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Asymmetric Organocatalysed [1,3]-Sigmatropic Rearrangements

Sara Kobbelgaard, Sebastian Brandes, and Karl Anker Jørgensen*[a]

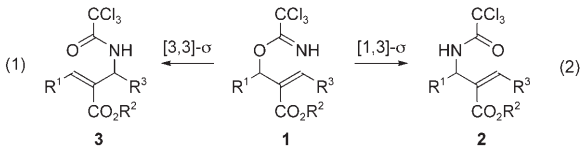
Abstract: The first organocatalysed enantioselective [1,3]-sigmatropic *O*- to *N*-rearrangement reactions are presented. The reactions take place under regio- and enantioselective control, and are catalysed by cinchona alkaloids. Two reactions have been developed the first one is the rearrangement of imidates to amides, while the other rearrangement occurs from carbamates to amines via a decarboxylation. Both transformations give nitrogen protected β-amino acid derivatives as the product. These novel asymmetric organocatalysed [1,3]-sigmatropic *O*- to *N*-rearrangement reactions provide a reliable and efficient synthetic method for obtaining enantioenriched β-amino acid derivates in good yield from racemic starting materials.

Keywords: asymmetric synthesis · cinchona alkaloids · organocatalysis · rearrangement · stereoselective catalysis

Introduction

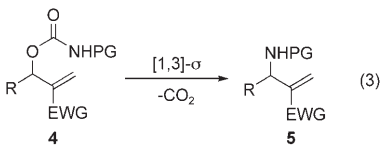
β-Amino acid and allyl amine derivatives are important building blocks found in many bioactive molecules, such as antibiotics, cytostatics and peptides.[1] The significance of these chemical structures requires reliable and efficient synthetic methods for obtaining them as chiral compounds. The asymmetric synthesis of chiral β-amino acids is possible via several synthetic approaches.[1,2] One approach to obtain α-alkylidene substituted β-amino acids is the aza-Morita–Baylis–Hillman reaction, in which protected imines react with α,β-unsaturated carboxyl compounds.[3] Enantioselective variations of this reaction have used chiral thioureas,[4] chiral phosphine Lewis bases[5] or cinchona alkaloid bases[6] as the catalyst.

Another approach to access α-alkylidene substituted β-amino acid derivatives is the enantioselective formation of the C–N bond, rather than the C–C bond. This former approach can be accomplished via the asymmetric rearrangement of trichloroacetimidates. The [3,3]-sigmatropic rearrangement of allylic trichloroacetimidates to allylic trichloroacetamides [Eq. (1)], is known as the Overman rearrangement.[7] This reaction can be conducted thermally or by metal catalysis, and stereoselective variations have been developed using either metal catalysis[8] or metal-catalysed substrate directed reactions.[9]



Another possible transformation of trichloroacetimidates is the less known [1,3]-sigmatropic rearrangement to trichloroacetamides [Eq. (2)].[10] This reaction readily transforms α-disubstituted allylic alcohols into allylic amines.

An additional enantioselective formation of the C–N bond, is the undemanding transformation of α-disubstituted allylic alcohols into allylic amines, the [1,3]-sigmatropic *O*- to *N*-rearrangement of carbamates into *N*-protected β-amino acid derivatives [Eq. (3)].[11] A decarboxylation takes place during this rearrangement, which provides lower atom efficiency than the rearrangement of trichloroacetimidates, but the reaction affords the prospect of altering the protecting group at the nitrogen atom.



[a] S. Kobbelgaard, Dr. S. Brandes, Prof. Dr. K. A. Jørgensen
The Danish National Research Foundation
Center for Catalysis, Department of Chemistry
Aarhus University, 8000 Aarhus C (Denmark)
Fax: (+45) 8916-6199
E-mail: kaj@chem.au.dk

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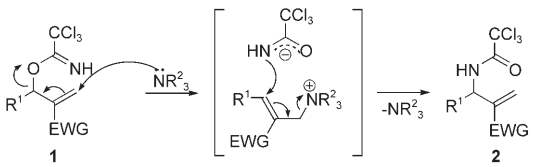
In the following, a new approach to these important rearrangement reactions will be outlined. We will show the development of the first organocatalytic enantioselective [1,3]-sigmatropic rearrangement reaction of trichloroacetimidates and carbamates, both leading to optically active α-alkylidene substituted β-amino acid derivatives [Eqs. (2) and (3)].

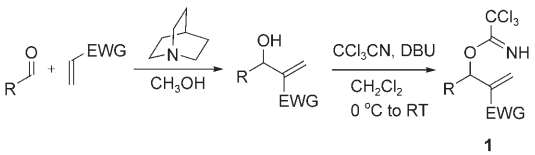
Results and Discussion

[1,3]-Sigmatropic rearrangement of imidates to amides: This [1,3]-sigmatropic rearrangement is thought to be catalysed via a S_N2' mechanism (Scheme 1), in which a nucleophilic amine attacks the terminal alkene and eliminates the trichloroacetimidate, thus establishing an ionic interaction between the quaternary ammonium bound substrate and the ambident nucleophile. Mechanistically similar eliminations of leaving groups, like acetates or carbamates, with a concomitant attack of another nucleophile present in the reaction mixture are also known.[11,12] As the trichloroacetamide anion is more stable than the trichloroacetimidate anion, the following S_N2' reaction is initiated by the attack of the nitrogen nucleophile of the anionic trichloroacetamide and the catalyst is released. The reaction is assumed to proceed by a rearrangement, rather than a double S_N2' addition. The latter assumption has been tested by the introduction of a tosylate as an external nucleophile, however, only the rearranged product was obtained. The reaction mechanism assures complete regioselectivity, since the covalently bound catalyst in the intermediate precludes the Overman rearrangement.



Scheme 1. Mechanism for the [1,3]-sigmatropic rearrangement of *O*-allyl trichloroacetimidates.

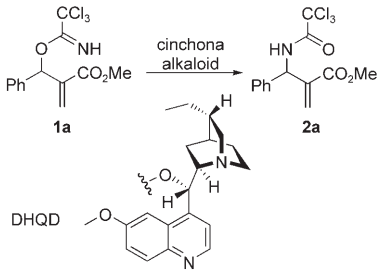
The starting compounds for the investigation of the organocatalysed [1,3]-rearrangement, the *O*-allyl trichloroacetimidates **1**, were synthesised via a two-step sequence. The sequence consisted of a Baylis–Hillman reaction between an aldehyde and an acrylate derivative,[13] followed by formation of **1** from treatment with trichloroacetonitrile and DBU[10a] (Scheme 2, EWG: electron-withdrawing group).



Scheme 2. Synthesis of *O*-allyl trichloroacetimidates **1**.

Initial trials of the asymmetric [1,3]-rearrangement of imidates were performed with the racemic *O*-allyl trichloroacetimidate **1a**, which was transformed into **2a** in the presence of a cinchona alkaloid as the catalyst.[14] For the first tests, the common cinchona alkaloids were chosen (Table 1, entries 1–4). Cinchonine (CN) gave the *N*-allyl amide **2a** in −12% *ee* (entry 1), while the pseudo-enantiomer cinchonidine (CD) increased the enantioselectivity to −39% *ee* (entry 2). Surprisingly, these two catalysts favoured the same enantiomer. This was not the case for the pseudo-enantiomers quinine (QN) and quinidine (QD), which afforded the allylic trichloroacetamide **2a** in 20% *ee* and −60% *ee*, respectively (entries 3, 4). Further screening led us to conduct a series of experiments with the dimeric cinchona alkaloids based on dihydroquinidine (DHQD).

Table 1. Screening of catalysts and reaction conditions in the [1,3]-sigmatropic rearrangement of imidates to amides.[a]



Entry	Catalyst	Solvent (T [°C])	t [d]	ee[b] [%]
1	CN	PhMe (RT)	1	−12
2	CD	PhMe (RT)	1	−39
3	QN	PhMe (RT)	1	20
4	QD	PhMe (RT)	1	−60
5	$[DHQD]_2$AQN	PhMe (RT)	1	0[c]
6	$[DHQD]_2$PYR	PhMe (RT)	4	0
7	$[DHQD]_2$PHAL	PhMe (RT)	3	83
8	$[DHQD]_2$PHAL	dioxane (40)	1	87[d]

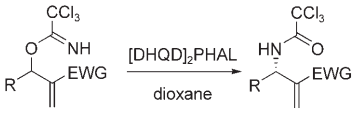
[a] All reactions were performed with 0.05 mmol of *O*-allyl trichloroacetimidate **1a** and 0.2 equiv of catalyst in 1 mL of solvent until full conversion was obtained. [b] *ee* determined by HPLC. [c] Only one enantiomer of **1a** was completely converted. [d] 0.1 equiv of catalyst.

Investigation of different dimeric cinchona catalysts (entries 5–8) revealed that the linkage between the two cinchona alkaloid moieties was of great importance for the enantioselectivity of the reaction. The cinchona alkaloid $[DHQD]_2$AQN selectively transformed a single enantiomer of **1a**, but the amide product **2a** was racemic (entry 5). No selectivity at all was observed with $[DHQD]_2$PYR (entry 6), whereas the catalyst $[DHQD]_2$PHAL with the 1,4-phthalazinediyl diether linkage, gave the rearranged product **2a** in

83% *ee* (entry 7). Examination of the reaction conditions led to dioxane as the solvent of choice, an increase in the reaction temperature and a decrease in catalyst loading. Performing the reaction under these conditions, the enantioselectivity of **2a** was improved to 87% *ee* (entry 8). Increasing the reaction temperature to 40°C resulted in the anticipated raise in reaction rate with a minor erosion of enantioselectivity. Elevating the temperature further had the effect of accelerating the thermally induced Overman rearrangement.

To determine the yield of this irreversible *O*,*N*-rearrangement, the reaction was performed in larger scale and at higher concentration, which accelerated the conversion (Table 2). The substrate used for the screening (**1a**) gave the rearranged product **2a** in 77% yield and 90% *ee* under the given conditions (entry 1).

Table 2. Asymmetric [1,3]-sigmatropic rearrangement reaction of various *O*-allylic trichloroacetimidates **1**.[a]



1 **2**

Entry	**1**	R	EWG	*T* [°C]	*t* [d]	Yield[b] [%]	*ee*[c] [%]
1	**a**	Ph	CO_2Me	40	on[d]	77	90
2	**b**	4-NO_2-Ph	CO_2Me	rt	1	89[e]	74
3	**c**	2-pyridyl	CO_2Me	40	2	64[e]	87
4	**d**	2-naphthyl	CO_2Me	40	on[d]	74	74
5	**e**	Ph	CO_2tBu	RT	5	89	92
6	**f**	Et	CO_2Me	RT	4	83	56
7	**g**	*i*Pr	CO_2Me	RT	3	57	78
8	**h**	*i*Pr	CN	RT	2	73	40

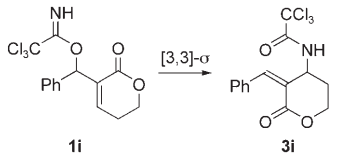
[a] Reactions were performed with 0.25 mmol of *O*-allyl trichloroacetimidate **1**, 0.1 equiv of catalyst in 0.5 mL of dioxane at the given temperature. The reaction was monitored by TLC and stopped at the indicated time. [b] Isolated yield. [c] Determined by HPLC. [d] on = overnight. [e] 5 mL of dioxane.

To examine the scope of this new asymmetric imidate rearrangement reaction, different *O*-allyl trichloroacetimidates **1b–h** were synthesised and tested (Table 2, entries 2–8). Alteration of the aromatic group by substituting in the *para*-position with an electron-withdrawing group, such as the nitro group, afforded the *N*-allyl amide **2b** in 89% yield and with 74% *ee* (entry 2). Changing the phenyl ring to the 2-pyridyl (**1c**), reduced the reaction rate, as well as the yield slightly and the trichloroacetamide **2c** was obtained in 64% yield and 87% *ee* (entry 3). Increasing the bulk of the aromatic group to the 2-naphthyl (**1d**) provided the amide product **2d** in 74% yield and with 74% *ee* (entry 4).

Expanding the size of the ester to a *tert*-butyl ester (**1e**) enhanced both yield and enantioselectivity to 89% and 92% *ee*, respectively (entry 5). Allylic trichloroacetimidates with aliphatic R groups were also synthesised, such as imidate **1f** having an ethyl attached to the chiral centre. This resulted in a lower enantioselectivity of 56% *ee* for the rearranged product **2f**, which was isolated in 83% yield (entry 6). The larger isopropyl group (**1g**) gave the trichloroacetamide **2g** in 57% yield and with 78% *ee*, improving the selectivity significantly compared to **2f**.

Other electron-withdrawing groups reacted as well, as demonstrated by the nitrile compound **1h**, which rearranged to the amide product in 73% yield and moderate 40% *ee*. This considerable drop in enantioselectivity is likely due to the linear structure of the sp-hybridized nitrile which limits spatial occupation.

Several attempts to synthesise allylic trichloroacetimidates with electron-donating aromatic R groups failed, because it was not possible to access the imidates from the Baylis–Hillman adducts. Sterically hindered *O*-allylic trichloroacetimidates were synthesised, but the reaction rate was significantly decreased; for example, the *tert*-butyl ester (R = *i*Pr) gave 50% conversion after nine days. Large R groups, such as *tert*-butyl (EWG = CO_2Me), prohibited the rearrangement. Experimental investigation of the importance of the substitution pattern of the alkene led to the synthesis of **1i**, containing a trisubstituted alkene [Eq. (4)]. Unfortunately, this imidate (**1i**) did not undergo the [1,3]-sigmatropic rearrangement, but only the Overman rearrangement giving the racemic amide **3i**. This result is in agreement with the proposed S_N2' mechanism, in which the trisubstituted alkene prevents the nucleophilic attack of the catalyst.[15]



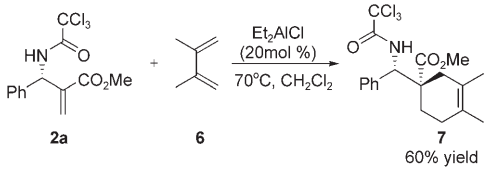
(4)

1i **3i**

The optically active products obtained by the asymmetric [1,3]-sigmatropic rearrangement reaction, have several functional groups, which can be modified, offering a broad range of applications. The ester functionality can be hydrolysed under acidic conditions; this gives the *N*-protected β-amino acid derivatives.

Another possible transformation is the addition of an electron-rich diene, such as 2,3-dimethylbuta-1,3-diene **6** in a Diels–Alder reaction to the optically active addition product **7** (Scheme 3).

The Diels–Alder reaction of **2a** with **6** proceeds in good yield and the enantioenrichment at the stereocenter α to the nitrogen atom is maintained from the starting material. The reaction ensures high diastereoselectivity >95:5 according

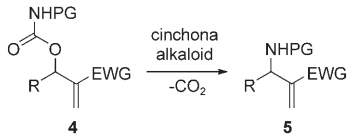


2a **6** **7**
60% yield

Scheme 3. Diels–Alder reaction between amide product (**2a**) and 2,3-dimethylbuta-1,3-diene **6**.

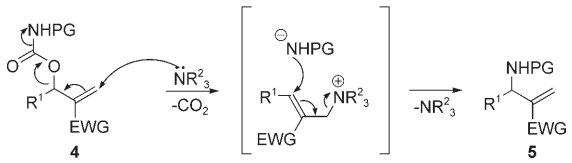
to ^{1}H NMR spectroscopy, as a result of the high *endo*/*exo* selectivity. The relative configuration has been determined and is shown in Scheme 3,[16] and the absolute configuration can be deduced from the stereocenter in **2a** which was determined by the next rearrangement.

[1,3]-Sigmatropic rearrangement of carbamates to amines: The other [1,3]-sigmatropic rearrangement reaction studied, also leading to β-amino acid derivatives, is the rearrangement of carbamates **4** via a decarboxylative reaction (Scheme 4). This rearrangement reaction gives rise to the same structures, as the first rearrangement presented, but the advantage of this rearrangement reaction is the possibility for varying the protection group on the nitrogen atom.



Scheme 4. [1,3]-Sigmatropic decarboxylative rearrangement.

The rearrangement is also believed to take place via a domino S_N2'–S_N2' mechanism (Scheme 5).[11] Initially the catalyst attacks the terminal alkene (**4**) leading to a decarboxylation and the generation of an amine nucleophile, which performs the second S_N2' reaction, and the *N*-protected amine **5** is formed.

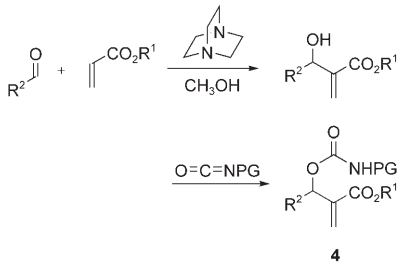


Scheme 5. The domino S_N2'–S_N2' mechanism for the decarboxylating rearrangement reaction of carbamate **4**.

The reaction demonstrates high regioselectivity since only the amine **5** from the [1,3]-rearrangement was obtained, the [3,3]-rearranged product was never isolated.

The starting compounds for the investigation of the organocatalysed [1,3]-rearrangement of carbamates **4** were synthesised via a two-step procedure (Scheme 6). The initial reaction was a Baylis–Hillman reaction between an aldehyde and an acrylate derivative in the presence of DABCO,[13] giving the Baylis–Hillman alcohol. The alcohol was treated with an isocyanate, forming the carbamate **4**.[11c]

p-Toluenesulfonyl (PG = Ts) was chosen as the first protecting group in the model substrate **4a** for this rearrangement reaction. The initial screening of reaction conditions are summarised in Table 3. The reaction was performed with different dimeric cinchona alkaloid catalysts, as these were found to be the most successful for the rearrangement of trichloroacetimidates. It appears that $[DHQD]_2PHAL$ gave the product **5a** in −16% *ee* (entry 1); on the other hand, with $[DHQD]_2AQN$ **5a** was isolated in 53% yield and in 69% *ee* (entry 3). The dihydroquinidine (DHQD) based catalyst gave higher selectivity, than the pseudo-enantiomere dihydroquinine (DHQ); for example, **5a** was obtained in 69% *ee* with $[DHQD]_2AQN$ as catalyst (entry 3), whereas the alkaloid $[DHQ]_2AQN$ afforded **5a** in −11% *ee* (entry 5) (see also entry 1 vs. 4).



Scheme 6. Synthesis of carbamates **4**.

Table 3. Screening of catalysts and reaction conditions for the [1,3]-sigmatropic rearrangement of carbamates to amines.[a]

Entry	PG, **5**	Catalyst	Solvent (T[°C])	t[d]	*ee*[b] [%]
1	Ts, **5a**	$[DHQD]_2PHAL$	CH_2Cl_2 (35)	2	−16
2	Ts, **5a**	$[DHQD]_2PYR$	CH_2Cl_2 (35)	2	29
3	Ts, **5a**	$[DHQD]_2AQN$	CH_2Cl_2 (35)	2	69[c]
4	Ts, **5a**	$[DHQ]_2PHAL$	CH_2Cl_2 (35)	1	−9
5	Ts, **5a**	$[DHQ]_2AQN$	CH_2Cl_2 (35)	4	−11
6[d]	Ts, **5a**	$[DHQD]_2AQN$	$CDCl_3$ (35)	4	−12
7	Ts, **5a**	$[DHQD]_2AQN$	dioxane (35)	2	0
8	$COCCl_3$, **5b**	$[DHQD]_2PHAL$	CH_2Cl_2 (35)	2	48
9[d]	$COCCl_3$, **5b**	$[DHQD]_2PHAL$	$CDCl_3$ (35)	1	65

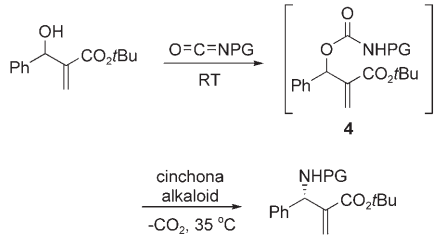
[a] Reactions were performed with 0.10 mmol of **4**, 0.2 equiv of catalyst in 2.0 mL of solvent at the given temperature. The reaction was monitored by TLC, and stopped when full conversion was observed at the indicated time. [b] Determined by HPLC. [c] 53% isolated yield. [d] 3 mL of solvent.

Examination of solvents revealed that this factor had a remarkable influence on the enantioselectivity of the reaction; the impact of the solvent was larger than of the catalyst. Changing the solvent form CH_2Cl_2 to $CDCl_3$ decreased the enantioselectivity from 69% *ee* (entry 3) to −12% *ee*, respectively (entry 6) and in dioxane the product obtained was formed as a racemic (entry 7).

The trichloroacetamide has also been employed as a protecting group for the amine, giving the same products as in the [1,3]-rearrangement of trichloroacetimidates (**5b**=**2e**). In this case, changing solvent from CH_2Cl_2 to $CDCl_3$ improved the enantioselectivity from 48% *ee* (entry 8) to 65% *ee* (entry 9). Preliminary results have disclosed that phenyl and benzyl also can be used as protecting groups for the nitrogen atom in this *O*- to *N*-rearrangement reaction.

The synthesis of the carbamates **4**, by addition of isocyanate to the alcohol in the Baylis–Hillman adduct takes place without any assistance, hence this reaction and the *O,N*-rearrangement can be performed as a domino reaction from the Baylis–Hillman products to the *N*-protected β-amino acid derivatives. This approach has been tested and the results are presented in Table 4.

Table 4. One-pot reaction from Baylis–Hillman adduct to protected β-amino acid derivative **5**.[a]



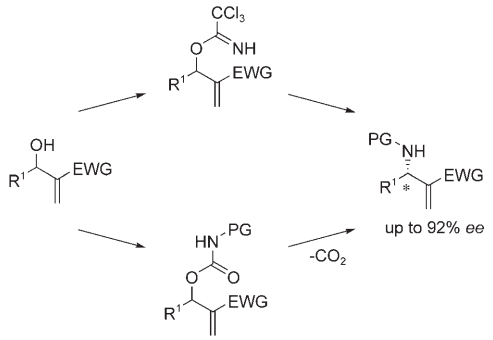
Entry	PG, **5**	Catalyst	Solvent	*t* 1)/2) step [h]	Yield[b] [%]	*ee*[c] [%]
1	Ts, **5a**	$[DHQD]_2AQN$	CH_2Cl_2	6/43	43	71
2	$COCCl_3$, **5b**	$[DHQD]_2PHAL$	$CHCl_3$	0.5/6	72	62

[a] Reactions were performed with 0.25 mmol of Baylis–Hillman adduct, 0.24 mmol of isocyanate in 2.0 mL of solvent at the given temperature. The reaction was monitored by TLC and after consumption of the isocyanate (1. step), 0.2 equiv of the catalyst was added and the reaction was stopped at the indicated time. [b] Isolated yield. [c] Determined by HPLC.

The one-pot reaction with the sulphonamide as protecting group (Table 4, entry 1), can be performed within 49 h and the product was obtained in 43% yield and 71% *ee*. The low yield is reasonable, considering the last step is proceeding with 53% yield (Table 3, entry 3), hence the addition of *p*-toluenesulfonyl isocyanate was proceeding with 81% yield. The product **5a** can be crystallised and has been isolated with an enantiopurity of >99% *ee*. The trichloroacetamide protected compound (entry 2) completed the addition reaction of trichloroacetyl isocyanate after 30 min and the rearrangement reaction within 6 h and the product **5b** was isolated with 62% *ee* and in 72% yield, meaning that each step in the reaction takes place with an average of 85% yield per step. The absolute configuration was determined after transesterification of **5a** to the methyl ester, the optical rotation was measured and compared to the optical rotation previously reported in literature.[17]

Conclusion

We have presented the first organocatalytic [1,3]-sigmatropic rearrangement reaction of racemic allylic trichloroacetimidates to enantiomerically enriched allylic trichloroacetamides (for general scheme, see below). This irreversible transformation is catalysed by $[DHQD]_2PHAL$, which assures complete regioselectivity as well as high enantioselectivity. The reaction is carried out with excellent conversion and the rearranged products are obtained in high isolated yields and enantiomeric excess.



The second [1,3]-sigmatropic rearrangement reaction presented in this paper is also catalysed by cinchona alkaloids. This *O*- to *N*-rearrangement regioselectively converts racemic carbamates to enantioenriched *N*-protected β-amino acid derivatives through a decarboxylation. This transformation can be performed as a one-pot reaction from the Baylis–Hillman product to the rearranged amine with high enantioselectivity. A range of protecting group can be applied in this procedure. These methods are an efficient way for obtaining nitrogen protected α-alkylidene-β-amino acid derivatives with high enantiopurity from readily accessible Baylis–Hillman adducts.

Experimental Section

General methods: The ^1H NMR and ^{13}C NMR spectra were recorded at 400 and 101 MHz, respectively. The chemical shifts are reported in ppm downfield to TMS ($\delta=0$) for ^1H NMR and for ^{13}C NMR relative to the central $CDCl_3$ resonance ($\delta=77.0$). Flash chromatography (FC) was carried out using Merck silica gel 60 (230–400 mesh). Analytical thin layer chromatography (TLC) was performed using pre-coated aluminium-backed plates (Merck Kieselgel 60 F254) and visualized by ultraviolet irradiation or appropriate stains. Optical rotations were measured on a Perkin–Elmer 241 polarimeter. The enantiomeric excess (*ee*) of the products was determined by HPLC using Chiralcel OD or OJ columns at the given wavelength with *i*PrOH/hexane mixtures as the eluent and the flow was 1 mL min^{-1} unless otherwise stated.

Materials: Analytical grade solvents were used as received. All commercially available reagents were used as received.

General procedure for the Baylis–Hillman reaction: The Baylis–Hillman adducts were synthesised according to known literature procedures.[13]

General procedure for synthesis of allylic trichloroacetimidates (1): The Baylis–Hillman adduct (1.0 equiv) was dissolved in trichloroacetonitrile (5 equiv) and cooled to 0 °C, then DBU (0.2 equiv) was added. The reaction was warmed slowly to room temperature. After 2 h the reaction was concentrated, and purified by FC.

*2-[Phenyl-(2,2,2-trichloroacetimidoyloxy)methyl]acrylic acid methyl ester (**1a**)*: $R_f=0.42$ (pentane/Et_2O 3:1); m.p. 84 °C (white solid); ^1H NMR (400 MHz, $CDCl_3$, TMS): $\delta=8.43$ (s, 1H), 7.48–7.44 (m, 2H), 7.39–7.29

(m, 3H), 6.79 (s, 1H), 6.43 (s, 1H), 5.98 (dd, $J=0.8$ Hz, 1.2 Hz, 1H), 3.75 ppm (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$): $\delta=165.5$, 160.7, 139.3, 137.2, 128.5, 128.4, 127.5, 126.3, 77.3, 52.1 ppm; HRMS: *m/z*: calcd for: 357.9780; found: 357.9778 $[M+Na]^+$.

*2-[(4-Nitrophenyl)-(2,2,2-trichloroacetimidoyloxy)methyl]acrylic acid methyl ester (**1b**)*: Synthesised according to known literature procedure.[10a] $R_f=0.26$ (pentane/Et_2O 1:1).

*2-[Pyridin-2-yl-(2,2,2-trichloroacetimidoyloxy)methyl]acrylic acid methyl ester (**1c**)*: $R_f=0.15$ (pentane/Et_2O 1:1); ^{1}H NMR (400 MHz, $CDCl_3$, TMS): $\delta=8.62$–8.59 (m, 1H), 8.50 (brs, 1H), 7.73 (dt, $J=1.3$ Hz, 7.6 Hz, 1H), 7.56 (d, $J=7.9$ Hz, 1H), 7.27–7.22 (m, 1H), 6.89 (s, 1H), 6.52 (s, 1H), 5.97 (s, 1H), 3.74 ppm (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$): $\delta=$ 165.4, 160.9, 156.6, 149.3, 137.7, 136.6, 127.9, 123.0, 122.0, 91.0, 78.0, 52.0 ppm; HRMS: *m/z*: calcd for: 358.9733; found: 358.9724 $[M+Na]^+$.

*2-[Naphthalen-2-yl-(2,2,2-trichloroacetimidoyloxy)methyl]acrylic acid methyl ester (**1d**)*: $R_f=0.50$ (pentane/Et_2O 1:1); m.p. 65 °C (off-white solid); ^{1}H NMR (400 MHz, $CDCl_3$, TMS): $\delta=8.47$ (brs, 1H), 7.96 (brs, 1H), 7.89–7.81 (m, 3H), 7.58 (dd, $J=1.7$ Hz, 8.6 Hz, 1H), 7.53–7.46 (m, 2H), 6.98 (s, 1H), 6.49 (brs, 1H), 6.07 (brs, 1H), 3.75 ppm (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$): $\delta=165.5$, 160.7, 139.2, 134.4, 133.2, 132.9, 128.2, 128.2, 127.7, 127.1, 126.4, 126.2, 125.0, 91.3, 77.4, 52.1 ppm; HRMS: *m/z*: calcd for: 407.9937; found: 407.9932 $[M+Na]^+$.

*2-[Phenyl-(2,2,2-trichloroacetimidoyloxy)methyl]acrylic acid tert-butyl ester (**1e**)*: Synthesised according to known literature procedure.[10a] $R_f=$ 0.50 (pentane/Et_2O 1:4).

*2-Methylene-3-(2,2,2-trichloroacetimidoyloxy)pentanoic acid methyl ester (**1f**)*: The compound was slightly yellow liquid. $R_f=0.54$ (pentane/Et_2O 1:1); ^{1}H NMR (400 MHz, $CDCl_3$, TMS): $\delta=8.32$ (s, 1H), 6.32 (s, 1H), 5.93 (s, 1H), 5.67 (dd, $J=4.1$ Hz, 7.6 Hz, 1H), 3.79 (s, 3H), 2.01–1.88 (m, 1H), 1.85–1.72 (m, 1H), 1.01 ppm (t, $J=7.4$ Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$): $\delta=165.8$, 161.2, 139.2, 124.9, 91.5, 77.4, 52.0, 27.7, 9.6 ppm; HRMS: *m/z*: calcd for: 309.9780; found: 309.9795 $[M+Na]^+$.

*4-Methyl-2-methylene-3-(2,2,2-trichloroacetimidoyloxy)pentanoic acid methyl ester (**1g**)*:[10a] $R_f=0.57$ (pentane/Et_2O 1:1); ^{1}H NMR (400 MHz, $CDCl_3$, TMS): $\delta=8.30$ (s, 1H), 6.36 (d, $J=0.8$ Hz, 1H), 5.89 (brs, 1H), 5.57 (d, $J=4.4$ Hz, 1H), 3.80 (s, 3H), 2.17–2.07 (m, 1H), 1.03 (d, $J=$ 6.9 Hz, 3H), 0.99 ppm (d, $J=6.8$ Hz, 3H);^{13}C NMR (101 MHz, $CDCl_3$): $\delta=165.9$, 161.3, 138.4, 125.5, 80.4, 52.1, 32.2, 19.0, 16.6 ppm; HRMS: *m/z*: calcd for: 323.9937; found: 323.9943 $[M+Na]^+$.

*2,2,2-Trichloroacetimidic acid 2-cyano-1-isopropyl-allyl ester (**1h**)*: The compound was a slightly yellow liquid. $R_f=0.49$ (pentane/Et_2O 1:1); ^{1}H NMR (400 MHz, $CDCl_3$, TMS): $\delta=8.45$ (brs, 1H), 6.13 (s, 1H), 6.07–6.06 (m, 1H), 5.15 (d, $J=7.3$ Hz, 1H), 2.25 (octet, $J=6.8$ Hz, 1H), 1.08 (d, $J=6.7$ Hz, 3H), 1.03 ppm (d, $J=6.9$ Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$): $\delta=161.3$, 133.3, 121.0, 116.4, 82.0, 31.4, 18.5, 17.4 ppm; HRMS: *m/z*: calcd for: 290.9835; found: 290.9840 $[M+Na]^+$.

*2,2,2-Trichloroacetimidic acid (2-oxo-5,6-dihydro-2H-pyran-3-yl)phenyl-methyl ester (**1i**)*: $R_f=0.18$ (pentane/Et_2O 1:1); m.p. 123 °C (white solid); ^{1}H NMR (400 MHz, $CDCl_3$, TMS): $\delta=8.45$ (s, 1H), 7.51–7.46 (m, 2H), 7.40–7.28 (m, 3H), 6.97 (t, $J=4.4$ Hz, 1H), 6.84 (s, 1H), 4.44–4.30 (m, 2H), 2.55–2.49 ppm (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$): $\delta=162.7$, 160.4, 140.3, 137.2, 132.2, 128.4, 128.4, 127.1, 91.2, 76.1, 66.0, 24.2 ppm; HRMS: *m/z*: calcd for: 369.9780; found: 369.9790 $[M+Na]^+$.

General procedure for asymmetric syntheses of allylic trichloroacetamides (2)

Method A: The imidate (**1**, 1 equiv) was weighed in a 4 mL vial, solvent (0.5 mL dioxane) and catalyst (0.1 equiv) were added. The reaction was stirred at 40 °C and monitored by TLC. Upon completion the solvent was evaporated and the crude product was directly purified by FC.

Method B: The imidate (**1**, 1 equiv) was weighed in a 4 mL vial, solvent (0.5 mL dioxane) and catalyst (0.1 equiv) were added. The reaction was stirred at room temperature and monitored by TLC. Upon completion the solvent was evaporated and the crude product was directly purified by FC.

Method C: The imidate (**1**, 1 equiv) was weighed in a 4 mL vial, solvent (5.0 mL dioxane) and catalyst (0.1 equiv) were added. The reaction was stirred at 40 °C and monitored by TLC. Upon completion the solvent was evaporated and the crude product was directly purified by FC.

Method D: The imidate (**1**, 1 equiv) was weighed in a 4 mL vial, solvent (5.0 mL dioxane) and catalyst (0.1 equiv) were added. The reaction was stirred at room temperature and monitored by TLC. Upon completion the solvent was evaporated and the crude product was directly purified by FC.

*2-[Phenyl-(2,2,2-trichloroacetylamino)methyl]acrylic acid methyl ester (**2a**)*: This imidate was obtained according to the general procedure (Method A, overnight) and isolated as a white solid (77% yield). $R_f=$ 0.31 (pentane/Et_2O 3:1); m.p. 81 °C. $[\alpha]_D=-22.7°$ ($c=0.98$, $CHCl_3$) (90% *ee*); HPLC (OD, 250 mm, hexane/*i*PrOH 98:2): $\tau_{major}=8.7$ min, $\tau_{minor}=$ 10.4 min; ^{1}H NMR (400 MHz, $CDCl_3$, TMS): $\delta=8.16$ (d, $J=8.4$ Hz, 1H), 7.39–7.32 (m, 2H), 7.33–7.27 (m, 3H), 6.44 (brs, 1H), 6.02 (brs, 1H), 5.92 (d, $J=8.8$ Hz, 1H), 3.73 ppm (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$): $\delta=166.1$, 161.1, 137.9, 137.4, 128.8, 128.7, 128.0, 126.0, 92.5, 56.9, 52.3 ppm; HRMS: *m/z*: calcd for: 357.9780; found: 357.9792 $[M+Na]^+$.

*2-[(4-Nitrophenyl)-(2,2,2-trichloroacetylamino)methyl]acrylic acid methyl ester (**2b**)*: This imidate was obtained according to the general procedure (Method D, 1 d) and isolated as a slightly yellow, clear oil (89% yield). $R_f=0.42$ (pentane/Et_2O 1:1); $[\alpha]_D=-34.0°$ ($c=7.7$, $CHCl_3$) (74% *ee*); HPLC (OD, 250 mm, hexane/*i*PrOH 90:10): $\tau_{major}=16.5$ min, $\tau_{minor}=$ 21.6 min; ^{1}H NMR (400 MHz, $CDCl_3$, TMS): $\delta=8.35$ (d, $J=8.4$ Hz, 1H), 8.20 (dd, $J=2.0$ Hz, 7.2 Hz, 2H), 7.48 (d, $J=8.6$ Hz, 2H), 6.50 (s, 1H), 6.14 (s, 1H), 5.97 (d, $J=8.8$ Hz, 1H), 3.75 ppm (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$): $\delta=166.1$ 161.6, 147.7, 145.5, 136.5, 130.7, 127.1, 124.2, 92.4, 56.9, 52.8 ppm; HRMS: *m/z*: calcd for: 402.9631; found: 402.9629 $[M+Na]^+$.

*2-[Pyridin-2-yl-(2,2,2-trichloroacetylamino)methyl]acrylic acid methyl ester (**2c**)*: This imidate was obtained according to the general procedure (Method C, 2 d) and isolated as a slightly yellow, clear oil (64% yield). $R_f=0.22$ (pentane/Et_2O 1:1); $[\alpha]_{365\,nm\ Hg}=+14.8°$ ($c=1.00$, $CHCl_3$) (80% *ee*); HPLC (OD, 250 mm, hexane/*i*PrOH 95:5): $\tau_{major}=10.1$ min, $\tau_{minor}=$ 12.5 min; ^{1}H NMR (400 MHz, $CDCl_3$, TMS): $\delta=8.83$ (brd, $J=6.8$ Hz, 1H), 8.55 (ddd, $J=0.9$ Hz, 1.8 Hz, 4.9 Hz, 1H), 7.70 (d, $J=1.8$ Hz, 7.7 Hz, 1H), 7.43 (d, $J=7.9$ Hz, 1H), 7.24 (dddd, $J=0.4$ Hz, 1.1 Hz, 4.9 Hz, 7.5 Hz, 1H), 6.40 (s, 1H), 6.03 (brs, 1H), 5.95 (d, $J=7.5$ Hz, 1H), 3.74 ppm (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$): $\delta=165.9$, 161.0, 155.9, 149.0, 138.2, 137.2, 127.8, 123.1, 122.1, 92.5, 56.0, 52.2 ppm; HRMS: *m/z*: calcd for: 358.9733; found: 358.9727 $[M+Na]^+$.

*2-[Naphthalen-2-yl-(2,2,2-trichloroacetylamino)methyl]acrylic acid methyl ester (**2d**)*: This imidate was obtained according to the general procedure (Method A, overnight) and isolated as a slightly yellow, clear oil (74% yield). $R_f=0.42$ (pentane/Et_2O 1:1); $[\alpha]_D=+4.5°$ ($c=0.98$, $CHCl_3$) (74% *ee*); HPLC (OD, 250 mm, hexane/*i*PrOH 95:5): $\tau_{major}=10.2$ min, $\tau_{minor}=$ 15.0 min; ^{1}H NMR (400 MHz, $CDCl_3$, TMS): $\delta=8.26$ (d, $J=8.7$ Hz, 1H), 7.88–7.81 (m, 3H), 7.76 (brs, 1H), 7.54–7.46 (m, 2H), 7.42 (dd, $J=$ 1.9 Hz, 8.5 Hz, 1H), 6.50 (brs, 1H), 6.12–6.08 (m, 1H), 3.73 ppm (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$): $\delta=166.1$, 161.1, 143.8, 137.4, 135.3, 133.1, 132.8, 128.8, 128.0, 127.6, 126.4, 126.3, 125.0, 124.0, 92.6, 57.0, 52.3 ppm; HRMS: *m/z*: calcd for: 407.9937; found: 407.9953 $[M+Na]^+$.

*2-[Phenyl-(2,2,2-trichloroacetylamino)methyl]acrylic acid tert-butyl ester (**2e**)*:[10a] This imidate was obtained according to the general procedure (Method B, 5 d) and isolated as a clear, colourless oil (89% yield). $R_f=$ 0.39 (pentane/Et_2O 4:1); $[\alpha]_D=-33.3°$ ($c=1.00$, $CHCl_3$) (92% *ee*); HPLC (OD, 250 mm, hexane/*i*PrOH 98:2): $\tau_{major}=5.5$ min, $\tau_{minor}=$ 6.1 min; ^{1}H NMR (400 MHz, $CDCl_3$, TMS) $\delta=7.99$ (d, $J=8.2$ Hz, 1H), 7.4–7.2 (m, 5H), 6.37 (s, 1H), 5.9–5.8 (m, 2H), 1.36 ppm (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$): $\delta=164.7$, 161.1, 139.0, 138.3, 128.7, 128.1, 127.8, 125.9, 92.7, 82.3, 56.8, 27.8 ppm.

*2-Methylene-3-(2,2,2-trichloroacetylamino)pentanoic acid methyl ester (**2f**)*: This imidate was obtained according to the general procedure (Method B, 4 d) and isolated as a clear, colourless oil (83% yield). $R_f=$ 0.28 (pentane/Et_2O 3:1); $[\alpha]_D=-20.2°$ ($c=1.01$, $CHCl_3$) (46% *ee*); HPLC (OJ, 500 mm, hexane/*i*PrOH 98:2): $\tau_{major}=23.9$ min, $\tau_{minor}=$ 25.6 min; ^{1}H NMR (400 MHz, $CDCl_3$, TMS): $\delta=7.82$ (d, $J=7.2$ Hz, 1H), 6.27 (s, 1H), 5.83 (s, 1H), 4.55 (q, $J=7.8$ Hz, 1H), 3.79 (s, 3H), 1.85–1.65 (m, 2H), 0.92 ppm (t, $J=7.4$ Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$): $\delta=$

166.4, 161.1, 137.3, 128.6, 92.7, 56.3, 52.1, 27.3, 10.7 ppm; HRMS: *m/z*: calcd for: 309.9780; found: 309.9794 $[M+Na]^+$.

*4-Methyl-2-methylene-3-(2,2,2-trichloroacetylamino)pentanoic acid methyl ester (**2g**)*: This imidate was obtained according to the general procedure (Method B, 3 d) and isolated as a slightly yellow, clear oil (57% yield). $R_f=0.22$ (pentane/Et_2O 1:1); $[\alpha]_D=-39.3°$ ($c=1.00$, $CHCl_3$) (78% *ee*); HPLC (OJ, 500 mm, hexane/*i*PrOH 99:1): $\tau_{major}=15.7$ min, $\tau_{minor}=18.0$ min; ^1H NMR (400 MHz, $CDCl_3$, TMS): $\delta=7.88$ (br d, $J=8.4$ Hz, 1H), 6.29 (s, 1H), 5.82 (s, 1H), 4.28 (t, $J=9.6$ Hz, 1H), 3.80 (s, 3H), 2.13–2.01 (m, 1H), 1.00 (d, $J=6.7$ Hz, 3H), 0.87 ppm (d, $J=6.8$ Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$): $\delta=166.6$, 161.2, 136.8, 129.3, 92.8, 61.2, 52.2, 31.3, 20.1, 19.1 ppm; HRMS: *m/z*: calcd for: 323.9937; found: 323.9943 $[M+Na]^+$.

*2,2,2-Trichloro-N-(2-cyano-1-isopropylallyl)acetamide (**2h**)*: This imidate was obtained according to the general procedure (Method B, 2 d) and isolated as a clear, colourless oil (73% yield). $R_f=0.38$ (pentane/Et_2O 1:1); $[\alpha]_D=+17.2°$ ($c=1.00$, $CHCl_3$) (40% *ee*); HPLC (OD, 250 mm, hexane/*i*PrOH 95:5): $\tau_{minor}=14.1$ min, $\tau_{major}=16.7$ min; ^1H NMR (400 MHz, $CDCl_3$, TMS): $\delta=6.81$ (br d, $J=7.2$ Hz, 1H), 6.09 (s, 1H), 6.01 (s, 1H), 4.20 (t, $J=8.6$ Hz, 1H), 2.11 (dsept, $J=8.7$ Hz, 6.7 Hz, 1H), 1.05 (d, $J=6.7$ Hz, 3H), 1.02 ppm (d, $J=6.7$ Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$): $\delta=161.6$, 133.4, 121.6, 116.3, 92.2, 60.3, 30.6, 19.4, 18.2 ppm; HRMS: *m/z*: calcd for: 290.9835; found: 290.9836 $[s+Na]^+$.

***N*-(3-Benzylidene-2-oxo-tetrahydropyran-4-yl)-2,2,2-trichloroacetamide (3i)**: ^1H NMR (400 MHz, $CDCl_3$, TMS): $\delta=8.09$ (s, 1H), 7.44 (br s, 1H), 7.42–7.34 (m, 5H), 5.26 (dd, $J=10.6$ Hz, 4.8 Hz, 1H), 4.62–4.53 (m, 1H), 4.41 (td, $J=11.1$ Hz, 4.0 Hz, 1H), 2.32–2.20 ppm (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$): $\delta=166.4$, 161.7, 147.9, 132.9, 130.6, 130.0, 129.0, 123.3, 92.2, 64.6, 46.6, 28.0 ppm; HRMS: *m/z*: calcd. for: 369.9780; found: 369.9771 $[M+Na]^+$.

Diels–Alder reaction between amide product (2a) and 2,3-dimethylbuta-1,3-diene (6): In an ordinary 2 mL vial the amide (40 mg, 0.12 mmol, 1 equiv) was dissolved in CH_2Cl_2 (0.3 mL). Then Et_2AlCl (25% sol. in toluene, 10 μL, 0.024 mmol) was added followed by 2,3-dimethylbuta-1,3-diene (68 μL, 0.60 mmol, 5 equiv). The vial was safely closed and stirred in an oil bath at 70 °C for 48 h. After complete consumption of the starting material (monitored by ^1H NMR), the crude was directly charged in FC (pentane/Et_2O 90:10) affording the pure product as a white solid, which can be easily recrystallised in colourless crystals in 60% yield.

3,4-Dimethyl-1-[phenyl-(2,2,2-trichloroacetylamino)methyl]cyclohex-3-enecarboxylic acid methyl ester (7): The *ee* was determined by HPLC using a Daicel Chiralcel OD column (hexane/*i*PrOH 98:2); flow rate 1.0 mL min^{-1}; $\tau_{minor}=6.0$ min, $\tau_{major}=12.4$ min; $[\alpha]_D=+46.8°$ ($c=1.00$, $CHCl_3$) (89% *ee*); ^1H NMR (400 MHz, $CDCl_3$, TMS): $\delta=8.63$ (d, $J=8.3$ Hz, 1H), 7.3–7.2 (m, 3H), 7.10 (dd, $J=7.8$, 2.0 Hz, 2H), 4.79 (d, $J=8.5$ Hz, 1H), 3.58 (s, 3H), 2.41 (d, $J=16.7$ Hz, 1H), 2.17 (d, $J=17.1$ Hz, 1H), 1.98 (br d, $J=5.9$ Hz, 2H), 1.83 (dt, $J=13.5$ Hz, 6.7 Hz, 1H), 1.54 (s, 6H), 1.43 ppm (dt, $J=13.5$ Hz, 7.1 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$): $\delta=176.3$, 161.0, 137.2, 128.4, 128.2, 127.3, 125.4, 121.9, 92.9, 59.9, 52.2, 49.0, 38.6, 28.6, 26.9, 19.2, 18.7 ppm; HRMS: calcd for $C_{19}H_{22}Cl_3NO_3Na$: 440.0563, found: 440.0564 $[M+Na]^+$; relative configuration was determined.[16]

General procedure for synthesis of carbamates (4): The Baylis–Hillman adduct (1.0 equiv) was dissolved in dry dichloromethane at room temperature, then isocyanate (1.1 equiv) was added. Reaction was monitored by TLC, and after completion, the reaction was concentrated, and purified by FC.

*2-[Phenyl-(tosylcarbamoyloxy)methyl]acrylic acid tert-butyl ester (**4a**)*: $R_f=0.32$ (pentane/Et_2O 1:1 + 8% MeOH); ^1H NMR (400 MHz, $CDCl_3$, TMS): $\delta=8.84$ (s, 1H), 7.81 (d, $J=7.3$ Hz, 2H), 7.3–7.1 (m, 7H), 6.52 (s, 1H), 6.30 (s, 1H), 5.70 (s, 1H), 2.35 (s, 3H), 1.28 ppm (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$): $\delta=163.7$, 149.1, 145.0, 139.9, 136.5, 135.3, 129.6, 128.7, 128.4, 128.3, 127.8, 126.4, 125.6, 81.8, 76.3, 27.8, 21.7 ppm; HRMS: *m/z*: calcd for: 454.1300; found: 454.1300 $[M+Na]^+$.

*2-[Phenyl-(2,2,2-trichloroacetylcarbamoyloxy)methyl]acrylic acid tert-butyl ester (**4b**)*: $R_f=0.33$ (pentane/Et_2O 1:2); ^1H NMR (400 MHz, $CDCl_3$, TMS): $\delta=8.46$ (s, 1H), 7.5–7.3 (m, 5H), 6.71 (s, 1H), 6.41 (s, 1H), 5.91 (s, 1H), 1.39 ppm (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$): $\delta=164.3$, 164.0, 155.9, 141.1, 138.0, 128.3, 127.7, 124.7, 81.5, 74.2, 27.8 ppm; HRMS: *m/z*: calcd for: 444.0148; found: 444.0146 $[M+Na]^+$.

General procedure for asymmetric syntheses of *N*-protected amine (5)

*From carbamates **4** to N-protected amine **5***: The carbamate (**4**, 1 equiv) was weighed in a 4 mL vial, solvent and catalyst (0.2 equiv) were added. The reaction was stirred at 35 °C and monitored by TLC. Upon completion the solvent was evaporated and the crude product was directly purified by FC.

*From Baylis–Hillman adduct to N-protected amine **5***: The Baylis–Hillman adduct (1.05 equiv) was weighed in a 4 mL vial, solvent and isocyanate (1.00 equiv) were added. The reaction was stirred at room temperature and monitored by TLC. After consummation of Baylis–Hillman, the catalyst (0.2 equiv) was added, and the reaction was warmed to 35 °C and monitored by TLC. Upon completion the solvent was evaporated and the crude product was directly purified by FC.

*2-[Phenyl-(toluene-4-sulfonylamino)methyl]acrylic acid tert-butyl ester (**5a**)*:[34] This amine was obtained from Baylis–Hillman adduct and isolated as a slightly yellow, clear oil (43% yield). $R_f=0.19$ (pentane/Et_2O 2:1); $[\alpha]_D=-12.8°$ ($c=1.01$, $CHCl_3$) (>99% *ee*); HPLC (AD, 250 mm, hexane/*i*PrOH 90:10): $\tau_{major}=16.0$ min, $\tau_{minor}=13.3$ min; ^1H NMR (400 MHz, $CDCl_3$, TMS): $\delta=7.68$ (d, $J=8.2$ Hz, 2H), 7.3–7.1 (m, 7H), 6.10 (s, 1H), 5.67 (s, 1H), 5.60 (d, $J=9.1$ Hz, 1H), 5.25 (d, $J=9.0$ Hz, 1H), 2.40 (s, 3H), 1.29 ppm (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$): $\delta=164.6$, 143.3, 139.8, 139.0, 137.7, 129.5, 128.4, 127.6, 127.2, 126.3, 81.8, 59.2, 27.8, 21.5 ppm.

*2-[Pyridin-2-yl-(2,2,2-trichloroacetylamino)methyl]acrylic acid methyl ester (**5b**=**2e**)*: This amine was obtained from Baylis–Hillman adduct isolated as a clear, colourless oil (72% yield). $R_f=0.39$ (pentane/Et_2O 4:1); $[\alpha]_D=-33.3°$ (c 1.00, $CHCl_3$) (92% *ee*); HPLC (OD, 250 mm, hexane/*i*PrOH 98:2): $\tau_{major}=5.5$ min, $\tau_{minor}=6.1$ min; ^1H NMR (400 MHz, $CDCl_3$, TMS): $\delta=7.99$ (d, $J=8.2$ Hz, 1H), 7.4–7.2 (m, 5H), 6.37 (s, 1H), 5.9–5.8 (m, 2H), 1.36 ppm (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$): $\delta=164.7$, 161.1, 139.0, 138.3, 128.7, 128.1, 127.8, 125.9, 92.7, 82.3, 56.8, 27.8 ppm.

Absolute configuration: Compound **5a** was transesterified, according to known literature procedure,[18] to the methyl ester, for which the absolute configuration is known.[17] The optical rotation of the compound was determined and compared. Since **5b** was generated via same mechanism, the absolute configuration is assumed to be similar; hence **5b**=**2e**, the configuration of the **2** can be deduced. $[\alpha]_D=-11.3°$ ($c=0.52$, $CHCl_3$) (68% *ee*); HPLC (AS, 250 mm, 0.60 mL min^{-1} hexane/*i*PrOH 60:40): $\tau_{minor}=17.1$ min, $\tau_{major}=20.2$ min; ^1H NMR (400 MHz, $CDCl_3$, TMS) $\delta=7.68$ (dd, $J=2.0$ Hz, 8.2 Hz, 2H), 7.3–7.2 (m, 5H), 7.2–7.1 (m, 2H), 6.22 (s, 1H), 5.83 (s, 1H), 5.60 (d, $J=9.0$ Hz, 1H), 5.29 (d, $J=9.0$ Hz, 1H), 3.60 (s, 3H), 2.41 ppm (s, 3H).

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