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Some unusual reactivities in the SmI_2-mediated reductive coupling of acrylamides and acrylates with imides

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ABSTRACT

A serendipitous discovery of some intra-molecular enolate addition reactions following a SmI_2-mediated reductive cross-coupling between imides and electron-deficient olefins leading to some novel compounds was investigated to determine the generality of the protocol and the possible mechanistic pathways involved. This provided a *Z*-selective synthesis of γ-ketoenediamides in good yields, albeit as of now the substrate scope remains limited. It was also shown that the seemingly similar acrylate substrates can behave differently compared to the corresponding acrylamides in their SmI_2-mediated reductive cross-coupling reaction with imides, and it was argued that these diverging reactivities are dominated by the ability of the acrylates to coordinate the samarium metal centre.

1. Introduction

SmI_2-mediated carbonyl–olefin couplings hold an increasingly important position in the growing family of C–C bond forming reactions mediated by SmI_2.[1] The outcome of such coupling reactions depends strongly on the relative reactivity of the coupling partners towards SmI_2 as has been elegantly demonstrated in an example by the group of Procter, in which a carbonyl–olefin coupling can proceed either through a 'carbonyl first' or an 'alkene first' mechanism.[2] Most carbonyl–olefin couplings are carried out in the presence of a proton donor.[3,8f,g] Little is known about the role of proton donors in the initial mechanistic steps in the carbonyl–olefin coupling, however, substantial effort has been made by the laboratories of Flowers,[4] Hoz[5] and Hilmersson[6] to understand the role of proton donors in carbonyl reductions mediated by SmI_2. Imides, β-keto amides and β-keto esters[7,8] have shown to be particularly good alternative carbonyl coupling partners in carbonyl–olefin couplings, and Flowers[9] has revealed that β-keto amides and esters are reduced 6 and 2 orders of magnitude faster, respectively, than the equivalent alkyl ketone. Moreover, the resulting hemiaminal obtained from addition to an imide carbonyl will be stabilised by the bidentate coordination of samarium preventing hemiaminal collapse, and hence preventing over-reduction of the resulting ketone. In our hands, imides have proven to be excellent acyl equivalents in carbonyl–olefin couplings, and have demonstrated their utility in a variety of applications.[8]

In this paper, we seek to highlight some recent unusual reactivities observed in the course of our studies on SmI_2-mediated carbonyl–olefin couplings between imides and electron-deficient alkenes, namely the reactivity of arising samarium enolates towards intra-molecular acyl substitution and aldol-condensation type reactions and the notable reactivity difference between seemingly similar coupling partners, acrylamides and acrylates.

2. Results and discussion

Recently, we published a novel application of *N*-acyl succinimides as acyl transfer reagents in the SmI_2-mediated reductive cross-coupling reactions (RCCRs) between electron-deficient olefins and imides.[10] It was proposed that the acyl transfer followed a mechanism similar to the coupling reactions with *N*-acyl oxazolidinones.[10] Hence, reductive coupling through a chelated transition state resulted in the formation of enolate intermediate **1** (Scheme 1). Subsequent protonation by H_2O afforded hemiaminal **2**, which collapses to the ketone during workup. The *N*-acyl succinimides were utilised to provide evidence for the influence of C–N bond rotation on the outcome of aforementioned reactions.

During the course of these studies, we isolated an interesting byproduct **6** in a 15% yield upon the reaction of *N*-acetyl succinimide **3** with *N*-*tert*-butylacrylamide **4** (Scheme 2). The double enamide motif in **6** was supported by the presence of four olefinic carbons in the ^{13}C NMR spectrum, two of which were shifted upfield (106.6 and 100.9 ppm). Significantly, only one olefinic proton was identified by ^1H NMR and was observed as a quartet with a coupling constant of J=1.2 Hz, indicative of an allylic coupling to a methyl. Moreover, the identification of two amides, one

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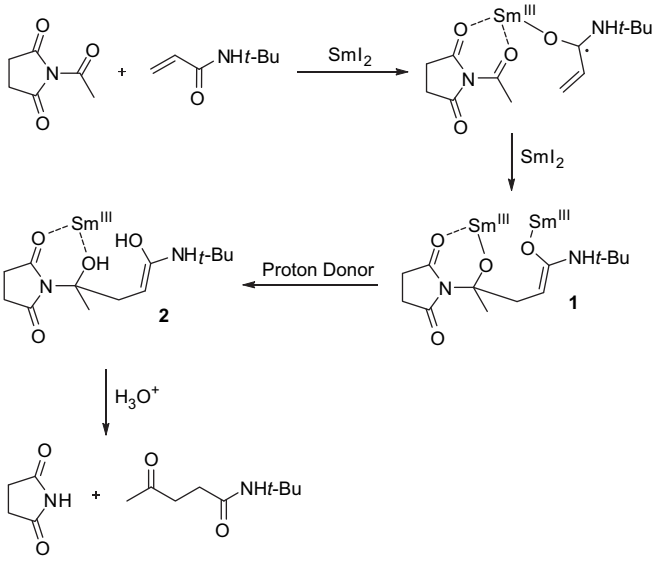
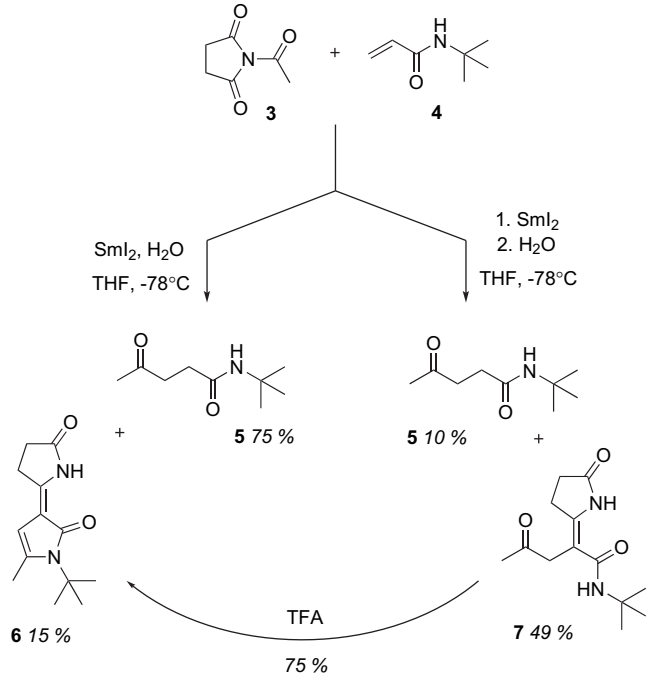


Scheme 1.

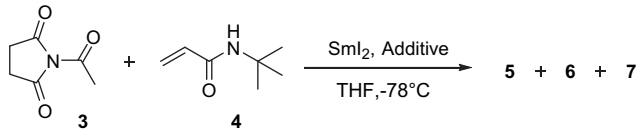
secondary and one tertiary by ^{1}H and ^{13}C NMR spectroscopy helped to substantiate the proposed structure **6**. Intrigued by its structure, we therefore set out to identify reaction conditions, which could favour its formation in higher yields, as well as to understand its mechanism of formation. It was expected that **6** would most likely involve the enolate addition to one of the ring carbonyls succeeding the reductive coupling of the substrates.



Scheme 2.

Both the collapse of the hemiaminal formed upon reaction onto the acyl carbonyl and the premature protonation of an intermediate enolate to produce the γ-keto amide **5** were expected to be strongly influenced by the nature of the proton donor, and we therefore conducted a small screening of proton donors in an attempt to promote the formation of **6** (Table 1). Not surprisingly, the more acidic proton donor trifluoroethanol (TFE) and the TEA/H_2O mixture resulted in suppression of the formation of **6** (Table 1, entries 1 and 2). MeOH produced a range of unidentified products, while the addition of *t*-BuOH and the exclusion of the proton donor to our surprise resulted in a new product **7** in a modest yield of 37% (Table 1, entries 5 and 6, and Scheme 2).[11]

Table 1
Influence of the proton donor ability on the SmI_2-mediated reductive coupling of *N*-acetyl succinimide[13] (1.5 equiv) and *tert*-butylacrylamide (1 equiv)



Entry	Additive	Yield[a] of **5**	Yield[a] of **6**	Yield[a] of **7**
1	TEA/H_2O	Major	Trace	—
2	TFE	Major	Trace	—
3	H_2O	75%	15%	—
4	MeOH	—	—	—
5	*t*-BuOH	18%	Trace	37%
6	None	Trace	12%	36%
7[b]	None	11%	—	49%
8[c]	None	10%	—	58%

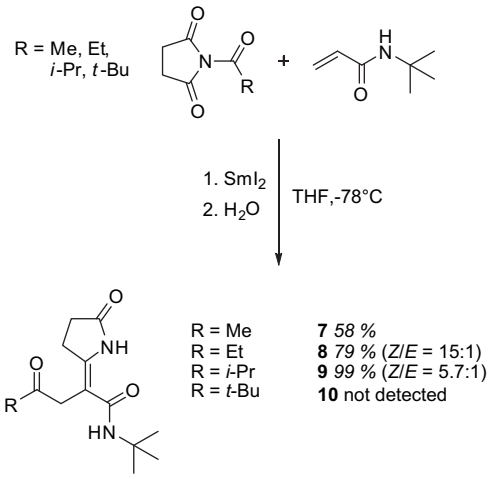
[a] Isolated yields after column chromatography.
[b] The order of addition is reversed, i.e., the substrates were added as a solution in THF to a stirring cold solution of SmI_2 in THF.
[c] *N*-Acetyl succinimide (1 equiv) and 1.5 equiv of acrylamide. Yield is based on the *N*-acetyl succinimide. The order of addition as for entry 7.

Transformation of **7** into **6** could be achieved with catalytic amounts of either *p*-TsOH or TFA in dichloromethane in a 50% and 75% yield, respectively (Scheme 2) suggesting that **7** does not derive from an alternative reaction path, but rather **7** is an intermediate in the formation of **6**. Although, intra-molecular enamide formation seems remarkable given the sterically congested nature of the *tert*-butyl amide, this kind of transformation has been reported previously proceeding under mild acidic conditions with γ-keto amides.[12] Reversing the order of addition, by adding a THF solution of the substrates to a pre-cooled solution of freshly formed SmI_2, resulted in an increased yield of **7** to 49%. Finally, a 58% yield of **7** was achieved based on *N*-acetyl succinimide by using an excess of acrylamide (Table 1, entries 7 and 8). Gratifyingly, the reaction between the intermediate reactive enolate and a second equivalent of *N*-acetyl succinimide was suppressed resulting in a di-acetylated acrylamide (**13**, Scheme 5), which was observed as a byproduct (~3%) in the reactions described in entries 6 and 7 of Table 1.

While the reaction appears to be tolerant to increase in the bulk of the *N*-acyl moiety as was also observed by us in previous studies for the RCCR utilising *N*-acyl oxazolidinones, in this transformation *N*-pivaloyl succinimide provides none of the desired enamide product. Surprisingly, both *N*-pivaloyl succinimide and *N*-*tert*-butylacrylamide were recovered unreacted in the absence of water. This suggests that the RCCR between *N*-acyl succinimides and acrylamides without water progresses through a different mechanism, as opposed to the RCCR between *N*-acyl oxazolidinones and acrylamides, where the acrylamide is reduced independently of the *N*-acyl oxazolidinone in the presence of water. Alternatively, the coupling reaction between imides and acrylamides in general may not progress through any intermediates of acrylamide reduction, but rather in direct competition. For example, the reaction may occur by way of a concerted reductive C–C bond formation.

It was observed that yields increased with the bulk of the *N*-acyl moiety (Scheme 3), going from R=Me (58%) to R=Et (79%) to R=*i*-Pr (99%). This could be attributed to either the stability of the resulting ketone and/or the effectiveness of hemiaminal collapse. Compounds **8** and **9** were obtained as two stereoisomers, easily separable by column chromatography, *Z*/*E*=15:1 and *Z*/*E*=5.7:1, respectively. A crystal structure was acquired for the major

Z-isomer of **9** (Fig. 1), the preference for which clearly is a result of the formation of an intra-molecular hydrogen bond (NH–O, 2.018 Å). To our surprise, *N*-pivaloyl succinimide provided none of the enamide product **10**, and both coupling precursors were recovered unreacted in the absence of water. This suggests that the reductive coupling reaction between *N*-acyl succinimides and acrylamides without water progresses through a different mechanism, as opposed to the coupling reaction with *N*-acyl oxazolidinones.



Scheme 3.

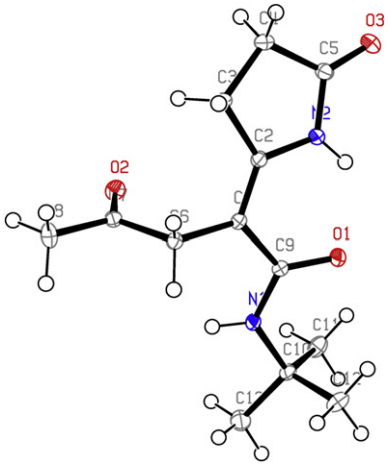
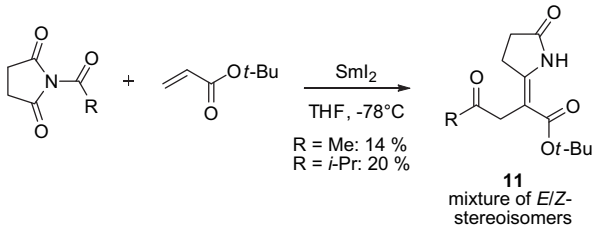


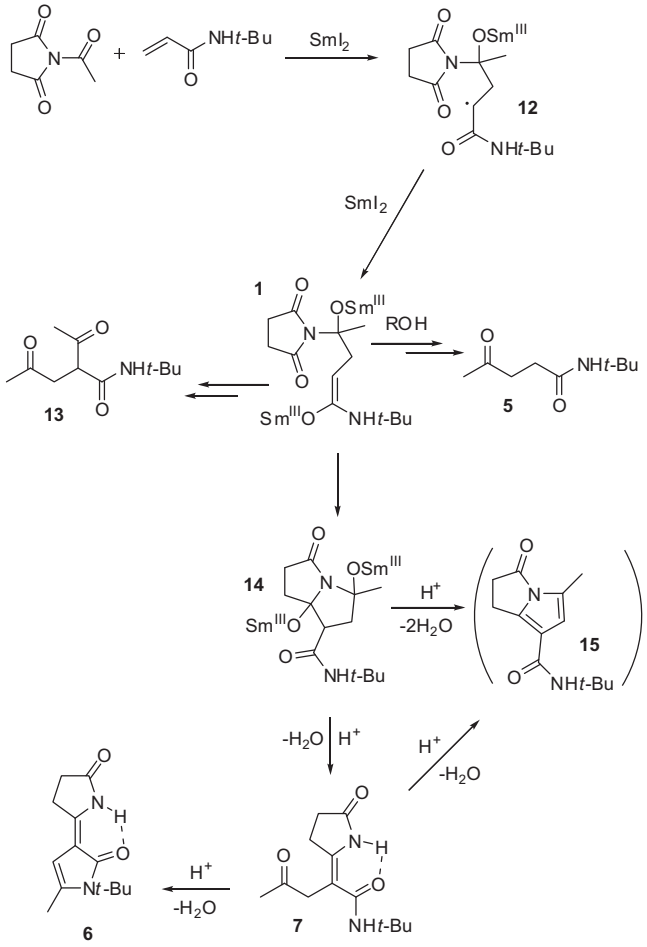
Figure 1. X-ray crystal structure of compound **9** (*Z*-isomer).

Unfortunately, the utility of the reaction is somewhat limited by the poor stability of the *N*-acyl succinimides making the synthesis and purification of the starting materials a difficult task. Also, it appears that there exists a delicate balance between the successful reduction of the intermediate α-radical followed by enolate addition to the ring carbonyl and a variety of intermolecular side reactions (e.g., radical or anionic addition reactions), possibly also with resulting polymerisation processes. Preliminary studies suggest that simple variations of the *N*-acyl moiety is tolerated (Scheme 3), yet small changes to the electron-deficient olefin, such as changing from *tert*-butyl to *n*-butylacrylamide or from secondary to tertiary amide results in substantial decomposition/polymerisation under the reaction conditions. The di-acetylated acrylamide (**13**, Scheme 5) was isolated as a significant byproduct (13%) with *n*-butylacrylamide as a coupling partner. The application of acrylates does show some promise and provided **11** in a 14 and 20% yield for R=Me and R=*i*-Pr, respectively, as a mixture of *E*/*Z*-stereoisomers (Scheme 4).



Scheme 4.

A mechanistic proposal for the reaction is depicted in Scheme 5. It is expected that the formation of **7** proceeds via a C–C bond formation between the *N*-acyl carbonyl and the β-carbon of the intermediate acrylamide derived radical anion, followed by reduction of the resulting stabilised α-radical **12** to the corresponding amide enolate **1** and succeeding addition to the ring carbonyl of the succinimide unit.

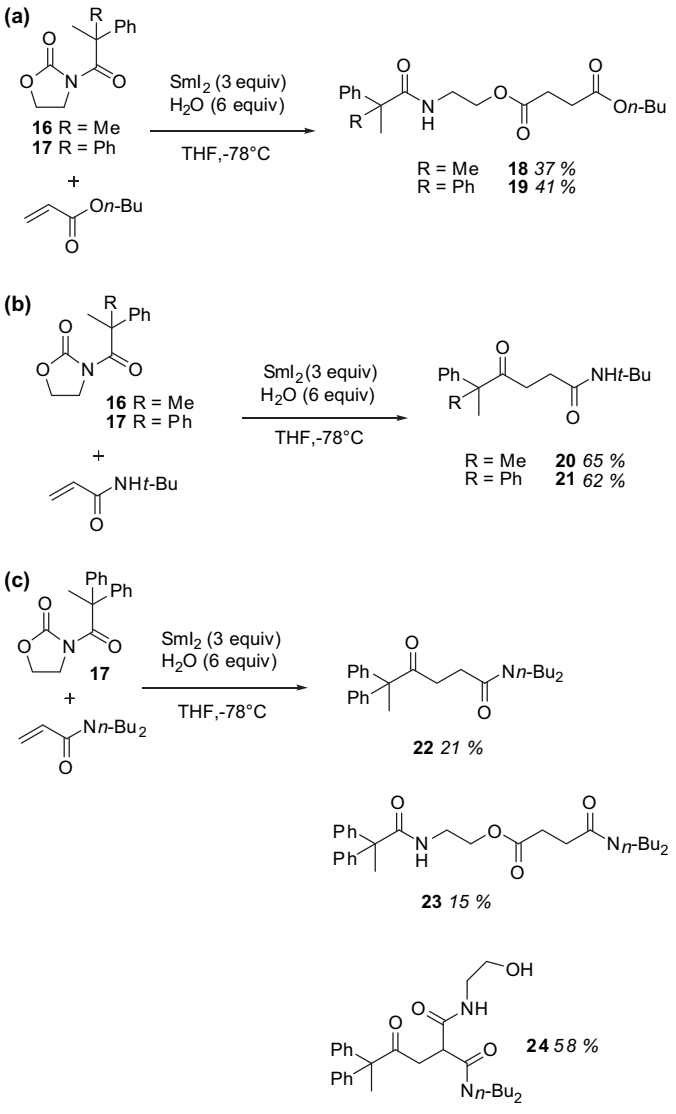


Scheme 5.

The resulting double hemiaminal **14** should then readily eliminate one molecule of H_2O and ringopen to produce the γ-ketoenamide **7**. At first, we assigned **6** to the bicyclic pyrrole structure **15**, however, at a later stage it was acknowledged that the same

spectroscopic data could be assigned to the dienamide structure **6**. Extensive efforts to crystallise the compound has so far failed, albeit the most likely structure is **6**, as the ^{1}H NMR spectrum suggests the presence of an amide proton participating in a hydrogen bond (10.3 ppm in deuterated acetonitrile), being only possible for the structure **6**.

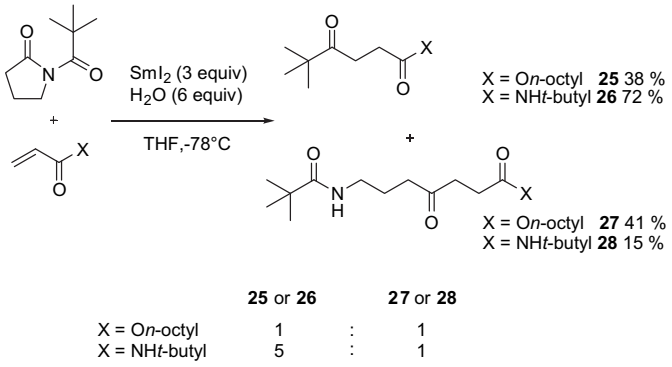
In the course of our studies on this type of SmI_2-mediated RCCRs we have observed that even small changes to the electron-deficient alkene can have a profound effect on the reactions. This effect has manifested itself in more than one way, e.g., ease of reduction, regioselectivity in the C–C bond forming step, reactivity of the intermediate enolate and product stability. An example of the diverging reaction pathways experienced for acrylamides and acrylates in SmI_2-mediated coupling of *N*-acyl oxazolidinones and electron-deficient olefins is outlined in Scheme 6. Curiously, when the *N*-acyl oxazolidinones **16** and **17** were reacted with *n*-butyl acrylate, we isolated products **18** and **19** in a 37% and 41% yield, respectively, as the sole coupling products (Scheme 6a), bearing witness to a cross-coupling between the oxazolidin-2-one carbonyl group and the olefin with concomitant ring opening. Contrary to this, their reaction with *tert*-butylacrylamide provides the expected γ-keto amides **20** and **21** in a 65% and 62% yield, respectively (Scheme 6b).[14] The divergence in regioselectivity observed is reminiscent of the results obtained by Evans et al. upon hydrolysis of sterically congested *N*-acyl oxazolidinones with LiOH, preferring attack on the ring carbonyl, as opposed to LiOOH, which prefers attack on the acyl carbonyl.[15]



Scheme 6.

When the *N*-acyl oxazolidinone **17** was reacted with di-*n*-butylacrylamide, to our surprise, a third compound **24** was formed as the major product in a 58% yield (Scheme 6c), possibly arising from an enolate intermediate similar to **1** (Scheme 5) proposed for the *N*-acyl succinimide olefin couplings. Enolate addition to the *endo*-cyclic carbonyl group would be followed by ring opening, providing a primary alkoxide, which is rapidly protonated by H_2O. Two other products were isolated from the reaction mixture, being the expected coupling product **22** (21% yield), as well as compound **23** (15% yield), the latter of which arises from attack of the reduced acrylamide at the oxazolidinone carbonyl group, as observed for the acrylates (Scheme 5a). Because the products **22** and **24** are derived from the addition to the acyl carbonyl group and **23** originates from the addition to the *endo*-cyclic carbonyl group, this signifies that in the SmI_2-mediated RCCR, tertiary acrylamides exhibit properties intermediate to those of the secondary acrylamides and acrylates.

The divergence in regioselectivity between acrylamides and acrylates can also be observed in their reaction with *N*-pivaloyl pyrrolidin-2-one. It was found that *tert*-butylacrylamide preferred addition to the acyl carbonyl group, affording **26** and **28** in a 72% and 15% yield (5:1 ratio), respectively. Whereas *n*-octyl acrylate was essentially unselective giving a 1:1 mixture of **25** and **27** derived from addition to the acyl carbonyl in a 38% yield and the ring carbonyl in a 41% yield, respectively (Scheme 7). This regioselectivity is in contrast to that reported by Namy,[16] in which selectivity for reaction at the ring carbonyl of *N*-acyl lactams was observed in their reductive coupling with ketones.

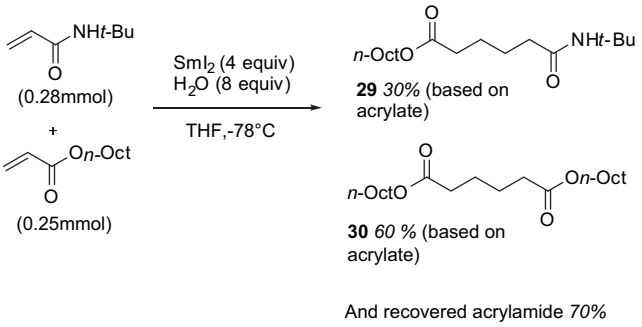


	25 or 26		27 or 28
X = O*n*-octyl	1	:	1
X = NH*t*-butyl	5	:	1

Scheme 7.

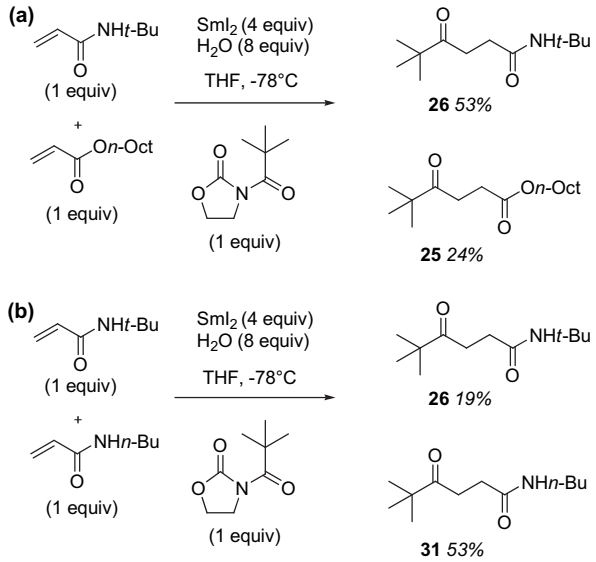
In an attempt to pinpoint the determining factors for the observed reactivity differences between acrylamides and acrylates, we conducted a few competition experiments. A 1:1 ratio of *N*-*tert*-butylacrylamide and *n*-octyl acrylate was subjected to the dropwise addition of an excess of SmI_2 at −78 °C in the absence of an imide coupling partner (Scheme 8). This resulted in a 2:1 mixture of compounds **30** (60%) and **29** (30%), and a 70% yield of recovered acrylamide. This result can be explained by one of two possible scenarios. Either the acrylates are initially more reactive towards reduction by SmI_2 (corroborating rates of reduction obtained in collaboration with Flowers et al.[14]) or the two alkenes are reduced at similar rates by the lanthanide reagent, and the radical anions produced react preferentially with acrylates. This latter point could be expected when considering the relative rates for the addition of carbon-centred radicals to acrylates and acrylamides ($1.2–1.9\times10^8$ and $3.2–5.4\times10^7$ M^{-1} s^{-1}, respectively) reported by Wojnárovits.[17] We have also previously noted that under the same reaction

conditions, acrylates alone are more prone to dimerisation, whereas acrylamides are preferentially reduced to the corresponding propionic amide,[14] signifying that acrylates are better acceptors (anionic or radical) than acrylamides given that a radical dimerisation pathway can be excluded.[18]



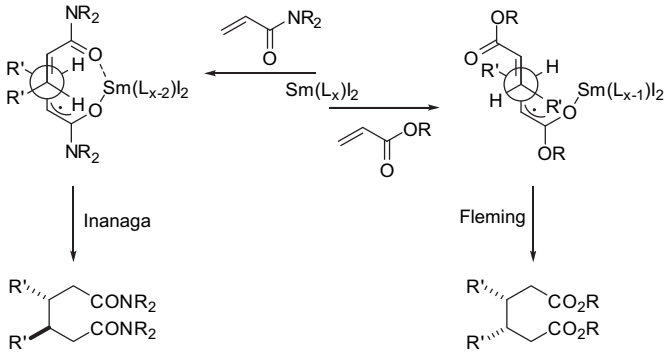
Scheme 8.

When the same two alkenes were reacted with a limiting amount of *N*-pivaloyl oxazolidinone, 53% of the *N*-acyl oxazolidinone reacted to produce the γ-keto amide **26**, and 24% to produce the γ-keto ester **25** (Scheme 9a).



Scheme 9.

This result is difficult to explain with either of the hypotheses stated above and therefore the explanation for the higher reactivity of acrylamides towards *N*-acyl oxazolidinones must be sought elsewhere. An obvious possibility is that the *N*-acyl oxazolidinone plays a central role in the selection between acrylates and acrylamides. This can be envisioned in two ways. (1) Reduction of the *N*-acyl oxazolidinone precedes addition to the olefin, whereby the radical addition steps become decisive for the selectivity. However, in collaboration with the Flowers group, we previously rejected this pathway.[14] A cyclopropyl probe on the acyl carbonyl provided coupling products with an intact cyclopropane ring suggesting that a ketyl-radical is not formed. (2) After bidentate coordination of the *N*-acyl oxazolidinone to SmI_2 the more Lewis basic of the two olefins can be expected to coordinate preferentially and thereby react fastest, effectively circumventing their individual reduction potentials. Whereas the first can be ruled out by our previous work,[14] the second coincides surprisingly well with the combined results of Kim[19] and Inanaga[20] on hydrodimerisation of acrylamides and the results of Fleming[21] on hydrodimerisation of acrylates. Inanaga reported a diastereoselective hydrodimerisation of *N*,*N*-dibenzyl crotonamide to achieve the corresponding DL-3,4-dimethyladipiamide, exclusively.[20a] Inanaga[20b] and Kim[19] later reported enantioselective versions with the same diastereoselective outcome. Both Kim and Inanaga rationalised that the diastereoselectivity arises by a tight coordination of the two reacting acrylamides to the same samarium centre, as depicted in Scheme 10. Inanaga also noted that the hydrodimerisation of acrylamides slowed significantly with increasing bulk in the β-position in good accordance with the proposed transition state, resulting in competing reduction of the C=C bond.[20b] Fleming, however, successively reported a *meso*-selective hydrodimerisation of both *cis*- and *trans*-acrylic esters, most likely arising from a transition state, whereby only one acrylate is coordinated to the samarium centre and the incoming olefin positions itself so as to minimise interactions between the two bulky β-substituents (Scheme 10).[21]



Scheme 10.

Reacting a 1:1 mixture of *tert*-butylacrylamide and *n*-butylacrylamide with a limiting amount of *N*-pivaloyl oxazolidinone results in the formation of the γ-keto amide **26** in a 19% yield and the γ-keto amide **31** in a 53% yield (Scheme 9b). Again, it can be proposed that the aptitude for the olefin to coordinate samarium is decisive. With the *tert*-butyl group being a better electron donating group than *n*-butyl in terms of inductive effects, one could argue that *tert*-butylacrylamide should provide the more Lewis basic carbonyl. However, it is not hard to imagine that the bulk of the *tert*-butyl group will interfere significantly with the coordination sphere of samarium, hence with the result that the *n*-butylacrylamide becomes the better ligand.

3. Conclusion

A SmI_2-mediated reductive cross-coupling reaction between *N*-acyl succinimides and *N*-*tert*-butylacrylamide has provided an entry into some novel enediamide[22] and dienediamide structures by way of two consecutive C–C bond formations followed by dehydration to generate the enediamide core. Although at present the bicyclic pyrrole **15** structure has been ruled out, it seems plausible that careful manipulation of **7**–**9** could provide an entry into these compounds. Alternatively, optimisation of the protocol to facilitate the use of either *N*,*N*-dialkyl acrylamides or acrylates should allow for the possible formation of the bicyclic pyrrole. On the basis of the observed differences in reactivity for the acrylamide and acrylate coupling partners investigated, we propose that the relative rate of reductive cross-coupling with imides could be governed by the strength of coordination to the samarium metal and follow the trend; *n*-butylacrylamide>*tert*-butylacrylamide>*n*-octyl acrylate. Also, it is postulated that reduction and dimerisation of acrylamides and acrylates are in direct competition with cross-coupling between imides and acrylamides/acrylates. The two pathways may

not share intermediates, such as a distinct radical anion or allyl radical species. This could be the case if the cross-coupling between imides and acrylamides/acrylates proceeded through a concerted mechanism, whereas, e.g., acrylamide reduction naturally must proceed through a distinct radical anion or allyl radical species. These hypotheses are currently under investigation.

4. Experimental section

4.1. General methods

Unless otherwise noted all reactions were carried out under an inert atmosphere. Solvents were dried according to standard procedures, reactions were monitored by thin-layer chromatography (TLC) analysis. All other chemicals were used as received from the appropriate suppliers. Flash chromatography was carried out on silica gel 60 (230–400 mesh). SmI_2 was prepared according to a literature method.[23]

The ^{1}H NMR spectra were recorded at 400 MHz and ^{13}C NMR spectra were recorded at 100 MHz. The chemical shifts are reported in parts per million downfield to TMS (δ=0) and referenced using the residual $CHCl_3$ resonance (δ=7.26) or CHD_2CN centre peak resonance (δ=1.94) for ^{1}H NMR and the central $CDCl_3$ resonance (δ=77.16) or CD_3CN centre peak resonance (δ=1.39) for ^{13}C NMR. ^{1}H NMR spectra are reported as follows (s=singlet, d=doublet, t=triplet, q=quartet, quin=quintet, sext=sextet, sept=septet, oct=octet, br=broad; coupling constant(s) in Hz; integration).

4.2. Experimental procedures

4.2.1. N-Propionyl succinimide[13]. Succinimide (5.00 g, 50.5 mmol) in pyridine (30 mL) under an atmosphere of argon was cooled to 0 °C and propionic anhydride (13 mL, 101 mmol) was added. The reaction mixture was allowed to reach room temperature and left stirring for two days, after which TLC analysis showed complete conversion to a less polar compound. Solvent was removed in vacuo (65 °C) and co-evaporated with toluene and dichloromethane to remove pyridine. The resulting crude oil was subjected to column chromatography with massive decomposition to succinimide as a consequence, therefore the remaining *N*-propionyl succinimide was recrystallised from EtOAc/heptanes to give the title compound (1.57 g, 10.1 mmol, 20%) as colourless crystals. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 2.89 (q, *J*=7.2 Hz, 2H), 2.78 (s, 4H), 1.18 (t, *J*=7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 174.5 (2C), 173.7, 32.4, 28.5 (2C), 7.7.

4.2.2. N-iso-Butyroyl succinimide[13]. Succinimide (5.00 g, 50.5 mmol) in pyridine (30 mL) under an atmosphere of argon was cooled to 0 °C and *iso*-butyroyl chloride (8.0 mL, 76 mmol) was added. The reaction mixture was allowed to reach room temperature over 30 min, after which TLC analysis showed complete conversion to a less polar compound. Pyridinium chloride formed in the reaction was removed by filtration and the solvent was removed in vacuo (65 °C) and co-evaporated with toluene and dichloromethane to remove pyridine. The resulting heterogeneous mixture was taken up in EtOAc and washed once with H_2O, once with brine, dried over Na_2SO_4 followed by evaporation to dryness. Recrystallisation from EtOAc/heptanes gave the title compound (6.76 g, 40.0 mmol, 79%) as colourless crystals. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 3.31 (sept, *J*=7.2 Hz, 1H), 2.77 (s, 4H), 1.15 (d, *J*=7.2 Hz, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 177.3, 174.6 (2C), 36.9, 28.6 (2C), 17.9 (2C).

*4.2.3. N-tert-Butyl-5-methyl-3-oxo-2,3-dihydro-1H-pyrrolizine-7-carboxamide (**6**) from **7***. To compound **5** (32.0 mg, 0.127 mmol) dissolved in dichloromethane (13 mL) under an atmosphere of argon at room temperature was added activated 4 Å molecular sieves. Then a solution of TFA in dichloromethane (0.13 mL, 0.01 M, 1 mol %) was added to the mixture and left stirring for 21 h. TLC analysis revealed a poor conversion to the less polar UV-active compound **4**, and more TFA in dichloromethane was added (0.05 mL, 0.1 M, 4 mol %). After 3 h complete conversion was observed by TLC, the molecular sieves were filtered off and washed with dichloromethane (20 mL). Subsequently the organics were washed with a 1:1 mixture of satd aq $NaHCO_3$ and H_2O (10 mL), brine, dried over Na_2SO_4, filtered and evaporated in vacuo. The resulting crude oil was subjected to column chromatography (increasing polarity from 10% to 50% EtOAc in pentane as the eluant) to achieve the title compound **4** (22.3 mg, 0.0952 mmol, 75%) as a weakly yellow solid. Despite numerous attempts, recrystallisation of the compound failed in our hands and often led to decomposition. ^{1}H NMR (400 MHz, CD_3CN) δ (ppm) 10.34 (br s, 1H), 5.47 (br q, *J*=1.2 Hz, 1H), 2.96–2.91 (m, 2H), 2.49–2.44 (m, 2H), 2.25 (br s, 3H), 1.57 (s, 9H). ^{13}C NMR (100 MHz, CD_3CN) δ (ppm) 178.9, 170.6, 150.5, 139.3, 106.6, 100.9, 58.3, 30.2 (3C), 28.4, 25.6, 20.0. MS (ES) $C_{13}H_{18}N_2O_2$ [M+Na$^+$]; calculated: 257.1, found: 257.1.

4.3. General procedure for the SmI_2-mediated reductive coupling of acrylamides or acrylates with *N*-acyl succinimides with no additive

SmI_2 in THF (1.00 mmol, 2.3 equiv) under an atmosphere of argon was cooled to −78 °C. Then *N*-acyl succinimide (0.436 mmol, 1 equiv) and *N-tert*-butylacrylamide (0.502 mmol, 1.15 equiv) as a solution in THF (5 mL) were added to the stirring solution and kept at −78 °C for 2 h. Quenching of excess SmI_2 was achieved with O_2 with concomitant change in colour from dark blue to yellow, followed by addition of H_2O (3 mL) and heating to room temperature. Next satd aq $Na_2S_2O_3$ (40 mL), EtOAc (20 mL) and HCl (1 M, 8 mL) were added sequentially. Extraction of the aqueous phase with EtOAc (3×20 mL) followed by washing of the collected organic phases with brine, drying over Na_2SO_4, filtration and evaporation in vacuo resulted in a heterogeneous mixture of oil and solid. The pure product(s) were obtained by column chromatography using the stated solvent system.

*4.3.1. (Z)-N-tert-Butyl-4-oxo-2-(5-oxopyrrolidin-2-ylidene)pentanamide (**7**)*. The title compound was prepared according to the general method above using *N*-acetyl succinimide (33.1 mg, 0.220 mmol) and *N-tert*-butylacrylamide (32.6 mg, 0.256 mmol). Purification by column chromatography (increasing polarity from 30% to 100% EtOAc in pentane) afforded the title compound **7** (32.1 mg, 0.127 mmol, 58%) as a weakly yellow solid. ^{1}H NMR (400 MHz, CD_3CN) δ (ppm) 10.92 (br s, 1H), 5.90 (br s, 1H), 3.25 (s, 2H), 2.82–2.78 (m, 2H), 2.42–2.38 (m, 2H), 2.15 (s, 3H), 1.31 (s, 9H). ^{13}C NMR (100 MHz, CD_3CN) δ (ppm) 208.0, 177.3, 167.8, 152.0, 97.9, 51.6, 43.3, 29.4, 28.9 (3C), 28.0, 25.9. HRMS $C_{13}H_{20}N_2O_3$ [M+Na$^+$] calculated: 275.1366, found: 275.1368.

*4.3.2. (Z)-N-tert-Butyl-4-oxo-2-(5-oxopyrrolidin-2-ylidene)hexanamide (**8**)*. The title compound was prepared according to the general method above using *N*-propionyl succinimide (68.0 mg, 0.443 mmol) and *N-tert*-butylacrylamide (65.3 mg, 0.551 mmol). Purification by column chromatography (increasing polarity from 40% to 100% EtOAc in pentane) afforded two pure stereoisomers: **8** (*Z*-isomer) (87.5 mg, 0.329 mmol, 74%) as a colourless solid and **8** (*E*-isomer) (6.0 mg, 0.023 mmol, 5%) as a colourless solid. *Compound **8** (Z-isomer)*: ^{1}H NMR (400 MHz, CD_3CN) δ (ppm) 10.90 (br s, 1H), 6.00 (br s, 1H), 3.24 (s, 2H), 2.82–2.78 (m, 2H), 2.53 (q, *J*=7.2 Hz, 2H), 2.41–2.38 (m, 2H), 1.31 (s, 9H), 0.98 (t, *J*=7.2 Hz, 3H). ^{13}C NMR (100 MHz, CD_3CN) δ (ppm) 211.2, 178.7, 169.5, 154.1, 98.7, 52.0, 41.9, 35.9, 29.0 (3C), 28.6, 26.5, 8.1. HRMS $C_{14}H_{22}N_2O_3$ [M+Na$^+$] calculated: 289.1523, found: 289.1523. *Compound **8** (E-isomer)*: ^{1}H NMR (400 MHz, CD_3CN) δ (ppm) 8.08 (br s, 1H), 5.94 (br s, 1H), 3.25 (s, 2H), 3.05–3.01 (m, 2H), 2.51 (q, *J*=7.2 Hz, 2H), 2.42–2.38 (m, 2H),

1.31 (s, 9H), 0.98 (t, J=7.2 Hz, 3H). HRMS $C_{14}H_{22}N_2O_3$ [M+Na^+] calculated: 289.1523, found: 289.1517.

*4.3.3. (Z)-N-tert-Butyl-5-methyl-4-oxo-2-(5-oxopyrrolidin-2-ylidene)hexanamide (**9**).* The title compound was prepared according to the general method above using *N-iso*-butyroyl succinimide (73.8 mg, 0.436 mmol) and *N-tert*-butylacrylamide (63.8 mg, 0.502 mmol). Purification by column chromatography (increasing polarity from 60% to 100% EtOAc in pentane) afforded the two pure stereoisomers: **9** (*Z*-isomer) (93.2 mg, 0.332 mmol, 76%) as colourless crystals and **9** (*E*-isomer) (16.4 mg, 0.058 mmol, 13%) as a colourless solid. *Compound **9** (Z-isomer)*: ^{1}H NMR (400 MHz, CD_3CN) δ (ppm) 10.88 (br s, 1H), 5.82 (br s, 1H), 3.33 (s, 2H), 2.83–2.72 (m, 3H), 2.42–2.36 (m, 2H), 1.31 (s, 9H), 1.07 (d, J=6.8 Hz, 6H). ^{13}C NMR (100 MHz, CD_3CN) δ (ppm) 214.2, 178.6, 169.5, 154.0, 98.6, 52.0, 40.6, 40.5, 29.0 (3C), 28.6, 26.5, 18.8. HRMS $C_{15}H_{24}N_2O_3$ [M+Na^+] calculated: 303.1679, found: 303.1686. *Compound **9** (E-isomer)*: ^{1}H NMR (400 MHz, CD_3CN) δ (ppm) 8.06 (br s, 1H), 5.84 (br s, 1H), 3.33 (s, 2H), 3.05–2.99 (m, 2H), 2.72 (sept, J=7.2 Hz, 1H), 2.43–2.37 (m, 2H), 1.30 (s, 9H), 1.06 (d, J=7.2 Hz, 6H). HRMS $C_{15}H_{24}N_2O_3$ [M+Na^+] calculated: 303.1679, found: 303.1683.

*4.3.4. n-Butyl 2-(2-methyl-2-phenylpropionylamino)ethyl succinate (**18**)*[14]. *N*-Acyl oxazolidinone **16** (109 mg, 0.467 mmol) was dissolved in THF (7.5 mL), then water (54 μL, 3.00 mmol) and *n*-butyl acrylate (216 μL, 1.50 mmol) were added. The mixture was cooled to −78 °C and then SmI_2 in THF (0.1 M, 15 mL, 1.50 mmol) was added dropwise over 10 min. The mixture was stirred at −78 °C for 18 h and then the flask was flushed with O_2. Satd aq NH_4Cl (5 mL) was added, and then the mixture poured into 0.5 M HCl (40 mL) and extracted with EtOAc (3×15 mL). The combined organic portions were washed with satd aq $Na_2S_2O_5$ (30 mL), dried ($MgSO_4$) filtered and evaporated in vacuo. The pure product was obtained by column chromatography (increasing polarity from 5% to 30% diethyl ether in 1:1 DCM/pentane as eluant), which gave the title compound **18** (62 mg, 0.171 mmol, 36.5%) as a colourless oil, and recovered **16** (15 mg, 0.063 mmol, 13.8%). ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.36–7.20 (m, 5H), 5.60 (br t, J=5.2 Hz, 1H), 4.08 (t, J=5.2 Hz, 2H), 4.03 (t, J=6.8 Hz, 2H), 3.40 (q, J=5.2 Hz, 2H), 2.49 (AA′BB′ system, 4H), 1.57 (pent, J=7.2 Hz, 2H), 1.54 (s, 6H), 1.34 (hex, J=7.6 Hz, 2H), 0.91 (t, J=7.6 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 177.5, 172.3, 172.1, 145.0, 128.5 (2C), 126.3 (2C), 64.6, 63.1, 46.8, 38.6, 30.5, 29.0, 28.9, 26.8 (2C), 19.0, 13.6. HRMS $C_{20}H_{29}NO_5$ [M+Na^+] calculated: 386.1944, found: 386.1943.

*4.3.5. n-Butyl 2-(2,2-diphenylpropanamido)ethyl succinate (**19**)*[14]. *N*-Acyl oxazolidinone **17** (138 mg, 0.467 mmol) was dissolved in THF (7.5 mL), then water (54 μL, 3.00 mmol) and *n*-butyl acrylate (216 μL, 1.50 mmol) were added. The mixture was cooled to −78 °C and then SmI_2 in THF (0.1 M, 15 mL, 1.50 mmol) was added dropwise over 10 min. The mixture was stirred at −78 °C for 18 h and then the flask was flushed with O_2. Satd aq NH_4Cl (5 mL) was added, and then the mixture poured into 0.5 M HCl (40 mL) and extracted with EtOAc (3×15 mL). The combined organic portions were washed with satd aq $Na_2S_2O_5$ (30 mL), dried ($MgSO_4$), filtered and evaporated in vacuo. The pure product was obtained by column chromatography (increasing polarity from 5% to 20% diethyl ether in 1:1 pentane/DCM as eluant), which gave the title compound **19** (115 mg, 0.270 mmol, 57.8%) as a colourless oil and recovered **17** (57 mg, 0.193 mmol, 41.3%) as colourless solids. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.35–7.20 (m, 10H), 5.82 (br t, J=5.6 Hz, 1H), 4.14 (t, J=5.6 Hz, 2H), 4.05 (t, J=6.8 Hz, 2H), 3.51 (q, J=5.6 Hz, 2H), 2.51 (AA′BB′ system, 4H), 1.99 (s, 3H), 1.59 (pent, J=7.2 Hz, 2H), 1.35 (hex, J=7.6 Hz, 2H), 0.93 (t, J=7.6 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 175.2, 172.1, 172.0, 144.8 (2C), 128.4 (4C), 128.0 (4C), 126.9 (2C), 64.6, 63.1, 56.9, 38.8, 30.5, 29.0, 28.9, 26.9, 19.0, 13.6. HRMS $C_{25}H_{31}NO_5$ [M+Na^+] calculated: 448.2100, found: 448.2113.

4.3.6. N,N-Di-n-butylacrylamide. Di-*n*-butylamine (1.00 g, 7.737 mmol) and triethylamine (1.95 mL, 14.00 mmol) were dissolved in CH_2Cl_2 (20 mL) and then the mixture was cooled to 0 °C. Acryloyl chloride (0.63 mL, 700 mg, 7.737 mmol) was added dropwise, the mixture was stirred at 0 °C for 2 h and then at room temperature for 18 h. The mixture was poured into water (50 mL) and extracted with CH_2Cl_2 (3×20 mL). The combined organic portions were dried ($MgSO_4$), filtered and evaporated in vacuo. The pure product was obtained by column chromatography (increasing polarity from 5% to 35% EtOAc in pentane as eluant), which gave the title compound (1.118 g, 6.10 mmol, 79%) as a colourless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 6.50 (dd, J=16.4, 10.4 Hz, 1H), 6.47 (dd, J=16.4, 2.0 Hz, 1H), 5.60 (dd, J=10.4, 2.0 Hz, 1H), 3.33 (t, J=7.6 Hz, 2H), 3.25 (t, J=7.6 Hz, 2H), 1.56–1.45 (m, 4H), 1.28 (app. hex, J=7.2 Hz, 4H), 0.90 (t, J=7.2 Hz, 3H), 0.88 (t, J=7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 165.8, 127.9 (2C), 127.4 (2C), 47.9, 46.4, 31.8, 29.9, 20.3, 20.0, 13.9, 13.8. HRMS $C_{11}H_{21}NO$ [M+Na^+] calculated: 206.1521, found: 206.1518.

4.4. Experimental procedure for Scheme 6c

N-Acyl oxazolidinone **17** (97 mg, 0.33 mmol) and *N*,*N*-di-*n*-butylacrylamide (46 mg, 0.25 mmol) were dissolved in THF (5 mL) and then water (36 mg, 2.00 mmol) was added. The mixture was cooled to −78 °C under a strict argon atmosphere before a solution of SmI_2 (10 mL, 1.00 mmol, 0.1 M in THF) was added dropwise over 5 min. The mixture was stirred at −78 °C for 18 h, and then the flask was flushed with oxygen to quench excess SmI_2. It was poured into satd aq $Na_2S_2O_3$ (40 mL) and extracted with EtOAc (3×20 mL). The combined organic portions were dried ($MgSO_4$), filtered and evaporated in vacuo. The pure products were obtained by column chromatography (increasing polarity from 5% to 50% EtOAc in pentane, and then 2% to 10% MeOH in DCM as eluant), which gave the products **22** (21 mg, 0.053 mmol, 21%), **23** (18 mg, 0.037 mmol, 15%), **24** (69 mg, 0.144 mmol, 58%) and recovered *N*-acyl oxazolidinone **17** (21 mg, 0.071 mmol, 23%).

*4.4.1. N,N-Di-n-butyl-4-oxo-5,5-diphenylhexanamide (**22**).* ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.34–7.17 (m, 10H), 3.27 (t, J=7.6 Hz, 2H), 3.21 (t, J=7.6 Hz, 2H), 2.82 (t, J=6.8 Hz, 2H), 2.47 (t, J=6.8 Hz, 2H), 1.94 (s, 3H), 1.57–1.42 (m, 4H), 1.36–1.22 (m, 4H), 0.93 (t, J=7.6 Hz, 3H), 0.90 (t, J=7.6 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 221.2, 171.2, 144.1 (2C), 128.5 (4C), 128.4 (4C), 126.9 (2C), 61.9, 47.8, 46.1, 35.2, 31.2, 30.0, 27.6, 26.6, 20.4, 20.2, 14.0, 13.9. HRMS $C_{26}H_{35}NO_2$ [M+Na^+] calculated: 416.2565, found: 416.2558.

*4.4.2. 2-(2,2-Diphenylpropanamido)ethyl 4-(di-n-butylamino)-4-oxobutanoate (**23**).* ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.34–7.20 (m, 10H), 6.00 (br t, J=4.8 Hz, 1H), 4.15 (t, J=4.8 Hz, 2H), 3.51 (q, J=4.8 Hz, 2H), 3.27–3.17 (m, 4H), 2.53 (AA′BB′ system, 4H), 1.99 (s, 3H), 1.58–1.49 (m, 2H), 1.49–1.40 (m, 2H), 1.37–1.20 (m, 4H), 0.95 (t, J=7.6 Hz, 3H), 0.89 (t, J=7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 175.4, 173.3, 170.0, 145.1 (2C), 128.5 (4C), 128.3 (4C), 127.0 (2C), 63.1, 57.1, 47.7, 45.9, 39.0, 31.1, 30.0, 29.5, 28.2, 27.1, 20.4, 20.3, 14.0, 13.9. HRMS $C_{29}H_{40}N_2O_4$ [M+Na^+] calculated: 503.2886, found: 503.2892.

*4.4.3. N^1,N^1-Di-n-butyl-N^3-(2-hydroxyethyl)-2-(2-oxo-3,3-diphenylbutyl)malonamide (**24**).* ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.34–7.20 (m, 6H), 7.17–7.09 (m, 4H), 7.00 (t, J=6.0 Hz, 1H), 3.86 (dd, J=10.0, 3.2 Hz, 1H), 3.61 (ddd, J=15.6, 10.0, 5.2 Hz, 1H), 3.55 (t, J=5.6 Hz, 2H), 3.46 (dt, J=13.6, 7.2, 1H), 3.35 (dd, J=18.4, 10.8 Hz, 1H), 3.33–3.15 (m, 4H), 2.89 (br s, 1H), 2.84 (dd, J=18.4, 3.2 Hz, 1H) 1.89 (s, 3H), 1.70–1.45 (m, 4H), 1.37–1.23 (m, 4H), 0.93 (t, J=7.2 Hz,

3H), 0.91 (t, J=7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 209.4, 170.6, 170.5, 143.6, 143.5, 128.4 (2C), 128.4 (2C), 128.3 (2C), 128.3 (2C), 127.9 (2C), 61.9, 61.4, 48.6, 46.9, 46.3, 42.5, 42.1, 31.2, 29.6, 26.5, 20.1, 20.1, 13.9, 13.8. HRMS $C_{29}H_{40}N_2O_4$ [M+Na$^+$] calculated: 503.2886, found: 503.2881.

4.4.4. 1-Pivaloylpyrrolidin-2-one. 2-Pyrrolidinone (0.454 mL, 5.87 mmol) was dissolved in THF (20 mL) and the solution was cooled to 0 °C. *n*-BuLi (3.5 mL, 5.88 mmol) was added dropwise and the solution was stirred at 0 °C for 30 min, before pivaloyl chloride (1.1 mL, 8.81 mmol) was added. The mixture was stirred at room temperature for 1 h, and then poured into aqueous $NaHCO_3$ (40 mL) and extracted with EtOAc (3×20 mL). The combined organic portions were dried ($MgSO_4$), filtered and evaporated in vacuo. The pure product was obtained by column chromatography (6% EtOAc in pentane as eluant), which gave the title compound (917 mg, 5.42 mmol, 92%) as a colourless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 3.78 (t, J=7.6 Hz, 2H), 2.55 (t, J=7.6 Hz, 2H), 1.99 (pent., J=7.6 Hz, 2H), 1.29 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 180.2, 173.6, 48.5, 41.6 (3C), 34.5, 26.1, 17.8. HRMS $C_9H_{15}NO_2$ [M+Na$^+$] calculated: 192.1000, found: 192.0990.

*4.4.5. n-Octyl 4-oxo-7-pivalamidoheptanoate (**27**).* 1-Pivaloylpyrrolidin-2-one (75 mg, 0.44 mmol), *n*-octyl acrylate (92 μL, 0.44 mmol) and water (64 μL, 3.55 mmol) were dissolved in THF (5 mL) and then the solution was cooled to −78 °C. A 0.1 M solution of SmI_2 (17.7 mL, 1.77 mmol) was added dropwise over 30 min, and then the mixture was stirred at −78 °C for 22 h. Excess SmI_2 was quenched by flushing the flask with O_2, and then the mixture poured into aqueous $Na_2S_2O_3$ (30 mL) and extracted with EtOAc (3×15 mL). The combined organic portions were dried ($MgSO_4$), filtered and evaporated in vacuo. The pure product was obtained by column chromatography (increasing polarity from 1% to 3% MeOH as eluant), which gave the title compound **27** (64 mg, 0.18 mmol, 41%) as a colourless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 5.99 (br s, 1H), 4.01 (t, J=6.8 Hz, 2H), 3.19 (td, J=6.7, 5.7 Hz, 2H), 2.67 (t, J=6.7 Hz, 2H), 2.57 (t, J=6.3 Hz, 2H), 2.52 (t, J=6.3 Hz, 2H), 1.78 (pent., J=6.7 Hz, 2H), 1.58 (pent., J=6.8 Hz, 2H), 1.30–1.20 (m, 10H), 1.46 (s, 9H), 0.85 (t, J=6.9 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 209.3, 178.9, 173.1, 65.1, 40.4, 39.3, 38.8, 37.3, 32.0, 29.4, 29.3, 28.8, 28.3, 27.8, 26.1, 23.3, 22.8, 14.3. HRMS $C_{20}H_{37}NO_4$ [M+Na$^+$] calculated: 378.2620, found: 378.2605.

*4.4.6. N-tert-Butyl-4-oxo-7-pivalamidoheptanamide (**28**).* 1-Pivaloylpyrrolidin-2-one (75 mg, 0.44 mmol), *N-tert*-butylacrylamide (56 mg, 0.44 mmol) and water (64 μL, 3.55 mmol) were dissolved in THF (5 mL) and then the solution was cooled to −78 °C. A 0.1 M solution of SmI_2 (17.7 mL, 1.77 mmol) was added dropwise over 30 min, and then the mixture was stirred at −78 °C for 22 h. Excess SmI_2 was quenched by flushing the flask with O_2, and then the mixture poured into aqueous $Na_2S_2O_3$ (30 mL) and extracted with EtOAc (3×15 mL). The combined organic portions were dried ($MgSO_4$), filtered and evaporated in vacuo. The pure product was obtained by column chromatography (increasing polarity from 1% to 3% MeOH as eluant), which gave the title compound **28** (68 mg, 0.066 mmol, 15%) as a colourless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 6.15 (br s, 1H), 5.25 (s, 1H), 3.19 (q, J=6.6 Hz, 2H), 2.66 (t, J=6.5 Hz, 2H), 2.52 (t, J=6.6 Hz, 2H), 2.38 (t, J=6.5 Hz, 2H), 1.77 (pent., J=6.6 Hz, 2H), 1.15 (s, 9H), 1.05 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 210.4, 178.9, 171.2, 51.4, 40.2, 38.9, 38.8, 37.7, 31.2, 28.9, 27.8, 23.3. HRMS $C_{16}H_{30}N_2O_3$ [M+Na$^+$] calculated: 321.2154, found: 321.2153.

4.4.7. Experimental procedure for Scheme 8. tert-Butylacrylamide (36 mg, 0.281 mmol) and *n*-octyl acrylate (46 mg, 0.25 mmol) were dissolved in THF (2.5 mL) and then water (36 μL, 2.00 mmol) was added before the solution was cooled to −78 °C. A 0.1 M solution of SmI_2 (10 mL, 1.00 mmol) was added dropwise over 5 min, and then the solution was stirred at −78 °C for 18 h. Excess SmI_2 was quenched by flushing the flask with O_2, and then the mixture was poured into aqueous $Na_2S_2O_3$ (40 mL) and extracted with EtOAc (3×20 mL). The combined organic portions were dried ($MgSO_4$), filtered and evaporated in vacuo. The pure products were obtained by column chromatography (increasing polarity from 5% to 30% EtOAc in pentane as eluant), which gave di-*n*-octyl adipate **30** (28 mg, 0.0756 mmol, 60%), recovered *tert*-butylacrylamide (25 mg, 0.197 mmol, 70%), and the hetero dimer **29** (24 mg, 0.0766 mmol, 31%).

*4.4.8. n-Octyl 6-(tert-butylamino)-6-oxohexanoate (**29**).* ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 5.31 (br s, 1H), 4.04 (t, J=6.8 Hz, 2H), 2.35–2.26 (m, 2H), 2.12–2.05 (m, 2H), 1.66–1.55 (m, 6H), 1.33 (s, 9H), 1.36–1.20 (m, 10H), 0.87 (t, J=6.4 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 173.6, 171.8, 64.5, 51.1, 37.2, 34.0, 31.7, 29.2, 29.1, 28.8 (3C), 28.6, 25.9, 25.1, 24.4, 22.6, 14.0. HRMS $C_{18}H_{35}NO_3$ [M+Na$^+$] calculated: 336.2515, found: 336.2509.

*4.4.9. Di-n-octyl adipate (**30**).* ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 4.05 (t, J=6.9 Hz, 4H), 2.36–2.28 (m, 4H), 1.69–1.58 (m, 8H), 1.35–1.22 (m, 20H), 0.95–0.88 (m, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 173.6 (2C), 64.7 (2C), 34.1 (2C), 31.9 (2C), 29.4 (2C), 29.3 (2C), 28.8 (2C), 26.1 (2C), 24.6 (2C), 22.8 (2C), 14.2 (2C). HRMS $C_{22}H_{42}O_4$ [M+Na$^+$] calculated: 393.2981, found: 393.2991.

4.5. X-ray crystallographic data for 9 (*Z*-isomer)

The crystal structure illustration is produced with thermal-motion probability ellipsoids, using ORTEP-III.[24] CCDC 743683 **9** (*Z*-isomer) contains the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif, or by emailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033.

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