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# From Simple Cyclic 1,3-Ketoamides to Complex Spirolactams by Supported Heterogeneous Organocatalysis with PS-BEMP

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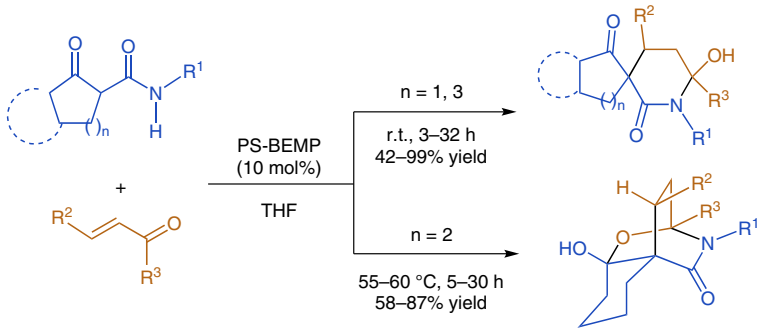
In the memory of Professor Jean Normant

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**Abstract** The reaction between cyclic 1,3-ketoamides and Michael acceptors in the presence of a catalytic amount of a polymer-supported organobase PS-BEMP has been developed for a direct access to spirocyclic 1,3-ketolactams through a domino Michael addition/hemiacetalization sequence. The products could be isolated in high chemical yields and purities after simple filtration, and the catalyst could be re-used without any re-activation. These spirolactams, containing a hemiaminal moiety, may be viewed as precursors of *N*-acyliminium intermediates upon Lewis acid activation, which allowed various subsequent functionalizations leading to original polycyclic lactams.

**Key words** supported organobase, Michael addition, spirolactam, heterogeneous organocatalysis, *N*-acyliminium intermediate

In the context of sustainable chemistry, the use of heterogeneous catalysts offers several advantages compared to homogeneous catalysis, notably in terms of isolation of the product, ease of handling, and recycling of the catalyst,[1] and to some extent, applications to automated systems and flow chemistry.[2] For several years, various catalytic species have been anchored to diverse insoluble supports, including some chiral organocatalysts for enantioselective synthesis.[3] The interest for polymer-supported organobases such as bicyclic guanidines (PS-TBD),[4] phosphines (PS-$PPh_3$)[5] or phosphazenes (PS-BEMP)][6] (Figure 1) started at the end of the nineties, essentially for the alkylation of amine derivatives.[7] Within this field of research, in 2004 we were the first group to report on the use of PS-BEMP as a heterogeneous catalyst for Michael additions. Indeed, this commercially available, user-friendly, and reusable chemical was found to promote the addition of 1,3-dicarbonyls onto various acceptors with high efficiency (Scheme 1, a).[8] Later on, several other groups applied this strategy to various synthetic methodologies,[9] including conjugate additions,[10] ring-opening of epoxides,[11] Henry reactions,[12] and hydrophosphonylation of aldehydes.[13]

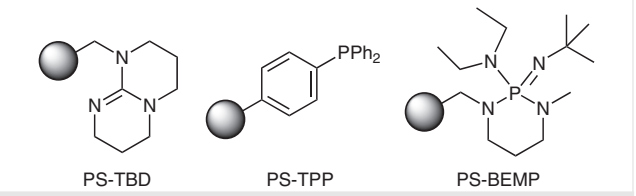
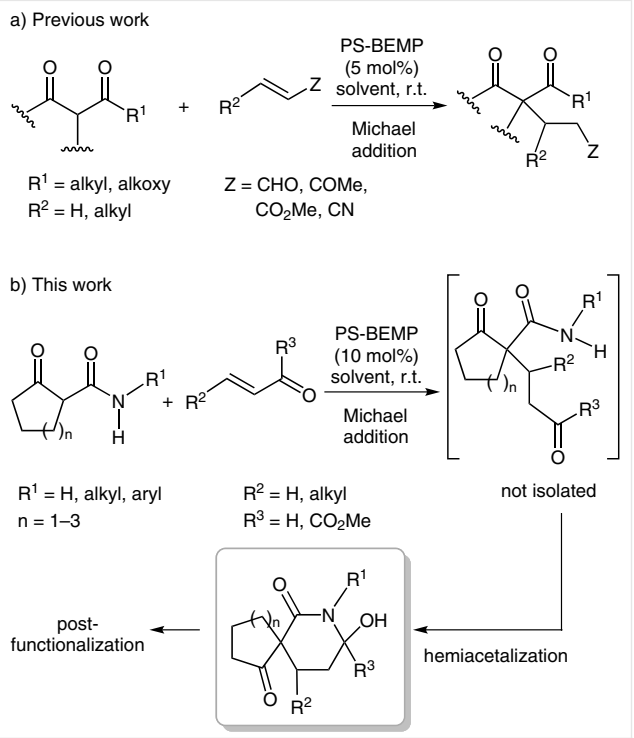



**Figure 1** Main polymer supported organobases

Remarkable contributions from the groups of Lectka and Dixon also demonstrated that the use of catalytic amounts of PS-BEMP can be cleverly combined with various others catalysts in sequential or domino reactions for the highly stereoselective synthesis of complex molecules.[14]

In the course of our studies on new domino and multicomponent reactions from 1,2- and 1,3-dicarbonyls for the synthesis of polyfunctionalyzed heterocycles,[15] we focused our interest on the use of 1,3-ketoamides. Indeed, compared with the more classical and intensively used 1,3-keto esters and 1,3-diketones containing different nucleophilic and electrophilic reactive sites, the amide moiety can be viewed as a supplementary aza-nucleophilic function, of-




**Scheme 1** PS-BEMP catalyzed Michael addition

fering new opportunities for domino reactions. Thus, in the PS-BEMP-catalyzed Michael addition, a suitably substituted secondary 1,3-ketoamide should offer a direct access to ketospirolactams through a domino Michael addition-hemiacetalization sequence (Scheme 1, b). In this formal [3+3] cyclization process, the 1,3-ketoamide reacts as 1,3-bis-nucleophile with the Michael acceptor acting as 1,3-bis-electrophile.

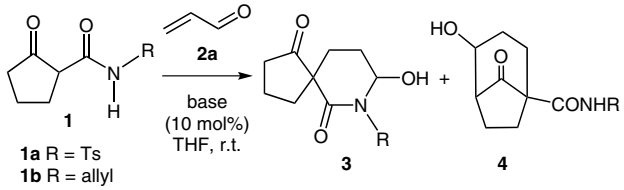
The spirocyclic 1,3-ketolactam scaffold is frequently associated with various biological activities, including action on cerebrovascular disorders,[16] anticancer,[17] antimicrobial,[18] and antifungal properties.[19] Consequently, owing to the great biological and synthetic importance of this heterocyclic core,[20] the synthesis of spirolactam derivatives has long been an area of intense development,[21] and still constitutes an active domain of research. In 2000, Cossy and co-workers identified cyclic 1,3-ketoamides as potential substrates for this purpose, as illustrated by their publication on the Mn(III)-induced radical cyclization of unsaturated 1,3-ketocarboxamides.[22] Later, gold- and palladium-based catalysts have also been used for the intramolecular addition of 1,3-ketoamides to alkenes[23] and allenes,[24] respectively. As reported by our team and by Marini's group, DBU[25] or N-heterocyclic carbenes[26] can alternatively promote Michael addition or alkylation of 1,3-ketoamides as key steps in sequences giving access to spirocyclic-1,3-ketolactams.

In this paper, we report a direct access to spirocyclic-1,3-ketolactams from easily accessible simple cyclic 1,3-ketoamides and Michael acceptors, using a catalytic amount of the commercially available polystyrene-supported organobase PS-BEMP. This methodology avoids the use of metal-based catalysts and harsh reactions conditions, and allows an easy isolation of the product from the re-usable catalyst. Post-functionalizations of the spirocyclic-1,3-ketolactams have been also studied, exploiting the reactivity of *N*-acyliminium intermediates generated from the hemiaminal moiety.

As illustrated in Table 1, some preliminary experiments confirmed our working hypothesis concerning the possibility of directly accessing spirocyclic 1,3-ketolactams from simple substrates, using a catalytic amount of a supported organobase. We started our study by reacting *N*-tosyl-1,3-ketoamide **1a** with 1.1 equivalent of acrolein (**2a**) in THF at room temperature in the presence of 10 mol% of PS-BEMP. Pleasingly, the desired spiro[4.5]decane ketolactam **3a** was formed as the only product and isolated by simple filtration in high yield as a 1.5:1 mixture of two diastereomers (Table 1, entry 1). Moreover, product purity was higher than 90%. In order to compare the efficiency of PS-BEMP with more classical mineral or organic bases, complementary experiments were run in standard conditions. A heterogeneous catalyst such as potassium carbonate (entry 2) or a homogeneous one such as DBU, BEMP, or guanidine (entries 3–5) afforded a mixture of the desired product **3aa** and bicyclic ketone **4aa** resulting from an intramolecular aldolization of the Michael adduct,[27] together with unidentified products. On the contrary, use of triphenylphosphine or its resin-supported version (entries 6 and 7) led to the formation of the desired product **3aa** with an efficiency and simplicity of use similar to PS-BEMP. However, $PPh_3$ performed less convincingly when *N*-allyl-1,3-ketoamide **1b** was used as substrate, leading to a 1:1 mixture of **3ba** and **4ba** (entries 8 and 9). In sharp contrast, we were pleased to note that the PS-BEMP-catalyzed reaction of **1b** with acrolein afforded exclusively the desired spiro compound in high yield after simple filtration (entry 10).

These preliminary results confirmed the relevance of using a supported organobase to reach our synthetic goal. Thus, we started to evaluate the scope of the reaction between various secondary 1,3-ketoamides **1**[28] and acceptors **2** in the presence of a catalytic amount of PS-BEMP, applying the previously established standard conditions (Scheme 2 and Scheme 3). Initially, the reactions between acrolein (**2a**) and *N*-homoallyl- and *N*-*o*-bromobenzyl-1,3-ketoamides **1c** and **1d** were investigated and found to afford after stirring at room temperature during 24 hours the corresponding spirobicyclic-1,3-ketolactams **3ca** and **3da** in good to excellent isolated yields, as a 1:1 mixture of two diastereomers. In the same conditions, 1,3-ketoamide **1e**, derived from 2-furylmethanamine, when treated with ei-

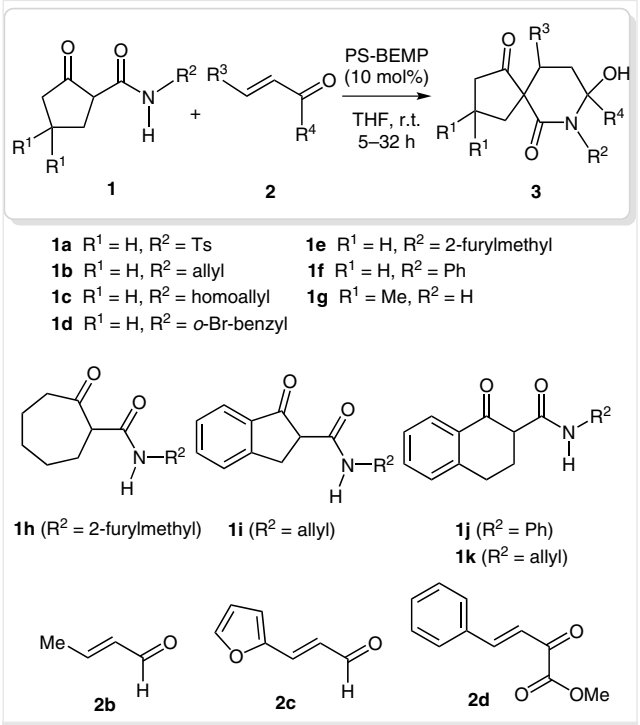
**Table 1** Preliminary Studies[a]




| Entry | Base | Substrate | Time (h)[b] | Product | Yield (%)[c] |
|---|---|---|---|---|---|
| 1 | PS-BEMP | **1a** | 3 | **3aa** | 94 |
| 2 | $K_2CO_3$[d] | **1a** | 16 | complex mixture | |
| 3 | DBU | **1a** | 16 | complex mixture | |
| 4 | BEMP | **1a** | 3 | complex mixture | |
| 5 | guanidine | **1a** | 3 | complex mixture | |
| 6 | $PPh_3$ | **1a** | 3 | **3aa** | 90 |
| 7 | PS-$PPh_3$ | **1a** | 3 | **3aa** | 92 |
| 8 | $PPh_3$ | **1b** | 24 | **3ba** + **4ba**[e] | 85 |
| 9 | PS-$PPh_3$ | **1b** | 24 | **3ba** + **4ba**[e] | 91 |
| 10 | PS-BEMP | **1b** | 24 | **3ba** | 87 |

[a] Reaction conditions: 1,3-ketoamide **1** (1.0 mmol), acrolein (**2a**; 1.1 mmol), and base (10 mol%) were mixed in anhyd THF (0.5 M) at r.t.
[b] Reaction time for total conversion of substrate, monitored by TLC.
[c] Isolated yield of product after simple filtration, obtained as a 1.5:1 mixture of diastereomers.
[d] Base used: 20 mol%.
[e] Ratio of **3ba**/**4ba** = 1:1.

ther crotonaldehyde (**2b**) or 3-(2-furyl)acrolein (**2c**) led to the formation of the desired products **3eb** and **3ec**, respectively, in almost quantitative yields and high chemical purity after simple filtration. Michael acceptor **2d**, derived from pyruvic acid, was found to be highly reactive in this sequence, leading quantitatively to **3ed** in only 5 hours at room temperature. This Michael acceptor allowed also the use of a less reactive *N*-aryl-1,3-ketoamide **1f**, allowing the formation of product **3fd** in 98% yield albeit after a prolonged reaction time (32 h).[29] Interestingly, primary 1,3-ketoamide **1g** turned out to be less efficient, but provided **3gd** with a free NH bond in 42%. Seven-membered cyclic 1,3-ketolactam **1h** gave also the desired product **3hd** in high yield, opening up a route to the spiro[5.6]dodecane family, for which only few synthetic methods have been reported to date.[14c,23a] Finally, substrates **1i**–**k**, containing a 1-indanone or a 1-tetralone ketoamide moiety, led to the desired spiro[4.5]decane **3ia** and spiro[5.5]undecanes **3ja** and **3ka** products, respectively, in good to excellent isolated yields. Although some products were obtained as a mixture of up to four diastereomers,[30] one major isomer was preferentially formed and could be systematically isolated and characterized. In the case of product **3ed**, the relative configuration of the major diastereomer was established by X-ray crystal structure analysis[31] (Figure 2).




**Scheme 2** PS-BEMP catalyzed Michael addition/hemiaminalization sequence for the synthesis of spiroketolactams **3**

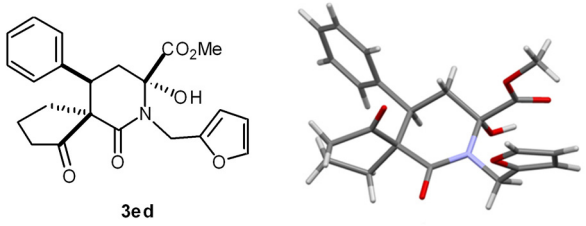
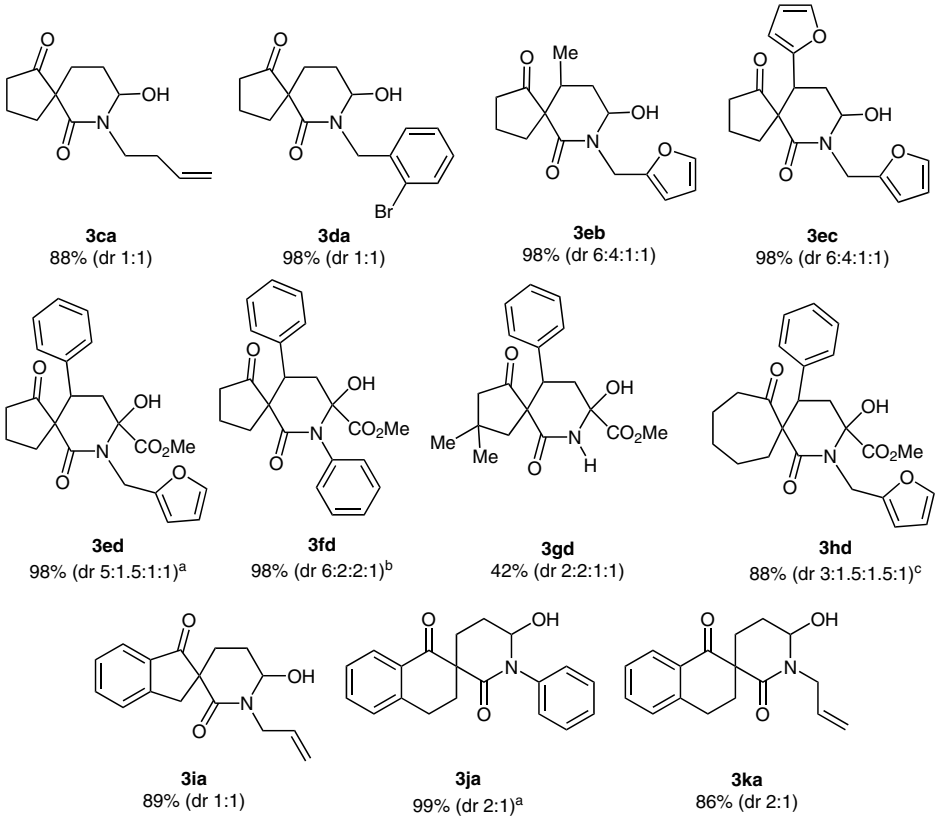



**Figure 2** X-ray crystal structure analysis of the major diastereomer of **3ed**

Six-membered alicyclic 1,3-ketoamides **1l** ($R^1$ = Ph), **1m** ($R^1$ = 2- furylmethyl), and **1n** ($R^1$ = benzyl) adopted a different behavior and in these cases the previous domino sequence was followed by an intramolecular hemiacetalization, leading to complex but stable and isolable tricyclic products **5** incorporating an original 2,6-oxazabicyclo[2.2.1]heptane core (Scheme 4). As already discussed for the case of compounds **3**, the major diastereomer of products **5** could be systematically isolated. Interestingly enough, compound **5nc** was formed with a good diastereoselectivity of 10:1. The structures of these tricyclic hemiacetals have been clearly confirmed by X-ray analysis[31] of a single crystal of product **5ld**, as depicted in Figure 3.




**Scheme 3** Scope of the reaction for the synthesis of spirocyclic-1,3-ketolactams **3**. *Reagents and conditions*: 1,3-ketoamide **1** (1.0 mmol), Michael acceptor **2** (1.1 mmol), and base (10 mol%) were mixed in anhyd THF (0.5 M) at r.t.. Unless otherwise noted reaction time is 24 h. [a] Reaction time: 5 h. [b] Reaction time: 32 h. [c] Reaction time: 9 h.

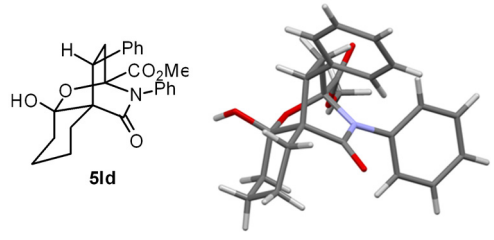


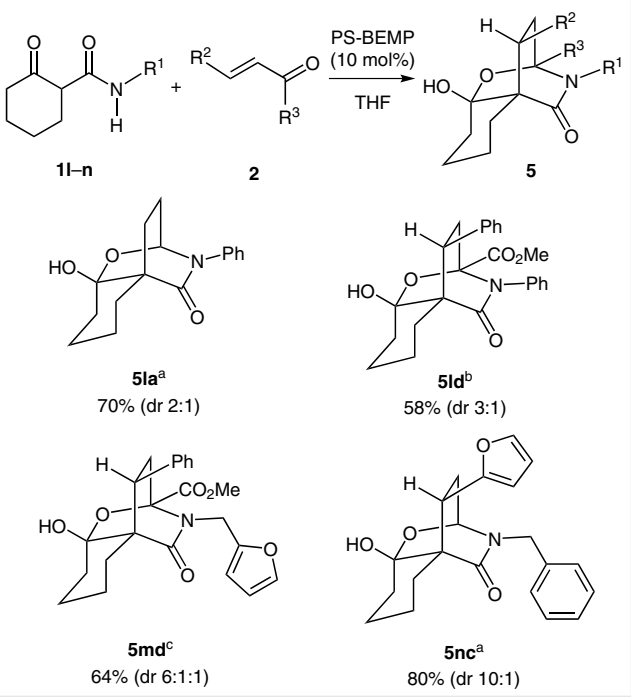

**Figure 3** X-ray crystal structure analysis of hemiacetal **5ld**

As a final refinement of the evaluation of the scope of our reaction we have run some experiments that clearly show the reusability of the catalyst (Table 2). Indeed, by systematically re-using the same sample of catalyst without any specific activation, we repeated several times the reaction between substrate **1a** and acrolein (**2a**), which initially led to the desired product **3aa** in 94% yield. For this study, we used a nondestructive rotatory stirring in order to limit degradation of the solid catalyst by mechanical stirring. PS-BEMP was isolated from each experiment by simple filtration and washing with THF, and re-used in the next one. Although it is necessary to increase the reaction time in each re-use of the catalyst to obtain complete conversion, the product is consistently obtained with the same efficiency in the first three recycles. Beyond the fifth use, performance starts to decline, reflecting a gradual deterioration of the catalyst, but isolated yields remain high.

The presence of the spirocyclic-1,3-ketolactam moiety would probably confer some interesting biological properties to products **3**, but the hemiaminal function also deserves to be considered for post-functionalizations. Thus, to start to illustrate the synthetic potential of platforms **3**, some dehydration reactions were conducted in the presence of the Burgess reagent in refluxing THF for 2 hours (Scheme 5).

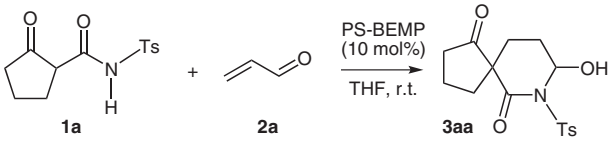
The corresponding enamides **6ia**, **6fd**, and **6gd**, obtained from substrates **3ia**, **3fd** and **3gd**, respectively, were isolated in good to excellent yields, as a 1:1 mixture of two diastereomers in the cases of **6fd** and **6gd**.

Another interesting feature of the hemiaminal function in substrates **3** is the possibility to generate *N*-acyliminium intermediates upon addition of Lewis acids, and subsequent trapping by an external nucleophile would result in substitution of the hydroxyl group. In order to translate this




**Scheme 4** Formation of polycyclic hemiacetals **5** from six-membered alicyclic 1,3-ketoamides **1l–n**. [a] Reaction conducted at 55 °C for 24 h. [b] Reaction conducted at r.t. for 30 h. [c] Reaction conducted at r.t. for 5 h.

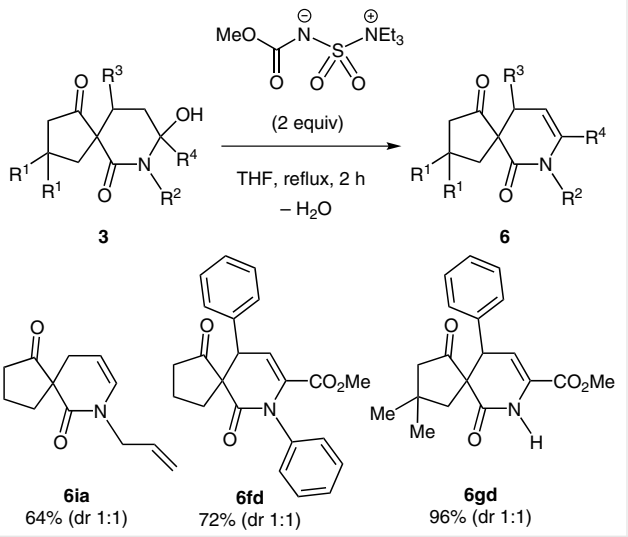
**Table 2** Recyclability of the Supported Catalyst[a]




| Run | Reaction time (h)[b] | Yield (%)[c] |
|---|---|---|
| 1 | 3 | 94 |
| 2 | 3 | 94 |
| 3 | 9 | 94 |
| 4 | 16 | 94 |
| 5 | 24 | 90 |
| 6 | 24 | 85 |

[a] Reaction conditions: 1,3-ketoamide **1a** (1.0 mmol), acrolein (**2a**; 1.1 mmol), and base (10 mol%) were mixed in anhyd THF (8 mL) at r.t..
[b] Reaction time for total conversion of substrate, monitored by TLC.
[c] Isolated yield of product after simple filtration, obtained as a 1.5:1 mixture of diastereomers.

idea into practice, substrates **3** were reacted with various silylated nucleophiles **7a–c** in the presence of $BF_3{\cdot}OEt_2$ at low temperature leading to functionalized products **8** in modest to excellent isolated yields, generally as a 1:1 mixture of two diastereomers (Scheme 6). Thus, the allyl moiety was successfully introduced in the structure of compounds **8baa**, **8caa**, **8daa**, **8iaa**, and **8jaa** through reaction with allyltrimethylsilane **7a**. Trimethylsilyl cyanide (**7b**) also reacted with the iminium intermediate derived from substrate **3fa**, but the corresponding product **8fab** was isolated in a moderate yield. It is noteworthy that only one diastereomer could be isolated, and its structure has been determined by X-ray analysis of a single crystal (Figure 4).[31] Similar results were obtained for the formation of product **8fac**, containing a synthetically relevant allene moiety, which was obtained through reaction of **3fa** with propargyl derivative **7c**, but in this case we were not able to ascertain the relative configuration.




**Scheme 5** Dehydration of spirohemiaminals **3**

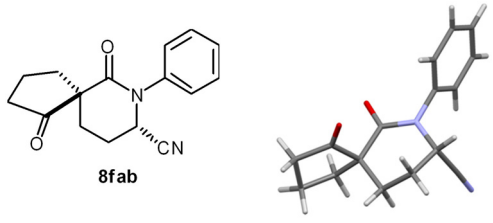
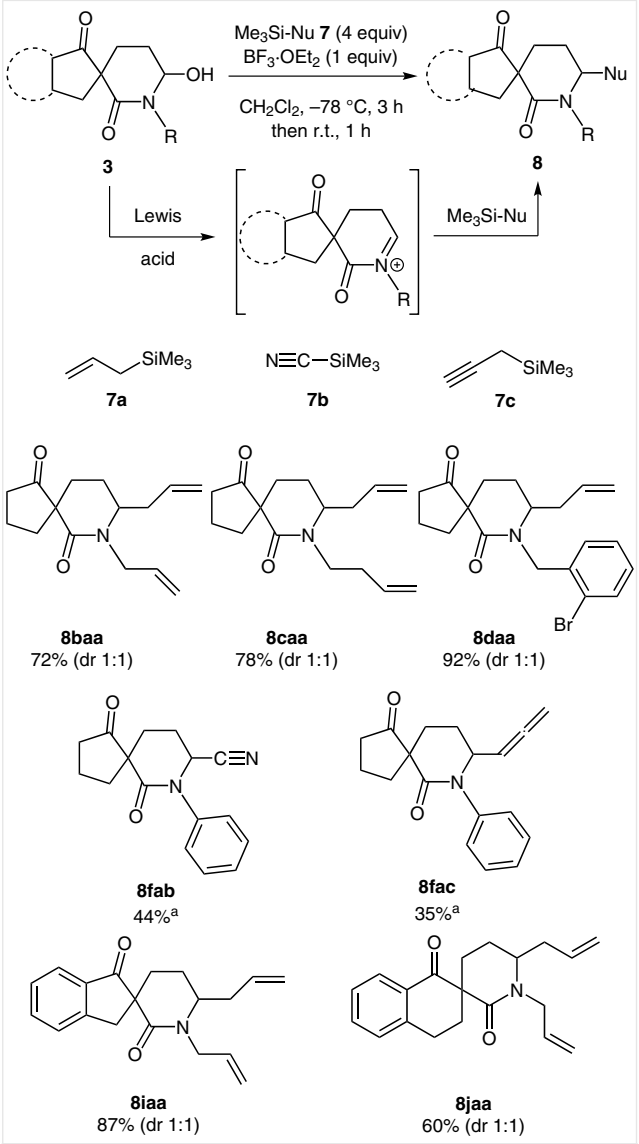


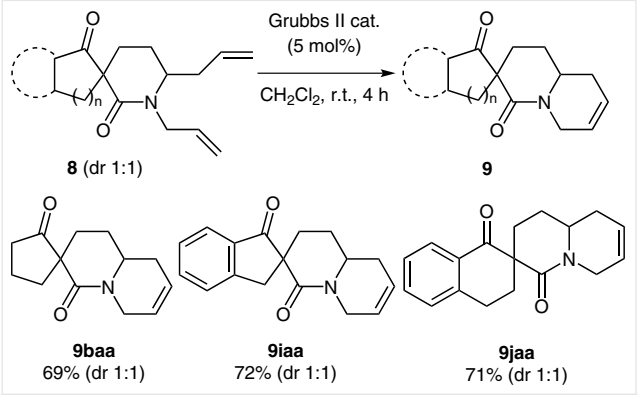

**Figure 4** X-ray crystal structure analysis of spirolactam **8fab**

Finally, we identified compounds **8**, bearing two allyl moieties, as potential substrates for ring closing-metathesis that could give access to original polycyclic spirolactams. Thus, treatment of spirolactams **8baa**, **8iaa**, and **8jaa** with 5 mol% of Grubbs second-generation catalyst resulted in the formation of the expected cyclized products **9baa**, **9iaa**, and **9jaa**, respectively, which were isolated in good yields (Scheme 7).

In conclusion, we have shown that the commercially available, user-friendly polymer-supported organobase PS-BEMP can be used as an efficient heterogeneous catalyst for




**Scheme 6** Functionalization of hemiaminals **3**. [a] Only one diastereomer could be isolated.




**Scheme 7** Ring-closing-metathesis reactions on compounds **8**

domino reactions between cyclic 1,3-ketoamides and Michael acceptors for the direct access to spiro[n.5]-1,3-ketolactams. The products can be isolated by simple filtration in high yields and chemical purities, and the catalyst can be re-used without specific activation. From a sustainable chemistry point of view, this methodology advantageously completes the arsenal of reactions already described with phosphazenes in homogeneous catalysis, by limiting the number of isolation and purification steps. It has been also demonstrated that these spiroketolactams constitute interesting synthetic platforms, especially because of the presence of a hemiaminal moiety that serves as a precursor of *N*-acyliminium intermediates. Our findings set the stage for the future development of supported chiral phosphazene catalysts for domino reactions aimed at the enantioselective synthesis of heterocycles.

Unless otherwise specified, all commercially available reagents were used as received. Reactions were carried out under an argon atmosphere and all reagents were weighed and handled in air at r.t. Anhyd THF, toluene, and $CH_2Cl_2$ were obtained from a solvent purification system (MBRAUN). The reactions were monitored by TLC visualized by UV (254 nm) and/or with *p*-anisaldehyde and $H_2SO_4$ in EtOH. Flash chromatography was performed on 40–63 µm silica gel eluted with EtOAc/PE or $Et_2O$/PE (bp 40–60 °C). NMR data were recorded at 300 or 400 MHz (Bruker Avance spectrometers) in $CDCl_3$ using as internal standards the residual $CHCl_3$ signal for $^1H$ NMR (δ = 7.26) and the deuterated solvent signal for $^{13}C$ NMR (δ = 77.16). Coupling constants (*J*) are in hertz (Hz) and standard abbreviations are used to describe the signal multiplicities.

### Spiroheterocycles 3 and 4; General Procedure

To a 10 mL one-necked round-bottomed flask, equipped with a magnetic stirring bar were added β-ketoamide **1** (1 equiv), freshly distilled THF (0.5 M), Michael acceptor **2** (1.1 equiv), and PS-BEMP (10 mol%). The mixture was stirred at r.t. or heated between 55 and 60 °C for the indicated time. After completion of the reaction (monitored by TLC), filtration, and concentration gave the resulting crude product, which was purified by chromatography on silica gel.

### 8-Hydroxy-7-tosyl-7-azaspiro[4.5]decane-1,6-dione (3aa)

Following the general procedure, the reaction of 4-methyl-*N*-(2-oxocyclopentanecarbonyl)benzenesulfonamide (300 mg, 1.06 mmol) with acrolein (**2a**; 77.90 µL, 1.16 mmol) in the presence of PS-BEMP (48.18 mg, 10 mol%) in THF (2 mL) at r.t. for 3 h afforded the product **3aa** as a white solid (336.5 mg, 94%). The crude product was obtained with 1.5:1 dr; $R_f$ = 0.48 ($Et_2O$/PE, 8:2). Data given are for the mixture of two diastereomers.

$^1H$ NMR (400 MHz, $CDCl_3$): δ = 7.91–7.85 (m, 4 H), 7.31 (d, *J* = 8.1 Hz, 4 H), 6.08–6.02 (m, 2 H), 4.18 (dd, *J* = 6.0, 0.9 Hz, 1 H), 3.83 (dd, *J* = 4.1, 1.6 Hz, 1 H), 2.67 (m, 1 H), 2.53–2.46 (m, 1 H), 2.42 (s, 6 H), 2.38–2.27 (m, 5 H), 2.24–2.03 (m, 5 H), 2.02–1.80 (m, 8 H).

$^{13}$C NMR (75 MHz, $CDCl_3$): δ = 216.10 (C), 214.73 (C), 171.12 (C), 170.34 (C), 144.83 (C), 144.79 (C), 135.80 (C), 135.74 (C), 129.40 (4 CH), 128.53 (2 CH), 128.39 (2 CH), 79.19 (CHOH), 78.56 (CHOH), 58.71 (C), 57.84 (C), 37.40 ($CH_2$), 36.49 ($CH_2$), 35.92 ($CH_2$), 27.80 ($CH_2$), 27.45 ($CH_2$), 26.39 ($CH_2$), 24.42 ($CH_2$), 24.24 ($CH_2$), 21.65 ($CH_3$), 21.05, ($CH_3$), 19.49 ($CH_2$), 19.3 ($CH_2$).

**7-Allyl-8-hydroxy-7-azaspiro[4.5]decane-1,6-dione (3ba)**

Following the general procedure, the reaction of *N*-allyl-2-oxocyclopentanecarboxamide (122 mg, 0.73 mmol) with acrolein (**2a**; 53.64 µL, 0.803 mmol) in the presence of PS-BEMP (33 mg, 10 mol%) in THF (1.5 mL) at r.t. for 24 h afforded the product **3ba** as a colorless oil (142 mg, 87%). The crude product was obtained with 1:1 dr; $R_f$ = 0.30 ($Et_2O$). Data given are for the mixture of two diastereomers.

$^1$H NMR (300 MHz, $CDCl_3$): δ = 5.79–5.65 (m, 2 H), 5.21–5.06 (m, 4 H), 4.93 (dd, *J* = 5.5, 3.1 Hz, 1 H), 4.86 (dd, *J* = 7.5, 3.4 Hz, 1 H), 4.64 (d, *J* = 5.9 Hz, 1 H), 4.50 (d, *J* = 8.1 Hz, 1 H), 4.37–4.27 (m, 2 H), 3.67 (dt, *J* = 15.4, 6.1 Hz, 2 H), 2.73–2.63 (m, 1 H), 2.51–2.39 (m, 3 H), 2.34–2.21 (m, 5 H), 2.18–2.04 (m, 3 H), 1.91–1.79 (m, 7 H), 1.47 (dt, *J* = 13.6, 4.1 Hz, 1 H).

$^{13}$C NMR (75 MHz, $CDCl_3$): δ = 219.2 (C), 216.2 (C), 170.6 (C), 170.2 (C), 132.6 (CH), 132.5 (CH), 116.9 ($CH_2$), 116.3 ($CH_2$), 78.6 (CH), 78.3 (CH), 56.6 (C), 55.8 (C), 46.7 ($CH_2$), 46.6 ($CH_2$), 38.9 ($CH_2$), 37.5 ($CH_2$), 36.1 ($CH_2$), 35.9 ($CH_2$), 27.5 ($CH_2$), 26.4 ($CH_2$), 24.6 ($CH_2$), 24.4 ($CH_2$), 19.6 ($CH_2$), 19.3 ($CH_2$).

HRMS (ESI+): *m*/*z* [M + H]$^+$ calcd for $C_{12}H_{18}NO_3$: 224.1281; found: 224.1277.

**7-(But-3-en-1-yl)-8-hydroxy-7-azaspiro[4.5]decane-1,6-dione (3ca)**

Following the general procedure, the reaction of *N*-(but-3-enyl)-2-oxocyclopentanecarboxamide (84 mg, 0.46 mmol) with acrolein (**2a**; 33.80 µL, 0.506 mmol) in the presence of PS-BEMP (21 mg, 10 mol%) in THF (1 mL) at r.t. for 24 h afforded the product **3ca** as a yellow oil (96 mg, 88%). The crude product was obtained with 1:1 dr; $R_f$ = 0.31 ($Et_2O$). Data given are for the mixture of two diastereomers.

$^1$H NMR (300 MHz, $CDCl_3$): δ = 5.87–5.70 (m, 2 H), 5.15 (d, *J* = 1.6 Hz, 1 H), 5.09–5.01 (m, 4 H), 4.90 (t, *J* = 3.5 Hz, 1 H), 3.63 (dt, *J* = 14, 7.2 Hz, 2 H), 3.33 (td, *J* = 14.1, 7.1 Hz, 2 H), 2.79–2.71 (m, 1 H), 2.57–2.45 (m, 2 H), 2.39–2.16 (m, 10 H), 1.96–1.75 (m, 12 H), 1.60–1.54 (m, 1 H).

$^{13}$C NMR (75 MHz, $CDCl_3$): δ = 219.5 (C), 216.7 (C), 170.6 (C), 170.3 (C), 135.4 (2 CH), 116.9 (2 $CH_2$), 80.1 (CH), 79.6 (CH), 56.7 (C), 55.8 (C), 45.3 ($CH_2$), 44.6 ($CH_2$), 39.1 (2 $CH_2$), 37.8 ($CH_2$), 36.4 ($CH_2$), 36.2 ($CH_2$), 32.4 (2 $CH_2$), 27.7 ($CH_2$), 26.8 ($CH_2$), 24.9 ($CH_2$), 19.8 ($CH_2$), 19.5 ($CH_2$).

HRMS (ESI+): *m*/*z* [M + H]$^+$ calcd for $C_{13}H_{20}NO_3$: 238.1438; found: 238.1441.

**7-(2-Bromobenzyl)-9-hydroxy-7-azaspiro[4.5]decane-1,6-dione (3da)**

Following the general procedure, the reaction of *N*-(2-bromobenzyl)-2-oxocyclopentanecarboxamide (264 mg, 0.89 mmol) with acrolein (65.40 µL, 0.979 mmol) in the presence of PS-BEMP (40.6 mg, 10 mol%) in THF (1.8 mL) at r.t. for 24 h afforded the product **3da** as a white solid (310 mg, 98%). The crude product was obtained with 1:1 dr; $R_f$ = 0.18 ($Et_2O$/PE, 7:3). Data given are for the mixture of two diastereomers.

$^1$H NMR (400 MHz, $CDCl_3$): δ = 7.53 (ddd, *J* = 8.1, 4.8, 1.0 Hz, 2 H), 7.36–7.28 (m, 3 H), 7.21 (dd, *J* = 8, 1.6 Hz, 1 H), 7.14–7.09 (m, 2 H), 5.12 (d, *J* = 16.3 Hz, 1 H), 5.00 (d, *J* = 15.7 Hz, 1 H), 4.95 (s, 1 H), 4.87 (s, 1 H), 4.52 (d, *J* = 15.7 Hz, 1 H), 4.44 (d, *J* = 16.3 Hz, 1 H), 2.88–2.82 (m, 2 H), 2.64–2.62 (m, 1 H), 2.57–2.48 (m, 1 H), 2.42–2.29 (m, 5 H), 2.23–1.87 (m, 10 H), 1.81–1.75 (m, 1 H), 1.67–1.58 (m, 2 H).

$^{13}$C NMR (75 MHz, $CDCl_3$): δ = 217.8 (C), 217.1 (C), 171.1 (C), 170.6 (C), 135.8 (C), 135.6 (CH),132.5 (CH), 132.3 (CH), 128.54 (CH), 128.51 (CH), 128.2 (CH), 127.67 (CH), 127.44 (2 CH), 123.03 (C), 122.7 (C), 79.1 (CH), 79.0 (CH), 56.6 (C), 55.9 (C), 48.2 ($CH_2$), 48.0 ($CH_2$), 38.7 ($CH_2$), 37.3 ($CH_2$), 36.0 ($CH_2$), 35.7 ($CH_2$), 27.5 ($CH_2$), 26.3 ($CH_2$), 25.4 ($CH_2$), 24.5 ($CH_2$), 24.3 ($CH_2$), 19.4 ($CH_2$).

HRMS (ESI+): *m*/*z* [M + H]$^+$ calcd for $C_{16}H_{19}BrNO_3$: 352.0543; found: 352.0545.

**7-(Furan-2-ylmethyl)-8-hydroxy-10-methyl-7-azaspiro[4.5]decane-1,6-dione (3eb)**

Following the general procedure, the reaction of *N*-(furan-2-ylmethyl)-2-oxocyclopentanecarboxamide (264 mg, 0.89 mmol) with crotonaldehyde (**2b**; 83.68 µL, 0.979 mmol) in the presence of PS-BEMP (40.6 mg, 10 mol%) in THF (1.8 mL) at r.t. for 24 h afforded the product **3eb** as a white solid (310 mg, 98%). The crude product was obtained with 6:4:1:1 dr. Two diastereomers were separated (silica gel chromatography).

First fraction: one diastereomer was isolated as a yellow solid (43 mg, 12%); $R_f$ = 0.7 ($Et_2O$/PE, 9:1).

$^1$H NMR (400 MHz, $CDCl_3$): δ = 7.33 (dd, *J* = 1.8, 0.7 Hz, 1 H), 6.30 (dd, *J* = 3.2, 1.9 Hz, 1 H), 6.24 (d, *J* = 3.2 Hz, 1 H), 5.30 (s, 1 H), 5.02 (d, *J* = 15.3 Hz, 1 H), 4.91 (t, *J* = 12.7 Hz, 1 H), 4.39 (d, *J* = 15.3 Hz, 1 H), 3.37 (d, *J* = 12.2 Hz, 1 H), 2.92 (t, *J* = 7.8 Hz, 1 H), 2.47–2.42 (m, 1 H), 2.24–2.20 (m, 2 H), 2.12–2.04 (m, 1 H), 2.07–1.94 (m, 3 H), 0.98 (d, *J* = 7.1 Hz, 3 H).

$^{13}$C NMR (75 MHz, $CDCl_3$): δ = 219.15 (C), 169.61 (C), 151.17 (C), 142.22 (CH), 110.44 (CH), 108.57 (CH), 78.77 (CHOH), 60.23 (C), 40.97 ($CH_2$), 39.64 ($CH_2$), 36.62 ($CH_2$), 34.35 (CH), 33.29 ($CH_2$), 20.76 ($CH_2$), 17.19 ($CH_3$).

Second fraction: incomplete separation; two diastereomers.

$^1$H NMR (400 MHz, $CDCl_3$): δ = 7.35 (s, 1 H), 7.33 (s, 1 H), 6.33 (d, *J* = 3.0 Hz, 1 H), 6.31 (d, *J* = 2.1 Hz, 2 H), 6.27 (d, *J* = 3.0 Hz, 1 H), 5.11 (s, 1 H), 4.94 (s, 1 H), 4.89 (d, *J* = 15.4 Hz, 1 H), 4.67 (d, *J* = 15.4 Hz, 1 H), 4.53 (d, *J* = 15.6 Hz, 1 H), 4.32 (d, *J* = 15.4 Hz, 1 H), 3.28–3.22 (m, 1 H), 2.69–1.62 (m, 19 H), 0.98 (d, *J* = 6.7 Hz, 2 H), 0.85 (d, *J* = 6.9 Hz, 4 H).

$^{13}$C NMR (75 MHz, $CDCl_3$): δ = 218.9 (C), 217.5 (C), 171.9 (C), 170.8 (C), 150.4 (2 C), 142.1 (2 CH), 110.4 (CH), 110.3 (CH), 108.4 (CH), 107.3 (CH), 78.7 (CH), 77.8 (CH), 60.2 (C), 59.2 (C),41.8 ($CH_2$), 40.4 ($CH_2$), 39.87 ($CH_2$), 39.81 ($CH_2$), 35.3 ($CH_2$), 34.5 ($CH_2$), 34.2 ($CH_2$), 30.9 (CH), 29.8 ($CH_2$), 27.4 (CH), 20.7 ($CH_2$), 19.9 ($CH_2$),16.2 ($CH_3$), 15.7 ($CH_3$).

Third fraction: one diastereomer was isolated as a yellow solid (30 mg, 10%); $R_f$ = 0.39 ($Et_2O$/PE, 9:1).

$^1$H NMR (300 MHz, $CDCl_3$): δ = 7.26 (t, *J* = 3.8 Hz, 1 H), 6.25–6.21 (m, 1 H), 6.19 (d, *J* = 3.0 Hz, 1 H), 4.90–4.81 (m, 1 H), 4.77 (d, *J* = 15.4 Hz, 1 H), 4.37 (d, *J* = 15.4 Hz, 1 H), 3.38 (dd, *J* = 14.9, 7.8 Hz, 1 H), 2.53 (m, 1 H), 2.11 (m, 5 H), 1.79 (ddd, *J* = 8.3, 6.9, 3.8 Hz, 1 H), 1.51 (m 1 H), 1.18 (s, 1 H), 0.77 (d, *J* = 6.8 Hz, 3 H).

$^{13}$C NMR (75 MHz, $CDCl_3$): δ = 217.86 (C), 172.25 (C), 150.79 (C), 142.15 (CH), 110.72 (CH), 108.69 (CH), 79.42 (CHOH), 59.78 (C), 39.91 ($CH_2$), 38.55 ($CH_2$), 36.51 ($CH_2$), 29.44 ($CH_2$), 29.34 (CH), 19.95 ($CH_2$), 16.03 ($CH_3$).

**10-(Furan-2-yl)-7-(furan-2-ylmethyl)-8-hydroxy-7-aza-spiro[4.5]decane-1,6-dione (3ec)**

Following the general procedure, the reaction of *N*-(furan-2-ylmethyl)-2-oxocyclopentanecarboxamide (264 mg, 0.89 mmol) with furylacrolein (**2c**; 70 mL, 0.979 mmol) in the presence of PS-BEMP (40.6 mg, 10 mol%) in THF (1.8 mL) at r.t. for 24 h afforded the product **3ec** as a white solid (310 mg, 98%). The crude product was obtained with 6:4:1:1 dr; $R_f$ = 0.18 ($Et_2O$/PE, 7:3). Data given are for the mixture of four diastereomers.

$^1$H NMR (300 MHz, $CDCl_3$): δ = 7.28 (s, 1 H), 7.26 (dd, *J* = 1.6, 0.8 Hz, 3 H), 7.24 (dd, *J* = 1.9, 0.6 Hz, 1 H), 7.23 (d, *J* = 1.3 Hz, 1 H), 7.22–7.20 (m, 2 H), 6.26–6.22 (m, 8 H), 6.22–6.19 (m, 4 H), 6.02 (d, *J* = 3.3 Hz, 1 H), 6.00 (d, *J* = 3.3 Hz, 1 H), 5.97 (d, *J* = 3.2 Hz, 2 H), 5.16–5.10 (m, 1 H), 5.09–5.02 (m, 2 H), 4.95 (d, *J* = 15.5 Hz, 4 H), 4.90 (d, *J* = 2.8 Hz, 1 H), 4.84 (d, *J* = 6.1 Hz, 3 H), 4.81 (d, *J* = 4.8 Hz, 1 H), 4.45–4.37 (m, 1 H), 4.33 (d, *J* = 15.8 Hz, 1 H), 4.19 (d, *J* = 15.5 Hz, 2 H), 4.08 (d, *J* = 7.2 Hz, 1 H), 4.05 (d, *J* = 2.6 Hz, 1 H), 4.04–4.01 (m, 1 H), 3.67 (dd, *J* = 13.7, 2.7 Hz, 1 H), 3.50 (dd, *J* = 13.5, 2.4 Hz, 1 H), 3.06 (dd, *J* = 13.9, 4.4 Hz, 1 H), 2.94 (dd, *J* = 13.8, 3.4 Hz, 1 H), 2.85 (d, *J* = 13.1 Hz, 1 H), 2.79–2.70 (m, 1 H), 2.49–2.38 (m, 3 H), 2.23–2.03 (m, 14 H), 1.98–1.81 (m, 10 H).

$^{13}$C NMR (75 MHz, $CDCl_3$): δ (major 1) = 218.4 (C), 171.3 (C), 153.2 (C), 150.2 (C), 142.2 (2 CH), 110.3 (2 CH), 108.6 (CH), 106.9 (CH), 77.3 (C), 59.8 (C), 40.1 ($CH_2$), 39.4 ($CH_2$), 39.3 ($CH_2$), 32.9 (CH), 31.5 ($CH_2$), 19.30 ($CH_2$); δ (major 2) = 216.8 (C), 170.1 (C), 153.6 (C), 150.4 (C), 142.0 (2 CH), 141.6 (CH), 141.3 (CH), 110.4 (CH), 107.8 (CH), 78.3 (C), 58.8 (C), 41.9 ($CH_2$), 36.5 (CH), 34.1 ($CH_2$), 31.7 ($CH_2$), 30.9 ($CH_2$), 19.7 ($CH_2$); δ (minor 1 + minor 2) = 218.2 (C), 217.5 (C), 171.5 (C), 171.4 (C), 152.6 (C), 152.5 (C), 150.5 (C), 150.4 (C), 142.1 (CH), 141.8 (CH), 141.7 (CH), 110.6 (CH),110.5 (CH), 108.5 (CH), 108.1 (CH), 107.4 (CH), 107.3 (CH), 107.28 (CH), 107.20 (CH), 110.2 (CH), 78.6 (C), 78.3 (C), 60.4 (C), 59.3 (C), 39.7 ($CH_2$), 39.5 ($CH_2$), 39.2 ($CH_2$), 37.86 ($CH_2$), 36.0 ($CH_2$), 35.9 ($CH_2$), 34.5 (CH), 33.1 ($CH_2$), 33.1 ($CH_2$), 31.0 ($CH_2$), 20.9 (CH),19.36 ($CH_2$).

**Methyl 7-(Furan-2-ylmethyl)-8-hydroxy-1,6-dioxo-10-phenyl-7-azaspiro[4.5]decane-8-carboxylate (3ed)**

Following the general procedure, the reaction of *N*-(furan-2-ylmethyl)-2-oxocyclopentanecarboxamide (200 mg, 0.96 mmol) with methyl (*E*)-2-oxo-4-phenylbut-3-enoate (**2d**; 201 mg, 1.05 mmol) in the presence of PS-BEMP (44 mg, 10 mol%) in THF (2 mL) at r.t. for 5 h afforded the product **3ed** as a white solid (368 mg, 98%). The crude product was obtained with 5:1.5:1:1 dr. One diastereiosomer was separated (silica gel chromatography).

First fraction: one diastereomer was isolated as a yellow solid (44 mg, 12%); mp 165 °C; $R_f$ = 0.56 ($Et_2O$/PE, 7:3).

$^1$H NMR (300 MHz, $CDCl_3$): δ = 7.23 (d, *J* = 0.9 Hz, 1 H), 7.19 (t, *J* = 5.2 Hz, 2 H), 7.14–7.06 (m, 2 H), 6.22 (dd, *J* = 3.1, 1.9 Hz, 1 H), 6.16 (d, *J* = 3.2 Hz, 1 H), 4.38 (s, 2 H), 3.69 (s, 3 H), 3.64–3.53 (m, 1 H), 3.43 (dd, *J* = 13.8, 2.1 Hz, 1 H), 2.79–2.69 (m, 1 H), 2.20–1.98 (m, 2 H), 1.92–1.81 (m, 1 H), 1.77 (dd, *J* = 12.9, 2.2 Hz, 1 H), 1.68–1.55 (m, 1 H), 1.10 (d, *J* = 14.8 Hz, 1 H), 0.87–0.76 (m, 1 H).

$^{13}$C NMR (75 MHz, $CDCl_3$): δ = 217.34 (C), 172.76 (C), 171.01 (C), 150.73 (C), 141.87 (CH), 139.16 (C), 128.93 (2 CH), 128.89 (2 CH), 127.92 (CH), 110.68 (CH), 108.76 (CH), 85.60 (COH), 60.63 (C), 54.39 ($CH_3$), 43.47 (CH), 40.75 ($CH_2$), 40.48 ($CH_2$), 36.02 ($CH_2$), 34.26 ($CH_2$), 20.18 ($CH_2$).

Second fraction: a mixture of two diastereomers was isolated (295 mg, 80%) as a yellow oil; $R_f$ = 0.44 ($Et_2O$/PE, 7:3). The major diastereomer partially crystallized as white needles for X-ray analysis.

$^1$H NMR (300 MHz, $CDCl_3$): δ = 7.41–7.26 (m, 8 H), 7.25–7.03 (m, 5 H), 6.31 (d, *J* = 1.8 Hz, 1 H), 6.29 (d, *J* = 1.9 Hz, 1 H), 6.28 (d, *J* = 3.4 Hz, 1 H), 6.25 (d, *J* = 3.2 Hz, 1 H), 4.80 (d, *J* = 15.5 Hz, 1 H), 4.67 (s, 1 H), 4.63 (d, *J* = 2.8 Hz, 1 H), 4.58 (d, *J* = 3.8 Hz, 2 H), 4.31 (d, *J* = 15.9 Hz, 1 H), 4.16 (dd, *J* = 13.9, 2.2 Hz, 1 H), 3.71 (s, 1 H), 3.67 (s, 3 H), 3.47–3.24 (m, 1 H), 2.91 (dd, *J* = 13.9, 6.7 Hz, 1 H), 2.75 (t, *J* = 13.6 Hz, 2 H), 2.45–2.07 (m, 8 H), 2.04–1.67 (m, 4 H), 1.11–0.95 (m, 2 H).

$^{13}$C NMR (75 MHz, $CDCl_3$): δ (major) = 217.1 (C), 172.7 (C), 172.3 (C), 150.5 (C), 141.8 (CH), 138.1 (C), 128.8 (CH), 128.5 (2 CH), 127.4 (2 CH), 110.5 (CH), 108.8 (CH), 84.8 (COH), 61.4 (C), 54.1 ($CH_3$),40.23 (CH), 39.8 ($CH_2$), 38.0 ($CH_2$), 36.1 ($CH_2$), 30.1 ($CH_2$), 19.5 ($CH_2$); δ (minor) = 217.6 (C), 172.1 (C), 170.2 (C), 150.8 (C), 141.7 (CH), 138.6 (C), 128.6 (2 CH), 128.2 (CH), 127.9 (2 CH), 110.4 (CH), 109.0 (CH), 84.9 (COH), 59.9 (C), 53.8 ($CH_3$), 49.9 (CH), 40.2 ($CH_2$), 38.1 ($CH_2$), 37.0 ($CH_2$), 33.6 ($CH_2$), 20.0 ($CH_2$).

HRMS (ESI+): *m*/*z* [M + H]$^+$ calcd for $C_{22}H_{20}NO_6$: 398.1598; found: 398.1597.

**Methyl 8-Hydroxy-1,6-dioxo-7,10-diphenyl-7-azaspiro[4.5]decane-8-carboxylate (3fd)**

Following the general procedure, the reaction of 2-oxo-*N*-phenylcyclopentanecarboxamide (500 mg, 2.46 mmol) with methyl (*E*)-2-oxo-4-phenylbut-3-enoate (**2d**; 514 mg, 2.70 mmol) in the presence of PS-BEMP (112.5 mg, 10 mol%) in THF (5 mL) at r.t. for 32 h afforded the product **3fd** as a white solid (96.5 mg, 98%). The crude product was obtained with 6:2:2:1 dr. Two diastereomers were separated.

First fraction: one diastereomer was isolated as a yellow oil (155 mg, 16%); $R_f$ = 0.75 ($Et_2O$/PE, 1:1).

$^1$H NMR (300 MHz, $CDCl_3$): δ = 7.37–7.28 (m, 6 H), 7.23–7.18 (m, 4 H), 5.27 (s, 1 H, OH), 4.56 (d, *J* = 2.2 Hz, 1 H), 4.39 (dd, *J* = 13.7, 2 Hz, 1 H), 3.71 (s, 3 H), 2.96 (t, *J* = 13.6 Hz, 1 H), 2.39–2.33 (m, 2 H), 2.31–2.24 (m, 1 H), 2.21 (dd, *J* = 13, 2.2 Hz, 1 H), 1.94–1.77 (m, 2 H).

$^{13}$C NMR (75 MHz, $CDCl_3$): δ = 217.02 (C), 172.21 (C), 170.85 (C), 139.22 (C), 138.51 (C), 129.28 (2 CH), 129.08 (2 CH), 129.04 (2 CH), 128.86 (2 CH), 128.48 (CH), 127.89 (CH), 86.16 (C), 60.61 (C), 53.63 ($CH_3$), 43.87 (CH), 39.98 (CH), 35.81 ($CH_2$), 34.03 ($CH_2$), 19.78 ($CH_2$).

Second fraction: one diastereomer was isolated as a yellow oil (464 mg, 48%); $R_f$ = 0.48 ($Et_2O$/PE, 1:1).

$^1$H NMR (300 MHz, $CDCl_3$): δ = 7.36–7.32 (m, 6 H), 7.24–7.19 (m, 5 H), 4.62 (s, 1 H), 4.40 (dd, *J* = 13.8, 2.2 Hz, 1 H), 3.70 (s, 3 H), 2.97 (t, *J* = 13.5 Hz, 1 H), 2.40–2.33 (m, 2 H), 2.30 (dd, *J* = 13.2, 6.7 Hz, 1 H), 2.20 (dd, *J* = 13.1, 2.4 Hz, 1 H), 1.94–1.77 (m, 2 H).

$^{13}$C NMR (75 MHz, $CDCl_3$): δ = 216.7 (C), 172.7 (C), 171.0 (C), 138.2 (C), 137.1 (C), 129.3 (2 CH), 128.8 (2 CH), 128.6 (CH), 128.5 (CH), 128.3 (2 CH), 127.2 (2 CH), 86.1 (C), 61.4 (C), 53.5 ($CH_3$), 39.6 ($CH_2$), 38.0 (CH), 35.5 ($CH_2$), 30.3 ($CH_2$), 19.3 ($CH_2$).

HRMS (ESI+): *m*/*z* [M + H]$^+$ calcd for $C_{23}H_{24}NO_5$: 394.1649; found: 394.1661.

**Methyl 8-Hydroxy-3,3-dimethyl-1,6-dioxo-10-phenyl-7-aza-spiro[4.5]decane-8-carboxylate (3gd)**

Following the general procedure, the reaction of 4,4-dimethyl-2-oxocyclopentanecarboxamide (170 mg, 1.09 mmol) with methyl (*E*)-2-oxo-4-phenylbut-3-enoate (**2d**; 229.69 mg, 1.20 mmol) in the presence of PS-BEMP (49 mg, 10 mol%) in THF (2.5 mL) at r.t. for 24 h afforded the product **3gd** as a white solid (160 mg, 42%). The crude product was obtained with 2:2:1:1 dr; $R_f$ = 0.35 ($Et_2O$). Data given are for the mixture of four diastereomers.

$^1$H NMR (300 MHz, $CDCl_3$): δ (characteristic peaks) = 3.87 (s, 2 H), 3.85 (s, 3 H ), 3.83 (s, 1 H), 3.81 (s, 1 H).

$^{13}$C NMR (75 MHz, $CDCl_3$): δ (major 1) = 216.9 (C), 182.6 (C), 174.87 (C), 138.8 (C), 129. 29 (2 CH), 129.27 (2 CH), 128.8 (CH), 81.2 (C), 68.0 ($CH_3$), 63.4 (C), 45.4 ($CH_2$), 43.3 (CH), 39.0 ($CH_2$), 33.1 (C), 30.6 ($CH_2$), 25.7 (2 $CH_3$); δ (major 2) = 215.7 (C), 171.1 (C), 171.1 (C), 139.2 (C), 131.9 (2 CH), 127.7 (CH), 120.6 (2 CH), 81.2 (C), 62.8 (C), 53.8 ($CH_3$), 53.1 ($CH_2$), 43.7 ($CH_2$), 43.2 (CH), 33.9 (2 $CH_3$), 30.6 (C), 29.7 ($CH_2$); δ (minor 1 + minor 2) = 216.5 (C), 216.4 (C), 174.6 (C), 172.4 (C), 171.4 (C), 171.3 (C), 138.7 (C), 138.6 (C), 134.1 (2 CH), 129.6 (2 CH), 129.4 (2 CH), 128.7 (2 CH), 128.6 (CH), 128.1 (CH), 128.01 (CH), 82.6 (C), 82.3 (C), 62.9 (C), 62.3 (C), 55.2 ($CH_3$), 54.8 ($CH_3$), 53.6 ($CH_2$), 53.5 ($CH_2$), 45.6 ($CH_2$), 45,29 (CH), 40.6 ($CH_2$), 32.6 (C), 34.6 (2 $CH_3$), 33.3 (2 $CH_3$), 32.5 (C), 30.0 ($CH_2$), 29.9 ($CH_2$).

HRMS (ESI+): *m*/*z* [M + H]$^+$ calcd for $C_{19}H_{24}NO_5$: 346.1649; found: 346.1646.

### Methyl 2-(Furan-2-ylmethyl)-3-hydroxy-1,7-dioxo-5-phenyl-2-azaspiro[5.6]dodecane-3-carboxylate (3hd)

Following the general procedure, the reaction of *N*-(furan-2-ylmethyl)-2-oxo-cycloheptanecarboxamide (163 mg, 0.69 mmol) with methyl (*E*)-2-oxo-4-phenylbut-3-enoate (**2d**; 144 mg, 0.76 mmol) in the presence of PS-BEMP (32 mg, 10 mol%) in THF (1.5 mL) at r.t. for 9 h afforded the product **3hd** as a white solid (262 mg, 88%). The crude product was obtained with 3:1.50:1.5:1 dr. One diastereomer was separated.

First fraction: one diastereomer was isolated as a yellow oil (110 mg, 42%); $R_f$ = 0.52 ($Et_2O$/PE, 7:3).

$^1$H NMR (300 MHz, $CDCl_3$): δ = 7.32–7.31 (m, 1 H), 7.30–7.29 (m, 1 H), 7.28 (d, *J* = 1.7 Hz, 2 H), 7.16–7.11 (m, 2 H), 6.30 (d, *J* = 1.4 Hz, 2 H), 4.60 (d, *J* = 15.9 Hz, 1 H), 4.39 (s, 1 H), 4.29 (d, *J* = 15.9 Hz, 1 H), 3.75 (s, 3 H), 3.41 (dd, *J* = 13.7, 2.1 Hz, 1 H), 3.14 (t, *J* = 13.4 Hz, 1 H), 2.42 (dt, *J* = 9.5, 6.4 Hz, 1 H), 2.09–2.03 (m, 3 H), 1.84 (dd, *J* = 13.2, 2.2 Hz, 1 H), 1.77–1.64 (m, 2 H), 1.35–1.25 (m, 1 H), 1.17 (d, *J* = 15.0 Hz, 1 H), 0.92–0.82 (m, 2 H).

$^{13}$C NMR (75 MHz, $CDCl_3$): δ = 213.1 (C), 172.7 (C), 170.2 (C), 150.9 (C), 141.7 (CH), 138.0 (C), 129.3 (2 CH), 128.5 (2 CH), 127.9 (CH), 110.5 (CH), 108.4 (CH), 85.0 (COH), 64.4 (C), 54.2 ($CH_3$), 45.5 ($CH_2$), 44.2 (CH), 40.7 ($CH_2$), 36.0 ($CH_2$), 35.0 ($CH_2$), 30.9 ($CH_2$), 25.6 ($CH_2$), 25.4 ($CH_2$).

Second fraction: a mixture of two diastereomers was obtained (105 mg, 40%); $R_f$ = 0.57 ($Et_2O$/PE, 7:3).

$^1$H NMR (300 MHz, $CDCl_3$): δ = 7.33–7.25 (m, 8 H), 7.13–7.08 (m, 4 H), 6.32–6.27 (m, 3 H), 6.24 (d, *J* = 3.2 Hz, 1 H), 4.75 (dd, *J* = 20.1, 3.0 Hz, 2 H), 4.57 (d, *J* = 8.0 Hz, 3 H), 4.28–4.12 (m, 3 H), 3.71 (s, 3 H), 3.70 (s, 3 H), 2.96 (t, *J* = 13.9 Hz, 1 H), 2.78 (t, *J* = 14.5 Hz, 1 H), 2.51 (dd, *J* = 18.8, 10.3 Hz, 2 H), 2.26–2.12 (m, 3 H), 2.02 (dd, *J* = 13.7, 2.8 Hz, 1 H), 1.84–1.66 (m, 11 H), 1.60–1.45 (m, 5 H).

$^{13}$C NMR (75 MHz, $CDCl_3$): δ = 213.3 (C), 213.2 (C), 173.0 (C), 172.4 (C), 171.7 (C), 171.5 (C), 150.9 (C), 150.8 (C), 141.6 (2 CH), 137.8 (2 C), 128.9 (2 CH), 128.8 (2 CH), 128.4 (2 CH), 127.6 (2 CH), 127.5 (CH), 121.0 (CH), 110.6 (CH), 110.5 (CH), 108.9 (CH), 108.5 (CH), 85.0 (COH), 84.4 (COH), 63.8 (C), 63.3 (C), 54.3 ($CH_3$), 54.2 ($CH_3$), 45.8 ($CH_2$), 45.7 ($CH_2$), 42.4 (CH), 42.0 (CH), 39.5 ($CH_2$), 37.7 ($CH_2$), 35.6 ($CH_2$), 35.0 ($CH_2$), 30.98 ($CH_2$), 30.92 ($CH_2$), 28.2 ($CH_2$), 27.7 ($CH_2$), 23.9 ($CH_2$), 24.0 ($CH_2$), 23.9 ($CH_2$), 23.8 ($CH_2$).

HRMS (ESI+): *m*/*z* [M + H]$^+$ calcd for $C_{24}H_{27}NO_6$: 426.1911; found: 426.1907.

### 1′-Allyl-6′-hydroxyspiro[indene-2,3′-piperidine]-1,2′(3*H*)-dione (3ia)

Following the general procedure, the reaction of 1-oxoindan-2-carboxylic acid allylamide (100 mg, 0.46 mmol) with acrolein (**2a**; 33.80 µL, 0.55 mmol) in the presence of PS-BEMP (40 mg, 10 mol%) in THF (1 mL) at r.t. for 24 h afforded the product **3ia** as a white solid (124 mg, 89%). The crude product was obtained with 1:1 dr; $R_f$ = 0.24 ($Et_2O$/PE, 8:2). Data given are for the mixture of two diastereomers.

$^1$H NMR (300 MHz, $CDCl_3$): δ = 7.77 (d, *J* = 7.7 Hz, 2 H), 7.63 (t, *J* = 7.4 Hz, 2 H), 7.48 (d, *J* = 7.7 Hz, 2 H), 7.40 (t, *J* = 7.7 Hz, 2 H), 5.92–5.78 (m, 2 H), 5.28–5.15 (m, 5 H), 5.04 (s, 2 H), 4.38–4.35 (m, 1 H), 4.34–4.30 (m, 1 H), 3.98–3.84 (m, 4 H), 3.75–3.65 (m, 2 H), 2.97 (d, *J* = 16.9 Hz, 2 H), 2.49 (ddd, *J* = 14.2, 10.5, 5.1 Hz, 2 H), 2.17 (s, 3 H), 1.87 (dt, *J* = 14.0, 5.9 Hz, 2 H).

$^{13}$C NMR (75 MHz, $CDCl_3$): δ (diastereomer 1) = 204.96 (C), 169.97 (C), 153.72 (C), 135.10 (CH), 134.11 (C), 132.75 (CH), 127.56 (CH), 126.30 (CH), 124.73 (CH), 116.46 ($CH_2$), 79.19 (CHOH), 60.42 ($CH_2$), 56.20 (C), 40.60 ($CH_2$), 26.52 ($CH_2$), 26.44 ($CH_2$); δ (diastereomer 2) = 206.42 (C), 169.71 (C), 153.84 (C), 135.68 (CH), 135.20 (C), 132.73 (CH), 127.84 (CH), 126.50 (CH), 124.80 (CH), 117.25 ($CH_2$), 78.81 (CHOH), 57.09 (C), 46.95 ($CH_2$), 41.17 ($CH_2$), 26.73 ($CH_2$), 28.12 ($CH_2$).

HRMS (ESI+): *m*/*z* [M + H]$^+$ calcd for $C_{16}H_{17}NO_3Na$: 294.1101; found: 294.1104.

### 6′-Hydroxy-1′-phenyl-3,4-dihydro-1*H*-spiro[naphthalene-2,3′-piperidine]-1,2′-dione (3ja)

Following the general procedure, the reaction of *N*-allyl-1-oxo-1-phenyl-1,2,3,4-tetrahydronaphthalene-2-carboxamide (33 mg, 0.12 mmol) with acrolein (**2a**; 9 µL, 0.13 mmol) in the presence of PS-BEMP (5 mg, 10 mol%) in THF (0.5 mL) at r.t. for 5 h afforded the product **3ja** as a white solid (39 mg, 99%). The crude product was obtained with 2:1 dr; $R_f$ = 0.15 ($Et_2O$/PE, 7:3). Data given are for the mixture of two diastereomers.

$^1$H NMR (400 MHz, $CDCl_3$): δ = 8.07–8.03 (m, 2 H), 7.51 (dd, *J* = 7.4, 1.3 Hz, 1 H), 7.48 (dd, *J* = 7.5, 1.3 Hz, 1 H), 7.43–7.41 (m, 1 H), 7.40 (dd, *J* = 3.0, 1.1 Hz, 2 H), 7.38 (d, *J* = 3.1 Hz, 2 H), 7.34–7.30 (m, 6 H), 7.29 (d, *J* = 1.1 Hz, 2 H), 7.24 (s, 1 H), 5.29 (s, 1 H), 5.24 (s, 1 H), 3.74 (d, *J* = 7.9 Hz, 1 H), 3.15 (d, *J* = 4.5 Hz, 1 H), 3.12 (dd, *J* = 7.6, 4.1 Hz, 1 H), 3.11–3.01 (m, 3 H), 2.99–2.89 (m, 1 H), 2.62–2.55 (m, 1 H), 2.40 (tt, *J* = 5.4, 3.6 Hz, 1 H), 2.32 (m, 1 H), 2.32–2.25 (m, 1 H), 2.18–2.15 (m, 1 H), 2.15–2.10 (m, 2 H), 2.10–2.00 (m, 2 H), 1.96 (dd, *J* = 7.7, 5.1 Hz, 1 H), 1.90 (ddd, *J* = 7.0, 6.0, 3.0 Hz, 1 H).

$^{13}$C NMR (75 MHz, $CDCl_3$): δ = 198.5 (C), 196.9 (C), 170.89 (C), 170.87 (C), 143.6 (C), 143.1 (C), 141.7 (C), 140.6 (C), 134.1 (CH), 133.7 (CH), 131.2 (C), 130.4 (C), 129.28 (2 CH), 129.22 (2 CH), 128.8 (CH), 128.7 (CH), 128.4 (CH), 128.2 (2 CH), 128.0 (2 CH), 127.9 (CH), 127.5 (2 CH), 126.97 (CH), 126.91 (CH), 82.2 (CHOH), 81.8 (CHOH), 54.3 (C), 54.1 (C), 32.6 ($CH_2$), 31.7 ($CH_2$), 27.5 ($CH_2$), 26.1 ($CH_2$), 25.6 ($CH_2$), 25.0 ($CH_2$), 24.6 ($CH_2$), 23.4 ($CH_2$).

HRMS (ESI+): *m*/*z* [M + H]$^+$ calcd for $C_{20}H_{20}NO_3$: 322.1438; found: 322.1437.

### 1′-Allyl-6′-hydroxy-3,4-dihydro-1*H*-spiro[naphthalene-2,3′-piperidine]-1,2'-dione (3ka)

Following the general procedure, the reaction of *N*-allyl-1-oxo-1,2,3,4-tetrahydronaphthalene-2-carboxamide (160 mg, 0.69 mmol) with acrolein (**2a**; 50.70 µL, 0.759 mmol) in the presence of PS-BEMP (31 mg, 10 mol%) in THF (1.5 mL) at r.t. for 24 h afforded the product **3ka** as a yellow solid (219 mg, 86%). The crude product was obtained with 2:1 dr.

First fraction: one diastereomer was isolated as a yellow solid (53 mg, 28%); $R_f$ = 0.29 (EtOAc/PE, 1:1).

$^1$H NMR (400 MHz, $CDCl_3$): δ = 7.95 (dd, *J* = 7.8, 2.8 Hz, 1 H), 7.42 (dtd, *J* = 11.2, 7.5, 2.2 Hz, 1 H), 7.24 (dd, *J* = 15.8, 7.9 Hz, 1 H), 7.18 (dd, *J* = 16.8, 6.4 Hz, 1 H), 5.87–5.66 (m, 1 H), 5.33–5.08 (m, 2 H), 4.98 (s, 1 H), 4.86 (t, *J* = 4.7 Hz, 1 H), 4.32 (ddd, *J* = 15.6, 10.7, 4.8 Hz, 1 H), 3.83 (dd, *J* = 15.7, 6.3 Hz, 1 H), 3.03–2.75 (m, 3 H), 2.39–2.13 (m, 1 H), 2.08–1.70 (m, 4 H).

$^{13}$C NMR (75 MHz, $CDCl_3$): δ = 198.59 (C), 170.33 (C), 143.61 (C), 134.16 (CH), 133.63 (CH), 131.31 (C), 128.82 (CH), 128.49 (CH), 127.04 (CH), 117.27 ($CH_2$), 79.46 (CHOH), 54.22 (C), 46.96 ($CH_2$), 31.75 ($CH_2$), 27.71 ($CH_2$), 25.10 ($CH_2$), 24.84 ($CH_2$).

Second fraction: one diastereomer was isolated as a yellow solid (109 mg, 58%); mp 51 °C; $R_f$ = 0.2 (EtOAc/PE, 1:1).

$^1$H NMR (300 MHz, $CDCl_3$): δ = 8.03 (d, *J* = 7.8 Hz, 1 H), 7.49 (td, *J* = 7.4, 1.0 Hz, 1 H), 7.31 (t, *J* = 7.3 Hz, 1 H), 7.22 (d, *J* = 4.6 Hz, 1 H), 5.92–5.78 (m, 1 H), 5.27–5.14 (m, 2 H), 4.98–4.90 (m, 1 H), 4.39 (dd, *J* = 15.3, 4.9 Hz, 1 H), 3.93 (dd, *J* = 15.3, 6.8 Hz, 1 H), 3.44 (d, *J* = 9.8 Hz, 1 H), 3.04 (dt, *J* = 9.9, 4.9 Hz, 1 H), 2.97–2.83 (m, 1 H), 2.48–2.37 (m, 1 H), 2.16 (ddd, *J* = 13.6, 8.7, 4.5 Hz, 1 H), 2.07–1.97 (m, 1 H), 1.96–1.74 (m, 3 H).

$^{13}$C NMR (75 MHz, $CDCl_3$): δ = 199.01 (C), 170.76 (C), 144.04 (C), 134.59 (CH), 134.05 (CH), 131.73 (C), 129.25 (CH), 128.91 (CH), 127.47 (CH), 117.69 ($CH_2$), 79.89 (CHOH), 54.65 (C), 47.39 ($CH_2$), 32.18 ($CH_2$), 28.14 ($CH_2$), 25.53 ($CH_2$), 25.27 ($CH_2$).

HRMS (ESI+): *m*/*z* [M + H]$^+$ calcd for $C_{17}H_{20}NO_3$: 286.1438; found: 286.1437.

### 8a-Hydroxy-10-phenylhexahydro-2*H*,5*H*-2,4a-(epiminomethano)chromen-9-one (5la)

Following the general procedure, the reaction of of 2-oxo-*N*-phenylcyclohexanecarboxamide (**1l**; 100 mg, 0.46 mmol) with acrolein (**2a**; 34 µL, 0.50 mmol) in the presence of PS-BEMP (21 mg, 10 mol%) in THF (1 mL) heated at 55–60 °C for 24 h, afforded the product **5la** as a yellow oil (88 mg, 70%). The crude product was obtained with 2:1 dr; $R_f$ = 0.34 ($Et_2O$/PE, 7:3). Data given are for the mixture of two diastereomers.

$^1$H NMR (300 MHz, $CDCl_3$): δ = 7.33–7.30 (m, 4 H), 7.28 (d, *J* = 1.6 Hz, 1 H), 7.25 (d, *J* = 3.0 Hz, 1 H), 7.17 (ddd, *J* = 6.9, 5.6, 1.4 Hz, 2 H), 5.44 (t, *J* = 2.2 Hz, 1 H), 5.36 (t, *J* = 2.2 Hz, 1 H), 3.71 (ddd, *J* = 6.6, 4.2, 2.6 Hz, 2 H), 2.38–2.26 (m, 1 H), 2.09–2.22 (m, 4 H), 2.01–1.89 (m, 3 H), 1.76–1.83 (m, 5 H), 1.61–1.32 (m, 13 H).

$^{13}$C NMR (75 MHz, $CDCl_3$): δ (major) = 172.49 (C), 139.40 (C), 128.95 (2 CH), 126.16 (2 CH), 123.95 (CH), 98.22 (COH), 84.24 (CH), 48.07 (C), 38.57 ($CH_2$), 28.30 ($CH_2$), 27.93 ($CH_2$), 22.67 ($CH_2$), 21.85 ($CH_2$), 20.10 ($CH_2$); δ (minor) = 172.12 (C), 138.99 (C), 128.93 (2 CH), 126.12 (2 CH), 124.23 (CH), 99.54 (COH), 84.30 (CH), 47.00 (C), 33.33 ($CH_2$), 28.07 ($CH_2$), 26.03 ($CH_2$), 22.95 ($CH_2$), 21.99 ($CH_2$), 20.29 ($CH_2$).

### Methyl 8a-Hydroxy-9-oxo-4,10-diphenylhexahydro-2*H*,5*H*-2,4a-(epiminomethano)chromene-2-carboxylate (5ld)

Following the general procedure, the reaction of 2-oxo-*N*-phenylcyclohexanecarboxamide (**1l**; 150 mg, 0.69 mmol) with methyl (*E*)-2-oxo-4-phenylbut-3-enoate (**2d**; 145 mg, 0.76 mmol) in the presence of PS-BEMP (32 mg, 10 mol%) in THF (1.5 mL) at r.t. for 30 h afforded the product **5ld** as a white solid (160.5 mg, 58%). The crude product was obtained with 3:1 dr; $R_f$ = 0.52 ($Et_2O$/PE, 7:3). The major diastereomer partially crystallized as white needles for X-ray analysis; mp 163 °C. Data given are for the mixture of two diastereomers.

$^1$H NMR (300 MHz, $CDCl_3$): δ = 7.46–7.27 (m, 20 H), 5.26 (s, 1 H), 4.19 (s, 1 H), 3.87 (dd, *J* = 10.4, 3.6 Hz, 1 H), 3.63 (dd, *J* = 10.3, 5.3 Hz, 1 H), 3.45 (d, *J* = 2.5 Hz, 1 H), 3.39 (s, 3 H), 3.38 (s, 1 H), 3.32 (d, *J* = 2.5 Hz, 1 H), 2.99 (dd, *J* = 13.8, 10.5 Hz, 1 H), 2.80 (dd, *J* = 13.9, 3.8 Hz, 2 H), 2.68 (dd, *J* = 13.5, 5.5 Hz, 1 H), 2.19–2.06 (m, 3 H), 1.68–1.37 (m, 13 H).

$^{13}$C NMR (75 MHz, $CDCl_3$): δ (minor) = 171.6 (C), 166.3 (C), 140.9 (C), 137.94 (C), 129.0 (2 CH), 128.9 (2 CH), 128.7 (CH), 128.6 (CH), 128.1 (2 CH), 127.4 (2 CH), 100.4 (C), 89.11 (C), 52.7 (CH), 51.8 ($CH_3$), 42.3 ($CH_2$), 36.8 (CH), 33.4 ($CH_2$), 23.4 ($CH_2$), 21.9 ($CH_2$), 19.5($CH_2$); δ (major) = 171.5 (C), 166.7 (C), 140.7 (C), 137.96 (C), 129.1 (2 CH), 128.8 (2 CH), 128.5 (2 CH), 128.3 (C), 127.9 (C), 127.2 (2 CH), 99.2 (C), 89.11 (C), 52.9 (CH), 52.8 ($CH_3$), 40.6 ($CH_2$), 38.7(CH), 38.4 ($CH_2$), 27.1 ($CH_2$), 22.3 ($CH_2$), 21.4 ($CH_2$).

### Methyl 10-(Furan-2-ylmethyl)-8a-hydroxy-9-oxo-4-phenylhexahydro-2*H*,5*H*-2,4a-(epiminomethano)chromene-2-carboxylate (5md)

Following the general procedure, the reaction of *N*-(furan-2ylmethyl)-2-oxocyclohexanecarboxamide (**1m**; 210 mg, 0.95 mmol) with methyl (*E*)-2-oxo-4-phenylbut-3-enoate (**2d**; 198.75 mg, 1.04 mmol) in the presence of PS-BEMP (41 mg, 10 mol%) in THF (2 mL) at r.t. for 5 h afforded the product **5md** as a yellow solid (250 mg, 64%). The crude product was obtained with 6:1:1 dr; $R_f$ = 0.47 ($Et_2O$/PE, 7:3). Data given are for the mixture of three diastereomers.

**Three diastereomers:**

$^1$H NMR (300 MHz, $CDCl_3$): δ (characteristic peaks, major) = 7.37 (d, *J* = 1.7 Hz, 1 H), 7.28 (br s, 1 H), 7.24 (br s, 2 H), 7.05 (d, *J* = 2.0 Hz, 1 H), 7.02 (d, *J* = 1.4 Hz, 1 H), 5.31 (s, 1 H), 6.33 (dd, *J* = 3.2, 1.9 Hz, 1 H), 6.27 (d, *J* = 3.2 Hz, 1 H),5.11 (d, *J* = 15.9 Hz, 1 H), 4.72 (d, *J* = 15.9 Hz, 1 H), 3.84 (s, 3 H), 3.68 (dd, *J* = 10.4, 3.6 Hz, 1 H), 2.89 (dd, *J* = 13.0, 4.6 Hz, 1 H), 2.51 (dd, *J* = 13.8, 3.6 Hz, 1 H).

$^{13}$C NMR (75 MHz, $CDCl_3$): δ (major) = 171.6 (C), 167.1 (C), 150.0 (C), 142.2 (CH), 140.4 (C), 128.7 (2 CH), 128.1 (2 CH), 127.0 (CH), 110.3 (CH), 108.8 (CH), 98.5 (C), 86.4 (C), 53.1 ($CH_3$), 52.2 (C), 40.8 ($CH_2$), 38.8 (CH), 38.1 ($CH_2$), 37.9 ($CH_2$), 27.0 ($CH_2$), 22.3 ($CH_2$), 21.4 ($CH_2$); δ (minor 1 + minor 2) = 172.9 (C), 171.8 (C), 166.7 (C), 163.3 (C), 151.2 (C), 150.1 (C), 142.3 (CH), 142.0 (CH), 140.7 (C), 139.9 (C), 129.5 (2 CH), 128.7 (2 CH), 128.3 (2 CH), 127.8 (2 CH), 127.2 (CH), 127.1 (CH), 114.0 (CH), 110.4 (CH), 110.4 (CH), 107.8 (CH), 99.8 (C), 99.1 (C), 86.5 (C), 82.5 (C), 54.4 ($CH_3$), 52.6 ($CH_3$), 51.6 (C), 50.2 (C), 44.7 (CH), 42.2 ($CH_2$), 41.8 ($CH_2$), 41.3 ($CH_2$), 38.4 ($CH_2$), 36.8 (CH), 36.3 ($CH_2$), 32.8 ($CH_2$), 23.3 ($CH_2$), 22.5 ($CH_2$), 22.0 ($CH_2$), 21.8 ($CH_2$), 21.17 ($CH_2$), 21.10 ($CH_2$).

HRMS (ESI+): *m*/*z* [M + H]$^+$ calcd for $C_{23}H_{26}NO_6$: 412.1755; found: 412.1754.

### 10-Benzyl-4-(furan-2-yl)-8a-hydroxyhexahydro-2*H*,5*H*-2,4a-(epiminomethano)chromen-9-one (5nc)

Following the general procedure, the reaction of *N*-benzyl-2-oxocyclohexanecarboxamide (**1n**; 300 mg, 1.29 mmol) with furylacrolein (**2c**; 101 µL, 1.41 mmol) in the presence of PS-BEMP (59 mg, 10 mol%) in THF (3 mL) heated at 55–60 °C for 24 h afforded the product **5nc** as a white solid (401 mg, 80%) with 10:1 dr. One diastereomer was separated.

First fraction: one diastereomer was isolated as a colorless oil (13%); $R_f$ = 0.43 ($Et_2O$/PE, 7:3).

$^1$H NMR (300 MHz, $CDCl_3$): δ = 7.36 (dd, *J* = 1.8, 0.7 Hz, 1 H), 7.31–7.25 (m, 6 H), 6.33 (dd, *J* = 3.2, 1.9 Hz, 1 H), 6.22 (d, *J* = 3.2 Hz, 1 H), 5.02 (dd, *J* = 3.1, 1.5 Hz, 1 H), 4.84 (d, *J* = 14.9 Hz, 1 H), 4.38 (d, *J* = 14.9 Hz, 1

H), 3.86 (d, $J$ = 1.8 Hz, 1 H), 3.07 (dd, $J$ = 10.8, 8.6 Hz, 1 H), 2.53 (ddd, $J$ = 13.6, 8.6, 1.6 Hz, 1 H), 2.05–1.97 (m, 2 H), 1.79 (dd, $J$ = 12.7, 8.6 Hz, 1 H), 1.56–1.45 (m, 3 H), 1.26–1.13 (m, 2 H).

$^{13}$C NMR (75 MHz, $CDCl_3$): δ = 173.0 (C), 151.8 (C), 142.1 (CH), 136.8 (C), 128.9 (2 CH), 128.0 (2 CH), 127.8 (CH), 111.0 (CH), 110.2 (CH), 99.6 (C), 80.7 (C–O), 51.8 ($CH_2$), 47.4 (C), 38.9 ($CH_2$), 36.2 (CH), 33.5 ($CH_2$), 26.1 ($CH_2$), 22.1 ($CH_2$), 21.7 ($CH_2$).

Second fraction: a mixture of two diastereomers was isolated (67%); $R_f$ = 0.16 ($Et_2O$/PE, 7:3).

$^1$H NMR (300 MHz, $CDCl_3$): δ = 7.42 (dd, $J$ = 11.8, 1.6 Hz, 1 H), 7.37 (d, $J$ = 2.0 Hz, 1 H), 7.34 (t, $J$ = 2.0 Hz, 3 H), 7.31 (d, $J$ = 1.9 Hz, 2 H), 7.29 (dd, $J$ = 4.0, 2.0 Hz, 3 H), 7.25 (dd, $J$ = 2.3, 1.6 Hz, 2 H), 7.20–7.17 (m, 1 H), 6.24 (dd, $J$ = 3.2, 1.9 Hz, 1 H), 6.20 (dd, $J$ = 3.2, 1.9 Hz, 1 H), 5.98 (d, $J$ = 3.2 Hz, 1 H), 5.88 (d, $J$ = 3.1 Hz, 1 H), 5.08–5.04 (m, 1 H), 4.98 (t, $J$ = 2.3 Hz, 1 H), 4.89 (s, 1 H), 4.84–4.77 (m, 1 H), 4.53 (dd, $J$ = 14.9, 3.3 Hz, 1 H), 3.68 (dd, $J$ = 10.3, 3.6 Hz, 1 H), 3.58 (dd, $J$ = 10.6, 4.8 Hz, 1 H), 3.44 (s, 1 H), 2.81 (s, 1 H), 2.56 (ddd, $J$ = 12.6, 10.3, 2.1 Hz, 1 H), 2.30 (td, $J$ = 10.5, 5.3 Hz, 1 H), 2.10–1.70 (m, 8 H), 1.63–1.13 (m, 10 H).

$^{13}$C NMR (75 MHz, $CDCl_3$): δ (major): = 171.19 (C), 154.84 (C), 141.84 (CH), 136.86 (C), 128.66 (2 CH), 128.58 (2 CH), 127.69 (CH), 110.14 (CH), 107.02 (CH), 98.14 (C), 80.97 (CH), 51.82 (C), 47.50 ($CH_2$), 38.52 ($CH_2$), 34.90 ($CH_2$), 33.30 (CH), 26.83 ($CH_2$), 22.43 ($CH_2$), 21.92 ($CH_2$); δ (minor) = 170.8 (C), 154.1 (C), 142.0 (CH), 136.9 (C), 128.7 (2 CH), 128.04 (CH), 127.7 (2 CH), 110.2 (CH), 107.06 (CH), 93.3 (C), 80.9 (CH), 51.2 (C), 47.8 (CH), 35.6 ($CH_2$), 33.4 ($CH_2$), 30.7 ($CH_2$), 23.5 ($CH_2$), 22.0 ($CH_2$), 19.6 ($CH_2$).

HRMS (ESI+): $m/z$ $[M + H]^+$ calcd for $C_{21}H_{24}NO_4$: 354.1700; found: 354.1694, 354.1700.

## Reactivity of Spirohemiaminals

### Dehydration; General Procedure 1

Under an argon atmosphere, Burgess reagent (1–2 equiv) was added to a 0.1 M solution of spirohemiaminal compound (1 equiv) in THF. The mixture was then stirred at reflux for 2 h. The solvent was removed under vacuum, the residue was washed with $H_2O$, and the organic layer was extracted with EtOAc (2 ×). The combined organic phases were dried ($Na_2SO_4$), filtered, and concentrated under vacuum to give the crude product. Finally, flash chromatography on silica gel afforded the desired product.

### 7-Allyl-7-azaspiro[4.5]dec-8-ene-1,6-dione (6ia)

Following the general procedure 1 for dehydration, the reaction of spirohemiaminal compund **3ba** (210 mg, 0.95 mmol) with Burgess reagent (187 mg, 0.98 mmol) in THF (2.5 mL) afforded the product **6ia** as a yellow oil (250 mg, 64%). The crude product was obtained with 1:1 dr; $R_f$ = 0.47 ($Et_2O$/PE, 7:3). Data given are for the mixture of two diastereomers.

$^1$H NMR (300 MHz, $CDCl_3$): δ = 6.02 (d, $J$ = 2.2 Hz, 1 H), 6.00 (d, $J$ = 2.2 Hz, 1 H), 5.75 (ddd, $J$ = 15.9, 10.7, 5.6 Hz, 2 H), 5.21–5.14 (m, 4 H), 5.10 (ddd, $J$ = 10.8, 5.5, 3.4 Hz, 2 H), 4.12 (ddt, $J$ = 15.6, 5.5, 1.5 Hz, 2 H), 4.04 (ddt, $J$ = 15.6, 5.6, 1.5 Hz, 2 H), 2.77–2.75 (m, 1 H), 2.73–2.71 (m, 1 H), 2.55–2.39 (m, 4 H), 2.35–2.24 (m, 2 H), 2.14–2.00 (m, 4 H), 1.95–1.84 (m, 4 H).

$^{13}$C NMR (75 MHz, $CDCl_3$): δ = 216.3 (2 C), 169.1 (2 C), 132.6 (2 CH), 128.8 (2 CH), 117.4 (2 $CH_2$), 103.7 (2 C), 55.0 (2 C), 48.1 (2 $CH_2$), 38.4 (2 $CH_2$), 35.1 (2 $CH_2$), 29.4 (2 $CH_2$), 19.1 (2 $CH_2$).

### Methyl 1,6-Dioxo-7,10-diphenyl-7-azaspiro[4.5]dec-8-ene-8-carboxylate (6fd)

Following the general procedure 1 for dehydration, the reaction of spirohemiaminal compound **3fd** (168 mg, 0.42 mmol) with Burgess reagent (203.7 mg, 0.84 mmol) in THF (5 mL) afforded the product **6fd** as a yellow solid (114 mg, 72%). The crude product was obtained with 1:1 dr; $R_f$ = 0.56 ($Et_2O$/PE, 7:3). Data given are for the mixture of two diastereomers.

$^1$H NMR (300 MHz, $CDCl_3$): δ = 7.36–7.27 (m, 10 H), 7.22–7.18 (m, 10 H), 6.51 (d, $J$ = 4.4 Hz, 1 H), 6.45 (d, $J$ = 3.5 Hz, 1 H), 4.36 (d, $J$ = 4.4 Hz, 1 H), 4.03 (d, $J$ = 3.4 Hz, 1 H), 3.49 (s, 3 H), 3.48 (s, 3 H), 2.83 (dt, $J$ = 13.4, 6.8 Hz, 1 H), 2.26 (ddd, $J$ = 16.4, 13.6, 6.5 Hz, 3 H), 1.99–1.79 (m, 6 H), 1.53 (dd, $J$ = 18.0, 6.7 Hz, 1 H), 1.24–1.12 (m, 1 H).

$^{13}$C NMR (75 MHz, $CDCl_3$): δ = 213.5 (C), 213.18 (C), 169.13 (C), 167.7 (C), 162.5 (C), 162.5 (C), 139.4 (C), 138.7 (C), 138.1 (C), 136.76 (C), 134.3 (C), 134.0 (C), 129.1 (2 CH), 129.08 (2 CH), 128.8 (2 CH), 128.7 (2 CH), 128.6 (2 CH), 128.5 (2 CH), 128.0 (CH), 127.8 (CH), 127.2 (CH), 127.1 (CH), 126.4 (2 CH), 126.2 (2 CH), 122.5 (CH), 122.1(CH), 59.9 (C), 59.14 (C), 52.2 ($CH_3$), 52.1 ($CH_3$), 47.8 (CH), 43.0 (CH), 39.8 ($CH_2$), 38.4 ($CH_2$), 31.8 ($CH_2$), 29.2 ($CH_2$), 19.1 ($CH_2$), 18.8 ($CH_2$).

### Methyl 3,3-Dimethyl-1,6-dioxo-10-phenyl-7-azaspiro[4.5]dec-8-ene-8-carboxylate (6gd)

Following the general procedure 1 for dehydration, the reaction of spirohemiaminal compound **3gd** (105 mg, 0.30 mmol) with Burgess reagent (145 mg, 0.60 mmol) in THF (3.5 mL) afforded the product **6gd** as a white solid (95 mg, 96%). The crude product was obtained with 1:1 dr; $R_f$ = 0.51 ($Et_2O$/PE, 7:3). Data given are for the mixture of two diastereomers.

$^1$H NMR (300 MHz, $CDCl_3$): δ = 7.89 (s, 1 H), 7.83 (s, 1 H), 7.33–7.28 (m, 5H), 7.20 (d, $J$ = 2.4 Hz, 1 H), 7.17 (d, $J$ = 1.5 Hz, 1 H), 7.14 (d, $J$ = 1.9 Hz, 1 H), 7.12 (d, $J$ = 2.4 Hz, 1 H), 6.33 (dd, $J$ = 4.7, 1.4 Hz, 1 H), 6.25 (dd, $J$ = 2.6, 1.6 Hz, 1 H), 4.08 (d, $J$ = 4.7 Hz, 1 H), 3.81 (s, 3 H), 3.80 (s, 3 H), 2.66 (d, $J$ = 13.7 Hz, 1 H), 2.36 (d, $J$ = 14.8 Hz, 1 H), 2.24 (d, $J$ = 14.3 Hz, 1 H), 1.98–1.91 (m, 2 H), 1.90–1.75 (m, 4 H), 1.09 (s, 4 H), 1.02 (s, 3 H), 0.70 (s, 3 H), 0.69 (s, 3 H).

$^{13}$C NMR (75 MHz, $CDCl_3$): δ = 213.2 (C), 212.2 (C), 169.2 (C), 168.1 (C), 162.0 (C), 162.0 (C), 138.0 (2 C), 129.9 (2 CH), 129.1 (2 CH), 128.9 (2 CH), 128.7 (2 CH), 128.3 (CH), 128.2 (CH), 127.9 (C), 127.1 (C), 117.1 (CH), 116.5 (CH), 60.2 (C), 60.0 (C), 54.8 ($CH_2$), 53.5 ($CH_2$), 52.7 ($CH_3$), 52.7 ($CH_3$), 49.7 (CH), 46.7 (CH), 43.9 ($CH_2$), 42.3 ($CH_2$), 32.8 (C), 32.5 (C), 29.9 ($CH_3$), 29.7 ($CH_3$), 29.6 ($CH_3$), 29.4 ($CH_3$).

### Nucleophilic Substitution; General Procedure 2

A solution of the corresponding spiro compound in anhyd $CH_2Cl_2$ (6 mL/mmol) was cooled to –78 °C, and then the corresponding silane (4 equiv) and the Lewis acid (1 equiv) were added via syringe. After stirring for 3 h at –78 °C and 1 h at r.t., sat. aq $NaHCO_3$ (10 mL/1 mmol) was added. The mixture was extracted with $CH_2Cl_2$ and the organic layer was dried ($Na_2SO_4$), filtered, and concentrated under vacuum to give the crude product. Finally, flash chromatography on silica gel afforded the desired product.

### 7,8-Aiallyl-7-azaspiro[4.5]decane-1,6-dione (8baa)

Following the general procedure 2 for substitution, the reaction of spirohemiaminal compound **3ba** (140 mg, 0.62 mmol) with allyltrimethylsilane (405 µL, 2.51 mmol) and $BF_3$·$OEt_2$ (77.5 µL, 0.62 mmol) in $CH_2Cl_2$ (4 mL) afforded the product **8baa** as a yellow oil (155 mg, 72%). The crude product was obtained with 1:1 dr; $R_f$ = 0.55 ($Et_2O$/PE, 9:1). Data given are for the mixture of two diastereomers.

$^1$H NMR (300 MHz, $CDCl_3$): δ = 5.76–5.56 (m, 4 H), 5.10–5.03 (m, 8 H), 4.50–4.41 (m, 1 H), 4.36 (ddt, *J* = 15.5, 4.4, 1.6 Hz, 1 H), 3.52–3.41 (m, 2 H), 3.39–3.31 (m, 1 H), 2.50–2.03 (m, 8 H), 2.19–2.03 (m, 6 H), 1.91–1.63 (m, 10 H), 1.46–1.39 (m, 1 H).

$^{13}$C NMR (75 MHz, $CDCl_3$): δ = 218.1 (C), 217.1 (C), 170.5 (C), 170.1 (C), 134.1 (CH), 133.7 (CH), 133.1 (CH), 132.7 (CH), 118.2 ($CH_2$), 118.1 ($CH_2$), 116.5 ($CH_2$), 116.5 ($CH_2$), 56.4 (CH), 55.5 (CH), 55.4 (C), 55.2 (C), 47.8 ($CH_2$), 47.6 ($CH_2$), 38.9 ($CH_2$), 37.8 ($CH_2$), 37.3 ($CH_2$), 37.2 ($CH_2$), 36.7 ($CH_2$), 36.6 ($CH_2$), 26.4 ($CH_2$), 25.9 ($CH_2$), 22.5 ($CH_2$), 22.1 ($CH_2$), 19.7 ($CH_2$), 19.6 ($CH_2$).

HRMS (ESI+): *m*/*z* [M + H]$^+$ calcd for $C_{15}H_{22}NO_2$: 248.1645; found: 248.1640, 248.1642.

### 8-Allyl-7-(but-3-en-1-yl)-7-azaspiro[4.5]decane-1,6-dione (8caa)

Following the general procedure 2 for substitution, the reaction of spirohemiaminal compound **3ca** (170 mg, 0.76 mmol) with allyltrimethylsilane (495 µL, 3.07 mmol) and $BF_3{\cdot}OEt_2$ (95 µL, 0.76 mmol) in $CH_2Cl_2$ (5 mL) afforded the product **8caa** as a white solid (155 mg, 78%). The crude product was obtained with 1:1 dr; $R_f$ = 0.20 ($Et_2O$/PE, 9:1). Data given are for the mixture of two diastereomers.

$^1$H NMR (300 MHz, $CDCl_3$): δ = 5.77–5.53 (m, 4 H), 5.08–4.91 (m, 8 H), 3.85–3.76 (m, 2 H), 3.39 (dt, *J* = 9.1, 4.3 Hz, 1 H), 3.30 (dt, *J* = 9.3, 7.3 Hz, 1 H), 2.83–2.72 (m, 2 H), 2.41–2.27 (m, 8 H), 2.20–2.07 (m, 8 H), 1.85–1.73 (m, 10 H), 1.41–1.34 (m, 2 H).

$^{13}$C NMR (75 MHz, $CDCl_3$): δ = 218.3 (C), 217.0 (C), 170.6 (C), 170.0(C), 135.2 (CH), 135.0 (CH), 134.0 (CH), 133.7 (CH), 118.2 ($CH_2$), 118.1 ($CH_2$), 116.7 ($CH_2$), 116.5 ($CH_2$), 56.3 (2 CH), 56.29 (C), 55.09 (C), 45.5 ($CH_2$), 45.2 ($CH_2$), 38.9 ($CH_2$), 37.7 ($CH_2$), 37.5 ($CH_2$), 37.4 ($CH_2$), 36.9 ($CH_2$), 36.5 ($CH_2$), 31.9 ($CH_2$), 31.8 ($CH_2$), 26.4 ($CH_2$), 25.7 ($CH_2$), 22.3 ($CH_2$), 22.1 ($CH_2$), 19.7 ($CH_2$), 19.5 ($CH_2$).

### 8-Allyl-7-(2-bromobenzyl)-7-azaspiro[4.5]decane-1,6-dione (8daa)

Following the general procedure 2 for substitution, the reaction of spirohemiaminal compound **3da** (208 mg, 0.59 mmol) with allyltrimethylsilane (382 µL, 2.37 mmol) and $BF_3{\cdot}OEt_2$ (74 µL, 0.59 mmol) in $CH_2Cl_2$ (5 mL) afforded the product **8daa** as a yellow solid (205 mg, 92%). The crude product was obtained with 1:1 dr; $R_f$ = 0.40 ($Et_2O$/PE, 7:3). Data given are for the mixture of two diastereomers.

$^1$H NMR (300 MHz, $CDCl_3$): δ = 7.47 (dt, *J* = 7.9, 1.5 Hz, 2 H), 7.32 (ddd, *J* = 9.2, 7.4, 1.4 Hz, 2 H), 7.18 (ddd, *J* = 9.4, 7.5, 1.4 Hz, 2 H), 7.06 (td, *J* = 7.9, 1.4 Hz, 2 H), 5.68–5.51 (m, 2 H), 5.23 (d, *J* = 16.3 Hz, 1 H), 5.12–5.02 (m, 4 H), 4.96 (d, *J* = 16.0 Hz, 1 H), 4.35 (d, *J* = 16.0 Hz, 1 H), 4.19 (d, *J* = 16.3 Hz, 1 H), 3.36–3.27 (m, 2 H), 2.76–2.44 (m, 4 H), 2.36–2.11 (m, 9 H), 1.93–1.71 (m, 10 H), 1.53–1.45 (m, 1 H).

$^{13}$C NMR (75 MHz, $CDCl_3$): δ = 217.97 (C), 217.09 (C), 171.01 (C), 170.54 (C), 136.19 (C), 135.61 (C), 133.88 (CH), 133.60 (CH), 132.64 (CH), 132.48 (CH), 128.62 (CH), 128.59 (CH), 128.51 (CH), 128.12 (CH), 127.89 (CH), 127.65 (CH), 123.12 (C), 123.11 (C), 118.46 ($CH_2$), 118.30 ($CH_2$), 56.54 (CH), 56.24 (CH), 55.55 (C), 55.32 (C), 48.72 ($CH_2$), 48.04 ($CH_2$), 38.80 ($CH_2$), 37.66 ($CH_2$), 37.16 ($CH_2$), 37.11 ($CH_2$), 36.89 ($CH_2$), 36.56 ($CH_2$), 26.35 ($CH_2$), 25.97 ($CH_2$), 22.57 ($CH_2$), 21.91 ($CH_2$), 19.77 ($CH_2$), 19.62 ($CH_2$).

HRMS (ESI+): *m*/*z* [M + H]$^+$ calc for $C_{19}H_{22}BrNO_2$: 376.0907; found: 376.0919, 376.0917.

### 1,6-Dioxo-7-phenyl-7-azaspiro[4.5]decane-8-carbonitrile (8fab)

Following the general procedure 2 for substitution, the reaction of spirohemiaminal **3fa** (260 mg, 1.28 mmol) with trimethylsilyl cyanide (382.55 µL, 5.12 mmol) and $BF_3{\cdot}OEt_2$ (158 µL, 1.28 mmol) in $CH_2Cl_2$ (9 mL) afforded the product **8fab** as a white solid (152 mg, 44%); $R_f$ = 0.23 ($Et_2O$/PE, 7:3) as a unique diastereomer that partially crystallized as white needles for X-ray analysis; mp 168 °C.

$^1$H NMR (300 MHz, $CDCl_3$): δ = 7.44–7.37 (m, 2 H), 7.31–7.27 (m, 3 H), 5.53 (d, *J* = 2.1 Hz, 1 H), 2.80–2.71 (m, 1 H), 2.57–2.33 (m, 3 H), 2.21–1.87 (m, 4 H), 1.80–1.58 (m, 2 H).

$^{13}$C NMR (75 MHz, $CDCl_3$): δ = 216.22 (C), 169.35 (C), 141.15 (C), 129.85 (2 CH), 128.55 (CH), 127.15 (2 CH), 118.18 (C), 55.58 (C), 52.71 (CH), 37.77 ($CH_2$), 36.30 ($CH_2$), 28.01 ($CH_2$), 23.71 ($CH_2$), 19.68 ($CH_2$).

### 7-Allyl-8-(propa-1,2-dien-1-yl)-7-azaspiro[4.5]decane-1,6-dione (8fac)

Following the general procedure 2 for substitution, the reaction of spirohemiaminal compound **3fa** (200 mg, 0.89 mmol) with propargyltrimethylsilane (401.55 µL, 2.68 mmol) and $BF_3{\cdot}OEt_2$ (110.60 µL, 0.89 mmol) in $CH_2Cl_2$ (8 mL) afforded the product **8fac** as a white oil (78 mg, 35%); $R_f$ = 0.23 ($Et_2O$/PE, 7:3). Only a single isomer was isolated.

$^1$H NMR (300 MHz, $CDCl_3$): δ = 5.80–5.67 (m, 1 H), 5.16–5.04 (m, 2 H), 4.83 (d, *J* = 5.9 Hz, 1 H), 4.53 (dd, *J* = 15.0, 3.7 Hz, 1 H), 4.00 (d, *J* = 5.9 Hz, 1 H), 3.43 (dd, *J* = 11.5, 3.6 Hz, 1 H), 2.99 (d, *J* = 17.4 Hz, 1 H), 2.70 (d, *J* = 17.4 Hz, 1 H), 2.27–2.11 (m, 4 H), 2.01–1.66 (m, 6 H).

$^{13}$C NMR (75 MHz, $CDCl_3$): δ = 212.3 (C), 208.4 (C), 174.1 (C), 133.6 ($CH_2$), 117.1 ($CH_2$), 92.3 (CH), 84.3 ($CH_2$), 54.5 (C), 48.9 ($CH_2$), 47.9 ($CH_2$), 40.5 ($CH_2$), 39.1 ($CH_2$), 31.4 (CH), 27.3 ($CH_2$), 26.9 ($CH_2$).

### 1′,6′-Diallylspiro[indene-2,3′-piperidine]-1,2′(3*H*)-dione (8iaa)

Following the general procedure 2 for substitution, the reaction of spirohemiaminal compound **3ia** (140 mg, 0.527 mmol) with allyltrimethylsilane (330 µL, 2.1 mmol) and $BF_3{\cdot}OEt_2$ (65 µL, 0,527 mmol) in $CH_2Cl_2$ (6 mL) afforded the product **8iaa** as a white oil (132.6 mg, 87%). The crude product was obtained with 1:1 dr; $R_f$ ($Et_2O$/PE, 7:3) = 0.28. Data given are for the mixture of two diastereomers.

$^1$H NMR (300 MHz, $CDCl_3$): δ = 7.74 (dd, *J* = 11.4, 7.7 Hz, 2 H), 7.57 (t, *J* = 7.4 Hz, 2 H), 7.43 (d, *J* = 7.7 Hz, 2 H), 7.36 (dt, *J* = 11.6, 5.8 Hz, 2 H), 5.87–5.63 (m, 4 H), 5.31 (d, *J* = 17.2 Hz, 1 H), 5.21–5.09 (m, 6 H), 4.65–4.56 (m, 1 H), 4.49 (dd, *J* = 15.5, 4.6 Hz, 1 H), 3.86 (d, *J* = 16.8 Hz, 1 H), 3.60 (ddd, *J* = 22.0, 20.2, 11.6 Hz, 5 H), 3.02 (d, *J* = 16.8 Hz, 1 H), 2.91 (d, *J* = 16.8 Hz, 1 H), 2.67–2.41 (m, 5 H), 2.33 (dq, *J* = 13.0, 4.1 Hz, 2 H), 2.01 (dd, *J* = 7.2, 5.2 Hz, 3 H), 1.83–1.69 (m, 2 H), 1.66–1.56 (m, 1 H).

$^{13}$C NMR (75 MHz, $CDCl_3$): δ (major) = 205.30 (C), 169.72 (C), 153.62 (C), 135.77 (C), 134.69 (CH), 134.01 (CH), 133.01 (CH), 127.63 (CH), 126.35 (CH), 124.80 (CH), 118.39 ($CH_2$), 116.81 ($CH_2$), 56.99 (C), 55.93 (CH), 47.92 ($CH_2$), 41.12 ($CH_2$), 37.50 ($CH_2$), 28.00 ($CH_2$), 22.16 ($CH_2$); δ (minor) = 205.71 (C), 170.10 (C), 153.76 (C), 135.12 (C), 134.25 (CH), 133.18 (CH), 127.68 (CH), 126.48 (CH), 124.97 (CH), 118.49 ($CH_2$), 116.97 ($CH_2$), 57.03 (C), 56.07 (CH), 48.12 ($CH_2$), 42.52 ($CH_2$), 37.04 ($CH_2$), 30.40 (CH), 28.14 ($CH_2$), 23.21 ($CH_2$).

### 1′,6′-Diallyl-3,4-dihydro-1*H*-spiro[naphthalene-2,3′-piperidine]-1,2′-dione (8jaa)

Following the general procedure 2 for substitution, the reaction of spirohemiaminal compound **3ka** (100 mg, 0.35 mmol) with allyltrimethylsilane (204.85 µL, 1.4 mmol) and $BF_3{\cdot}OEt_2$ (37 µL, 0,35 mmol) in $CH_2Cl_2$ (4 mL) afforded the product **8jaa** as a white solid (65

mg, 60%). The crude product was obtained with 1:1 dr; $R_f$ = 0.34 ($Et_2O$/PE, 7:3) for the first diastereomer; $R_f$ = 0.27 ($Et_2O$/PE, 7:3) for the second diastereomer. Data given are for the mixture of two diastereomers.

$^1$H NMR (300 MHz, $CDCl_3$): δ = 7.98 (d, *J* = 7.8 Hz, 2 H), 7.40 (t, *J* = 7.4 Hz, 2 H), 7.22 (d, *J* = 9.7 Hz, 2 H), 7.16 (d, *J* = 7.6 Hz, 2 H), 5.73 (dtdd, *J* = 24.1, 10.0, 7.3, 5.3 Hz, 4 H), 5.32 (d, *J* = 17.2 Hz, 1 H), 5.19–5.03 (m, 7 H), 4.62–4.54 (m, 1 H), 4.43 (dd, *J* = 15.6, 4.5 Hz, 1 H), 3.62 (dd, *J* = 15.7, 6.5 Hz, 1 H), 3.54–3.43 (m, 2 H), 3.38 (dt, *J* = 9.2, 4.6 Hz, 1 H), 3.02–2.92 (m, 4 H), 2.81 (ddd, *J* = 13.7, 9.1, 6.4 Hz, 1 H), 2.56–2.16 (m, 5 H), 2.06–1.88 (m, 6 H), 1.83–1.66 (m, 4 H).

$^{13}$C NMR (75 MHz, $CDCl_3$): δ (major) = 197.22 (C), 170.20 (C), 143.12 (C), 134.27 (CH), 133.61 (CH), 133.07 (CH), 130.61 (C), 128.47 (CH), 126.84 (CH), 118.31 ($CH_2$), 116.74 ($CH_2$), 55.25 (C), 53.40 (CH), 48.38 ($CH_2$), 37.19 ($CH_2$), 33.41 ($CH_2$), 29.81 (CH), 25.14 ($CH_2$), 24.87 ($CH_2$), 21.06 ($CH_2$); δ (minor) = 198.17 (C), 170.59 (C), 143.37 (C), 134.19 (CH), 133.55 (CH), 131.68 (C), 128.31 (CH), 128.69 (CH), 126.92 (CH), 118.38 ($CH_2$), 116.83 ($CH_2$), 55.90 (C), 54.15 (CH), 47.83 ($CH_2$), 37.49 ($CH_2$), 32.32 ($CH_2$), 30.42 (CH), 25.17 ($CH_2$), 25.00 ($CH_2$), 22.51 ($CH_2$).

### Metathesis Cyclization; General Procedure 3

To a one-necked round-bottomed flask, equipped with magnetic stirring bar under an argon atmosphere, were introduced spiro compound (1 equiv) and then the Grubbs catalyst (5 mol%). The mixture was stirred at r.t. for 4 h (the reaction was monitored by TLC). The mixture was then filtered and purified by flash chromatography on silica gel to separate the diastereomers.

### 1′,6′,9′,9a′-Tetrahydro-2′*H*,4′*H*-spiro[cyclopentane-1,3′-quinolizine]-2,4′-dione (9baa)

To a one-necked round-bottomed flask, equipped with a magnetic stirring bar under an argon atmosphere, were introduced spiro compound **8baa** (370 mg, 1.49 mmol) in $CH_2Cl_2$ (46 mL), followed by Grubbs II catalyst (64 mg, 5 mol%). The mixture was stirred at r.t. for 4 h (the reaction was monitored by TLC). The mixture was then filtered and purified by flash chromatography on silica gel. The two diastereomers were separated.

First fraction: one diastereomer was isolated as a brown solid (72 mg, 32%); mp 106 °C; $R_f$ = 0.23 ($Et_2O$/PE, 7:3).

$^1$H NMR (300 MHz, $CDCl_3$): δ = 5.75 (ddd, *J* = 11.7, 2.7, 1.5 Hz, 1 H), 5.67 (ddd, *J* = 4.2, 2.2, 1.0 Hz, 1 H), 4.59 (dd, *J* = 19.2, 2.4 Hz, 1 H), 3.57 (dd, *J* = 14.6, 7.8 Hz, 1 H), 3.48 (dd, *J* = 17.9, 1.1 Hz, 1 H), 2.58 (dd, *J* = 11.8, 7.0 Hz, 1 H), 2.54–2.43 (m, 1 H), 2.35–2.09 (m, 5 H), 2.06–1.84 (m, 3 H), 1.62–1.49 (dddd, *J* = 17.4, 10.9, 7.3, 3.2 Hz, 2 H).

$^{13}$C NMR (75 MHz, $CDCl_3$): δ = 217.69 (C), 170.06 (C), 124.23 (CH), 123.75 (CH), 56.0 (C), 52.9 (CH), 42.5 ($CH_2$), 38.9 ($CH_2$), 36.5 ($CH_2$), 32.9 ($CH_2$), 27.3 ($CH_2$), 25.6 ($CH_2$), 19.5 ($CH_2$).

Second fraction: one diastereomer was isolated as a brown oil (84 mg, 37%); $R_f$ = 0.18 ($Et_2O$/PE, 7:3).

$^1$H NMR (400 MHz, $CDCl_3$): δ = 5.78 (ddd, *J* = 10.0, 5.8, 2.1 Hz, 1 H), 5.66 (ddd, *J* = 5.3, 3.9, 2.6 Hz, 1 H), 4.69 (dd, *J* = 18.7, 3.0 Hz, 1 H), 3.55 (dt, *J* = 10.4, 4.3 Hz, 1 H), 3.43 (ddd, *J* = 18.8, 4.0, 2.2 Hz, 1 H), 2.67–2.62 (m, 1 H), 2.53–2.44 (m, 1 H), 2.40–2.28 (m, 2 H), 2.22–2.16 (m, 1 H), 2.15–2.09 (m, 1 H), 2.06 (dd, *J* = 7.3, 3.4 Hz, 1 H), 2.04–1.82 (m, 4 H), 1.53 (ddd, *J* = 13.3, 7.3, 3.1 Hz, 1 H).

$^{13}$C NMR (75 MHz, $CDCl_3$): δ = 217.3 (C), 169.6 (C), 124.6 (CH), 124.0 (CH), 56.2 (C), 52.4 (CH), 42.9 ($CH_2$), 38.7 ($CH_2$), 36.2 ($CH_2$), 32.5($CH_2$), 26.5 ($CH_2$), 24.3 ($CH_2$), 19.7 ($CH_2$).

### 1′,6′,9′,9a′-Tetrahydro-2′*H*,4′*H*-spiro[indene-2,3′-quinolizine]-1,4′(3*H*)-dione (9iaa)

To a one-necked round-bottomed flask, equipped with a magnetic stirring bar under an argon atmosphere, were introduced spiro compound **8iaa** (53 mg, 0.16 mmol) in $CH_2Cl_2$ (5.6 mL), followed by Grubbs II catalyst (7.13 mg, 5 mol%). The mixture was stirred at r.t. for 4 h (the reaction was monitored by TLC). The mixture was then filtered and was purified by flash chromatography on silica gel. The two diastereomers were separated.

First fraction: one diastereomer was isolated as a brown oil (12 mg, 39%); $R_f$ = 0.3 ($Et_2O$/PE; 8:2).

$^1$H NMR (400 MHz, $CDCl_3$): δ = 8.05 (d, *J* = 7.8 Hz, 1 H), 7.47 (td, *J* = 7.5, 1.2 Hz, 1 H), 7.30 (t, *J* = 7.6 Hz, 1 H), 7.23 (d, *J* = 7.6 Hz, 1 H), 5.79 (ddd, *J* = 9.7, 5.5, 1.9 Hz, 1 H), 5.71 (dd, *J* = 10.4, 1.4 Hz, 1 H), 4.75 (d, *J* = 18.9 Hz, 1 H), 3.69 (td, *J* = 10.5, 4.1 Hz, 1 H), 3.59 (ddd, *J* = 18.8, 3.9, 2.0 Hz, 1 H), 3.03 (dd, *J* = 11.6, 6.3 Hz, 1 H), 2.96 (dd, *J* = 15.4, 7.7 Hz, 1 H), 2.33–2.23 (m, 1 H), 2.22–2.12 (m, 1 H), 2.06 (dd, *J* = 18.6, 2.4 Hz, 1 H), 2.02–1.95 (m, 1 H), 1.89 (ddd, *J* = 13.8, 11.0, 3.1 Hz, 1 H), 1.69–1.59 (m, 1 H).

$^{13}$C NMR (101 MHz, $CDCl_3$): δ = 197.55 (C), 169.65 (C), 143.28 (C), 133.61 (CH), 131.34 (C), 128.73 (CH), 128.37 (CH), 126.89 (CH), 124.84 (CH), 124.37 (CH), 53.92 (C), 52.48 (CH), 43.29 ($CH_2$), 32.74 ($CH_2$), 25.59 ($CH_2$), 25.20 ($CH_2$), 23.56 ($CH_2$).

Second fraction: one diastereomer was isolated as a brown oil (10 mg, 33%); $R_f$ = 0.2 ($Et_2O$/PE, 8:2).

$^1$H NMR (400 MHz, $CDCl_3$): δ = 7.77 (d, *J* = 7.7 Hz, 1 H), 7.59 (t, *J* = 7.4 Hz, 1 H), 7.45 (d, *J* = 7.7 Hz, 1 H), 7.38 (t, *J* = 7.4 Hz, 1 H), 5.80 (ddd, *J* = 9.9, 5.0, 2.3 Hz, 1 H), 5.72 (dd, *J* = 10.2, 2.4 Hz, 1 H), 4.69 (d, *J* = 19.3 Hz, 1 H), 3.80–3.69 (m, 2 H), 3.59 (dd, *J* = 19.1, 2.3 Hz, 1 H), 3.00 (d, *J* = 16.9 Hz, 1 H), 2.55–2.46 (m, 1 H), 2.27–2.13 (m, 4 H), 1.90–1.84 (m, 1 H).

$^{13}$C NMR (101 MHz, $CDCl_3$): δ = 205.41 (C), 169.51 (C), 153.49 (C), 135.52 (C), 135.19 (C), 127.79 (CH), 126.46 (CH), 124.96 (CH), 124.47 (CH), 123.89 (CH), 56.65 (CH), 53.03 (CH), 42.88 ($CH_2$), 41.11 ($CH_2$), 33.15 ($CH_2$), 28.96 ($CH_2$), 25.55 ($CH_2$).

### 1′,3,4,6′,9′,9a′-Hexahydro-1*H*,2′*H*,4′*H*-spiro[naphthalene-2,3′-quinolizine]-1,4′-dione (9jaa)

To a one-necked round-bottomed flask, equipped with magnetic stirring bar under an argon atmosphere, were introduced spiro compound **8jaa** (105 mg, 0.33 mmol) in $CH_2Cl_2$ (10 mL), followed by Grubbs II catalyst (14.3 mg, 5 mol%). The mixture was stirred at r.t. for 4 h (the reaction was monitored by TLC). The mixture was then filtered and purified by flash chromatography on silica gel. The two diastereomers were separated.

First fraction: one diastereomer was isolated as a brown solid (21 mg, 32%); $R_f$ = 0.41 ($Et_2O$/PE, 9:1).

$^1$H NMR (300 MHz, $CDCl_3$): δ = 8.03 (d, *J* = 7.8 Hz, 1 H), 7.46 (t, *J* = 7.5 Hz, 1 H), 7.30 (d, *J* = 7.3 Hz, 1 H), 7.22 (d, *J* = 7.6 Hz, 1 H), 5.79 (dd, *J* = 12.1, 3.3 Hz, 1 H), 5.69 (d, *J* = 10.3 Hz, 1 H), 4.74 (d, *J* = 18.8 Hz, 1 H), 3.67 (dd, *J* = 10.3, 5.1 Hz, 1 H), 3.57 (d, *J* = 18.9 Hz, 1 H), 2.99 (dt, *J* = 16.0, 7.1 Hz, 3 H), 2.7–1.91 (m, 6 H), 1.63 (dd, *J* = 13.9, 6.8 Hz, 1 H).

$^{13}$C NMR (75 MHz, $CDCl_3$): δ = 197.3 (C), 169.4 (C), 143.1 (C), 133.4 (CH), 131.1 (C), 128.6 (CH), 128.1 (CH), 126.6 (CH), 124.5 (CH), 124.3 (CH), 53.7 (CH), 52.3 (C), 43.1 ($CH_2$), 32.5 ($CH_2$), 32.5 ($CH_2$), 25.4 ($CH_2$), 25.0 ($CH_2$), 23.3 ($CH_2$).

Second fraction: one diastereomer was isolated as a brown solid (2.5 mg, 38%); mp 128 °C; $R_f$ = 0.25 ($Et_2O$/PE, 9:1).

$^1$H NMR (400 MHz, $CDCl_3$): δ = 8.05 (d, *J* = 7.4 Hz, 1 H), 7.47 (td, *J* = 7.5, 1.1 Hz, 1 H), 7.30 (t, *J* = 7.5 Hz, 1 H), 7.23 (d, *J* = 7.6 Hz, 1 H), 5.82–5.76 (m, 1 H), 5.72 (dd, *J* = 10.5, 1.5 Hz, 1 H), 4.76 (d, *J* = 18.8 Hz, 1 H), 3.69 (td, *J* = 10.4, 4.1 Hz, 1 H), 3.59 (dd, *J* = 18.9, 1.7 Hz, 1 H), 3.03 (dd, *J* = 11.5, 6.0 Hz, 2 H), 2.97 (dd, *J* = 15.4, 7.6 Hz, 1 H), 2.33–2.12 (m, 4 H), 2.06 (dd, *J* = 15.3, 2.3 Hz, 1 H), 2.03–1.94 (m, 1 H), 1.89 (ddd, *J* = 13.8, 11.0, 3.1 Hz, 1 H).

$^{13}$C NMR (101 MHz, $CDCl_3$): δ = 197.41 (C), 169.51 (C), 143.15 (C), 133.47 (CH), 131.22 (C), 128.59 (CH), 128.25 (CH), 126.76 (CH), 124.72 (CH), 124.23 (CH), 53.79 (C), 52.34 (CH), 43.15 ($CH_2$), 32.61 ($CH_2$), 29.70 ($CH_2$), 25.47 ($CH_2$), 25.07 ($CH_2$), 23.43 ($CH_2$).

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## Supporting Information

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(31) CCDC 1429887 (**3ed**), CCDC 1429886 (**5ld**), and CCDC 1430278 (**8fb**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/getstructures.