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Transamidation of Carboxamides Catalyzed by Fe(III) and Water

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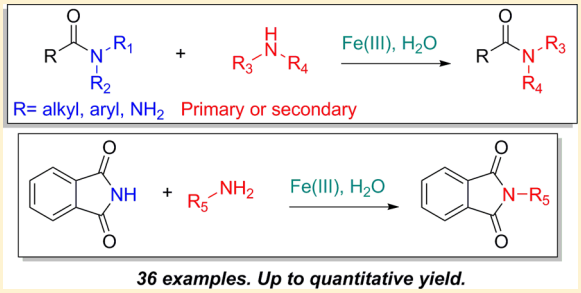
Supporting Information

ABSTRACT: The highly efficient transamidation of several primary, secondary, and tertiary amides with aliphatic and aromatic amines (primary and secondary) is described. The reaction is performed in the presence of a 5 mol % concentration of different hydrated salts of Fe(III), and the results show that the presence of water is crucial. The methodology was also applied to urea and phthalimide to demonstrate its versatility and wide substrate scope. An example of its use is an intramolecular application in the synthesis of 2,3-dihydro-5*H*-benzo[*b*]-1,4-thiazepin-4-one, which is the bicyclic core of diltiazem and structurally related drugs (Budriesi, R.; Cosimelli, B.; Ioan, P.; Carosati, E.; Ugenti, M. P.; Spisani, R. *Curr. Med. Chem.* **2007**, *14*, 279−287). A plausible mechanism that explains the role of water is proposed on the basis of experimental observations and previous mechanistic suggestions for transamidation reactions catalyzed by transition metals such as copper and aluminum. This methodology represents a significant improvement over other existing methods; it can be performed in air and with wet or technical grade solvents.



INTRODUCTION

The amide functional group is present in a vast number of naturally occurring complex structures, such as peptides, proteins, and alkaloids.[1] Furthermore, amides are extremely useful building blocks in organic synthesis, and they serve as precursors for many valuable compounds, including pharmaceuticals, agrochemicals, and organic materials.[2] Various synthetic methods to access amides are known and are well documented in the literature,[3] including the reactions of carboxylic acid derivatives (other than amides) with amines or ammonia,[4] the hydration of nitriles,[5] and the reaction of amines with aldehydes or alcohols,[6] in addition to some recognized name reactions.[7] Nevertheless, due to the poor electrophilic character of the amide carbonyl group, reactions with nucleophiles usually require strong reaction conditions and make the transamidation reaction an atypical synthetic methodology for amides.[8]

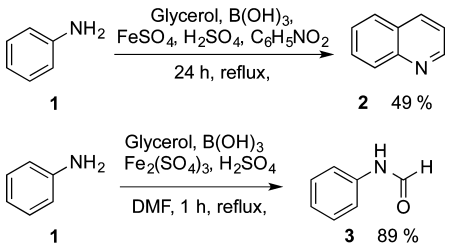
The exchange of the amine moiety of an amide is a conceptually simple but rare organic transformation, primarily due to the modest reactivity of amides. Some recent and clever examples of transamidation have been described,[9] including those using heterogeneous and homogeneous catalysis. However, even when effective, these methodologies have particular experimental issues, such as the use of expensive and waste-generating reagents and mixtures of products and the need for high temperatures and sealed tubes or stringent water- and oxygen-free conditions. During the preparation of this paper, the first Fe(III)-catalyzed transamidation reaction was published.[9n] However, the methodology is limited to the use of primary amides and primary amines, and at least one of the reagents must be a liquid to dissolve the reaction mixture; otherwise, the reagents will not be in contact with the porous solid catalyst.

Motivated by unexpected results, we present herein a highly efficient, selective, experimentally simple, and readily applicable method for the transamidation of carboxamides. In addition, this methodology can be utilized for the protection of primary amines with phthalimide and for the construction of symmetric and asymmetric ureas, making this methodology potentially applicable to the synthesis of organic catalysts.

RESULTS AND DISCUSSION

During our studies on the Skraup synthesis of quinolines, we explored different oxidizing agents to avoid the use of nitrobenzene (Scheme 1). Our first choice was $Fe_2(SO_4)_3$, as we were hoping for a combined effect from sulfate and the oxidizing agent. Curiously, after 1 h, the aniline was completely

Scheme 1. Unexpected Formylation of Aniline by Treatment with DMF



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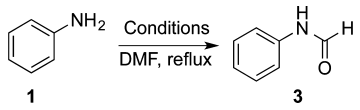
consumed, but the reaction product was identified as *N*-phenylformamide (**3**), which was obtained in 89% yield.

This fortuitous result motivated us to study the transformation carefully. The literature describes boric acid as a transamidation catalyst;[9h] thus, we decided to perform the same reaction while avoiding the use of glycerol, sulfuric acid, and iron(III) sulfate. After reflux for 3 days, only partial conversion of aniline was observed (Table 1). Consequently, we substituted the boric acid for 30 mol % iron(III) sulfate. After 8 h, we observed complete conversion, and the formylation product was obtained in 60% yield.

Table 1. Identification of the Reaction Catalyst



1 **3**

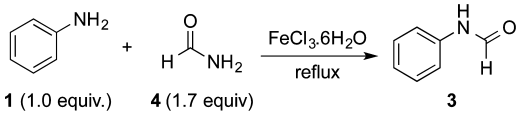
entry	conditions	time (h)	yield (%)
1	$B(OH)_3$ (0.3 equiv)	72	ND[a]
2	$Fe_2(SO_4)_3$ (0.3 equiv)	8	60

[a]The product was observed by TLC, but conversion was poor.

This preliminary result confirmed that Fe(III) is responsible for the transamidation process.[10] Nevertheless, the combination of iron(III) sulfate, $B(OH)_3$, and H_2SO_4 in glycerol was a more efficient catalytic system.

On the basis of this result, we decided to explore whether the reaction was viable with other amides used as a reagent instead of as the solvent and whether other sources of Fe(III) could be used. Accordingly, we performed a reaction between aniline and the highly reactive primary amide formamide in the presence of iron(III) chloride hexahydrate. The reaction was performed in different solvents to determine the best reaction conditions. The results summarized in Table 2 suggest that any

Table 2. Optimization of the Reaction Solvent



1 (1.0 equiv.) **4** (1.7 equiv) **3**

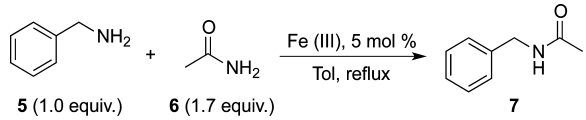
entry	solvent	time[a] (h)	yield[b] (%)
1	CH_3CN	38	97
2	THF	38	94
3	toluene	6.5	quantitative
4	*p*-xylene	12	97
5	toluene[c]	60	50
6	DMSO	18	48
7	EtOH	24	93
8	isoamyl alcohol	24	37
9	1,2-dichloroethane	60	80

[a]All these experiments were performed with 5 mol % catalyst; 2 and 1 mol % catalyst can be used as well, but the reaction time is much longer. [b]Isolated yield. [c]This reaction was performed with dry toluene and anhydrous $FeCl_3$.

Fe(III) source can be used and show that the reaction works well with primary amides. Concerning the solvent, it is clear that aromatic nonpolar solvents afforded better results in terms of reaction time. Nonetheless, if necessary (because of reagent solubility), the reaction can be conducted in polar protic solvents (entry 7), polar aprotic solvents, such as acetonitrile (entry 1), and ethers (entry 2) without losing effectiveness, but longer reaction times are necessary. The use of solvents with higher boiling points afforded low yields and mixtures of unidentified polar compounds (entries 6 and 8). Entries 3 and 5 also suggested that water plays an important role in the reaction mechanism and that its presence is imperative for complete conversion in a short reaction time. The presence of water in the first experiment (second reaction in Scheme 1) was assured by the presence of glycerol and sulfuric acid. Therefore, we decided to use hydrated Fe(III) salts and commercial toluene that was not purified.

The next step in the optimization process was to find the best source of Fe(III). Accordingly, we decided to use a less reactive amide, acetamide, and an aliphatic primary amine, benzylamine, because this is described in the literature as a more challenging transamidation reaction. As shown in Table 3,

Table 3. Identification of the Best Fe(III) Salt for the Transamidation Reaction



5 (1.0 equiv.) **6** (1.7 equiv.) **7**

entry	catalyst	time (h)	yield (%)
1	$Fe(NO_3)_3{\cdot}9H_2O$	8.5	90
2	$FeCl_3{\cdot}6H_2O$	6.5	80
3[a]	$Fe_2(SO_4)_3$	24	61
4		60	ND[b]

[a]A 30 mol % concentration of water was added to the reaction mixture. [b]The reaction product was undetectable by ^1H NMR of the crude mixture; however, it was visible by TLC analysis.

hydrated $Fe(NO_3)_3$ and $FeCl_3$ (entries 1 and 2) afforded better yields and shorter reaction times. However, when the reaction was performed with iron nitrate, the products were easily purified; thus, we decided to use hydrated $Fe(NO_3)_3$ in subsequent studies.

Transamidation and other exchange reactions are in equilibrium, and a driving force is needed to push this equilibrium toward the desired products. In all of the cases described above, amines with low boiling points or ammonia were exchanged and liberated during the reaction, and their release drove the equilibrium and allowed complete conversion of the starting material. When using amides that will result in the production of larger liquid amines, an excess of one of the reagents is expected to be necessary. The recent report of the use of Fe(III) in transamidation reported that changing the molar ratio of amide to amine from 1:1.1 to 1.1:1 resulted in a yield reduction.[9n] In our case, either an excess of amine or an excess of amide can be used without significantly affecting the yield (see Tables 4 and 5); nevertheless, greater excesses resulted in shorter reaction times. Stoichiometric amounts of reagents can only be used with highly reactive amides; otherwise, the reaction time is too long, and the yields can be poor (see Table 5, entries 1 and 6). To reduce the reaction time, we decided to use 1.7 equiv of amide and 1 equiv of amine. Although the amine is usually less expensive than the amide, due to local legislation, amides are more accessible than amines; thus, we commonly used excess amide. Control experiments under an argon atmosphere demonstrated that oxygen has no influence on the reaction time or yield and does not participate in the reaction mechanism.

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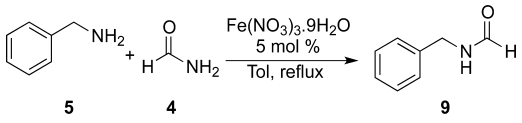
Table 4. Optimization of the Molar Ratio of Amine to Amide

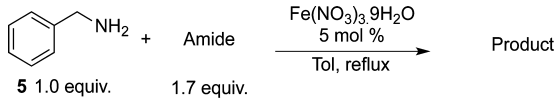


5 4 9

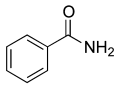
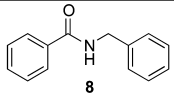
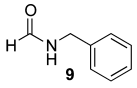
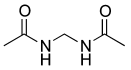
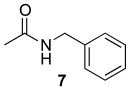
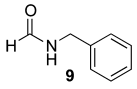
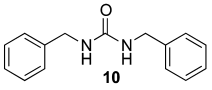
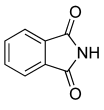
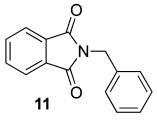
entry	amt of amine (equiv)	amt of amide (equiv)	time[a] (h)
1	1.0	1.7	2[b]
2	1.0	1.5	2.5
3	1.0	1.2	3.5
4	1.0	1.0	24[b]
5	1.2	1.0	4
6	1.5	1.0	4
7	1.7	1.0	3.5

[a]The yield was always >98% and was determined after purification and verification of purity by ^{1}H NMR. [b]A control experiment under an argon atmosphere showed no change in the reaction time or yield.

Table 5. Reaction of Benzylamine with Different Amides



5 1.0 equiv. 1.7 equiv.

Entry	Amide	Product	Time (h)	Yield (%)
1		 8	38; 48[b]	66; (53)[a]; 65[b]
2		 9	2	quant.
3		 7	24	60
4		 9	30	93
5		 10	48	63
6		 11	18; 19[b]	89; (58)[a]; 86[b]

[a]The yields shown in parentheses were obtained after 6 days of reaction of stoichiometric amounts of both reagents. [b]The yield and reaction time were obtained using 1.7 equiv of amide and 1 equiv of amine.

At this stage, we wanted to demonstrate the generality of the reaction. Thus, we used 5 mol % $Fe(NO_3)_3{\cdot}9H_2O$ (as indicated in Tables 2 and 3), 1 equiv of benzylamine, and 1.7 equiv of amide in toluene. As shown in Table 5, all amides were active under the reaction conditions. The more reactive primary amide formamide (entry 2) provides the expected formylation product in quantitative yield after 2 h; in contrast, the less reactive benzamide (entry 1) required 38 h to afford a 66% yield of isolated pure product. When using excess amine, the reaction time and yield were comparable, and the use of stoichiometric amounts of both reagents afforded slightly lower yields, presumably because there is no driving force other than evaporation of liberated amine. Secondary amides (entry 3) and the tertiary amide DMF (entry 4) were similarly active. *N,N*-Methylenediacetamide was selected because it is readily prepared in large quantities from acetamide.[11] Ureas (entry 5), which are generally much less reactive than amides, also afforded good yields among all the described methodologies for transamidation; only $Cu(AcO)_2$ is described as an active catalyst for this transformation.[9j] It is important to highlight that phthalimide (entry 6) was also active, and this result represents a useful method for the protection of primary amines, as described previously in the literature.

As shown in Tables 2 and 5, this methodology is attractive as a formylation method.[12] Table 6 presents our results from the formylation reactions of primary and secondary aromatic and aliphatic amines. Aromatic (to form compounds **3**, **13a**, and **13b**) and heteroaromatic (to form compounds **13d** and **13e**) primary amines reacted well. A special case is the reaction that used aminothiophenol as the nucleophile for the synthesis of **13c**. Surprisingly, the product obtained was benzothiazole (83% yield), suggesting that the initially formylated product readily dehydrates to produce the isolated heterocyclic compound. As expected, formylation proceeds easily with unhindered secondary amines (to form compounds **13f**, **13g**, **13h**, and **13i**); however, the use of hindered amines, such as dicyclohexylamine, occurs with slightly reduced yield (compound **13j**). The reaction to obtain **13k** showed complete selectivity for amines in the presence of alcohols. Free amino acids did not react; however, prior esterification and the use of 1 equiv of triethylamine to generate the free ester afforded the desired formylated products in excellent yields (compounds **13l** and **13m**).

Acetylation reactions using acetamide were slightly less effective in terms of reaction time, but this method is still effective for reactions with various amines, as good yields were obtained (Table 7).

According to the literature,[13] complexes between metallic centers and amidate ligands from aromatic amides are more stable than those formed with aliphatic amides; in spite of this stability, previous reports of transamidation reactions with homogeneous transition-metal catalysts afforded yields of only approximately 30%[9j] when aromatic amides were used. In our case, we obtained good yields with primary amines (Table 5, entry 1) and hydrazine (Scheme 2); unfortunately, the yields with secondary amines were exceptionally poor.

Although the generality of this method had been demonstrated, some questions remained unanswered. Could larger amides be used? Obviously, when small gaseous amines are produced, the equilibrium is easily driven. However, to achieve a more versatile and general version of this reaction, we need to demonstrate that this catalyst is also useful when larger liquid amines are exchanged. Therefore, we explored the reaction between formylpyrrolidine (**13f**) and benzylamine (**5**). To ensure that the equilibrium could be shifted, we used an excess (1.7 equiv) of amine. Gratifyingly, the desired product was isolated in good yield (Scheme 3).

On the basis of the results in Table 5, we decided to study the reaction with phthalimide as a method for protecting primary amines. This reaction is particularly useful when bifunctional amines are needed and the primary nitrogen must be protected. For example, in the case of ethanolamine, the literature reports the use of phthalic anhydride and the amine in a 1:1 molar ratio to afford yields of approximately 85%. In our case, the use of cheaper phthalimide gave the desired product **20a** in 95% yield (Table 8). This reaction also proceeds easily with branched amines (compound **20b**), nitrogen-containing

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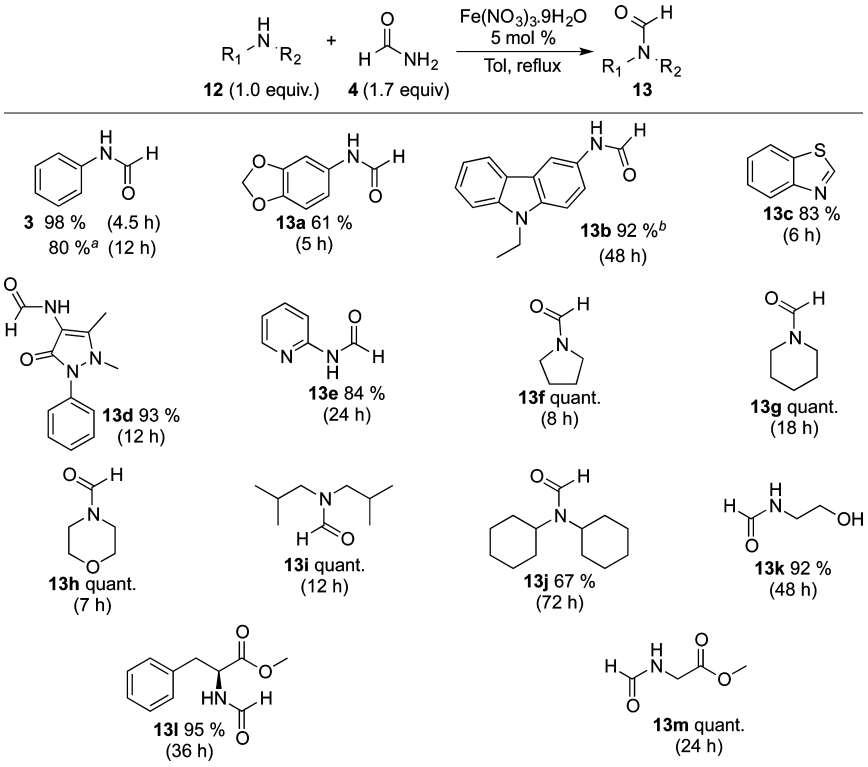
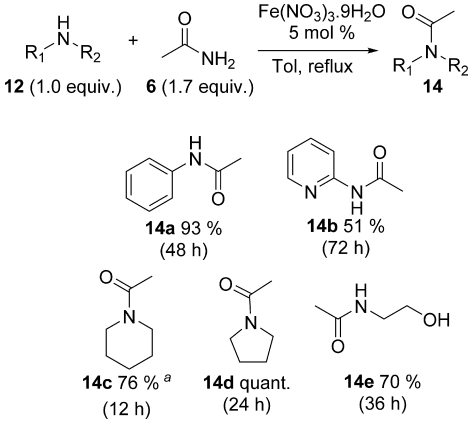
Table 6. Formylation of Amines Using Fe(III)



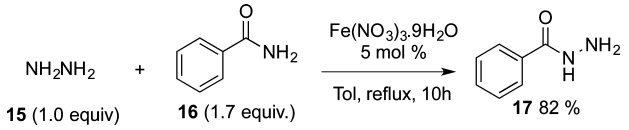
[a]DMF was used as the formylation agent. [b]This reaction was performed in CH_3CN because of poor substrate solubility in toluene.

Table 7. Acetylation Reaction of Amines with Acetamide and Fe(III)



[a]This reaction was performed in *p*-xylene.

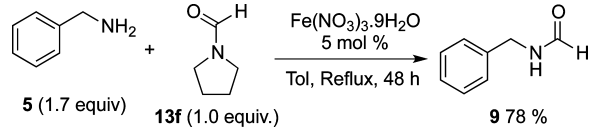
Scheme 2. Transamidation Reaction with Benzamide and Hydrazine



amines (compound **20c**), and small amino acid esters (compound **20d**).

The applicability of this reaction to the synthesis of symmetric and asymmetric ureas was explored. The reaction of urea with primary aliphatic and aromatic amines works extremely well (Table 4, entry 5 and compound **22a**) compared

Scheme 3. Transamidation Reaction with Displacement of Liquid Amines



with other transamidation methods. Curiously, the reaction of urea with aliphatic secondary amines yielded only the monosubstitution product **22b**, even with a large excess of the amine and/or large amounts of catalyst. This method was used for the synthesis of asymmetric ureas in a one-pot procedure to afford product **22c**. In this case, we used 1.3 equiv of piperidine and 1 equiv of urea; when the reaction was complete according to TLC analysis, 1 equiv of benzylamine and 5 mol % additional catalyst were added. Interestingly, asymmetric ureas can also be obtained in similar yields by reaction with primary amines first (Table 9).

Finally, we decided to utilize this reaction in an intramolecular process with 2-aminothiophenol (**23**) and acrylamide (**24**) (Scheme 4). The direct reaction of these two components afforded heterocyclic product **26** in only 11% yield. However, the open substrate (Michael addition product) **25** was isolated in 14% yield. This result shows that the Michael addition of a sulfur nucleophile is faster than the transamidation reaction. According to the literature, both nitrogen[14] and sulfur[15] can react via a Michael addition induced by Fe(III); nevertheless, no product from nitrogen addition was isolated.

Two factors were responsible for this unusual result. First, 2-aminothiophenol (**23**) is unstable under the reaction conditions; it oxidizes in the presence of air, and this oxidation is catalyzed by Fe(III). Nevertheless, we were unable to identify

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Table 8. Fe(III) as a Catalyst for the Protection of Primary Amines

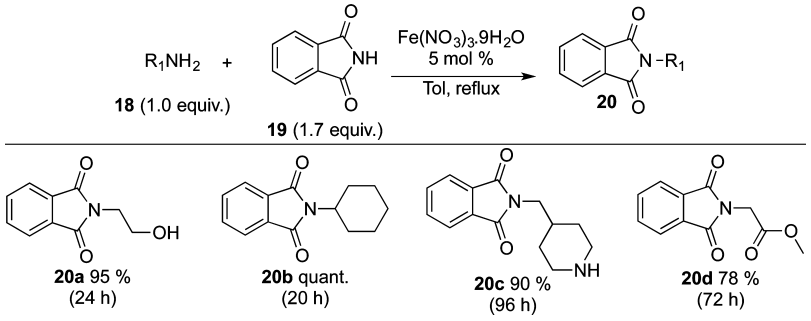
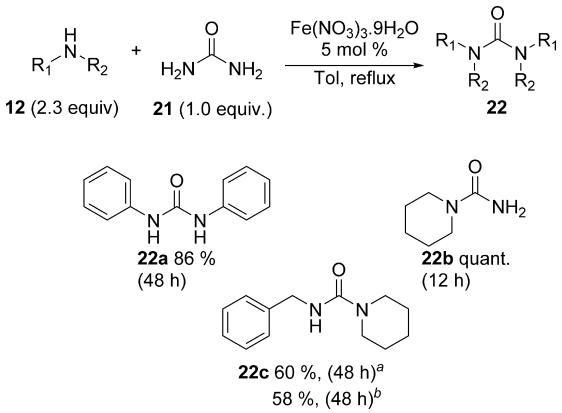
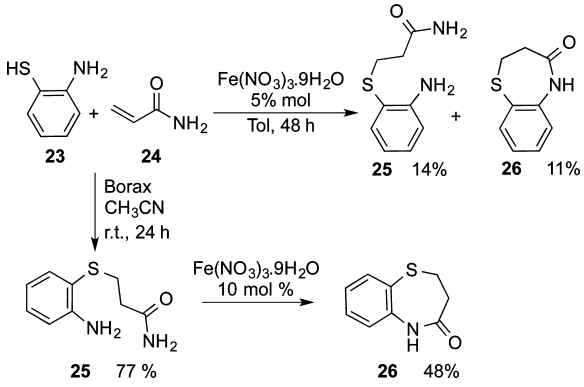


Table 9. Application to the Synthesis of Ureas



[a]The reaction procedure was initiated with 1.3 equiv of piperidine and 1.0 equiv of urea followed by 1 equiv of benzylamine and 5 mol % extra catalyst. [b]The reaction was initiated with 1.3 equiv of benzylamine and 1.0 equiv of urea followed by 1.0 equiv of piperidine and 5 mol % extra catalyst.

Scheme 4. Synthesis of 2,3-Dihydro-5*H*-benzo[*b*]-1,4-thiazepin-4-one by Intramolecular Transamidation

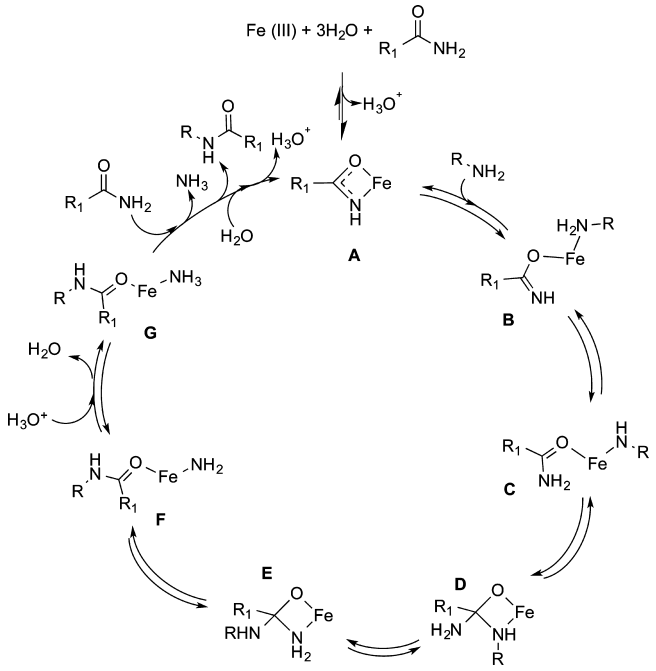


the products when we mixed the aminothiophenol with Fe(III) salts. Second, acrylamide readily polymerizes under these conditions. To address these problems and to apply our approach in an intramolecular process, we decided to use a known method[16] to induce Michael addition of the sulfur nucleophiles to acrylamide and thus avoid polymerization, and we were able to isolate the addition product **25** in 77% yield.

Through this approach, we avoided the oxidation issue. As anticipated, the transamidation reaction was successful, and the heterocyclic product **26** was isolated in 48% yield using 10 mol % Fe(III) catalyst. This constitutes a useful method with potential applications to the synthesis of diltiazem and analogues.

The reaction mechanism has not yet been elucidated; however, we can suggest a mechanistic pathway on the basis of previous studies by Stahl and co-workers.[17] This proposal is schematically represented in Scheme 5. Only one-third of the iron coordination sphere is shown for clarity.

Scheme 5. Plausible Reaction Mechanism



The first step is generation of the amidate complex **A**, which can be formed from free Fe(III) or from its hexahydrate complex. This transformation is part of an equilibrium; however, as complex **A** reacts with an amine, the equilibrium is shifted. The formation of **A** and its further reaction with an amine have been proposed in other similar mechanisms; usually, basic ligands (acetate or amines) exchange with the amide, and protonated free ligands are produced. In our case, this role is assumed by water, which generates an acidic proton that is important in a later step. The amine present in the reaction mixture cleaves the Fe−N bond to produce an unstable intermediate, **B**. This transformation is fast, and according to Stahl, it does not affect the reaction rate; proton exchange affords the more stable but reactive complex **C**. The interaction between the amine nitrogen and the carbonyl results in cyclic intermediate **D**, which is in equilibrium with its

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isomer **E**. **D** can also regenerate **C**, just as **E** can produce **F** (a **C** isomer). The previously formed **F** can abstract a proton from the hydronium ion formed during the first step, thus showing the catalytic role of water. Through the reaction of a new molecule of amide and another molecule of water, intermediate **G** produces the desired exchanged amide, the amidate complex **A**, ammonia (which is the driving force for this reaction), and the regenerated proton needed for the **F** → **G** step.

This proposed mechanism is essentially the same as that proposed by Stahl (with the exception of the participation of water), and it effectively explains the observed results with primary and secondary amides. Nevertheless, tertiary amides cannot exchange a proton (**B** → **C**), which suggests a different mechanism; Stahl and co-workers have performed additional studies and have proposed a slightly different mechanism to explain the reactivity of tertiary amides.[18]

Very recently, Sheppard suggested that ureas react by a different mechanism, most likely via isocyanate intermediates.[8]

The mechanism described in Scheme 5 also explains the low yield obtained with sulfur-containing amides. When nitrogen, oxygen, and sulfur are present in the same molecule, there is a preference to form complexes between iron and sulfur. These complexes cannot react in a transamidation process.[19]

To complement these results, we are currently applying this methodology to the synthesis of bioactive compounds, motivated by the slight toxicity of iron and the desire to elucidate the reaction mechanism.

CONCLUSION

In conclusion, we have developed a useful, simple, and general method for transamidation reactions using different sources of Fe(III) as the catalyst. The reaction is assisted by water, and no special care must be taken; the reaction can be performed in air and with technical grade or wet solvents. This reaction is also applicable to the synthesis of symmetric and asymmetric ureas and as an alternative protection method for primary amines.

We also described the application of an intramolecular transamidation process to demonstrate the versatility and the great potential of this transformation. This methodology illustrates the use of inexpensive and readily available Fe(III) salts as catalysts in organic synthesis.

EXPERIMENTAL SECTION

General Information. NMR spectra were recorded on a 300 MHz spectrometer, and the data are expressed in parts per million referenced to TMS. Data are reported as follows: δ (chemical shift), multiplicity (br, broad; s, singlet; d, doublet; t, triplet; q, quadruplet; quint, quintuplet; m, multiplet), coupling constants (J in hertz), and integration. The chemical shifts for APT experiments (75 MHz) are expressed in parts per million referenced to TMS. Infrared (IR) spectra are reported in terms of absorption frequency (ν, cm^{-1}) using KBr. Mass spectrometry (MS) was performed in electron impact (EI; 70 eV) mode. Mass spectral data are reported as m/z. High-resolution mass spectrometry (HRMS) was performed on a Q-TOF LC/MS instrument.

General Procedure for Transamidation Reaction. Amide (5.1 mmol) and amine (3.0 mmol) were dissolved or suspended in toluene (3.0 mL), $Fe(NO_3)_3{\cdot}9H_2O$ (61 mg, 0.15 mmol) was added, and the mixture was refluxed until complete conversion (by TLC) of the amine. The hot reaction mixture was filtered through a pad of Celite, concentrated, and purified by flash chromatography as indicated below.

***N*-Phenylformamide (3).** The crude mixture was purified by flash chromatography with DCM, and the product was obtained as a beige solid. Yield: 356 mg, 98%. Mp: 49−50 °C (lit.[20] 48−49 °C). The presence of two rotamers was observed in the NMR spectra in a 0.5 (M):0.5 (m) ratio. However, it is not possible to differentiate all signals corresponding to each rotamer. ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm) 8.71 (d, J = 11.3 Hz, 1H), 8.56 (br s, 1H), 8.37 (s, 1H), 7.55 (d, J = 8.6 Hz, 2H), 7.26−7.39 (m, 4H), 7.09−7.19 (m, 4H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$): δ (ppm) 162.7, 159.1, 136.8, 136.7, 129.7, 129.1, 125.3, 124.8, 120.0, 118.8. IR (ν, cm^{-1}, KBr): 3267, 3137, 1683, 1602, 1493, 1314, 755. MS (EI): 121 (100), 93 (95), 66 (80).

***N*-Benzylacetamide (7).** The crude mixture was purified by flash chromatography with DCM, and the product was obtained as white crystals. Yield: 393 mg, 88%. Mp: 61−62 °C (lit.[21] 62−64 °C). ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm) 7.21−7.39 (m, 5H), 5.94 (br s, 1H), 4.41 (d, J = 5.7 Hz, 2H), 2.01 (s, 3H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$): δ (ppm) 169.9, 138.2, 128.7, 127.8, 127.5, 43.7, 23.2. IR (ν, cm^{-1}, KBr): 3296, 3063, 3029,1644, 1554, 1452. MS (EI): 149 (62), 106 (100), 91 (34), 79 (19), 65 (9), 43 (38), 30 (12).

***N*-Benzylbenzamide (8).** The crude mixture was purified by flash chromatography with DCM/AcOEt (1:1), and the product was obtained as white crystals. Yield: 418 mg, 66%. Mp: 108−109 °C (lit.[22] 105−107 °C). ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm) 7.68−7.95 (m, 2H), 7.10−7.61 (m, 8H), 6.55 (br s, 1H), 4.63 (d, J = 5.7 Hz, 2H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$): δ (ppm) 167.3, 138.2, 134.4, 131.5, 128.7, 128.5, 127.9, 127.6, 126.9, 44.1. IR (ν, cm^{-1}, KBr): 3291, 3085, 1638, 1551, 1417, 1316, 1261, 726, 695. MS (EI): 211 (48), 105 (100), 77 (61), 51(15).

***N*-Benzylformamide (9).** The crude mixture was purified by flash chromatography with DCM/AcOEt (7:3), and the product was obtained as white crystals. Yield: 405 mg, quantitative. Mp: 61−63 °C (lit.[4d] 63−64 °C). The presence of two rotamers was observed in the NMR spectra in an 0.85 (M):0.15 (m) ratio. ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm) 8.20 (M) (s, 1H), 8.12 (m) (d, J = 11.9 Hz, 1H), 7.25−7.36 (m, 5H), 6.24 (br s, 1H), 4.44 (M) (d, J = 5.9 Hz, 2H), 4.37 (m) (d, J = 5.9 Hz, 1H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$): δ (ppm) 164.7(m), 161.1(M), 137.53, 128.84, 128.68, 127.87, 127.68, 127.57, 126.89, 45.6(m), 42.1(M). IR (ν, cm^{-1}, KBr): 3271, 3055, 2855, 2777, 1639, 1533, 1498, 1454, 1388. MS (EI): 135 (100), 91 (40), 79 (40).

***N,N′*-Dibenzylurea (10).** The crude mixture was purified by flash chromatography with pentane/AcOEt (9:1), and the product was obtained as white crystals. Yield: 454 mg, 63%. Mp: 170 °C (lit.[23] 170−171 °C). ^{1}H NMR (300 MHz, DMSO): δ (ppm) 7.02−7.51 (m, 10H), 6.45 (t, J = 5.9 Hz, 2H), 4.25 (d, J = 6.0 Hz, 4H). ^{13}C{^{1}H} NMR (75 MHz, DMSO): δ (ppm) 158.5, 141.4, 128.7, 127.4, 127.0, 43.4. IR (ν, cm^{-1}, KBr): 3321, 3030, 2922, 1626, 1574, 1453, 1258, 695. HRMS: calcd for $C_{15}H_{17}N_2O$, 241.1341; found, 241.1335.

2-Benzylisoindoline-1,3-dione (11). The crude mixture was purified by flash chromatography with DCM, and the product was obtained as a yellow solid. Yield: 633 mg, 89%. Mp: 115 °C (lit.[24] 115−116 °C). ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm) 7.60−7.92 (m, 4H), 7.07−7.59 (m, 5H), 4.85 (s, 2H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$): δ (ppm) 168.0, 136.3, 133.9, 132.1, 128.6, 127.8, 123.3, 41.6. IR (ν, cm^{-1}, KBr): 1772, 1702, 1611, 1424, 1393, 1359, 1323, 953. MS (EI): 237 (100), 130 (12), 104 (70), 91 (15).

***N*-(Benzo[1,3]dioxol-5-yl)formamide (13a).** The crude mixture was purified by flash chromatography with DCM, and the product was obtained as a light purple solid. Yield: 302 mg, 61%. Mp: 89−90 °C (lit.[25] 91−94 °C). The presence of two rotamers was observed in the NMR spectra in a 0.5 (M):0.5 (m) ratio. ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm) 8.49 (m) (d, J = 11.4 Hz, 1H), 8.31(M) (d, J = 1.6 Hz, 1H), 7.68 (m) (br s, 1H), 7.24 (M) (d, J = 2.1 Hz, 1H), 6.48−6.89(m, 6H), 5.99 (s, 2H), 5.96 (s, 2H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$): δ (ppm) 162.8, 158.7, 148.6, 147.8, 145.7, 144.7, 130.9, 130.6, 113.3, 113.1, 108.7, 108.1, 102.8, 102.2, 101.7, 101.4. IR (ν, cm^{-1}, KBr): 3068, 2972, 2902, 2780, 1737, 1653, 1511, 1486. HRMS: calcd for $C_8H_8NO_3$, 166.0504; found, 166.0494.

***N*-(9-Ethyl-9*H*-carbazol-3-yl)formamide (13b).** The crude mixture was purified by flash chromatography with DCM/AcOEt (8:2), and the product was obtained as white crystals. Yield: 657 mg, 92%. Mp: 149−150 °C (lit.[26] 148 °C). The presence of two rotamers was observed in the NMR spectra; however, it is not possible to

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differentiate all the signals corresponding to each isomer. ^{1}H NMR (300 MHz, DMSO): δ (ppm) 9.99−10.33 (m, 1H), 8.74 (d, J = 11.1 Hz, 1H), 8.26−8.57 (m, 1H), 7.93−8.17 (m, 1H), 7.47−7.78 (m, 3H), 7.12−7.50 (m, 2H), 4.41 (d, J = 7.1 Hz, 2H), 1.29 (t, J = 7.0 Hz, 3H). ^{13}C{^{1}H} NMR (75 MHz, DMSO): δ (ppm) 163.5, 159.6, 140.5, 140.5, 137.2, 136.8, 130.8, 130.6, 126.5, 126.3, 123.0, 122.4, 122.4, 122.3, 121.0, 120.7, 119.0, 118.7, 111.6, 110.7, 110.2, 109.6, 37.4, 14.1. IR (ν, cm^{-1}, KBr): 3240, 3049, 2967, 2872, 1654, 1541, 1474. HRMS: calcd for $C_{15}H_{15}N_2O$, 239.1184; found, 239.1177.

Benzothiazole (13c). The crude mixture was purified by flash chromatography with DCM/cyclohexane (1:1), and the product was obtained as a brown liquid. Yield: 336 mg, 83%. ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm) 9.00 (s, 1H), 8.15 (d, J = 8.2 Hz, 1H), 7.92−8.01 (m, 1H), 7.30−7.60 (m, 2H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$): δ (ppm) 159.3, 153.2, 133.7, 126.1, 125.5, 123.6, 121.9. IR (ν, cm^{-1}, KBr): 3060, 1555, 1471, 1423, 1315, 1291, 1266, 873, 758, 728. HRMS: calcd for C_7H_6NS, 136.0220; found, 136.0217.

***N*-Formyl-4-aminoantipyrine (13d).** The crude mixture was purified by flash chromatography with DCM, and the product was obtained as a beige solid. Yield: 644 mg, 93%. Mp: 188−190 °C (lit.[27] 192−194 °C). The presence of two rotamers was observed in the NMR spectra in an 0.85 (M):0.15 (m) ratio. ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm) 9.21 (s, 1H), 8.47 (m) (d, J = 11.4 Hz, 1H), 8.23 (M) (d, J = 1.2 Hz, 1H), 7.27−7.50 (m, 5H), 3.10 (s, 3H), 2.25 (s, 3H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$): δ (ppm) 160.5, 149.8, 134.2, 129.3, 127.4, 127.1, 124.7, 124.2, 107.0, 36.1, 35.7, 12.1. IR (ν, cm^{-1}, KBr): 3180, 3111, 3055, 2934, 2877, 1688, 1644, 1590. HRMS: calcd for $C_{12}H_{14}N_3O_2$, 232.1086; found, 232.1085.

***N*-(Pyridin-2-yl)formamide (13e).** The crude mixture was purified by flash chromatography with DCM/AcOEt (9:1), and the product was obtained as a white solid. Yield: 307 mg, 84%. Mp: 75−76 °C (lit.[28] 75−76 °C). The presence of two rotamers was observed in the NMR spectra in a 0.6 (M):0.4 (m) ratio. ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm) 9.97 (m) (br s, 1H), 9.77 (M) (br s, 1H), 9.33 (m) (d, J = 10.5 Hz, 1H), 8.53(M) (s, 1H), 8.30 (dd, 6.6 Hz, 1H), 7.56−7.88 (m, 1H), 7.09 (td, 1H), 6.94(m) (d, J = 8.2 Hz, 1H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$): δ (ppm) 162.9, 159.5, 151.0, 150.9, 148.5, 147.4, 138.8, 138.7, 120.2, 119.8, 115.1, 110.5. IR (ν, cm^{-1}, KBr): 3189. 3081, 2987, 1711, 1596, 1551, 1499. MS (EI): 122 (30), 94 (100), 67 (90).

Pyrrolidine-1-carbaldehyde (13f). The crude mixture was purified by flash chromatography with DCM/AcOEt (8:2), and the product was obtained as a yellow oil. Yield: 297 mg, quantitative. ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm) 8.27 (s, 1H), 3.43−3.51 (m, 4H), 1.91−1.93 (m, 4H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$): δ (ppm) 160.9, 46.0, 43.1, 24.9, 24.2. IR (ν, cm^{-1}, KBr): 2974, 2881, 1656, 1429, 1388, 1334. MS (EI): 99 (88), 71 (65), 56 (0,5), 43 (100).

Piperidine-1-carbaldehyde (13g). The crude mixture was purified by flash chromatography with DCM/AcOEt (9:1), and the product was obtained as a pale yellow oil. Yield: 339 mg, quantitative. ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm) 8.00 (s, 1H), 3.48 (t, J = 9 Hz, 2H), 3.31 (t, J = 12 Hz, 2H), 1.51−1.73 (m, 6H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$): δ (ppm) 160.8, 46.8, 40.6, 26.5, 25.0, 24.6. IR (ν, cm^{-1}, KBr): 2941, 2861, 1738, 1675, 1444, 1373, 1242. MS (EI): 113 (100), 98 (35), 84 (53) 70 (32), 56 (77), 42 (62).

Morpholine-4-carbaldehyde (13h). The crude mixture was purified by flash chromatography with DCM/AcOEt (1:1), and the product was obtained as a yellow oil. Yield: 345 mg, quantitative. ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm) 8.07 (s, 1H), 3.64−3.72 (m, 4H), 3.58 (t, J = 9 Hz, 2H), 3.40 (t, J = 9 Hz, 2H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$): δ (ppm) 160.8, 67.2, 66.4, 45.8, 40.6. IR (ν, cm^{-1}, KBr): 2979, 2924, 2863, 1655, 1442,1399, 1363, 1301, 1272, 1232, 1188, 1111, 1069, 1006, 855, 811. MS (EI): 115 (99), 100 (74), 86 (46), 72 (33), 56 (92), 42 (100).

***N*,*N*-Diisobutylformamide (13i).** The crude mixture was purified by flash chromatography with DCM, and the product was obtained as a yellow oil. Yield: 471 mg, quantitative. ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm) 8.07 (s, 1H), 3.13 (d, J = 7.6 Hz, 2H), 2.99 (d, J = 7.4 Hz, 2H), 1.64−2.19 (m, 2H), 0.89 (d, J = 6.7 Hz, 12H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$): δ (ppm) 163.3, 55.4, 49.4, 26.4, 26.1, 20.0, 19.8. IR (ν, cm^{-1}, KBr): 2960, 2872, 2359, 1672, 1468, 1468, 1432, 1389. MS (EI:) 157 (17), 114 (100), 102 (8), 86 (14), 72 (13).

***N*,*N*-Dicyclohexylformamide (13j).** The crude mixture was purified by flash chromatography with DCM/AcOEt (1:1), and the product was obtained as white crystals. Yield: 420 mg, 67%. Mp: 60−62 °C (lit.[29] 61 °C). ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm) 8.34 (s, 1H), 3.78−4.10 (m, 1H), 3.00−3.11 (m, 1H), 0.80−2.03 (m, 20H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$): δ (ppm) 161.6, 54.9, 52.3, 34.6, 30.4, 26.2, 25.8, 25.3, 25.2. IR (ν, cm^{-1}, KBr): 2931, 2852, 2666, 1661, 1446, 1422, 1379, 1292, 1231. MS (EI): 209 (24), 166 (20), 128 (100).

***N*-(2-Hydroxyethyl)formamide (13k).** The crude mixture was purified by flash chromatography with DCM/MeOH (9:1), and the product was obtained as a pale yellow oil. Yield: 246 mg, 92%. ^{1}H NMR (300 MHz, DMSO): δ (ppm) 8.00 (s. 1H), 4.71 (t, J = 5.4 Hz, 1H), 3.36−3.43 (m, 2H), 3.09−3.17 (m, 2H). ^{13}C{^{1}H} NMR (75 MHz, DMSO): δ (ppm) 161.6, 60.1, 40.5. IR (ν, cm^{-1}, KBr) 3380, 2888, 1666, 1538, 1389. MS (EI) [M − OH]:71 (56), 58 (70), 43(52), 30 (100).

***N*-Formyl-(*S*)-phenylalanine Methyl Ester (13l).** The crude mixture was purified by flash chromatography with DCM/MeOH (9:1), and the product was obtained as a viscous oil. Yield: 590 mg, 95%. ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm) 8.17 (s, 1H), 7.09−7.33(m, 5H), 6.11 (s, 1H), 4.94−5.01 (m, 1H), 3.75 (s, 3H), 3.16 (t, J = 5.9 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ (ppm) 172.0, 161.3, 136.0, 129.8, 129.2, 127.8, 53.0, 52.3, 38.3. IR (ν, cm^{-1}, KBr): 3301, 3030, 2953, 2960, 2870, 1744, 1668, 1543. MS (EI) [M − NHCOH]: 162 (17), 91 (20), 44 (18). $[\alpha]_D^{18}$ = 89.14 (c = 1.1).

Methyl Formylglycinate (13m). The crude mixture was purified by flash chromatography with DCM/MeOH (9:1), and the product was obtained as a colorless oil. Yield: 351 mg, quantitative. ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm) 7.28 (s, 1H), 4.11 (d, J = 5.3 Hz, 2H), 3.79 (s, 3H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$): δ (ppm) 170.0, 161.1, 52.5, 39.8. IR (ν, cm^{-1}, KBr): 3424, 2917, 2849, 1741, 1688, 1452, 1442, 1391, 1312, 1226, 1051. MS (EI) [M − CO]: 89 (22), 58 (65), 30 (100).

***N*-Phenylacetamide (14a).** The crude mixture was purified by flash chromatography with DCM, the product was obtained as white crystals. Yield: 377 mg, 93%. Mp: 112−113 °C (lit.[30] 112−114 °C). ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm) 7.51 (s, 1H), 7.49−7.50 (m, 2H), 7.25−7.30 (m, 2H), 7.10 (m, 1H), 2.16 (s, 3H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$): δ (ppm) 168.5, 137.9, 128.9, 124.3, 119.9, 24.5. IR (ν, cm^{-1}, KBr): 3293, 3259, 3194, 3135, 3059, 1663, 1598, 1556, 1508. MS (EI): 135 (26), 93(100), 43 (22).

***N*-Pyridin-2-ylacetamide (14b).** The crude mixture was purified by flash chromatography with DCM/AcOEt (7:3), and the product was obtained as a beige crystals. Yield: 208 mg, 51%. Mp: 73−75 °C (lit.[31] 73−74 °C). ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm) 8.91 (br s, 1H), 8.10−8.36 (m, 2H), 7.65−7.77 (m, 1H), 7.05 (m, 1H), 2.21 (s, 3H). ^{13}C{^{1}H}NMR (75 MHz, $CDCl_3$): δ (ppm) 168.9, 151.6, 147.5, 138.5, 119.7, 114.2, 24.6. IR (ν, cm^{-1}, KBr): 3191, 3112, 3007, 1692, 1600, 1579, 1535. MS (EI): 136 (17), 94 (100), 78 (7), 67 (71), 43 (36), 39 (14).

***N*-Acetylpiperidine (14c).** The crude mixture was purified by flash chromatography with DCM/AcOEt (1:1), and the product was obtained as a pale yellow liquid. Yield: 290 mg, 76%. ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm) 3.53−3.56 (m, 2H), 3.37−3.41 (m, 2H), 2.08 (s, 3H), 1.25−1.64 (m, 6H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$): δ (ppm) 168.8, 47.4, 42.5, 26.4, 25.5, 24.4, 21.4. IR (ν, cm^{-1}, KBr) 3458, 2935, 2856, 1625, 1445, 1268. MS (EI) 127 (50), 84 (75), 70 (35), 56 (47), 43 (68), 32 (100).

***N*-Acetylpyrrolidine (14d).** The crude mixture was purified by flash chromatography with AcOEt. and the product was obtained as a yellow oil. Yield: 339 mg, quantitative. ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm) 3.40−3.48 (m, 4H), 2.05 (s, 3H), 1.84−1.97 (m, 4H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$): δ (ppm) 172.9, 47.3, 45.5, 26.0, 24.5, 22.4. IR (ν, cm^{-1}, KBr): 3421, 1663, 1609, 1476. MS (EI): 113 (13), 70 (22), 43 (40), 32 (100).

***N*-(2-Hydroxyethyl)acetamide (14e).** The crude mixture was purified by flash chromatography with DCM/AcOEt (1:1), and the

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product was obtained as a yellow oil. Yield: 216 mg, 70%. ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm) 6.42 (br s, 1H), 3.63−3.87 (m, 2H), 3.23−3.56 (m, 2H), 2.02 (s, 3H). $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$): δ (ppm) 171.5, 61.9, 42.4, 23.1. IR (ν, cm^{-1}, KBr): 3317, 2942, 2883, 1632, 1565, 1433.

Benzoic Acid Hydrazide (17). The crude mixture was purified by flash chromatography with DCM/AcOEt (4:6), and the product was obtained as a white solid. Yield: 335 mg, 82%. Mp: 115−117 °C (lit.[32] 112−116 °C). ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm) 7.08−8.12 (m, 5H), 4.11 (br s, 2H). $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$): δ (ppm) 168.7, 132.6, 131.9, 128.7, 126.9. IR (ν, cm^{-1}, KBr): 3299, 3220, 3022, 2875, 1661, 1616, 1564, 1486, 1446. HRMS: calcd for $C_7H_9N_2O$: 137.0715; found, 137.0707.

***N*-(2-Hydroxyethyl)phthalimide (20a).** The crude mixture was purified by flash chromatography with DCM/AcOEt (9:1), and the product was obtained as white crystals. Yield: 544 mg, 95%. Mp: 128−129 °C (lit.[33] 126−127 °C). ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm) 7.79 (m, 4H), 3.90 (s, 4H), 2.40 (s, 1H). $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$): δ (ppm) 168.8, 134.1, 132.0, 123.4, 61.0, 40.8. IR (ν, cm^{-1}, KBr): 3472, 2982, 2952, 1767, 1692, 1606. MS (EI): 160 (100), 148 (50), 133 (28), 117 (7), 104 (28), 77 (39), 50 (22), 32 (28).

***N*-Cyclohexylphthalimide (20b).** The crude mixture was purified by flash chromatography with DCM/cyclohexane (8:2), and the product was obtained as white crystals. Yield: 687 mg, quantitative. Mp: 171−173 °C (lit.[34] 170−172 °C). ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm) 7.55−7.95 (m, 4H), 4.06−4.17 (m, 1H), 2.18−2.24(m, 2H), 1.59−1.89(m, 4H), 1.25−1.41 (m, 4H). $^{13}C\{^1H\}$NMR (75 MHz, $CDCl_3$): δ (ppm) 168.5, 133.7, 132.1, 123.0, 50.9, 29.9, 26.0, 25.1. IR (ν, cm^{-1}, KBr): 3452, 2927, 2855, 1767, 1705, 1612. MS (EI): 229 (26), 186 (26), 160 (8), 148 (100), 130 (46), 104 (16), 76 (21).

4-(Phthalimidomethyl)piperidine (20c). The crude mixture was purified by flash chromatography with DCM/MeOH (9:1), and the product was obtained as a yellow beige solid. Yield: 659 mg, 90%. Mp: 136 °C. ^{1}H NMR (300 MHz, DMSO): δ (ppm) 8.19 (s, 1H), 7.87 (d, J = 3.3 Hz, 4H), 3.48 (d, J = 6.8 Hz, 2H), 3.11−3.29 (m, 2H), 2.78 (t, J = 11.9 Hz, 2H), 1.96 (s, 1H), 1.77 (d, J = 13.1 Hz, 2H), 1.40 (dd, J = 23.1, 11.3 Hz, 2H). $^{13}C\{^1H\}$ NMR (75 MHz, DMSO): δ (ppm) 169.4, 135.8, 132.8, 124.4, 43.8, 43.4, 34.1, 27.4. IR (ν, cm^{-1}, KBr): 3356, 3013, 2939, 2856, 2766, 1770, 1712, 1606, 1466, 1427, 1398, 1366. HRMS: calcd for $C_{14}H_{17}N_2O_2$, 245.1290; found, 245.1281.

Methyl Phthalylglycinate (20d). The crude mixture was purified by flash chromatography with DCM/AcOEt (1:1), and the product was obtained as white crystals. Yield: 512 mg, 78%. Mp: 113−115 °C (lit.[24] 111−112 °C). ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm) 7.74−7.91 (m, 4H), 4.46 (s, 2H), 3.78 (s, 3H). $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$): δ (ppm) 167.7, 167.4, 134.2, 132.0, 123.6, 52.7, 38.7. IR (ν, cm^{-1}, KBr): 2923, 1773, 1750, 1720, 1610, 1559. MS (EI): 219 (8), 160 (100).

1,3-Diphenylurea (22a). The crude mixture was purified by flash chromatography with DCM, and the product was obtained as a white solid. Yield: 547 mg, 86%. Mp: 247−248 °C (lit.[35] 244−246 °C). ^{1}H NMR (300 MHz, DMSO): δ (ppm) 8.66 (s, 2H), 7.45 (d, J = 7.6 Hz, 4H), 7.28 (t, J = 7.9 Hz, 4H), 6.97 (t, J = 7.3 Hz, 2H). $^{13}C\{^1H\}$ NMR (75 MHz, DMSO): δ (ppm) 153.0, 140.2, 129.2, 122.3, 118,6. IR (ν, cm^{-1}, KBr): 3326, 3134, 1648, 1594, 1553, 1497, 1447. HRMS: calcd for $C_{13}H_{13}N_2O$, 213.1028; found, 213.1027.

Piperidine-1-carboxylic Acid Amide (22b). The crude mixture was purified by flash chromatography with AcOEt, and the product was obtained as white crystals. Yield: 384 mg, quantitative. Mp: 97−98 °C (lit.[36] 97−99 °C). ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm) 4.93 (s, 2H), 3.32−3.16 (m, 4H), 1.56−1.59 (m, 6H). $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$): δ (ppm) 158.6, 45.0, 25.5, 24.2. IR (ν, cm^{-1}, KBr): 3395, 3204, 2925, 2852, 1663, 1602, 1495, 1437. MS (EI): 128 (20), 113 (10), 84 (30), 70 (15), 56 (27), 44 (58), 32 (100).

***N*-Benzylpiperidine-1-carboxamide (22c).** The crude mixture was purified by flash chromatography with DCM/cyclohexane (1:1), and the product was obtained as white crystals. Yield: 392 mg, 60%. Mp: 102−104 °C (lit.[37] 103−104 °C). ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm) 7.26−7.35 (m, 5H), 4.77 (br s, 1H), 4.42 (d, J = 5.5 Hz, 2H), 3.32−3.36 (m, 4H), 1.54−1.58 (m, 6H). $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$): δ (ppm) 157.5, 139.6, 128.5, 127.7, 127.2, 45.0, 44.9, 25.6, 24.4. IR (ν, cm^{-1}, KBr): 3344, 2932, 2850, 1623, 1538, 1481. HRMS: calcd for $C_{13}H_{19}N_2O$, 219.1495; found, 219.1497.

3-((2-Aminophenyl)thio)propionamide (25). The crude mixture was purified by flash chromatography with DCM/AcOEt (7:3), and the product was obtained as white crystals. Yield: 435 mg, 74%. Mp: 102−104 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm) 7.38 (dd, J = 7.6, 1.4 Hz, 1H), 7.15 (td, J = 8.0, 1.5 Hz, 1H), 6.64−6.81 (m, 2H), 4.72 (s, 4H), 3.02 (t, J = 7.0 Hz, 2H), 2.43 (t, J = 7.0 Hz, 2H). $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$): δ (ppm) 174.3, 148.6, 136.3, 130.1, 118.6, 116.5, 115.1, 35.5, 30.0. IR (ν, cm^{-1}, KBr): 3304, 3061, 2927, 2875, 1665, 1536, 1496. MS (EI): 196 (28), 136 (19), 125 (100), 93 (35), 80 (48), 65 (13), 44 (43). HRMS: calcd for $C_9H_{13}N_2OS$, 197.0749; found, 197.0744.

2,3-Dihydro-5*H*-benzo[*b*][1,4]thiazepin-4-one (26). The crude mixture was purified by flash chromatography with DCM/AcOEt (6:4), and the product was obtained as a brown solid. Yield: 252 mg, 47%. Mp: 213-215 °C (lit.[38] 214.3−216.8 °C). ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 8.52 (s, 1H), 7.60 (dd, J = 7.7, 1.4 Hz, 1H), 7.36 (td, J = 7.7, 1.5 Hz, 1H), 7.01−7.24 (m, 2H), 3.46 (t, J = 7.0 Hz, 2H), 2.64 (t, J = 6.9 Hz, 2H). $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ (ppm) 173.9, 141.4, 135.45, 129.8, 126.9, 126.4, 123.3, 34.3, 33.5. IR (ν, cm^{-1}, KBr) 3355, 3179, 2957, 1682, 1475, 1383. HRMS: calcd for $C_9H_{10}NOS$, 180.0483; found, 180.0473.

■ ASSOCIATED CONTENT

Supporting Information

Copies of all NMR spectra. 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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