Experimental Section

DBEDOT was obtained according to ref. [14] with 76% yield: m.p. 96°C; ^{1}H NMR (500 MHz, $CDCl_3$, 25°C, TMS): $\delta = 4.27$ ppm (s, 4H); ^{13}C NMR (125 MHz, $CDCl_3$, 25°C, TMS): $\delta = 139.6$, 85.4, 64.9 ppm; CP-MAS ^{13}C NMR (75 MHz, solid state, 25°C, TMS): $\delta = 140.3$, 84.6, 65.1 ppm; MS (70 eV): m/z (%): 302 (55) [M^+], 300 (100), 298 (55); elemental analysis: found: C 23.79, H 1.28, Br 53.00, S 10.86; calcd for $C_6H_4Br_2O_2S$: C 24.02, H 1.34, Br 53.27, S 10.69.

PEDOT: In a typical experiment, DBEDOT (0.01–2 g) was incubated at 60°C for 24 h and dried in vacuum (0.1 mbar) at room temperature to give black crystals of bromine-doped PEDOT; elemental analysis: found: C 28.87, H 1.65, Br 38.42, S 12.90; calcd for $C_6H_4Br_{1.2}O_2S(H_2O)_{0.6}$: C 28.01, H 3.50, Br 38.73, S 12.45.

The well-ground material was additionally dried in vacuum (0.1 mbar) at 150°C overnight, then stirred with hydrazine hydrate (50% aqueous solution, in MeCN) overnight, filtered, and washed with neat MeCN. Vacuum drying afforded a nearly fully dedoped PEDOT; elemental analysis: found: C 46.84, H 2.42, N ~2, Br 0.42, S 19.04; calcd for $C_6H_4O_2Br_{0.01}S(NH_2NH_2{\cdot}3H_2O)_{0.12}$: C 47.63, H 3.44, N 2.22, Br 0.53, S 21.19. CP-MAS ^{13}C NMR (75 MHz, solid state, 25°C, TMS): $\delta_c = 136.5$, 108.7, 64.9 ppm; IR (KBr): $\tilde{\nu} = 1650$, 1431, 1358, 1203, 1066, 984, 918, 832, 690 cm^{-1}.

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Asymmetric Michael Addition

Highly Enantioselective Organocatalytic Conjugate Addition of Malonates to Acyclic α,β-Unsaturated Enones**

*Nis Halland, Pompiliu S. Aburel, and Karl Anker Jørgensen**

Even though the first reports of enantioselective organocatalysis by Wiechert et al. and Hajos and Parrish appeared almost three decades ago,[1] the field of asymmetric catalysis has been dominated by metal catalysis. It is only recently that asymmetric organocatalysis has received renewed attention and become the focus of intense research efforts.[2] This is primarily due to the operational simplicity, the cheap catalysts, and the obvious industrial applications.

Recently, a number of reports on organocatalytic transformations has appeared covering a wide range of reactions including Diels–Alder reactions,[3] aldol reactions,[4] Mannich

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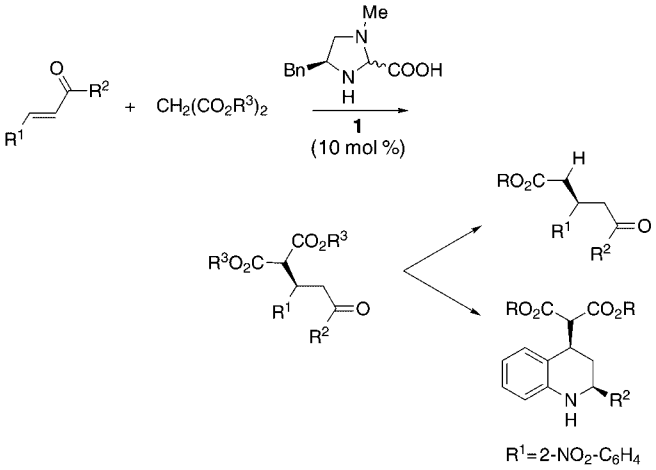
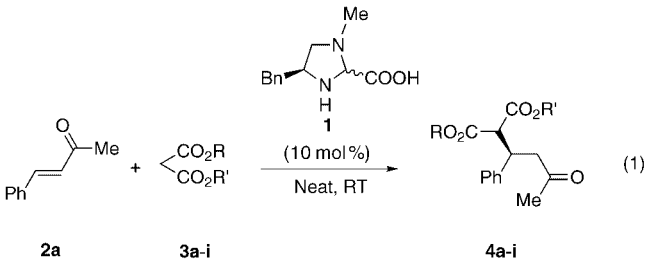
reactions,[5] 1,3-dipolar cycloadditions,[6] α amination,[7] synthesis of electron-rich benzene systems,[8] Robinson annulation,[9] Michael reaction,[10] Strecker reaction,[11] and others.[12] Although impressive results have been achieved in many organocatalytic asymmetric reactions, reports on enantioselective Michael addition reactions with excellent enantioselectivities (>90% *ee*) have until recently[10l] been limited to cyclic substrates[10e] or reactions with very low yields.[10f]

Herein we report the first enantioselective Michael addition of malonates to acyclic enones in excellent yields and enantioselectivities using an imidazolidine catalyst easily prepared from phenylalanine.[13] The potential of this new catalytic enantioselective C–C bond-forming reaction is demonstrated by an easy synthetic route to optically active δ ketoesters after a simple decarboxylation procedure and the formation of optically active tetrahydroquinolines (Scheme 1). This organocatalytic approach compares favorably to Lewis acid catalyzed[14] and indirect Lewis acid catalyzed[15] Michael additions to acyclic substrates in terms of ease of handling, yields, and enantioselectivities.



Scheme 1. Enantioselective Michael addition of malonates to acyclic enones.

The imidazolidine catalyst **1** is an efficient catalyst for the Michael addition of malonate nucleophiles to α,β-unsaturated enones [Eq. (1)], and a test reaction of benzylideneacetone (**2a**) with diethyl malonate (**3b**) and 10 mol% of catalyst **1** yielded the Michael adduct **4b** in high yield and 91% *ee* (Table 1, entry 2). A series of malonates were tested as it is known that the ester group has a large effect on the asymmetric induction of the reaction.[10a] The results of the screening of malonates **3a–i** in the reaction with **2a** in the presence of 10 mol% of **1** are presented in Table 1.



It turned out that the ester functionality has a large influence on the yield and enantioselective induction. The use of dimethyl malonate (**3a**) afforded only 73% *ee* (Table 1, entry 1), which is substantially lower than the 91% *ee* obtained in the initial test reaction with **3b** (Table 1, entry 2). For the sterically more hindered malonates **3c, 3d**, and **3i**, the reaction rate was decreased considerably and only low yields were obtained (Table 1, entries 3, 4, 9). The reactions of the medium-sized malonates **3e–h** all proceeded with excellent yields and enantioselectivities. For example, dibenzyl malonate (**3f**) afforded the Michael adduct in 93% yield and higher than 99% *ee* (Table 1, entry 6). Unfortunately the diastereoselectivities with the nonsymmetrical malonates **3g,h** were rather low (Table 1, entries 7, 8) as almost equal amounts of the isomers at the α-carbon atom were formed. This has been observed previously in amine-catalyzed Michael additions of nitroalkanes to enones.[10b,13]

To further explore the scope of the reaction, a series of α,β-unsaturated enones **2a–o** were reacted with dibenzyl malonate (**3f**) in the presence of 10 mol% of catalyst **1** [Eq. (2)]. The results are presented in Table 2. The aromatic

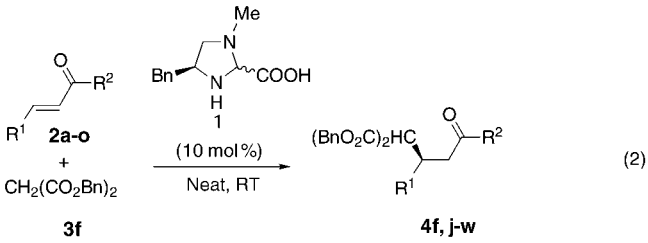


Table 1: Enantioselective Michael addition of malonates **3a-i** to benzylideneacetone (**2a**) catalyzed by **1** [Eq. (1)].[a]

Entry	Malonate	R	R′	*t* [h]	d.r.	Yield of **4** [%][b]	*ee* [%][c]
1	**3a**	Me	Me	120	–	66	73
2	**3b**	Et	Et	120	–	73	91
3	**3c**	*i*Pr	*i*Pr	210	–	26	71
4	**3d**	*t*Bu	*t*Bu	210	–	<5	nd
5	**3e**	allyl	allyl	150	–	92	89
6	**3f**	Bn	Bn	150	–	93	>99
7	**3g**	Bn	Me	150	1:1.5	92	98/97
8	**3h**	Bn	Et	150	1:1	90	90[d]
9	**3i**	Et	*t*Bu	150	1:1.3	<10	nd

[a] Experimental conditions: **2a** (0.5 mmol) and **1** (0.05 mmol) were added to **3** (1.0 mL) and the reaction mixture was stirred at ambient temperature for the time indicated in the table. [b] Unoptimized yields determined by GC. [c] Determined by chiral stationary-phase HPLC, see Supporting Information; nd: not determined. [d] Determined by chiral stationary-phase HPLC after decarboxylation, see Supporting Information.

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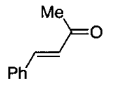
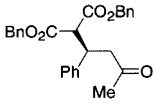
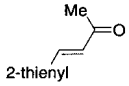
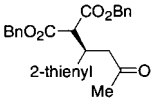
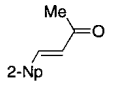
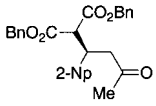
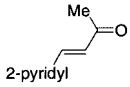
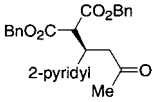
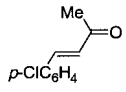
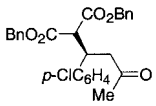
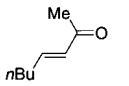
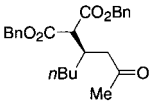
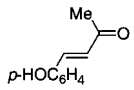
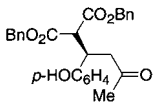
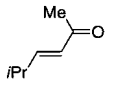
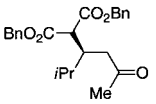
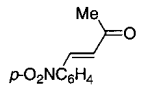
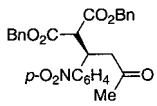
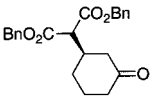
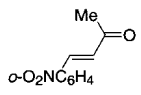
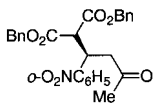
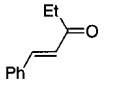
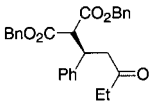
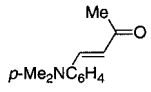
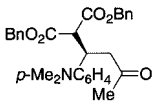
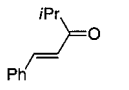
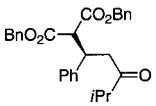
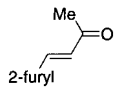
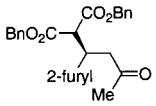
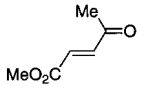
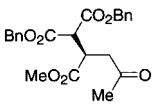
Table 2: Enantioselective Michael addition of dibenzyl malonate (**3f**) to **2a–o** catalyzed by **1** [Eq. (2)].[a]

Entry	Enone	Product	*t* [h]	Yield [%][b]	*ee* [%][c]	Entry	Enone	Product	*t* [h]	Yield [%][b]	*ee* [%][c]
1	 **2a**	 **4f**	165	86	99	9	 **2i**	 **4q**	165	75	92
2	 **2b**	 **4j**	165 165	99 74	90 93[d]	10	 **2j**	 **4r**	165	95	88
3	 **2c**	 **4k**	165	75	98	11	 **2k**	 **4s**	250	61	91[f]
4	 **2d**	 **4l**	165	75	93	12	 **2l**	 **4t**	170	33	84
5	 **2e**	 **4m**	165	84	89[e]	13	 **2m**	 **4u**	150	78	83
6	 **2f**	 **4n**	150	87	86	14	 **2n**	 **4v**	250	66	95[f]
7	 **2g**	 **4o**	170	58	77	15	 **2o**	 **4w**	170	2	94
8	 **2h**	 **4p**	150	75	92	16	 **2p**	 **4x**	288	59	59[e]

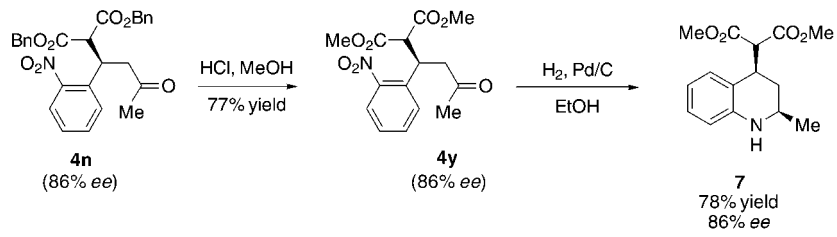
[a] Experimental conditions: Enone **2** (0.5 mmol) and **1** (0.05 mmol) were added to **3f** (1.0 mL) and the reaction mixture was stirred at ambient temperature for the time indicated in the table. [b] Yields after flash chromatography. [c] Determined by chiral stationary-phase HPLC, see Supporting Information. [d] Performed at 10 °C. [e] Performed at 0 °C. [f] Performed by using 20 mol% of catalyst.

enones **2a–f** reacted very well with **3f** and the Michael adducts **4f,j–n** were all formed in high yields and enantioselectivities (Table 2, entries 1–6). Both electron-withdrawing (NO_2, Cl) and -donating substituents (OH) can be introduced on the aromatic ring without compromising the yield or enantioselectivity of the reaction (Table 2, entries 3–6). The only exception to the generally high yields and enantioselectivities with aromatic enones was the *N,N*-dimethylaniline derivative **2g** (58% **4o** with 77% *ee*, Table 2, entry 7). The heteroaromatic enones **2h–j** were also successfully used in this Michael reaction (Table 2, entries 8–10). The alkyl-substituted enones **2k,l** were found to react quite slowly and with lower yields even when longer reaction times and higher catalyst loadings were employed (Table 2, entry 11), however high enantioselectivities were still obtained (Table 2, entries 11, 12).

It should be noted that no by-products were observed in any of the reactions, that the yields for the slowly reacting substrates **2k,l,n,o** are a consequence of the reaction time, and that higher yields could be obtained at longer reaction times. Higher yields[16] could also be achieved at elevated reaction temperatures, but generally accompanied by slightly decreased enantioselectivies: for instance, compound **4v** was formed in 82% yield and 87% *ee* at 60 °C (10 mol% of **1** and shorter reaction time). For the sterically more hindered enones **2n,o**, the reaction rate was decreased and lower yields resulted. This seems to be an effect of the added steric bulk on the ketone, hindering the catalyst approach, and thus slowing

down the reaction rate. The reduced reaction rate did not affect the asymmetric induction (Table 2, entries 14, 15). An ester-substituted enone, **2p**, was also tested; the Michael adduct **4x** was formed, although in moderate yield and enantioselectivity (Table 2, entry 16).

The absolute configuration of the Michael adduct **4k** was determined to be *R*.[17] This is in complete agreement with an iminium ion intermediate **5** (Figure 1),[18] obtained from activation of enone **2a** by the chiral catalyst. The *Re* face of the enone in this intermediate is shielded by the benzyl group of the chiral catalyst allowing the malonate to approach the open *Si* face of the enone as outlined in Figure 1.



Scheme 2. Synthesis of an optically active tetrahydroquinoline from **4n**.

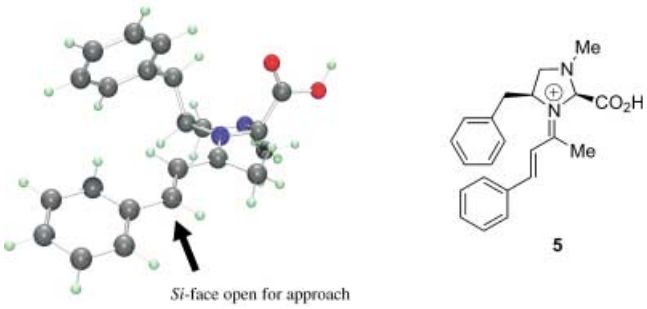
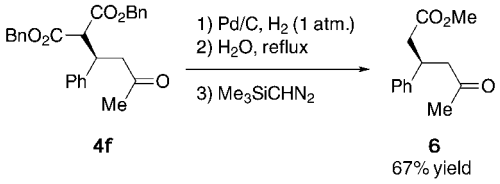


Figure 1. PM3-minimized structure and formula of the proposed iminium ion intermediate **5**.

The Michael adducts **4** could easily undergo a simple one-pot decarboxylation–transesterification procedure to give the corresponding optically active δ ketoesters **6** as shown in Equation (3) for Michael adduct **4f** which is decarboxylated in 67% yield (unoptimized) and without detectable loss of optical activity.



(3)

Michael adduct **4n** could be used for a facile synthesis of the biologically interesting optically active tetrahydroquinoline **7** (Scheme 2).[19] The transformation of dibenzyl ester **4n** into the corresponding dimethyl ester **4y** was followed by reductive amination giving tetrahydroquinoline **7** as a single diastereomer in 78% yield and without loss of otical purity.

In summary, we have developed the first highly enantioselective organocatalytic Michael addition of malonates to α,β-unsaturated enones using an imidazolidine catalyst easily prepared from phenylalanine. The reaction proceeds for a great diversity of α,β-unsaturated enones with excellent enantioselectivities. The scope of the reaction is demonstrated by the synthesis of optically active δ ketoesters and tetrahydroquinolines.

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[17] CCDC-194337 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/conts/retrieving.html (or from the Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge CB21EZ, UK; fax: (+44) 1223-336-033; or deposit@ccdc.cam.ac.uk).
[18] The calculations have been performed for the protonated carboxylic acid form of **5**.
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Structural Memory Reporters

Supramolecular Chirality: A Reporter of Structural Memory**

*Marco Ziegler, Anna V. Davis, Darren W. Johnson, and Kenneth N. Raymond**

Dedicated to Dr. Jide Xu
on the occasion of his 60th birthday

Herein we describe a molecular structure, formed from labile components, that exhibits structural memory. The macroscopic model in Figure 1 demonstrates this principle. The wooden icosohedral puzzle retains its structure (without any glue) despite dissociation of several pieces. These labile pieces can be removed and replaced without disassembly of the original structure. The structure itself is retained, or remembered, throughout the process of component substitution. In short, structural memory describes the substitution process itself and not merely the starting and ending states of the system.

Figure 1. A 3D puzzle made of labile wooden components retains its structure despite dissociation of several pieces.

Like the wooden puzzle, discrete supramolecular assemblies exhibit well-defined topologies, specified by the arrangement and connectivity of the constituent molecular components. If these molecular components can be substituted in a stepwise fashion and the supramolecular structure still persists, then there is structural memory. We describe such structural memory—as reported by retention of chirality—in

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