Hindered Brønsted bases as Lewis base catalysts

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KHMDS and KO*t*Bu are well established as strong, hindered, non-nucleophilic Brønsted bases. However, in the present work these bases are applied as highly active Lewis base catalysts for the formal [2+2] cycloaddition of ketenes with aldehydes and imines.

Introduction

Alkali metal hexamethyldisilazanes are well known as non-nucleophilic hindered Brønsted bases and are extensively used in synthesis.[1] HMDS has a pK_a of 26 and *N*,*N*-diisopropylamine a pK_a of 36 in THF. HO*t*Bu has a pK_a of 29.4 in DMSO.[2] The lower pK_a of HMDS can be explained by α-silyl stabilization.[3] However, a few examples where these bases act as nucleophiles are also known. Despite its lower basicity and the more pronounced sterical screening of the nitrogen atom of MHMDS compared to LDA, more examples[4] of the HMDS anion acting as a nucleophile are known than for LDA.[5] Moreover, KO*t*Bu may also act as a nucleophile.[6]

The Staudinger cycloaddition[7] as well as the formal [2+2] cycloaddition of aldehydes and ketenes, the Wynberg reaction,[8] are established methods to obtain β-lactams and β-lactones,[9] which are important compounds due to their biological activity and utility in synthesis.[10] The reactions are often promoted by Lewis base catalysts. These catalysts are normally weak Brønsted bases.

Here we report that the hindered strong base NaHMDS/KHMDS is an efficient Lewis base catalyst for the Staudinger reaction of disubstituted ketenes and imines with a *para*-nosyl group.[11] In addition hindered Brønsted bases are also active catalysts for the cycloaddition of ketenes with aldehydes and reactions were conducted to exclude some possible mechanistic pathways.

Results and discussion

Several Lewis bases were screened for their nucleophilic capacity to catalyze the Staudinger cycloaddition of imine **1a** with a *para*-nosyl group and phenylethyl ketene **2a** (Scheme 1). Along with strong amine bases, alkali metal amides were also tested under different reaction conditions as shown in Table 1. Due to their nucleophilic nature, the best results were observed in the cases when amide catalysts were applied. Furthermore, the character of the alkali metal had an influence on the reaction. NaHMDS and KHMDS resulted in total conversion at −78 °C in less than 5 min and 10 min respectively (Table 1, entries 1 and 5), however LiHMDS gave just a moderate yield of 28% in 3 h (Table 1, entry 6). LDA catalyzed the reaction in a good yield of 77% but the reaction time increased to 1.5 h, and a decrease in the diastereoselectivity was observed (Table 1, entry 8). This can be attributed to the lower nucleophilicity of the lithium amides, due to the stronger covalent bond character between the lithium and nitrogen.

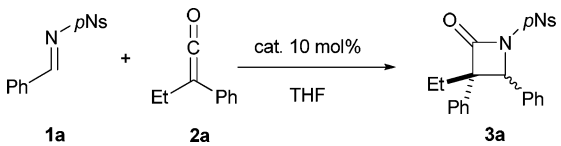
When toluene was used as a solvent instead of THF only traces of the product were obtained at −78 °C with KHMDS. This can be mainly explained by the poor solubility of the imines.[12] At room temperature the reaction proceeded in toluene with quantitative yield, and the diastereomeric ratio of the product was found to be similar to that obtained at −78 °C in THF (Table 1, entry 3). The reaction performed in THF at room temperature (Table 1, entry 2) resulted in a decrease in the diastereomeric ratio.

As shown in Scheme 2, it is known that NaHMDS reacts with aldehydes to form TMS-protected imines with liberation of NaOTMS. This reaction is much faster with LiHMDS and can be carried out at −40 °C, but it is much slower with KHMDS.[4i] Since alkoxides have not so far been used as Lewis base catalysts in [2+2] cycloadditions, the Staudinger reaction was repeated with NaOTMS as a potential catalyst (Table 1, entry 9). The reaction was stopped after 20 min in order to compare

Table 1 Staudinger reaction of **1a** and **2a** catalyzed by 10 mol% of catalysts at −78 °C in THF

entry	catalyst	T [min]	yield [%][a]	*trans*:*cis*
1	KHMDS	10 min	85	20:80
2[b]		5 min	99	33:66
3[b,c]		1 h	99	20:80
4[c]		24 h	0	—
5	NaHMDS	<5 min	99	20:80
6	LiHMDS	3 h	28	20:80
7	HMDS	24 h	0	—
8	LDA	1.5 h	77	28:72
9[d]	NaOTMS	20 min	48	37:63
10	DMAP	3.5 h	92	55:45
11	Et_3N	24 h	17	50:50
12	DABCO	24 h	44	50:50
13[b]	DBU	24 h	*traces*	—
14[b]	—	24 h	0	—

[a] Yields of isolated **3a**. [b] Reaction performed at rt. [c] Reaction performed in toluene. [d] Reaction was stopped by quenching with $NH_4Cl_{(aq)}$ at −78 °C.



Scheme 1 Staudinger reaction catalyzed by different Lewis bases.

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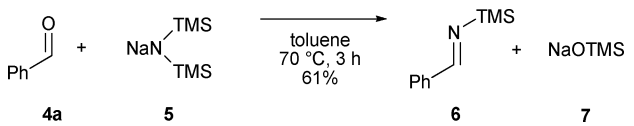
Table 2 Staudinger reaction with different imines **1** and ketenes **2**, catalyzed by 10 mol% MHMDS

entry	imine	ketene	base	T [min]	yield [%][a]	**3**[b] (*trans:cis*)
1	**1a** Ph	**2a** $R^1 = Et$, $R^2 = Ph$	NaHMDS	< 5	99	**3a** (20:80)
2	**1b** 2-Cl-C_6H_4	**2a**	KHMDS	< 3	99	**3b** (12:88)
3	**1c** 2-Thiophenyl	**2a**	KHMDS	15	68	**3c** (43:57)
4	**1d** 1-Naphthyl	**2a**	KHMDS	90	89	**3d** (14:86)
5	**1e** 2-Naphthyl	**2a**	NaHMDS	10	98	**3e** (45:55)
6	**1f** 4-CH_3-C_6H_4	**2a**	NaHMDS	< 10	87	**3f** (33:67)
7	**1g** 4-Cl-C_6H_4	**2a**	NaHMDS	< 5	92	**3g** (26:74)
8	**1h** 4-CF_3-C_6H_4	**2a**	KHMDS	10	99	**3h** (43:57)
9	**1i** 4-NC-C_6H_4	**2a**	NaHMDS	15	99	**3i** (36:64)
10	**1j** 4-F-C_6H_4	**2a**	KHMDS	10	98	**3j** (25:75)
11	**1k** 3,4-$(MeO)_2$-C_6H_3	**2a**	NaHMDS	120	88	**3k** (22:78)
12	**1a** Ph	**2b** $R^1 = Me$, $R^2 = Ph$	NaHMDS	10	72	**3l** (30:70)
13	**1j** 4-F-C_6H_4	**2b**	NaHMDS	10	94	**3m** (32:68)
14[c]	**1a** Ph	**2c** $R^1 = Ph$, $R^2 = Ph$	NaHMDS	180	99	**3n**
15[c]	**1j** 4-F-C_6H_4	**2c**	NaHMDS	180	97	**3o**
16	**1a** Ph	**2d** $R^1, R^2 = -(CH_2)_6-$	NaHMDS	90	48	**3p**

[a] Isolated yields. [b] Diastereomers were separated by column chromatography. [c] Reaction performed at −78 °C to rt.



Scheme 2 Reaction of aldehydes with NaHMDS.[4g]

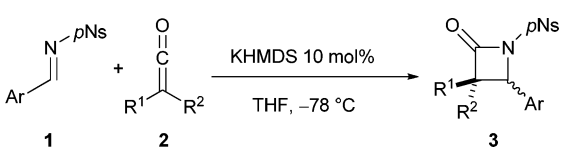
the results with NaHMDS and to eliminate the possibility that NaOTMS is formed with the ketene in analogy to Scheme 2. The yield and the diastereoselectivity were lower compared to the NaHMDS catalyzed reaction, but nevertheless NaOTMS showed good catalytic activity.

Commonly used tertiary amines were also applied in the reaction in order to compare their catalytic activity to MHMDS. In all cases poor yields were obtained under the reaction conditions (Table 1, entries 10–13). The reactions of tertiary amines with such highly substituted ketenes are normally performed over several hours at room temperature or on heating.[7f,7t,7u,7v] In the absence of a catalyst no reaction took place (Table 1, entry 14). An attempt to use a tosyl protected analogue of **1a** in the reaction gave an unidentified mixture of compounds and not the desired product.

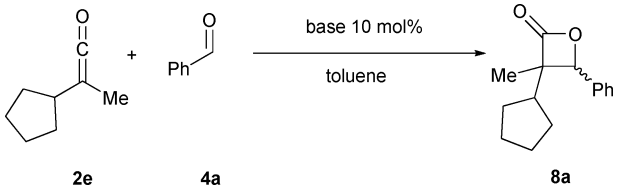
Next, several imines and ketenes were used in the Staudinger reaction under the optimized conditions (Table 2, Scheme 3). In general all imines gave the corresponding products in significant yields and diastereoselectivity with the *cis*-adduct prevailing. Exceptions were the imines **1c**, **1e** and **1h** which gave good yields, but a lower diastereoselectivity. In several cases the formation of the product was completed in less than 10 min.

Also, different disubstituted ketenes were applied in the reaction. Changing from an ethyl to a methyl substituent in the ketene gave the desired product in good yield and diastereoselectivity (Table 2, entry 12). The 1,1′-diphenylketene **2c** had a lower reactivity and reacted with imines **1a** and **1j** at room temperature in 98% yield (Table 2, entries 14 and 15). As an example for an alkyl-alkyl substituted ketene, imine **1a** was reacted with ketene **2d** to give the product in 49% yield (Table 2, entry 16). The lower yields of **3l** and **3p** can be attributed to the alternative possibility of oligomerization and dimerization of the ketene. In all cases the diketone dimers of the corresponding ketenes were observed.[13] The possible β-alkenyl-β-lactone dimers were not found.[14]

Due to the results for the Staudinger cycloaddition, we were interested to see whether NaHMDS has a catalytic effect in the formal [2+2] cycloaddition of ketenes and aldehydes. We focused on the ketene/aldehyde system shown in Scheme 4. Since there was no solubility issue expected, as for the Staudinger reaction, and due to the observation that in toluene a higher diastereomeric ratio was achieved (Table 1, entry 3), it was decided to carry out the subsequent cycloaddition in toluene. In analogy to other reports it was found with the presented catalytic system that aryl-aryl and aryl-alkyl ketenes were not active enough to react with benzaldehydes.[8h,8k] Therefore,



Scheme 3 Staudinger reaction with different imines and ketenes.



Scheme 4 Base catalyzed [2+2] reaction with ketene and benzaldehyde.

Table 3 Base catalyzed [2+2] reaction with ketene **2e** and aldehyde **4a**[a]

entry	base	t [°C]	time	yield [%][b]	*trans*:*cis*[c]
1	NaHMDS	−78	1 h	30	33:67
2	KHMDS	−78	1 h	36	22:78
3	LiHMDS	−78	1 h	0	—
4	KO*t*Bu	−78 to −20	5 h	traces	—
5	NaOTMS	−78	5 h	0	—
6	NaHMDS	−78 to rt	5 h	99	50:50
7	KHMDS	−78 to rt	5 h	99	50:50
8	KO*t*Bu	−78 to rt	5 h	54	37:63
9	NaOTMS	−10 to rt	5 h	98	50:50
10	—	−78 to rt	5 h	0	—

[a] Ketene (2 equiv.) in a 0.27 M toluene solution. [b] Isolated yield. [c] Determined by ^{1}H-NMR.

alkyl-alkyl ketenes were used in the reaction. Ketene **2e** was prepared from 2-cyclopentylpropanoylchloride in toluene with 1 equiv. of DABCO. After 3 h at 80 °C ketene **2e** was vacuum transferred together with the solvent to give a 0.27 M solution.

First, reactions with NaHMDS or KHMDS as catalysts were carried out at −78 °C for 1 h to give the product in low yields. With LiHMDS no product was obtained (Table 3, entries 1–3). In addition, KO*t*Bu was tested as a hindered non-nucleophilic base to give only traces of product at −20 °C. When the reaction was repeated with KHMDS and NaHMDS and the reaction mixture was allowed to warm to room temperature, quantitative yields were obtained. However, the diastereoselectivity decreased. With KO*t*Bu a yield of 54% was isolated at room temperature. In the absence of a catalyst no conversion occurred (Table 3, entry 10).

In order to exclude the possibility that NaOTMS is generated according to Scheme 2, a control reaction with NaOTMS as the catalyst was performed at −78 °C and no conversion was observed. If NaOTMS is applied as the catalyst between −10 °C and room temperature, product **8a** is formed in 98% yield (Table 3, entries 5 and 9). Thus, NaOTMS is less active than NaHMDS. Since NaHMDS, KHMDS and NaOTMS gave excellent yields, but a 50:50 ratio of diastereomers, when the reaction was warmed up to room temperature (Table 3, entries 6, 7 and 9) it is not possible to rule out completely that some NaOTMS was generated from NaHMDS at room temperature according to Scheme 2. However, the reaction in Scheme 2 normally proceeds at higher temperatures than room temperature and in the case of KHMDS even higher temperatures are needed.[4g]

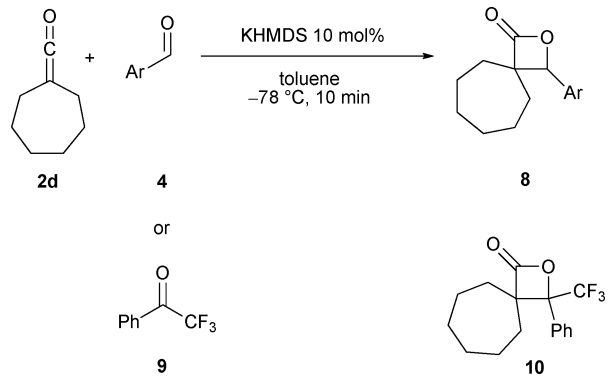
In addition, ketene **2d**[7e,15] was tested in the reaction with benzaldehyde, beginning with experiments at −78 °C or room temperature in the absence of a catalyst. No conversion into the product **8b** was observed. However, with 10 mol% KHMDS the less hindered ketene **2d** displayed with several aldehydes (Table 4) a far higher reactivity than ketene **2e**. Thus, the reactions were complete after 10 min to give the desired products (Scheme 5). Furthermore, it was even possible to apply α,α,α-trifluoroacetophenone (**9**) in the reaction with ketene **2d** and to isolate the tetrasubstituted β-lactone **10** in 49% yield (Table 4, entry 7).

Prolonged stirring did not result in a higher yield due to competing dimerization of the ketene to the corresponding diketone. Electron-rich and -deficient aldehydes gave similar yields. Furthermore, a reaction with ketene **2d**, benzaldehyde (**4a**) and

Table 4 KHMDS catalyzed Wynberg reaction with ketene **2d**[a]

entry	Ar	yield [%][b]	product
1	**4a** Ph	59	**8b**
2	**4b** 2-Me-C_6H_4	60	**8c**
3	**4c** 4-Cl-C_6H_4	60	**8d**
4	**4d** 4-Me-C_6H_4	56	**8e**
5	**4e** 4-CF_3-C_6H_4	55	**8f**
6	**4f** 4-F-C_6H_4	61	**8g**
7[c]	**9** PhCOCF3	49	**10**

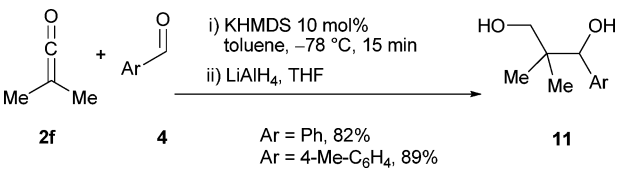
[a] Ketene **2d** (2 equiv.). [b] Isolated yield. [c] −78 °C to rt.



Scheme 5 KHMDS catalyzed Wynberg reaction with ketene **2d**.

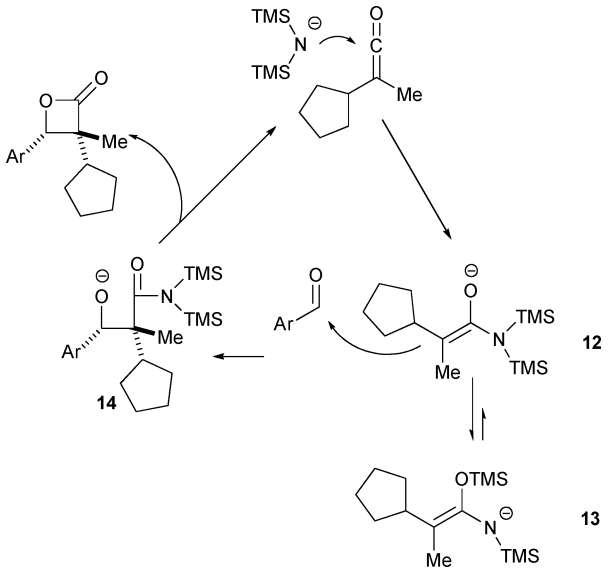
10 mol% NaOTMS at −78 °C gave the desired product in 32% yield after 10 min.

In addition, ketene **2f**[7e,15] was reacted with benzaldehyde or *para*-methylbenzaldehyde. The reactions were complete after 15 min. For easier handling, the products were directly transformed to diols **11** with $LiAlH_4$, with an overall yield of 82 and 89%, respectively (Scheme 6).



Scheme 6 KHMDS catalyzed Wynberg reaction.

Based on the present results, the mechanism in Scheme 7 can be proposed for the reaction of aldehydes with ketenes. After the initial nucleophilic attack of the HMDS anion at the ketene, the amide enolate **12** is formed, which obviously must allow a 1,3 silyl shift to anion **13**. The process would be encouraged by the oxophilicity of silicon. However, this rearrangement could be slow or lead to an equilibrating mixture from which **12** is consumed by the aldehyde. Taking into consideration that the HMDS group in enolate **12** is far larger than the cyclopentyl ring, the aldehyde approaches from the side opposite to the HMDS group and the *cis* product is formed, which is observed in the majority of examples of Lewis base catalysed [2+2] cycloadditions of ketenes with imines or aldehydes.[7,8]



Scheme 7 Proposed mechanism.

Conclusions

In conclusion it has been shown that potassium and sodium hexamethyldisilazane amides can act as highly active Lewis base catalysts in the formal [2+2] cycloaddition of ketenes with imines or aldehydes. The Staudinger cycloaddition was completed in a short time of 5 to 15 min at −78 °C. The useful *para*-nosyl group can be removed in high yield under mild conditions.[16] The speed and simplicity of the reported procedure makes it a valuable tool for preparing libraries of β-lactams and β-lactones. It was also possible to obtain a tetrasubstituted β-lactone *via* the Wynberg reaction. In addition, it was shown that KO*t*Bu and NaOTMS are also good Lewis base catalysts for these cycloadditions. These findings may encourage the exploration of tandem reactions with these bases or the development of chiral analogues.

Experimental

General experimental

All reactions were conducted under an atmosphere of dry nitrogen. Glassware was dried in an oven or flame-dried under vacuum prior to use. THF was distilled from sodium benzophenone ketyl. Toluene was distilled from sodium. Reactions were monitored by TLC with MERCK Silica gel 60 F_{254} plates. Flash column chromatography was performed on silica gel 60 (70–230 mesh ASTM) from MERCK. Ketenes **2**[7e,8h,15] and imines **1**[12] were prepared according to literature procedures. Aldehydes **4** were distilled or sublimed. All other chemicals, were purchased from commercial sources. Melting points were taken on a Dr. Tottoli apparatus from BÜCHI and are uncorrected. Infrared spectra were recorded on a Vector 22 FT-IR from BRUKER. The absorption of solids was measured by potassium bromide pellets, the absorption of liquids by using a thin layer between sodium chloride plates. ^{1}H-NMR spectra were taken on an AMX 400 (400 MHz) or an AC 250 P (200 MHz) from BRUKER in $CDCl_3$ unless otherwise stated. ^{13}C-NMR spectra were taken on an AMX 400 (100 MHz) or on an AC 250 P (50 MHz) from BRUKER in $CDCl_3$ unless otherwise stated.

General experimental procedure for the Staudinger cycloaddition. An imine **1** (0.1 mmol) and a ketene **2** (0.25 mmol) were dissolved in dry THF (1 mL) and cooled down to −78 °C. KHMDS or NaHMDS (0.01 mmol) was added, and the reaction was monitored by TLC. After total conversion the reaction mixture was sujected to column chromatography and the products were eluted with 1:8 ethyl acetate/petrol ether to give the desired diastereomers mostly as white solids (yields: 48–99%) For yields and ratios see Tables 1 and 2.

3a: *trans*-Isomer: white crystals, mp 144 °C. ^{1}H NMR (200 MHz): $\delta = 0.57$ (t, $J = 7.4$ Hz, 3 H), 1.25–1.43 (m, 1 H), 1.64–1.89 (m, 1 H), 5.24 (s, 1 H), 7.21–7.44 (m, 10 H), 8.12 (d, $J = 8.9$ Hz, 2 H), 8.34 (d, $J = 8.98$ Hz, 2 H). ^{13}C NMR (50 MHz): $\delta =$ 8.7, 27.1, 68.1, 69.9, 124.6, 126.2, 127.2, 128.1, 128.9, 129.2, 129.3, 133.6, 137.4, 143.9, 151.0, 168.6. IR (KBr) ν/cm^{-1}: 1792 (C=O). MS (ES$^+$): m/z = 459.1 [M + Na]$^+$ Anal. Calcd for $C_{23}H_{20}N_2O_5S$: C, 63.29; H, 4.62; N, 6.42%. Found: C, 63.20; H, 4.67; N, 6.35%.

cis-Isomer: white crystals, mp 144–145 °C. ^{1}H NMR (200 MHz): $\delta = 0.94$ (t, $J = 7.4$ Hz, 3 H), 2.20 (q, $J = 7.4$ Hz, 2 H), 5.15 (s, 1 H), 6.70–6.76 (m, 2 H), 6.82–6.91 (m, 2 H), 6.94–7.16 (m, 6 H), 7.95 (d, $J = 8.9$ Hz, 2 H), 8.26 (d, $J = 8.9$ Hz, 2 H). ^{13}C NMR (50 MHz): $\delta = 9.3$, 32.6, 69.1, 70.3, 124.4, 127.2, 127.4, 128.2, 128.2, 128.3, 128.9, 129.0, 133.7, 134.5, 144.4, 150.8, 167.8. IR (KBr) ν/cm^{-1}: 1792 (C=O). MS (ES$^+$): m/z = 459.1 [M + Na]$^+$. Anal. Calcd for $C_{23}H_{20}N_2O_5S$: C, 63.29; H, 4.62; N, 6.42%. Found: C, 63.38; H, 4.73; N, 6.28%.

3b: *trans*-Isomer: white crystals, mp 107 °C. ^{1}H NMR (400 MHz): $\delta = 0.83$ (t, $J = 8.0$ Hz, 3 H), 2.09–2.17 (m, 1 H), 2.24–2.33 (m, 1 H), 5.64 (s, 1 H), 6.70–6.72 (m, 1 H), 6.81–6.84 (m, 1 H), 6.95–6.98 (m, 2 H), 7.03–7.07 (m, 3 H), 7.29–7.23 (m, 2 H), 8.22 (d, $J = 8.8$ Hz, 2 H), 8.43 (d, $J = 8.8$ Hz, 2 H). ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 9.3$, 30.7, 64.7, 71.5, 124.8, 126.9, 128.5, 129.3, 129.4, 129.7, 132.3, 133.1, 134.1, 143.8, 151.2, 168.4. IR (KBr) ν/cm^{-1}: 1787 (C=O). MS (ES$^+$): m/z = 493.1 [M + Na]$^+$. Anal. Calcd for ($C_{23}H_{19}ClN_2O_5S$): C, 58.66; H, 4.07; N, 5.95%. Found: C, 58.45; H, 4.05; N, 5.97%.

cis-Isomer: white crystals, mp 107 °C. ^{1}H NMR (200 MHz): $\delta = 0.59$ (t, $J = 7.4$ Hz, 3 H), 1.70 (q, $J = 7.3$ Hz, 2 H), 5.56 (s, 1 H), 7.03–7.07 (m, 5 H), 7.34–7.48 (m, 4 H), 8.15 (d, $J = 8.8$ Hz, 2 H), 8.37 (d, $J = 8.8$ Hz, 2 H). ^{13}C NMR (50 MHz): $\delta = 8.6$, 25.4, 64.7, 69.5, 124.7, 126.7, 127.9, 128.3, 130.0, 129.2, 132.2, 133.1, 133.9, 143.6, 151.1, 168.1. IR (KBr) ν/cm^{-1}: 1793 (C=O). MS (ES$^+$): m/z = 493.1 [M + Na]$^+$. Anal. Calcd for ($C_{23}H_{19}ClN_2O_5S$): C, 58.66; H, 4.07; N, 5.95%. Found: C, 58.71; H, 4.09; N, 5.81%.

3c: *trans*-Isomer: white crystals, mp 116 °C. ^{1}H NMR (200 MHz): $\delta = 0.64$ (t, $J = 7.6$ Hz, 3 H), 1.50–1.68 (m, 1 H), 1.85–2.03 (m, 1 H), 5.53 (s, 1 H), 7.04–7.11 (m, 2 H), 7.24–7.37 (m, 6 H), 8.10 (d, $J = 9.0$ Hz, 2 H), 8.34 (d, $J = 9.2$ Hz, 4 H). ^{13}C NMR (50 MHz): $\delta = 8.7$, 27.7, 65.8, 68.3, 124.5, 126.2, 126.7, 127.5, 127.9, 128.2, 129.2, 129.2, 136.5, 137.1, 144.0, 168.2. IR (KBr) ν/cm^{-1}: 1782 (C=O). MS (ES$^+$): m/z = 465.0 [M + Na]$^+$. Anal. Calcd for ($C_{21}H_{18}N_2O_5S_2$): C, 57.00; H, 4.10; N, 6.33%. Found: C, 56.99; H, 4.10; N, 6.30%.

cis-Isomer: white crystals, mp 124 °C. ^{1}H NMR (200 MHz): $\delta = 0.97$ (t, $J = 7.2$ Hz, 3 H), 2.25 (q, $J = 8.0$ Hz, 2 H), 5.49 (s, 1 H), 6.73–6.75 (m, 2 H), 6.97–7.04 (m, 3 H), 7.11–7.18 (m, 3 H), 7.93 (d, $J = 9.04$ Hz, 2 H), 8.25 (d, $J = 9.04$ Hz, 2 H). ^{13}C NMR (50 MHz): $\delta = 9.3$, 32.4, 64.9, 70.5, 124.4, 126.4, 127.2, 127.9, 128.5, 128.9, 129.1, 134.5, 137.2, 144.4, 150.8, 167.2. IR (KBr)

ν/cm^{-1}: 1790 (C=O). MS (ES$^+$): m/z = 465.0 [M + Na]$^+$. Anal. Calcd for ($C_{21}H_{18}N_2O_5S_2$): C, 57.00; H, 4.10; N, 6.33%. Found: C, 57.13; H, 4.15; N, 6.26%.

3d: *trans*-Isomer: white crystals, mp 182 °C. ^{1}H NMR (200 MHz): δ = 0.66 (t, J = 7.4 Hz, 3 H), 1.26–1.43 (m, 1 H), 1.58–1.78 (m, 1 H), 5.82 (s, 1 H), 7.05–7.10 (m, 2 H), 7.34–7.38 (m, 3 H), 7.43–7.63 (m, 5 H), 7.87–7.97 (m, 2 H), 8.27 (d, J = 9.0 Hz, 2 H), 8.46 (d, J = 9.0 Hz, 2 H). ^{13}C NMR (50 MHz): δ = 8.9, 24.1, 68.5, 68.8, 122.9, 124.8, 125.1, 125.2, 126.5, 126.9, 128.6, 129.5, 129.5, 129.6, 129.7, 130.9, 133.9, 136.6, 144.0, 169.7. IR (KBr) ν/cm^{-1}: 1787 (C=O). MS (ES$^+$): m/z = 509.2 [M + Na]$^+$. Anal. Calcd for ($C_{27}H_{22}N_2O_5S$): C, 66.65; H, 4.56; N, 5.76%. Found: C, 66.77; H, 4.78; N, 5.59%.

cis-Isomer: white crystals, mp 186 °C. ^{1}H NMR (200 MHz): δ = 0.97 (t, J = 7.6 Hz, 3 H), 2.26–2.47 (m, 2 H), 6.05 (s, 1 H), 6.69–6.99 (m, 6 H), 7.50–7.69 (m, 4 H), 7.83 (d, J = 7.8 Hz, 1 H), 8.02 (d, J = 8.2 Hz, 1 H), 8.15 (d, J = 9.0 Hz, 2 H), 8.38 (d, J = 9.0 Hz, 2 H). ^{13}C NMR (50 MHz): δ = 9.5, 31.2, 64.9, 71.6, 121.7, 124.7, 125.1, 126.1, 126.8, 127.2, 127.6, 128.1, 129.0, 129.3, 129.5, 129.6, 131.3, 133.5, 134.1, 138.3, 144.4, 168.6. IR (KBr) ν/cm^{-1}: 1782 (C=O). MS (ES$^+$): m/z = 509.2 [M + Na]$^+$. Anal. Calcd for ($C_{27}H_{22}N_2O_5S$): C, 66.65; H, 4.56; N, 5.76%. Found: C, 66.58; H, 4.87; N, 5.54%.

3e: *trans*-Isomer: white crystals, mp = 155 °C. ^{1}H NMR (400 MHz): δ = 0.56 (t, J = 7.2 Hz, 3 H), 1.31–1.40 (m, 1 H), 1.74–1.83 (m, 1 H), 5.42 (s, 1 H), 7.30–7.41 (m, 6 H), 7.54–7.58 (m, 2 H), 7.73–7.77 (m, 2 H), 7.87–7.91 (m, 2 H), 8.13 (d, J = 8.8 Hz, 2 H), 8.34 (d, J = 8.8 Hz, 2 H). ^{13}C NMR (100 MHz): δ = 8.6, 27.0, 29.7, 68.2, 69.9, 124.2, 124.4, 126.2, 126.7, 126.9, 127.0, 127.8, 127.9, 128.0, 128.7, 129.0, 129.1, 130.8, 132.9, 133.4, 137.3, 143.9, 150.9, 168.4. IR (KBr) ν/cm^{-1}: 1783 (C=O). MS (ES$^+$): m/z = 508.8 [M + Na]$^{+\cdot}$. Anal. Calcd for $C_{27}H_{22}N_2O_5S$: C 66.65; H 4.56; N 5.76%. Found: C 66.70; H 4.43; N 5.71%.

cis-Isomer: white crystals, mp = 177 °C. ^{1}H NMR (200 MHz): δ = 0.99 (t, J = 7.4 Hz, 3 H), 2.17–2.36 (m, 2 H), 5.33 (s, 1 H), 6.51 (d, J = 8.6 Hz, 1 H), 6.89–7.01 (m, 5 H), 7.29 (d, J = 8.6 Hz, 1 H), 7.41–7.50 (m, 3 H), 7.57–7.69 (m, 2 H), 7.86 (d, J = 9.2 Hz, 2 H), 8.12 (d, J = 9.0 Hz, 2 H). ^{13}C NMR (50 MHz): δ = 9.2, 32.8, 69.3, 70.0, 124.2, 124.5, 126.6, 126.9, 127.1, 127.3, 127.7, 127.7, 128.2, 128.6, 128.8, 130.9, 132.5, 133.0, 134.3, 144.2, 150.6, 167.6. IR (KBr) ν/cm^{-1}: 1788 (C=O). MS (ES$^+$): m/z = 995.0 [2M + Na]$^+$. Anal. Calcd for $C_{27}H_{22}N_2O_5S$: C 66.65; H 4.56; N 5.76%. Found: C 66.78; H 4.55; N 5.80%.

3f: *trans*-Isomer: white crystals, mp 142 °C. ^{1}H NMR (200 MHz): δ = 0.57 (t, J = 7.4 Hz, 3 H), 1.25–1.43 (m, 1 H), 1.59–1.83 (m, 1 H), 2.39 (s, 3 H), 5.21 (s, 1 H), 7.21–7.43 (m, 9 H), 8.12 (d, J = 9.0 Hz, 2 H), 8.35 (d, J = 9.04 Hz, 2 H). ^{13}C NMR (50 MHz): δ = 8.7, 21.4, 27.2, 68.0, 70.0, 124.6, 126.2, 127.2, 128.1, 129.2, 130.5, 137.5, 139.2, 144.0, 151.1, 168.7. IR (KBr) ν/cm^{-1}: 1785 (C=O). MS (ES$^+$): m/z = 473 [M + Na]$^+$. Anal. Calcd for ($C_{24}H_{22}N_2O_5S$): C, 63.98; H, 4.92; N, 6.22%. Found: C, 64.05; H, 5.17; N, 6.02%.

c*is*-Isomer: white crystals, mp 147 °C. ^{1}H NMR (200 MHz): δ = 0.93 (t, J = 8.0 Hz, 3 H), 2.18 (q, J = 7.2 Hz, 2 H), 2.20 (s, 3 H), 5.11 (s, 1 H), 6.60 (d, J = 8.0 Hz, 2 H), 6.78 (d, J = 8.0 Hz, 2 H), 6.85–6.89 (m, 2 H), 7.02–7.09 (m, 3 H), 7.87 (d, J = 9.0 Hz, 2 H), 8.18 (d, J = 9.0 Hz, 2 H). ^{13}C NMR (50 MHz): δ = 9.3, 21.2, 32.8, 69.2, 70.0, 124.3, 127.3, 127.4, 128.2, 128.3, 128.9, 129.0, 130.5, 134.6, 138.9, 144.4, 150.8, 167.9. IR (KBr) ν/cm^{-1}: 1781 (C=O). MS (ES$^+$): m/z = 473 [M + Na]$^+$. Anal. Calcd for ($C_{24}H_{22}N_2O_5S$): C, 63.98; H, 4.92; N, 6.22%. Found: C, 63.99; H, 5.02; N, 6.21%.

3g: *trans*-Isomer: white crystals, mp = 163 °C. ^{1}H NMR (200 MHz): δ = 0.59 (t, J = 7.4 Hz, 3 H), 1.25–1.43 (m, 1 H), 1.62–1.80 (m, 1 H), 5.17 (s, 1 H), 7.16–7.21 (m, 2 H), 7.29–7.35 (m, 5 H), 7.42 (d, J = 8.6 Hz, 2 H), 8.14 (d, J = 9.0 Hz, 2 H), 8.36 (d, J = 9.0 Hz, 2 H). ^{13}C NMR (50 MHz): δ = 8.6, 27.1, 68.0, 69.1, 124.5, 126.0, 128.1, 128.4, 129.0, 129.1, 129.2, 132.2, 135.1, 136.9, 143.5, 151.0, 168.2. IR (KBr) ν/cm^{-1}: 1789 (C=O). MS (ES$^+$): m/z = 493.0 [M + Na]$^+$. Anal. Calcd for $C_{23}H_{19}ClN_2O_5S$: C 58.66; H 4.07; N 5.93%. Found: C 58.79; H 3.95; N 5.92%.

cis-Isomer: white crystals, mp = 134 °C. ^{1}H NMR (200 MHz): δ = 0.90 (t, J = 7.4 Hz, 3 H), 2.16 (q, J = 7.4 Hz, 2 H), 5.11 (s, 1 H), 6.72 (d, J = 8.4 Hz, 2 H), 6.83–6.87 (m, 2 H), 7.01 (d, J = 8.6 Hz, 2 H), 7.05–7.12 (m, 2 H), 8.02 (d, J = 9.2 Hz, 2 H), 8.33 (d, J = 9.2 Hz, 2 H). ^{13}C NMR (50 MHz): δ = 9.1, 32.2, 68.2, 70.3, 124.4, 127.0, 127.6, 128.4, 128.9, 129.2, 132.4, 133.9, 134.8, 144.1, 150.9, 167.5. IR (KBr) ν/cm^{-1}: 1792 (C=O). MS (ES$^+$): m/z = 493.1 [M + Na]$^+$. Anal. Calcd for $C_{23}H_{19}ClN_2O_5S$: C 58.66; H 4.07; N 5.93%. Found: C 58.80; H 4.09; N 6.05%.

3h: *trans*-Isomer: white crystals, mp = 158–159 °C. ^{1}H NMR (200 MHz): δ = 0.61 (t, J = 7.2 Hz, 3 H), 1.23–1.42 (m, 1 H), 1.60–1.78 (m, 1 H), 5.22 (s, 1 H), 7.16–7.20 (m, 2 H), 7.31–7.37 (m, 3 H), 7.53 (d, J = 8.0 Hz, 2 H), 7.72 (d, J = 8.2 Hz, 2 H), 8.16 (d, J = 9.0 Hz, 2 H), 8.38 (d, J = 9.0 Hz, 2 H). ^{13}C NMR (50 MHz): δ = 8.6, 27.0, 68.2, 69.1, 124.6, 125.9, 126.0, 127.4, 128.3, 129.0, 129.2, 136.7, 137.8, 143.3, 151.0, 168.0. IR (KBr) ν/cm^{-1}: 1783 (C=O). MS (ES$^+$): m/z = 527.0 [M + Na]$^+$. Anal. Calcd for $C_{24}H_{19}F_3N_2O_5S$: C 57.14; H 3.80; N 5.55%. Found: C 56.98; H 3.85; N 5.40%.

cis-Isomer: white crystals, mp = 131 °C. ^{1}H NMR (200 MHz): δ = 0.91 (t, J = 7.4 Hz, 3 H), 2.17 (q, J = 7.0 Hz, 2 H), 5.16 (s, 1 H), 6.81–6.81 (m, 2 H), 6.94 (d, J = 8.0 Hz, 2 H), 7.10–7.30 (m, 3 H), 7.30 (d, J = 8.0 Hz, 2 H), 8.37 (d, J = 9.0 Hz, 2 H), 8.35 (d, J = 9.0 Hz, 2 H). ^{13}C NMR (50 MHz): δ = 9.1, 31.9, 68.0, 70.7, 124.5, 125.0, 125.1, 125.2, 127.0, 127.7, 128.1, 128.4, 128.9, 133.6, 138.0, 143.9, 150.9, 167.4. IR (KBr) ν/cm^{-1}: 1796 (C=O). MS (ES$^+$): m/z = 526.8 [M + Na]$^+$. Anal. Calcd for $C_{24}H_{19}F_3N_2O_5S$: C 57.14; H 3.80; N 5.55%. Found: C 56.87; H 3.85; N 5.39%.

3i: *trans*-Isomer: white crystals, mp = 168 °C. ^{1}H NMR (200 MHz): δ = 0.61 (t, J = 7.4 Hz, 3 H), 1.22–1.42 (m, 1 H), 1.56–1.76 (m, 1 H), 5.18 (s, 1 H), 7.12–7.17 (m, 2 H), 7.31–7.37 (m, 3 H), 7.55 (d, J = 8.2 Hz, 2 H), 7.78 (d, J = 8.4 Hz, 2 H), 8.16 (d, J = 9.0 Hz, 2 H), 8.38 (d, J = 9.0 Hz, 2 H). ^{13}C NMR (50 MHz): δ = 8.6, 27.0, 68.4, 69.0, 113.2, 118.0, 124.6, 125.8, 127.7, 128.4, 129.0, 129.3, 132.6, 136.4, 139.1, 143.1, 151.1, 167.8. IR (KBr) ν/cm^{-1}: 1797 (C=O). MS (ES$^+$): m/z = 484.09 [M + Na]$^+$. Anal. Calcd for $C_{24}H_{19}N_3O_5S$: C 62.46; H 4.15; N 9.11%. Found: C 62.61; H 4.19; N 9.15%.

cis-Isomer: white crystals, mp = 103–104 °C. ^{1}H NMR (200 MHz): δ = 0.87 (t, J = 7.4 Hz, 3 H), 2.05–2.25 (m, 2 H), 5.13 (s, 1 H), 6.80–6.86 (m, 2 H), 6.99 (d, J = 8.4 Hz, 2 H), 7.04–7.09 (m, 3 H), 7.37 (d, J = 8.4 Hz, 2 H), 8.13 (d, J = 9.0 Hz, 2 H), 8.41 (d, J = 9.0 Hz, 2 H). ^{13}C NMR (50 MHz): δ = 9.1, 31.5, 67.8, 71.1, 112.3, 112.6, 118.0, 124.7, 126.9, 127.9, 128.2, 128.6, 129.0, 131.9, 133.3, 139.5, 143.7, 151.1, 167.2. IR (KBr) ν/cm^{-1}: 1786 (C=O). MS (ES$^+$): m/z = 484.09 [M + Na]$^+$. Anal. Calcd for $C_{24}H_{19}N_3O_5S$: C 62.46; H 4.15; N 9.11%. Found: C 62.45; H 4.19; N 9.36%.

3j: *trans*-Isomer: white crystals, mp = 79 °C. ^{1}H NMR (200 MHz): δ = 0.59 (t, J = 7.4 Hz, 3 H), 1.25–1.43 (m, 1 H), 1.63–1.81 (m, 1 H), 5.19 (s, 1 H), 7.09–7.21 (m, 4 H), 7.29–7.39 (m, 5 H), 8.13 (d, J = 9.2 Hz, 2 H), 8.36 (d, J = 9.0 Hz, 2 H). ^{13}C NMR (50 MHz): δ = 8.5, 27.0, 68.0, 69.1, 115.7, 116.2, 124.5, 126.0, 128.1, 128.7, 128.9, 129.0, 129.1, 129.3, 129.4, 137.0, 143.6, 168.3. IR (KBr) ν/cm^{-1}: 1786 (C=O). MS (ES$^+$): m/z = 477.0 [M + Na]$^+$.

cis-Isomer: white crystals, mp = 124 °C. ^{1}H NMR (200 MHz): δ = 0.91 (t, J = 7.4 Hz, 3 H), 2.16 (q, J = 7.4 Hz, 2 H), 5.13 (s, 1 H), 6.72–6.76 (m, 4 H), 6.82–6.87 (m, 2 H), 7.04–7.11 (m, 3 H), 8.01 (d, J = 9.0 Hz, 2 H), 8.33 (d, J = 9.0 Hz, 2 H). ^{13}C NMR (50 MHz): δ = 9.2, 32.2, 68.2, 70.3, 115.0, 115.4, 124.4, 127.1, 127.5, 128.3, 128.9, 129.6, 129.6, 129.7, 134.1, 144.2, 150.8, 160.2, 165.1, 167.6. IR (KBr) ν/cm^{-1}: 1784 (C=O). MS (ES$^+$): m/z = 477.0 [M + Na]$^+$.

3k: *trans*-Isomer: light yellow crystals, mp 143 °C. ^{1}H NMR (200 MHz): δ = 0.59 (t, J = 7.4 Hz, 3 H), 1.26–1.49 (m, 1 H), 1.69–1.87 (m, 1 H), 3.86 (s, 3 H), 3.92 (s, 3 H), 5.16 (s, 1 H), 6.84 (s, 1 H), 6.88–6.89 (m, 2 H), 7.18–7.39 (m, 5 H), 8.13 (d, J = 9.0 Hz, 2 H), 8.35 (d, J = 9.0 Hz, 2 H). ^{13}C NMR (50 MHz): δ = 8.7, 27.1, 56.1, 56.2, 68.2, 69.9, 110.2, 111.3, 119.9, 124.6, 125.9, 126.2, 128.1, 129.2, 137.5, 143.9, 149.3, 149.8, 151.1, 168.8. IR (KBr) ν/cm^{-1}: 1793 (C=O). MS (ES$^+$): m/z = 518.8 [M + Na]$^+$, 829.0. Anal. Calcd for ($C_{25}H_{24}N_2O_7S$): C, 60.47; H, 4.87; N, 5.64%. Found: C, 60.41; H, 4.83; N, 5.63%.

cis-Isomer: yellow crystals, mp 146 °C. ^{1}H NMR (200 MHz): δ = 0.94 (t, J = 7.4 Hz, 3 H), 2.18 (q, J = 7.4 Hz, 2 H), 3.21 (s, 3 H), 3.79 (s, 3 H), 5.08 (s, 1 H), 5.82 (s, 1 H), 6.57–6.59 (m, 2 H), 6.84–6.92 (m, 2 H), 7.06–7.09 (m, 3 H), 7.93 (d, J = 9.0 Hz, 2 H), 8.26 (d, J = 9.0 Hz, 2 H). ^{13}C NMR (50 MHz): δ = 9.3, 32.6, 55.4, 55.9, 69.2, 69.9, 110.3, 110.6, 121.8, 124.3, 125.7, 127.2, 127.5, 128.4, 129.0, 129.2, 134.9, 144.4, 148.5, 149.5, 150.8, 167.9. IR (KBr) ν/cm^{-1}: 1787 (C=O). MS (ES$^+$): m/z = 518.8 [M + Na]$^+$, 829.0. Anal. Calcd for ($C_{25}H_{24}N_2O_7S$): C, 60.47; H, 4.87; N, 5.64%. Found: C, 60.47; H, 4.90; N, 5.67%.

3l: *trans*-Isomer: white crystals, mp 163 °C. ^{1}H NMR (200 MHz): δ = 1.18 (s, 3 H), 5.28 (s, 1 H), 7.20–7.42 (m, 10 H), 8.15 (d, J = 9.0 Hz, 2 H), 8.37 (d, J = 9.0 Hz, 2 H). ^{13}C NMR (50 MHz): δ = 20.0, 64.1, 70.0, 124.6, 125.4, 127.0, 128.2, 129.0, 129.2, 129.3, 129.4, 133.6, 139.6, 144.0, 151.1, 169.1. IR (KBr) ν/cm^{-1}: 1787 (C=O). MS (ES$^+$): m/z = 445.1 [M + Na]$^+$. Anal. Calcd for ($C_{22}H_{18}N_2O_5S$): C, 62.55; H, 4.29; N, 6.63%. Found: C, 63.19; H, 4.64; N, 6.63%.

cis-Isomer: white crystals, mp 142 °C. ^{1}H NMR (200 MHz): δ = 1.81 (s, 3 H), 5.12 (s, 1 H), 6.71–6.77 (m, 2 H), 6.86–6.93 (m, 2 H), 6.95–7.16 (m, 6 H), 7.98 (d, J = 9.0 Hz, 2 H), 8.29 (d, J = 9.0 Hz, 2 H). ^{13}C NMR (50 MHz): δ = 25.4, 66.0, 71.1, 124.5, 126.8, 127.6, 127.9, 128.3, 128.5, 129.0, 129.1, 133.6, 135.8, 144.2, 150.9, 168.5. IR (KBr) ν/cm^{-1}: 1791 (C=O). MS (ES$^+$): m/z = 445.1 [M + Na]$^+$. Anal. Calcd for ($C_{22}H_{18}N_2O_5S$): C, 62.55; H, 4.29; N, 6.63%. Found: C, 63.14; H, 4.60; N, 6.50%.

3m: *trans*-Isomer: white crystals, mp = 59 °C. ^{1}H NMR (400 MHz): δ = 1.18 (s, 3 H), 5.23 (s, 1 H), 7.11–7.19 (m, 4 H), 7.28–7.35 (m, 5 H), 8.16 (d, J = 8.8 Hz, 2 H), 8.38 (d, J = 8.8 Hz, 2 H). ^{13}C NMR (100 MHz): δ = 19.8, 29.7, 64.0, 69.3, 115.9, 116.2, 124.6, 125.2, 128.2, 128.6, 128.7, 129.0, 129.3, 139.1, 143.6, 151.0, 168.8. IR (KBr) ν/cm^{-1}: 1795 (C=O).). MS (ES$^+$): m/z = 463.08 [M + Na]$^+$. HRMS Calcd for $C_{22}H_{17}FN_2O_5SNa$: 463.0740. Found: 463.0758.

cis-Isomer: white crystals, mp = 139 °C. ^{1}H-NMR (200 MHz): δ = 1.77 (s, 3 H), 5.09 (s, 1 H), 6.68–6.79 (m, 4 H), 6.85–6.91 (m, 2 H), 7.04–7.11 (m, 3 H), 8.04 (d, J = 9.0 Hz, 2 H), 8.35 (d, J = 9.0 Hz, 2 H). ^{13}C NMR (50 MHz): δ = 24.9, 69.9, 70.2, 115.0, 115.5, 124.5, 126.6, 127.6, 128.5, 128.9, 129.3, 129.5, 129.6, 129.6, 135.4, 143.8, 150.9, 160.2, 165.1, 168.2. IR (KBr) ν/cm^{-1}: 1794 (C=O). MS (ES$^+$): m/z = 463.1 [M + Na]$^+$. HRMS Calcd for $C_{22}H_{17}FN_2O_5SNa$: 463.0740. Found: 463.0741.

3n: white crystals, mp 156 °C. ^{1}H NMR (200 MHz): δ = 5.86 (s, 1 H), 6.87–7.21 (m, 10 H), 7.28–7.48 (m, 5 H), 8.00 (d, J = 9.0 Hz, 2 H), 8.26 (d, J = 9.0 Hz, 2 H). ^{13}C NMR (50 MHz): δ = 69.6, 73.3, 124.4, 126.9, 127.6, 127.8, 128.0, 128.3, 128.4, 129.0, 129.1, 129.2, 133.4, 135.6, 138.7, 143.9, 150.9, 166.7. IR (KBr) ν/cm^{-1}: 1781 (C=O). MS (ES$^+$): m/z = 507.0 [M + Na]$^+$. Anal. Calcd for ($C_{27}H_{20}N_2O_5S$): C, 66.93; H, 4.16; N, 5.78%. Found: C, 66.97; H, 4.31; N, 5.77%.

3o: white crystals, mp 121 °C. ^{1}H NMR (200 MHz): δ = 5.84 (s, 1 H), 6.75–6.96 (t, 6 H), 7.01–7.09. (m, 3 H), 7.28–7.44 (m, 5 H), 8.04 (d, J = 9.0 Hz, 2 H), 8.30 (d, J = 9.0 Hz, 2 H). ^{13}C NMR (50 MHz): δ = 29.7, 68.8, 115.2, 115.6, 124.4, 126.8, 127.7, 128.3, 128.4, 128.9, 129.1, 129.5, 129.7, 135.2, 138.3, 143.6, 166.5. IR (KBr) ν/cm^{-1}: 1791 (C=O). MS (ES$^+$): m/z = 524.8 [M + Na]$^+$. Anal. Calcd for $C_{27}H_{19}FN_2O_5S$: C 64.53; H 3.81; N 5.57%. Found: C 64.83; H 3.89; N 5.67%.

3p: white crystals, mp 168 °C. ^{1}H NMR (200 MHz): δ = 1.06–1.38 (m, 4 H), 1.46–1.66 (m, 6 H), 1.72–2.02 (m, 2 H), 4.85 (s, 1 H), 7.11–7.33 (m, 5 H), 8.12 (d, J = 8.8 Hz, 2 H), 8.38 (d, J = 8.8 Hz, 2 H). ^{13}C NMR (50 MHz): δ = 22.8, 23.7, 29.0, 29.1, 30.0, 35.4, 64.3, 70.5, 124.6, 127.1, 128.8, 129.0, 129.2, 134.1, 144.2, 151.0, 171.3. IR (KBr) ν/cm^{-1}: 1787 (C=O). MS (ES$^+$): m/z = 437.2 [M + Na]$^+$. Anal. Calcd for ($C_{21}H_{22}N_2O_5S$): C, 60.85; H, 5.35; N, 6.76%. Found: C, 60.71; H, 5.47; N, 6.69%.

Preparation of cyclopentyl methyl ketene 2e. The ketene was prepared by dehydrochlorination of 2-cyclopentylpropanoyl chloride (2.73 g, 17 mmol) with DABCO (1.9 g 17 mmol) in toluene (20 mL) under a nitrogen atmosphere at 80 °C. After 3 h the reaction mixture was allowed to cool down to room temperature and the ketene and toluene were vacuum transferred into another flask. To quantify the amount of ketene generated by this procedure, 0.5 mL of yellow ketene solution was quenched with an excess of *n*-propylamine. Evaporation of the solvent and excess amine furnished 2-cyclopentyl-*N*-propylpropanamide as a white solid (24.4 mg). The concentration of ketene solution was 0.27 M. ^{1}H NMR (200 MHz) δ = 0.88 (t, J = 7.5 Hz, 3 H), 1.00–1.16 (m, 5 H), 1.43–1.61 (m, 6 H), 1.65–1.82 (m, 2 H), 1.84–1.96 (m, 2 H), 3.07–3.27 (m, 2 H), 5.83 (s, 1 H).

General experimental procedure for Table 3. To a ketene solution of **2e** (0.75 mmol, 2.82 mL toluene) was added benzaldehyde (**4a**) (30μL, 0.3 mmol) at −78 °C followed by the addition of MHMDS (0.5 M solution in toluene), NaOTMS or KO*t*Bu (0.03 mmol). After the given times and temperatures in Table 3, the reaction mixture was subjected directly to column chromatography on silica gel and the diastereomers were eluted with a 1:19 diethyl ether–petrol ether mixture to give the desired compounds as oils. For yields and diastereomeric ratios see Table 3.

8a: *trans*-Diastereomer: ^{1}H NMR (200 MHz) δ = 0.91 (s, 3 H), 1.26–1.58 (m, 2 H), 1.62–1.78 (m, 4 H), 1.79–2.06 (m, 2 H), 2.21–2.38 (m, 1 H), 5.39 (s, 1 H), 7.22–7.46 (m, 5 H); ^{13}C NMR (50 MHz) δ = 15.5, 25.5, 25.6, 27.8, 28.3, 44.3, 63.3, 79.5, 125.4, 128.3, 128.6, 135.6, 174.5. The spectral data were consistent with literature values.[8h]

cis-Diastereomer: ^{1}H NMR (200 MHz) δ = 0.89–1.29 (m, 3 H), 1.30–1.53 (m, 5 H), 1.55 (s, 3 H), 1.97–2.08 (m, 1 H), 5.30 (s, 1 H), 7.28–7.44 (m, 5 H); ^{13}C NMR (50 MHz) δ = 17.0, 25.6, 25.8, 26.7, 28.2, 39.8, 63.3, 83.7, 126.1, 128.5, 128.6, 135.6, 174.7. The spectral data were consistent with literature values.[8h]

General experimental procedure for Table 4. Ketene **2d** (93 mg, 0.75 mmol) and an aldehyde **4** or **9** (0.3 mmol) were placed into a dry Schlenk flask with dry toluene (2 mL) at −78 °C. KHMDS (0.5 M solution in toluene, 0.03 mmol, 10 mol%) was slowly added. The reaction mixture was stirred for 10 min. The solvent was removed under reduced pressure giving the crude products **8**, which were purified by column chromatography (2/98 diethyl ether/hexane) to give the desired lactones. For yields see Table 4.

8b: oil; ^{1}H NMR (400 MHz) δ = 1.25–1.42 (m, 4 H), 1.55–1.64 (m, 4 H), 1.85–1.90 (m, 2 H), 2.14–2.25 (m, 2 H), 5.30 (s, 1 H), 7.25–7.46 (m, 5 H); ^{13}C-NMR (100 MHz) δ = 22.9, 23.8, 29.1, 29.2, 30.4, 35.4, 64.0, 84.2, 125.9, 128.7, 135.5, 175.5. Spectral data were consistent with literature values.[8h]

8c: oil, ^{1}H NMR (400 MHz) δ = 1.44–1.57 (m, 9 H), 1.74–1.76 (m, 1 H), 1.90–1.94 (m, 1 H), 2.16–2.22 (m, 1 H), 2.30 (s, 3 H), 2.42–2.48 (m, 1 H), 5.40 (s, 1 H), 7.19 (d, J = 8.0 Hz) 7.27–7.35 (m, 2 H), 7.47–7.49 (m, 1 H); ^{13}C NMR (100 MHz) δ = 18.4, 22.0, 22.7, 28.4, 28.7, 30.9, 34.9, 62.7, 81.7, 124.4, 125.3, 127.1, 129.2, 128.9, 132.9, 133.1, 174.2. IR (NaCl) ν/cm^{-1} 1827, 1458, 1460, 1102, 937.

8d: oil, ^{1}H NMR (400 MHz) δ = 1.26–1.37 (m, 5 H), 1.60–1.69 (m, 4 H), 1.85–1.90 (m, 1 H), 2.13–2.19 (m, 1 H), 2.27–2.31 (m, 1 H), 5.31 (s, 1 H), 7.30 (d, J = 8.0 Hz, 2 H),7.45 (d, J = 8.0 Hz, 2 H); ^{13}C NMR (100 MHz) δ = 22.7, 23.7, 28.98, 29.03, 30.3, 35.2, 64.1, 83.4, 127.2, 128.9, 134.0, 134.4, 175.0. IR (NaCl) ν/cm^{-1} 1827, 1460, 1092, 940.

8e: oil, ^{1}H NMR (200 MHz) δ = 1.22–1.25 (m, 5 H), 1.50–1.57-(m, 4 H), 1.70–1.90 (m, 1 H), 1.90–1.94 (m, 1 H), 2.05–2.25 (m, 2 H), 2.30 (s, 3 H), 5.20 (s, 1 H), 7.05–7.18 (m, 4 H); ^{13}C NMR (50 MHz) δ = 21.4, 22.9, 23.8, 29.2, 29.8, 30.3, 35.4, 63.8, 84.3, 125.9, 129.4, 132.5, 138.5, 175.7. IR (NaCl) ν/cm^{-1} 1823, 1459, 1260, 1106, 938.

8f: oil, ^{1}H NMR (200 MHz) δ = 1.20–1.63 (m, 9 H), 1.84–1.97 (m, 1 H), 2.09–2.37 (m, 2 H), 5.34 (s, 1 H), 7.44 (d, J = 8.0 Hz, 2 H), 7.71 (d, J = 8.0 Hz, 2 H); ^{13}C NMR (50 MHz), δ = 22.7, 23.6, 28.9, 29.0, 30.4, 35.3, 64.5, 83.2, 121.2, 125.6, 125.8, 126.1, 130.4, 131.1, 139.5, 174.6. IR (NaCl) ν/cm^{-1} 1827, 1512, 1264, 1108, 939.

8g: oil, ^{1}H NMR (200 MHz) δ = 1.25–1.45 (m, 4 H), 1.63–1.68 (m, 4 H), 1.82–1.92 (m, 2 H), 2.06–2.32 (m, 2 H), 2.30 (s, 3 H), 5.28 (s, 1 H), 7.07–7.15 (m, 2 H), 7.24–7.31 (m, 2 H); ^{13}C NMR (50 MHz), δ = 22.3, 23.2, 27.8, 28.5, 29.6, 34.8, 63.5, 83.0, 115.2 (d, J = 22 Hz), 127.1 (d, J = 8 Hz), 131.1, 162.2 (d, J = 245 Hz), 174.6. IR (NaCl) ν/cm^{-1} 1826, 1512, 1459, 1261, 1109, 939.

10: oil, ^{1}H NMR (200 MHz) δ = 1.20–1.91 (m, 10 H), 2.15–2.40 (m, 2 H), 7.24–7.55 (m, 5 H); ^{13}C NMR (50 MHz), δ = 22.7, 23.1, 29.3 (q, J = 2.8 Hz), 29.5, 29.7, 34.3, 66.7, 84.7 (q, J = 30.2 Hz), 124.1 (q, J = 281.6 Hz), 125.3 (q, J = 2.2 Hz), 126.5, 128.2, 129.2, 129.4, 131.2, 172.2. IR (NaCl) ν/cm^{-1} 3055, 2987, 1845, 1422, 1266, 1179, 748.

General experimental procedure for the reaction with ketene 2f. Ketene **2f** (0.6 mmol, 1.62 mL, 0.37 M solution in THF) and aldehyde **4a** or **4d** (0.3 mmol) were added at −78 °C to toluene (2 mL) followed by the addition of KHMDS (0.03 mmol, 0.5 M solution in toluene). The reaction was monitored by TLC. After 15 min the reaction was completed. The reaction was worked up with sat. $NH_4Cl_{(aq)}$ (5 mL) and the aqueous phase was extracted with CH_2Cl_2 (3 × 5 mL). The combined organic phases were dried (Na_2CO_3) and the solvent removed. The resulting product was dissolved in THF (5 mL) and $LiAlH_4$ (1.2 mmol) was added. After 1 h stirring the reaction was carefully quenched with 1 M NaOH (5 mL) and H_2O (5 mL). The aqueous solution was extracted with EtOAc (3 × 5 mL) and the combined phases were dried (Na_2SO_4) and the solvent removed. The crude product was purified on silica gel and the products were eluted with 1:2 diethyl ether–petrol ether mixture to give the desired compounds as white solids. The spectral data were consistent with literature values.[8h]

11a: Ar = Ph, solid, yield 82%. ^{1}H NMR (200 MHz) δ = 0.89–1.29 (m, 3 H), 1.30–1.53 (m, 5 H), 1.55 (s, 3 H), 1.97–2.08 (m, 1 H), 5.30 (s, 1 H), 7.28–7.44 (m, 5 H); ^{13}C NMR (50 MHz) δ = 17.0, 25.6, 25.8, 26.7, 28.2, 39.8, 63.3, 83.7, 127.4, 128.4, 137.1, 138.4.

11b: Ar = 4-Me-C_6H_4-, solid, yield 89%. ^{1}H NMR (200 MHz) δ = 0.81 (s, 3 H), 0.86 (s, 3 H), 2.34 (s, 3 H), 3.15 (s, 2 H), 3.48 (d, J = 10.2 Hz, 1 H), 3.58 (d, J = 10.5 Hz, 1 H), 4.59 (s, 1 H), 7.11–7.59 (m, 4 H). ^{13}C NMR (50 MHz) δ = 18.9, 21.7, 22.7, 39.0, 72.0, 82.1, 127.4, 127.5, 128.4, 137.1, 138.4.

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