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New chiral basic heterogeneous catalyst based on Csβ zeolite

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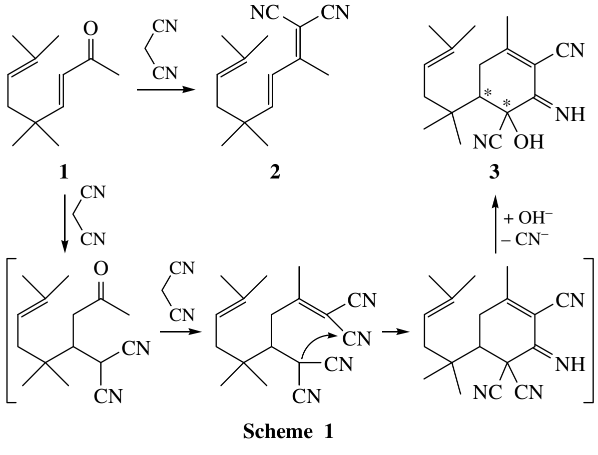
A new basic chiral catalyst Met-Csβ has been synthesised for preparing optically active products of the Michael reaction and tandem transformations by the interaction of starting achiral α,β-unsaturated carbonyl compounds with malononitrile.

The Michael reaction is of importance for forming new carbon–carbon bonds.[1] Special attention has recently been paid to the enantioselective Michael addition.[2] Asymmetric catalysis of the Michael reaction generally employs various homogeneous metallocomplex catalysts,[3] while heterogeneous chiral systems were almost not used for this purpose.[4–6] At the same time, the use of heterogeneous catalysts often permits one to avoid typical disadvantages of homogeneous systems such as difficulties of catalyst separation and recycling.[7]

Previously, we showed that basic zeolite Csβ is an effective catalyst for reactions of α,β-unsaturated carbonyl compounds from the terpenoid series with CH acids.[8,9] The reaction products were the typical products of Michael and Knoevenagel reactions, or tandem transformations, which depended on the structure of the terpenoid. For example, when ketone **1** reacted with malononitrile (Scheme 1) in the presence of zeolite Csβ, the Knoevenagel reaction (product **2**) competed with the Michael



Scheme 1

reaction, and the latter initiated tandem transformations leading to polyfunctional compound **3**, which is formed as a mixture of two diastereomers.

The mechanism suggested for the reaction forming compound **3** was confirmed by the fact that starting dinitrile **2** was not converted to compound **3** under the conditions of its reaction with malononitrile.

The formation of asymmetric centres in product **3** in the course of the above transformations prompted us to synthesise from Csβ a heterogeneous chiral catalyst suitable for asymmetric catalysis of reactions of α,β-unsaturated carbonyl compounds with malononitrile. For test reaction, we chose the transformation of ketone **1** into polyfunctional compound **3**. Currently, we know of only two catalytic systems suitable for Michael reactions between malononitrile and α,β-unsaturated carbonyl compounds; the systems use homogeneous complexes of Mg^{2+} and Ni^{2+} ions with hardly accessible chiral ligands based on substituted phenyloxazoles.[10]

Heterogeneous chiral catalysts described in the literature were created by modifying zeolites with optically active compounds. Thus, zeolites NaX and NaY modified with (–)- or (+)-ephedrine were employed for asymmetric catalysis of the Norrish–Young photoreaction.[11] Chiral 1,3-dithiane-1-oxide applied to the zeolite HY support was used for investigating dehydration of a mixture of *S*- and *R*-isomers of butan-2-ol, which led to preferable conversion of one of the enantiomers.[12] No examples of chiral compounds applied to zeolites and designed for the preparation of asymmetric basic catalysts have been found in the literature.

The structure of zeolite Csβ involves caesium oxide clusters, the caesium content being ~34 wt.%.[8] For the chiral modifier, we chose L-methionine. Its interaction with caesium oxides led to caesium methionate, which is insoluble in nonpolar solvents and is tightly held by the zeolite surface. We prepared catalyst samples with different mass contents of L-methionine: 8%, 11%, and 14%.[†] For zeolite with 8% L-methionine (8%Met-Csβ), the area of the specific free surface decreased considerably: 23 $m^2 g^{-1}$ (as determined by argon adsorption at 77 K) *versus* 51 $m^2 g^{-1}$ for the starting Csβ. Table 1 presents the results of the catalytic activity test for the catalysts in the reaction of ketone **1** with malononitrile.

When 8%Met-Csβ was used as a catalyst, the yields of reaction products **2** and **3** were 28 and 10%, respectively (conversion was nearly 100%) (Table 1).[‡] Product **3** is an optically active compound; the diastereomeric excess (ee, 3.3%) was determined from ^{1}H NMR spectral data using $Eu(hfc)_3$ as a chiral shift reagent. Using 8%Met-Csβ resulted in a considerable retardation of the reaction and decreased total yield of the products compared to the case with Csβ used as a catalyst. The ratio between the yields of dinitrile **2** and polyfunctional compound **3** changed in favour of the latter. This change may be explained, at least partially, by a reaction between dinitrile **2** and malononitrile leading to compound **3** in the presence of the 8%Met-Csβ catalyst,[§] which does not occur in the presence of Csβ. The product did not possess optical activity. Thus, in the presence of modified zeolite 8%Met-Csβ as a catalyst, the reaction follows one of the routes possible in this case: primary formation of a Michael or Knoevenagel reaction product, the latter leading to a racemic compound.

Table 1 Interaction of ketone **1** with malononitrile.

Catalyst	Conversion (%)	Reaction time (days)	Yield[a] (%)		**2/3**	$[\alpha]^{20}_{D}$ for **3**	ee[b] (%)
			2	**3**			
Csβ[8]	73	2	40	7	5.7	0	0
Cs_xO_y[8]	100	2	30	0	—	—	—
8%Met-Csβ	98	14	28	10	2.8	+11	3.3
8%Met-Csβ	88[c]	18	—[c]	9	—	0	0
11%Met-Csβ	67	28	44	11	4	+20	6
14%Met-Csβ	100	18	5	25	0.2	0	0
Met-Cs	100	18	10	15	0.67	0	0

[a]Yield given based on the converted terpenoid **1** or **2**. [b]Determined using ^{1}H NMR spectral data and a $Eu(hfc)_3$ addition as a chiral shift reagent. [c]Compound **2** was employed as a starting compound.

When the content of L-methionine in the catalyst was raised to 11%, the total yield of the reaction products increased to 55%, while conversion decreased to 67%, and the optical purity of **3** increased to 6%.

To check if the optical purity of the product has been changed, *e.g.*, by racemization or kinetic separation, we kept compound **3** on the 11%Met-Csβ catalyst (mass ratio of compound **3** to catalyst was 1:2) for 14 days under reaction conditions. This gave tar product **3** (only 10% of compound **3** was recovered) whose optical purity did not change.

With 14% L-methionine in the catalyst, the reaction of ketone **1** with malononitrile led to racemic compound **3** as the major reaction product. The absence of optically active products in this case may be explained by the fact that due to excess L-methionine applied to zeolite, the reaction is catalysed by caesium methionate lying on the surface of the zeolite and is not affected by the crystal structure of the zeolite. Indeed, when this reaction was carried out using amorphous caesium methionate as a catalyst, compound **3** isolated as a product did not possess optical activity. Thus, the crystal structure of zeolite proved to be essential to enantioselective catalysis.

The resulting heterogeneous chiral catalyst was tested in a reaction of another α,β-unsaturated ketone, benzalacetone **4**, with malononitrile (Scheme 2). When conducted in the presence of 8%Met-Csβ, this reaction gave compound **5** in 26% yield based on the converted ketone (conversion 43%).[¶] The isolated product was optically active (ee, 3%). The interaction of benzalacetone **4** with malononitrile on the starting zeolite Csβ led to the formation of racemic compounds **5** and **6** in 3 and 6% yields, respectively.

When the reaction of benzalacetone **4** with malononitrile was carried out in the presence of caesium L-methionate, we isolated racemic compounds **5** and **6**, in 7% yield each. A similar result was obtained using caesium oxides modified with L-methionine as catalysts (yields of racemic products **5** and **6** were 9% for

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[†] A methanol solution of the calculated amount of L-methionine was poured into zeolite Csβ (100 mg) preliminarily calcined for 2 h at 500 °C. The solvent was distilled off on a rotary vacuum evaporator. The resulting white powder was dried in a vacuum (0.07 Torr) at 50 °C for 2 h immediately before use.

[‡] *In the presence of 8%Met-Csβ.* A solution of malononitrile (0.151 g, 2.3 mmol) in diethyl ether (2 ml) was added to Met-Csβ (0.05 g). The ether was distilled off, and 5,5,8-trimethylnona-3,7-dien-2-one **1** (0.106 g, 0.6 mmol) was added. The mixture was allowed to stand for 14 days at 20 °C and then treated with ethyl acetate. The reaction products were separated on a silica gel column using hexane as an eluent with a diethyl ether gradient from 0 to 100%. This gave starting ketone **1** (0.002 g, conversion 98%), 2-(1,4,4,7-tetramethylocta-2,6-dienylidene)malononitrile **2** (0.038 g, yield 28% based on converted ketone **1**) and 1-hydroxy-2-imino-4-methyl-6-(1,1,4-trimethylpent-3-enyl)cyclohex-3-ene-1,3-dinitrile **3** (0.018 g, yield 10% based on converted ketone **1**). For compound **3** $[\alpha]^{20}_{580}$ = +11 (*c* 0.6, $CHCl_3$).

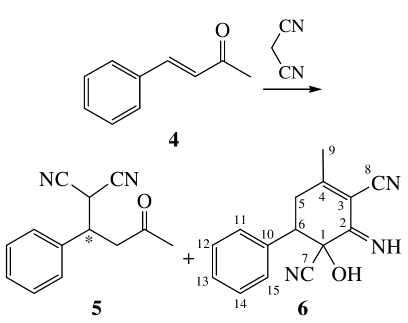
In the presence of 11%Met-Csβ. Similarly, when malononitrile (0.472 g, 7.2 mmol) reacted with ketone **1** (0.333 g, 1.8 mmol) in the presence of 11%Met-Csβ, (0.158 g) for 28 days, the products were starting ketone **1** (0.109 g, conversion 67%), compound **2** (0.124 g, yield 44% based on converted ketone **1**), and compound **3** (0.036 g, yield 11% based on converted ketone **1**). For compound **3** $[\alpha]^{20}_{580}$ = +20 (*c* 1.2, $CHCl_3$).

In the presence of 14%Met-Csβ. Similarly, the reaction of malononitrile (0.158 g, 2.4 mmol) with ketone **1** (0.104 g, 0.6 mmol) in the presence of 14%Met-Csβ (0.108 g) for 18 days gave compound **2** (0.007 g, yield 5%) and racemic compound **3** (0.042 g, yield 25%).

In the presence of caesium L-methionate. Similarly, in the reaction of malononitrile (0.339 g, 5.2 mmol) and ketone **1** (0.336 g, 1.9 mmol) in the presence of caesium methionate (0.173 g) for 18 days, the product was compound **2** (0.045 g, yield 10%) and racemic compound **3** (0.080 g, yield 15%).

[§] A solution of malononitrile (0.032 g, 0.5 mmol) in diethyl ether (1 ml) was added to 8%Met-Csβ (0.01 g). The ether was distilled off, and compound **2** (0.016 g, 0.07 mmol) was added. The mixture was kept at 20 °C for 18 days, and treated with ethyl acetate as an extractant. The reaction products were separated on a silica gel column using hexane as an eluent with a gradient of diethyl ether from 0 to 100%. The products were starting dinitrile **2** (0.002 g, conversion 88%) and racemic compound **3** (0.002 g, yield 9% based on converted dinitrile **2**).

each). These facts suggest that the crystal structure of zeolite is essential to the formation of optically active products.



Scheme 2

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¶ *In the presence of 8%Met-Csβ.* A solution of malononitrile (0.2 g, 3.0 mmol) in diethyl ether (4 ml) was added to 8%Met-Csβ (0.020 g). The ether was distilled off, and benzalacetone **4** (0.212 g, 1.5 mmol) was added. The mixture was kept at 20 °C for 48 h and treated with ethyl acetate. The reaction products were separated on a silica gel column using hexane as an eluent with a gradient of diethyl ether from 0 to 100%. This procedure afforded starting ketone **4** (0.112 g, conversion 43%) and 2-(3-oxo-1-phenylbutyl)malononitrile **5** (0.033 g, yield 26% based on converted benzalacetone **4**). The ^{1}H NMR spectrum of compound **5** is similar to the published data.[13] $[\alpha]^{20}_{580} = +3$ (c 1.1, $CHCl_3$). The enantiomeric excess (3%) was determined from ^{1}H NMR spectral data for compound **5** with the addition of the Eu(tfc)$_3$ chiral shift reagent.

In the presence of Csβ. Similarly, when malononitrile (0.224 g, 3.3 mmol) reacted with benzalacetone **4** (0.195 g, 1.3 mmol) in the presence of Csβ (0.053 g) at 20 °C for 10 days, the products were starting ketone **4** (0.074 g, conversion 62%), compound **5** (0.013 g, yield 3% based on converted benzalacetone **4**) and 1-hydroxy-2-imino-4-methyl-6-phenylcyclohex-3-ene-1,8-dicarbonitrile **6** (0.032 g, yield 6% based on converted benzalacetone **4**).

For **6**: ^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.21 (br. s, 3H, C^9H_3), 2.59 (dd, 1H, H^5, $J_{5,5'}$ 18 Hz, $J_{5,6}$ 7 Hz), 2.83 (ddq, 1H, $H^{5'}$, J 18 Hz, $J_{5',6}$ 8.5 Hz, $J_{5',9}$ 1 Hz), 3.73 (dd, 1H, H^6, $J_{6,5'}$ 8.5 Hz, $J_{6,5}$ 7 Hz), 4.82 (br. s, 2H, OH, =NH), 7.15 (dd, 2H, H^{11}, H^{15}, $J_{11,12}$ 7.5 Hz, $J_{11,13}$ 1.5 Hz), 7.24 (tt, 1H, H^{13}, $J_{13,12}$ 7.5 and 1.5 Hz), 7.31 (br. t, 2H, H^{12}, H^{14}, J 7.5 Hz). ^{13}C NMR, δ: 75.21 (s, C^1), 146.44 (s, C^2), 105.21 (s, C^3), 161.32 (s, C^4), 39.13 (t, C^5), 37.80 (d, C^6), 118.30 (s, C^7), 113.57 (s, C^8), 23.98 (q, C^9), 141.48 (s, C^{10}), 126.99 (d, C^{11}, C^{15}), 127.67 (d, C^{13}), 129.01 (d, C^{12}, C^{14}). MS, *m/z*: 234.10268 [$M^+ - OH$]. Calc. for $C_{15}H_{13}N_3O$: 234.10312.

In the presence of caesium L-methionate. A similar reaction between malononitrile (0.14 g, 2.3 mmol) and benzalacetone **4** (0.121 g, 0.8 mmol) in the presence of caesium L-methionate (0.2 g) at 20 °C for 10 days gave compounds **5** (0.016 g, yield 9%) and **6** (0.018 g, yield 9%). The products did not possess optical activity.

In the presence of caesium oxides modified with L-methionine (Met-Cs). A solution of L-methionine (0.04 g, 0.27 mmol) in methanol was added to the mixture of caesium oxides obtained by calcinating caesium formate (0.06 g, 0.34 mmol) at 500 °C for 2 h. The solvent was distilled off. Malononitrile (0.299 g, 4.8 mmol) in diethyl ether (2 ml) was added to the resulting catalyst, the ether was evaporated, and benzalacetone **4** (0.316 g, 2.2 mmol) was added to the mixture. The mixture was kept at 20 °C for 168 h. Conventional treatment yielded starting ketone **4** (0.059 g, conversion 81%), compound **5** (0.08 g), and a 1:0.94 mixture of compounds **5** and **6** (^{1}H NMR data). The yield was 7% for each of compounds, **5** and **6**, based on converted ketone **4**; the products did not possess optical activity.