Ruthenium and Iron-Catalysed Decarboxylyative
N-alkylation of Cyclic α-Amino Acids with Alcohols:
Sustainable Routes to Pyrrolidine and Piperidine Derivatives

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A modular and waste-free strategy for constructing N-substituted cyclic amines via decarboxylyative N-alkylation of α-amino acids employing ruthenium- and iron-based catalysts is presented. The reported method allows the synthesis of a wide range of five- and six-membered N-alkylated heterocycles in moderate-to-excellent yields starting from predominantly proline and a broad range of benzyl alcohols, and primary and secondary aliphatic alcohols. Examples using pipecolic acid for the construction of piperidine derivatives, as well as the one-pot synthesis of α-amino nitriles, are also shown.

Introduction

Saturated azaheterocycles, especially pyrrolidine and piperidine, are ubiquitous scaffolds in biologically active compounds[1] and key building blocks in diverse areas of organic chemistry.[2] Numerous pharmaceuticals comprise five- and six-membered azaheterocyclic moieties (Figure 1). Therefore, over the past decades considerable efforts have focused on the development of novel approaches for the efficient and environmentally friendly synthesis of substituted pyrrolidines and piperidines, employing affordable and widely available substrates and sustainable catalysts.

Traditional methods for the construction of the core heterocyclic centre[3] such as the Mitsunobu[3b] and Appel-type reactions[3c] (Scheme 1a, pathway 1) or classical reductive aminations[3d] (Scheme 1a, pathway 2) face a number of limitations including the use of toxic solvents and/or reagents as well as poor atom economy.

The discovery of metal-catalysed “hydrogen borrowing” methods for the N-alkylation of amines with alcohols[4] (Scheme 1b, pathway 3) has led to cleaner synthesis of saturated azaheterocycles by judicious selection of appropriate combinations of coupling partners (e.g., benzyl amines and diols or cyclic amines with alcohols). These methods only produce water as a by-product, may employ bio-derived alcohol substrates[5, 6] and, as recently reported, can also be performed using earth-abundant metal catalysts[7–9].

An elegant catalytic strategy for the construction of various cyclic amines was recently illustrated by Darcel and co-workers (Scheme 1b, pathway 4).[10] They achieved the Fe- and Ru-catalysed reductive amination of carbonyl compounds with ω-amino fatty acids to furnish various pyrrolidines, piperidines and azepanes.

A distinctly different method for the construction of N-heterocycles involves the decarboxylyation of amino acids already containing such core moiety via coupling with carbonyl compounds (inspired by the classical Strecker degradation[11, 12] followed by a reaction of the formed azomethine ylides with various non-traditional dipolarophiles[13] (Scheme 1b, pathway 5).

A highly interesting approach for the one-pot construction of valuable N-heterocyclic scaffolds would be the combination of the hydrogen-borrowing with the decarboxylyation/azomethine ylide chemistry: this would enable the catalytic coupling of naturally abundant amino acids with widely available and potentially bio-derived alcohol substrates (Scheme 1c). In this case, the carbonyl compounds necessary for imine formation...
could be generated in situ by means of the transition-metal catalyst while the amino acids would provide the core N-heterocyclic scaffold upon decarboxylation. Surprisingly, to the best of our knowledge, the first and only example for such homogeneously catalysed decarboxylative N-alkylation of natural α-amino acids with alcohols has been reported by Zhao and co-workers, employing pentamethylcyclopentadienyl iridium dichloride imer ([Cp*IrCl$_2$])$_2$/NaHCO$_3$ as catalyst. Despite the potential of earth-abundant Fe- or Ru-based systems in diverse N-alkylation reactions, no decarboxylative N-alkylation methods have been developed yet using such catalysts. This is not surprising given the highly functionalized and potentially strongly coordinating nature of amino-acid substrates or reaction intermediates.

Recently, we have shown that base-free N-alkylation of unprotected α-amino acids with a broad range of alcohols is feasible using Shvo’s catalyst and Knölker’s complex and have introduced the Fe-based catalytic N-alkylation of amines with alcohols with a broad scope, including the construction of N-heterocyclic scaffolds. Herein, we set to establish the first decarboxylative N-alkylation methods using these Fe- and Ru-based half-sandwich complexes.

### Results and Discussion

Following our initial observations regarding the N-alkylation of natural α-amino acids with various alcohols using Shvo’s complex (C1), we first selected DL-proline (1a) and 4-methoxybenzyl alcohol (2a) as starting materials for establishing the desired decarboxylative N-alkylation methodology (Table 1). The initially selected conditions using a 1:2 molar ratio of 1a and 2a, 1 mol% C1 at 120 °C delivered excellent results. Applying these parameters, excellent (88–99%) product (3aa) yields were detected in various solvents such as cyclopentyl methyl ether (CPME), toluene, 1,4-dioxane, and tert-amyl alcohol (entries 4–7). In chloroform (entry 8), only traces of the product were observed, whereas in acetonitrile moderate yield was seen (52%, entry 9). While 1,4-dioxane furnished the highest 3aa yield, and toluene also gave excellent results. Taking into account solvent sustainability guidelines, we chose toluene as preferred solvent for further investigation; the product yield was further improved from 90% to 94% using 4 equiv. of 2a at 120 °C (entry 4 vs entry 11). Further decrease of reaction temperature to 110 °C negatively affected the product yield (entry 10). Blank reactions in the absence of catalyst (entry 1) or in the absence of alcohol (entry 2) gave no product.

#### Scheme 1

a) Classical synthetic pathways to N-substituted cyclic amines

b) Previously reported catalytic or synthetic routes to saturated azaheterocycles

c) Ruthenium and Iron-catalysed decarboxylative N-alkylation of amines with alcohols

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**Table 1.** Establishing the decarboxylative N-alkylation of DL-proline with 4-methoxybenzyl alcohol using iron- and ruthenium-based catalysts.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Alcohol [mmol]</th>
<th>Catalyst [mol%]</th>
<th>T [°C]</th>
<th>Solvent</th>
<th>Yield [%]</th>
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<tbody>
<tr>
<td>1</td>
<td>1</td>
<td>-</td>
<td>120</td>
<td>toluene</td>
<td>-</td>
</tr>
<tr>
<td>2</td>
<td>-</td>
<td>C1/1</td>
<td>120</td>
<td>toluene</td>
<td>-</td>
</tr>
<tr>
<td>3</td>
<td>1</td>
<td>C1/1</td>
<td>120</td>
<td>CF$_3$CH$_2$OH</td>
<td>96 [a]</td>
</tr>
<tr>
<td>4</td>
<td>1</td>
<td>C1/1</td>
<td>120</td>
<td>toluene</td>
<td>90</td>
</tr>
<tr>
<td>5</td>
<td>1</td>
<td>C1/1</td>
<td>120</td>
<td>tert-amyl alcohol</td>
<td>88</td>
</tr>
<tr>
<td>6</td>
<td>1</td>
<td>C1/1</td>
<td>120</td>
<td>CPME</td>
<td>89</td>
</tr>
<tr>
<td>7</td>
<td>1</td>
<td>C1/1</td>
<td>120</td>
<td>1,4-dioxane</td>
<td>99</td>
</tr>
<tr>
<td>8</td>
<td>1</td>
<td>C1/1</td>
<td>120</td>
<td>CHCl$_3$</td>
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<tr>
<td>9</td>
<td>1</td>
<td>C1/1</td>
<td>120</td>
<td>CH$_2$CN</td>
<td>52</td>
</tr>
<tr>
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<td>2</td>
<td>C1/1</td>
<td>110</td>
<td>toluene</td>
<td>81</td>
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<tr>
<td>11</td>
<td>2</td>
<td>C1/1</td>
<td>120</td>
<td>toluene</td>
<td>94</td>
</tr>
<tr>
<td>12</td>
<td>2</td>
<td>C2/4</td>
<td>120</td>
<td>toluene</td>
<td>77</td>
</tr>
<tr>
<td>13</td>
<td>2</td>
<td>C2/8</td>
<td>110</td>
<td>toluene</td>
<td>75</td>
</tr>
<tr>
<td>14[a]</td>
<td>2</td>
<td>C2/4</td>
<td>110</td>
<td>toluene</td>
<td>71</td>
</tr>
<tr>
<td>15[a]</td>
<td>2</td>
<td>C2/4</td>
<td>110</td>
<td>1,4-dioxane</td>
<td>73</td>
</tr>
<tr>
<td>16</td>
<td>2</td>
<td>C2/4</td>
<td>120</td>
<td>1,4-dioxane</td>
<td>70</td>
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</table>

[a] General reaction conditions: 0.5 mmol of 1, 1 or 2 mmol of 2, 1 mol% C1 or 4–8 mol% C2, 2 mL of solvent, 24 h, 100–120 °C, under argon.
[b] Isolated yields. [c] N-alkylated non-decarboxylated product was observed. [d] 48 h.
as expected. For comparison with our previous studies,[74] the
treaction was also conducted in trifluoroethanol, indeed result-
ing in 90 % yield of the N-alkylation product without decarbox-
ylation, presumably due to the increased acidity of the reaction
medium.

Next, we turned our attention to the Fe catalyst C2.[16] Ap-
plying C2 in the model reaction at 120 °C in toluene 77 % yield
was achieved (entry 12) within 24 h. However, further attempts
to enhance 3aa yield either by doubling the catalyst loading
to 8 mol % or by increasing the reaction time to 48 h did not
significantly influence the yield of the reaction (75 % and 71 %,
to entries 13 and 14, respectively). The lower yield achieved with
C2 compared to C1 could be attributed to a slower dehydro-
genation and/or a slower reduction step involved in the hydro-
gen-borrowing cycle (see also Scheme 3).

In further studies, the scope and limitations of the newly es-
established Ru- and Fe-catalysed decarboxylative N-alkylation
methodologies were explored. Benzyl alcohol with electron-
donating substituents such as 4-methoxybenzyl alcohol (2a)
and 4-methylbenzyl alcohol (2b) as well as bulky substituents
(2c, 2d) were successfully coupled with 1a, furnishing the cor-
responding products (3aa, 3ab, 3ac, 3ad) with excellent iso-
lated yields (86–94 %) with C1 as catalyst, whereas poorer
yields (19–77 %) were obtained when applying the Fe-based
catalyst C2 (Table 2, entries 1–4). Interestingly, piperylon alco-
hol (2e) gave excellent isolated yields (94 %) of 3ae in both
systems (entry 5). With 3-pyridine methanol (2g) and 2-thio-
ephene methanol (2h), moderate product yields were observed
with C1, while reactivity was completely blocked using 2g
with C2. The latter system appeared more compatible with 2h
(33 % 3ah with C1 vs. 45 % with C2).

When para-halide-substituted benzyl alcohols were em-
ployed, 75 % of 3ai and 90 % of 3aj were successfully isolated.
Moreover, desired products bearing deactivating functional
groups such as –CF3, –CN, –CH2COOH, and –NO2 were
formed in good-to-excellent isolated yields (65–99 %, 3ak–
3an). Considerably lower yields were observed for the above-
mentioned substrates using C2 as catalyst (14–37 %, 3ak–3an).
Selected aliphatic alcohols such as 2o and 2p reacted smooth-
ly with DL-proline, affording 3ao and 3ap in very good yields
(83–86 %), albeit only with C1 as catalyst (entries 15 and 16).

Notably, the developed methodology could be extended to
piperolic acid (1b) as well, and the target N-substituted piperi-
dines 3ba–3bn were obtained in 31 and 64 % isolated yields,
respectively, using C1. In the case of product 3ba, the Fe-
based catalyst (C2) gave a 54 % isolated yield.

Other acyclic α- and β-amino acids (glycine, DL-alanine, DL-
phenylalanine, β-alanine) as well as N-alkyl α-amino acids (N-
methyl glycine, N-isopropyl valine) were attempted to couple
with 4-methoxybenzyl alcohol (2a) under the optimized reac-
tion conditions; however, low yields were obtained in both
systems (using C1 and C2). Additionally, employing C1 as a
catalyst we examined reactions between N-methyl glycine (sar-
cosine)/N-isopropyl valine and 2a with the addition of a base
(KOtBu, KOH, K2CO3, NaHCO3) in various solvents (1,4-dioxane,
t-amy al alcohol, CPME); however, no significant improvement in
product yield could be established.

Table 2. Decarboxylative N-alkylation of amino acids with primary
alcohols.[8]

<table>
<thead>
<tr>
<th>Entry</th>
<th>Product</th>
<th>Yield [%]</th>
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<tbody>
<tr>
<td></td>
<td></td>
<td>C1</td>
</tr>
<tr>
<td>1</td>
<td>3aa</td>
<td>94</td>
</tr>
<tr>
<td>2</td>
<td>3ab</td>
<td>86</td>
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<tr>
<td>3</td>
<td>3ac</td>
<td>93</td>
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<tr>
<td>4</td>
<td>3ad</td>
<td>91</td>
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<tr>
<td>5</td>
<td>3ae</td>
<td>94</td>
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<td>6</td>
<td>3af</td>
<td>42</td>
</tr>
<tr>
<td>7</td>
<td>3ag</td>
<td>40</td>
</tr>
<tr>
<td>8</td>
<td>3ah</td>
<td>33</td>
</tr>
<tr>
<td>9</td>
<td>3ai</td>
<td>75</td>
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<td>16</td>
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<tr>
<td>17</td>
<td>3ba</td>
<td>31[8]</td>
</tr>
<tr>
<td>18</td>
<td>3bn</td>
<td>64</td>
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</table>

[a] General reaction conditions: 0.5 mmol of 1, 0.5 mmol of 2, 1 mol % C1
or 4 mol % C2, 2 mL toluene, 24 h, 120 °C, under argon. [b] Isolated yields.
[c] Yields are based on 1H NMR spectroscopy, using 1,3,5-trimethoxyben-
zeine as an internal standard.

To further expand the scope of the reaction, we turned our
attention to the use of secondary and long-chain primary ali-
phatic alcohols applying the more active Ru-based catalytic
system (Table 3). Cyclohexanol (2q) and 4-isopropylhexan-1-ol
(2r) smoothly reacted with 1a, providing good yields (57 %
and 76 %) of the corresponding products (3aq, 3ar, respective-
ly). However, no product was observed in the reaction of DL-proline with menthol (2s), presumably due to the steric bulk of the alcohol substrate. Similarly, other secondary alcohols such as 2t, 2u, and 2v furnished the desired products in reasonable yields. Interestingly, the use of cinnamyl alcohol 2w or 2x led to the formation of products 3aw and 3ax in good yields, although the double bond of 3aw was found to be reduced. Several long-chain aliphatic alcohols were also found to react with 1a and 1b, affording the corresponding products (3ay, 3by) in 54% and 55% isolated yields, respectively.

Encouraged by the above results showing a broad range of alcohols suitable for the Ru-catalysed decarboxylative N-alkylation of α-amino acids, we investigated the possibility of employing 5α-cholestan-3β-ol as substrate for the decarboxylative N-alkylation of DL-proline (Scheme 2). The corresponding product was successfully obtained in 50% isolated yield, which demonstrates the applicability of the developed methodology for the functionalization of biologically active compounds.

Next, we investigated the use of mandelonitriles (4) as unique substrates for the formation of nitriles and the possibility of accessing cyclic amino nitriles in a straightforward and one-pot approach based on mechanistic considerations present in literature.[17] Notably, the use of mandelonitrile (4a) and its derivatives 4-methylmandelonitrile (4b) and 4-chloromandelonitrile (4c) led to the formation of products 5a, 5b and 5c as well as their regioisomers 5'a, 5'b and 5'c in good combined isolated yields (71–76%) when applying both catalytic systems C1 and C2 (Table 4). A preliminary proposal for the formation of these regioisomers is provided (Supporting Information, Figure S5, Note 1). Basic DL-proline, used in slight excess in the system, is assumed to play a role in α-aminonitrile isomerization in favour of regioisomer 5 (Supporting Information, Figure S5, Note 1).[17] This is supported by the fact that 5:5' ratios followed a specific trend (Table 4) related to the nature of the substituents on the aromatic ring, where electron-withdrawing substituents would stabilize dipoles with a partial negative

<table>
<thead>
<tr>
<th>Entry</th>
<th>Product</th>
<th>Yield [%]</th>
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<tr>
<td>1</td>
<td>3aq</td>
<td>57</td>
</tr>
<tr>
<td>2</td>
<td>3ar</td>
<td>76[16]</td>
</tr>
<tr>
<td>3</td>
<td>3as</td>
<td>0</td>
</tr>
<tr>
<td>4</td>
<td>3at</td>
<td>49</td>
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<tr>
<td>5</td>
<td>3au</td>
<td>62</td>
</tr>
<tr>
<td>6</td>
<td>3av</td>
<td>42[16]</td>
</tr>
<tr>
<td>7</td>
<td>3aw</td>
<td>81[16]</td>
</tr>
<tr>
<td>8</td>
<td>3ax</td>
<td>51[16]</td>
</tr>
<tr>
<td>9</td>
<td>3ay</td>
<td>54</td>
</tr>
<tr>
<td>10</td>
<td>3by</td>
<td>55</td>
</tr>
</tbody>
</table>

Table 3. Decarboxylative N-alkylation of amino acids with secondary and long-chain alcohols.\([a]\)

\([a]\) General reaction conditions: 0.5 mmol of 1, 1 mmol of 2, 1 mol% C1, 2 mL toluene, 24 h, 120 °C, under argon. \([b]\) Isolated yields. \([c]\) Yields are based on 1H NMR spectroscopy, using 1,3,5-trimethoxybenzene as an internal standard. \([d]\) Reduced double bond in the product (note: 2 equiv. of alcohol used).

![Table 4](image)

Table 4. Construction of α-amino nitriles from mandelonitrile and its derivatives using an N-alkylation/decarboxylation strategy.\([a]\)

\([a]\) General reaction conditions: 1.1 mmol of 1a, 1 mmol of 4, 1 mol% C1 or 4 mol% C2, 2 mL toluene, 24 h, 120 °C, under argon. \([b]\) Reported value refers to combined isolated yield of both regioisomers 5 and 5'.

![Scheme 2](image)
charge predominantly in the benzylic position. Thus, regioselectivity of the reaction could be attributed to the unlike charge distribution of the differently substituted azomethine ylides.\(^{[13a]}\)

A plausible mechanism of the decarboxylative \(N\)-alkylation of \(\alpha\)-amino acids with alcohols is depicted in Scheme 3. The proposed reaction sequence is based on control experiments and 1D, 2D NMR spectroscopic investigations as well as earlier literature reports\(^{[13a, 14]}\) (further specified below). The sequence begins with the metal-catalysed dehydrogenation of an alcohol (II) to the carbonyl compound (III), which readily undergoes condensation with an amino acid (I; here, DL-proline). Condensation and water elimination results in the formation of an oxazolidin-5-one derivative (IV\(a\)), which is in equilibrium with the acyclic iminium carboxylate intermediate (IV\(a\)). The formation of oxazolidones by reaction of \(\alpha\)-amino acids with carbonyl compounds was previously extensively investigated by Grigg et al.\(^{[17]}\) and Seebach et al.\(^{[18]}\) whereas oxazolidine/iminium equilibria were proposed during mechanistic studies of proline-mediated aldol condensation reactions.\(^{[19]}\) Decarboxylation of thermally labile oxazolidin-5-one derivative (IV\(a\)) furnishes azomethine ylides (IV\(a\) and IV\(b\)) in a dipolar [3+2] cycloaddition step,\(^{[20,21]}\) as also discussed in literature for various oxazolidinone derivatives.\(^{[17b, 18]}\) As a final step, the azomethine ylides would undergo protonation and subsequent reduction by means of the metal hydride generated during the first dehydrogenation step, leading to the formation of the \(N\)-alkylated cyclic amine product (VI). The existence of a dehydrogenation step (Scheme 3, VI to IV\(a\) and IV\(b\)) through involvement of a Ru- and Ir-based transfer hydrogenation catalyst similar to C1 was previously described in literature.\(^{[16c, 17]}\)

Several control experiments were conducted to confirm the central role of the catalyst (C1) in the proposed reaction scheme. As discussed above, no reaction occurred between the alcohol and amino acid in the absence of C1 (entry 1, Table 1) and C1 did not induce decarboxylation of the \(\alpha\)-amino acid in the absence of the alcohol (entry 2, Table 1).

Next, 1D and 2D NMR spectroscopic investigations of a reaction mixture containing 4-methoxybenzyl alcohol (2\(a\)) and 1\(a\) in [D\(_6\)]toluene at 120 °C in the presence of Shvo’s catalyst (C1) were conducted to confirm several proposed reaction intermediates (Supporting Information, Figures S1–S4). These studies allowed the detection of key intermediate 4-methoxybenzaldehyde (III), and the ester (III\(b\)) as side product originating from the aldehyde (Supporting Information, Figure S2). Although we were not able to detect the oxazolidin-5-one derivative (IV\(a\)) or the acyclic iminium carboxylate species (IV\(a\)), the corresponding \(N\)-alkyl-proline (IV\(b\)) formed by hydrogenation of (IV\(a\)) via the metal hydride generated by dehydrogenation—was observed as indirect evidence (Supporting Information, Figure S3). The presence of the Ru–H species expected in the catalytic cycle was also affirmed by its typical distinct chemical shift (−9.65 ppm, Supporting Information, Figure S4).

More experiments were conducted to further elaborate on the role of intermediate IV\(b\). A direct decarboxylation pathway starting from separately synthetized benzyl-pyrrolidine-2-carboxylic acid (IV\(b\)) under the reaction conditions but in absence of C1 could be ruled out. However, excellent yield (> 99%) of the target cyclic amine (VI) was achieved starting from (IV\(b\)) in the presence of (C1), confirming the proposed hydrogenation/dehydrogenation equilibrium between IV\(a\) and IV\(b\). Indeed, C1 was previously shown to efficiently catalyse imine hydrogenation as well as the dehydrogenation of secondary or tertiary amines.\(^{[22, 23]}\) This result is particularly interesting, since, to the best of our knowledge, the decarboxylation of \(N\)-alkyl amino acids into their \(N\)-alkylamine analogues has not yet been accomplished by using a dehydrogenation catalyst.

Further, aiming to prove that the alcohol is a genuine hydrogen source, 1\(a\) was allowed to react with \(\alpha\)-tert-[D\(_2\)]benzyl alcohol (2\(f\)–d\(_2\)) under standard reaction conditions. The product distribution analysis employing \(^1\)H NMR spectroscopy (Supporting Information, Figure S6, Note 2) displayed deuterium incorporation at the 2 and 5 positions of the pyrrolidine ring as well as at the benzylic position of the desired product, which addi-
ationally supported the above-proposed mechanism (for discussion see the Supporting Information, Note 2).

Lastly, during the 1D and 2D NMR spectroscopic investigations, where significant amount of product was detected already after 1 h reaction time, it became apparent that the reaction proceeds faster than initially assumed based on our earlier studies that frequently displayed sluggish imine hydrogenation step. Therefore we have followed the evolution of detectable intermediates (III, IVb, Ru-H) and product (VI) over time (Supplementary Figure S7, Note 3). Gratifyingly, already after 2 h full conversion and excellent product yield was achieved, confirmed by an isolated yield of 96% for 1-(4-methoxybenzyl)pyrrolidine (3aa). Although certainly substrate dependent, at 120 °C the decarboxylation of the thermally labile oxazolidin-5-one derivative to the proposed azomethine ylides is expected to be rapid; hence, it appears that the proposed hydrogen transfer from the substrate alcohol to the ylides is facile as well. This presents a unique advantage of the method presented herein.

Conclusions

We have developed the decarboxylative N-alkylation of α-amino acids with alcohols applying Ru- and Fe-based catalytic systems for the synthesis of N-substituted cyclic amines. The described methods demonstrate high selectivity, wide alcohol scope and excellent functional-group tolerance, in particular regarding the Ru-based system. Although the iron-based method would require further optimization in terms of efficiency possibly by switching to alternative catalyst structures capable of borrowing hydrogen, the proof of principle presented here opens the way toward fully sustainable methodologies for the construction of saturated azaheterocycles since both the α-amino acid as well as the alcohol substrates can be obtained from renewable resources and the employed catalyst uses an earth-abundant, non-toxic metal.

Experimental Section

General procedure for the decarboxylative N-alkylation of amino acids

An oven-dried 20 mL Schlenk tube, equipped with a stirring bar, was charged with amino acid (0.5 mmol, 1 equiv.), corresponding alcohol (1 or 2 mmol, 2 or 4 equiv.), Shvo’s catalyst (C1, 0.005 mmol, 1 mol%) or Knüll’s complex (C2, 0.02 mmol, 4 mol%) and toluene (as a solvent, 2 mL). Solid materials were weighed into the Schlenk tube under air. Then the Schlenk tube was subsequently connected to an argon line and vacuum–argon treatment mixture was cooled down to room temperature, the crude reaction mixture was filtered through silica gel, eluted with ethyl acetate and solvent were charged under an argon stream. The Schlenk tube was capped, and the mixture was rapidly stirred at room temperature. The reaction mixture was cooled down to room temperature, the crude mixture was filtered through silica gel, eluted with ethyl acetate and concentrated in vacuo. The residue was purified by flash column chromatography to provide the pure amine product.

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Conflict of interest

The authors declare no conflict of interest.

Keywords: decarboxylation • iron • N-alkylation • N-heterocycles • proline


