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# Auto Tandem Catalysis: Asymmetric Vinylogous Cycloaddition / Kinetic Resolution Sequence for the Enantioselective Synthesis of Spiro-Dihydropyranone from Benzylidene Meldrum's Acid.

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*Dedicated to Prof. Jean-Claude Fiaud on the occasion of his 77th birthday*

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**Abstract:** A catalytic enantioselective vinylogous domino reaction has been achieved from ketone-derived benzylidene Meldrum's acid and  $\alpha$ -ketolactones to provide spiro-lactone dihydropyranones with more than 99% ee. An Auto Tandem Catalysis (ATC) process resulting from dual and complementary role of (DHQ)<sub>2</sub>PHAL organocatalyst resulted in a sequence involving an asymmetric vinylogous formal (4+2) cycloaddition of benzylidene and the subsequent kinetic resolution operating through a 1,3-prototropic shift leading to good yields (> 50%) and the high selectivity.

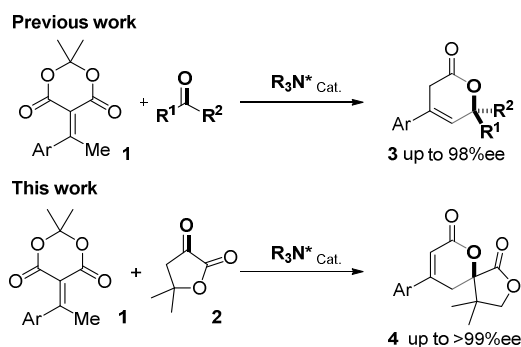
**Keywords:** Auto Tandem Catalysis; Asymmetric Catalysis; Kinetic Resolution; Organocatalysis; Meldrum's acid; 1,3 prototropic shift

Accessing chiral enantioenriched molecules is still a major challenge in organic chemistry. Producing highly complex structures while preserving energy, resources and time as well as minimizing waste is even more difficult. Over the years, great attention has been given to domino, tandem, one-pot, multi-components and multi-catalyzed reactions in the synthesis of natural products as well as biologically active compounds.<sup>[1]</sup> Among these, the enantioselective Auto Tandem Catalysis (ATC) offers a powerful tool owing to the same chiral catalyst promotes at least two different chemical transformations in a single pot, while ensuring the asymmetric induction (**Figure 1**). The main advantages of this strategy consist both in the multiple role of a single catalyst and the challenging compatibility between reagents to achieve an economical domino process.<sup>[2,3]</sup> However, despite considerable efforts in this area,<sup>[4]</sup> examples of ATC process with high enantioselectivity are limited.<sup>[5]</sup> Moreover, an auto-tandem catalysis in the presence of a Brønsted base is highly desirable to expand its practice in organic synthesis.<sup>[4n]</sup>



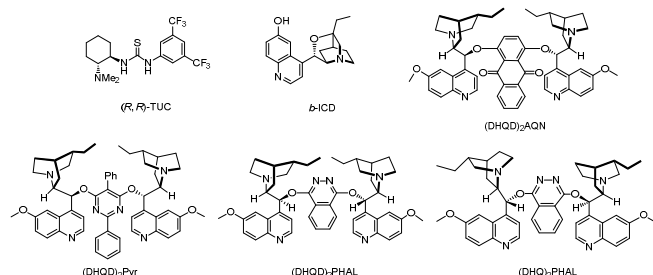
**Figure 1.** Schematic representation of ATC.

Chiral enantioenriched 5,6-dihydropyran-2-ones is an important heterocyclic structure found in numerous bioactive compounds. Many synthetic strategies have been developed to obtain this motif.<sup>[6]</sup> Among them, the enantioselective vinylogous reaction is a very important and simple way to construct such a structure bearing a quaternary stereocenter.<sup>[7]</sup> As such, the development of new reagents to obtain novel chiral 5,6-dihydropyran-2-ones is still of high interest. In the course of our development of efficient enantioselective transformations, we have recently discovered an unprecedented route to 3,6-dihydropyran-2-one **3** as spiro-[4,5] decane derivatives with up to 98% ee, from a novel platform in vinylogous series i.e. ketone-derived benzylidene Meldrum's acids **1**.<sup>[8],[9]</sup> The reaction proceeded through a formal (4+2) cycloaddition.<sup>[10]</sup> Herein, we report a highly enantioselective ATC including a formal (4+2) cycloaddition followed by a kinetic resolution of the intermediate to give access to spiro(bis-lactone) 5,6-dihydropyran-2-ones **4** with excellent enantiomeric excesses (Scheme 1). The access to enantioenriched compounds **4** from benzylidene Meldrum's acids has never been described so far.



**Scheme 1.** Benzylidene Meldrum's acid **1** as an original vinylogous platform.

In our previous work, concerning the vinylogous addition reaction of benzylidene **1** to ketones, we observed that triethylamine could isomerize the obtained product **3** into the conjugated product **4** for longer reaction. We therefore envisaged that a basic chiral catalyst could deliver directly the enantioenriched  $\alpha,\beta$ -unsaturated lactone **4**, through an economical domino-sequence. Initial investigations examined the base-catalyzed reaction of benzylidene **1a** with dihydro-4,4-dimethyl-2,3-furandione **2** in the presence of Cinchona-derived catalysts (Scheme 2 and Table 1).



**Scheme 2.** Catalysts.

**Table 1.** Asymmetric catalysis with benzylidene **1a** and dihydro-4,4-dimethyl-2,3-furandione **2** in the presence of alkaloid catalysts. <sup>[a]</sup>

Reaction scheme showing the asymmetric Diels-Alder reaction of chiral diene **1a** and maleimide **2** catalyzed by various catalysts to form products **3a** and **4a**. The reaction conditions are 25°C, 24h in CH<sub>2</sub>Cl<sub>2</sub> with 20mol% catalyst.

Entry	Cat	Conv. [%]	<b>3a/4a</b>	Yields [%] <b>3a/4a</b>	ee <sub>3a</sub> [%]	ee <sub>4a</sub> [%]
1	( <i>R,R</i> )-TUC	81	99/1	76/nd	92-( <i>R</i> )	nd
2	β-ICD	78	96/4	76/nd	35-( <i>R</i> )	nd
3	(DHQD) <sub>2</sub> AQN	91	3/97	nd/71	nd	71-( <i>R</i> )
4	(DHQD) <sub>2</sub> Pyr	94	21/79	7,5/69	86-( <i>S</i> )	89-( <i>R</i> )
5	(DHQD) <sub>2</sub> PHAL	97	25/75	20/74	89-( <i>S</i> )	92-( <i>R</i> )
6	(DHQ) <sub>2</sub> PHAL	99	13/87	11/86	75-( <i>R</i> )	98-( <i>S</i> )

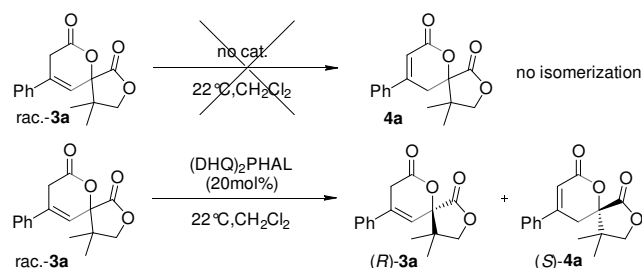
7 <sup>[b]</sup>	(DHQ) <sub>2</sub> PHAL	97	14/86	13/82	12-( <i>S</i> )	99-( <i>S</i> )
8 <sup>[c]</sup>	(DHQ) <sub>2</sub> PHAL	99	15/85	13/80	66-( <i>R</i> )	94-( <i>S</i> )
9 <sup>[d]</sup>	(DHQ) <sub>2</sub> PHAL	97	14/86	11/81	51-( <i>R</i> )	99-( <i>S</i> )

[a] Reaction conditions: **1a** (0.15 mmol), **2** (0.15 mmol), catalyst (20 mol%) in DCM (0.5 M) at 25 °C otherwise noted. Percentage of isolated yields after separation of **3a** and **4a** by column chromatography. The conversion and ratio of isomers (**3a/4a**) were determined by <sup>1</sup>H NMR on the crude product. Enantiomeric excess (ee) was determined by chiral HPLC. The absolute configuration of **3a** and **4a** were determined by X-Ray analysis of pure crystal [b] Performed at 10°C. [c] Performed at 40°C. [d] Performed with 10 mol% catalyst at [C]=1.0 M.

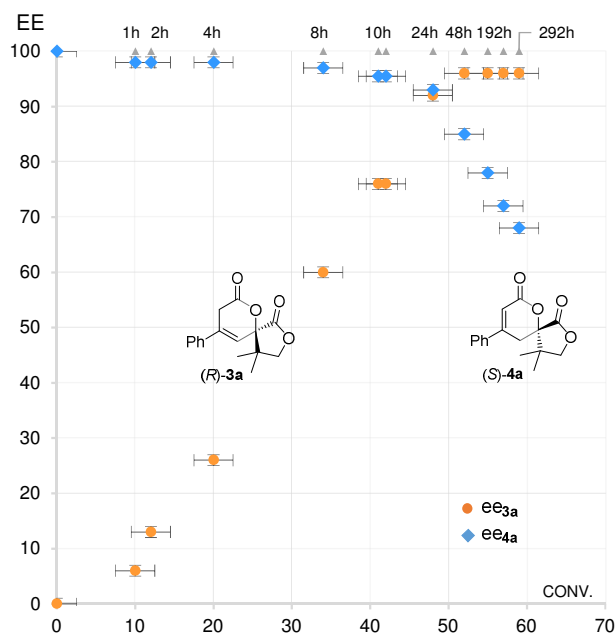
Reaction with β-ICD as catalyst proceeded smoothly to give the non-conjugated product **3a** as the major product with low enantioselectivity (Table 1, entry 2). This result is in agreement with our previous work (entry 1), which showed that many catalysts with an inadequate basicity led to the kinetic product **3a**, without subsequent conversion into the conjugated compound **4a**.<sup>[8]</sup> Dimeric alkaloid catalysts afforded **4a** as the major product with better selectivity than β-ICD and in excellent conversion. Thus (DHQD)<sub>2</sub>AQN gave an excellent ratio (**3a/4a**: 3/97) with 71% ee for **4a** (Table 1, entry 3). (DHQD)<sub>2</sub>Pyr and (DHQD)<sub>2</sub>PHAL provided the conjugated product **4a** with lower **3a/4a** selectivity with (21/79) and (25/75) respectively. Compounds **3a** and **4a** were isolated in satisfactory yields, but with a significant difference of enantiomeric excesses of (86%ee<sub>3a</sub> / 89%ee<sub>4a</sub>) and (89%ee<sub>3a</sub> / 92%ee<sub>4a</sub>) respectively (Table 1, entries 4 and 5). This observation was confirmed when using (DHQ)<sub>2</sub>PHAL as catalyst. In this case, a 13/87 ratio of **3a/4a** with 75% ee for (*R*)-**3a** and excellent 98% ee for (*S*)-**4a** were obtained (Table 1, entry 6). At lower temperature (10°C), the conjugated spiro(bis-lactone) (*S*)-**4a** was isolated in good yield of 82% and very high enantiomeric excess of 99%, whereas only 13% of the non-conjugated compound (*S*)-**3a** was obtained with a low enantiomeric excess of 12% (Table 1, entry 7). Higher temperature or higher concentration in the presence of lower catalyst loading do not improve the results (Table 1, entries 8 and 9). These results are in contradiction with a simple chemical isomerization process of the carbon-carbon double bond of the β, γ-unsaturated lactone **3a** to the conjugated lactone **4a**. At this stage, we supposed a possible ATC process including an enantioselective formal cycloaddition following by a kinetic resolution (KR) of **3a** to **4a**. Surprisingly, this KR would proceed through a 1,3-proton shift.

To prove the existence of KR, we first verified that **3a** is thermodynamically stable in the reaction conditions without the catalyst. Further investigations were conducted into the isomerization of a racemic mixture of **3a** to **4a** in the presence of (DHQ)<sub>2</sub>PHAL at room temperature in order to determine the ratio **3a/4a** as well as the enantiomeric excesses of **3a** and **4a** and the conversion (Scheme 3).<sup>[11]</sup> To our delight,

a clear kinetic resolution of racemic **3a** was observed with high efficiency in the presence of (DHQ)<sub>2</sub>PHAL (Figure 2).



**Scheme 3.** Thermodynamic stability and kinetic resolution of racemic **3a**.<sup>[a]</sup>



**Figure 2.** Kinetic resolution of **3a** in the presence of (DHQ)<sub>2</sub>PHAL. [a] Enantiomeric excesses were determined by HPLC. Conversion and ratio **3a/4a** were determined by <sup>1</sup>H NMR (see SI for experimental data).

The enantioenriched conjugated (*S*)-**4a** was obtained by the preferentially isomerization of (*S*)-**3a** promoted by the basic (DHQ)<sub>2</sub>PHAL catalyst. While the reaction rate was relatively rapid at low conversion, the transformation slowed after 10 hours (41% of conversion in 10 hours and 48% in 24 hours). To achieve conversions of 59%, 292 hours of reaction time was required. This is proof of the real efficiency of the KR process with an enantioselectivity factor *E* > 100.<sup>[12]</sup> Subsequently, to demonstrate the role of the ATC process during the reaction, a kinetic study was undertaken. Several parameters were investigated such as conversion, **3a/4a** ratio and enantiomeric excesses of **3a** and **4a** during the reaction between **1a** and **2** catalyzed by (DHQ)<sub>2</sub>PHAL (Table 2).

**Table 2.** Auto Tandem Catalysis with benzylidene **1a** and dihydro-4,4-dimethyl-2,3-furandione **2** in the presence of (DHQ)<sub>2</sub>PHAL catalyst.<sup>[a]</sup>

Entry	Time [h]	Conv. [%]	<b>3a/4a</b>	ee <sub>3a</sub> [%]	ee <sub>4a</sub> [%]
1	2	51	95/5	91-( <i>S</i> )	>99-( <i>S</i> )
2	4	75	89/11	88-( <i>S</i> )	99-( <i>S</i> )
3	6	86	75/25	83-( <i>S</i> )	>99-( <i>S</i> )
4	8	90	64/36	76-( <i>S</i> )	>99-( <i>S</i> )
5	10	92	51/49	67-( <i>S</i> )	>99-( <i>S</i> )
6	12	92	39/61	55-( <i>S</i> )	>99-( <i>S</i> )
7	27	96	13/87	27-( <i>R</i> )	99-( <i>S</i> )
8	33	97	11/89	64-( <i>R</i> )	99-( <i>S</i> )

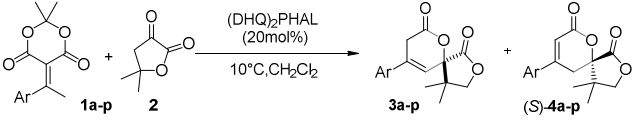
[a] Reaction conditions: **1a** (0.15 mmol), **2** (0.15 mmol), catalyst (20 mol%) in DCM (0.5 M) at 21 °C Conversion and ratio of isomers (**3a/4a**) were determined by <sup>1</sup>H NMR on the crude product after filtration on a pad of silica gel. Enantiomeric excess (ee) determined by chiral HPLC analysis.

Half conversion was observed after 2 hours (Table 2, entry 1). The ratio of 95/5 confirms the preliminary formation of the non-conjugated compound **3a**. The good selectivity of 91% ee for (*S*)-**3a**, reflects probably the high selectivity when creating the spiro stereogenic center during the first step of the process. At this stage, the enantiomeric excess of **4a** was determined to (*S*)-99% ee. During the progress of reaction, we observed a loss of the enantiomeric excess of (*S*)-**3a** correlating with the variation of **3a/4a** ratio (entries 2-5). The equivalent quantity of **3a** and **4a** was obtained around 10 hours of reaction (entry 5). The variation of **3a/4a** ratio in favor of **4a** isomer in the course of reaction is related to the decrease of enantiomeric excess of **3a** in reserving the high enantiomeric excess (99% ee) of **4a**, confirming the predominant action of the KR. This proceeded until the change of the major enantiomer of **3a** from (*S*) to (*R*) between 12h and 27h reaction time, proving the efficient consumption of (*S*)-**3a** and resulting in the enrichment of (*R*) enantiomer (Table 2, entries 6 and 7). This was confirmed by the enantiomeric excess of (*R*)-**3a** increasing from 27 to 64% ee for a reaction time from 27 to 33 h (Table 2, entries 7 and 8). After 27 h of reaction, 96% of conversion was obtained with 13/87 ratio in favor of **4a** product. (*R*)-**3a** was detected with 27% ee whereas (*S*)-**4a** was isolated with an excellent enantiomeric excess of 99% ee.

Obtaining the ideal conditions of this ATC reaction through our experiments, our focus turned to the

substrates scope. A series of benzylidene Meldrum's acid **1a-p** were used in the ATC reaction in the presence of dihydro-4,4-dimethyl-2,3-furandione **2** leading to the formation of 5,6-dihydropyran-2-ones **4a-p** as expected (Table 3).<sup>[13]</sup>

**Table 3.** Substrates scope for Auto Tandem Catalysis of 5,6-dihydropyran-2-ones **4a-p**.<sup>[a]</sup>



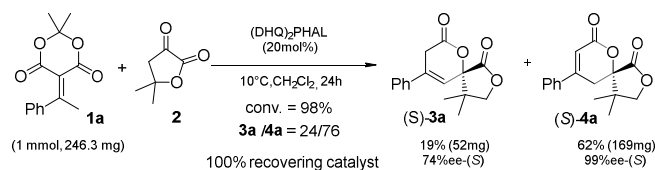
Entry	Ar	Conv. [%]	3/4	Yields [%] <sup>[c]</sup> 3/4	ee <sub>3a-p</sub> [%]	ee <sub>4a-p</sub> [%] <sup>[d]</sup>
1 <sup>[b]</sup>	<b>4a</b> : Ph	99	13/87	11/86	75( <i>R</i> )	98-( <i>S</i> )
2 <sup>[b]</sup>	<b>4b</b> : 4-(CN)C <sub>6</sub> H <sub>4</sub>	99	14/86	11/82	75	94-( <i>S</i> )
3	<b>4a</b> : Ph	97	14/86	13/82	12( <i>S</i> )	99-( <i>S</i> )
4	<b>4b</b> : 4-(CN)C <sub>6</sub> H <sub>4</sub>	99	16/84	13/64	57	>99-( <i>S</i> )
5	<b>4c</b> : 4-ClC <sub>6</sub> H <sub>4</sub>	96	8/92	7/87	96	>99-( <i>S</i> )
6	<b>4d</b> : 4-(MeO)C <sub>6</sub> H <sub>4</sub>	97	20/80	11/73	37	>99-( <i>S</i> )
7	<b>4e</b> : 4-(NO <sub>2</sub> )C <sub>6</sub> H <sub>4</sub>	98	25/75	8/65	33	>99
8	<b>4f</b> : 4-(CH <sub>3</sub> )C <sub>6</sub> H <sub>4</sub>	98	11/89	9/86	13	>99
9	<b>4g</b> : 4-(CF <sub>3</sub> )C <sub>6</sub> H <sub>4</sub>	98	10/90	8/72	21	>99-( <i>S</i> )
10 <sup>[b]</sup>	<b>4h</b> : 2-naphthyl	99	14/86	8/76	62	>99
11	<b>4i</b> : 4-(MeO <sub>2</sub> C)C <sub>6</sub> H <sub>4</sub>	93	20/80	14/67	2	97-( <i>S</i> )
12	<b>4j</b> : 3,4-(-OCH <sub>2</sub> O-)C <sub>6</sub> H <sub>4</sub>	98	24/76	21/67	67.5	98-( <i>S</i> )
13	<b>4k</b> : 3-BrC <sub>6</sub> H <sub>4</sub>	98	52/48	40/44	74	>99-( <i>S</i> )
14	<b>4l</b> : 3-(CH <sub>3</sub> )C <sub>6</sub> H <sub>4</sub>	91	82/18	64/15	89	99
15 <sup>[e]</sup>	<b>4l</b> :	99	10/90	9/87	- 55	98
16	<b>4m</b> : 4-( <i>tert</i> -Bu)C <sub>6</sub> H <sub>4</sub>	67	95/5	58/nd	91	nd
17 <sup>[e]</sup>	<b>4m</b> :	97	26/74	22/65	67	>99
18	<b>4n</b> : 2-furyl	85	99/1	62/nd	83	nd
19 <sup>[e]</sup>	<b>4n</b> :	99	7/93	6/82	- 60	97-( <i>S</i> )
20	<b>4o</b> : 2-ClC <sub>6</sub> H <sub>4</sub>	61	97/3	57/nd	64	nd
21 <sup>[e]</sup>	<b>4o</b> :	93	56/44	50/38	23	>99
22	<b>4p</b> : 1-naphthyl	81	96/4	64/nd	44	nd
23 <sup>[e]</sup>	<b>4p</b> :	82	86/14	65/9	41	96

[a] Reaction conditions: Benzylidene **1** (0.15 mmol), **2** (0.15mmol), catalyst (20 mol%) in DCM (0.5 M) at 10 °C for 24h otherwise noted. Conversion and ratio of isomers (**3a-p/4a-p**) were determined by <sup>1</sup>H NMR on the crude product. Enantiomeric excess (ee) determined by chiral HPLC. [b] Reaction performed at 25°C. [c] Isolated yields after column chromatography. [d] Absolute configuration

for **4a**, **4b**, **4c**, **4d**, **4g**, **4i**, **4j**, **4k** and **4n** was determined to be (*S*) by X-Ray analysis (see ref [14]). [e] 72h reaction time.

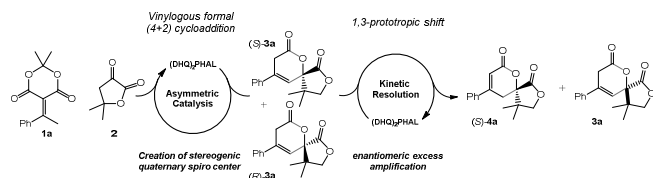
As indicated in Table 3, a better enantioselectivity was observed at 10 °C with benzylidene Meldrum's acids **1a** and **1b** (entries 1-2 vs 3-4). In all cases, excellent conversions of substrates **4a-j** were obtained in 24hours. In the most of cases, the ratio **3a-j/4a-j** in favor of conjugated **4a-j** product ranging from 25/75 to 8/92 was detected, leading to satisfactory isolated yields (64 to 87%). Interestingly, all conjugated products were obtained with very high enantiomeric excess with the majority greater than 99% ee (entries **3-13**). The absolute configuration for compounds **4a**, **4b**, **4c**, **4d**, **4g**, **4i**, **4j**, **4k** and **4n** were determined to be (*S*) by X-ray analysis.<sup>[14]</sup> The high enantioselectivity of the process seems to be independent of the electronic nature of the benzylidene, since the presence of electron-withdrawing or donating group do not affect the excellent enantioselectivity of the process. However, the steric effect and more precisely, the *ortho* or *meta* position of substituent on the aryl group showed more impact on the ratio **3/4**. For example, substrate **1k** led to an equivalent ratio of 52/48 suggesting probably a slower KR rate compared to other substrates **4a-j**. In this case, **3k** was isolated with 74% ee and more than 99% ee for **4k** (entry 13). The steric effect on the KR rate was confirmed with compounds **1l-p**. Despite compound **1l** bearing a *meta*-methyl group on the aryl offered a good conversion, compound **4l** was obtained as minor product with only 15% yield and 99% ee (entry 14). Extending the reaction time to 72 h led to the inversion of the ratio **3l/4l** from 82/18 to 10/90 in favor of the conjugated product **4l** with a limited loss of the enantiomeric excess to 98% ee (entry 15). Moreover, an inversion of the absolute configuration for the unreactive major enantiomer **3l** (-55% ee) suggests an active KR process. A similar effect was observed for substrates **1m** and **1n** which requires a longer reaction time to give predominantly the desired conjugated products **4m-n**. After 72h, the ratio value is totally reversed from 99/1 to 7/93 for **3n/4n** (entries 18, 19) and from 95/5 to 26/74 for **3m/4m** (entries 16, 17). Conjugated compound **1m** was isolated with excellent enantioselectivity over 99% ee and **1n** with 97% ee. The limit of the reaction was observed for substrates **1o** and **1p**. After 24 h lower conversions and non-conjugated products **3o** and **3p** were obtained as major product with 97/3 and 96/4 ratio respectively along with moderate enantiomeric excesses (64 and 44% ee, entries 20, 22). Longer reaction time slightly increase the ratio of conjugated product to only 56/44 for **3o/4o** and 86/14 for **3p/4p** suggesting the KR rate is particularly slow for these substrates (entries 21, 23). However, **4o** and **4p** were isolated with 99% and 96% ee respectively. Based on these results, the efficiency of this process depends both on the enantioselectivity of the vinylogous cycloaddition (first step), determining

the chemical yield and on the KR (second step) establishing the enantioselectivity of the general process. This ATC process is efficient in 1 mmol scale to produce **4a** as enantioenriched compound with 99% ee (scheme 4). Moreover, all the catalyst is easily recovered.<sup>[15]</sup>



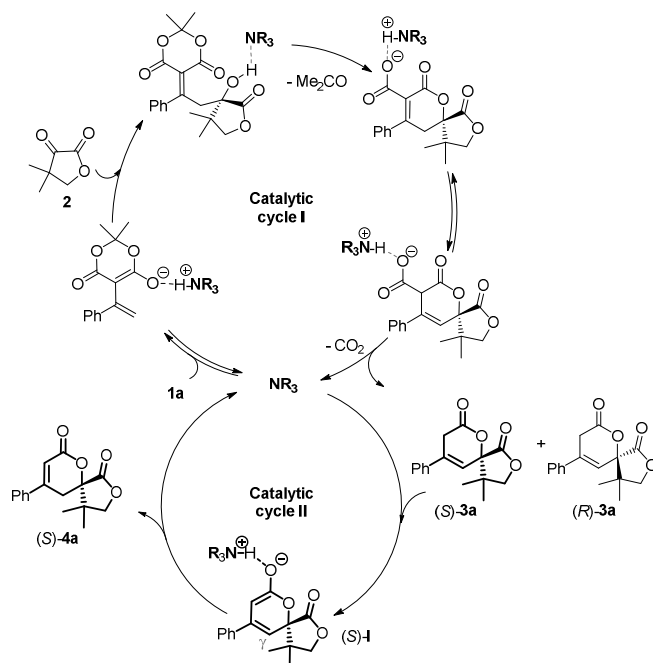
**Scheme 4.** Large scale Auto Tandem Catalysis with benzylidene **1a** and dihydro-4,4-dimethyl-2,3-furandione **2**.

The chemical process is summarized in scheme 5. It is related to the asymmetric formation of the spiro stereogenic center catalyzed by (DHQ)<sub>2</sub>PHAL leading to the non-conjugated lactone **3a** as an enantioenriched mixture (cycle I).<sup>[8]</sup> The second cycle consists in the isomerization of (*S*)-**3a** to conjugated lactone (*S*)-**4a** via a kinetic resolution process controlled by the same catalyst (cycle II). This kinetic resolution operates through a 1,3-prototropic shift. Despite such transformation being well-documented in enantioselective catalysis,<sup>[16]</sup> the present process ensures the amplification of enantiomeric excess. To the best of our knowledge, a kinetic resolution that proceeds through a 1,3-prototropic shift leading to an enantiomeric excess amplification has never been reported yet.



**Scheme 5.** Proposed enantioselective ATC process for the synthesis of spiro 5,6-dihydropyran-2-ones **4a-p**.

The proposed catalytic sequence is shown in scheme 6. The inside mechanism of the first cycle is based on our previous body of work.<sup>[8]</sup> Based on a study by Dixon and co-workers,<sup>[16d]</sup> basic catalyst deprotonates the weakly acidic  $\alpha$ -position of (*S*)-**3a** to form the intermediate (*S*)-**I**. A regioselective reprotonation of the extended enolate (*S*)-**I** would then occur preferentially at the  $\gamma$ -position to afford the product (*S*)-**4a**.



**Scheme 6.** Proposed mechanism for the synthesis of spiro 5,6-dihydropyran-2-ones **4a-p** by ATC process.

In conclusion, we describe for the first time an Auto Tandem Catalysis (ATC) process including an enantioselective vinyllogous formal (4+2) cycloaddition followed by a kinetic resolution (KR) leading to enantioenriched-final product. This KR process proceeds through a 1,3-prototropic shift. The system leads to a high selectivity for the preparation of 5,6-dihydropyran-2-one as original spiro-[4,5]decanes **4a-p** with a quaternary stereocenter. This ATC sequence capitalizes on the cooperative effect of (DHQ)<sub>2</sub>PHAL organocatalyst on the two enantiodeterminating steps allowing to overcome the maximum of 50% yield which could be usually reached in regular KR-processes.

## Experimental Section

**General procedure for Auto Tandem Catalysis of 5,6-dihydropyran-2-ones 4a-p:** Meldrum's acid derivative **1a-p** (0.15 mmol) and dihydro-4,4-dimethyl-2,3-furandione **2** (0.15 mmol, 19.5 mg) were diluted in dry CH<sub>2</sub>Cl<sub>2</sub> (0.3 mL, 0.5 M) and (DHQ)<sub>2</sub>PHAL (20 mol%, 23.9 mg) was added. After stirring at the desired temperature for 24 hours under argon atmosphere, the reaction was filtered on a pad of silica gel [eluent: Petroleum Ether/EtOAc (6/4)] to remove catalyst and concentrated in vacuo at 30°C to avoid the possible non-catalyzed thermodynamic isomerization of **3a** to **4a**. Conversion and **3a-p**/**4a-p** ratio were determined by <sup>1</sup>H NMR on the crude product. The residue was purified by column chromatography on silica gel to separate the desired spiro lactones **3a-p** and **4a-p**. 23.9 mg of clean (DHQ)<sub>2</sub>PHAL were isolated by washing the pad of silica with eluent [CH<sub>2</sub>Cl<sub>2</sub>/MeOH (9/1)] and concentrated in vacuo (100% recovered).

Detailed experimental procedures for substrates synthesis, kinetic resolution of racemic **3a**, NMR-, HPLC-spectra and crystallographic data can be found in the supporting information.

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- [13] The optimal temperature at 10 °C was determined to offer the best enantioselectivity (Table 1). The preparation of new racemic compounds **3a-p** or **4a-p** were obtained from basic catalysis to give pure samples (see SI).
- [14] Based on the (S)-absolute configuration and the levorotation for compounds **4a**, **4b**, **4c**, **4d**, **4g**, **4i**, **4j**, **4k** and **4n**, we suppose a same (S)-configuration for **4e**, **4f**, **4h**, **4l**, **4m**, **4o** and **4p** which are levorotary compounds.

CCDC 1992495, 2062725 & 2045183-2045189 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre via <http://www.ccdc.cam.ac.uk/Community/>.

[15] 100% of the catalyst was recovered after reaction (see experimental section)

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Enantioselective Auto Tandem Catalysis

