12.6 and 3.3 Hz, 1H, CH_2), 4.68–4.60 (m, 1H, CH_2), 4.20 (q, *J* = 7.2 Hz, 2H, OCH_2) 3.81 (s, 3H, OCH_3), 3.54–3.47 (m, 1H, CH), 2.49–2.43 (m, 2H, CH_2), 2.37–2.26 (m, 1H, CH_2), 2.18–1.99 (m, 3H, CH_2), 1.28 (t, *J* = 7.0 Hz, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.0, 19.4, 32.3, 38.1, 45.4, 55.4, 61.2, 61.9, 76.4, 110.9, 120.5, 123.3, 124.9, 127.0, 129.2, 131.3, 156.8, 169.7, 213.1; MS (Q-TOF): *m/z* = 384.1051 $(M+Na)^+$.

(*E*)-(*S*)-Ethyl 1-[(*R*)-4′-(4″-methoxyphenyl)-1′-nitrobut-3′-en-2′-yl]-2-oxocyclopentanecarboxylate (8e): Yellow oil; yield: 91%; *dr* 89:11; $[\alpha]_D^{20}$: +68.0 (*c* 0.5, $CHCl_3$); *ee* 93%; HPLC [Chiralpak AD-H, hexane/*i*-PrOH (80:10), 0.5 mL min^{-1}, 209 nm]: t_R = 25.7 mim (major) and t_R = 35.4 min (minor); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.26 (d, *J* = 5.1 Hz, 2H, ArH), 6.82 (d, *J* = 8.4 Hz, 2H, ArH), 6.44 (d, *J* = 15.9 Hz, 1H, CH), 5.97 (dd, *J* = 14.4 and 9.6 Hz, 1H, CH), 4.99–4.88 (m, 1H, CH_2), 4.65–4.58 (m, 1H, CH_2), 4.20 (q, *J* = 6.9 Hz, 2H, OCH_2) 3.79 (s, 3H, OCH_3), 3.50–3.45 (m, 1H, CH), 2.45–1.99 (m, 6H, $3CH_2$) 1.27 (t, *J* = 6.9 Hz, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.0, 19.4, 32.1, 38.0, 45.1, 55.2, 61.2, 62.0, 76.4, 113.9, 120.4, 127.8, 128.6, 135.9, 159.6, 169.6, 213.0; MS (Q-TOF): *m/z* = 384.1082 $(M+Na)^+$.

(*E*)-(*S*)-Ethyl 1-[(*R*)-4′-(4″-acetoxy-3″-methoxyphenyl)-1′-nitrobut-3′-en-2′-yl]-2-oxocyclopentanecarboxylate (8f): Yellow oil; yield: 97%; *dr* 93:7; $[\alpha]_D^{20}$: +52.5 (c 1.0, $CHCl_3$); *ee* 98%; HPLC [Chiralpak IB, hexane/*i*-PrOH (80:20), 0.5 mL min^{-1}, 214 nm]: t_R = 35.5 mim (major) and t_R = 40.6 min (minor)]; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.98–6.89 (m, 3H, ArH), 6.47 (d, *J* = 15.9 Hz, 1H, CH), 6.09 (dd, *J* = 15.7 and 9.4 Hz, 1H, CH), 5.00 (dd, *J* = 12.6 and 3.3 Hz, 1H, CH_2), 4.67–4.59 (m, 1H, CH_2), 4.21 (q, *J* = 7.0 Hz, 2H, OCH_2) 3.84 (s, 3H, OCH_3), 3.51–3.45 (m, 1H, CH), 2.53–2.42 (m, 2H, CH_2), 2.37–2.34 (m, 1H, CH_2), 2.31 (s, 3H, $COCH_3$) 2.11–1.98 (m, 3H, CH_2), 1.28 (t, *J* = 6.9 Hz, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.0, 19.5, 20.6, 32.3, 38.0, 45.0, 55.9, 61.0, 62.1, 76.2, 110.5, 119.1, 122.8, 123.2, 134.9, 135.9, 139.7, 151.1, 169.0, 169.6, 212.9; MS (Q-TOF): *m/z* = 442.1070 $(M+Na)^+$.

(*E*)-(*S*)-Ethyl 1-[(*R*)-3′-methyl-1′-nitro-4′-phenylbut-3′-en-2′-yl]-2-oxocyclopentanecarboxylate (8g): Yellow oil; yield: 74%; *dr* > 99:1; $[\alpha]_D^{20}$: +50.0 (*c* 1.0, $CHCl_3$); *ee* 88%; HPLC [Chiralpak AD-H, hexane/*i*-PrOH (85:15), 0.5 mL min^{-1}, 207 nm]: t_R = 12.7 mim (major) and t_R = 14.4 min (minor); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.39–7.29 (m, 2H, ArH), 7.26–6.22 (m, 1H, ArH), 7.18–7.16 (m, 2H, ArH), 6.42 (s, 1H), 5.21 (dd, *J* = 13.0 and 3.1 Hz, 1H, CH_2), 4.96 (dd, *J* = 12.9 and 11.1 Hz, 1H, CH_2), 4.20 (q, *J* = 7.2 Hz, 2H, OCH_2), 3.35–3.31 (m, 1H, CH), 2.65–2.57 (m, 1H, CH_2), 2.48–2.43 (m, 2H, CH_2), 2.15–2.01 (m, 3H, CH_2), 1.80 (s, 3H, CH_3), 1.29 (t, *J* = 7.2 Hz, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.9, 15.2, 19.1, 32.2, 37.5, 50.5, 60.8, 62.1, 75.5, 127.0, 128.1, 128.9, 132.4, 132.7, 136.6, 169.0, 212.3; MS (Q-TOF): *m/z* = 368.1116 $(M+Na)^+$.

(*E*)-(*S*)-Ethyl 1-[(*R*)-4,8-dimethyl-1-nitrononа-3,7-dien-2-yl]-2-oxocyclopentanecarboxylate (8h): Colorless oil; yield: 77%; *dr* 65:35; $[\alpha]_D^{20}$: +32.0 (*c* 1.0, $CHCl_3$); *ee* 91% (95%); HPLC [Chiralpak IB, hexane/*i*-PrOH (90:10), 0.5 mL min^{-1}, 205 nm]: major diastereomer t_R = 7.0 min (major) and t_R = 11.2 min (minor), minor diastereomer t_R = 6.9 min (major) and t_R = 13.2 min (minor)]; ^{1}H NMR (300 MHz,$CDCl_3$): δ = 5.13–4.99 (m, 2H, CH_2), 4.91- 4.73 (m, 1H, CH), 4.44–4.35 (m, 1H, CH), 4.18 (q, *J* = 6.9 Hz, 2H, OCH_2), 3.89–3.68 (m, 1H, CH), 2.43–2.40 (m, 2H, CH_2), 2.33–2.22 (m, 1H, CH_2), 2.06–1.97 (m, 7H, CH_2), 1.71–1.59 (m, 9H, $3\times CH_3$), 1.30–1.25 (m, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.0, 16.4, 17.6, 19.6, 19.8, 23.4, 25.6, 26.2, 26.4, 32.1, 31.6, 32.1, 38.1, 39.3, 39.6, 39.9, 61.4, 61.6, 76.9, 77.2, 118.1, 118.7, 123.6, 123.8, 131.8, 143.7, 169.7, 212.7; MS (Q-TOF): *m/z* = 374.1732 $(M+Na)^+$.

(*E*)-(*S*)-Methyl 1-[(*R*)-1′-nitro-4′-phenylbut-3′-en-2′-yl]-2-oxocyclopentanecarboxylate (8i): Colorless oil; yield: 99%; *dr* 89:11; $[\alpha]_D^{20}$: +58.0 (*c* 0 .5, $CHCl_3$); *ee* 90%; HPLC [Chiralpak AD-H, hexane/*i*-PrOH (99/1), 1.3 mL min^{-1}, 206 nm]: t_R = 36.4 min (major) and t_R = 46.4 min (minor); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.34–7.24 (m, 5H, ArH), 6.50 (d, *J* = 15.9 Hz, 1H, CH), 6.11 (dd, *J* = 16.5 and 9.3 Hz, 1H, CH), 5.00 (dd, *J* = 9.3 and 3.6 Hz,1H, CH_2), 4.63 (dd, *J* = 12.6 and 10.5 Hz, 1H, CH_2), 3.74 (s, 3H, CH_3), 3.54–3.46 (m, 1H, CH), 2.47–2.40 (m, 2H, CH_2) 2.35–2.23 (m, 1H, CH_2), 2.16–1.96 (m, 3H, CH_2); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 19.8, 32.5, 38.4, 45.3, 53.2, 61.4, 76.6, 123.1, 126.9, 128.6, 128.9, 136.2, 136.9, 170.5, 213.2; MS (Q-TOF): *m/z* = 340.0803 $(M+Na)^+$.

(*E*)-(*S*)-*iso*-Propyl 1-[(*R*)-1′-nitro-4′-phenylbut-3′-en-2′-yl]-2-oxocyclopentanecarboxylate (8j): Light yellow oil; yield: 88%; *dr* 96:4; $[\alpha]_D^{20}$: +67.0 (*c* 1.0, $CHCl_3$); *ee* 93%; HPLC [Chiralpak AD-H, hexane/*i*-PrOH (85/15), 0.5 mL min^{-1}, 211 nm]: t_R = 15.2 min (major) and t_R = 18.4 min (minor); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.30–7.27 (m, 5H, ArH), 6.49 (d, *J* = 15.6 Hz, 1H, CH), 6.13 (dd, *J* = 15.7 and 9.4 Hz, 1H, CH), 5.08–4.96 (m, 2H, CH_2 and OCH), 4.64–4.57 (m, 1H, CH_2), 3.51–3.44 (m, 1H, CH), 2.50–2.39 (m, 2H, CH_2), 2.33–2.21 (m, 1H, CH_2), 2.12–1.97 (m, 3H, CH_2) 1.26–1.23 (m, 6H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 19.4, 21.5, 21.6, 32.3, 38.0, 45.0, 61.1, 69.9, 76.3, 122.9, 126.6 128.2, 128.5, 135.9, 136.4, 169.1, 213.0; MS (Q-TOF): *m/z* = 368.1078 $(M+Na)^+$.

(*E*)-(*S*)-*tert*-Butyl-1-[(*R*)-1′-nitro-4′-phenylbut-3′-en-2′-yl]-2-oxocyclopentanecarboxylate (8k): Light yellow oil; yield: 92%; *dr* 97:3; $[\alpha]_D^{20}$: +62.5 (*c* 1.0, CH_2Cl_2); *ee* 97%; HPLC [Chiralpak AD-H, hexane/*i*-PrOH (90/10), 1.0 mL min^{-1}, 208 nm]: t_R = 7.0 min (major) and t_R = 8.2 min (minor); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.32–7.25 (m, 5H, ArH), 6.49 (d, *J* = 15.9 Hz, 1H, CH), 6.15 (dd, *J* = 15.7 and 9.4 Hz, 1H, CH), 5.07–4.97 (m, 1H, CH_2), 4.63–4.56 (m, 1H, CH_2), 3.49–3.43 (m, 1H, CH), 2.48–2.41 (m, 2H, CH_2), 2.31–2.18 (m, 1H, CH_2), 2.05–1.97 (m, 3H, CH_2) 1.47 (s, 9H, $3\times CH_3$); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 19.5, 27.9, 32.5, 38.0, 45.2, 61.6, 76.4, 83.3, 123.1, 126.6, 128.2, 128.6, 136.0, 136.3, 168.8, 213.4; MS (Q-TOF): 382.1190 $(M+Na)^+$.

(*E*)-(*S*)-*tert*-Butyl 1-[(*R*)-4′-(4″-methoxyphenyl)-1′-nitrobut-3′-en-2′-yl]-2- oxocyclohexanecarboxylate (8l): Yellow oil; yield: 80%; *dr* 98:2; $[\alpha]_D^{20}$: +52.0 (*c* 0.5, $CHCl_3$); *ee* 98%; HPLC [Chiralpak AD-H, hexane/*i*-PrOH (90:10), 1 mL min^{-1}, 265 nm]: t_R = 9.7 min (major) and t_R = 14.4 min (minor); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.27–7.24 (m, 2H, ArH), 6.84–6.81 (m, 2H, ArH), 6.42 (d, *J* = 15.9 Hz, 1H, CH), 6.99 (dd, *J* = 15.6 and 9.6 Hz, 1H, CH),5.01 (dd, *J* = 15.4 and 3.3 Hz, 1H, CH_2), 4.57 (dd, *J* = 17.7 and 10.6 Hz, 1H, CH_2), 3.79 (s, 3H, OCH_3), 3.47–3.49 (m, 1H, CH), 2.47–2.41 (m, 2H, CH_2), 2.31–2.21 (m, 1H, CH_2), 2.06–1.96 (m, 3H, CH_2) 1.46 (s, 9H, 3 × CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 19.5, 27.8, 32.4, 38.0, 45.2, 55.3, 61.7, 76.5, 83.2, 113.9, 120.7, 127.8, 128.8, 135.8, 159.6, 168.8, 213.3; MS (Q-TOF): *m/z* = 412.1213 $(M+Na)^+$.

(*E*)-(*S*)-Benzyl 1-[(*R*)-1′-nitro-4′-phenylbut-3′-en-2′-yl]-2-oxocyclopentanecarboxylate (8m): Colorless wax; yield: 94%; *dr* 88:12; $[\alpha]_D^{20}$: +64.0 (*c* 1.0, $CHCl_3$); *ee* 95%; HPLC [Chiralpak IB, hexane/*i*-PrOH (80/20), 0.5 mL min^{-1}, 210 nm]: t_R = 20.4 min (major) and t_R = 26.0 min (minor); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.38–7.25 (m, 10H, ArH), 6.54–6.46 (m, 1H, CH), 6.15–6.07 (m, 1H, CH), 5.20–5.18 (m, 2H, OCH_2), 4.98–4.90 (m, 1H, CH_2), 4.63–4.53 (m, 1H, CH_2), 3.54–3.51 (m, 1H, CH), 2.45–1.96 (m, 6H, CH_2); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 19.4, 32.2, 38.1, 45.1, 61.2, 67.7, 76.1, 122.6, 126.6, 128.2, 128.3, 128.6, 128.7, 134.9, 135.8, 136.6, 169.4, 212.7; MS (Q-TOF): 416.0997 $(M+Na)^+$.

(*E*)-Ethyl 1-(1′-nitro-4′-phenylbut-3′-en-2′-yl)-2-oxocyclohexanecarboxylate (8n): Colorless oil; yield: 82%; *dr* 99:1; $[\alpha]_D^{20}$: −60.0 (*c* 0.5, $CHCl_3$); *ee* 99%; HPLC [Chiralpak AD-H, hexane/*i*-PrOH (90/10), 0.5 mL min^{-1}, 210 nm]: t_R = 20.2 min (major) and t_R = 28.2 min (minor); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.31–7.26 (m, 5H, ArH), 6.45 (d, *J* = 15.9 Hz, 1H, CH), 6.08 (dd, *J* = 15.7 and 10.0 Hz, 1H, CH), 4.80–4.76 (m, 1H, CH_2), 4.45–4.38 (m, 1H, CH_2), 4.27- 4.21 (m, 2H, OCH_2), 3.52–3.45 (m, 1H, CH), 2.46–2.52 (m, 3H, CH_2), 2.05–2.00 (m, 1H, CH_2), 1.85–1.81 (m, 1H, CH_2), 1.66–1.60 (m, 3H, CH_2), 1.31–1.25 (m, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.1, 22.3, 27.4, 38.3, 41.2, 46.4, 61.9, 62.5, 77.1, 123.5, 126.5, 126.6, 128.0, 128.5, 135.9, 136.0, 170.1, 207.1; MS (Q-TOF): *m/z* = 368.1018 $(M+Na)^+$.

(*E*)-Ethyl 1-[4′-(4″-methoxyphenyl)-1′-nitrobut-3′-en-2′-yl]-2-oxocyclohexanecarboxylate (8o): Light yellow oil; yield: 73%; *dr*; 99:1; $[\alpha]_D^{20}$: −63.6 (*c* 0.5, $CHCl_3$); *ee* 98%; HPLC [Chiralpak AD-H, hexane/*i*-PrOH (90/10), 0.5 mL min^{-1}, 210 nm]: t_R = 29.1 min (major) and t_R = 41.9 min (minor); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.27–7.22 (m, 2H, ArH), 6.83–6.79 (m, 2H, ArH), 6.39 (d, *J* = 15.6 Hz, 1H, CH), 5.92 (dd, *J* = 15.7 and 10.0 Hz, 1H, CH), 4.75 (dd, *J* = 12.3 and 3.0 Hz, 1H, CH_2), 4.40 (dd, *J* = 12.4 and 10.3 Hz, 1H, CH_2), 4.25–4.21 (m, 2H, OCH_2), 3.79 (m, 3H, CH_3), 3.48–3.40 (m, 1H, CH), 2.57–2.44 (m, 3H, CH_2), 2.03–2.00 (m, 1H, CH_2), 1.82–1.81 (m, 1H, CH_2), 1.69–1.56 (m, 3H, CH_2), 1.28 (t, *J* = 7.2 Hz, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.1, 22.3, 27.4, 36.3, 41.2, 46.5, 55.3, 61.9, 62.6, 77.3, 113.9, 121.1, 127.8, 128.8, 128.9, 135.3, 139.0, 159.5, 170.1, 207.1; MS (Q-TOF): *m/z* = 398.1033 $(M+Na)^+$.

(*E*)-Ethyl 2-acetyl-2-methyl-3-(nitromethyl)-5-phenylpent-4-enoate (8p): Yellow oil; yield: 63%; *dr* 65:35; $[\alpha]_D^{20}$: −7.3 (*c* 0.25, $CHCl_3$); *ee* 96% (*ee* 75% minor diastereomer); HPLC [Chiralpak IB, hexane/*i*-PrOH (90/10), 0.5 mL min^{-1}, 204 nm]: major diastereomer t_R = 16.2 min (major) and tR = 22.6 min (minor), minor diastereomer t_R = 16.6 min (major) and t_R = 19.6 min (minor); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.28–7.23 (m, 5H, ArH), 6.54–6.47 (m, 1H, CH), 6.07–5.94 (m, 1H, CH), 4.72–4.66 (m, 1H, CH_2), 4.61–4.49 (m, 1H, CH_2), 4.27–4.17 (m, 2H, OCH_2), 3.70–3.75 (m, 1H, CH), 2.17 (s, 3H, CH_3), 1.47 (m, 3H, CH_3), 1.30–1.23 (m, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.0, 17.8, 27.0, 46.2, 61.4, 62.2, 76.8, 122.9, 126.6, 128.2, 128.5, 135.9, 136.5, 170.8, 204.4; MS (Q-TOF): *m/z* = 342.1698 $(M+Na)^+$.

(*E*)-Ethyl 2-acetyl-2-chloro-3-(nitromethyl)-5-phenylpent-4-enoate (8q): Yellow oil; yield: 93%; *dr* 56:44; $[\alpha]_D^{20}$: + 25.0 (*c* 1.0, $CHCl_3$); *ee* 93% (*ee* 89% minor diastereomer); HPLC [Chiralpak OD-H, hexane/*i*-PrOH (90/10), 1.0 mL min^{-1}, 210 nm]: major diastereomer t_R = 11.8 min (major) and t_R = 13.9 min (minor), minor diastereomer t_R = 8.7 min (major) and t_R = 10.2 min (minor); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.31–7.25 (m, 5H, ArH), 6.59 (d, *J* = 7.8 Hz, 1H, CH) diastereomer, 6.54 (d, *J* = 7.8 Hz, 1H, CH), 6.13–6.01 (m, 1H, CH), 4.89–4.49 (m, 2H, CH_2), 4.30–4.04 (m, 3H, CH and OCH_2), 2.36 (s, 3H, CH_3) diastereomer, 2.34 (s, 3H, CH_3), 1.30–1.20 (m, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.9, 25.5, 27.1, 46.4, 48.2, 63.7, 64.0, 76.2, 76.4, 120.7, 120.9, 126.7, 128.5, 128.6, 135.5, 137.5, 137.9, 165.0, 196.5; MS (Q-TOF): *m/z* = 362.1164 $(M+Na)^+$.

(*E*)-2-Acetyl-2-(1′-nitro-4′-phenylbut-3′-en-2′-yl)cyclopentanone (8r): Yellow oil; yield: 92%; *dr* 72:28; $[\alpha]_D^{20}$: +38.0 (*c* 0.5, $CHCl_3$); *ee* 92%; [Chiralpak AD-H, hexane/*i*-PrOH (90/10), 0.1 mL min^{-1}, 207 nm]: t_R = 24.9 min (major) and t_R = 26.9 min (minor); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.32–7.24 (m, 5H, ArH), 6.54 (d, *J* = 14.4 Hz, 1H, CH), 6.02 (dd, *J* = 15.6 and 9.0 Hz, 1H, CH), 4.52–4.35 (m, 2H, OCH_2), 3.84–3.72 (m, 1H, CH), 2.58–2.32 (m, 3H, CH_2), 2.29 (s, 3H, CH_3), 2.08–1.85 (m, 3H, 2 × CH_2); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 19.5, 26.5, 28.1, 38.6, 45.0, 70.1, 76.1, 122.0, 126.6, 128.4, 128.6, 135.7, 136.7, 137.0, 202.9, 213.7; MS (Q-TOF): *m/z* = 324.0924 $(M+Na)^+$.

Procedure for the Synthesis of 9

The mixture of zinc powder (305.0 mg, 4.70 mmol), optically pure **8n** (110 mg, 0.32 mmol) and EtOH (3.0 mL) was stirred in a 10-mL round-bottom flask at 35 °C for 10 min. After which 2 mL of 4 M aqueous HCl were added dropwise over 2 h and the resulting mixture was stirred at 35 °C for 24 h. To maintain the pH of the mixture in the range of 0–1, additional 4 M aqueous HCl was added. On completion of the reaction (as monitored by TLC), the solvent was removed under reduced pressure and aqueous 3 M NaOH (6 mL) was added, and the solution stirred for 5 min. Dichloromethane (20 mL) was added to the mixture. The mixture was filtered and the two layers were separated. The aqueous layer was extracted with CH_2Cl_2 (3 × 10 mL), and the combined organic layers were washed with brine and dried over anhydrous Na_2SO_4 and concentrated to obtain crude blackish oil. The crude oil was purified by column chromatography on silica gel (hexane:EtOAc = 7:3) to afford the product **9**; yield: 87 mg (91%).

(*E*)-Ethyl 3,3a,4,5,6,7-hexahydro-3-styryl-2*H*-indole-3a-carboxylate (9): Brown oil; yield 91%; *dr* 99:1; $[\alpha]_D^{20}$: +108.5 (*c* 1.0, $CHCl_3$); *ee* 99%; HPLC [Chiralpak OD-H, hexane/*i*-PrOH (95/5), 1 mL min^{-1}, 207 nm]: t_R = 12.3 min (minor) and t_R = 20.2 min (major); ^{1}H NMR(300 MHz, $CDCl_3$): δ =

7.30–7.22 (m, 5H, ArH), 6.47–6.41 (m,1H, CH), 6.05–5.96 (m, 1H, CH), 4.32–4.04 (m, 3H, CH_2 and OCH_2), 3.77–3.69 (m, 1H, CH_2), 2.98–2.92 (m, 1H, CH), 2.77–2.67 (m, 2H, CH_2), 2.35–2.14 (m, 1H, CH_2), 1.98–1.81 (m, 1H, CH_2), 1.77–1.74 (m, 1H, CH_2), 1.49–1.43 (m, 2H, CH_2), 1.31–1.20 (m, 4H, CH_3 and CH_2); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.4, 23.3, 26.1, 31.4, 36.5, 54.6, 61.0, 63.7, 65.0, 126.2, 126.3, 127.5, 128.5, 132.8, 136.8, 170.5, 185.3; MS (Q-TOF): m/z = 320.1393 $(M+Na)^+$.

Procedure for the Synthesis of 10

A mixture of 60 mg (0.2 mmol) of **9**, 200 μL AcOH, and 3 mL MeCN was stirred in a 25-mL round-bottom flsak. The mixture was cooled to 0 °C for 10 min, Then 63 mg of $NaCNBH_3$ (1.0 mmol, 5 equiv.) were added in one portion. The reaction mixture was stirred at room temperature for 24 h. After the completion of the reaction, MeCN was removed under reduced pressure, aqueous 2M NaOH (12 mL) was added, and then the solution was stirred for 5 min. The reaction mixture was diluted with 15 mL CH_2Cl_2 and the mixture was filtered and the two layers were separated. The aqueous layer was extracted with CH_2Cl_2 (3× 10 mL) and then the combined organic layer was washed with brine, dried over anhydrous Na_2SO_4, and concentrated. The crude oil was diluted with 5 mL CH_2Cl_2. The reaction mixture was cooled to 5 °C for 10 min, then $(Boc)_2O$ (0.4 mmol, 2 equiv.) was added over 5 min. The contents were stirred at room temperature for 2 h. After the reaction was completed, aquous 2M NaOH (12 mL) was added, and then the solution was stirred for 30 min. The reaction mixture was diluted with 15 mL CH_2Cl_2 and two layers were separated. The aqueous layer was extracted with CH_2Cl_2 (3×10 mL), and then the combined organic layer was washed with brine, dried over anhydrous Na_2SO_4, and concentrated. The crude oil was purified by column chromatography on silica gel (hexane:ethyl acetate = 8:2) to afford the **10**; yield: 53%.

3a-Ethyl 1-*tert*-Butyl octahydro-3-styrylindole-1,3a-dicarboxylate (10): Dark brown oil; yield: 53%; $[\alpha]_D^{20}$: +28.5 (*c* 1.0, $CHCl_3$); 99% *ee*; HPLC [Chiralpak ODH, hexane/*i*-PrOH (95/5), 0.5 mL min^{-1}, 250 nm]: t_R = 12.5 min (minor) and t_R = 16.6 min (major); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.27–7.12 (m, 5H, ArH), 6.35 (d, J = 15.6 Hz, 1H, CH),6.02 (dd, J = 15.7 and 8.5 Hz, 1H, CH), 4.16–4.04 (m, 3H), 3.58–3.51 (m, 1H), 3.42–3.36 (m, 1H), 3.04–2.96 (m, 1H), 1.99–1.94 (m, 1H, CH_2), 1.83–1.77 (m, 1H), 1.56–1.44 (m, 1H), 1.40 (s, 9H, CH_3) 1.33–1.25 (3H, m), 1.21–1.12 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 12.3, 21.4, 22.2, 28.5, 32.0, 44.8, 58.3, 60.5, 61.5, 78.1, 79.2, 126.2, 126.7, 127.5, 128.5, 130.9, 132.9, 136.9, 137.0, 154.5, 173.9; MS (Q-TOF): m/z = 422.2775 $(M+Na)^+$.

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