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ARTICLE

Cinchona Alkaloid Based Chiral Catalysts act as Highly Efficient Multifunctional Organocatalyst for the Asymmetric Conjugate Addition of Malonates to Nitroolefins

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Abstract: New type of pentaerythritol tetrabromide based chiral quaternary ammonium act as organocatalysts **7** (**7a** and **7b**) have prepared and used as organocatalysts for enantioselective Michael addition reactions between the various nitroolefin and Michael donors (malonates) under mild reaction conditions such as lower concentration of base, catalyst and room temperature with very good chemical yields (up to 97%) and ee's (up to 99).

Introduction

In recent organic synthesis, most of the researchers were concentrated new smart design, practical, cost-effective and environmental friendly catalytic systems.[1] In particularly synthesis and optimisation of chiral organocatalysts were very much needed to achieve highly enantioselective controlled optically active enantiopure products with very good yield.[2-3] Generally, there are many types of organocatalyst available for the synthesis of efficient enantiopure products which includes chiral catalyst such as proline,[4] cinchona alkaloids [5] via quinine, cinchonine, and various sugar,[6] amino acid,[7] ionic liquid [8a] or amide-derived compounds.[8b] Asymmetric synthesis, available in great varieties, were the vital source of a large number of chiral compounds that have become essential for human society.[9]

Among these enantioselective asymmetric Michael addition reaction of electron deficient olefins, particularly α, β-unsaturated ketones such as chalcone, nitroolefins, have been investigated and reported lower to moderate yield and ee's under organocatalysts and phase transfer catalysts (PTC).[10-23] In this connection Lee et. al., have been reported the 2-aminobenzimidazole bifunctional organocatalyst 1a and 1b with the commercially available diethyl malonate as Michael donor at 0°C to RT for the effective Michael addition of nitroolefins in the presence of 10 mol% of catalyst with better yields (82-99%) and ee's (90-93%).[24a] Consecutively, Suez et al.,[24b] reported the enantioselective Michael addition of nitroolefins in the presence of 20 mol% of quanine based organocatalyst 2a and 2b at room temperature but the reaction was carried out longer time (24-144 h) with moderate yield (41-94%) and ee's (84-88%). Even though there are numerous reports[25] available for enantioselective Michael addition of nitroolefins, their full potential is not yet to be reached or explained in terms of both enantioselectivity and general applicability. Both the previous reports were used higher concentration of catalyst loading 10 mol% and 20 mol% and longer reaction time (24-40h). Previously, we reported a series of tri-functional mesitylene and triazine based cinchona alkaloids as a chiral phase transfer catalysts (CPTC) for highly enantioselective Michael addition reactions of chalcones with very good yield and ee's.[26] In this work is also the extending of our research interest of the organocatalyst in asymmetric catalysis and also first time we report the tetrafunctional organocatalysts for effective enantioselective Michael addition reaction under mild reaction conditions such as catalyst loading (1 mol%) and time (30 mins) at room temperature conditions.

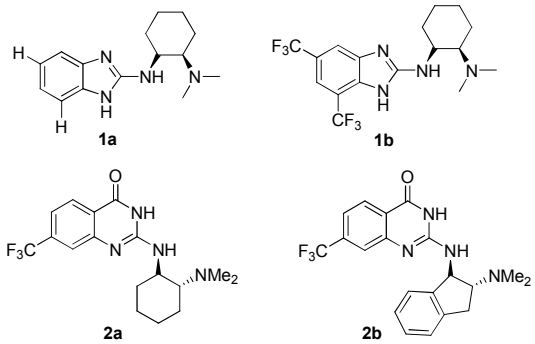

Fig. 1 Previously reported chiral organocatalysts

Here, we focused on the enantioselectivity and the chemical yield of Michael addition of nitroolefins reactions (Scheme 1) using new types of tetra functional organocatalysts derived from cinchonine **6** under mild reaction conditions. Here, we synthesized a new series of tetrafunctional organocatalyst using pentaerythritol tetrabromide as a core.[27] In this work, we reported very good yield (up to 97%) and excellent ee's (up to 99%) at ambient temperature conditions.

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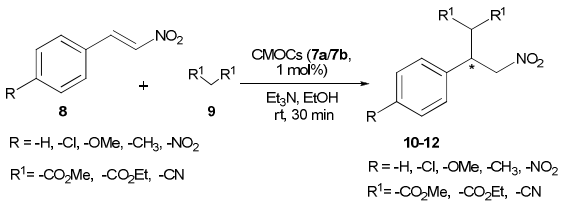
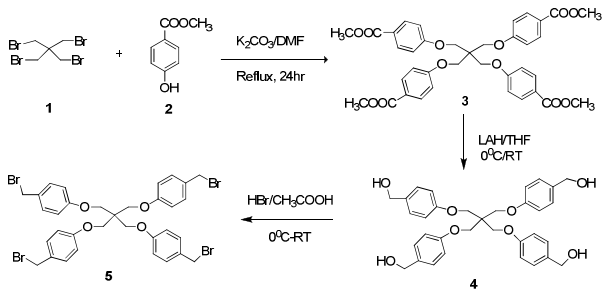
† Footnotes relating to the title and/or authors should appear here.
Electronic Supplementary Information (ESI) available: [details of any supplementary information available should be included here]. See DOI: 10.1039/x0xx00000x

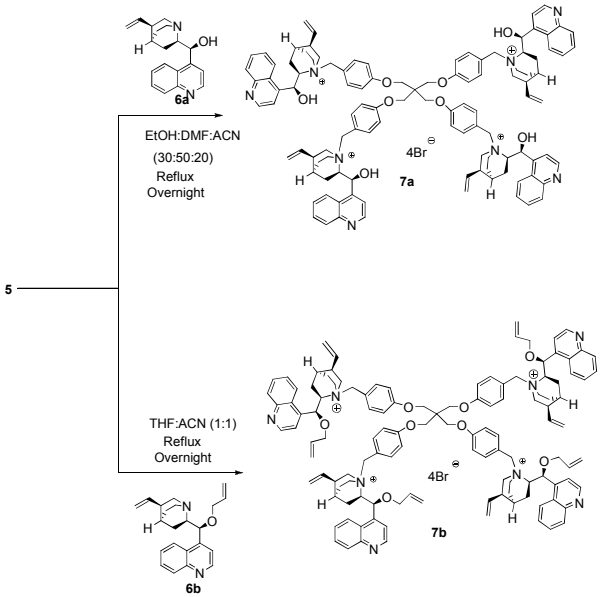
Results and discussion



Scheme 1 Synthesis of Enantioselective Michael addition of Nitroolefins with various Michael donors.



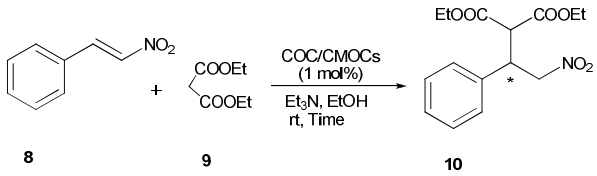
Scheme 2 Synthesis of Scaffold **5**.



Scheme 3 Synthesis of CMOCs 7 (7a and 7b).

The tetraester **3**, obtained from the modified procedure[27] of the four fold *O*-alkylation of pentaerythritol tetrabromide with methyl-4-hydroxybenzoate, then it was reduced with $LiAlH_4$ in THF to afford the tetra-alcohol **4** with 90% yield. Further, the tetraalcohol **4** was treated with HBr in CH_3COOH to give tetrabromide **5** with 92% yield (Scheme 2). The pentaerythritol tetrabromide based chiral multifunctional organocatalysts ((CMOCs) (**7a** and **7b**)) were synthesized from the reaction of tetrabromide **5** with cinchonine free C_9-OH **6a** and *O*- allylcinchonine [26] **6b** respectively as depicted in scheme 3.Thus, an initial attempt was made by treating nitroolefin (**8**) with diethyl malonate (**9)** in the presence of different chiral organocatalysts (COCs) **1**, **2** and CMOCs **7** (1 mol%) in ethanol at room temperature. This revealed that **1**, **2** are indeed able to act as catalyst, though its activity and stereoselectivity is insufficient even increased the reaction time from 12 to 144 hrs (entry 1-4 in Table 1). But our newly synthesized CMOCs **7a** and **7b** influenced the reaction rate and we got very good yield upto 96% and ee's upto 99% (entries 5 and 6, Table 1) under same conditions with lesser time (only 30 min). This is due to the multiactive sites are present in the catalysts **7** and ion pair interaction is more with the catalysts and the anions of the Michael donor. Further, we believe that the simultaneously cooperative neigboring group of the cinchonium cation with the Michael donors.

Table 1 Catalytic asymmetric Michael addition reaction of diethyl malonate 9 to nitroolefin 8 with different COCs 1, 2 and CMOCs 7 (7a/ 7b) in room temperature.



Entry	Catalysts	Time (hours) [a]	Yield % [b]	ee % [c]	Abs. Conf [d]
1	1a	6	45	78	R
2	1b	24	99	93	R
3	2a	24	94	84	R
4	2b	144	33	45	R
5	7a	0.5	96	99	R
6	7b	0.5	96	99	R

[a] The Michael reaction of Nitroolefin **8** (0.067 mmol), diethyl malonate **9** (0.073 mmol), COCs (**1a**, **1b**, **2a**, **2b**) CMOCs **7** (**7a**/**7b**, 1 mol%), with 1 ml of ethanol and triethylamine (0.073 mmol) in room temperature. [b] Isolated yield of purified material. [c] Enantiopurity was determined by HPLC analysis of the Michael adduct **10** using a chiral column (Chiralcel OD-H) with hexane-IPA as an eluent. [d] Absolute configuration was determined by comparison of the HPLC retention time.[12b]

Further, we carried out the optimization of bases for Michael addition of Nitroolefin 8 with diethylmalonate 9 in the presence of CMOCs 7 under identical reaction conditions. From that results, we observed that the triethylamine, DIEA are the more effective bases than the other bases such as pyridine, piperidine, K^tOBu, Cs_2CO_3, K_2CO_3, (entries 1-14 in Table 2).

Table 2 Effect of bases in the Michael addition reaction in the presence of the nitroolefin 8 and diethyl malonate 9 with CMOCs 7 (7a/7b), under room temperature.

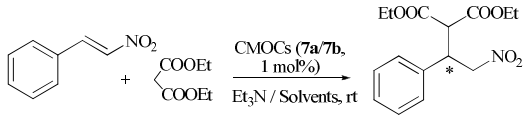
8 9 10

Entry	Base	Catalyst	Time (min)[a]	Yield (%)[b]	% of ee[c]	Abs. conf.[d]
1	K^{t}OBu	7a	70	80	83	R
2	K^{t}OBu	7b	70	80	84	R
3	K_2CO_3	7a	60	90	85	R
4	K_2CO_3	7b	60	90	86	R
5	CS_2CO_3	7a	50	93	86	R
6	CS_2CO_3	7b	50	93	87	R
7	TEA	7a	30	96	99	R
8	TEA	7b	30	96	99	R
9	DIEA	7a	40	95	89	R
10	DIEA	7b	40	95	90	R
11	Pyridine	7a	60	75	71	R
12	Pyridine	7b	60	75	73	R
13	Piperidine	7a	60	70	71	R
14	Piperidine	7b	60	70	73	R

[a] The Michael reaction of nitroolefin **8** (0.067 mmol), diethyl malonate **9** (0.073 mmol), CMOCs **7** (**7a/7b**, 1 mol%), with 1 ml of ethanol and various bases (0.073 mmol) in room temperature. [b] Isolated yield of purified material. [c] Enantiopurity was determined by HPLC analysis of the Michael adduct **10** using a chiral column (Chiralcel OD-H) with hexane-IPA as an eluent. [d] Absolute configuration was determined by comparison of the HPLC retention time.[12b]

Then the asymmetric Michael addition reaction was carried out in different solvents using CMOCs 7 (7a and 7b) under room temperature, the other parameters are kept as constant. The obtained results (Table 3) show that, the change of solvent is found to be an important crucial factor in the Michael addition reaction due to their polarity of the solvents. The product yield and ee's have been found to decrease gradually, using polar to nonpolar solvents (entries 1-14, Table 3), among solvents THF and toluene mediated reactions are reduced the activity of 7a and 7b resulted in poor yield and ee's of Michael adduct 10 (entries 11-14, Table 3). Further, we get moderate yields and ee's of 10 using aprotic solvents such as acetone, chloroform and DCM (entries 5-10, Table 3) and we found very good yield and ee's of 10 when we are using protic polar solvents such as methanol and ethanol. (entries 1-4, Table 3). The optimization of the Michael addition reaction of nitroolefin **8** with diethyl malonate **9** was carried out in the presence of different reaction temperature conditions. From the observed results, higher chemical yield and ee's are obtained at room temperature when compared with other temperature conditions (i.e. -10 °C, ultrasonic and 50 °C) (entries 1-8, Table 4). Through extensive screening, the optimized reaction conditions are found to be 1 mol % of catalyst **7**, triethylamine as base and ethanol as solvent at room temperature.

Table 3 Effect of solvents in the Michael addition reaction of nitroolefin 8, diethyl malonate 9, CMOCs 7 (7a/7b), under room temperature.



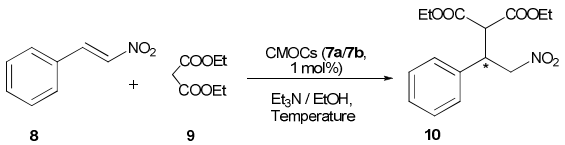
8 9 10

Entry	Solvents	Catalyst	Time (min)[a]	Yield %[b]	% of ee[c]	Abs. conf.[d]
1	Methanol	7a	35	95	99	R
2	Methanol	7b	35	95	99	R
3	Ethanol	7a	30	96	99	R
4	Ethanol	7b	30	96	99	R
5	Acetone	7a	40	88	89	R
6	Acetone	7b	40	88	90	R
7	DCM	7a	50	86	84	R
8	DCM	7b	50	86	88	R
9	$CHCl_3$	7a	50	80	83	R
10	$CHCl_3$	7b	50	80	86	R
11	THF	7a	55	70	83	R
12	THF	7b	55	70	85	R
13	Toluene	7a	60	65	82	R
14	Toluene	7b	60	65	83	R

[a] The Michael reaction of nitroolefin **8** (0.067 mmol), diethyl malonate **9** (0.073 mmol), CMOCs **7** (**7a/7b**, 1 mol%), with 1 ml of various solvents and triethylamine (0.073 mmol), in room temperature. [b] Isolated yield of purified material. [c] Enantiopurity was determined by HPLC analysis of the Michael adduct **10** using a chiral column (Chiralcel OD-H) with hexane-IPA as solvents. [d] Absolute configuration was determined by comparison of the HPLC retention time.[12b]

Further, the catalytic efficiencies were studied by the Michael addition reaction of various nitroolefins **8**(**a-e**) and Michael donors **9**(**a-c**) under the optimized reaction conditions described above (1 mol% of the catalysts **7a** or **7b**, triethylamine, ethanol, room temperature). From the observed results in table 5, independent of the substitution on the aryl group of the nitroolefins, both the electron withdrawing and electron donating groups are present on the aryl groups which could not affect the product yield and ee's, we found an excellent yields and ee's (entries 1-30, Table 5).

Table 4 Optimization of asymmetric Michael addition between the nitroolefin 8 and diethyl malonate 9 with CMOCs 7 (7a/ 7b) in various conditions.



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Entry	Catalyst	Condition	Time (hrs)[a]	Yield %[b]	% of ee[c]	Abs. conf[d]
1	7a	US[e]	10	85	71	R
2	7b	US[e]	10	86	73	R
3	7a	50^0C	6	65	73	R
4	7b	50^0C	5	68	73	R
5	7a	-10^0C	8	75	88	R
6	7b	-10^0C	9	77	88	R
7	7a	RT	0.5	96	99	R
8	7b	RT	0.5	96	99	R

[a] The Michael reaction of Nitroolefin **8** (0.067 mmol), diethyl malonate **9** (0.073 mmol), CMOCs **7** (**7a**/**7b**, 1 mol%), with 1 ml ethanol and triethylamine (0.073 mmol) in various conditions. [b] Isolated yield of purified material [c] Enantiopurity was determined by HPLC analysis of the Michael adduct **10** using a chiral column (Chiralcel OD-H) with hexane-IPA as solvents. [d] Absolute configuration was determined by comparison of the HPLC retention time.[12b] [e] Ultrasonication

Further, from the established optimized reaction conditions for the model reaction, the scope of this Michael addition was studied and the results were listed in Table 5. From the observed results, almost all the substituted β-nitroalkenes bearing either electron-donating or withdrawing substituents on the aromatic ring gave the desired Michael adducts in very good yields (up to 97%) and good enantioselectivities (89-95%) (entries 7-30, Table 5). Unsubstituted β-nitroalkenes gave better enantioselectivity compared with substituted β-nitroalkenes bearing electron-withdrawing or electron-donating groups in the aromatic ring (entries, 1-6, Table 5). When 2-(nitrovinyl)-benzene used highest yield (97%) and excellent enantioselectivity (99% ee) is achieved irrespective of the catalysts **7a** or **7b** (entries, 5 and 6, Table 5). The formation of higher chemical yield and ee's for C_9 (*O*) protected CMOC **7b** is due to the presence of effective formation of contact ion-pair between the R_4N^+ of CMOCs with anion of the substrate via co-operative influenced by close spatial arrangement of two active-site (Fig 2). Further, the formation of lower/moderate yield and ee's in the Michael addition of nitroolefin due to the electronic effect. That is, as we observed in tetra-site based CMOCs **7** (**7a** and **7b**) contain lone-pair of electrons on the oxygen atoms (present in each corner of pentaerythritol) shift the electron density to the electron deficient terminal R_4N^+ site of the CMOCs via aromatic ring spacer chain, as a result no bond resonance is formed (Fig 3). This leads to detachment/deactivation of catalytic site, thus lose their attracting power (electrophile attracting power) towards the anions of nitroolefin. As a result, the formation of degree of ion-pair between R_4N^+ of tetra-site CMOCs (**7a** and **7b**) with anions of the nitroolefin is relatively lower hence we got moderate yield and ee's.

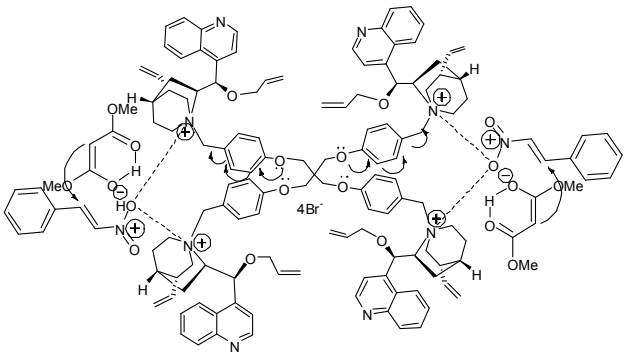


Fig. 2 Ion-pair interaction between the R_4N^+ of CMOCs with anion of the substrate via co-operative influenced due to electrostatic attractions.

Further, the formation of the yield and ee's of Michael adduct 10 in the presence of C_9(O) protected CMOCs such as cinchonine derived 7 (entries 1-14, Table 2) is purely based on the stereochemistry/molecular assembly of CMOCs with substrates. That is, in general irrespective of C_9 free OH or C_9 (O) protected CMOC's, there should be three factors which influence chemical yield and ee's: (i) effective contacts of ion-pair formed between R_4N^+ of CMOC's with anion of nitroolefin (ii) with the same ion-pair interaction of the enolate of the diethylmalonate with R_4N^+ of CMOC's (iii) intermolecular hydrogen bonding between C_9 free -OH of CMOC's with anions of nitroolefin and α-carbon of diethylmalonate. We strongly believed that the above three possible electrostatic processes are responsible for deciding the yield 10 and ee's.[28]

In the reaction, on deprotonation of the α-carbon of the diethylmalonate 9 by the triethylamine, the α-carbon anion of the diethylmalonate is generated which in turn forms an ion pair with the R_4N^+ of the CMOCs and a subsequently negative charge is developed on the enolate of the substrate leading to an ion-pair with the R_4N^+ of the CMOC's. These ion-pair formation brings the substrates closer by reducing the bonding distance of R_4N^+ of CMOC's (Fig 4a). Subsequently, there is the possibility for hydrogen bonding through the same electrostatic attraction between the anion of α-carbon of diethylmalonate with C_9 free -OH of the CMOC's in turn prevents the movements of anionic substrate

species towards R_4N^+ of the CMOC's (Fig 4b). Whereas, in C_9 (O) protected CMOCs catalysed reaction (entries 5-14 , Table 3), the possibility for formation of hydrogen bond between the C_9 free-OH with α-carbon anion of dimethylmalonate is completely unobserved since the free –OH at C_9 position is protected through allylation (Fig 4c). As a result, the first two electrostatic processes (i) and (ii) may be more dominant and thus anionic substrate (nitroolefin) are moved very fast closer to R_4N^+ active site of CMOC's without any constraint and followed by further attraction of anion of α-carbon of diethylmalonate with the nitroolefin facilitating higher order of chemical yield and enantioselectivity parallely.

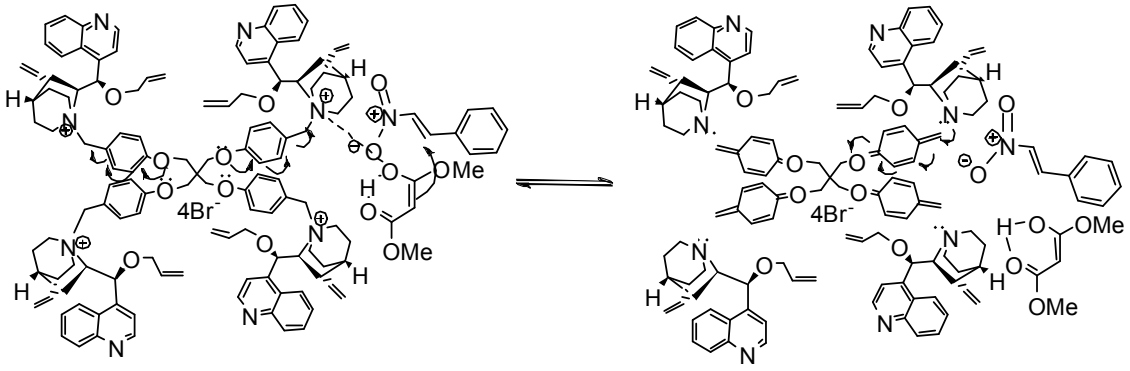
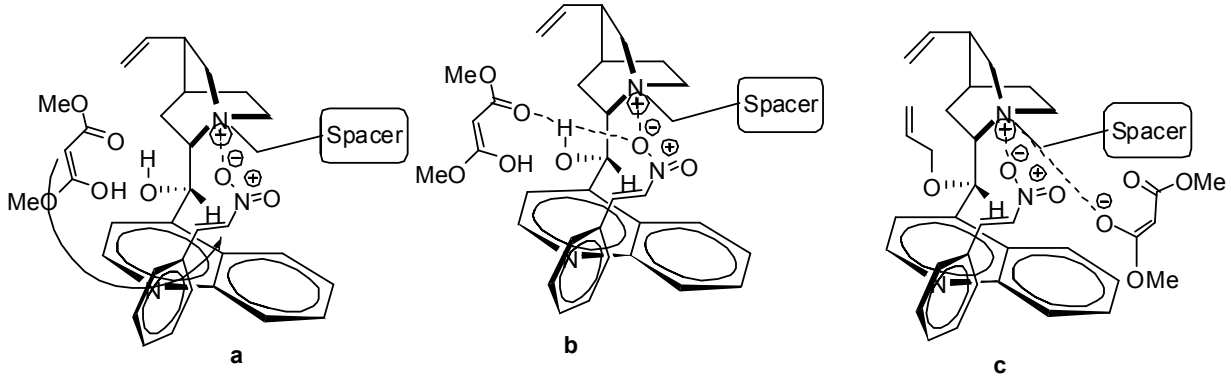


Fig. 3 Detachment/deactivation of CMOC due to no bond resonance formation.



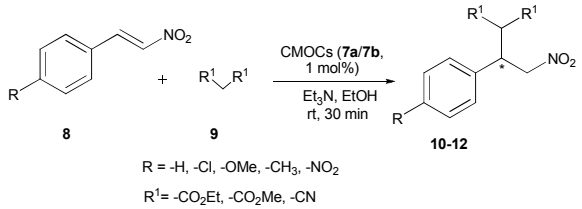
Ion -pair formed between R_4N^+ of CMOCs with anion of the nitro olefin due to electrostatic attraction

Hydrogen bonding between enolate anion of dimethylmalonate, nitro olefin and free -OH present in C_9 position of CMOCs

Ion -pair formed between R_4N^+ of CMOCs with anion of the nitroolefin and dimethylmalonate due to electrostatic attraction

Fig. 4 Formation of various intermediates/molecular assemblies during enantioselective Michael addition of nitroolefin using C_9 free –OH & allyl protected CMOCs.

Table 5 Catalytic asymmetric Michael addition reaction of various Michael donors 9 (a-c) to nitrostyrene derivatives 8 (a-e) under CMOCs conditions.



Entry	Nitroolefins	R	R^1	Catalyst	Product[a]	Yield %[b]	% of ee[c]	Abs. conf.[d]
1	8a	-H	-COOEt	7a	10a	96	99	R
2	8a	-H	-COOEt	7b	10a	96	99	R
3	8a	-H	-COOMe	7a	11a	94	98	R
4	8a	-H	-COOMe	7b	11a	94	98	R
5	8a	-H	-CN	7a	12a	97	99	R
6	8a	-H	-CN	7b	12a	97	99	R
7	8b	-Cl	-COOEt	7a	10b	93	95	R
8	8b	-Cl	-COOEt	7b	10b	93	95	R
9	8b	-Cl	-COOMe	7a	11b	90	91	R
10	8b	-Cl	-COOMe	7b	11b	90	92	R
11	8b	-Cl	-CN	7a	12b	97	96	R
12	8b	-Cl	-CN	7b	12b	97	96	R
13	8c	-OMe	-COOEt	7a	10c	92	95	R
14	8c	-OMe	-COOEt	7b	10c	92	95	R
15	8c	-OMe	-COOMe	7a	11c	90	91	R
16	8c	-OMe	-COOMe	7b	11c	90	91	R
17	8c	-OMe	-CN	7a	12c	94	96	R
18	8c	-OMe	-CN	7b	12c	94	96	R
19	8d	$-CH_3$	-COOEt	7a	10d	92	90	R
20	8d	$-CH_3$	-COOEt	7b	10d	92	90	R
21	8d	$-CH_3$	-COOMe	7a	11d	90	89	R
22	8d	$-CH_3$	-COOMe	7b	11d	90	89	R
23	8d	$-CH_3$	-CN	7a	12d	95	97	R
24	8d	$-CH_3$	-CN	7b	12d	95	97	R
25	8e	$-NO_2$	-COOEt	7a	10e	85	95	R
26	8e	$-NO_2$	-COOEt	7b	10e	85	95	R
27	8e	$-NO_2$	-COOMe	7a	11e	80	93	R
28	8e	$-NO_2$	-COOMe	7b	11e	80	93	R
29	8e	$-NO_2$	-CN	7a	12e	90	95	R
30	8e	$-NO_2$	-CN	7b	12e	90	95	R

[a] The Michael reaction of different Nitroolefins **8 (a-e)** (0.067 mmol), various Michael donors **9(a-c)** (0.073 mmol), **CMOCs 7** (**7a/7b**, 1 mol%), with 1 ml Ethanol and triethylamine (0.073 mmol) in room temperature. [b] Isolated yield of purified material. [c] Enantiopurity was determined by HPLC analysis of the Michael adduct (**10-12 (a-e))** using a chiral column (Chiralcel OD-H) with hexane-IPA as solvents. [d] Absolute configuration was determined by comparison of the HPLC retention time.[12b]

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Conclusion

We have designed a new class of tetrafunctional chiral organocatalysts by a reasonable combination of readily available cinchona alkaloid with penta erythritrol based tetrabromide. The catalysts 7 (7a and 7b) exhibited the best performance in the asymmetric Michael addition of nitroolefins with various Michael donors such as dimethylmalonate, diethylmalonate and malononitrile. The corresponding products can be obtained in moderate to high yields with excellent enantioselectivities (up to 99%) under mild reaction conditions.

Experimental section

Materials and Methods

All the chemicals and reagents used in this work were of analytical grade. Allylbromide, (+)-cinchonine, HBr in acetic acid, benzaldehyde, 4-chlorobenzaldehyde, 4-methylbenzaldehyde, anisaldehyde, were obtained from Alfa Aesar, pentaerythritol tetra bromide,4-hydroxy benzoic acid, $LiAlH_4$, 4-nitrobenzaldehyde, nitromethane, potassium *tert*-butoxide, cesium carbonate and potassium carbonate were obtained from Sigma Aldrich, sodium hyroxide, pottassium hydroxide, were obtained from Merck and all the solvents were obtained from Laboratory reagent grade. The melting points were measured in open capillary tubes and are uncorrected.

The ^1H and ^{13}C NMR spectra were recorded on a Bruker (Avance) 300 and 400 MHz NMR instrument using TMS as an internal standard and $CDCl_3$ as a solvent. Standard Bruker software was used throughout. Chemical shifts are given in parts per million (δ-scale) and the coupling constants are given in Hertz. Silica gel-G plates (Merck) were used for TLC analysis with a mixture of n-hexane and ethyl acetate as an eluent. Column chromatography was carried out in silica gel (60-120 mesh) using n-hexane and ethyl acetate as an eluent. FT-IR spectroscopy measured in a JASCO FT/IR-410 spectrometer and KBr used as pellets. Mass spectra were analysed by Voyager DE PRO Biospectrometry Workstation (Applied Biosystems) matrix-assisted laser desorption ionization time-of-flight (MALDI-TOF) mass spectroscopy (MS) instrument. A pulsed nitrogen laser of 337 nm was used, and the TOF was operated in the delayed extraction mode. The HPLC were recorded in SHIMADZU LC-6AD with Chiral Column (Chiral Cel OD-H), using HPLC grade n-hexane and isopropanol solvent. Optical rotations were measured on Rudolph Research Analytical AUTOPOL-II (readability ±0.01°) and AUTOPOL-IV (readability ±0.001°) automatic polarimeters.

Preparation of tetraester (3).[27] A stirred mixture of pentaerythritol tetrabromide (5g, 12.89 mmol), methyl-4-hydroxybenzoate (7.84g, 51.52 mmol) and K_2CO_3 (23.15g, 167.49 mmol) in DMF was heated at 150^0C and reflux for about 32 h. The solution was then cooled, water (100 mL) was added, and the mixture was extracted twice with ethyl acetate. The organic layers were combined, washed with water and brine, and dried over Na_2SO_4. Removal of volatiles under reduced pressure left a residue that was purified by column chromatography (silica, ethyl acetate (4%)/hexane (96%), isolated yield of 3 (8.46g, 97%). Colourless solid. Mp: 199-200 °C. FT-IR = 1710cm^{-1}(C=O stretching), ^1H NMR (300 MHz, $CDCl_3$) δ_H: 7.97 (d, *J* = 8.9 Hz, 8H), 6.89 (d, *J* = 8.8 Hz, 8H), 3.87 (s, 12H), 3.84 (s, 8H); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C: 166.72, 163.04, 131.21, 122.36, 113.27, 55.03, 51.37, 42.11.

Preparation of tetra alcohol (4).[27] The tetraester 3 (3g, 4.45 mmol) was reduced with $LiAlH_4$ (1g, 26.61 mmol) using THF (40 mL) as a solvent and the reaction mass was cooled to 0°C for 4 hours. The reaction mixture was extracted with ethyl acetate. The organic layers were combined, washed with water and brine, and dried over Na_2SO_4. Removal of volatiles under reduced pressure left a residue that was purified by column chromatography, ethyl acetate/hexane (20:80), isolated yield of 4 (2.25g, 90%). Colourless solid: Mp: 135-136 °C. FT-IR= 3255(O-H stretching), 2920cm^{-1}(C-H stretching), ^1H NMR (300 MHz, $CDCl_3$) δ_H: 7.29 (d, *J* = 8.4 Hz, 8H), 6.89 (d, *J* = 8.6 Hz, 8H), 4.61 (s, 8H), 3.81 (s, 8H); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C: 158.91, 132.98, 128.46, 113.71, 64.68, 55.10, 41.54.

Preparation of tetra bromide (Scaffold 5).[27] HBr in acetic acid (30 mL) was taken in a pre-dried RB flask and tetra alcohol 4 (2g, 3.56 mmol) was added under nitrogen atmosphere at 0 °C. After stirring for about 6hrs, the reaction was monitored by TLC, the reaction mixture was poured on to 10% sodium bicarbonate solution and extracted with ethyl acetate, washed with brine and dried over sodium sulphate. Concentrated it and purified by column chromatography using pet. Ether and ethyl acetate as an eluent (8:2). Isolated yield of 5 is (2.45g, 85%). Off-white solid, Mp: 169-170 °C. ^1H NMR (300 MHz, $CDCl_3$) δ_H: 7.31(d, *J* = 8.5 Hz, 8H), 6.91 (d, *J* = 8.6 Hz, 8H), 4.64 (s, 8H), 3.83 (s, 8H); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C: 158.91, 132.98, 128.46, 113.71, 55.10, 41.85, 35.09.

Synthesis of cinchonine (contains free C_9-OH) based multifunctional organocatalyst (7a). A mixture of (0.1g, 10 mmol), tetra bromide 5 and cinchonine free C_9-OH 6a (30 mmol) was dissolved in 5 ml of EtOH:DMF:ACN (30:50:20 ratio) and whole reaction mixture was refluxed for overnight, the white solid was filtered off, washed with diethylether and dried it, to get pure white tetra-site containing organocatalyst (7a) (95% yield). ^1H NMR (400 MHz, $CDCl_3$) δ_H: 8.82 (d, *J* = 4.5 Hz, 4H), 8.13 (d, *J* = 8.2 Hz, 4H), 8.04 (d, *J* = 5.6 Hz, 4H), 7.76 (d, *J* = 4.5 Hz, 4H), 7.64 (d, *J* = 4.4

Hz, 4H), 7.58 (m, 8H), 7.14 (m, 4H), 6.65 (d, *J* = 8.6 Hz, 8H), 6.48 (s, 4H), 5.83 (d, *J* = 12.0 Hz, 4H), 5.66 (m, 4H), 5.50 (d, *J* = 12.0 Hz, 4H), 5.41 (m, 4H), 4.93 (m, 4H), 3.77 (s, 16H), 3.17 (m, 8H), 2.78 (m, 8H), 2.38 (m, 4H), 1.86 (m, 16H), 1.46 (m, 4H).); ^{13}C NMR (100 MHz, $CDCl_3$) δ_C: 156.84, 149.40, 149.24, 148.58, 137.13, 129.82, 129.36, 127.68, 125.48, 123.30, 120.38.119.14, 117.22, 114.31, 81.02, 66.42, 63.78, 61.80, 59.17, 52.08, 40.43, 38.01, 28.80, 26.10, 23.19; MS (MALDI- TOF): m/z calculated for $C_{109}H_{120}Br_4N_8O_8$: 1984.5941; found 1984.5459. $[\alpha]_D^{25}$ = +0.71 (*c*=0.14, $CHCl_3$).

Synthesis of allylated cinchonine based multifunctional organocatalyst (7b). A mixture of (0.1g, 10 mmol), tetra bromide 5 and *O*-allylcinchonine[26] 6b (30 mmol) was dissolved in 5 ml THF:ACN (1:1 ratio) and heated to reflux for about overnight, the off white solid was filtered, washed with diethylether and dried it, to get pure off white tetra-site organocatalyst (7b) (96% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ_H: 8.83 (d, *J* = 4.5 Hz, 4H), 8.14 (d, *J* = 8.2 Hz, 4H), 8.05 (d, *J* = 5.6 Hz, 4H), 7.77 (d, *J* = 4.5 Hz, 4H), 7.64 (d, *J* = 4.4 Hz, 4H), 7.60 (m, 8H), 7.13 (m, 4H), 6.65 (d, *J* = 8.6 Hz, 8H), 5.90 (m, 4H), 5.69 (dd, *J* = 17.2, 9.3 Hz, 4H), 5.28 (dd, *J* = 17.2, 9.3 Hz, 12H), 4.92 (d, *J* = 17.1 Hz, 4H), 4.87 (d, *J* = 11.5 Hz, 4H), 3.91 (m, 8H), 3.71 (s, 16H), 3.41 (s, 4H), 3.06 (dd, *J* = 13.6, 12.8 Hz, 8H), 2.64 (m, 4H), 2.25 (s, 4H), 1.79 (s, 4H), 1.52 (d, *J* = 11.2 Hz, 12H), 0.81 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ_C: 156.66, 149.97, 149.49, 148.27, 137.57, 134.59, 129.30, 129.15, 127.14, 125.64, 122.63, 120.43, 118.95, 117.69, 114.47, 78.05, 75.49, 72.24, 65.75, 61.54, 59.56, 52.36, 40.67, 38.43, 28.74, 26.51, 22.79; MS (MALDI- TOF): m/z calculated for $C_{121}H_{136}Br_4N_8O_8$: 2144.7193; found 2144.7438. $[\alpha]_D^{25}$ = +0.71 (*c*=0.14, $CHCl_3$).

General method for the synthesis of nitroolefins (8a-e).[14-15] The nitroolefins 8 obtained by the modified procedure.[14] Aromatic aldehyde (1 mmol), nitromethane (1 mmol) was dissolved in methanol and the reaction mass was cooled to -5^{0}C. Further NaOH (1.2 mmol) was added slowly into the reaction mass through addition funnel. Finally the reaction mixture was stirred for about 1hr, the reaction was monitored by TLC, after completion of the reaction, the mixture was neutralized by 4N HCl, and after neutralization the pale yellow colour solid nitroolefin was formed.

General method for the synthesis of enantioselective catalytic Michael addition of nitroolefins with various Michael donors under CMOCs conditions (10-12 (a-e)). To a mixture of nitroolefin 8 (a-e, 0.1 mmol), Michael donor (diethyl malonate, dimethyl malonate, malononitrile 9 (a-c, 0.12 mmol) and CMOCs (1 mol %) 7 (7a/7b) were dissolved in 1 ml of ethanol and added of triethylamine. Then the reaction mixture was stirred for 30 min, after that the reaction mixture was extracted with ethylacetate, washed with water (3 × 2 ml), then washed with brine (5 ml), dried over sodium sulphate and concentrated it. The crude material was purified by column chromatography on silica gel (ethylacetate and n-hexane as an eluent), to afford the corresponding Michael adducts (10-12 (a-e)). The enantiomeric excess of Michael adducts were determined by chiral stationary-phase HPLC analysis.

Characterization of nitroolefins (8a-e)

(E)- (2-nitrovinyl) benzene (8a). Light yellow colour solid, yield: 96%, Mp: 57-58 °C.^{1}H NMR (300 MHz, $CDCl_3$) δ_H 8.02 (d, J = 13.6 Hz, 1H), 7.60 (d, J = 13.7 Hz, 1H), 7.54 (m, 2H), 7.43 (m, 3H); ^{13}C NMR (75 MHz, DMSO-d_6) δ_C 140.10, 138.83, 132.96, 131.10, 130.63, 130.05.

(E)-1-chloro-4-(2-nitrovinyl) benzene (8b). Light yellow colour solid, yield: 97%, Mp: 113-114 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 7.97 (d, J = 13.6 Hz, 1H), 7.62 (d, J = 13.6 Hz, 1H), 7.46 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C 137.51, 137.39, 137.27, 130.39, 129.07, 128.40.

(E)-1-methoxy-4-(2-nitrovinyl) benzene (8c). Yellow colour solid, yield: 87%, Mp: 85-88 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 7.98 (d, J = 13.5 Hz, 1H), 7.53 (d, J = 7.3 Hz, 1H), 7.50 (m, 2H), 6.96 (d, J = 8.8 Hz, 2H), 3.87 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C 163.04, 139.15, 135.13, 131.29, 122.69, 115.10, 55.65.

(E)-1-methyl-4-(2-nitrovinyl) benzene (8d). Yellow colour solid, isolated yield: 96%, Mp: 106-107 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 7.99 (d, J = 13.6 Hz, 1H), 7.58 (d, J = 13.6 Hz, 1H), 7.45 (d, J = 7.8 Hz, 2H), 7.23 (d, J = 7.4 Hz, 2H), 2.42 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C 143.23, 139.29, 136.39, 130.25, 129.31, 127.38, 21.79.

(E)-1-nitro-4-(2-nitrovinyl) benzene (8e). Yellow colour solid, isolated yield: 90%, Mp: 198-200 °C. ^{1}H NMR (300 MHz, DMSO-d_6) δ_H 8.30 (d, J = 13.4 Hz, 2H), 8.23 (d, J = 12.2 Hz, 2H), 8.06 (d, J = 8.5 Hz, 2H); ^{13}C NMR (75 MHz, DMSO-d_6) δ_C 149.15, 141.06, 137.00, 136.72, 131.06, 124.32.

Characterization of Michael adducts (10-12 (a-e))

(R)-Diethyl 2-(2-nitro-1-phenylethyl) malonate (10a). Colourless solid, yield: 96%, Mp: 59-61 °C, ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 7.35 (m, 5H), 4.93 (m, 2H), 4.25 (m, 4H), 4.01 (q, *J* = 7.1 Hz, 1H), 3.82 (d, *J* = 9.3 Hz, 1H), 1.29 (t, *J* = 7.1 Hz, 3H), 1.05 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C 168.00, 167.37, 136.92, 129.46, 128.86, 128.59, 78.21 62.64, 62.38, 55.61, 43.57, 14.57, 14.25. The enantiomeric excess was determined by HPLC, Chiral cel (OD-H), 240 nm, hexane: IPA 99: 1, flow rate: 1 mL min^{-1}, retention time: 2.23 min (major), 16.61 min (minor). $[\alpha_]_D^{25.4}$ = +2.85 (*c*=0.22, CH_2Cl_2), (99% ee, (*R*)-isomer).The absolute stereochemistry of the addition product was assigned as (*R*) by comparison of the optical data with literature reported value [29]: $[\alpha]_D^{28}$ = +6.04 (*c*=1.10, $CHCl_3$), (95% ee, (*R*)-isomer).

(R)-Diethyl 2-(1-(4-chlorophenyl)-2-nitroethyl) malonate (10b). Pale yellow solid, yield: 93%, Mp: 43-47 °C, ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 7.30 (d, *J* = 8.5, 2H), 6.83 (d, , *J* = 8.4 2H), 4.90 (m, 2H), 4.25 (m, 4H), 4.04 (q, *J* = 7.1, 1H), 3.78 (d, *J* = 9.3 Hz, 1H), 1.27 (t, *J* = 7.1 Hz, 3H), 1.07 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C 167.10, 166.54, 134.46, 134.23, 129.72, 129.42, 77.65, 62.74, 62.52, 54.58, 42.73, 14.17, 14.02. The enantiomeric excess was determined by HPLC, Chiral cel (OD-H), 245 nm, hexane: IPA 99:1, flow rate: 1 mL min^{-1}, retention time: 2.33 min (major), 22.37 min (minor). $[\alpha]_D^{27.2}$ = +2.19 (*c*= 0.32, CH_2Cl_2), (95% ee, (*R*)-isomer).

(R)-Diethyl 2-(1-(4-methoxyphenyl)-2-nitroethyl) malonate (10c). Colourless oil, yield: 92%, ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 7.15 (d, *J* = 8.5, 2H), 6.83 (d, *J* = 8.4, 2H), 4.85 (m, 2H), 4.25 (m, 4H), 4.02 (q, *J* = 7.1, 1H), 3.79 (d, J= 8.6 Hz, 1H), 3.77 (s, 3H) (merged), 1.26 (t, *J* = 7.1, 3H), 1.06 (t, , *J* = 7.1, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C 167.66, 167.01, 159.65, 129.30, 128.31, 114.47, 78.05, 62.18, 61.93, 55.35, 42.51, 14.08, 13.90. The enantiomeric excess was determined by HPLC, Chiral cel (OD-H), 245 nm, hexane: IPA 99: 1, flow rate: 1 mL min^{-1}, retention time: 2.78 min (major), 10.87 min (minor). $[\alpha]_D^{27.2}$ = +2.95 (*c*=0.17, CH_2Cl_2), (95% ee, (*R*)-isomer).

(R)-Diethyl 2-(2-nitro-1-p-tolylethyl) malonate (10d). Colourless oil, yield: 92%, ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 7.45 (d, *J* = 7.8 Hz, 2H), 7.25 (d, , *J* = 7.4 Hz, 2H), 4.90 (m, 2H), 4.23 (m, 4H), 4.01 (q, *J* = 7.1 Hz, 1H), 3.79 (d, *J* = 9.3 Hz, 1H), 2.29 (s, 3H), 1.25 (t, *J* = 7.1 Hz, 3H), 1.05 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C 167.60, 166.98, 138.13, 133.21, 129.68, 127.93, 77.88, 62.24, 61.93, 55.14, 42.34, 21.12, 14.06, 13.85. The enantiomeric excess was determined by HPLC, Chiral cel (OD-H), 245 nm, hexane: IPA 99: 1, flow rate: 1 mL min^{-1}, retention time: 2.07 min (major), 20.75 min (minor). $[\alpha]_D^{25}$ = +2.86 (*c* = 0.35, CH_2Cl_2), (90% ee, (*R*)-isomer).

R)-Diethyl 2-(2-nitro-1-(4-nitrophenyl) ethyl) malonate (10e). Yellow colour oil, yield: 85%, ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 8.20 (d, *J* = 8.7 Hz, 2H), 7.45 (d, , *J* = 8.5Hz, 2H), 4.95 (m, 2H), 4.33 (m, 4H), 4.06 (q, *J* = 7.1 Hz, 1H), 3.82 (d, *J* = 9.0 Hz, 1H), 1.27 (t, *J* = 7.0 Hz, 3H), 1.10 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C 166.87, 166.31, 147.78, 143.67, 129.22, 124.08, 77.42, 62.51, 62.30, 55.36, 42.50, 13.94, 13.79. The enantiomeric excess was determined by HPLC, Chiral cel (OD-H), 245 nm, hexane: IPA 99: 1, flow rate: 1 mL min^{-1}, retention time: 2.33 min (major), 22.37 min (minor). $[\alpha]_D^{25}$ = +2.12 (*c* =0.33, CH_2Cl_2), (95% ee, (*R*)-isomer).

(R)-Dimethyl 2-(2-nitro-1-phenylethyl) malonate (11a). White solid, yield: 94%, Mp: 64-65 °C, ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 7.30 (m, 3H), 7.25 (m, 2H), 4.90 (m, 2H), 4.23 (m, 1H), 3.86 (d, *J* = 6.9 Hz, 1H), 3.73 (s, 3H), 3.53 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C 167.85, 167.25, 136.19, 128.97, 128.37, 127.89, 76.84, 54.71, 52.96, 52.75,42.95. The enantiomeric excess was determined by HPLC, Chiral cel (OD-H), 240 nm, hexane: IPA 99: 1, flow rate: 1 mL min^{-1}, retention time: 2.09 min (major), 26.89 min (minor). $[\alpha]_D^{27}$ = +2.73 (*c* =0.95, $CHCl_3$), (98% ee, (*R*)-isomer). The absolute stereochemistry of the addition product was assigned as (*R*) by comparison of the optical data with literature reported value [29]: $[\alpha]_D^{25}$ = +4.40 (*c*=1.02, $CHCl_3$), (93% ee, (*S*)-isomer).

(R)-Dimethyl 2-(1-(4-chlorophenyl)-2-nitroethyl)malonate (11b). White solid, yield: 90%, Mp: 80-81 °C, ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 7.29 (d, J= 8.2 Hz, 2H), 7.19 (d, J= 8.4 Hz, 2H), 4.93 (m, 2H), 4.23 (m, 1H), 3.87 (d, *J* = 6.9 Hz, 1H), 3.74 (s, 3H), 3.53 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C 167.26, 166.67, 134.37, 134.22, 129.04, 128.98, 76.51, 54.03, 53.22, 53.07, 42.41. The enantiomeric excess was determined by HPLC, Chiral cel (OD-H), 245 nm, hexane: IPA 99: 1, flow rate: 1 mL min^{-1}, retention time: 2.68 min (major), 23.23 min (minor). $[\alpha]_D^{25}$ = +2.41 (*c* =0.75, $CHCl_3$), (92% ee, (*R*)-isomer).

(R)-Dimethyl 2-(1-(4-methoxyphenyl)-2-nitroethyl)malonate (11c). Yellow oil, yield: 90%, ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 7.12 (d, J= 8.7 Hz, 2H), 6.82 (d, J= 8.7 Hz, 2H), 4.90 (m, 2H), 4.19 (m, 1H), 3.82 (d, *J* = 9.2 Hz, 1H), 3.75 (s, 3H), 3.73 (s, 3H), 3.53 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C 168.00, 167.40, 159.54, 129.11, 127.97, 114.46, 77.75, 55.29, 54.95, 53.08, 52.91, 42.40. The enantiomeric excess was determined by HPLC, Chiral cel (OD-H), 245 nm, hexane: IPA 99: 1, flow rate: 1 mL min^{-1}, retention time: 2.50 min (major), 12.19 min (minor). $[\alpha]_D^{25}$ = +1.38 (*c*=0.94, $CHCl_3$), (91% ee, (*R*)-isomer).

(R)-Dimethyl 2-(2-nitro-1-p-tolylethyl)malonate (11d). Colourless oil, yield: 90%, ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 7.63 (d, J= 13.6 Hz, 2H), 7.45 (d, J= 7.8 Hz, 2H), 4.91 (m, 2H), 4.23 (m, 1H), 3.87 (d, *J* = 6.9 Hz, 1H), 3.74 (s, 3H), 3.61 (s, 3H), 2.42 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C 167.81, 167.20, 138.25, 133.19, 129.05, 127.77, 77.55, 54.94, 52.89, 52.72, 42.20, 21.41. The enantiomeric excess was determined by HPLC, Chiral cel (OD-H), 240 nm, hexane: IPA 99: 1, flow rate: 1 mL min^{-1}, retention time: 2.50 min (major), 12.19 min (minor). $[\alpha]_D^{25}$ = +2.29 (*c*= 0.07, $CHCl_3$), (89% ee, (*R*)-isomer).

(R)-Dimethyl 2-(2-nitro-1-(4-nitrophenyl) ethyl)malonate (11e). Yellow oil, yield: 80%, ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 8.20 (d, J= 8.7 Hz, 2H), 7.46 (d, J= 8.7 Hz, 2H), 4.95 (m, 2H), 4.39 (m, 1H), 3.87 (d, *J* = 8.8 Hz, 1H), 3.78 (s, 3H), 3.61 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C 167.42, 166.89, 147.99, 143.68, 129.26, 124.32, 77.58, 54.25, 53.44, 53.29, 42.63. The enantiomeric excess was determined by HPLC, Chiral cel (OD-H), 240 nm, hexane: IPA 99: 1, flow rate: 1 mL min^{-1}, retention time: 2.07 min (major), 20.74 min (minor). $[\alpha]_D^{25}$ = +2.32 (*c*= 0.45, $CHCl_3$), (93% ee, (*R*)-isomer).

(R)-2-(2-nitro-1-phenylethyl) malononitrile (12a). White solid, yield: 97%, Mp: 55-56 °C, ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 7.56 (m, 3H), 7.45 (m, 2H), 4.91 (m, 2H), 4.50 (d, J= 6.6 Hz, 1H), 4.22 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C 131.86, 130.09, 129.30, 127.76, 110.51, 110.21, 77.97, 42.68, 29.23. The enantiomeric excess was determined by HPLC, Chiral cel (OD-H), 240 nm, hexane: IPA 99: 1, flow rate: 1 mL min^{-1}, retention time: 2.15 min (major), 15.34 min (minor). $[\alpha]_D^{25}$ = +2.78 (*c* =0.18, CH_2Cl_2), (99% ee, (*R*)-isomer). The absolute stereochemistry of the addition product was assigned as (*R*) by comparison of the optical data with literature reported value [29] $[\alpha]_D^{24.1}$ = +5.4 (c= 0.5, $CHCl_3$).

(R)-2-(1-(4-chlorophenyl)-2-nitroethyl) malononitrile (12b). White solid, yield: 97%, Mp: 88-90 °C, ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 7.43 (d, J= 8.5 Hz 2H), 7.36 (d, J= 8.9 Hz, 2H), 4.95 (m, 2H), 4.40 (d, J= 8.6 Hz, 1H), 4.24 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C 135.70, 129.30, 128.75, 128.31, 110.77, 110.59, 78.05, 42.39, 27.06. The enantiomeric excess was determined by HPLC, Chiral cel (OD-H), 245 nm, hexane: IPA 99: 1, flow rate: 1 mL min^{-1}, retention time: 2.12 min (major), 11.31 min (minor). $[\alpha]_D^{25}$ = +3.16 (*c*=0.19, CH_2Cl_2), (96% ee, (*R*)-isomer). The absolute stereochemistry of the addition product was assigned as (*R*) by comparison of the optical data with literature reported value [29]: $[\alpha]_D^{24.4}$ = +7.2 (*c* =0.5, $CHCl_3$), (76% ee, (*R*)-isomer).

(R)-2-(1-(4-methoxyphenyl)-2-nitroethyl) malononitrile (12c). White solid, yield: 94%, Mp: 82-94 °C, ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 7.13 (d, J= 8.7 Hz, 2H), 6.82 (d, J= 8.7 Hz, 2H), 4.90 (m, 2H), 4.41 (d, J= 5.7 Hz, 1H) 4.06 (m, 1H), 3.80 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C 160.93, 129.21, 123.33, 115.47, 110.55, 110.28, 76.75, 55.37, 43.12, 27.61. The enantiomeric excess was determined by HPLC, Chiral cel (OD-H), 245 nm, hexane: IPA 99: 1, flow rate: 1 mL min^{-1}, retention time: 2.12 min (major), 11.31 min (minor). $[\alpha]_D^{25.2}$ = +3.74 (*c* =0.33, CH_2Cl_2), (96% ee, (*R*)-isomer). The absolute stereochemistry of the addition product was assigned as (*R*) by comparison of the optical data with literature reported value [29]: $[\alpha]_D^{27.2}$ = +7.1 (*c* = 1.0, $CHCl_3$), (78% ee, (*R*)-isomer).

(R)-2-(2-nitro-1-p-tolylethyl) malononitrile (12d). White solid, yield: 95%, Mp: 99-100 °C, ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 7.29 (m, 4H), 4.91 (m, 2H), 4.28 (d, J= 6.0 Hz, 1H), 4.05 (m, 1H), 2.37 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C 139.31, 130.09, 128.34, 127.23, 109.80, 109.61, 76.74, 42.38, 27.23, 21.79. The enantiomeric excess was determined by HPLC, Chiral cel (OD-H), 245 nm, hexane: IPA 99: 1, flow rate: 1 mL min^{-1}, retention time: 2.12 min (major), 15.93 min (minor). $[\alpha]_D^{29}$ = +2.73 (*c* = 0.22, CH_2Cl_2), (97% ee, (*R*)-isomer).

(R)-2-(2-nitro-1-(4-nitrophenyl) ethyl) malononitrile (12e). Yellow solid, yield: 90%, Mp: 141-143 °C, ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 8.20 (d, J= 8.7Hz, 2H), 7.46 (d, J= 8.5 Hz, 2H), 5.21 (d, J= 6.9 Hz,

1H), 4.55 (d, J= 7.4 Hz, 1H), 3.62 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C 149.62, 142.62, 130.68, 125.50, 112.50, 112.20, 78.05, 42.34, 27.46. The enantiomeric excess was determined by HPLC, Chiral cel (OD-H), 245 nm, hexane: IPA 99: 1, flow rate: 1 mL min^{-1}, retention time: 2.33 min (major), 22.37 min (minor). $[\alpha]_D^{25}$ = +1.54 (*c* = 0.13, CH_2Cl_2), (95% ee, (*R*)-isomer).

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