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Combination of Rearrangement with Metallic and Organic Catalyses – a Step- and Atom-Economical Approach to α-Spirolactones and -lactams

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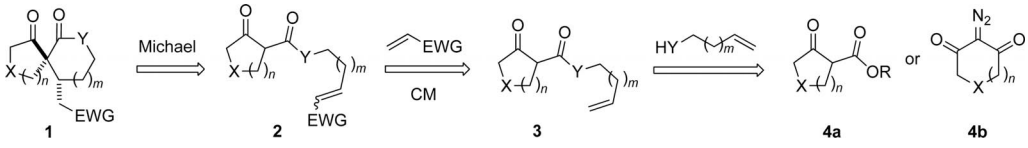
A general synthetic route to α-spirolactones and -lactams from 2-diazo-1,3-dicarbonyl compounds, (homo)allylic alcohols or amines and acrylic derivatives, involving a single consecutive reaction consisting of a Wolff rearrangement/α-oxo ketene trapping/cross metathesis/Michael addition sequence is described. During the consecutive reaction optimization, the organocatalytic activity of *N*,*N*-diaryl-1,3-imidazol(in)-2-ylidene N-heterocyclic carbenes (NHCs) in the Michael addition of 1,3-dicarbonyl compounds was discovered. A conceptually attractive version of the consecutive reaction was then developed, involving the Grubbs–Hoveyda ruthenium-based precatalyst containing the SIMes [1,3-bis(2,4,6-trimethylphenyl)imidazolin-2-ylidene] NHC ligand as the source of both the organometallic catalyst of the cross metathesis and the organic catalyst of the intramolecular Michael addition.

Introduction

Spiro compounds form a class of molecules with unique chemical and conformational features often associated with important biological properties. They have attracted considerable attention from the synthetic community and still constitute an active domain of research.[1] In complex bioactive molecules containing a spiro moiety, it often occurs that simplified analogs retaining the spiro structural domain exhibit a biological profile comparable to that of the parent compounds.[2] Therefore, original stereoselective synthetic strategies targeting spiro compounds are of importance for the development of new medicinally relevant scaffolds. An important focus for contemporary organic synthesis is economy.[3] Indeed, the efficiency of a synthetic sequence is determined by issues of brevity and sustainability, as witnessed by the tremendous efforts currently directed at the development of multiple-bond-forming transformations (MBFTs)[4] and catalytic chemical processes[5] for the simple creation of molecular complexity and functional diversity. It is now recognized that the step count is one of the most important criteria when evaluating the efficiency of a synthesis.

In this context, and in connection with our interest in the applications of 1,3-dicarbonyl compounds in MBFTs[6] and the construction of functionalized spirocyclic scaffolds,[7] we present a new synthetic approach to α-spirolactones and -lactams **1**. Retrosynthetic analysis involves a catalytic Michael-based spirocyclization of substrates **2**, which should be available by olefin cross metathesis (CM) between acrylic derivatives and the terminal olefin in esters (or amides) **3**,[8] obtained from **4a** by transesterification (or transamidation), or alternatively from the 2-diazo-1,3-diketones **4b** following a Wolff rearrangement and trapping of the resultant α-oxo ketene (Scheme 1). Ideally, all of these transformations should be conducted in a single consecutive reaction.[4]



Scheme 1. Retrosynthetic analysis for α-spirolactones and -lactams (n = 1, 2; m = 0, 1).

In this article, we report our efforts to develop a general synthetic route to the spiro compounds **1** in a single consecutive reaction, and how this work has led to the discovery

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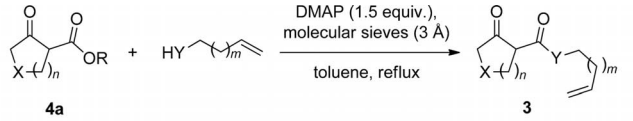
of the excellent organocatalytic activity of *N*,*N*-diaryl-1,3-imidazol(in)-2-ylidenes in the Michael addition of 1,3-dicarbonyl compounds.

Results and Discussion

The study started with the preparation of 1,3-dicarbonyl compounds of type **3** in the five- to seven-membered ring series either by transesterification and transamidation reactions from **4a** (Table 1),[9] or by our recently developed microwave-assisted Wolff rearrangement/α-oxo ketene trapping reaction from **4b** (Table 2).[10] It must be highlighted that, although the transesterification (and transamidation) strategy is quite general, it requires an excess of nucleophile and additives, prolonged reaction times to proceed efficiently and a final purification step. Conversely, when applicable, the Wolff rearrangement/α-oxo ketene trapping reactions require no excess of substrate or additive, the reactions are efficient and require no purification (only nitrogen gas was produced as byproduct), the reaction times were short, and the sequence required a minimum of energy.

Table 1. Transesterification and transamidation reactions.[a]

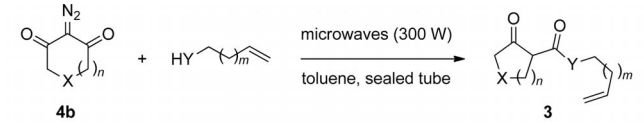


4a 3

Entry	R'–YH	Product[b]	Entry	R'–YH	Product[b]
1	HO (3 equiv., 7 h)	**3a** (79%)	6	HO (solvent, 72 h)	**3f** (65%)
2	HO (3 equiv., 6 h)	**3b** (79%)	7	HN (15 equiv., 56 h)	**3g** (63%)
3	HN (5 equiv., 27 h)	**3c** (94%)	8	HO (solvent, 48 h)	**3h** (77%)
4	HN (5 equiv., 10 h)	**3d** (58%)	9	HO (solvent, 48 h)	**3i** (74%)
5	HN (5 equiv., 48 h)	**3e** (63%)			

[a] Products of Entries 1–6 were obtained from the corresponding methyl esters and those of Entries 7–9 were obtained from the corresponding ethyl esters; see Supporting Information for the preparation of substrates **4a** for Entries 4–7. [b] Yields for isolated products after flash chromatography. DMAP = 4-(dimethylamino)pyridine, MMP = 3-methoxyphenyl.

Table 2. Wolff rearrangement/α-oxo ketene trapping reactions.[a]



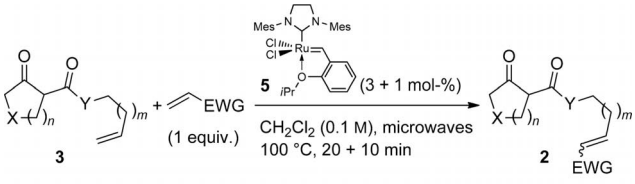
4b 3

Entry	R'–YH	Product[b]	Entry	R'–YH	Product[b]
1	HO (1 equiv., 3 min)	**3a** (99%)	4	HO (1 equiv., 3 min)	**3i** (94%)
2	HO (1 equiv., 3 min)	**3b** (96%)	5	HO (1 equiv., 3 min)	**3j** (96%)
3	HN (1 equiv., 3 min)	**3c** (96%)	6	HN, Ph (1 equiv., 2 min)	**3k** (93%)

[a] Results of Entries 5 and 6 are reproduced from ref.[10] for comparison. [b] Yields for isolated clean crude products.

With a series of olefinic substrates **3** in hand, we turned our attention to their required CM reactions with a variety of acrylic derivatives, keeping in mind our objective of a single consecutive reaction for the sequence **4** → **1**. Thus, we optimized the CM reactions on a few substrates **3** considering only reaction conditions involving a single equivalent of the acrylic derivative reaction partners. This should secure a subsequent Michael-based spirocyclization in a consecutive manner without competition with intermolecular processes with the excess of acrylic reagent. Based on our previous work with the microwave-assisted CM of olefins,[11] and owing to the efficiency and cleanliness of the metathesis reactions under these conditions,[12] we only considered dielectric heating as the activation mode. After a short optimization study, we found that these CM reactions were best performed in dichloromethane with the Grubbs–Hoveyda precatalyst **5** introduced in two portions (3 then 1 mol-%) at 100 °C. These reaction conditions proved quite general (see Table 3 and below), and few limitations were encountered. Among these, substrate **3d** containing a basic nitrogen atom was recovered unchanged probably due to catalyst deactivation.[13] From the results reported in Table 3, it also appears that allylic esters (or amides, see below) are less reactive than their homoallylic counterparts (Entries 1 and 2 vs. 3–6). This is most likely due to the formation of stabilized six-membered-ring ruthenium chelate complexes with allylic esters (or amides), which inhibit the reactions.[14] It must be mentioned here that the spiro product **1** was not detected after the CM in any case, indicating that **5** and the ruthenium species derived from **5** do not catalyze the Michael-induced spirocyclization (see below).

Table 3. CM reactions of **3** with 1 equiv. of acrylic derivatives.



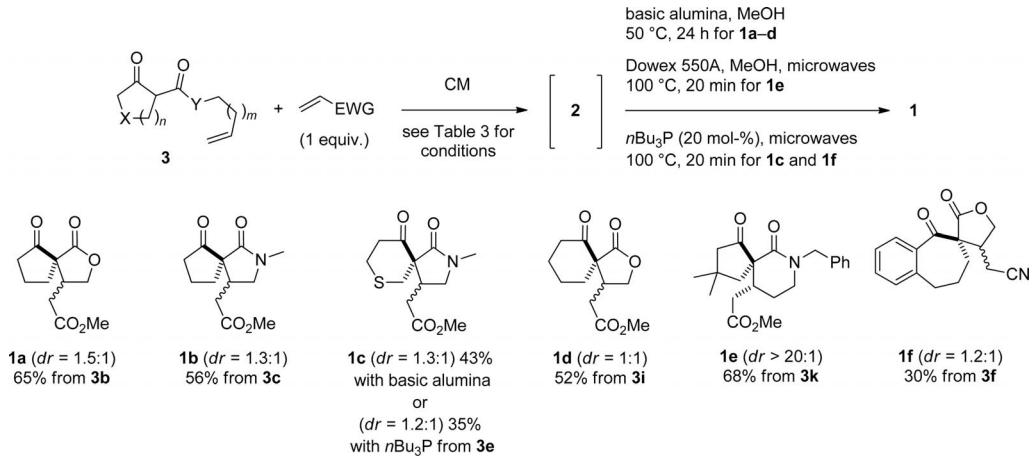
Entry	Substrate **3**	EWG	Product	Yield [(*E*)/(*Z*)][a]
1	**3b**	CO_2Me	**2a**	53% (> 10:1)
2	**3i**	CN	**2b**	52% (1:3)
3	**3a**	CN	**2c**	85% (1:3)
4	**3a**	COMe	**2d**	66% (> 10:1)
5	**3j**	CO_2Me	**2e**	78% (> 10:1)
6	**3k**	CO_2Me	**2f**	73% (> 10:1)

[a] Yields for isolated products after silica gel flash chromatography. The diastereomeric ratios were determined from ^1H and ^{13}C NMR spectroscopy of the crude material.

When the CM reactions were performed under the above conditions, relatively clean final reaction mixtures were obtained (essentially dichloromethane solutions of **2**), which were used directly in the next transformation. Therefore, our early attempts for the consecutive reaction of **3** → **1** were realized with various known catalysts for the Michael addition. Among these, we have successfully examined basic alumina,[15] Dowex 550A resin[16] and tributylphosphane.[17] Practically, basic alumina or Dowex resin and methanol were added directly to the cooled CM reaction mixture to afford the expected spiro compounds **1** upon heating in good yields for the consecutive CM/Michael reaction (Scheme 2). However, basic alumina was found to be ineffective for the formation of δ-latones and δ-lactams, and the Dowex resin promoted only the spirocyclization of β-keto amide substrates. This first set of experiments also revealed an excellent diastereoselectivity for the spiro[4,5] series (e.g. δ-lactams **1e**), a feature later found to be general regardless of the nature of the catalyst used to promote the Michael-based spirocyclization. Finally, when a catalytic amount of tributylphosphane was used for the spirocyclization step of the consecutive reaction, no methanol was required, and spiro compounds **1c** and **1f** were obtained in moderate yields from **3e** and **3f**, respectively (Scheme 2).

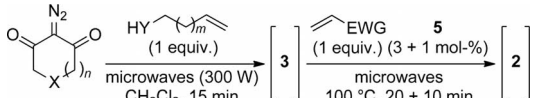
At this point, we surmised that the entire sequence Wolff rearrangement/α-oxo ketene trapping/CM/Michael reaction corresponding to the desired transformation **4b** → **1** could be performed in a single consecutive reaction, provided that the Wolff rearrangement could be performed in the CM reaction solvent (i.e. dichloromethane) rather than toluene. Accordingly, we briefly examined the microwave-assisted Wolff rearrangement in dichloromethane, and not surprisingly (both solvents have similar loss tangent, $\tan\delta \approx 0.04$[18]) the reaction was found to be equally efficient and clean as in toluene, although somewhat slower. Thus, the consecutive reaction leading to **1** from **4b** was attempted as follows: microwave-assisted Wolff rearrangement/α-oxo ketene trapping in dichloromethane for 15 min (300 W), addition of the acrylic derivative (1 equiv.) and the CM precatalyst **5** (3 + 1 mol-%) to the reaction mixture followed by microwave irradiation at 100 °C, and finally addition of tributylphosphane (20 mol-%) and microwave irradiation at 100 °C. Rewardingly, a variety of α-spirolactones and -lactams **1** were obtained under these conditions involving a single consecutive reaction, and the products were all obtained in good yields considering that four chemical bonds are created (and one broken) in the transformation. The results are presented in Table 4. A single diastereomer of α-spiro-δ-lactones **1i** and **1j** was obtained (Entries 4 and 5, respectively), probably due to the existence of a well-defined six-membered chair-like transition state in these cases with both (*E*) and (*Z*) CM products **2**, whereas the formation of α-spiro-γ-lactones and -γ-lactams **1a**, **1g** and **1h** was found to be poorly diastereoselective (Entries 1–3). With the in situ formed CM product **2** derived from the chiral α-oxo ketene obtained from **4b** (X = CHMe), homoallyl alcohol and acrylonitrile (Entry 6), a modest but effective chiral induction was observed, the Michael-based spirocyclization occurring preferentially *anti* to the methyl group on the cyclopentane ring. The structures of spiro compounds **1j** and **1k** (major diastereomer) have been obtained by X-ray diffraction analysis (Figure 1).[19] Finally, it is important to note that, quite surprisingly, no α-spiro-δ-lactams (e.g. **1e**) were obtained under these conditions leaving the corresponding monocyclic intermediates **2** unchanged (see below).

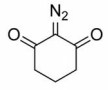
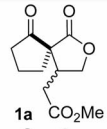
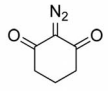
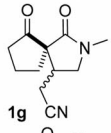
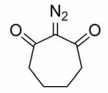
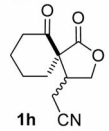
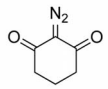
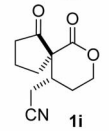
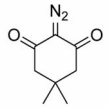
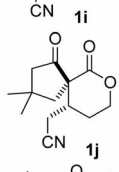
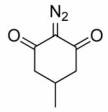
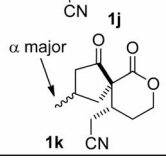
In order to better evaluate the efficiency (as defined in the Introduction) of the consecutive reaction **4b** → **1** vs. the three-step sequence **4b** → **3** → **2** → **1**, the yield of the tributylphosphane-promoted spirocyclization step was needed starting from pure compound **2**. We chose the transformation **2c** → **1i** for this purpose. Thus, in separate experiments, a dichloromethane solution of pure β-oxo ester **2c** was treated with up to 1 equiv. of tributylphosphane and irradiated with microwaves at 100 °C, according to the conditions developed for the last elemental transformation of the consecutive reactions presented in Scheme 2 and Table 4. To our great surprise, substrate **2c** was totally inert



Scheme 2. Consecutive CM/Michael reactions.

Table 4. Consecutive Wolff rearrangement/α-oxo ketene trapping/CM/Michael reactions.



Entry	4b	Product 1	Yield (*dr*)[a]
1			51% (1.6:1)
2			34% (1.2:1)
3			49% (1.8:1)
4[b]			60% (> 20:1)
5			40% (> 20:1)
6			41% (> 70:20:3.5:1)

[a] Yields for isolated products after flash chromatography. The diastereomeric ratios were determined by ^{1}H and ^{13}C NMR spectroscopy of the crude material. [b] Conditions for the last step: nBu$_3$P (10 mol-%), microwaves, 100 °C, 10 min.

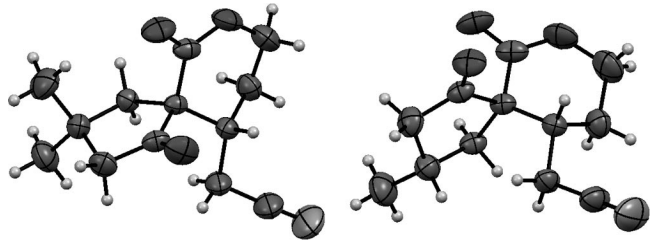
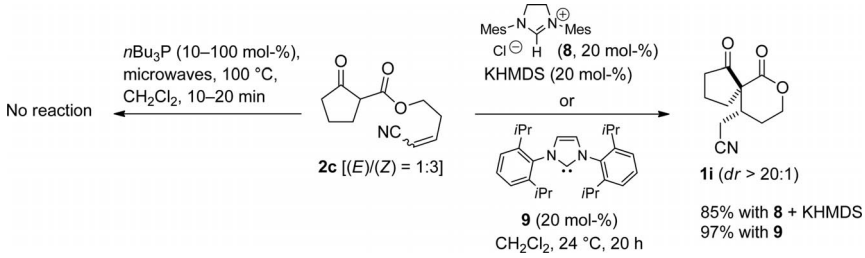


Figure 1. ORTEP diagrams of **1j** (left) and **1k** (major diastereomer, right) displayed at 50% probability.[19]

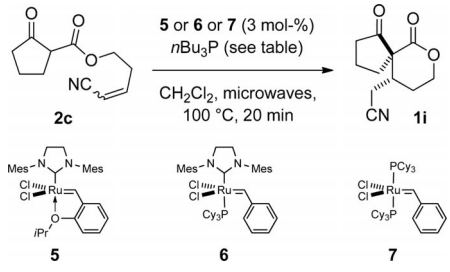
under these conditions and was recovered quantitatively (Scheme 3, left). From these results, we concluded that, although tributylphosphane is an excellent promoter of the transformation **2** → **1** under the consecutive reaction conditions, it is not a catalyst for this transformation. Logically, we searched for the actual catalyst of the Michael-based spirocyclization. The most reasonable hypothesis was that tributylphosphane was acting as a competing ligand at the ruthenium centre in **5**, or more likely in the other ruthenium complexes formed during the CM reaction. Several control experiments were conducted with the three metathesis precatalysts **5**–**7** and tributylphosphane (Table 5). From this set of experiments it was concluded that (1) only **5** and **6** containing a SIMes NHC ligand led to the catalyst for the Michael addition (compare Entries 2, 4, 6 and 7 with 8), and (2) this catalyst is generated only when the reactions are performed under ethylene (Entries 2, 4, 6, 7). Related domino CM/Michael addition reactions have been reported in the past few years, invoking the Lewis acidity of either the (methylidene)ruthenium 14-electron complex [(SIMes)(Cl)$_2$Ru=CH$_2$] generated during the metathesis catalytic cycle or the ruthenium hydride species derived from degradation of the latter[20] as the activation mode of the Michael addition.[8b,21] However, in this case, the Lewis acidity of the ruthenium species formed during the reaction should be quenched by the excess phosphane (relative to the ruthenium), and thus, such an activation mode for the



Scheme 3. NHC-catalyzed Michael-induced spirocyclization. Mes = mesityl = 2,4,6-trimethylphenyl.

Michael addition is unlikely. The fact that the NHC-free **7** combined with tributylphosphane and ethylene did not promote the Michael addition (Entry 8) brought the hypothesis that the SIMes NHC in **5** and **6** is responsible for the observed catalytic activity. Yet another set of control experiments allowed us to confirm this hypothesis: to a dichloromethane solution of **5** under ethylene was added 5 equiv. of tributylphosphane, the mixture was irradiated with microwaves at 100 °C for 20 min, and a preparative TLC of the concentrated product mixture allowed the isolation of the chlorohydrate of the NHC SIMes (**8**, confirmed by comparison of ^{1}H NMR spectroscopic data with those of an authentic sample) together with unidentified ruthenium species. This experiment indicated that a NHC/tributylphosphane exchange occurred at the metal centre, presumably involving the 14-electron complex [(SIMes)(Cl)$_2$Ru=CH$_2$]. Such NHC/phosphane ligand exchange reactions are rare due to the strong NHC–metal interaction, and the tributylphosphane analogue of **6** [(SIMes)(Cl)$_2$(*n*Bu$_3$P)Ru=CHPh] was reported to be stable in the presence of an excess of tributylphosphane at room temperature.[22] Finally, we examined the intramolecular Michael addition of β-oxo ester **2c** with 20 mol-% of SIMes {generated from **8** and KHMDS [potassium bis(trimethylsilyl)amide]} at room temperature, and the spiro product **1i** was obtained in 85% yield with excellent diastereoselectivity, demonstrating the organocatalytic activity of NHCs in the Michael addition of 1,3-dicarbonyl compounds (Scheme 3, right).[23] With the commercially available stable NHC IPr [**9**, 1,3-bis(2,6-diisopropylphenyl)imidazol-2-ylidene], the same reaction afforded a 97% yield of the spiro product **1i**. It was concluded that, under the conditions of the consecutive reactions involving a tributylphosphane-promoted spirocyclization (Table 4 and in part Scheme 2), the actual catalyst of the intramolecular Michael addition step is the NHC SIMes originally present as an ancillary ligand on **5**.[24] These reactions represent examples of a par-

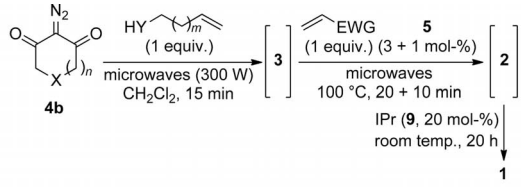
Table 5. Control experiments with metathesis precatalysts and tributylphophane.

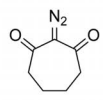
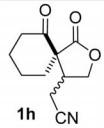
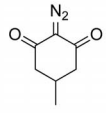
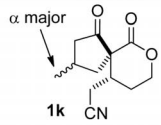
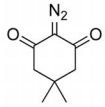
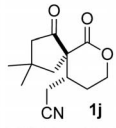
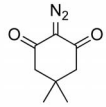
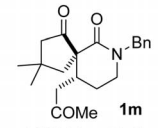
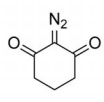
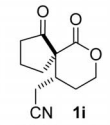
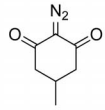
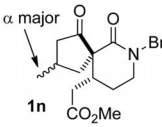
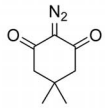
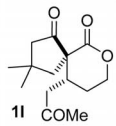
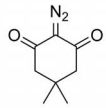
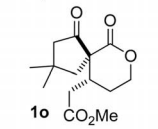


Entry	Conditions	*n*Bu$_3$P	Spirocyclization[a]
1	**5** under argon	10 mol-%	no
2	**5** under ethylene	10 mol-%	yes
3	**5** under argon	50 mol-%	no
4	**5** under ethylene	50 mol-%	yes
5	**5** under argon	100 mol-%	no
6	**5** under ethylene	100 mol-%	yes
7	**6** under ethylene	100 mol-%	yes
8	**7** under ethylene	100 mol-%	no

[a] These qualitative experiments were analyzed by TLC, and full conversion was not achieved when spirocyclization occurred.

Table 6. Modified consecutive Wolff rearrangement/α-oxo ketene trapping/CM/Michael reactions.



Entry	4b	Product 1[a]	Entry	4b	Product 1[a]
1		 **1h** 50% (*dr* = 2.7:1)	5		 **1k** 41% (*dr* > 80:20:4:1)
2		 **1j** 39% (*dr* > 20:1)	6		 **1m** 77% (*dr* > 20:1)
3		 **1i** 54% (*dr* > 20:1)	7		 **1n** 50% (*dr* > 56:20:2.8:1)
4		 **1l** 44% (*dr* > 20:1)	8		 **1o** 55% (*dr* > 20:1)

[a] Yields for isolated products after flash chromatography. The diastereomeric ratios were determined by ^{1}H and ^{13}C NMR spectroscopy of the crude material.

ticularly attractive concept of consecutive reactions involving the same organometallic precatalyst as the successive source of both metallic and organic catalysts.

Having demonstrated that the Michael addition elemental step could be efficiently catalyzed by the NHC **9**, we briefly explored a modified version of the consecutive Wolff rearrangement/α-oxo ketene trapping/CM/Michael reaction involving a catalytic amount of **9** instead of tributylphosphane (Table 6). These modified conditions proved equally efficient and general, leading to the same observations, with the advantage of generalizing the method to the preparation of α-spiro-δ-lactams (**1m** and **1n**, Entries 6 and 7, respectively) unavailable under the previous conditions (see Table 4).

Conclusions

A general stereoselective synthetic route to α-spirolactones and -lactams from 2-diazo-1,3-dicarbonyl compounds, (homo)allylic alcohols or amines, and acrylic derivatives, involving a single consecutive reaction consisting of a Wolff rearrangement/α-oxo ketene trapping/CM/Michael addition sequence is described in full. The yields are typically in the 40–60% range (up to 77%), but the simplicity and cleanliness of the reactions, combined with the chemical diversity accessible and the rapid increase in molecular complexity largely make up for this small limitation. In the course of this work, the superiority of the microwave-assisted Wolff rearrangement/α-oxo ketene trapping reaction over the classical transesterification/transamidation strategy was confirmed for the preparation of β-oxo esters and β-oxo amides where applicable. Thanks to microwave technology, we have developed "clean" conditions for the CM of terminal olefins with acrylic derivatives using only 1 equiv. of each olefinic substrate and 4 mol-% of metallic precatalyst in reduced reaction times. The organocatalytic activity of *N*,*N*-diaryl-1,3-imidazol(in)-2-ylidene NHCs in the Michael addition of 1,3-dicarbonyl compounds and analogues was discovered and exploited in the consecutive reaction leading to α-spirolactones and -lactams. A conceptually attractive version of this consecutive reaction was developed, which involved the Grubbs–Hoveyda precatalyst **5** containing the SIMes NHC ligand as the successive source of both the organometallic CM catalyst and the organic catalyst for the intramolecular Michael addition when the last step is promoted by a catalytic amount of tributylphosphane to release the NHC from the ruthenium centre. Overall, it can be emphasized that the consecutive reaction described here has allowed the preparation of the target α-spirolactones and -lactams by using only a single equivalent of each of the three reaction partners and a catalytic amount of additives, which was designed to produce only nitrogen and ethylene gases as byproducts, and required minimum energy thanks to microwave technology.

Experimental Section

General Remarks: Reactions were generally performed in oven-dried round-bottomed flasks equipped with a Teflon-coated stirring bar in anhydrous solvents under argon. Reactions under microwave irradiation were performed in oven-dried 10 mL sealable Pyrex tubes equipped with a Teflon-coated stirring bar (obtained from CEM). All reactions under microwave irradiation (ν = 2.45 GHz) were performed in a CEM Discover 1–300 W system equipped with build-in pressure measurement sensor and a vertically focused IR temperature sensor. All reagents were obtained from commercial sources and used as supplied unless otherwise stated. Anhydrous CH_2Cl_2 and toluene were obtained from an MBraun SPS-800 solvent purification system. MeOH was dried by heating to reflux with magnesium turnings and then distilled under argon. All acrylic derivatives were distilled prior use. Petroleum ether refers to the fraction distilled between 40 °C and 65 °C. The reactions were monitored by TLC, which was performed with Merck 60F254 plates and visualized with an ethanolic solution of *p*-anisaldehyde and sulfuric acid or an ethanolic solution of molybdophosphoric acid. Flash chromatography was performed with Merck 230–400 mesh silica gel. NMR spectroscopic data were recorded with a Bruker Avance 300 spectrometer in $CDCl_3$, and chemical shifts (δ) are given in ppm relative to the residual nondeuterated solvent signal for ^1H ($CHCl_3$: δ = 7.26 ppm) and relative to the deuterated solvent signal for ^{13}C ($CDCl_3$: δ = 77.0 ppm); coupling constants (J) are in Hz. Mass spectra were recorded with a Bruker Esquire 6000 spectrometer equipped with an electrospray ionization source and an ion trap detector. Melting points were measured with a Büchi B-540 apparatus and are uncorrected. High-resolution mass spectra were obtained from Spectropole (http://www.spectropole.u-3mrs.fr/).

Compounds of Tables 1 and 2: The substrates of Entries 4,[25] 5,[26] 6[27] and 7[28] in Table 1, the diazo substrates[29] and the nucleophile of Entry 6[30] in Table 2 were prepared according to literature procedures.

General Procedure for the Preparation of Compounds in Table 1: To a solution of β-oxo ester **4a** (1.0 mmol) in anhydrous toluene (0–5 mL) were successively added the nucleophile (3.0 equiv. to solvent), DMAP (1.5 mmol) and molecular sieves (3 Å) (0.5 g). The reaction mixture was stirred with heating to reflux for 6–120 h with periodic monitoring by TLC. When full conversion was reached, the reaction was quenched with an aqueous solution of hydrochloric acid (1 M). The resulting acidic aqueous medium was washed three times with ethyl acetate, the combined organic layers were washed with water then brine, dried with anhydrous sodium sulfate, filtered and concentrated under vacuum to give the crude product, which was purified by silica gel flash chromatography with EtOAc/petroleum ether to afford pure **3**.

General Procedure for the Preparation of Compounds in Table 2:[10] A solution of 2-diazo-1,3-diketone **4b** (1.0 mmol) and nucleophile (1.0 mmol) in toluene (2 mL) in a 10 mL sealed tube equipped with a Teflon-coated stirring bar was irradiated with microwaves at 300 W until the temperature reached 180 °C, the pressure reached 17 bars or for a maximum time of 3 min, whereupon the reaction mixture was cooled to 40 °C with an air flow. Concentration of the reaction mixture followed by high-vacuum removal of volatiles afforded the clean crude product **3** without need for purification. Compounds **3b**,[31] **3c**,[32] **3j**[10] and **3k**[10] exhibited physical and spectroscopic properties identical to previously reported data.

Compound 3a: According to the general procedure, **3a** was obtained as a colourless oil (144 mg, 79% for Table 1, and 180 mg, 99% for Table 2). R_f (50% EtOAc in petroleum ether) = 0.75. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 212.2 (C), 169.3 (C), 133.7 (CH), 117.3 (CH_2), 64.2 (CH_2), 54.7 (CH), 38.0 (CH_2), 33.0 (CH_2), 27.4 (CH_2), 20.9 (CH_2) ppm. ^1H NMR (300 MHz, $CDCl_3$): δ = 5.77 (dddd, J

= 6.7, 6.9, 10.2, 17.0 Hz, 1 H), 5.16–5.01 (m, 2 H), 4.17 (dd, *J* = 6.7, 6.8 Hz, 2 H), 3.13 (dd, *J* = 8.8, 9.0 Hz, 1 H), 2.53–2.01 (m, 6 H), 1.93–1.77 (m, 2 H) ppm. MS (ESI+): *m*/*z* = 183 $[M + H]^+$, 205 $[M + Na]^+$, 221 $[M + K]^+$.

Compound 3d: According to the general procedure, **3d** was obtained as a colourless oil (167 mg, 58%). R_f (30% EtOAc in petroleum ether) = 0.42. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 207.0 (C), 206.8 (C), 166.3 (C), 165.8 (C), 160.8 (2 C), 148.6 (C), 148.6 (C), 132.6 (CH), 132.2 (CH), 130.1 (2CH), 117.5 (CH_2), 116.9 (CH_2), 105.8 (2 CH), 103.3 (2 CH), 99.3 (2 CH), 55.8 (CH_2), 55.7 (CH_2), 55.1 (2 CH_3), 52.3 (CH_2), 51.6 (CH_2), 51.3 (CH), 50.6 (CH), 49.0 (CH_2), 48.7 (CH_2), 35.2 (CH_3), 34.3 (CH_3) ppm. ^1H NMR (300 MHz, $CDCl_3$): δ = 7.19 (dd, *J* = 8.2, 8.2 Hz, 2 H), 6.40 (dd, *J* = 2.3, 8.0 Hz, 2 H), 6.29 (ddd, *J* = 2.3, 2.6, 7.9 Hz, 2 H), 6.25–6.20 (m, 2 H), 5.93–5.69 (m, 2 H), 5.30–5.14 (m, 4 H), 4.14–3.70 (m, 14 H), 3.8 (s, 6 H), 3.15 (s, 3 H), 3.0 (s, 3 H) ppm. MS (ESI+): *m*/*z* = 289 $[M + H]^+$, 311 $[M + Na]^+$, 227 $[M + K]^+$.

Compound 3e: According to the general procedure, **3e** was obtained as a colourless oil (134 mg, 63%). R_f (60% EtOAc in petroleum ether) = 0.65. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 204.6 (C), 204.3 (C), 168.7 (C), 168.4 (C), 132.7 (CH), 132.4 (CH), 117.3 (CH_2), 117.1 (CH_2), 57.2 (CH), 56.8 (CH), 52.2 (CH_2), 50.2 (CH_2), 44.3 (CH_2), 44.0 (CH_2), 34.6 (CH_3), 33.7 (CH_3), 32.9 (CH_2), 32.8 (CH_2), 30.2 (CH_2), 30.0 (CH_2) ppm. ^1H NMR (300 MHz, $CDCl_3$): δ = 5.84–5.69 (m, 2 H), 5.29–5.10 (m, 4 H), 4.17–3.65 (m, 6 H), 3.48–3.33 (m, 2 H), 3.11–2.63 (m, 10 H), 2.97 (s, 3 H), 2.83 (s, 3 H) ppm. MS (ESI+): *m*/*z* = 214 $[M + H]^+$, 236 $[M + Na]^+$, 252 $[M + K]^+$.

Compound 3f: According to the general procedure, **3f** was obtained as a colourless oil (159 mg, 65%). R_f (10% EtOAc in petroleum ether) = 0.63. ^{13}C NMR (75 MHz, $CDCl_3$): keto form (ca. 30%): δ = 200.4 (C), 170.0 (C), 141.2 (C), 138.0 (C), 132.4 (CH), 131.8 (CH), 129.8 (CH), 129.1 (CH), 126.7 (CH), 118.4 (CH_2), 65.7 (CH_2), 56.6 (CH), 32.8 (CH_2), 25.3 (CH_2), 24.3 (CH_2); enol form (ca. 70%): δ = 172.6 (C), 170.7 (C), 141.0 (C), 135.6 (C), 132.2 (CH), 130.1 (CH), 128.9 (CH), 127.1 (CH), 126.3 (CH), 117.9 (CH_2), 100.1 (C), 65.0 (CH_2), 33.5 (CH_2), 31.7 (CH_2), 21.7 (CH_2) ppm. ^1H NMR (300 MHz, $CDCl_3$): δ = 12.61 (s, 0.7 H), 7.78–7.59 (m, 1 H), 7.47–7.27 (m, 2 H), 7.25–7.17 (m, 1 H), 6.00 (dddd, *J* = 5.5, 6.7, 10.5, 16.0 Hz, 0.7 H), 5.91 (dddd, *J* = 5.8, 6.8, 10.5, 16.1 Hz, 0.3 H), 5.41–5.22 (m, 2 H), 4.77–4.73 (m, 1.4 H), 4.70–4.64 (m, 0.6 H), 3.89–3.82 (m, 0.3 H), 2.98–2.92 (m, 0.6 H), 2.65 (dd, *J* = 6.9, 6.5 Hz, 1.4 H), 2.27–2.01 (m, 3.7 H), 1.94–1.76 (m, 0.3 H) ppm. MS (ESI+): *m*/*z* = 245 $[M + H]^+$, 267 $[M + Na]^+$, 283 $[M + K]^+$.

Compound 3g: According to the general procedure, **3g** was obtained as a colourless oil (186 mg, 63%). R_f (40% EtOAc in petroleum ether) = 0.50. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 203.9 (C), 203.6 (C), 167.6 (C), 167.3 (C), 154.4 (2 C), 132.6 (CH), 132.3 (CH), 117.3 (2CH_2), 80.7 (C), 80.6 (C), 53.6 (2 CH), 52.2 (2 CH_2), 50.1 (2 CH_2), 40.9 (2 CH_2), 40.7 (2 CH_2), 34.7 (2 CH_3), 28.3 (6 CH_3) ppm. ^1H NMR (300 MHz, $CDCl_3$): δ = 5.77 (dddd, *J* = 6.7, 6.9, 10.2, 17.2 Hz, 1 H), 5.75 (dddd, *J* = 6.7, 6.9, 10.2, 17.2 Hz, 1 H), 5.30–5.14 (m, 4 H), 4.30–3.83 (m, 6 H), 3.79–3.47 (m, 6 H), 3.40–3.25 (m, 2 H), 2.95 (s, 3 H), 2.87 (s, 3 H), 2.64–2.39 (m, 4 H), 1.47 (s, 9 H), 1.46 (s, 9 H) ppm. MS (ESI+): *m*/*z* = 297 $[M + H]^+$, 320 $[M + Na]^+$, 336 $[M + K]^+$.

Compound 3h: According to the general procedure, **3h** was obtained as a colourless oil (151 mg, 77%). R_f (20% EtOAc in petroleum ether) = 0.56–0.78. ^{13}C NMR (75 MHz, $CDCl_3$): keto form (ca. 40%): δ = 206.1 (C), 169.9 (C), 133.8 (CH), 117.2 (CH_2), 64.0 (CH_2), 57.1 (CH), 41.5 (CH_2), 32.9 (CH_2), 29.0 (CH_2), 23.2 (CH_2), 22.3 (CH_2); enol form (ca. 60%): δ = 172.5 (C), 172.1 (C), 133.9 (CH), 117.2 (CH_2), 97.7 (C), 63.1 (CH_2), 33.0 (CH_2), 29.9 (CH_2), 27.0 (CH_2), 22.3 (CH_2), 21.9 (CH_2) ppm. ^1H NMR (300 MHz, $CDCl_3$): δ = 12.16 (s, 0.9 H), 5.80 (dddd, *J* = 6.8, 6.9, 10.2, 17.0 Hz, 0.9 H), 5.71 (dddd, *J* = 6.7, 6.9, 10.2, 17.1 Hz, 0.1 H), 5.16–4.98 (m, 2 H), 4.18 (dd, *J* = 6.7, 6.7 Hz, 1.8 H), 4.14–4.10 (m, 0.2 H), 3.38–3.33 (m, 0.1 H), 2.41 (dddd, *J* = 1.2, 1.3, 6.8, 13.4 Hz, 2 H), 2.28–2.16 (m, 4 H), 1.72–1.54 (m, 4 H) ppm. MS (ESI+): *m*/*z* = 197 $[M + H]^+$, 219 $[M + Na]^+$, 235 $[M + K]^+$.

Compound 3i: According to the general procedure, **3i** was obtained as a colourless oil (135 mg, 74% for Table 1, and 171 mg, 94% for Table 2). R_f (20% EtOAc in petroleum ether) = 0.57–0.86. ^{13}C NMR (75 MHz, $CDCl_3$): keto form (ca. 30%): δ = 206.0 (C), 169.6 (C), 131.7 (CH), 118.4 (CH_2), 65.6 (CH_2), 57.1 (CH), 41.4 (CH_2), 29.9 (CH_2), 27.0 (CH_2), 23.2 (CH_2); enol form (ca. 70%): δ = 172.4 (C), 172.2 (C), 132.2 (CH), 117.7 (CH_2), 97.5 (C), 64.6 (CH_2), 29.0 (CH_2), 22.3 (CH_2), 22.3 (CH_2), 21.8 (CH_2) ppm. ^1H NMR (300 MHz, $CDCl_3$): δ = 12.13 (s, 0.7 H), 5.95 (dddd, *J* = 5.5, 6.7, 10.5, 17.2 Hz, 0.7 H), 5.91 (dddd, *J* = 5.8, 6.0, 10.5, 17.2 Hz, 0.3 H), 5.27 (dddd, *J* = 1.4, 1.5, 10.5, 17.2 Hz, 1.4 H), 5.40–5.10 (m, 0.6 H), 4.65 (ddd, *J* = 1.4, 1.5, 5.5 Hz, 1.4 H), 4.75–4.55 (m, 0.6 H), 3.41 (m, 0.3 H), 2.56–2.45 (m, 0.3 H), 2.42–2.10 (m, 3.7 H), 1.94–1.77 (m, 0.3 H), 1.72–1.56 (m, 3.7 H) ppm. MS (ESI+): *m*/*z* = 197 $[M + H]^+$, 219 $[M + Na]^+$, 235 $[M + K]^+$.

General Procedure for the Preparation of Compounds in Table 3: To a solution of **3** (0.50 mmol) in anhydrous dichloromethane (5 mL) were successively added the acrylic derivative (0.50 mmol) and **5** in two portions (0.015 mmol at the start, and 0.005 mmol after 20 min). The reaction vessel was sealed and irradiated with microwaves at 100 °C for 30 min (20, then 10 min). The solvent and volatiles were removed under vacuum, and the resulting crude product was purified by silica gel flash chromatography with EtOAc/petroleum ether to afford pure **2**. Compounds **2b**,[11b] **2c**[11a] and **2f**[23a] exhibited physical and spectroscopic properties identical to previously reported data.

Compound 2a: According to the general procedure, **2a** was obtained as a brown oil (60 mg, 53%). R_f (25% EtOAc in petroleum ether) = 0.33. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 211.7 (C), 168.6 (C), 166.2 (C), 140.8 (CH), 122.0 (CH), 63.2 (CH_2), 54.6 (CH), 51.7 (CH_3), 38.0 (CH_2), 27.3 (CH_2), 20.9 (CH_2) ppm. ^1H NMR (300 MHz, $CDCl_3$): δ = 6.97–6.87 (m, 1 H), 6.12–6.05 (m, 1 H), 4.84–4.77 (m, 2 H), 3.74 (s, 3 H), 3.22 (dd, *J* = 9.2, 9.0 Hz, 1 H), 2.44–2.24 (m, 4 H), 2.20–2.08 (m, 1 H), 1.94–1.79 (m, 1 H) ppm. HRMS (ESI+): *m*/*z* $[M + H]^+$: calcd. for $C_{11}H_{15}O_5^+$ 227.0916, obsd 227.0920.

Compound 2d: According to the general procedure, **2d** was obtained as a brown oil (74 mg, 66%). R_f (30% EtOAc in petroleum ether) = 0.45. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 211.9 (C), 198.2 (C), 169.1 (C), 142.7 (CH), 133.1 (CH), 62.9 (CH_2), 54.6 (CH), 37.8 (CH_2), 31.5 (CH_2), 27.1 (CH_2), 26.7 (CH_3), 20.8 (CH_2) ppm. ^1H NMR (300 MHz, $CDCl_3$): δ = 6.73 (ddd, *J* = 6.8, 6.9, 16.0 Hz, 1 H), 6.09 (ddd, *J* = 1.3, 1.4, 16.0 Hz, 1 H), 4.32–4.16 (m, 2 H), 3.12 (dd, *J* = 9.2, 9.1 Hz, 1 H), 2.59–2.50 (m, 2 H), 2.30–2.01 (m, 5 H), 2.23 (s, 3 H), 1.90–1.74 (m, 1 H) ppm. MS (ESI+): *m*/*z* = 225 $[M + H]^+$, 247 $[M + Na]^+$, 263 $[M + K]^+$.

Compound 2e: According to the general procedure, **2e** was obtained as a brown oil (104 mg, 78%). R_f (30% EtOAc in petroleum ether) = 0.63. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 211.1 (C), 169.2 (C), 166.4 (C), 143.8 (CH), 123.2 (CH), 62.9 (CH_2), 54.0 (CH), 52.8 (CH_2), 51.4 (CH_3), 40.6 (CH_2), 34.3 (C), 31.2 (CH_2), 28.8 (CH_3), 27.5 (CH_3) ppm. ^1H NMR (300 MHz, $CDCl_3$): δ = 6.9 (ddd, *J* = 6.9, 7.0, 15.8 Hz, 1 H), 5.90 (ddd, *J* = 1.2, 1.5, 15.8 Hz, 1 H), 4.35–4.15 (m, 2 H), 3.72 (s, 3 H), 3.36 (dd, *J* = 9.0, 11.0 Hz, 1 H), 2.64–2.28 (m, 3 H), 2.18 (s, 2 H), 2.21–1.97 (m, 1 H), 1.21 (s, 3 H), 1.04 (s, 3

H) ppm. MS (ESI+): *m*/*z* = 269 $[M + H]^+$, 291 $[M + Na]^+$, 307 $[M + K]^+$.

General Procedure for the Preparation of Compounds 1a–1d in Scheme 2: To a solution of **3** (0.50 mmol) in anhydrous dichloromethane (5 mL) were successively added the acrylic derivative (0.50 mmol) and **5** in two portions (0.015 mmol at the start and 0.005 mmol after 20 min), and the reaction vessel was sealed and irradiated with microwaves at 100 °C for 30 min (20, then 10 min). To the cooled reaction mixture was added basic alumina (0.8 g) and methanol (0.7 mL), and the resulting mixture was heated at 50 °C for 24 h. The reaction mixture was filtered through a pad of Celite and concentrated under vacuum to give the crude product, which was purified by silica gel flash chromatography with EtOAc/petroleum ether to afford pure **1a**–**d**. Compound **1a**[8a] exhibited physical and spectroscopic properties identical to previously reported data.

Compound 1b (*dr* = 1.3:1): According to the general procedure, **1b** was obtained as a brown oil (67 mg, 56%). Minor diastereomer (isolated): R_f (60% EtOAc in petroleum ether) = 0.22. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 216.9 (C), 172.4 (C), 172.1 (C), 60.9 (C), 52.6 (CH_2), 51.8 (CH_3), 39.4 (CH_2), 38.6 (CH), 32.9 (CH_2), 32.6 (CH_2), 29.9 (CH_3), 20.1 (CH_2) ppm. ^1H NMR (300 MHz, $CDCl_3$): δ = 3.66 (s, 3 H), 3.47 (dd, *J* = 8.5, 9.2 Hz, 1 H), 3.36 (dd, *J* = 10.0, 9.2 Hz, 1 H), 2.86 (s, 3 H), 2.72–260 (m, 1 H), 2.58–2.45 (m, 3 H), 2.41–2.11 (m, 3 H), 1.97–1.82 (m, 2 H) ppm. HRMS (ESI+): *m*/*z* $[M + H]^+$: calcd. for $[C_{12}H_{18}NO_4]^+$ 240.1230, found 240.1228. Major diastereomer: R_f (60% EtOAc in petroleum ether) = 0.27. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 216.5 (C), 172.5 (C), 171.8 (C), 61.2 (C), 52.6 (CH_2), 51.9 (CH_3), 38.7 (CH), 37.3 (CH_2), 34.6 (CH_2), 29.8 (CH_3), 28.5 (CH_2), 19.4 (CH_2) ppm. ^1H NMR (300 MHz, $CDCl_3$): δ = 3.67 (s, 3 H), 3.05–2.93 (m, 2 H), 2.83 (s, 3 H), 2.59–2.12 (m, 7 H), 1.98–1.82 (m, 2 H) ppm.

Compound 1c (*dr* = 1.3:1 with Al_2O_3 or *dr* = 1.2:1 with *n*Bu_3P): According to the general procedures, **1c** was obtained as a brown oil (58 mg, 43% with Al_2O_3, and 47 mg, 35% with *n*Bu_3P). R_f (60% EtOAc in petroleum ether) = 0.13. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 206.2 (C), 205.3 (C), 171.9 (C), 171.9 (C), 171.2 (C), 170.8 (C), 60.1 (C), 61.8 (C), 52.4 (CH_2), 51.9 (CH_3), 51.8 (CH_3), 51.1 (CH_2), 41.5 (CH_2), 41.4 (CH), 40.6 (CH_2), 36.6 (CH_2), 35.1 (CH), 34.8 (CH_2), 33.0 (CH_2), 31.5 (CH_2), 29.9 ($2CH_3$), 28.5 (CH_2), 26.7 (CH_2) ppm. ^1H NMR (300 MHz, $CDCl_3$): δ = 3.67 (s, 3 H), 3.66 (s, 3 H), 3.77–3.44 (m, 4 H), 3.28–2.66 (m, 16 H), 2.85 (s, 3 H), 2.84 (s, 3 H), 2.55–2.22 (m, 2 H) ppm. HRMS (ESI+): *m*/*z* $[M + H]^+$: calcd. for $[C_{12}H_{18}NO_4S]^+$ 272.0951, found 272.0953.

Compound 1d (*dr* = 1:1): According to the general procedure, **1d** was obtained as a brown oil (63 mg, 52%). First diastereomer eluted (isolated): R_f (30% EtOAc in petroleum ether) = 0.54. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 205.9 (C), 174.7 (C), 172.0 (C), 71.1 (CH_2), 59.2 (C), 52.0 (CH_3), 42.9 (CH), 40.8 (CH_2), 34.6 (CH_2), 31.6 (CH_2), 24.8 (CH_2), 20.6 (CH_2) ppm. ^1H NMR (300 MHz, $CDCl_3$): δ = 4.52 (dd, *J* = 8.5, 9.2 Hz, 1 H), 4.16 (dd, *J* = 8.7, 9.2 Hz, 1 H), 3.68 (s, 3 H), 2.86 (dd, *J* = 10.0, 16.1 Hz, 1 H), 2.57 (dd, *J* = 3.8, 16.1 Hz, 1 H), 2.76–2.59 (m, 2 H), 2.42–2.27 (m, 2 H), 2.24–2.14 (m, 1 H), 2.07–1.96 (m, 1 H), 1.91–1.60 (m, 3 H) ppm. HRMS (ESI+): *m*/*z* $[M + H]^+$: calcd. for $[C_{12}H_{17}O_5]^+$ 241.1071, found 241.1074. Second diastereomer eluted: R_f (30% EtOAc in petroleum ether) = 0.50. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 204.7 (C), 174.1 (C), 171.5 (C), 69.9 (CH_2), 59.1 (C), 52.0 (CH_3), 39.5 (CH_2), 36.2 (CH), 34.6 (CH_2), 30.2 (CH_2), 26.6 (CH_2), 20.2 (CH_2) ppm. ^1H NMR (300 MHz, $CDCl_3$): δ = 4.53 (dd, *J* = 7.4, 9.2 Hz, 1 H), 3.93 (dd, *J* = 8.7, 9.2 Hz, 1 H), 3.70 (s, 3 H), 3.10–2.98 (m, 1 H), 2.51 (dd, *J* = 4.9, 15.9 Hz, 1 H), 2.28 (dd, *J* = 10.5, 15.9 Hz, 1 H), 2.76–2.62 (m, 1 H), 2.40–2.20 (m, 2 H), 2.23–2.08 (m, 1 H), 2.07–1.96 (m, 1 H), 1.80–1.60 (m, 3 H) ppm.

Procedure for 1e: To a solution of **3l** (0.50 mmol) in anhydrous dichloromethane (5 mL) were successively added methyl acrylate (0.50 mmol) and **5** in two portions (0.015 mmol at the start and 0.005 mmol after 20 min), and the reaction vessel was sealed and irradiated with microwaves at 100 °C for 30 min (20, then 10 min). To the cooled reaction mixture was added Dowex 550A resin (230 mg), and the resulting mixture was irradiated with microwaves at 100 °C for 20 min, and the product **1e** was isolated as above. Compound **1e** exhibited physical and spectroscopic properties identical to previously reported data.[23a]

General Procedure for 1c and 1f: To a solution of **3e** or **3f**, respectively, (0.50 mmol) in anhydrous dichloromethane (5 mL) were successively added the acrylic derivative (0.50 mmol) and **5** in two portions (0.015 mmol at the start and 0.005 mmol after 20 min), and the reaction vessel was sealed and irradiated with microwaves at 100 °C for 30 min (20, then 10 min). To the cooled reaction mixture was added tributylphosphane (0.10 mmol), and the resulting mixture was irradiated with microwaves at 100 °C for 20 min. The products **1c** and **1f** were isolated as above.

Compound 1f (*dr* = 1.2:1): According to the general procedure, **1f** was obtained as a brown oil (40 mg, 30%). R_f (10% EtOAc in petroleum ether) = 0.47. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 205.5 (C), 204.2 (C), 174.0 (C), 172.9 (C), 138.7 (C), 138.3 (C), 138.3 (C), 137.9 (C), 133.2 (CH), 132.7 (CH), 129.1 (CH), 129.0 (CH), 128.7 (CH), 127.6 (CH), 127.4 (CH), 127.1 (CH), 116.8 (C), 116.4 (C), 69.7 (CH_2), 68.4 (CH_2), 60.6 (C), 59.5 (C), 43.4 (CH), 41.8 (CH), 32.0 (CH_2), 30.9 (CH_2), 30.4 (CH_2), 25.4 (CH_2), 22.8 (CH_2), 21.5 (CH_2), 17.0 (CH_2), 16.0 (CH_2) ppm. ^1H NMR (300 MHz, $CDCl_3$): δ = 7.52–7.29 (m, 6 H), 7.18 (d, *J* = 7.4 Hz, 2 H), 4.56 (dd, *J* = 7.8, 9.0 Hz, 1 H), 4.53 (dd, *J* = 6.9, 9.0 Hz, 1 H), 4.34 (dd, *J* = 8.2, 9.0 Hz, 1 H), 4.09 (dd, *J* = 7.2, 9.0 Hz, 1 H), 3.47 (ddd, *J* = 6.9, 8.3, 13.8 Hz, 1 H), 3.32 (ddd, *J* = 5.4, 9.6, 15.0 Hz, 1 H), 3.09 (ddd, *J* = 7.2, 7.3, 14.6 Hz, 1 H), 3.92 (dt, *J* = 1.3, 7.8 Hz, 1 H), 2.88–2.73 (m, 2 H), 2.71–2.51 (m, 6 H), 2.20–1.81 (m, 6 H) ppm. MS (ESI+): *m*/*z* = 270 $[M + H]^+$, 292 $[M + Na]^+$, 308 $[M + K]^+$.

General Procedure for the Preparation of Compounds in Table 4: A solution of 2-diazo-1,3-diketone **4b** (0.50 mmol) and allyl alcohol, homoallyl alcohol or allyl(methyl)amine (0.50 mmol) in dichloromethane (5 mL) in a 10 mL sealed tube equipped with a Teflon-coated stirring bar was irradiated with microwaves at 300 W for 15 min, whereupon the reaction mixture was cooled to 40 °C with an air flow. To the resulting solution were added the acrylic derivative (0.50 mmol) and **5** in two portions (0.015 mmol at the start and 0.005 mmol after 20 min), and the reaction vessel was sealed and irradiated with microwaves at 100 °C for 30 min (20, then 10 min). To the cooled reaction mixture was added tributylphosphane (0.10 mmol), and the resulting mixture was irradiated with microwaves at 100 °C for 20 min. The cooled reaction mixture was filtered through a pad of Celite and concentrated under vacuum to give the crude product, which was purified by silica gel flash chromatography with EtOAc/petroleum ether to afford pure **1a** and **1g**–**k**. Compounds **1h**–**k** exhibited physical and spectroscopic properties identical to previously reported data.[8a] Compounds **1j** and **1k** (major diastereomer) were obtained as white needles suitable for X-ray diffraction analysis.[19]

Compound 1g (*dr* = 1.2:1): According to the general procedure, **1g** was obtained as a brown oil (35 mg, 34%). R_f (50% EtOAc in petroleum ether) = 0.27. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 216.5 (C), 215.4 (C), 171.8 (C), 171.0 (C), 117.4 (C), 117.3 (C), 61.3 (C), 60.6 (C), 52.0 (CH_2), 51.9 (CH_2), 39.3 (CH_2), 38.2 (CH), 37.1 (CH_2),

34.9 (CH), 30.0 (CH_3), 30.0 (CH_3), 29.7 (CH_2), 28.4 (CH_2), 19.9 (CH_2), 19.3 (CH_2), 19.0 (CH_2), 16.3 (CH_2) ppm. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.86 (dd, J = 7.2, 10.0 Hz, 1 H), 3.50–3.36 (m, 1 H), 3.44 (dd, J = 7.9, 10.0 Hz, 1 H), 3.15 (dd, J = 4.1, 10.0 Hz, 1 H), 3.89 (s, 3 H), 3.88 (s, 3 H), 2.69–2.52 (m, 4 H), 2.51–2.23 (m, 9 H), 2.16–1.86 (m, 5 H) ppm. MS (ESI+): m/z = 207 [M + H]$^+$, 229 [M + Na]$^+$, 245 [M + K]$^+$.

General Procedure for the Preparation of Compounds in Scheme 3: To a suspension of SIMes chlorohydrate **8** (17 mg, 0.05 mmol) in anhydrous toluene (0.5 mL) was added a 0.05 M solution of KHMDS in toluene (1 mL, 0.05 mmol), and the resulting mixture was stirred at room temperature for 30 min. To the reaction mixture was added a solution of pure **2c** (52 mg, 0.25 mmol) in anhydrous dichloromethane (2.5 mL), and the reaction mixture was stirred at 24 °C for 20 h. The solvent was removed under vacuum, and the resulting crude product was purified by silica gel flash chromatography with EtOAc/petroleum ether to afford 44 mg (85%) of pure **1i** as a colourless oil. Alternatively, to a solution of **2c** (104 mg, 0.50 mmol) in dichloromethane (5 mL) was added **9** (38 mg, 0.10 mmol), and the reaction mixture was stirred at 24 °C for 20 h. The solvent was removed under vacuum, and the resulting crude product was purified by silica gel flash chromatography with EtOAc/petroleum ether to afford 100 mg (97%) of pure **1i** as a colourless oil.

General Procedure for the Preparation of Compounds in Table 6: A solution of 2-diazo-1,3-diketone **4b** (0.50 mmol) and allyl alcohol, homoallyl alcohol or benzyl homoallylamine (0.50 mmol) in dichloromethane (5 mL) in a 10 mL sealed tube equipped with a Teflon-coated stirring bar was irradiated with microwaves at 300 W for 15 min, whereupon the reaction mixture was cooled to 40 °C with an air flow. To the resulting solution were added the acrylic derivative (0.50 mmol) and **5** in two portions (0.015 mmol at the start and 0.005 mmol after 20 min), and the reaction vessel was sealed and irradiated with microwaves at 100 °C for 30 min (20, then 10 min). To the cooled reaction mixture was added **9** (0.10 mmol), and the resulting mixture was stirred at 24 °C for 20 h. The reaction mixture was filtered through a pad of Celite and concentrated under vacuum to give the crude product, which was purified by silica gel flash chromatography with EtOAc/petroleum ether to afford pure **1h**–**o**. Compounds **1l**–**n** exhibited physical and spectroscopic properties identical to previously reported data.[8a]

Compound 1o: According to the general procedure, **1o** was obtained as a brown oil (95 mg, 71%). R_f (40% EtOAc in petroleum ether) = 0.27. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 212.8 (C), 171.5 (C), 171.5 (C), 68.0 (CH_2), 61.0 (C), 53.5 (CH_2), 52.0 (CH_3), 44.7 (CH_2), 35.2 (CH_2), 34.4 (CH), 32.8 (C), 31.1 (CH_3), 30.0 (CH_3), 24.6 (CH_2) ppm. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 4.48–4.40 (m, 2 H), 3.68 (s, 3 H), 2.82–2.73 (m, 1 H), 2.64 (d, J = 17.7 Hz, 1 H), 2.37–2.21 (m, 5 H), 1.87 (d, J = 14.2 Hz, 1 H), 1.71–1.59 (m, 1 H), 1.13 (s, 3 H), 1.24 (s, 3 H) ppm. HRMS (ESI+): m/z [M + H]$^+$ calcd. for $C_{14}H_{21}O_5^+$ 269.1384, obsd 269.1385.

Supporting Information (see footnote on the first page of this article): Copies of NMR spectra of all new compounds.

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