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Reduction of *N*-Allylamides by $LiAlH_4$: Unexpected Attack of the Double Bond with Mechanistic Studies of Product and Byproduct Formation

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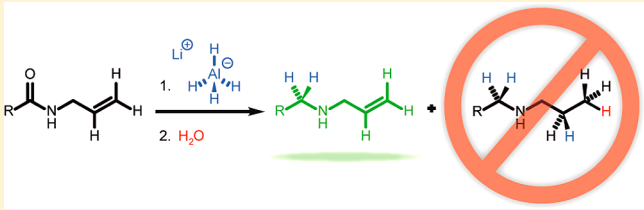
Supporting Information

ABSTRACT: The reduction of secondary allyl amides with $LiAlH_4$ can lead to a concomitant reduction of the double bond. Previously, an excess of $LiAlH_4$ in hazardous solvents was used for the reduction. This work discusses optimized reaction conditions in *t*BuOMe as a safe solvent, with only a 1.5-fold excess of $LiAlH_4$, without reduction of the double bond in most cases. ^1H and ^2D NMR spectroscopic studies give evidence for the mechanism of the reduction of the amide as well as the double bond: Amide reduction generally precedes double bond reduction. Sterically hindered allylamides are an exception. They are reduced considerably more slowly at higher temperatures, and double bond reduction is observed before amide reduction has gone to completion.



INTRODUCTION

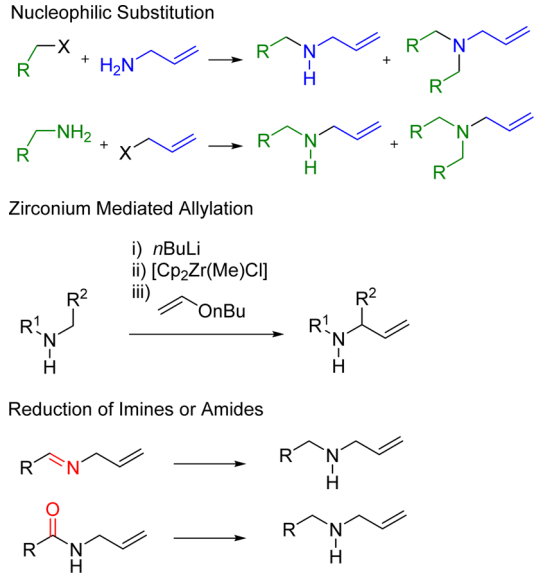
In organic chemistry, the allylamine motif constitutes a highly interesting unit, especially in the pharmaceutical industry. Allylamines are often present in pharmaceuticals including the potent antifungal drugs naftifine,[1] terbinafine,[1] cytosinine,[2] oryzoxymicine,[3−5] and gabaculine.[6−9] In combination with a phosphate unit, as a phosphoramidate, allylamine moieties were investigated as flame retardants in polyurethane foams due to their low volatility, easy synthesis, and low evolution of toxic gases and smoke.[10] Furthermore, allylamines are used in synthesis of indoles[11] and various heterocycles[12−14] or as precursor to important compounds as α- and β-amino acids,[15−18] alkaloids,[19,20] carbohydrate derivatives,[21] and for the synthesis of poly(allylamines) as weak polyelectrolytes.[22−24]

There are several methods to synthesize allylamines (Scheme 1). For symmetrical tertiary allylamines, $AllylNR_2$, easy synthetic routes are available for example by allylation of primary[25,26] or secondary amines.[27] In contrast, secondary allylamines represent a major difficulty because of overalkylation to tertiary allylamines.[25] Very recent developments are the introduction of allylamine by the Petasis raction[28] or by a zirconium mediated coupling reaction between amines and enol ethers. This method is very efficient, but it relies on bis(cyclopentadienyl)zirconium methyl chloride, which is not commercially available.[29] A more commonly used route to secondary allylamines is therefore the reduction of imines or iminium salts.[30−33]

However, many imines and iminium salts are unstable toward hydrolysis, and therefore, these precursors may be difficult to isolate. The reduction of the much more hydrolytically stable amides, which are easily accessible from acyl halides and allylamine, using $LiAlH_4$ as the reductant is therefore the most versatile route to secondary allylamines (Scheme 1).[34−36] However, as we demonstrate in this report, the double bond of the allylamine can be reduced under some conditions, leading to a *n*-propylamine byproduct which cannot be removed from the product mixture.

That issue prompted this investigation into the factors contributing to this problem. This study leads to general recommendations for performing that important reaction.

Scheme 1. Overview of Synthetic Routes to Secondary Allylamines (X = Halides)



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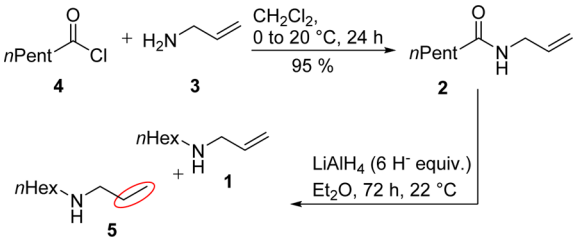
RESULTS

For our current research program, we required the secondary *N*-allyl-*N*-*n*-hexylamine **1**, which we wished to prepare by simply reducing the easily synthesized amide **2** with $LiAlH_4$. The amide **2** was readily accessible from allylamine **3** and *n*-hexanoyl chloride **4** in an excellent yield of 95% (Scheme 2).[37]

Scheme 2. Syntheses of Allylamine 1 and the Unexpected Byproduct 5



For the subsequent reduction of the amide functional group, half an equivalent of $LiAlH_4$ (two hydride equivalents with respect to the functional group) should be sufficient. A literature procedure for the reduction of the very similar *N*-*n*-heptylacetamide, a compound which does not have the additional complication of a double bond present, described the use of 12 hydride equivalents.[37] This seemed not only excessive, but also the quenching of the reaction was a major safety concern due to its exothermic nature and release of hydrogen. We therefore opted for using a smaller excess of $LiAlH_4$ (6 H^- equiv) in Et_2O. After 72 h at 22 °C, we did indeed obtain the secondary allylamine product **1**, but an NMR analysis revealed that it was contaminated with byproduct **5** where the double bond had also been reduced in a ratio of **1**:**5** = 1:2 (Figure 1).

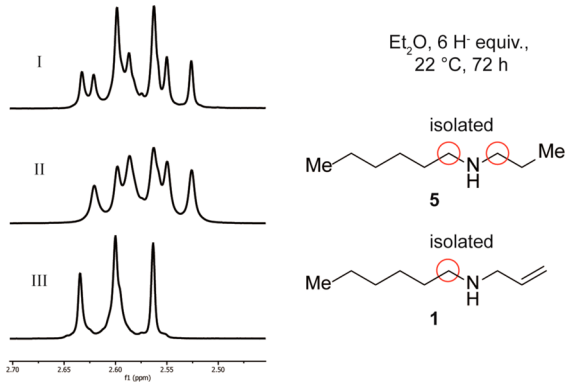


Figure 1. Section of stacked ^1H NMR spectra of crude reaction mixture (I), isolated byproduct **5** (II), and isolated product **1** (III).

Due to these results, the procedure of Wu et al.[38] was used, which employed 16 H^- equivalents on the related *N*-allyl-5-phenylpent-4-ynamide, but did not report an attack of the double bond. This large excess of $LiAlH_4$ in combination with Et_2O as solvent led to a very violent and potentially dangerous quenching procedure even though it was performed by the slow addition of ice cold water with ice cooling the reaction vessel. However, surprisingly, GC analysis showed a better yield of 96% amine **1** accompanied by 1% of hydrogenated byproduct **5** compared to the previously described procedure with six hydride equivalents. This result was unexpected because, intuitively, with more equivalents of hydride, the potential for reducing the double bond should be increased. These strikingly different results prompted us to investigate the reduction reaction systematically (Table 1).

Our aims were, first, to find reaction conditions that give the product **1** in high yields without over-reduction to product **5**. Second, the amount of $LiAlH_4$ should be minimized, both for atom and financial economy, as well as for safety reasons. Third, the solvent used should in the ideal case be safe, with a high boiling point and no danger of peroxide formation, because the production of secondary allylamines is of high importance in industry. Lastly, we decided to investigate the mechanism of the reaction and the behavior of other allylamides to be able to draw general conclusions for conducting allylamide reductions. For this, all reductions were carried out on a 20 mmol scale and a concentration of 0.33 mol/L in *t*BuOMe. As over-reduction could potentially happen during the exothermic first reduction step, we investigated cooling during addition of amide **2** to 0 °C (Table 1, entries 1, 2, 3). However, this led to similar results compared to the reaction carried out without cooling; the yield of **1** and **5** was 96% and 1%, respectively. To achieve the first aim of the optimization, to reduce the amount of $LiAlH_4$, reactions with the theoretical minimum amount of $LiAlH_4$ (2 H^- equiv), at 22 °C, were performed in the solvents (*t*BuOMe, THF, and Me-THF).[40] All of these solvents have a higher boiling point than diethyl ether, although THF and Me-THF both can form peroxides and are not ideal from a safety perspective. In all of these cases, GC analysis showed that the conversion stopped at approximately 40% (Table 1, entries 6, 7, 8) with no formation of the byproduct **5**. Even reactions at higher temperatures of 35 and 55 °C in *t*BuOMe showed no significant difference (Table 1, entries 9, 10) with a product yield of ca. 40%, but no over-reduced byproduct. Because of this surprising result, the amount of $LiAlH_4$ was raised to three H^- equivalents. For both *t*BuOMe and Me-THF as solvents after 24 h at 22 °C, good yields of product **1** of 89% and 76%, respectively, were found, without significant amount of hydrogenated byproduct **5** (1% and no detectable amounts, respectively). However, the same reaction in THF showed almost no conversion, giving only 8% of the product (Table 1, entry 14). Because the type of solvent was clearly important, we reintroduced Et_2O to our comparative studies. In comparison to *t*BuOMe as solvent, Et_2O showed a similar yield (Table 1, entries 11, 12) of 91%, with ca. 1% of over-reduced product **5**. The increase in temperature (35 °C) reduced the reaction time to 4 h with similar yields as those obtained at 22 °C of 82%, 87% ,and 83%, respectively, except for THF (8%). In none of these was byproduct **5** detected (Table 1, entries 15−18).

Longer reaction times, however, led to a marked increase of the amount of **5** up to 15% (Table 1 in the Supporting Information; entries 4−6, 12−15, 21, 24). The tendency to faster reaction times at higher temperatures was confirmed by obtaining similar yields (82% to 87%) at 55 °C with half the reaction times compared to reactions at 35 °C, because the higher thermal energy allowed a faster hydride transfer. Even in THF, the reduction at 55 °C reached a similar yield of 78%. That THF is only a good solvent at higher temperatures can be explained by the lower solubility of $LiAlH_4$ in this solvent (compared to Et_2O)[41] and the type of solvation (contact ion pairs or separated ion pairs).[42]

In order to understand the formation of the hydrogenated byproducts, there were several questions to address: First, does the attack of the double bond by hydride happen before or during

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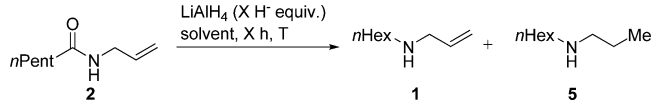
Table 1. Optimization of the Reaction Conditions for Reduction of *n*-Hexylallylamide (2) by Adapting Solvent, Temperature, and $LiAlH_4$ (H^- equiv), and Monitoring the Reaction Time[39]



entry	solvent	$LiAlH_4$ (H^- equiv)	T (°C)	time (h)	**2**[a] (%)	**1**[a] (%)	**5**[a] (%)
1	Et_2O	16	0 °C → 22 °C[b]	12	22	77	0
2	Et_2O	16	0 °C → 22 °C[c]	12	3	96	1
3	Et_2O	16	22 °C	12	3	96	1
4	Et_2O	6	22 °C	4 (24)	9 (3)	90 (80)	1 (15)
5	Et_2O	6	35 °C	1 (2)	15 (6)	82 (86)	0 (3)
6	*t*BuOMe	2	22	24	50	40	0
7	THF	2	22	24	58	37	0
8	Me-THF	2	22	24	52	26	0
9	*t*BuOMe	2	35	24	49	44	0
10	*t*BuOMe	2	55	24	49	39	0
11	Et_2O	3	22	24	7	91	1
12	*t*BuOMe	3	22	24	9	89	1
13	THF	3	22	24	92	8	0
14	Me-THF	3	22	24	14	76	0
15	Et_2O	3	35	4	16	82	0
16	*t*BuOMe	3	35	4	12	87	0
17	THF	3	35	4	92	8	0
18	Me-THF	3	35	4	13	83	0
19	*t*BuOMe	3	55	2	9	84	0
20	THF	3	55	2	11	78	0
21	Me-THF	3	55	2	3	87	1

[a]Yields measured by GC using 1,3,5-triisopropylbenzene as an internal standard. [b]Ice bath slowly warmed up. [c]Ice bath removed after amide addition.

quenching reaction? Second, does the hydride attack the double bond selectively on one carbon or does it attack randomly both double bond positions? Third, if the hydride attacks selectively, which position of the double bond is attacked and does this allow drawing conclusions as to the geometry of the substrate–lithium aluminum hydride complex or the partially oxidized aluminum hydride species respectively?

To investigate the reaction mechanism the reduction process was monitored by No-D ^1H NMR spectroscopy. For this purpose, we used *N*-allylbenzamide **6** as starting material because this compound has fewer alkyl proton signals than **2** and its products, which was expected to simplify the analysis. For the reduction of the amide **6**, we had detected 14% of over-reduced byproduct **7** after 2 days. As reducing agents, $LiAlH_4$ (Figure 2a) as well as $LiAlD_4$ (Figure 2b) were used, and for quenching both H_2O and D_2O were employed.

Immediately after the addition of $LiAlH_4$ to **6**, which proceeds with a marked exotherm, a substantial shift of the protons of the allyl group was observed: Both doublets of doublet of triplets for the protons H1a and H2a were shifted upfield from 5.69 to 5.59 ppm and 5.57 to 5.53 ppm, respectively, whereas the apparent triplet for the allylic methylene group at 4.53 ppm shifted to 4.29 ppm. All peaks became broader and less well-defined. After about 47 min, the signal intensity for the starting material started to decrease, and gradually a new set of signals at 5.46, 5.44, and 4.46 ppm appeared. This was fully developed after 19 h 21 min and corresponds most likely to metal complex of amine **8**, which releases the amine **8** after quenching with water (Figure 2).

These signal assignments were further supported by conducting the experiment with $LiAlD_4$ as the reducing agent (Figure 2b). The methylene proton signals H4 of the product **8** did not appear at all (4.55 and 4.46 ppm), indicating deuteration at this position (Figure 2b). In the reduction with $LiAlH_4$, aside from the signals for the product **8**, after 1 d 21 h a further signal at 4.62 ppm appeared. Although this singlet signal can be ascribed to benzylic protons of Ph–CH_2–N (Figure 2, red circle), its shift reveals that it belongs to the prequenching species (i.e., the metal complex) of byproduct **7**. This assignment was further supported by newly emerged alkyl signals at 3.07, 2.30, and 0.54 ppm which are indicative of the propyl chain of **7** (Figures 59 and 60, Supporting Information).

To gain further insight in the position of the aluminum hydride complex during attack on the double bond, we quenched the reaction once with H_2O and once with D_2O. ^1H NMR analysis showed different byproducts for each approach. First, reducing the amide **6** by $LiAlH_4$ and quenching with H_2O led to product **8** (with the significant signals at 5.93, 5.20, 5.11, and 3.28 ppm, for the allyl moiety) accompanied by a triplet at 2.54 ppm, a triplet of quartet at 1.50 ppm, and a triplet at 0.85 ppm for the byproduct **7** (Figure 3a). By choosing $LiAlD_4$ as reductant and quenching by H_2O, we obtained a doublet at 2.54 ppm for the α proton, a signal for the β proton with reduced intensity, and also a doublet signal for the γ proton. This result supports the selective hydride attack in the β position (Figure 3b). For the identification of the origin of the proton of the reduced double bond in the *n*-propylamide byproduct, we chose $LiAlH_4$ as reductant in a further experiment and quenched it with D_2O. In the corresponding ^1H NMR spectrum, the triplet signal at 2.54 ppm, the quartet of doublet signal at 1.48 ppm, and the intensity reduced triplet signal at 0.85 ppm indicated the presence of a deuterium atom at γ position (Figure 3c). This assignment was further supported by the ^1H

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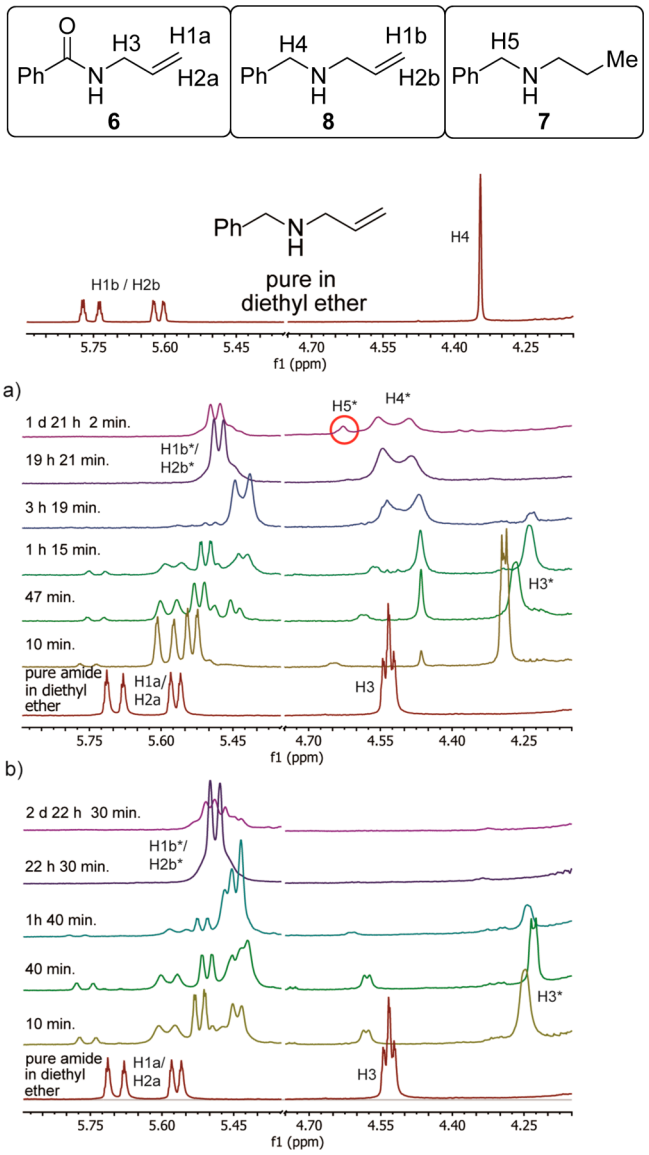

Figure 2. Section of No-D ^{1}H NMR spectra for the sequence of the reduction of *N*-allylbenzamide (**6**) by $LiAlH_4$ (a) and by $LiAlD_4$ (b) in Et_2O. Only a selection of spectra is displayed. For the fully recorded sequence see Supporting Information.

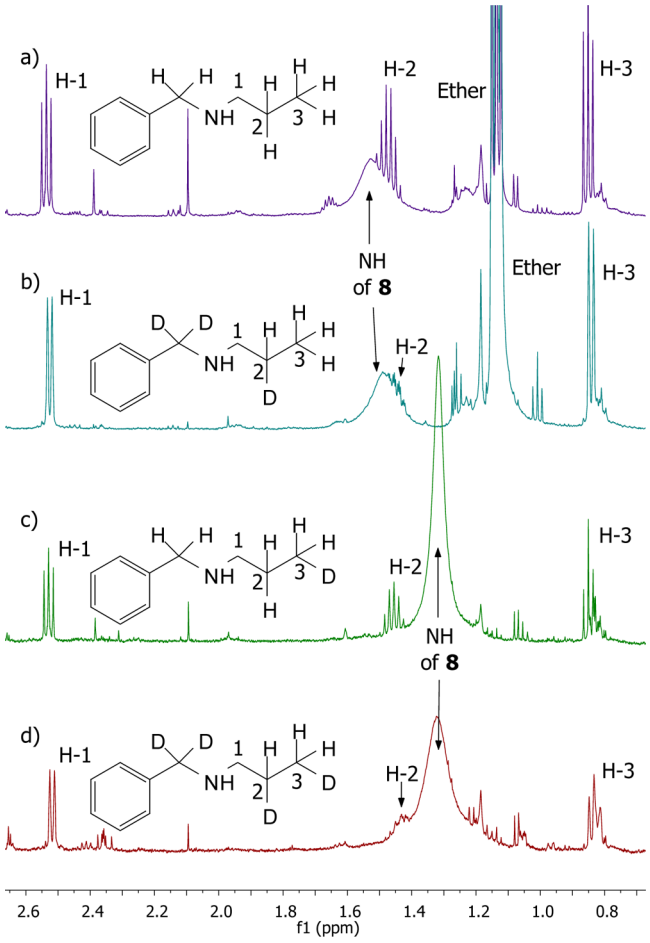

Figure 3. Stacked section of ^{1}H NMR spectra of the deuteration experiments zoomed in for clearly visible byproduct signals. The spectra were obtained from mixtures and contained residual solvent (Et_2O): (a) 1. $LiAlH_4$, 2. H_2O; (b) 1. $LiAlD_4$, 2. H_2O; (c) 1. $LiAlH_4$, 2. D_2O; (d) $LiAlD_4$, 2. D_2O.

NMR of the approach with $LiAlD_4$ as reductant and D_2O as quenching reagent (Figure 3d).

It was then important to elucidate if other secondary amides would behave similarly under the same conditions. For this purpose, a range of amides were prepared from the corresponding acid chlorides and allylamine in excellent yields or in one case from ethyl formiate and allylamine. All amides were subjected to the optimized reaction conditions for the reduction of *N*-allyl-*N*-*n*-hexylamide **2**, using three hydride equivalents in *t*BuOMe as a solvent at 35 °C, while the reaction was monitored by GC analysis (Table 2).

First, as a comparison to the amide **2** (Table 2, entry 1), where the corresponding amine **1** was isolated in a yield of 69%, we tested the reaction conditions with a longer (Table 2, entry 2) and shorter (Table 2, entry 3) alkyl chain moiety. Both starting materials **9** and **10** were reduced in similar yields (65−68%) in a reaction time of 4 h, without any observation of the over-reduced byproduct. For volatile amines, high yields could only be obtained by transforming them to the hydrochloride before removing the solvent. The formyl allylamide **11** reacted much faster with full conversion after 1 h. Although no reduction of the double bond was observed, an entirely unexpected new byproduct emerged: 22% of allylamine hydrochloride **12** was unequivocally identified (Table 2, entry 4). To the best of our knowledge, this is the first carbon−nitrogen cleavage reaction as side reaction in a reduction of an amide by $LiAlH_4$.[43,44]

To investigate more sterically hindered amides, isobutyramide **13** was reduced, which gave a slightly lower yield of 58% of amine **14** than the linear alkylated amines (Table 2, entry 5). However, when the steric hindrance was only slightly increased further to butyl-2-ethyl, ^{1}H NMR and GC analysis showed no allylamine **15** after 6 h at 35 °C. If the reduction was heated to 55 °C, we obtained 25% of amine **15** after 2 h (Table 2, entry 6). The mesitylallylamide **16** with a similar bulky residue compared to butyl-2-ethylamide **17** revealed the same behavior with no conversion after 4 h at 35 °C. But even additional heating of 2 h at 55 °C failed to yield any of the amine **18**.

The similarly bulky but less flexible cyclohexyl moiety on the other hand led to a much higher isolated yield of 79% in respect to the linear alkylated amides (Table 2, entry 8). This high yield decreased to 65%, if the cyclohexyl ring was replaced by a flat aromatic ring as amide substituent (Table 2, entry 9). A CH_2 group as spacer between phenyl and amide functional group

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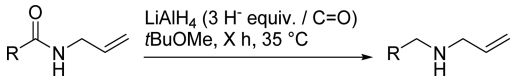
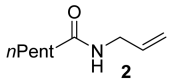
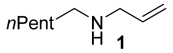
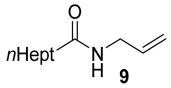
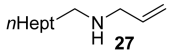
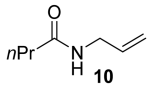
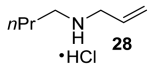
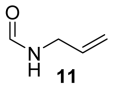
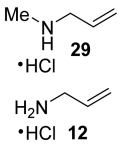
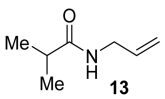
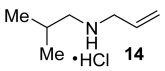
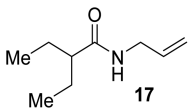
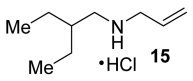
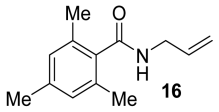
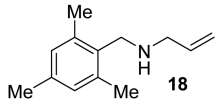
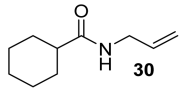
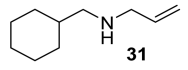
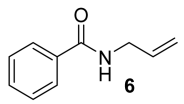
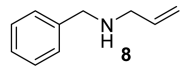
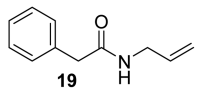
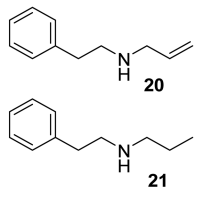
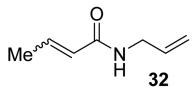
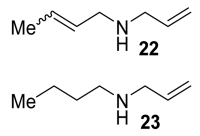
Table 2. Overview of Several Synthesized Amides and Their Corresponding Amines by Optimized Reduction Conditions



Entry	Amide	Amine
1		 4 h 69 %
2		 4 h 65 %
3		 4 h 68 %
4		 1 h: 100 % conversion **29** / **12** = 78 / 22
5		 4 h 58 %
6		 6 h 0 % + 2 h at 55 °C 25 %
7		 6 h 0 % + 2 h at 55 °C 0 %
8		 4 h 79 %
9		 4 h 65 %
10		 4 h 0 % + 2 h at 55 °C 26 % (**20**) 8 % (**21**)
11		 After 2 h: Both DB attacked; Several not assignable signals.

which allows more torsional flexibility for this substituent led to a poorer reduction. However, in this case, the limited solubility of the amide **19** forced us to add the amide as suspension, which could have artificially reduced the yield. After 6 h, ^{1}H NMR spectroscopy of the crude mixture showed only 26% allylamine **20**, which was already accompanied by 8% of the *n*-propylamine byproduct **21** (Table 2, entry 10).

To expand the range of allylamides, we also investigated a α,β-unsaturated compound (Table 2, entry 11). After 2 h, all starting material was converted, but a large amount of the α,β-double bond had also been attacked.[45] ^{1}H NMR indicated the presence of product **22** and about 50% of butylallylamine **23** as byproduct.

DISCUSSION

Although the reduction of amides by $LiAlH_4$ in general is a relatively common reaction, very little research effort has been dedicated to elucidating its mechanism.[46,47]

Reduction of the Amide. For reductions of carbonyl functional groups by $LiAlH_4$, a reasonable assumption is the coordination of the Lewis acidic Li^+ ion to the oxygen atom of the carbonyl functional group (Scheme 3, **A**).

This assumption is supported by the immediately observed exotherm of the reaction straight after the addition of $LiAlH_4$ to the solution of the amide. This exotherm cannot be the result of the reduction reaction itself: This happens on a much slower time scale as was clearly proved by the NMR experiments. The addition of $LiAlH_4$ only shifted the signals of the allyl protons and only after ca. 40−50 min new sets of signals started to appear. By the help of the deuteration studies, the hydrides or deuterides which were transferred to the carbonyl group were clearly identified. Further support of the hypothesis that coordination by Li^+ is a vital step in the reaction includes the observations of the reactions with sterically hindered carbonyl compounds. In extreme cases, we obtained only starting material after quenching under the same reaction conditions as for unhindered allylamides (Table 2, entries 6, 7). For the 2-ethyl-butyl moiety, heating up to 55 °C for 2 h led to a reduction reaction of 37% (Table 2, entry 6). We purport that the flexible steric residues only allow the

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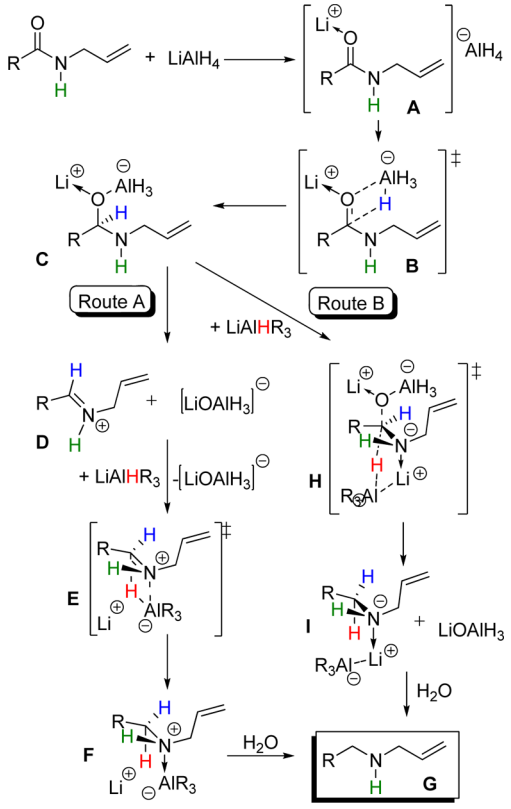
Scheme 3. Proposed Mechanism Based on the Results of the Mechanistic Study



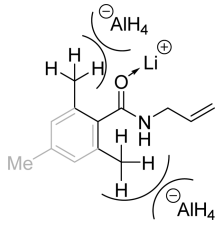


Figure 4. Prevention of the reduction by steric repulsion between bulky moieties and aluminum hydride anions.

coordination of the Li^+ on the less hindered side of the allylamide residue. It thereby prevents the approach of the AlH_4^- ion to the carbonyl center (Figure 4).

Once the lithium cation has coordinated to the oxygen and leads to an even more polarized carbonyl group, the aluminum hydride ion could transfer a hydride to the carbonyl carbon atom via a four membered ring intermediate (**B**). Originating from the hemiaminal species formed (**C**), where the lithium aluminum hydride ion pair is coordinated or bonded to the oxygen, we can consider two possible routes.

Route A presupposes that the hemiaminal compound (**C**) is unstable and decomposes to the corresponding iminium ion by elimination (**D**). Then, a second aluminum hydride species transfers the hydride to the iminium double bond via a four membered ring intermediate (hydroalumination) (**E**). The aminoaluminate (**F**) which is then formed can be quenched by water to give the secondary allylamine as product (**G**).

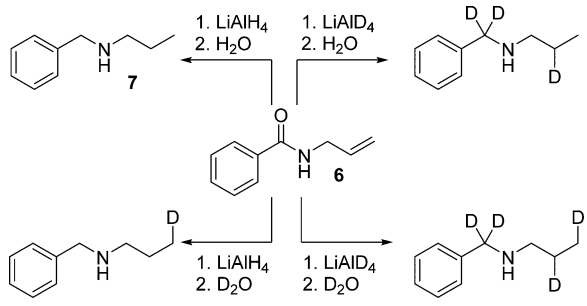
Route B assumes that the hemiaminal compound (**C**) is stable and a second lithium aluminum compound can coordinate to the nitrogen and then transfer a hydride to the double bond via a five membered ring intermediate (**H**). The lithiated aluminum oxide compound serves as leaving group. For the coordination of the second reducing reagent to the nitrogen, it is likely that the lithium cation plays a crucial role in coordinating directly to the nitrogen and bringing the aluminum hydride into close proximity. By quenching the complexed amine species (**I**) with water, the secondary allylamine (**G**) will then also be obtained (Scheme 3). Route A appears less likely, because no signal could be identified that would correspond to a proton of a N=C—*H* group which would have a chemical shift similar to aldehyde protons.[48] Moreover, such a species would also be comparatively unhindered and should be easily reduced, even in sterically crowded cases. However, such amides were very resistant to reduction, and double bond reduction was an earlier side reaction (for a discussion see below).

The first reduction step of the polarized carbonyl group is no doubt faster than the second one as was shown by the No-D ^{1}H NMR spectroscopic measurements of the reduction of **6** (Figure 2). It can clearly be seen that this step has gone to completion before 3 h 19 min. It is then the second reduction step that is rate limiting. This is also a possible explanation for why the reaction comes to a halt if only two equivalents of hydride are used: The $LiAlH_xOR_y$ species which are formed in the reaction should have a decreasing reducing power with decreased hydride content, due to the electron withdrawing effects of the oxygen substituents. Therefore, not only is the amide more susceptible to reduction, but also it is more likely to be reduced by a more powerful reductant than are species **C** or **D**.

Reduction of the Allylic Double Bond. ^{1}H NMR spectra (Figure 1) and GC analysis (Figures 49−53 Supporting Information) show clearly that the allylic double bond in the allylamide **2** was attacked by $LiAlH_4$ (or a related species, $AlH_xR_y^-$ with $x + y = 4$) during the reduction to give amine **1**. However, this problem could not be overcome by reducing the amount of $LiAlH_4$ to the formally required two hydrogen equivalents, because the reduction of the amide comes to a halt (see above).

The hydride attack on the allylic double bond by the aluminum species was investigated with No-D NMR sequences of the reduction of allylbenzamide **6** (Figure 2) and several deuteration experiments (Scheme 4).

Scheme 4. Overview of Deuteration Results with Reactions Carried out in Et_2O at 22 °C



After a reaction time of about 3 h, when the first reduction step is complete, a downfield shift of the terminal allylic proton signal and the presence of a second similarly shifted signal (Figure 2a, H4*) appeared. This could indicate the coordination of the lithium aluminum hydride species to the double bond (**24**, Scheme 5). At this stage, no double bond reduction takes place, presumably because the reduction of the hemiaminal species is faster. However, this shift indicates already that the double bond

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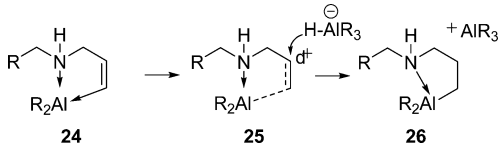
Scheme 5. Possible Mechanism of the Allylic Double Bond Attack



is capable of an interaction with the reductant. Such a coordination may lead to a polarization of the double bond and enable a second lithium aluminum species to transfer a hydride to the allylic β-position (**25**, Scheme 5). This double bond coordination was confirmed by deuteration experiments, which clearly demonstrated the selective hydride transfer to the allylic β carbon as well as continuance of the lithium aluminum species on γ position (**26**, Scheme 5). The high regioselectivity suggests that the reaction proceeds via a five membered ring as an intermediate. That this hydride transfer happened *in situ* before quenching the reaction was confirmed by proton signals at 4.62 ppm accompanied by the signals at 3.07, 2.30, and 0.54 ppm belonging to the propyl chain (Figures 59 and 60 Supporting Information).

In the case of sterically hindered amides, however, species **H** (Scheme 3) may be formed only with difficulty if the substituent R on the hemiaminal species is large. In this case, it is conceivable that hydrogen transfer to the double bond, which is comparatively unhindered, could proceed with a higher rate constant than the second reduction.

CONCLUSION

In the reduction of allylamides, $LiAlH_4$ can also reduce the double bond of the allyl group. Consequently, a mixture of inseparable products (allylamines and *n*-propylamines) may be obtained. An analysis of the reaction parameters solvent, temperature, and added hydride$^-$ equivalents was performed with a view of finding safe and generally applicable reaction conditions. From these investigations, *t*BuOMe emerged as the best solvent, at a slightly elevated reaction temperature of 35 °C. Contrary to previous reports, only three hydride equivalents are required. Under those conditions, byproduct formation can be entirely suppressed. Mechanistic NMR studies and deuteration experiments revealed that, in the unhindered case, the allylic double bond attack occurred as a sequential reaction *after* product formation and at a much slower reaction rate compared to the amide reduction

However, if the amide is sterically hindered in the α-position, the temperature will have to be increased to reflux, and longer reaction times will be required. In such cases, concomitant reduction of the allylic double bond may be observed.

In summary, the reduction of allylamides with $LiAlH_4$ is a very useful method, but great care has to be taken to analyze the reaction carefully for the occurrence of over-reduced byproducts, which may be very easy to overlook.

EXPERIMENTAL SECTION

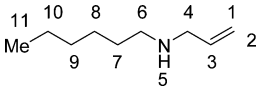
All reagents used were commercially available and used without further purification. For their purities see the Supporting Information. All solvents that were used in reactions were dried prior to use. For exact drying procedures see Supporting Information.

All syntheses were carried out using standard Schlenk techniques or in a glovebox under a dry and inert nitrogen atmosphere. Glassware and NMR tubes were dried in an oven at 200 °C for at least 2 h before use. Reaction vessels were heated under vacuum and purged with nitrogen three times before adding reagents. The container with $LiAlH_4$ was opened in the glovebox. For all reductions with $LiAlH_4$ or $LiAlD_4$, the entire reaction apparatus was assembled in the glovebox. The reaction vessels were charged with $LiAlH_4$ or $LiAlD_4$ in the glovebox and were then brought out of the glovebox and attached to the Schlenk line under vigorous exclusion of air and moisture.

All NMR spectra were recorded on a 500 or 600 MHz spectrometer (with respect to the proton resonance). ^{1}H NMR and ^{13}C NMR spectra were referenced against the solvent residual proton signals (^{1}H) or the solvent itself (^{13}C).

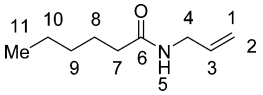
The exact assignment of the peaks was proved by ^{1}H, ^{13}C DEPT and two-dimensional NMR spectroscopy such as ^{1}H COSY, ^{13}C HSQC, or ^{1}H/^{13}C HMBC when possible.

***N*-Allylhexanamine (1).**[49]



This compound has also been synthesized by Yadav et al. using a different method.[49] To a suspension of $LiAlH_4$ (656 mg, 15.1 mmol) in dry *t*-BuOMe (60 mL) in a Schlenk flask under a nitrogen atmosphere was added *N*-allylhexanamide (3.129 g, 20.20 mmol) via a syringe. The addition was continued while the reaction mixture started to reflux. The overall addition time was 3 min. The suspension was heated and stirred at 35 °C oil bath temperature for 4 h and quenched by adding H_2O (5 mL) while cooling the mixture (ice bath). The resulting suspension was dried over $MgSO_4$ and filtered. The filter cake was washed with Et_2O (120 mL). Evaporation of solvent on a rotary evaporator and subsequent Kugelrohr distillation (70 °C; 10 mbar) yielded in 1.960 g (13.9 mmol; 69%) isolated product as colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ = 5.91 (1 H, ddt, J = 17.1, 10.2, 6.0 Hz, 3-H), 5.16 (1 H, ddt, J = 17.1, 1.7, 1.6 Hz, 1-H), 5.08 (1 H, ddt, J = 10.2, 1.7, 1.3 Hz, 2-H), 3.25 (2 H, ddd, J = 6.0, 1.6, 1.3 Hz, 4-H), 2.60 (2 H, t, J = 7.3, 7.3 Hz, 6-H), 1.48 (2 H, m, 7-H), 1.30 (6 H, m, 8-H, 9-H, 10-H), 1.10 (1 H, s, 5-H), 0.88 (3 H, t, J = 7.0 Hz, 11-H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$) δ = 137.2 (C-1), 115.8 (C-2), 52.7 (C-4), 49.7 (C-6), 32.0 (C-8/9/10), 30.3 (C-7), 27.2 (C-8/9/10), 22.8 (C-8/9/10), 14.2 (C-11) ppm. IR (ATR): 2957 (m), 2925 (s), 2872 (m), 2857 (m), 2810 (m), 1456 (m), 1124 (m), 993 (m), 915 (s), 724 (m) cm^{-1}. HRMS (EI-TOF) m/z: [M]$^+$ calcd for $C_9H_{19}N_1$ 141.1518; found 141.1512.

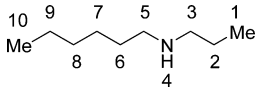
***N*-Allylhexanamide (2).**[50]



This compound has also been synthesized by Cadierno et al. using a different method.[50] In a dried flask, a solution of allylamine (**3**) (20.0 mL, 267 mmol) and triethylamine (50.0 mL, 270 mmol) in CH_2Cl_2 (250 mL) was cooled in an ice bath (<0 °C). Hexanoyl chloride (**4**) (37.0 mL, 265 mmol) was gradually added over the course of 10 min. The ice bath was removed, and the solution was allowed to warm to 20 °C. After 24 h, water (150 mL) was added, and the organic layer was separated. The aqueous layer was extracted with CH_2Cl_2 (3 × 180 mL). The combined organic extracts were washed with a 10% aqueous HCl solution (70 mL), a saturated $NaHCO_3$ solution (70 mL), and brine (70 mL). The organic phase was dried over $MgSO_4$. After removal of solvent in vacuo, the crude mixture was distilled by using a distillation bridge (oil bath: 155 °C; 7 mbar). The first fraction gave 39.016 g (95%) of the pure product. ^{1}H NMR (500 MHz, $CDCl_3$) δ = 5.83 (1 H, ddt, J = 17.1, 10.2, 5.7 Hz, 3-H), 5.58 (1 H, s, 5-H), 5.17 (1 H, ddt, J = 17.1, 1.5, 1.5 Hz, 1-H), 5.12 (1 H, ddt, J = 10.2, 1.5, 1.5 Hz, 2-H), 3.88 (1 H, dddd, J = 5.7, 5.7, 1.5, 1.5 Hz, 4-H), 2.18 (2 H, t, J = 7.7 Hz, 7-H), 1.64 (2 H, m, 8-H), 1.31 (4 H, m, 9-H, 10-H), 0.89 (3 H, t, J = 7.0 Hz, 11-H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$) δ = 173.1 (C═O), 134.6 (C-1), 116.4 (C-3), 42.0 (C-4), 36.9 (C-7), 31.6 (C-9/10), 25.6 (C-8), 22.5 (C-9/10), 14.1 (C-11) ppm. IR (ATR): 3282 (br), 3084 (w), 2958 (s), 929 (s), 2873 (m), 2860 (m), 1641 (vs), 1544 (vs), 1256 (s), 988 (s), 916 (s) cm^{-1}. HRMS (EI-TOF) m/z: [M + H]$^+$ calcd for $C_9H_{18}N_1O_1$ 156.1383; found 156.1390.

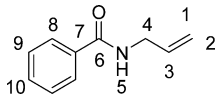
dx.doi.org/10.1021/jo501907v | J. Org. Chem. 2014, 79, 10284−10295

***N*-Propylhexanamine (5).**[51]



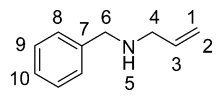
This compound has also been synthesized by Stein and Breit using a different method.[51] A solution of *N*-propylhexanamide (1.30 g, 8.27 mmol) in THF (2 mL) was added dropwise over a course of 2 min to a suspension of $LiAlH_4$ (940 mg, 24.8 mmol) in dry THF (10 mL). The suspension was heated to reflux temperature for 16 h, cooled in an ice bath, and quenched with H_2O (1 mL), 15% aqueous NaOH solution (1.5 mL), and additional H_2O (1 mL). The resulting suspension was filtered and flushed with Et_2O (10 mL), and the filtrate was dried over $MgSO_4$. After removal of the solvent on a rotary evaporator (40 °C, 10 mbar), 0.634 g (54%) of the product was obtained as colorless oil. ^{1}H NMR (600 MHz, $CDCl_3$) δ = 2.58 (4 H, m, 3-H, 5-H), 1.68 (1 H, s, 4-H), 1.51 (4 H, m, 2-H, 6-H), 1.28 (6 H, m, 7-H, 8-H, 9-H), 0.91 (3 H, t, J = 7.4 Hz, 1-H), 0.88 (3 H, t, J = 6.9 Hz, 10-H) ppm. ^{13}C NMR (151 MHz, $CDCl_3$) δ = 52.1 (C-3), 50.2 (C-5), 31.9 (C-7/8/9), 30.2 (C −6), 27.2 (C-7/8/9), 23.3 (C-2), 22.8 (C-7/8/9), 14.2 (C-10), 11.9 (C-1) ppm. IR (ATR): 2957 (m), 2927 (s), 2874 (m), 2856 (m), 2809 (m), 1458 (m), 1131 (m), 723 (m) cm^{-1}. HRMS (EI-TOF) m/z: $[M]^+$ calcd for $C_9H_{21}N_1$ 143.1674; found 143.1668.

***N*-Allylbenzamide (6).**[52]



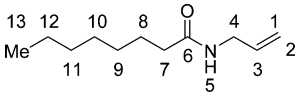
This compound has also been synthesized by Prediger et al.[52] In a dried flask under an atmosphere of nitrogen, a solution of allylamine (**3**) (9.00 mL, 120 mmol) and triethylamine (16.5 mL, 120 mmol) in CH_2Cl_2 (120 mL) was cooled in an ice bath to 0 °C. Then benzoyl chloride (17.5 mL, 150 mmol) was added over the course of 1 h. After this time, the ice bath was removed, and the solution was allowed to warm to 22 °C. After 1 h at 22 °C, water (150 mL) was added, and the organic layer was separated. The aqueous layer was extracted with CH_2Cl_2 (3 × 150 mL). The combined organic extracts were washed with brine (100 mL) and dried over Na_2SO_4 and the solvent removed. The crude product was purified by column chromatography [silica; eluent, gradient *n*-hexane/Et_2O from 90% *n*-hexane to 100% Et_2O; R_f of product = 0.25; R_f of acid chloride = 0.53 (in Et_2O/*n*-hexane = 1:1)]. After removal of the solvent in vacuo, 19.223 g (99%) of the product was obtained as colorless oil. ^{1}H NMR (600 MHz, $CDCl_3$) δ = 7.78 (2 H, m, 8-H), 7.47 (1 H, m, 10-H), 7.40 (2 H, m, 9-H), 6.55 (1 H, a br s, 5-H), 5.91 (1 H, ddt, J = 17.2, 10.3, 5.7 Hz, 3-H), 5.23 (1 H, ddt, J = 17.2, 1.7, 1.7 Hz, 1-H), 5.15 (1 H, ddt, J = 10.3, 1.6, 1.6 Hz, 2-H), 4.06 (1 H, dddd, J = 5.7, 5.7, 1.7, 1.6 Hz, 4-H) ppm. ^{13}C NMR (151 MHz, $CDCl_3$) δ = 167.5 (C-6), 134.5 (C-7), 134.3 (C-3), 131.6 (C-10), 128.6 (C-9), 127.1 (C-8), 116.6 (C-1), 42.5 (C-4) ppm. IR (ATR): 3073 (w), 3068 (w), 2913 (w), 1636 (vs), 1603 (m), 1578 (m), 1531 (vs), 1489 (s), 1294 (s), 917 (s), 691 (m) cm^{-1}. HRMS (EI-TOF) m/z: $[M]^+$ calcd for $C_{10}H_{11}NO$ 161.0841; found 161.0836.

***N*-Allylbenzenemethanamine (8).**[53]



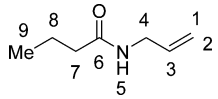
This compound has also been synthesized by Petersen et al. using a different method.[53] To a suspension of $LiAlH_4$ (657 mg, 15.1 mmol) in dry *t*-BuOMe (60 mL) in a Schlenk flask under nitrogen atmosphere was added *N*-allylbenzamide (3.241 g, 20.10 mmol) via syringe. Addition was continued while the reaction mixture started to reflux. The overall addition time was 3 min. The suspension was heated and stirred at 35 °C oil bath temperature for 4 h and quenched by adding H_2O (5 mL) while cooling the mixture (ice bath). The resulting suspension was dried over $MgSO_4$ and filtered. The filter cake was washed with Et_2O (120 mL). Evaporation of the solvent with a rotary evaporator and subsequent Kugelrohr distillation (50 °C; 2 × 10^{-1} mbar) yielded 1.910 g (13.0 mmol; 65%) of the product as colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.32 (4 H, m, 8-H, 9-H), 7.25 (1 H, m, 10-H), 5.93 (1 H, ddt, J = 17.3, 10.3, 6.0 Hz, 3-H), 5.20 (1 H, ddt, J = 17.3, 1.7, 1.4 Hz, 1-H), 5.11 (1 H, ddt, J = 10.3, 1.7, 1.4 Hz, 2-H), 3.79 (2 H, s, 6-H), 3.28 (2 H, ddd, J = 6.0, 1.4, 1.4 Hz, 4-H), 1.40 (1 H, s, 5-H)[54] ppm. ^{13}C NMR (126 MHz, $CDCl_3$) δ = 140.4 (C-7), 136.9 (C-3), 128.5 (C-9), 128.3 (C-8), 127.1 (C-10), 116.1 (C-1), 53.4 (C-6), 51.9 (C-4) ppm. IR (ATR): 3064 (w), 3028 (w), 2914 (w), 2812 (w), 1454 (m), 993 (m), 915 (s), 733 (s), 697 (vs) cm^{-1}. HRMS (EI-TOF) m/z: $[M]^+$ calcd for $C_{10}H_{13}N$ 147.1048; found 147.1043.

***N*-Allyloctanamide (9).**[55]



This compound has also been synthesized by Allen et al. using a different method.[55] In a dried flask under an atmosphere of nitrogen, a solution of allylamine (**3**) (9.00 mL, 120 mmol) in CH_2Cl_2 (120 mL) and triethylamine (16.6 mL, 120 mmol) was cooled in an ice bath. Octanoyl chloride (20.5 mL, 120 mmol) was added over the course of 1 h. The cooling bath was removed, and the reaction mixture stirred for a further 1 h. Then, water (150 mL) was added, and the organic layer was separated. The aqueous layer was extracted with CH_2Cl_2 (2 × 150 mL). The combined organic extracts were washed with brine (1 × 100 mL) and dried over Na_2SO_4. The solvent and the remaining triethylamine were removed on a rotary evaporator. The product was obtained without further purification as colorless oil that solidifies slightly below 22 °C (ambient temperature) in a yield of 19.595 g, 89%. Mp: 25 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ = 5.84 (1 H, ddt, J = 17.1, 10.2, 5.7 Hz, 3-H), 5.52 (1 H, s, 5-H), 5.18 (1 H, ddt, J = 17.1, 1.6, 1.4 Hz, 1-H), 5.12 (1 H, ddt, J = 10.2, 1.4, 1.4 Hz, 2-H), 3.88 (2 H, dddd, J = 5.7, 5.7, 1.6, 1.4 Hz, 4-H), 2.19 (2 H, t, J = 7.5 Hz, 7-H), 1.63 (2 H, tt, J = 7.5, 7.5 Hz, 8-H), 1.29 (8 H, m, 12-H, 11-H, 10-H, 9-H), 0.87 (3 H, t, J = 7.0 Hz, 13-H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$) δ = 173.1 (C-6), 134.6 (C-3), 116.4 (C-1), 42.0 (C-4), 37.0 (C-7), 31.8 (C-9/10/11/12), 29.4 (C-9/10/11/12), 29.1 (C-9/10/11/12), 25.9 (C-8), 22.7 (C-9/10/11/12), 14.2 (C-13) ppm. IR (ATR): 3297 (br), 3083 (w), 2956 (s), 2923 (m), 2856 (m), 1638 (vs), 1544 (vs), 1247 (m), 988 (m), 918 (s) cm^{-1}. HRMS (EI-TOF) m/z: $[M]^+$ calcd for $C_{11}H_{21}N_1O_1$ 183.1623; found 183.1616.

***N*-Allylbutanamide (10).**[56]



This compound has also been synthesized by Forjan et al.[56] In a dried flask under an atmosphere of nitrogen, a solution of allylamine (**3**) (9.00 mL, 6.85 g, 120 mmol) in CH_2Cl_2 (120 mL) was prepared. This solution was cooled in an ice bath, and triethylamine (16.6 mL, 120 mmol) was added. Butanoyl chloride (12.5 mL, 120 mmol) was added over the course of 1 h. After this time, the ice bath was removed, and the solution was allowed to warm to 22 °C. A colorless salt was formed. After 1 h, deionized water (150 mL) was added, and the organic layer was separated. The aqueous layer was extracted with CH_2Cl_2 (3 × 150 mL). The combined organic extracts were washed with brine (100 mL) and dried over Na_2SO_4. The solvent and the remaining triethylamine were removed on a rotary evaporator. A yellowish liquid was obtained. The liquid was again dissolved in $CHCl_3$ (250 mL) and was washed with half saturated Na_2CO_3 and dried over Na_2SO_4. The solvent was removed on a rotary evaporator to give the pure product (14.40 g; 94%) as colorless liquid. ^{1}H NMR (500 MHz, $CDCl_3$) δ = 5.84 (1 H, ddt, J = 17.2, 10.2, 5.7 Hz, 3-H), 5.55 (1 H, s, 5-H), 5.17 (1 H, ddt, J = 17.2, 1.6, 1.4 Hz, 1-H), 5.12 (1 H, ddt, J = 10.2, 1.4, 1.4 Hz, 2-H), 3.88 (2 H, dddd, J = 5.7, 5.7, 1.6, 1.4 Hz, 4-H), 2.17 (2 H, t, J = 7.4 Hz, 7-H), 1.67 (2 H, tq, J = 7.4, 7.4 Hz, 8-H), 0.95 (3 H, t, J = 7.4 Hz, 9-H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$) δ = 172.9 (C-6), 134.6 (C-3), 116.4 (C-1), 42.0 (C-4), 38.8 (C-7), 19.3 (C-8), 13.9 (C-9) ppm. IR (ATR): 3289 (br), 3078 (w), 2964 (m), 2932 (w), 2874 (w), 1640 (vs), 1545 (vs), 989 (m), 917 (m) cm^{-1}. HRMS (EI-TOF) m/z: $[M]^+$ calcd for $C_7H_{13}N_1O_1$ 127.0997; found 127.0994.

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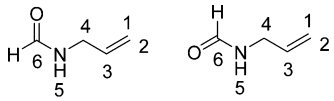
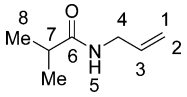
***N*-Allylformamide (11).**[52]



cisoid *transoid*

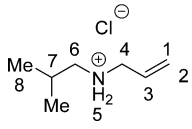
This compound has also been synthesized by Prediger et al.[52] A solution of allylamine (11.2 mL, 8.56 g, 150 mmol) in CH_2Cl_2 (50 mL) was cooled in an ice bath. To this solution, ethyl formate (10.1 mL, 18.5 g, 250 mmol) was added over the course of 10 min. After 30 min, the ice bath was removed, the solution was allowed to warm to 22 °C, and the reaction mixture was allowed to stir for 16 h. Then the solvent and residual starting materials were removed under reduced pressure (30 °C, 6 mbar). The crude product was purified by Kugelrohr distillation (70 °C, 0.5 mbar) to give a clear colorless liquid (4.745 g, 37%) in a mixture of cisoid/transoid of ca. 17/83. As the compound is relatively volatile, it is likely that prolonged application of vacuum reduces the yield substantially. ^{1}H NMR (500 MHz, $CDCl_3$), cisoid, δ = 8.09 (1H, s, 6-H), 6.80 (1H, s, 5-H) 5.82−5.68 (1H, m, 3-H), 5.15−5.08 (1H, m, 1-H), 5.05 (1H, ddd, J = 10.3, 2.9, 1.5 Hz, 2-H), 3.83−3.77 (2H, m, 4-H); transoid, δ = 7.93 (1H, d, J_{trans} = 12.0 Hz, 6-H; for C*H*-N*H* coupling constants of similar amides, see LaPlanche, L. A.; Rogers, M. T. *J. Am. Chem. Soc.* **1964**, *86*, 337), 6.44 (1H, as, 5-H), 5.82−5.68 (1H, m, 3-H), 5.18−5.11 (2H, m, 1-H, 2-H), 3.77−3.72 (2H, m, 4-H). ^{13}C NMR (126 MHz, $CDCl_3$), cisoid, δ = 161.5 (C-6), 133.5 (C-3), 116.3 (C-2), 40.4 (C-4); transoid, δ = 165.1 (C-6), 134.4 (C-3), 116.7 (C-2), 44.0 (C-4). IR (of cisoid/transoid mixture) (ATR): 3280 (br), 3048 (br), 2865 (br), 1655 (vs), 1643 (vs), 1528 (m), 1382 (s), 917 (m) cm^{-1}. HRMS (EI-TOF) m/z: $[M]^+$ calcd for $C_4H_7N_1O_1$ 85.0528; found 85.0525.

***N*-Allylisobutyramide (13).**[57]



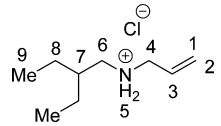
This compound has also been synthesized by Buswell et al.[57] In a dried flask under an atmosphere of nitrogen, a solution of allylamine (**3**) (9.00 mL, 120 mmol) and triethylamine (16.6 mL, 120 mmol) in CH_2Cl_2 (120 mL) was cooled in an ice bath to 0 °C. Then, isobutyryl chloride (15.7 mL, 150 mmol) was added over the course of 1 h. After this time, the ice bath was removed, and the solution was allowed to warm to 22 °C. After 1 h at 22 °C, water (150 mL) was added, and the organic layer was separated. The aqueous layer was extracted with CH_2Cl_2 (3 × 150 mL). The combined organic extracts were washed with brine (100 mL) and dried over Na_2SO_4 and the solvent removed. The crude product was purified by column chromatography (silica; eluent, gradient *n*-hexane/chloroform from 100% *n*-hexane to 100% chloroform; R_f in chloroform = 0.13). As the product contained ca. 10% of isobutyric acid, it was dissolved in chloroform (200 mL) and extracted with a solution of half-saturated Na_2CO_3 (2 × 100 mL). The organic phase was dried over Na_2SO_4 and the solvent removed to obtain the product as a colorless solid (11.565 g, 76%). Mp: 36 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ = 5.83 (1 H, ddt, J = 17.1, 10.3, 5.7 Hz, 3-H), 5.61 (1 H, s, 5-H), 5.16 (1 ddt, J = 17.1, 1.7, 1.5 Hz, 1-H), 5.12 (1 H, ddt, J = 10.3, 1.7, 1.5 Hz, 2-H), 3.87 (2 H, ddd, J = 5.7, 1.5, 1.5 Hz, 4-H), 2.38 (1 H, sept, J = 6.9 Hz, 7-H), 1.16 (6 H, d, J = 6.9 Hz, 8-H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$) δ = 177.0 (C-6), 134.5 (C-3), 116.3 (C-1), 41.9 (C-4), 35.8 (C-7), 19.8 (C-8) ppm. IR (ATR): 3289 (br), 3083 (w), 2968 (m), 2935 (w), 2877 (w), 1642 (vs), 1539 (vs), 1240 (s), 988 (m), 917 (s) cm^{-1}. HRMS (EI-TOF) m/z: $[M]^+$ calcd for $C_7H_{13}N_1O_1$ 127.0997; found 127.0995.

***N*-Allylisobutanamine Hydrochloride (14).**



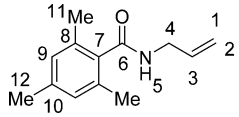
To a suspension of $LiAlH_4$ (658 mg, 15.2 mmol) in dry *t*-BuOMe (55 mL) in a Schlenk flask under a nitrogen atmosphere was added *N*-allylisobutyramide (2.554 g, 20.1 mmol) in dry *t*-BuOMe (5 mL) via syringe. Addition was continued while the reaction mixture started to reflux. The overall addition time was 3 min.. The suspension was heated and stirred at 35 °C oil bath temperature for 4 h and quenched by adding H_2O (5 mL) while cooling the mixture (ice bath). The resulting suspension was filtered, and the filter cake was washed with Et_2O (120 mL). To the filtrate was added hydrochloric acid (37%; 4 mL), and the mixture was stirred for 5 min. By evaporation of solvent on a rotary evaporator, a colorless salt was obtained which contained residual amide (~24%). A subsequent Kugelrohr distillation (60 °C; 5 × 10^{-2} mbar) yielded 1.743 g (11.6 mmol; 58%) of isolated product as colorless hygroscopic solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ = 9.56 (2 H, as, 5-H), 6.12 (1 H, ddt, J = 17.2, 10.3, 7.0 Hz, 3-H), 5.46 (2 H, m, 1-H, 2-H), 3.62 (2 H, m, 4-H), 2.71 (2 H, m, 6-H), 2.23 (1 H, tsept, J = 6.7, 6.7 Hz, 7-H), 1.09 (6 H, d, J = 6.7 Hz, 8-H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$) δ = 128.2 (C-3), 124.2 (C-1/2), 53.6 (C-6), 50.2 (C-4), 26.0 (C-7). 20.7 (C-8) ppm. IR (ATR): 2962 (br s), 2755 (br s), 2425 (br), 446 (s), 993 (s), 928 (s) cm^{-1}. HRMS (EI-TOF) m/z: $[M - HCl]^+$ calcd for $C_7H_{15}N$ 113.1205; found 113.1205.

***N*-Allyl-2-ethylbutanamine Hydrochloride (15).**



To a suspension of $LiAlH_4$ (656 mg, 15.1 mmol) in dry *t*-BuOMe (55 mL) in a Schlenk flask under nitrogen atmosphere was added *N*-allyl-2-ethylbutanamide (3.112 g, 20.04 mmol) in dry *t*-BuOMe (5 mL) via syringe. Addition was continued while the reaction mixture started to reflux. The overall addition time was 3 min. The suspension was heated and stirred at 35 °C oil bath temperature for 4 h and an additional 2 h at 55 °C. Then the reaction mixture was quenched by adding H_2O (5 mL) while cooling the mixture (ice bath). The resulting suspension was filtered, and the filter cake was washed with Et_2O (120 mL). To the filtrate was added hydrochloric acid (37%; 4 mL), and the mixture was stirred for 5 min. By evaporation of solvent on a rotary evaporator, a colorless salt was obtained which contained residual amide (~63%). A subsequent Kugelrohr distillation (80 °C; 2 × 10^{-1} mbar) yielded 874 mg (4.92 mmol; 25%) of the isolated product as colorless hygroscopic solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ = 9.50 (2 H, as, 5-H), 6.13 (1 H, ddt, J = 17.2, 10.3, 7.0 Hz, 3-H), 5.46 (2 H, m, 1-H, 2-H), 3.61 (2 H, m, 4-H), 2.78 (2 H, m, 6-H), 1.83 (1 H, m, 7-H), 1.51 (4 H, m, 8-H), 0.89 (6 H, t, J = 7.4 Hz, 9-H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$) δ = 128.3 (C-3), 124.1 (C-1/2), 50.2 (C-4), 49.0 (C-6), 37.7 (C-7), 23.3 (C-8), 10.4 (C-9) ppm. IR (ATR): 2963 (s), 2932 (m), 2877 (m), 2798 (w), 2737 (m), 1462 (m), 1449 (m), 993 (m), 925 (s) cm^{-1}. HRMS (EI-TOF) m/z: $[M]^+$ calcd for $C_9H_{19}N_1$ 141.1518; found 141.1521.

***N*-Allyl-(2,4,6-trimethyl)benzamide (16).**

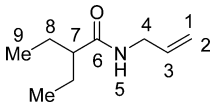


In a dried flask under an atmosphere of nitrogen, a solution of allylamine (4.30 mL, 3.28 g, 57.5 mmol) in CH_2Cl_2 (50 mL) and triethylamine (7.97 mL, 5.82 g, 57.5 mmol) was cooled in an ice bath. 2,4,6-Trimethylbenzoyl chloride (9.55 mL, 10.5 g, 57.5 mmol) was added over the course of 60 min. The cooling bath was removed and the reaction mixture stirred for a further 1 h. Then, water (150 mL) was added, and the organic layer was separated. The aqueous layer was extracted with CH_2Cl_2 (2 × 150 mL). The combined organic extracts were washed with brine (1 × 100 mL) and dried over Na_2SO_4. The solvent and the remaining triethylamine were removed on a rotary evaporator. The product was obtained without further purification as a colorless solid in a yield of 10.4538 g, 99%. Mp: 112 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ = 6.84 (as, 1H, 9-H), 5.93 (1 H, ddt, J = 16.2, 10.4, 5.8 Hz, 3-H), 5.66 (1 H, s, 5-H), 5.27 (1 H, m, 1-H), 5.18 (1 H, m, 2-H), 4.09 (1 H, dd, J = 5.8, 5.8 Hz, 4-H), 2.29 (6 H, s, 11-H), 2.27 (3H, s, 12-H). ^{13}C NMR (151 MHz, $CDCl_3$) δ = 170.5 (C-6), 138.6 (C-11), 135.0 (C-12), 134.3 (C-7/9), 134.2 (C-7/9), 128.4 (C-8), 117.0 (C-1), 42.1 (C-4), 21.2 (C-12), 19.3 (C-11). IR (ATR): 3255 (br), 3083 (w), 2977 (w), 2916 (w), 2855 (w), 1635 (s), 1613 (m), 1545 (m), 1294 (m), 917

dx.doi.org/10.1021/jo501907v | *J. Org. Chem.* 2014, 79, 10284−10295

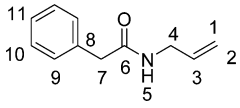
(m), 858 (m) cm^{-1}. HRMS (EI-TOF) *m/z*: $[M]^+$ calcd for $C_{13}H_{17}N_1O_1$ 203.1310; found 203.1312.

***N*-Allyl-2-ethylbutanamide (17).**



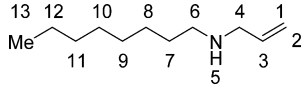
In a dried flask under an atmosphere of nitrogen was prepared a solution of allylamine (**3**) (8.98 mL, 6.85 g, 120 mmol) in CH_2Cl_2 (120 mL). This solution was cooled in an ice bath, and triethylamine (16.63 mL, 120 mmol) was added. 2-Ethylbutanoyl chloride (20.60 mL, 150 mmol) was added over the course of 1 h. After this time, the ice bath was removed, and the solution was allowed to warm to 22 °C. A colorless precipitate was formed. After 1 h, water (150 mL) was added, and the organic layer was separated. The aqueous layer was extracted with CH_2Cl_2 (3 × 150 mL). The combined organic extracts were washed with brine (100 mL) and dried over Na_2SO_4 and the solvent removed. The crude product was purified by column chromatography (silica; eluent, gradient cyclohexane/chloroform from 100% cyclohexane to 100% chloroform; R_f in chloroform = 0.25). After removing solvent, we obtained the pure product as colorless solid (18.316 g, 98%). Mp: 62 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ = 5.84 (1 H, ddt, *J* = 17.1, 10.2, 5.7 Hz, 3-H), 5.53 (1 H, s, 5-H), 5.19 (1 H, ddt, *J* = 17.1, 1.6, 1.4 Hz, 1-H), 5.12 (1 H, ddt, *J* = 10.2, 1.4, 1.3 Hz, 2-H), 3.91 (2 H, dddd, *J* = 5.7, 1.6, 1.3, 1.3, 4-H), 1.86 (1 H, m, 7-H), 1.62 (2 H, m, 8-H), 1.43 (2 H, m, 8-H), 0.87 (6 H, t, *J* = 7.5 Hz, 9-H) ppm. ^{13}C NMR (151 MHz, $CDCl_3$) δ = 175.7 (C-6), 134.8 (C-3), 116.4 (C-1), 51.8 (C-7), 41.9 (C-4), 25.9 (C-8), 12.3 (C-9) ppm. IR (ATR): 3287 (br s), 3077 (w), 2963 (s), 2928 (s), 2876 (m), 2862 (m), 1637 (s), 1538 (s), 1238 (m), 925 (s), 709 (s) cm^{-1}. HRMS (EI-TOF) *m/z*: $[M]^+$ calcd for $C_9H_{17}N_1O_1$ 155.1310; found 155.1306.

***N*-Allyl-2-phenylacetamide (19).[58]**



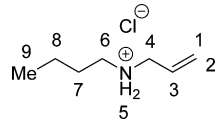
This compound has also been synthesized by Mahé et al. using a different method.[58] In a dried flask under an atmosphere of nitrogen was prepared a solution of allylamine (**3**) (8.98 mL, 120 mmol) in CH_2Cl_2 (120 mL). This solution was cooled in an ice bath, and triethylamine (16.6 mL, 120 mmol) was added. Phenylacetyl chloride (19.84 mL, 150 mmol) was added over the course of 1 h. Then the solution was allowed to warm to 22 °C. A colorless solid was formed. After 1 h, water (150 mL) was added, and the organic layer was separated. The aqueous layer was extracted with CH_2Cl_2 (3 × 150 mL). The combined organic extracts were washed with brine (100 mL) and dried over Na_2SO_4 and the solvent removed. A colorless solid was obtained. Recrystallization from Et_2O yielded in 10.38 g (49%) of product. Mp: 63 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.32 (5 H, m, 11/10/9-H), 5.76 (1 H, ddt, *J* = 17.0, 10.4, 5.5 Hz, 3-H), 5.47 (1 H, s, 5-H), 5.06 (1 H, ddt, *J* = 10.4, 1.4, 1.4 Hz, 1-H), 5.05 (1 H, ddt, *J* = 17.0, 1.6, 1.4 Hz, 2-H), 3.84 (2 H, dddd, 5.6, 1.6, 1.4, 1.4 Hz, 4-H), 3.60 (2 H, s, 7-H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$) δ = 170.9 (C-6), 135.0 (C-8), 134.2 (C-3), 129.6 (C-10/9), 129.2 (C-10/9), 127.5 (C-11), 116.2 (C-1), 44.0 (C-7), 42.0 (C-4) ppm. IR (ATR): 3236 (m), 3073 (w), 3066 (w), 3008 (w), 1625 (s), 1556 (br s), 1493 (m) cm^1. HRMS (EI-TOF) *m/z*: $[M]^+$ calcd for $C_{11}H_{13}N_1O_1$ 175.0997; found 175.0991.

***N*-Allyloctanamine (27).[59]**



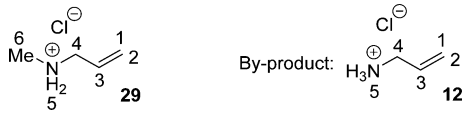
This compound has also been synthesized by Carrera et al. using a different method.[59] To a suspension of $LiAlH_4$ (657 mg, 15.1 mmol) in dry *t*-BuOMe (60 mL) in a Schlenk flask under nitrogen atmosphere was added *N*-allyloctanamide (3.678 g, 20.1 mmol) via syringe. Addition was continued while the reaction mixture started to reflux. The overall addition time was 3 min. The suspension was heated and stirred at 35 °C oil bath temperature for 4 h and quenched by adding H_2O (5 mL) while cooling the mixture (ice bath). The resulting suspension was dried over $MgSO_4$ and filtered. The filter cake was washed with Et_2O (120 mL). Evaporation of solvent and subsequent Kugelrohr distillation (40 °C; 2 × 10^{-1} mbar) yielded 2.192 g (16 mmol; 65%) of isolated product. ^{1}H NMR (500 MHz, $CDCl_3$) δ = 5.91 (1 H, ddt, *J* = 17.1, 10.2, 6.0 Hz, 3-H), 5.17 (1 H, ddt, *J* = 17.1, 1.6, 1.4 Hz, 1-H), 5.08 (1 H, ddt, *J* = 10.2, 1.7, 1.3 Hz, 2-H), 3.25 (2 H, ddd, *J* = 6.0, 1.5, 1.4 Hz, 4-H), 2.60 (2 H, t, *J* = 7.3 Hz, 6-H), 1.48 (2 H, m, 7-H), 1.30 (10 H, m, 12-H, 11-H, 10-H, 9-H, 8-H), 1.16 (1 H, s, 5-H), 0.87 (3 H, t, *J* = 7.0 Hz, 13-H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$) δ = 137.3 (C-3), 115.7 (C-1), 52.7 (C-4), 49.7 (C-6), 32.0 (C-7), 30.3 (C-12/11/10/9/8), 29.7 (C-7), 29.4 (C-12/11/10/9/8), 27.5 (C-12/11/10/9/8), 22.8 (C-12/11/10/9/8), 14.2 (C-13) ppm. IR (ATR): 2957 (m), 2924 (vs), 2855 (s), 2811 (m), 1458 (m), 1123 (m), 993 (m), 916 (s), 723 (m) cm^{-1}. HRMS (EI-TOF): $[M]^+$ calcd for $C_{11}H_{23}N$ 169.1831; found 169.1829.

***N*-Allylbutanamine Hydrochloride (28).**



To a suspension of $LiAlH_4$ (655 mg, 15.1 mmol) in dry *t*-BuOMe (60 mL) in a Schlenk flask under nitrogen atmosphere was added *N*-allylbutanamide (2.578 g, 20.3 mmol) via syringe. Addition was continued while the reaction mixture started to reflux. The overall addition time was 3 min. The suspension was heated and stirred at 35 °C oil bath temperature for 4 h and quenched by adding H_2O (5 mL) while cooling the mixture (ice bath). The resulting suspension was filtered, and the filter cake was washed with Et_2O (120 mL). To the filtrate, hydrochloric acid (37%, 4 mL) was added, and the mixture was stirred for 5 min. By evaporation of solvent on a rotary evaporator, a colorless salt was obtained which contained residual amide (~18%). A subsequent Kugelrohr distillation (60 °C; 5 × 10^{-2} mbar) yielded 2.036 g (13.6 mmol; 68%) of the isolated product as colorless hygroscopic solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ = 9.64 (2 H, s, 5-H), 6.09 (1 H, ddt, *J* = 17.2, 10.2, 6.9 Hz, 3-H), 5.47 (1 H, ddt, *J* = 17.2, 1.3, 1.0 Hz, 1-H), 5.44 (1 H, dd, *J* = 10.2, 1.0 Hz, 2-H), 3.57 (2 H, m, 4-H), 2.87 (2 H, m, 6-H), 1.84 (2 H, m, 7-H), 0.95 (3 H, t, *J* = 7.4 Hz, 9-H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$) δ = 128.0 (C-3), 124.0 (C-1), 49.6 (C-4), 46.3 (C-6), 27.9 (C-7), 20.3 (C-8), 13.6 (C-9) ppm. IR (ATR): 2962 (br s), 2935 (br s), 2877 (m), 2735 (br s), 2439 (m), 1453 (s), 992 (m), 930 (m) cm^{-1}. HRMS (EI-TOF): $[M - HCl]^+$ calcd for $C_7H_{15}N$ 113.1205; found 113.1204.

***N*-Allylmethylamine Hydrochloride (29).**



To a suspension of $LiAlH_4$ (653 mg, 15.1 mmol) in dry *t*-BuOMe (60 mL) in a Schlenk flask under a nitrogen atmosphere was added *N*-allylformamide (1.718 g, 20.2 mmol) via syringe. Addition was continued while the reaction mixture started to reflux. The overall addition time was 3 min. The suspension was heated and stirred at 35 °C oil bath temperature for 1 h and quenched by adding H_2O (5 mL) while cooling the mixture (ice bath). The resulting suspension was filtered, and the filter cake was washed with Et_2O (120 mL). To the filtrate was added hydrochloric acid (37%, 4 mL), and the mixture was stirred for 5 min. By evaporation of solvent on a rotary evaporator, a colorless high hygroscopic salt (1.826 g: 85%) was obtained which contained allylamine hydrochloride **12** (~22%). ^{1}H NMR (**29**, 500 MHz, $CDCl_3$) δ = 9.51 (2 H, s, 5-H), 6.04 (1 H, m, 3-H), 5.51 (1 H, m, 1-H), 5.49 (1 H, m, 2-H), 3.61 (2 H, m, 4-H), 2.65 (3 H, t, *J* = 7.4 Hz, 6-H) ppm. ^{1}H NMR (**12**, 500 MHz, $CDCl_3$): δ = 8.46 (3 H, s, 5-H), 6.04 (1 H, m, 3-H), 5.50 (1 H, m, 1-H), 5.38 (1 H, m, 2-H), 3.63 (2 H, m, 4-H) ppm. ^{13}C NMR (**29**, 126 MHz, $CDCl_3$) δ = 127.6 (C-3), 124.5 (C-1), 51.1 (C-4), 31.8 (C-6) ppm. ^{13}C NMR (**12**, 126 MHz, $CDCl_3$) δ = 129.5 (C-3), 121.8 (C-1), 42.1 (C-4) ppm. IR (mixture of **29** and **12**; ATR): 2951 (br s), 2711 (br s), 2425 (m), 1465 (m), 1427 (m), 995 (m), 940 (s) cm^{-1}. HRMS (**29**; EI-TOF) *m/z*: $[M - HCl]^+$ calcd for C_4H_9N

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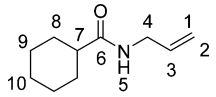
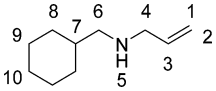
71.0735; found 71.0733. HRMS (**12**; EI-TOF) *m*/*z*: the mass of **12** was too low for detecting high resolution mass on our systems.

***N*-Allylcyclohexanamide (30).**



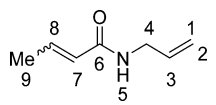
In a dried flask under an atmosphere of nitrogen was cooled a solution of allylamine (**3**) (9.0 mL, 120 mmol) in CH_2Cl_2 (120 mL) and triethylamine (16.6 mL, 120 mmol) in an ice bath. Cyclohexanoyl chloride (20.2 mL, 150 mmol) was added over the course of 1 h. The cooling bath was removed and the reaction mixture stirred for a further 1 h. Then, water (150 mL) was added, and the organic layer was separated. The aqueous layer was extracted with CH_2Cl_2 (3 × 150 mL). The combined organic extracts were washed with brine (1 × 100 mL) and dried over Na_2SO_4. The solvent and the remaining triethylamine were removed on a rotary evaporator. The crude product was purified by column chromatography (silica; eluent, gradient *n*-hexane/diethyl ether from 90% to 50% *n*-hexane; R_f in *n*-hexane/diethyl ether 1:1 = 0.15). After removal of the solvent on the rotary evaporator, the product was obtained as colorless solid (17.210 g, 82%). Mp: 74 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ = 5.83 (1 H, ddt, *J* = 17.1, 10.3, 5.7, 3-H), 5.56 (1 H, s, 5-H), 5.16 (1 H, ddt, *J* = 17.1, 1.6, 1.5, 1-H), 5.11 (1 H, ddt, *J* = 10.2, 1.5, 1.3, 2-H), 3.87 (2 H, dddd, *J* = 5.7, 5.7, 1.5, 1.3, 4-H), 2.09 (1 H, tt, *J* = 11.9, 3.4, 7-H), 1.86 (2 H, m, 10/9/8-H), 1.79 (2 H, m, 10/9/8-H), 1.66 (1 H, m, 10/9/8-H), 1.44 (1 H, m, 10/9/8-H), 1.23 (3 H, m, 10/9/8-H) ppm. ^{13}C NMR (151 MHz, $CDCl_3$) δ = 176.0 (C-6), 134.6 (C-3), 116.3 (C-1), 45.7 (C-7), 41.8 (C-4), 29.9 (C-8), 25.9 (C-10, C-9) ppm. IR (ATR): 3291 (s), 3082 (w), 2928 (vs), 2853 (s), 1638 (vs), 1547 (vs), 1255 (m), 997 (s), 919 (vs), 702 (s) cm^{-1}. HRMS (EI-TOF) *m*/*z*: $[M]^+$ calcd for $C_{10}H_{17}N_1O_1$ 167.1310; found 167.1307.

***N*-Allyl-(cyclohexylmethan)amine (31).[60]**



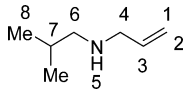
This compound has also been synthesized by Denes et al. using a different method.[60] To a suspension of $LiAlH_4$ (659 mg, 17.143 mmol) in dry *t*-BuOMe (45 mL) in a Schlenk flask under nitrogen atmosphere was added *N*-allylcyclohexanamide (3.349 g, 20 mmol) in dry *t*-BuOMe (15 mL) via syringe. Addition was continued while the reaction mixture started to reflux. The overall addition time was 3 min. The suspension was heated and stirred at 35 °C oil bath temperature for 4 h and quenched by adding H_2O (5 mL) while cooling the mixture (ice bath). The resulting suspension was dried over $MgSO_4$ and filtered. The filter cake was washed with Et_2O (120 mL). Evaporation of solvent and subsequent Kugelrohr distillation (30 °C; 2 × 10^{-1} mbar) yielded 2.413 g (15.7 mmol; 79%) of colorless oil as isolated product. ^{1}H NMR (500 MHz, $CDCl_3$) δ = 5.90 (1 H, ddt, *J* = 17.1, 10.3, 6.0 Hz, 3-H), 5.16 (1 H, ddt, *J* = 17.1, 1.7, 1.6 Hz, 1-H), 5.07 (1 H, ddt, *J* = 10.3, 1.7, 1.4 Hz, 2-H), 3.22 (2 H, ddd, *J* = 6.0, 1.6, 1.4 Hz, 4-H), 2.43 (2 H, d, *J* = 6.7 Hz, 6-H), 1.68 (5 H, m, 10/9/8-H, 5-H), 1.45 (1 H, m, 7-H), 1.19 (4 H, m, 10/9/8-H), 0.90 (2 H, m, 10/9/8-H). ^{13}C NMR (151 MHz, $CDCl_3$) δ = 137.4 (C-3), 115.7 (C-1), 56.4 (C-6), 52.9 (C-4), 38.2 (C-7), 31.6 (C-8), 26.8 (C-10/9) 26.2 (C-10/9) ppm. IR (ATR): 2920 (vs), 2852 (m), 2810 (w), 1449 (s), 1123 (w), 993 (m), 915 (s) cm^{-1}. HRMS (EI-TOF) *m*/*z*: $[M]^+$ calcd for $C_{10}H_{19}N_1$ 153.1518; found 153.1518.

***N*-Allylbut-2-enamide (32).**



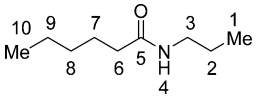
To a solution of allylamine (**3**) (8.98 mL, 6.85 g, 120 mmol) and triethylamine (16.63 mL, 120 mmol) in CH_2Cl_2 (120 mL) at 0 °C was added crotonyl chloride (14.37 mL, 150 mmol, *trans*/*cis* = 90/10) over the course of 1 h. The ice bath was removed, and the solution was allowed to stir at 22 °C for a further 1 h. Then, water (150 mL) was added, and the organic layer was separated. The aqueous layer was extracted with CH_2Cl_2 (3 × 150 mL). The combined organic extracts were washed with brine (100 mL) and dried over Na_2SO_4. The solvent and the remaining triethylamine were removed on a rotary evaporator, and the remaining material was distilled with a 10 cm Vigreux column. The product could be isolated as a colorless liquid (10.946 g, 84%, *trans*/*cis* = 98/2) that easily solidified at a steam temperature of *T* = 104 °C, pressure = 1 mbar. Because the product was obtained as a cis/trans mixture, no mp was determined. ^{1}H NMR (600 MHz, $CDCl_3$, trans product) δ = 6.84 (1 H, dq, *J* = 15.2, 6.9 Hz, 8-H), 5.85 (1 H, ddt, *J* = 17.1, 10.3, 5.7 Hz, 3-H), 5.81 (1 H, dq, *J* = 15.2, 1.7 Hz, 7-H), 5.63 (1 H, s, 5-H), 5.19 (1 H, ddt, *J* = 17.1, 1.6, 1.2 Hz, 1-H), 5.13 (1 H, ddt, *J* = 10.3, 1.4, 1.2 Hz, 2-H), 3.94 (2 H, dddd, *J* = 5.7, 5.7, 1.6, 1.2 Hz, 4-H), 1.85 (3 H, dd, *J* = 6.9, 1.7 Hz, 9-H) ppm. ^{1}H NMR (600 MHz, $CDCl_3$, cis product)[61] δ = 6.12 (dq, *J* = 11.5, 7.2 Hz, 8-H), 5.73 (dq, *J* = 11.5, 1.8 Hz, 7-H), 2.13 (dd, *J* = 7.2, 1.8 Hz, 9-H) ppm. ^{13}C NMR (151 MHz, $CDCl_3$, trans product)[62] δ = 165.9 (C-6), 140.2 (C-8), 134.4 (C-3), 125.0 (C-7), 116.5 (C-1), 42.0 (C-4), 17.8 (C-9) ppm. IR (ATR): 3281brm, 3076 (br w), 2916 (w), 1675 (s), 1632 (s), 1545 (m) cm^{-1}. HRMS (EI-TOF) *m*/*z*: $[M]^+$ calcd for $C_7H_{11}N_1O_1$ 125.0841; found 125.0841.

***N*-Allylisobutanamine (33).[63]**



This compound has also been synthesized by D'hooghe et al. using a different method.[63] To a suspension of $LiAlH_4$ (654 mg, 15.1 mmol) in dry *t*-BuOMe (55 mL) in a Schlenk flask under nitrogen atmosphere was added *N*-allylisobutyramide (2.584 g, 20.3 mmol) in dry *t*-BuOMe (5 mL) via syringe. Addition was continued while the reaction mixture started to reflux. The overall addition time was 3 min. The suspension was heated and stirred at 35 °C oil bath temperature for 4 h and quenched by adding H_2O (5 mL) while cooling the mixture (ice bath). The resulting suspension was dried over $MgSO_4$ and filtered. The filter cake was washed with Et_2O (120 mL). Evaporation of solvent on a rotary evaporator and subsequent Kugelrohr distillation (60 °C; 60 mbar) yielded 0.648 g (5.7 mmol; 29%) of isolated product as a colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ = 5.91 (1 H, ddt, *J* = 17.1, 10.3, 6.0 Hz, 3-H), 5.17 (1 ddt, *J* = 17.1, 1.7, 1.5 Hz, 1-H), 5.08 (1 H, ddt, *J* = 10.3, 1.7, 1.4 Hz, 2-H), 3.24 (2 H, ddd, *J* = 6.0, 1.5, 1.4 Hz, 4-H), 2.42 (2 H, d, *J* = 6.7 Hz, 6-H), 1.75 (1 H, tsept, *J* = 6.7, 6.7 Hz, 7-H), 1.09 (1 H, s, 5-H), 0.91 (6 H, d, *J* = 6.7 Hz, 8-H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$) δ = 137.4 (C-3), 115.7 (C-1), 57.7 (C-6), 52.8 (C-4), 28.5 (C-7), 20.3 (C-8) ppm. IR (ATR): 2955 (s), 2837 (m), 2810 (m), 1470 (m), 1449 (m), 993 (m), 917 (vs) cm^{-1}. HRMS (EI-TOF) *m*/*z*: $[M]^+$ calcd for $C_7H_{15}N$ 113.1205; found 113.1207.

***N*-Propylhexanamide (34).[64]**



This compound has also been synthesized by Zyryanov and Rudkevich using a different method.[64] In a dried flask, a solution of allylamine (**3**) (4.1 mL, 50 mmol) and triethylamine (7.3 mL, 54 mmol) in toluene (100 mL) was cooled in an ice bath (<0 °C). Hexanoyl chloride (8.0 mL, 58 mmol) was gradually added over the course of 5 min. The ice bath was removed, and the solution was allowed to warm to 18 °C. After 12 h, water (50 mL) was added, and the organic layer was separated. The aqueous layer was extracted CH_2Cl_2 (3 × 200 mL). The combined organic extracts were washed with a 10% aqueous HCl solution (30 mL), a saturated $NaHCO_3$ solution (50 mL), and brine (50 mL). The organic phase was dried over $MgSO_4$. After removal of solvent in vacuo, 8.720 g (91%) of the product was obtained as a colorless oil. ^{1}H NMR (600 MHz, $CDCl_3$) δ = 5.46 (1 H, s, 4-H), 3.21 (2 H, td, *J* = 7.3, 6.7 Hz, 3-H), 2.15 (2 H, t, *J* = 7.6 Hz, 6-H), 1.63 (2 H, tt, *J* = 7.6, 7.6 Hz, 7-H), 1.51 (2 H, tq, *J* = 7.3, 7.3 Hz, 2-H), 1.31 (4 H, m, 8-H, 9-H), 0.92 (3 H, t, *J* = 7.3 Hz, 1-H), 0.89 (3 H, t, *J* = 7.0 Hz, 10-H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$) δ = 173.3 (C-5), 41.3 (C-3), 37.0 (C-z6), 31.6 (C-8), 25.7 (C-7), 23.1 (C-2), 22.6 (C-9), 14.1 (C-10), 11.5 (C-1) ppm. IR (ATR): 3292 (br), 3084 (w), 2960 (s), 2931 (s), 2874 (m), 863 (m), 1642 (vs), 1549 (vs), 1254 (m) cm^{-1}. HRMS (EI-TOF): $[M]^+$ calcd for $C_9H_{19}N_1O_1$ 157.1467; found 157.1468.

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■ ASSOCIATED CONTENT

Supporting Information

Purities of the compounds used, drying procedures for the solvents, ^{1}H NMR and ^{13}C NMR spectra for all compounds, calculations and spectra of the $LiAlH_4$ titration, complete optimization data, and additional ^{1}H NMR spectra of the mechanistic study. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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