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Copper-Catalyzed Synthesis of Substituted Furans and Pyrroles by Heterocyclodehydration and Tandem Heterocyclodehydration–Hydration of 3-Yne-1,2-diols and 1-Amino-3-yn-2-ol Derivatives

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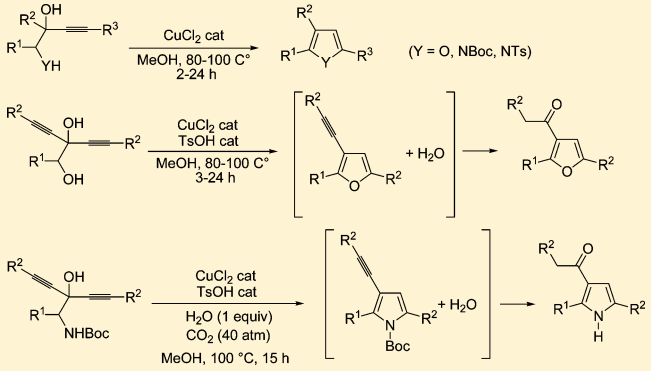
Supporting Information

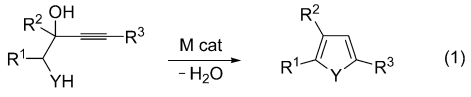
ABSTRACT: $CuCl_2$-catalyzed heterocyclodehydration of readily available 3-yne-1,2-diols and 1-amino-3-yn-2-ol derivatives afforded substituted furans and pyrroles, respectively, in good to high yields (53–99%) under mild conditions (MeOH as the solvent, 80–100 °C, 1–24 h). In the case of 2,2-dialkynyl-1,2-diols, bearing an additional alkynyl substituent at C-2, a cascade process, corresponding to copper-catalyzed heterocyclodehydration followed by acid-catalyzed hydration of the triple bond, was realized when the reaction was carried out in the presence of both $CuCl_2$ and TsOH, leading to 3-acylfurans in one step and high yields (75–84%). Under the same conditions, *N*-Boc-2-alkynyl-1-amino-3-yn-2-ols were converted into the corresponding *N*-unsubstituted 3-acylpyrroles in low to fair yields (19–59%). However, working in the presence of added water and a large excess of CO_2 (40 atm), in addition to $CuCl_2$ and TsOH, caused a significant improvement of the yields of 3-acylpyrroles (68–87%), thus making the method of general synthetic applicability.



INTRODUCTION

Copper catalysis has recently acquired an increasing importance, in view of the availability, lower toxicity and higher environmental compatibility of copper when compared with other transition metal catalysts.[1,2] The growing importance of copper-based catalysts in organic synthesis is testified by the increasing number of publications in this field during the past years,[2] including reviews.[1]

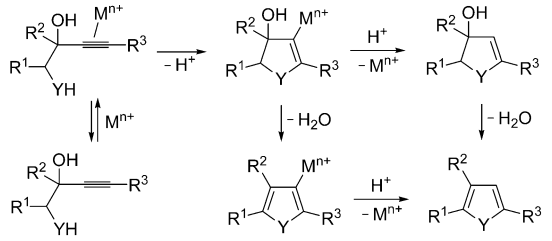
On the other hand, metal-catalyzed heterocyclodehydration of suitably functionalized acyclic precursors is currently established as a versatile and powerful method for the direct synthesis of heterocyclic derivatives under mild reaction conditions starting from readily available precursors.[3,4] A particularly attractive process consists of the heterocyclodehydration of 3-yne-1,2-diols **1** and 1-amino-3-yn-2-ol derivatives **3** to give the corresponding furans **2** and pyrroles **4**, respectively, according to eq 1. The heterocyclodehydration occurs by 5-*exo*-



1 (Y = O); **3** (Y = NR) **2** (Y = O); **4** (Y = NR) (1)

dig intramolecular nucleophilic attack of the hydroxyl group to the triple bond coordinated to the metal center, followed by protonolysis and aromatization or vice versa (Scheme 1).

Scheme 1. Formation of Substituted Furans (2) and Pyrroles (4) by Metal-Catalyzed Heterocyclodehydration of 3-Yne-1,2-diols (1) and 1-Amino-3-yn-2-ol Derivatives (3), Respectively



1 (Y = O); **3** (Y = NR) **2** (Y = O); **4** (Y = NR)

This reaction has been reported to occur under the catalysis of various transition metals, including gold,[3b,c] ruthenium,[3d] silver,[3e,g] molybdenum,[3i,j] and palladium.[3k,l] However, before our short report,[5] no general method based on the use of copper catalysts had been disclosed. In this work, we report a full account on $CuCl_2$-catalyzed heterocyclodehydration of **1** and **3** to give furans **2** and pyrroles **4**, respectively, which allows an efficient, convenient, and economical synthesis of these

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important classes of heterocycles[6,7] under mild conditions using a very simple and ligand-free catalyst.

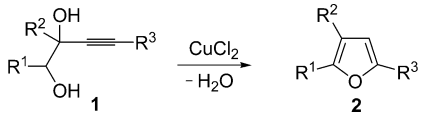
RESULTS AND DISCUSSION

$CuCl_2$-Catalyzed Heterocyclization of 3-Yne-1,2-diols to Give Substituted Furans. The reactivity of 3-yne-1,2-diols **1**, easily obtained by alkynylation of the suitable α-hydroxy carbonyl compound, was investigated first. The reaction of 2-methyl-4-phenylbut-3-yne-1,2-diol **1a**, carried out in the presence of 2 mol % of $CuCl_2$, in MeOH as the solvent (0.2 mmol of **1a** per mL of MeOH) at 80 °C for 1 h, led to the formation of the desired 4-methyl-2-phenylfuran **2a** in 37% GLC yield at 47% substrate conversion (entry 1, Table S1, Supporting Information). After a brief optimization study (Table S1, Supporting Information), **2a** could be obtained in 75% isolated yield at total conversion of **1a**, working at 100 °C for 2 h (Table 1, entry 1). Under the same conditions, 2,4-diphenylbut-3-yne-1,2-diol **1b** led to the corresponding 2,4-diphenylfuran **2b** in 53% isolated yield after 3 h reaction time (Table 1, entry 2). Quite interestingly, the reactivity of 3-yne-1,2-diols bearing an alkyl group on the triple bond (R^3 = alkyl) was higher with respect to the analogous substrates substituted with a phenyl group (R^3 = phenyl). Thus, 2-phenyloct-3-yne-1,2-diol **1c** could be converted into 2-butyl-4-phenylfuran **2c** in 80% yield by conducting the reaction at 80 °C for 2 h (Table 1, entry 3), and under the same conditions, 1,2-diphenyloct-3-yne-1,2-diol **1d** afforded 5-butyl-2,3-diphenylfuran **2d** in 81% yield (Table 1, entry 4).

Of particular interest was the reaction of 2,2-dialkynyl-1,2-diols **1e–i**, bearing an additional alkynyl substituent at C-2. These substrates, in fact, were smoothly converted into the corresponding furans **2e–i** in high yields (81–91%) without affecting the additional alkynyl substituent (Table 1, entries 5–9). The reaction worked nicely even in the presence of a bulky substituent, such as *tert*-butyl, on the triple bond, as shown in entry 8 of Table 1.

Having assessed the possibility to obtain 3-alkynylfurans from 2,2-dialkynyl-1,2-diols, we then verified the possibility to directly obtain 3-acylfurans by tandem heterocyclodehydration/water addition to the 3-alkynyl substituent. In order to realize this process, we allowed 2,2-dialkynyl-1,2-diols **1f–i** to react under conditions similar to those reported in Table 1, entries 6–9 but in the presence of an organic acid such as TsOH (20 mol %). Gratifyingly, after 3–24 h at 80–100 °C, the corresponding 3-acylfurans **5f–i** were formed in high yields, based on starting **1f–i** (Table 2).[8]

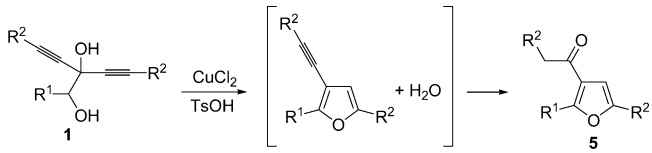
Table 1. Synthesis of Substituted Furans 2 by $CuCl_2$-Catalyzed Heterocyclodehydration of 3-Yne-1,2-diols 1[a]



entry	1	R^1	R^2	R^3	T (°C)	time (h)	2	yield of 2[b] (%)
1	**1a**	H	Me	Ph	100	2	**2a**	75
2	**1b**	H	Ph	Ph	100	3	**2b**	53
3	**1c**	H	Ph	Bu	80	2	**2c**	80
4	**1d**	Ph	Ph	Bu	80	2	**2d**	81
5	**1e**	H	C≡CBu	Bu	80	2	**2e**	87
6[c]	**1f**	Me	C≡CBu	Bu	80	2	**2f**	91
7	**1g**	Ph	C≡CBu	Bu	80	2	**2g**	84
8[c]	**1h**	Me	C≡C^{t}Bu	^{t}Bu	80	2	**2h**	81
9[c]	**1i**	Me	C≡CPh	Ph	100	3	**2i**	84

[a]All reactions were carried out in MeOH in the presence of 2 mol % of $CuCl_2$ (0.20 mmol of **1** per mL of MeOH, 1 mmol scale based on **1**). Conversion of **1** was quantitative in all cases. [b]Isolated yield based on starting **1**. [c]The substrate employed was the *S* enantiomer [prepared from commercially available ethyl (*S*)-α-hydroxypropionate].[4b]

Table 2. Synthesis of 3-Acylfurans 5 by Tandem $CuCl_2$-Catalyzed Heterocyclodehydration of 2,2-Dialkynyl-1,2-diols/Acid-Catalyzed Water Addition to the Triple Bond[a]



entry	1	R^1	R^2	T (°C)	time (h)	5	yield of 5[b] (%)
1[c]	**1f**	Me	Bu	80	3	**5f**	84
2	**1g**	Ph	Bu	80	24	**5g**	89
3[c]	**1h**	Me	*t*-Bu	80	3	**5h**	78
4[c]	**1i**	Me	Ph	100	15	**5i**	75

[a]All reactions were carried out in MeOH in the presence of 2 mol % of $CuCl_2$ and 20 mol % of TsOH·H_2O (0.20 mmol of **1** per mL of MeOH, 1 mmol scale based on **1**). Conversion of **1** was quantitative in all cases. [b]Isolated yield based on starting **1**. [c]The substrate employed was the *S* enantiomer [prepared from commercially available ethyl (*S*)-α-hydroxypropionate].[4b]

$CuCl_2$-Catalyzed Heterocyclization of 1-Amino-3-yn-2-ol Derivatives to Give Substituted Pyrroles. A variety of *N*-Boc-1-amino-3-yn-2-ols **3** were allowed to react under conditions similar to those successfully employed for 3-yne-1,2-diols **1**, in order to develop a general synthesis of substituted pyrroles **4**. The results obtained by varying the nature of the substituent α to the amino group, α to the hydroxyl group, and on the triple bond are reported in Table 3. As can be seen, good to excellent yields of the corresponding *N*-Boc-pyrroles were obtained with all the substrates tested, at 80–100 °C and after 1–24 h reaction time. Monoalkynyl substrates **3a–f** turned out to be less reactive than monoalkynyl 3-yne-1,2-diols, and a higher catalyst loading (5 mol % instead of 2 mol %) was necessary in order to achieve acceptable reaction rates and product yields (Table 3, entries 1–7). As already observed with 3-yne-1,2-diols, conjugation of the triple bond with an aromatic ring caused a slight decrease of reactivity, as can be seen by comparing entry 2 (**3b**, R^1 = Bn, R^2 = H, R^3 = Bu) with entry 7 (**3f**, R^1 = Bn, R^2 = H, R^3 = Ph). In this latter case, the reaction of (*S*)-*N*-Boc-4-amino-1,5-diphenylpent-1-yn-3-ol **3f** led to the formation of a mixture of *N*-Boc-2-benzyl-5-phenylpyrrole **4f** (32%) and 2-benzyl-5-phenyl-1*H*-pyrrole **6f** (21%), deriving from in situ deprotection of **4f**. After treatment of the reaction crude with NaOMe (3 equiv with respect to starting **3f**), **6f** was selectively obtained in 53% yield, according to Scheme 2. On the other hand, dialkynyl substrates **3g–k** were significantly more reactive than monoalkynyl substrates **3a–f**, as shown by entries 8–12 (Table 3). The reaction could also be successfully applied to *N*-tosyl derivatives, as shown by entry 13 (Table 3).

The influence of the substrate stereochemistry on the reaction outcome was also investigated, by reacting the racemic (3*RS*,4*RS*) *syn* diastereomer of *N*-Boc-3-amino-2-methyldec-5-

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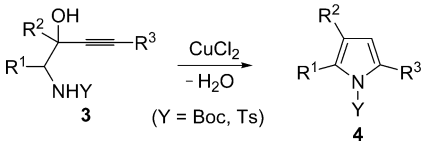
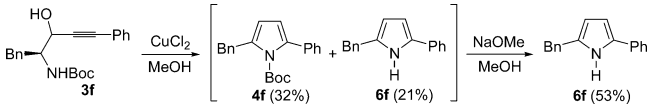
Table 3. Synthesis of Substituted Pyrroles 4 by $CuCl_2$-Catalyzed Heterocyclodehydration of 1-Amino-3-yn-2-ol Derivatives 3[a]



entry	3	R^1	R^2	R^3	Y	mol % $CuCl_2$	T (°C)	time (h)	4	yield of 4[b] (%)
1[c]	**3a**	Me	H	Bu	Boc	5	100	15	**4a**	56
2[c]	**3b**	Bn	H	Bu	Boc	5	100	15	**4b**	70
3[c]	**3c**	*i*-Pr	H	Bu	Boc	5	100	8	**4c**	76
4[d]	*syn*-**3c**	*i*-Pr	H	Bu	Boc	5	100	8	**4c**	71
5[c]	**3d**	Bn	Me	Bu	Boc	5	100	15	**4d**	75
6	**3e**	H	H	Bu	Boc	5	100	18	**4e**	97
7[c]	**3f**	Bn	H	Ph	Boc	5	100	24	**4f**	32[e]
8[f]	**3g**	Me	C≡CBu	Bu	Boc	2	80	1	**4g**	99
9	**3h**	Bn	C≡CBu	Bu	Boc	2	80	8	**4h**	73
10[f]	**3i**	*i*-Bu	C≡CBu	Bu	Boc	2	100	1	**4i**	78
11	**3j**	H	C≡CBu	Bu	Boc	2	80	2	**4j**	73
12[f]	**3k**	Me	C≡CPh	Ph	Boc	2	80	1	**4k**	82
13[f]	**3l**	Me	C≡CBu	Bu	Ts	2	80	8	**4l**	83

[a]All reactions were carried out in MeOH in the presence of $CuCl_2$ as the catalyst (0.20 mmol of **3** per mL of MeOH, 1 mmol scale based on **1**). Conversion of **3** was quantitative in all cases. [b]Isolated yield based on starting **3**. [c]The substrate employed was a (*S*,*S*) + (*S*,*R*) diastereomeric mixture (obtained starting from the corresponding commercially available methyl *N*-Boc-L-amino ester).[4c] [d]The substrate employed was the racemic (3*RS*,4*RS*) *syn* diastereomer (obtained starting from commercially available *N*-Boc-D/L-valine methyl ester).[4c] [e]The reaction also led to the formation of 2-benzyl-5-phenyl-1*H*-pyrrole **6f** in 21% isolated yield. [f]The substrate employed was the *S* enantiomer (obtained starting from the corresponding commercially available methyl L-amino ester).[4c]

Scheme 2. Synthesis of 2-Benzyl-5-phenyl-1*H*-pyrrole 6f by $CuCl_2$-Catalyzed Heterocyclodehydration of (*S*)-*N*-Boc-4-amino-1,5-diphenylpent-1-yn-3-ol 3f Followed by Base-Promoted Deprotection

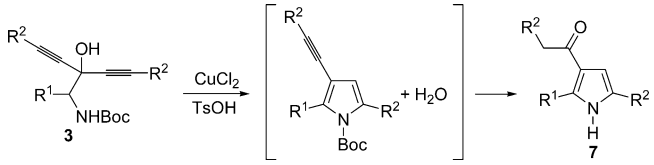


yn-4-ol, *syn*-**3c**, and comparing its reactivity with that of the corresponding diastereomeric mixture (3*S*,4*S*) + (3*S*,4*R*), **3c**. As shown in Table 3, entries 3 and 4, the *syn* diastereomer (Table 3, entry 4) gave practically the same results as those obtained with the diastereomeric mixture (3*S*,4*S*) + (3*S*,4*R*) (Table 3, entry 3), so it can be concluded that the stereochemistry of the substrate does not significantly affect the reaction outcome.

Also in the case of *N*-Boc-2-alkynyl-1-amino-3-yn-2-ols, we verified the possibility to realize the one-pot sequential Cu-catalyzed heterocyclodehydration/acid-catalyzed water addition to the triple bond. The results obtained working in the presence of 2 mol % of $CuCl_2$ and 20 mol % of TsOH are shown in Table 4. Under these conditions, triple bond hydration was accompanied by acid-promoted *N*-deprotection, with formation of the corresponding *N*-unsubstituted-3-acylpyrrole **7**. As can be seen from Table 4, moderate to fair yields (48−59%) of **7** were obtained in almost all cases, with the exception of 2-methyl-3-phenylacetyl-5-phenylpyrrole **7k**, which was formed in low yield (19%, Table 4, entry 4).

With the aim of improving these results, we carried out the cascade reaction also in the presence of added water and of a large excess of carbon dioxide, in addition to $CuCl_2$ and TsOH. In fact, it is known that CO_2, under appropriate conditions, can cause β-carboxylation of the pyrrole ring.[9] Therefore, working in the presence of CO_2 and TsOH, the formation of the

Table 4. Formation of 3-Acylpyrroles 7 by Tandem $CuCl_2$-Catalyzed Heterocyclodehydration of *N*-Boc-2-Alkynyl-1-amino-3-yn-2-ols/Acid-Catalyzed Water Addition to the Triple Bond[a]



entry	3	R^1	R^2	T (°C)	time (h)	7	yield of 7[b] (%)
1[c]	**3g**	Me	Bu	100	15	**7g**	54
2	**3h**	Bn	Bu	100	15	**7h**	59
3[c]	**3i**	*i*-Bu	Bu	100	15	**7i**	48
4[c]	**3k**	Me	Ph	100	15	**7k**	19
5[c]	**3m**	Me	*t*-Bu	100	15	**7m**	56

[a]All reactions were carried out in MeOH in the presence of 2 mol % of $CuCl_2$ and 20 mol % of TsOH·H_2O (0.20 mmol of **3** per mL of MeOH, 1 mmol scale based on **3**). Conversion of **3** was quantitative in all cases. [b]Isolated yield based on starting **3**. [c]The substrate employed was the *S* enantiomer (obtained starting from the corresponding commercially available methyl *N*-Boc-L-amino ester).[4c]

cationic carboxylated intermediate **I** from the reaction between the 3-alkynyl intermediate, CO_2 and TsOH should take place. This would favor triple bond protonation, thus promoting the subsequent water attack to the triple bond with simultaneous decarboxylation. In this way, CO_2 would actually act as an efficient cocatalyst for the triple bond hydration of the 3-alkynyl intermediate (Scheme 3).

Indeed, working in the presence of added water and large excess of CO_2 (40 atm), in addition to $CuCl_2$ and TsOH, caused a significant improvement of the yields of acylpyrroles **7**, thus making the method of general synthetic applicability, as shown by the results reported in Table 5. In particular,

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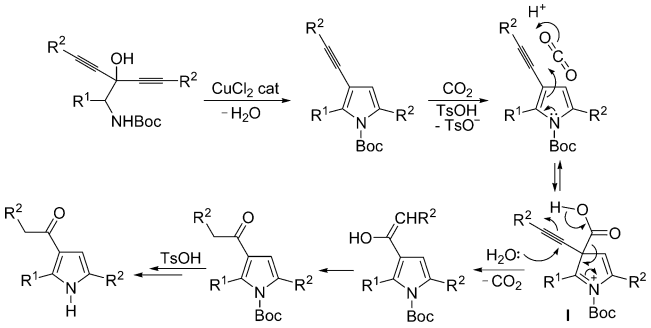
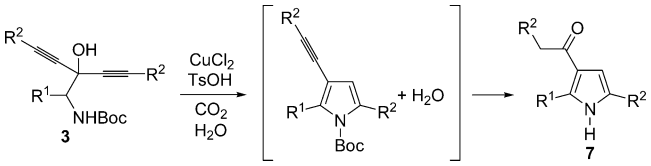
Scheme 3. Possible Mechanism for the CO_2/TsOH-Promoted Hydration of 3-Alkynylpyrrole Intermediates (Obtained by $CuCl_2$-Catalyzed Heterocyclodehydration of *N*-Boc-2-alkynyl-1-amino-3-yn-2-ols) Leading to 3-Acylpyrroles[a]



[a]The acid-promoted deprotection is shown to occur as the end of the process, but it can also take place in an earlier stage.

Table 5. Synthesis of 3-Acylpyrroles 7 by Tandem $CuCl_2$-Catalyzed Heterocyclodehydration of *N*-Boc-2-Alkynyl-1-amino-3-yn-2-ols/Acid- and CO_2-Promoted Water Addition to the Triple Bond[a]



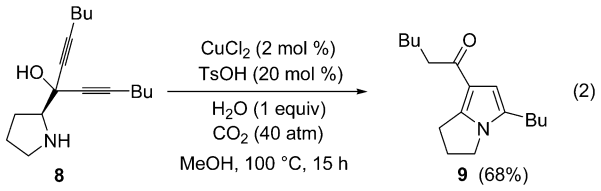
entry	3	R^1	R^2	7	yield of 7[b] (%)
1[c]	**3g**	Me	Bu	**7g**	70
2	**3h**	Bn	Bu	**7h**	82
3[c]	**3i**	*i*-Bu	Bu	**7i**	68
4[c]	**3k**	Me	Ph	**7k**	80
5[c]	**3m**	Me	*t*-Bu	**7m**	87
6	**3n**	*i*-Pr	Bu	**7n**	71
7[c]	**3o**	*i*-Bu	*t*-Bu	**7o**	78
8[c]	**3p**[d]	*i*-Bu	H	**7p**	82[e]

[a]All reactions were carried out at 100 °C for 15 h in MeOH (0.20 mmol of **3** per mL of MeOH, 1 mmol scale based on **3**), in the presence of $CuCl_2$ (2 mol %), TsOH·H_2O (20 mol %), H_2O (1 equiv) and CO_2 (40 atm). Conversion of **3** was quantitative in all cases. [b]Isolated yield based on starting **3**. [c]The substrate employed was the *S* enantiomer (obtained starting from the corresponding commercially available methyl *N*-Boc-L-amino ester).[4c] [d]Crude substrate. [e]Based on the *bis*-(trimethylsilyl) precursor of **3p**, that is, (*S*)-*N*-Boc-4-amino-6-methyl-1-(trimethylsilyl)-3-[2-(trimethylsilyl)ethynyl]hept-1-yn-3-ol **3p′**. (Substrate **3p**, obtained by deprotection of **3p′**, was used crude without further purification. See the Experimental Section for details.)

acylpyrrole **7k** was now obtained in a yield as high as 80% (to be compared with 19% obtained in Table 4, entry 4).[10] The method could also be successfully applied to a substrate bearing terminal triple bonds, such as (*S*)-*N*-Boc-4-amino-3-ethynyl-6-methylhept-1-yn-3-ol **3p** (Table 5, entry 8), and to a substrate bearing a secondary unprotected amino group, such as (*S*)-7-(pyrrolidin-2-yl)trideca-5,8-diyn-7-ol **8** (eq 2).

CONCLUSIONS

In conclusion, we have reported a general and convenient method for the synthesis of furans **2** and pyrroles **4** by copper-catalyzed heterocyclodehydration of 3-yne-1,2-diols **1** and 1-amino-3-yn-2-ol derivatives **3**, respectively. The process is catalyzed by a simple and inexpensive catalyst ($CuCl_2$) and takes place under mild conditions (MeOH as the solvent, 80–100 °C, 1–24 h).



Of particular interest was the reaction of 2,2-dialkynyl-1,2-diols and *N*-Boc-2-alkynyl-1-amino-3-yn-2-ols, bearing an additional alkynyl substituent at C-2, which were converted into the corresponding 3-alkynylfurans and 3-alkynylpyrroles in high yields without affecting the additional alkynyl substituent. Moreover, under appropriate conditions, these substrates could be converted in one step into the corresponding 3-acylfurans **5** and *N*-unsubstituted 3-acylpyrroles **7** by a cascade process, corresponding to copper-catalyzed heterocyclodehydration followed by acid-catalyzed hydration of the triple bond. This latter approach was also successfully applied to (*S*)-7-(pyrrolidin-2-yl)trideca-5,8-diyn-7-ol **8** to give a novel dihydropyrrolizine derivative **9** in good yield.

EXPERIMENTAL SECTION

General Experimental Methods. Melting points are uncorrected. ^{1}H NMR and ^{13}C NMR spectra were recorded at 25 °C in $CDCl_3$ or DMSO-d_6 solutions at 300 or 500 MHz and 75 or 126 MHz, respectively, with Me_4Si as internal standard. Chemical shifts (δ) and coupling constants (J) are given in ppm and in Hz, respectively. IR spectra were taken with an FT-IR spectrometer. Mass spectra were obtained using a GC–MS apparatus at 70 eV ionization voltage or a mass spectrometer equipped with a turbo ion spray ionization source in the positive mode [ion spray voltage (IS) 4500 V; curtain gas 10 psi; temperature 25 °C; ion source gas (1) 20 psi; declustering and focusing potentials 50 and 400 V, respectively]. Microanalyses were carried out at our analytical laboratory. All reactions were analyzed by TLC on silica gel 60 F_{254} or on neutral alumina and by GLC using a gas chromatograph and capillary columns with polymethylsilicone +5% phenylsilicone as the stationary phase. Column chromatography was performed on silica gel 60 (70–230 mesh). Evaporation refers to the removal of solvent under reduced pressure.

Preparation of Substrates. 3-Yne-1,2-diols **1a–c**, **1e,f**,[4b] *N*-Boc-1-amino-3-yn-2-ols **3a–i**, **3k**, **3m–o**,[4c] and (*S*)-7-(pyrrolidin-2-yl)-trideca-5,8-diyin-7-ol **8**[4c] were prepared as we previously described. 3-Yne-1,2-diols **1d**, **1g–i**, *N*-Boc-1-amino-3-yn-2-ols **3j** and **3p**, *N*-Ts-7-(1-aminoethyl)trideca-5,8-diyn-7-ol **3l** were prepared as described below. All other materials were commercially available and were used without further purification.

Preparation of 1,2-Diphenyl-oct-3-yne-1,2-diol 1d. A solution of 1-hexyne (4.55 g; 44.5 mmol) in anhydrous THF (6 mL) was added dropwise under nitrogen to a stirred, cooled (−40 °C) mixture of BuLi (28 mL of a 1.6 M solution in hexanes, 44.8 mmol) in anhydrous THF (18 mL) and anhydrous hexane (28 mL). To the resulting mixture, maintained at −40 °C, was added, with stirring, a solution of LiBr (1.56 g, 18 mmol) in THF (6 mL). After 0.5 h, 2-hydroxy-1,2-diphenylethanone (3.61 g, 17 mmol), diluted in anhydrous THF (5 mL), was slowly added under nitrogen at the same temperature. The resulting mixture was stirred for additional 2 h and then allowed to warm up to room temperature. After quenching with a saturated solution of NH_4Cl (20 mL), the mixture was extracted with Et_2O (3 × 50 mL). The combined organic layers were washed with water (40 mL) and then dried over Na_2SO_4. After filtration, the solvent was evaporated, and the crude 1,2-diphenyl-oct-3-yne-1,2-diol **1d** was purified by column chromatography on silica gel using hexane–AcOEt

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6:4 as eluent. Yield: 4.25 g, starting from 3.61 g of 2-hydroxy-1,2-diphenylethanone (85%). Yellow amorphous solid: mp 94−95 °C, lit.[11] 96 °C; IR (KBr) ν = 3489 (m, br), 3451 (m, br), 2219 (v w), 1450 (w), 1384 (m), 1181 (w), 1061 (m), 735 (w), 697 (m), 631 (w) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ = 7.44−7.35 (m, 2 H), 7.30−7.04 (m, 8 H), 4.82 (s, 1 H), 2.87 (s, 1 H), 2.81 (d, J = 3.0, 1 H), 2.29 (t, J = 7.3, 2 H), 1.60−1.33 (m, 4 H), 0.92 (t, J = 7.3, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 140.5, 137.7, 128.0, 127.93, 127.87, 127.3, 126.7, 88.8, 81.1, 76.3, 30.5, 22.0, 18.5, 13.6; MS (ESI+, direct infusion) m/z = 317 [$(M + Na)^+$]. Anal. calcd for $C_{20}H_{22}O_2$ (294.39): C, 81.60; H, 7.53. Found: C, 81.71; H, 7.52.

General Procedure for the Preparation of 2-Alkynyl-3-yne-1,2-diols 1g−i. A solution of 1-alkyne (51.0 mmol) (1-hexyne: 4.19 g; 3,3-dimethyl-1-butyne: 4.19 g; phenylacetylene: 5.21 g) in anhydrous THF (8 mL) was added dropwise under nitrogen to a stirred, cooled (−78 °C) mixture of BuLi (34 mL of a 1.6 M solution in hexanes, 54.4 mmol) in anhydrous THF (22 mL) and anhydrous hexane (34 mL). To the resulting mixture, maintained at −78 °C, was added, with stirring, a solution of LiBr (2.13 g, 24.5 mmol) in THF (7 mL). After 0.5 h, a solution of methyl DL-mandelate (2.82 g, 17 mmol) or ethyl L-lactate (2.01 g, 17 mmol) in anhydrous THF (5 mL) was slowly added under nitrogen at the same temperature. The resulting mixture was stirred for additional 2 h and then allowed to warm up to room temperature. After quenching with a saturated solution of NH_4Cl (20 mL), the mixture was extracted with Et_2O (3 × 50 mL). The combined organic layers were washed with water (40 mL) and then dried over Na_2SO_4. After filtration and evaporation of the solvent, the product was purified by column chromatography on silica gel using as eluent 9:1 hexane−AcOEt (**1h**, **1g**) or 8:2 hexane−AcOEt (**1i**).

*2-Hex-1-ynyl-1-phenyl-oct-3-yne-1,2-diol (**1g**).* Yield: 4.26 g, starting from 2.82 g of methyl DL-mandelate (84%). Yellow solid: mp 34−35 °C; IR (KBr) ν = 3372 (s, br), 2955 (s), 2929 (s), 2860 (m), 2237 (m), 1454 (m), 1378 (m), 1062 (m), 727 (s), 696 (m), 646 (s) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ = 7.57−7.48 (m, 2 H), 7.36−7.29 (m, 3 H), 4.77 (s, 1 H), 3.10 (s, 1 H), 3.00 (s, 1 H), 2.20 (t, J = 7.0, 4 H), 1.54−1.27 (m, 8 H), 0.89 (t, J = 7.0, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 137.5, 128.24, 128.18, 127.4, 87.0, 86.8, 80.0, 78.5, 77.8, 68.1, 30.3, 21.9, 18.4, 13.6; GC−MS m/z = 298 (M^+, absent), 280 (54), 265 (5), 238 (23), 237 (100), 207 (6), 191 (12), 178 (9), 165 (27), 152 (14), 135 (5), 121 (13), 108 (21), 107 (19), 105 (34), 91 (19), 79 (33), 77 (66). Anal. calcd for $C_{20}H_{26}O_2$ (298.42): C, 80.50; H, 8.78. Found: C, 80.44; H, 8.80.

*(S)-3-(3,3-Dimethylbut-1-ynyl)-6,6-dimethylhept-4-yne-2,3-diol (**1h**).* Yield: 2.81 g, starting from 2.01 g of ethyl L-lactate (70%). Colorless solid: mp 71−72 °C; $[\alpha]^{25}_D$ (MeOH, c = 1.04 × 10^{-2} g mL^{-1}) = −6°; IR (KBr) ν = 3333 (m, br), 2669 (s), 2238 (w), 1477 (m), 1340 (m), 1266 (m), 1205 (w), 1135 (m), 1098 (w), 1023 (m), 992 (m), 871 (m) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ = 3.81 (q, J = 6.1, 1 H), 3.39 (s, 1 H), 2.67 (s, 1 H), 1.33 (d, J = 6.1, 3 H), 1.24 (s, 3 H), 1.23 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 93.7, 93.1, 77.9, 76.5, 74.4, 67.8, 30.8, 30.7, 27.4, 27.3, 17.5; GC−MS m/z = 236 (M^+, absent), 188 (28), 187 (28), 159 (5), 147 (11), 146 (100), 131 (21), 117 (14), 115 (31), 109 (13), 105 (35), 91 (16), 77 (44), 59 (64). Anal. calcd for $C_{15}H_{24}O_2$ (236.35): C, 76.23; H, 10.24. Found: C, 76.30; H, 10.21.

*(S)-5-Phenyl-3-(2-phenylethynyl)pent-4-yne-2,3-diol (**1i**).* Yield: 3.76 g, starting from 2.01 g of ethyl L-lactate (80%). Yellow solid: mp 90−92 °C, lit.[11] 106−107 °C; $[\alpha]^{25}_D$ (MeOH, c = 1.04 × 10^{-2} g mL^{-1}) = −7°; IR (KBr) ν = 3395 (m, br), 2200 (w), 1489 (w), 1443 (m), 1384 (m), 1293 (w), 1132 (m), 1092 (m). 1048 (m), 986 (w), 898 (w), 757 (m), 691 (m) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ = 7.52−7.44 (m, 4 H), 7.35−7.24 (m, 6 H), 4.11 (q, J = 6.1, 1 H), 3.74 (s, 1 H), 2.88 (s, 1 H), 1.52 (d, J = 6.1, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 132.0, 131.9, 128.9, 128.3, 121.84, 121.79, 87.1, 86.0, 85.5, 85.0, 74.5, 68.7, 17.8; GC−MS m/z = 276 (M^+, absent), 232 (41), 231 (64), 214 (55), 203 (28), 187 (7), 150 (3), 129 (100), 102 (21), 75 (17). Anal. calcd for $C_{19}H_{16}O_2$ (276.33): C, 82.58; H, 5.84. Found: C, 82.54; H, 5.83.

Preparation of *N*-Boc-7-aminomethyl-trideca-5,8-diyn-7-ol (3j). To a suspension of Mg turnings (0.6 g, 24.7 mmol) in anhydrous THF (3 mL), maintained under nitrogen and under reflux, was added pure ethyl bromide (0.5 mL) to start the formation of the Grignard reagent. The remaining bromide was added dropwise in THF solution (1.3 mL of EtBr in 12 mL of THF; total amount of EtBr added: 2.63 g, 24.1 mmol). The mixture was then allowed to reflux for additional 20 min. After cooling, the resulting solution of EtMgBr was transferred under nitrogen to a dropping funnel and added dropwise under nitrogen to a solution of the 1-hexyne (1.98 g, 24.1 mmol) in anhydrous THF (6 mL) at 0 °C with stirring. After additional stirring at 0 °C for 15 min, the mixture was allowed to warm up to room temperature and then was heated at 45 °C and stirred for 2 h. To the hot solution of the 1-hexynylmagnesium bromide thus obtained was added, dropwise and under nitrogen, a solution of *N*-Boc-glycine methyl ester (1.17 g, 6.21 mmol) in anhydrous THF (7 mL). The resulting mixture was allowed to stir at 35 °C overnight. After cooling to room temperature, saturated NH_4Cl (50 mL) and AcOEt (50 mL) were sequentially added, phases were separated, and the aqueous phase was extracted with AcOEt (3 × 50 mL). The collected organic layers were washed with brine and dried over Na_2SO_4. After filtration and evaporation of the solvent, product **3j** was purified by column chromatography on silica gel using 8:2 hexane−AcOEt as the eluent. Yield: 0.80 g, starting from 1.17 g of *N*-Boc-glycine methyl ester (40%). Yellow oil: IR (film) ν = 3413 (m, br), 2960 (m), 2932 (m), 2873 (w), 2240 (vw), 1701 (s), 1511 (m), 1457 (w), 1367 (m), 1251 (m), 1173 (m), 1077 (w) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ = 5.12−5.03 (m, br, 1 H), 3.54−3.44 (m, 2 H), 3.32 (s, br, 1 H), 2.22 (t, J = 6.9, 4 H), 1.56−1.33 (m, 8 H), 1.46 (s, 9 H), 0.91 (t, J = 7.2, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 156.5, 84.9, 79.8, 79.1, 63.9, 52.0, 30.4, 28.4, 21.9, 18.4, 13.6; MS (ESI+, direct infusion) m/z = 344 [$(M + Na)^+$]. Anal. calcd for $C_{19}H_{31}NO_3$ (321.45): C, 70.99; H, 9.72; N, 4.36. Found: C, 71.08; H, 9.75; N, 4.35.

Preparation of (*S*)-*N*-Boc-4-amino-6-methyl-1-trimethylsilanyl-3-trimethylsilanylethynylhept-1-yn-3-ol (3p′). To a suspension of Mg turnings (1.8 g, 74.1 mmol) in anhydrous THF (9 mL), maintained under nitrogen and under reflux, was added pure ethyl bromide (1.5 mL) to start the formation of the Grignard reagent. The remaining bromide was added dropwise in THF solution (3.9 mL of EtBr in 36 mL of THF; total amount of EtBr added: 7.89 g, 72.3 mmol). The mixture was then allowed to reflux for an additional 20 min. After cooling, the resulting solution of EtMgBr was transferred under nitrogen to a dropping funnel and added dropwise under nitrogen to a solution of trimethylsilylacetylene (7.10 g, 72.3 mmol) in anhydrous THF (18 mL) at 0 °C with stirring. After additional stirring at 0 °C for 15 min, the mixture was allowed to warm up to room temperature and then was heated at 45 °C and stirred for 2 h. To the hot solution of the 1-trimethylsilylethynylmagnesium bromide thus obtained was added, dropwise and under nitrogen, a solution of *N*-Boc-L-leucine methyl ester (4.56 g, 18.6 mmol) in anhydrous THF (21 mL). The resulting mixture was allowed to stir at 35 °C overnight. After cooling to room temperature, saturated NH_4Cl (100 mL) and AcOEt (100 mL) were sequentially added, phases were separated, and the aqueous phase was extracted with AcOEt (3 × 100 mL). The collected organic layers were washed with brine and dried over Na_2SO_4. After filtration and evaporation of the solvent, the crude product was purified by column chromatography on silica gel using 8:2 hexane−AcOEt as the eluent to give pure (*S*)-*N*-Boc-4-amino-6-methyl-1-trimethylsilanyl-3-trimethylsilanylethynyl-hept-1-yn-3-ol **3p**. Yield: 5.87 g, starting from 4.56 g of *N*-Boc-L-leucine methyl ester (77%). Colorless solid: mp 82−84 °C; $[\alpha]^{25}_D$ (MeOH, c = 1.04 × 10^{-2} g mL^{-1}) = −38°; IR (KBr) ν = 3446 (m, br), 2956 (m), 2171 (w), 1701 (s), 1511 (s), 1386 (w), 1341 (m), 1250 (m), 1178 (m), 1123 (w), 1062 (m), 1011 (m), 886 (m), 842 (s), 761 (m) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ = 4.63 (d, br, J = 10.3, 1 H), 4.00−3.88 (m, 1 H), 3.41 (s, br, 1 H), 1.75−1.63 (m, 2 H), 1.50−1.35 (m, 1 H), 1.46 (s, 9 H), 0.95 (d, J = 6.0, 6 H), 0.19 (s, 9 H), 0.18 (s, 9 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 156.9, 104.0, 102.9, 89.9, 89.7, 80.2, 68.4, 58.3, 40.5, 28.7, 25.3, 24.1, 21.9; MS (ESI+, direct infusion) m/z = 432 [$(M + Na)^+$]. Anal. calcd for $C_{21}H_{39}NO_3Si_2$ (409.71): C, 61.56; H, 9.59; N, 3.42. Found: C, 61.61; H, 9.58; N, 3.43.

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Preparation of (*S*)-*N*-Tosyl-7-(1-aminoethyl)trideca-5,8-diyn-7-ol 3l. *Preparation of Crude N-Tosyl-L-alanine methyl ester.* To a cold (0 °C) solution of L-alanine methyl ester hydrochloride (8.0 g, 57.3 mmol) in anhydrous CH_2Cl_2 (80 mL) was added under nitrogen tosyl chloride (2.02 g, 63.0 mmol). To the resulting mixture was added dropwise Et_3N (12.7 g, 126.1 mmol) under nitrogen at 0 °C. The mixture was allowed to warm up to room temperature, stirred for 20 h, and then diluted with water (50 mL). Phases were separated, and the aqueous phase was extracted with CH_2Cl_2 (50 mL). The collected organic layers were washed with brine and dried over Na_2SO_4. After filtration, the solvent was evaporated to obtain crude *N*-tosyl-L-alanine methyl ester as a colorless amorphous solid (13.1 g, 89% yield based on starting L-alanine methyl ester hydrochloride), which was sufficiently pure to be used as such in the next step.

Preparation of (S)-N-Tosyl-7-(1-aminoethyl)trideca-5,8-diyn-7-ol. To a suspension of Mg turnings (0.6 g, 24.7 mmol) in anhydrous THF (3 mL), maintained under nitrogen and under reflux, was added pure ethyl bromide (0.5 mL) to start the formation of the Grignard reagent. The remaining bromide was added dropwise in THF solution (1.3 mL of EtBr in 12 mL of THF; total amount of EtBr added: 2.63 g, 24.1 mmol). The mixture was then allowed to reflux for additional 20 min. After cooling, the resulting solution of EtMgBr was transferred under nitrogen to a dropping funnel and added dropwise under nitrogen to a solution of 1-hexyne (1.98 g, 24.1 mmol) in anhydrous THF (6 mL) at 0 °C with stirring. After additional stirring at 0 °C for 15 min, the mixture was allowed to warm up to room temperature and then stirred for additional 2 h. To the solution of 1-hexynylmagnesium bromide thus obtained was then added, dropwise under nitrogen at room temperature, a solution of crude *N*-tosyl-L-alanine methyl ester (1.60 g, 6.21 mmol) in anhydrous THF (7 mL). The resulting mixture was allowed to stir at 35 °C overnight. After cooling, saturated NH_4Cl (50 mL) and AcOEt (50 mL) were sequentially added, and the phases were separated. The aqueous phase was extracted with AcOEt (3 × 50 mL). The collected organic layers were washed with brine and dried over Na_2SO_4. After filtration and evaporation of the solvent, the products were purified by column chromatography on silica gel using 7:3 hexane−AcOEt as the eluent to give *N*-tosyl-7-(1-aminoethyl)-trideca-5,8-diyn-7-ol **3l** as a colorless oil (1.72 g, 71% based on crude *N*-tosyl-L-alanine methyl ester): $[\alpha]^{25}_{D}$ (MeOH, c = 1.04 × 10^{-2} g mL^{-1}) = −122°; IR (film) ν = 3479 (m, br), 2934 (m), 2240 (w), 1430 (m), 1333 (s), 1165 (s), 1093 (m), 916 (w), 816 (w), 662 (m) cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.82−7.77 (m, 2 H), 7.33−7.28 (m, 2 H), 4.92 (d, br, J = 8.9, 1 H), 3.54−3.43 (m, 1 H), 2.99 (s, br, 1 H), 2.42 (s, 3 H), 2.18 (t, J = 7.1, 2 H), 2.16 (t, J = 7.1, 2 H), 1.53−1.29 (m, 8 H), 1.22 (d, J = 6.5, 3 H), 0.90 (t, J = 7.1, 3 H), 0.88 (t, J = 7.1, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 143.5, 137.7, 129.7, 127.2, 86.3, 85.9, 78.3, 77.6, 66.8, 58.9, 30.4, 30.3, 22.00, 21.97, 21.6, 18.3, 17.8, 15.3, 13.6; MS (ESI+, direct infusion) m/z = 412 [$(M + Na)^+$, 100], 394 (21), 216 (21). Anal. calcd for $C_{22}H_{31}NO_3S$ (389.55): C, 67.83; H, 8.02; N, 3.60; S, 8.23. Found: C, 67.63; H, 8.02; N, 3.62; S, 8.24.

General Procedure for the $CuCl_2$-Catalyzed Heterocyclodehydration of 3-Yne-1,2-diols 1a−i and *N*-1-Amino-3-yn-2-ol Derivatives 3a−l To Give Furans 2a−i and Pyrroles 4a−l. A solution of pure **1** [**1a** (176 mg), **1b** (238 mg), **1c** (218 mg), **1d** (294 mg), **1e** (321 mg), **1f** (236 mg), **1g** (298 mg), **1h** (236 mg), **1i** (276 mg), **3a** (255 mg), **3b** (331 mg), **3c** (283 mg), **3d** (345 mg), **3e** (241 mg), **3f** (351 mg), **3g** (335 mg), **3h** (412 mg), **3i** (378 mg), **3j** (321 mg), **3k** (375 mg), **3l** (390 mg); 1.0 mmol] in anyhydrous MeOH (5.0 mL) was added to $CuCl_2$ (2.7 mg, 2.0 × 10^{-2} mmol, for **1a−i** and **3g−l**; 6.8 mg, 5 × 10^{-2} mmol, for **3a−f**) under nitrogen in a Schlenk flask. The resulting mixture was stirred under nitrogen at 100 °C (for **1a**, **1b**, **1i**, **3a−f**) or 80 °C (for **1c−h**, **3g−l**) and was monitored in TLC until complete conversion of the substrate (1 h for **3g**, **3i**, and **3k**; 2 h for **1a**, **1c−h** and **3j**; 3 h for **1b** and **1i**; 8 h for **3c**, **3h** and **3l**; 15 h for **3a**, **3b** and **3d**; 18 h for **3e**; 24 h for **3f**). Solvent was evaporated, and the crude products were purified by column chromatography on silica gel [99:1 hexane−acetone for **2a−c**; hexane−AcOEt from 9:1 to 8:2 for **2d**, **2e**, and **2h**; pure hexane for **2g**; 8:2 hexane−AcOEt for **4a**, **4b**, **4d**, **4g**, and **4l**; 9:1 hexane−AcOEt for **4c**, **4h**, **4i**, and **4k**; 6:4 hexane−AcOEt for **4e**; 95:5 hexane−AcOEt for **4f**, **6f** (order of elution: **4f**, **6f**) and **4j**] or neutral alumina (99:1 hexane−acetone for **2f** and **2i**).

*4-Methyl-2-phenylfuran (**2a**).* Yield: 119 mg, starting from 176 mg of **1a** (75%) (Table 1, entry 1). Colorless solid: mp 37−39 °C, lit.[12] 38−40 °C; IR (KBr) ν = 2960 (m), 1601 (w), 1495 (w), 1449 (w), 1266 (m), 1116 (w), 739 (m), 702 (m) cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.65−7.57 (m, 2 H), 7.37−7.28 (m, 2 H), 7.23−7.15 (m, 2 H, 1 H), 6.48 (s, 1 H), 2.02 (d, J = 1.2, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 154.0, 138.9, 131.2, 128.6, 127.1, 123.7, 122.0, 107.8, 9.8; GC−MS (EI, 70 eV) m/z = 158 (M^+, 100), 129 (70), 128 (43), 127 (21), 115 (39), 102 (11), 89 (5), 77 (20). Anal. calcd for $C_{11}H_{10}O$ (158.20): C, 83.51; H, 6.37. Found: C, 83.74; H, 6.36.

*2,4-Diphenylfuran (**2b**).* Yield: 117 mg, starting from 238 mg of **1b** (53%) (Table 1, entry 2). Colorless solid: mp 108−110 °C, lit.[12] 109.5−110.5 °C; IR (KBr) ν = 3062 (m), 1610 (w), 1538 (w), 1492 (w), 1453 (m), 1200 (w), 914 (m), 809 (m), 749 (m), 691 (m) cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.75−7.65 (m, 3 H, 2 H), 7.55−7.47 (m, 2 H), 7.43−7.32 (m, 4 H), 7.31−7.21 (m, 2 H), 6.94 (s, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 154.8, 137.9, 132.3, 130.6, 128.8, 128.7, 128.4, 127.6, 127.1, 125.8, 123.8, 104.0; GC−MS (EI, 70 eV) m/z = 220 (M^+, 100), 192 (29), 191 (85), 190 (10), 189 (32), 165 (26), 139 (5), 115 (12), 94 (11), 63 (10). Anal. calcd for $C_{16}H_{12}O$ (220.27): C, 87.25; H, 5.49. Found: C, 87.16; H, 5.48.

*2-Butyl-4-phenylfuran (**2c**).* Yield: 160 mg, starting from 218 mg of **1c** (80%) (Table 1, entry 3). Colorless solid: mp 32−34 °C; IR (KBr) ν = 2957 (s), 2930 (s), 2871 (m), 1601 (m), 1449 (m), 1128 (m), 747 (s), 695 (s) cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.55 (s, 1 H), 7.46−7.35 (m, 2 H), 7.34−7.24 (m, 2 H), 7.22−7.12 (m, 1 H) 6.27 (s, 1 H), 2.61 (t, J = 7.7, 2 H), 1.69−1.57 (m, 2 H), 1.44−1.30 (m, 2 H), 0.92 (t, J = 7.3, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 157.7, 136.6, 133.0, 128.7, 127.0, 126.7, 125.7, 104.0, 30.1, 27.8, 22.3, 13.8; GC−MS (EI, 70 eV) m/z = 200 (M^+, 55), 171 (7), 158 (29), 157 (100), 141 (6), 129 (53), 128 (61), 127 (24), 115 (15), 102 (7), 77 (9). Anal. calcd for $C_{14}H_{16}O$ (200.28): C, 83.96; H, 8.05. Found: C, 83.90; H, 8.06.

*5-Butyl-2,3-diphenylfuran (**2d**).* Yield: 224 mg, starting from 294 mg of **1d** (81%) (Table 1, entry 4). Yellow oil: IR (film) ν = 3060 (m), 3030 (m), 2871 (m), 1558 (m), 1502 (m), 1448 (m), 1330 (m), 1130 (m), 1071 (m), 952 (m), 762 (m), 695 (m) cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.54−7.47 (m, 2 H), 7.42−7.36 (m, 2 H), 7.34−7.12 (m, 6 H), 6.14 (s, 1 H), 2.68 (t, J = 7.6, 2 H), 1.76−1.63 (m, 2 H), 1.43 (sextuplet, J = 7.3, 2 H), 0.95 (t, J = 7.3, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 155.7, 146.6, 134.8, 131.6, 128.60, 128.53, 128.3, 127.0, 126.9, 125.9, 123.0, 109.3, 30.1, 27.8, 22.4, 13.9; GC−MS m/z = 276 (M^+, 70), 234 (21), 233 (100), 215 (2), 203 (9), 189 (8), 178 (3), 127 (6), 105 (26), 77 (20). Anal. calcd for $C_{20}H_{20}O$ (276.37): C, 86.92; H, 7.29. Found: C, 86.94; H, 7.28.

*2-Butyl-4-hex-1-ynylfuran (**2e**).* Yield: 178 mg, starting from 321 mg of **1e** (87%) (Table 1, entry 5). Yellow oil: IR (film) ν = 2958 (m), 2933 (m), 2863 (m), 2230 (w), 1603 (m), 1466 (m), 1333 (m), 1133 (m), 944 (w), cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.39 (s, 1 H), 5.98 (s, 1 H) 2.56 (t, J = 7.5, 2 H), 2.36 (t, J = 6.9, 2 H), 1.65−1.24 (m, 8 H), 0.92 (t, J = 7.0, 3 H), 0.91 (t, J = 7.0, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 156.7, 143.2, 108.4, 107.8, 91.4, 71.9, 30.9, 29.9, 27.5, 22.2, 22.0, 19.2, 13.8, 13.6; GC−MS m/z = 204 (M^+, 63), 189 (11), 175 (5), 161 (100), 147 (14), 133 (11), 119 (32), 105 (30), 91 (54), 77 (23). Anal. calcd for $C_{14}H_{20}O$ (204.31): C, 82.30; H, 9.87. Found: C, 82.24; H, 9.88.

*5-Butyl-3-hex-1-ynyl-2-methylfuran (**2f**).* Yield: 199 mg, starting from 236 mg of **1f** (91%) (Table 1, entry 6). Pale yellow oil: IR (film) ν = 2958 (m), 2932 (m), 2862 (m), 2230 (w), 1580 (m), 1465 (m), 1232 (m), 1124 (w), 951 (w), 799 (m), 734 (m) cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 5.87 (s, 1 H), 2.51 (t, J = 7.7, 2 H), 2.37 (t, J = 6.9, 2 H), 2.28 (s, 3 H), 1.63−1.24 (m, 8 H), 0.93 (t, J = 7.4, 3 H), 0.91 (t, J = 7.4, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 154.0, 153.5, 107.6, 103.7, 92.0, 72.9, 31.1, 30.1, 27.5, 22.2, 22.0, 19.2, 13.8, 13.7, 12.5; GC−MS (EI, 70 eV) m/z = 218 (M^+, 28), 203 (1), 175 (100), 161 (2), 145 (4), 133 (11), 115 (4), 105 (5), 91 (8), 77 (6). Anal. calcd for $C_{15}H_{22}O$ (218.33): C, 82.52; H, 10.16. Found: C, 82.32; H 10.19.

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*5-Butyl-3-hex-1-ynyl-2-phenylfuran (**2g**).* Yield: 235 mg, starting from 298 mg of **1g** (84%) (Table 1, entry 7). Colorless oil: IR (film) ν = 2957 (m), 2927 (m), 2872 (m), 2232 (vw), 1600 (m), 1533 (w), 1493 (m), 1466 (m), 1254 (m), 1134 (m), 804 (m), 763 (m) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ = 8.07−7.99 (m, 2 H), 7.41−7.33 (m, 2 H), 7.28−7.19 (m, 1 H), 6.06 (t, J = 0.9, 1 H), 2.62 (td, J = 7.1, 0.9, 2 H), 2.47 (t, J = 6.9, 2 H), 1.70−1.32 (m, 8 H), 0.96 (t, J = 7.3, 3 H), 0.93 (t, J = 7.3, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 155.1, 152.3, 131.0, 128.3, 127.1, 124.1, 110.4, 103.9, 94.7, 74.1, 30.8, 30.0, 27.6, 22.2, 22.1, 19.5, 13.8, 13.6; GC−MS m/z = 280 (M^+, 55), 265 (2), 237 (100), 207 (4), 195 (9), 178 (8), 165 (22), 152 (11), 115 (5), 105 (22), 77 (28). Anal. calcd for $C_{20}H_{24}O$ (280.40): C, 85.67; H, 8.63. Found: C, 85.79; H, 8.62.

*5-tert-Butyl-3-(3,3-dimethyl-but-1-ynyl)-2-methylfuran-5-butyl-2,3-diphenylfuran (**2h**).* Yield: 177 mg, starting from 236 mg of **1h** (81%) (Table 1, entry 8). Yellow oil: IR (film) ν = 2968 (m), 2869 (w), 2217 (vw), 1575 (w), 1462 (m), 1362 (m), 1293 (m), 1232 (w), 1184 (w), 943 (m), 802 (m) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ = 5.86 (s, 1 H), 2.28 (s, 3 H), 1.28 (s, 9 H), 1.21 (s, 9 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 161.8, 153.2, 104.9, 103.4, 100.3, 71.4, 32.4, 31.3, 28.9, 28.1, 12.4; GC−MS m/z = 218 (M^+, 30), 203 (100), 188 (6), 173 (4), 145 (2), 115 (4), 105 (4), 91 (6). Anal. calcd for $C_{15}H_{22}O$ (218.33): C, 82.52; H, 10.16. Found: C, 82.59; H, 10.16.

*2-Methyl-5-phenyl-3-phenylethynylfuran (**2i**).* Yield: 217 mg, starting from 276 mg of **1i** (84%) (Table 1, entry 9). Colorless solid: mp 72−73 °C; IR (KBr) ν = 2213 (w), 1600 (m), 1556 (m), 1489 (m), 1439 (m), 1235 (w), 1154 (m), 1113 (w), 1048 (w), 1023 (w), 928 (m), 816 (m), 753 (s), 689 (s) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ = 7.64−7.58 (m, 2 H), 7.53−7.45 (m, 2 H), 7.38−7.16 (m, 6 H), 6.64 (s, 1 H) 2.48 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 155.9, 151.9, 131.4, 130.3, 128.7, 128.3, 128.0, 127.4, 123.6, 107.6, 105.4, 92.1, 81.6, 12.9; GC−MS m/z = 258 (M^+, 100), 229 (9), 216 (9), 215 (46), 213 (20), 189 (6), 163 (3), 152 (4), 129 (6), 105 (4), 77 (8). Anal. calcd for $C_{19}H_{14}O$ (258.31): C, 88.34; H, 5.56. Found: C, 88.59; H, 5.57.

*N-Boc-2-butyl-5-methylpyrrole (**4a**).* Yield: 134 mg, starting from 255 mg of **3a** (56%) (Table 3, entry 1). Yellow oil: IR (film) ν = 2958 (s), 2930 (s), 1737 (s), 1626 (w), 1539 (m), 1480 (w), 1388 (m), 1369 (m), 1314 (s), 1256 (m), 1219 (s), 1015 (w), 852 (m), 783 (m) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ = 5.82−5.78 (m, 2 H), 2.82−2.72 (m, 2 H), 2.37 (s, 2 H), 1.60−1.50 (m, 2 H), 1.59 (s, 9 H), 1.46−1.31 (m, 2 H), 0.93 (t, J = 7.3, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 150.5, 136.1, 131.2, 110.1, 109.0, 83.2, 31.4, 29.4, 28.1, 22.6, 16.5, 14.1; MS (ESI+, direct infusion) m/z = 260 [$(M + Na)^+$]. Anal. calcd for $C_{14}H_{23}NO_2$ (237.34): C, 70.85; H, 9.77; N, 5.90. Found: C, 70.80; H, 9.75; N, 5.91.

*N-Boc-2-benzyl-5-butylpyrrole (**4b**).* Yield: 219 mg, starting from 331 mg of **3b** (70%) (Table 3, entry 2). Yellow oil: IR (film) ν = 3019 (m), 2928 (w), 1734 (s), 1496 (m), 1371 (w), 1335 (m), 1216 (s), 1160 (m), 1126 (w), 755 (s) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ = 7.30−7.08 (m, 5 H), 5.84 (d, br, J = 3.2, 1 H), 5.68 (d, br, J = 3.2, 1 H), 4.16 (s, 2 H), 2.83−2.74 (m, 2 H), 1.65−1.50 (m, 2 H), 1.48−1.33 (m, 2 H), 1.42 (s, 9 H), 0.93 (t, J = 7.3, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 150.3, 140.2, 136.8, 133.4, 128.5, 128.2, 125.9, 111.5, 108.9, 83.4, 35.7, 31.3, 29.2, 27.7, 22.6, 14.0; MS (ESI+, direct infusion) m/z = 336 [$(M + Na)^+$]. Anal. calcd for $C_{20}H_{27}NO_2$ (313.43): C, 76.64; H, 8.68; N, 4.47. Found: C, 76.49; H, 8.70; N, 4.46.

*N-Boc-2-butyl-5-isopropylpyrrole (**4c**).* Yield: 202 mg, starting from 283 mg of **3c** (76%) (Table 3, entry 3). Yellow oil: IR (film) ν = 2966 (m), 2933 (m), 2873 (w), 1739 (s), 1458 (w), 1393 (w), 1369 (m), 1321 (m), 1159 (m), 1115 (m), 757 (m) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ = 5.87 (dd, J = 3.2, 0.8, 1 H); 5.83 (dt, J = 3.2, 0.8, 1 H), 3.50−3.35 (m, 1 H), 2.77−2.69 (m, 2 H), 1.63−1.50 (m, 2 H), 1.60 (s, 9 H), 1.46−1.32 (m, 2 H), 1.20 (d, J = 6.5, 6 H), 0.93 (t, J = 3.6, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 150.6, 142.4, 135.9, 108.6, 106.3, 83.3, 31.4, 29.3, 27.9, 27.1, 23.2, 22.6, 14.0; MS (ESI^+, direct infusion) m/z = 266 [$(M + H)^+$]. Anal. calcd for $C_{16}H_{27}NO_2$ (265.39): C, 72.41; H, 10.25; N, 5.28. Found: C, 72.30; H, 10.26; N, 5.27.

*N-Boc-2-benzyl-5-butyl-3-methylpyrrole (**4d**).* Yield: 246 mg, starting from 345 mg of **3d** (75%) (Table 3, entry 5). Yellow oil: IR (film) ν = 2962 (m), 2931 (m), 2877 (w), 1733 (s), 1373 (m), 1328 (m), 1252 (m), 1135 (m), 851 (m), 702 (m) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ = 7.25−7.17 (m, 2 H), 7.15−7.07 (m, 1 H), 7.02−6.95 (m, 2 H), 5.82 (s, 1 H), 4.18 (s, 2 H), 2.77 (t, J = 7.6, 2 H), 1.98 (s, 3 H), 1.64−1.50 (m, 2 H), 1.47−1.32 (m, 2 H), 1.30 (s, 9 H), 0.93 (t, J = 7.3, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 150.2, 141.0, 135.6, 128.1, 127.6, 127.3, 125.5, 119.4, 111.8, 82.9, 31.7, 31.4, 29.0, 27.5, 22.6, 14.1, 11.2; MS (ESI^+, direct infusion) m/z = 328 [$(M + H)^+$]. Anal. calcd for $C_{21}H_{29}NO_2$ (327.46): C, 77.02; H, 8.93; N, 4.28. Found: C, 77.09; H, 8.91; N, 4.28.

*N-Boc-2-butylpyrrole (**4e**).* Yield: 217 mg, starting from 241 mg of **3e** (97%) (Table 3, entry 6). Yellow oil: IR (film) ν = 2958 (m), 2932 (m), 1747 (s), 1405 (m), 1371 (m), 1330 (s), 1254 (w), 1171 (m), 1132 (m), 1064 (w), 852 (w), 717 (m) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ = 7.18 (dd, J = 3.2, 1.6, 1 H), 6.06 (t, J = 3.2, 1 H), 5.97−5.92 (m, 1 H), 2.83 (t, J = 7.6, 2 H), 1.66−1.50 (m, 2 H), 1.47−1.33 (m, 2 H), 1.59 (s, 9 H), 0.94 (t, J = 7.3, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 149.6, 136.5, 120.8, 110.7, 109.9, 83.1, 31.1, 28.6, 28.0, 22.5, 14.0; MS (ESI^+, direct infusion) m/z = 246 [$(M + Na)^+$]. Anal. calcd for $C_{13}H_{21}NO_2$ (223.31): C, 69.92; H, 9.48; N, 6.27. Found: C, 69.85; H, 9.50; N, 6.28.

*N-Boc-2-benzyl-5-phenylpyrrole (**4f**).* Yield: 106 mg, starting from 351 mg of **3f** (32%) (Table 3, entry 7). Colorless solid: mp 89−90 °C, lit.[13] 93−94 °C; IR (KBr) ν = 1736 (s), 1602 (w), 1527 (w), 1453 (w), 1369 (m), 1308 (s), 1213 (w), 1146 (m), 1066 (m), 790 (m), 763 (s), 698 (m) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ = 7.36−7.15 (m, 10 H), 6.10 (d, J = 3.2, 1 H), 5.84 (dt, J = 3.2, 0.9, 1 H), 4.22 (s, br, 2 H), 1.12 (s, 9 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 150.1, 139.5, 135.6, 135.3, 135.1, 128.8, 128.2, 127.7, 126.7, 126.1, 111.8, 111.4, 83.5, 34.8, 27.1; MS (ESI^+, direct infusion) m/z = 356 [$(M + Na)^+$]. Anal. calcd for $C_{22}H_{23}NO_2$ (331.17): C, 79.25; H, 6.95; N, 4.20. Found: C, 79.19; H, 6.97; N, 4.19.

*N-Boc-5-butyl-3-hex-1-ynyl-2-methylpyrrole (**4g**).* Yield: 314 mg, starting from 335 mg of **3g** (99%) (Table 3, entry 8). Pale yellow oil: IR (film) ν = 2968 (m), 2878 (m), 2229 (w), 1752 (s), 1548 (w), 1459 (w), 1338 (s), 1171 (m), 1108 (m), 856 (w) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ = 5.87 (t, J = 0.9, 1 H), 2.77−2.69 (m, 2 H), 2.43 (s, 3 H), 2.39 (t, J = 7.0, 2 H), 1.62−1.30 (m, 8 H), 1.58 (s, 9 H), 0.93 (t, J = 7.1, 3 H), 0.92 (t, J = 7.1, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 150.1, 135.3, 134.4, 111.8, 106.4, 91.6, 83.7, 74.9, 31.3, 29.0, 28.1, 22.5, 22.0, 19.3, 14.8, 14.0, 13.6; MS (ESI+, direct infusion) m/z = 340 [$(M + Na)^+$]. Anal. calcd for $C_{20}H_{31}NO_2$ (317.47): C, 75.67; H, 9.84; N, 4.41. Found: C, 75.75; H, 9.81; N, 4.43.

*N-Boc-2-benzyl-5-butyl-3-hex-1-ynylpyrrole (**4h**).* Yield: 287 mg, starting from 412 mg of **3h** (73%) (Table 3, entry 9). Colorless oil: IR (film) ν = 2958 (m), 2932 (m), 2872 (w), 2231 (vw), 1743 (s), 1455 (w), 1335 (s), 1167 (m), 1131 (m), 850 (w), 703 (w) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ = 7.26−7.18 (m, 2 H), 7.17−7.03 (m, 3 H), 5.96 (s, 1 H), 4.32 (s, 2 H), 2.72 (t, J = 7.5, 2 H), 2.35 (t, J = 6.9, 2 H), 1.60−1.46 (m, 4 H), 1.46−1.32 (m, 4 H), 1.31 (s, 9 H), 0.92 (t, J = 7.3, 3 H); 0.88 (t, J = 7.3, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 149.6, 140.5, 135.9, 135.6, 128.2, 127.9, 125.7, 111.4, 107.9, 91.7, 83.8, 74.7, 33.1, 31.1, 28.8, 27.5, 22.5, 22.0, 19.3, 14.0, 13.6; MS (ESI^+, direct infusion) m/z = 416 [$(M + Na)^+$]. Anal. calcd for $C_{26}H_{35}NO_2$ (393.56): C, 79.35; H, 8.96; N, 3.56. Found: C, 79.56; H, 8.95; N, 3.57.

*N-Boc-5-butyl-3-hex-1-ynyl-2-isobutylpyrrole (**4i**).* Yield: 280 mg, starting from 378 mg of **3i** (78%) (Table 3, entry 10). Colorless oil: IR (film) ν = 2957 (m), 2925 (m), 2879 (w), 2231 (vw), 1741 (s), 1469 (w), 1372 (w), 1322 (s), 1167 (m), 1123 (m), 759 (m) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ = 5.87 (s, br), 2.79 (d, J = 7.3, 2 H), 2.71 (t, J = 7.7, 2 H), 2.38 (t, J = 6.7, 2 H), 1.94−1.73 (m, 1 H), 1.60−1.29 (m, 8 H), 1.59 (s, 9 H), 0.98−0.81 (m, 12 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 150.1, 138.0, 135.3, 111.6, 107.4, 91.3, 83.6, 75.6, 36.4, 31.32, 31.26, 29.5, 29.0, 28.0, 27.9, 22.5, 22.4, 22.0, 19.3, 13.9, 13.6; MS (ESI^+, direct infusion) m/z = 382 [$(M + Na)^+$]. Anal. calcd for $C_{23}H_{37}NO_2$ (359.55): C, 76.83; H, 10.37; N, 3.90. Found: C, 76.70; H, 10.38; N, 3.89.

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*N-Boc-2-butyl-4-hex-1-ynylpyrrole (**4j**).* Yield: 222 mg, starting from 321 mg of **3j** (73%) (Table 3, entry 11). Yellow oil: IR (film) ν = 2958 (m), 2933 (m), 2872 (w), 2226 (w), 1749 (s), 1458 (w), 1370 (s), 1342 (s), 1272 (m), 1156 (m), 1109 (w), 1088 (w) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ = 7.26 (d, J = 2.0, 1 H), 5.97−5.94 (m, 1 H), 2.83−2.74 (m, 2 H), 2.36 (t, J = 6.9, 2 H), 1.63−1.32 (m, 8 H), 1.58 (s, 9 H), 0.93 (t, J = 7.2, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 148.9, 136.5, 123.6, 113.5, 106.8, 89.9, 83.6, 74.4, 31.0, 30.8, 28.3, 28.0, 22.4, 22.0, 19.2, 14.0, 13.7; MS (ESI$^+$, direct infusion) m/z = 326 [(M + Na)$^+$]. Anal. calcd for $C_{19}H_{29}NO_2$ (303.44): C, 75.21; H, 9.63; N, 4.62. Found: C, 75.34; H, 9.65; N, 4.61.

*N-Boc-2-methyl-5-phenyl-3-phenylethynylpyrrole (**4k**).* Yield: 293 mg, starting from 375 mg of **3k** (82%) (Table 3, entry 12). Colorless oil: IR (film) ν = 2983 (w), 2922 (w), 2210 (m), 1744 (s), 1489 (m), 1370 (m), 1327 (s), 1291 (m), 1250 (m), 1152 (m), 1133 (m), 1067 (w), 850 (m), 775 (m) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ = 7.52−7.47 (m, 2 H), 7.38−7.24 (m, 8 H), 6.24 (s, 1 H), 2.61 (s, 3 H), 1.25 (s, 9 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 149.6, 137.0, 134.5, 134.3, 131.3, 128.5, 128.3, 127.8, 127.7, 127.1, 123.9, 114.1, 106.0, 91.4, 84.1, 83.8, 27.3, 14.1; MS (ESI$^+$, direct infusion) m/z = 380 [(M + Na)$^+$]. Anal. calcd for $C_{24}H_{23}NO_2$ (357.44): C, 80.64; H, 6.49; N, 3.92. Found: C, 80.51; H, 6.50; N, 3.91.

*N-Tosyl-5-butyl-3-hex-1-ynyl-2-methylpyrrole (**4l**).* Yield: 308 mg, starting from 390 mg of **3l** (83%) (Table 3, entry 13). Brown oil: IR (film) ν = 2931 (m), 2872 (m), 2232 (w), 1739 (s), 1597 (w), 1457 (w), 1366 (s), 1251 (m), 1106 (m), 1092 (m), 813 (m), cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ = 7.55−7.48 (m, 2 H), 7.29−7.21 (m, 2 H), 5.94 (s, br, 1 H), 2.80−2.70 (m, 2 H), 2.44 (s, 3 H), 2.38 (s, 3 H), 2.37 (t, J = 6.9, 2 H), 1.63−1.28 (m, 8 H), 0.92 (t, J = 7.1, 3 H), 0.89 (t, J = 7.1, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 144.6, 137.2, 136.6, 135.3, 130.0, 126.2, 113.1, 108.1, 92.9, 73.9, 31.1, 31.0, 28.3, 22.4, 22.0, 21.5, 19.2, 14.1, 13.9, 13.6; MS (ESI+, direct infusion) m/z = 394 [(M + Na)$^+$]. Anal. calcd for $C_{22}H_{29}NO_2S$ (371.54): C, 71.12; H, 7.87; N, 3.77; S, 8.63. Found: C, 71.32; H, 7.86; N, 3.78; S, 8.61.

General Procedure for the Synthesis of 3-Acylfurans 5f−i by $CuCl_2$-Catalyzed Cyclodehydration/Acid-Catalyzed Water Addition of 2-Alkynyl-3-yne-1,2-diols 1f−i. In a typical experiment, a solution of pure **1** [**1f** (236 mg), **1g** (298 mg), **1h** (236 mg), **1i** (276 mg); 1.0 mmol] in anyhydrous MeOH (5.0 mL) was added to $CuCl_2$ (2.7 mg, 2.0 × 10^{-2} mmol) and TsOH monohydrate (38.1 mg, 0.2 mmol) under nitrogen in a Schlenk flask. The resulting mixture was stirred under nitrogen at 80 °C (for **1f−h**) or 100 °C (for **1i**) and was monitored by TLC until complete conversion of the substrate (3 h for **1f** and **1h**; 15 h for **1i**; 24 h for **1g**). Solvent was evaporated, and the crude products were purified by column chromatography on silica gel using as eluent 99:1 hexane−acetone (for **5f**, **5h**, and **5i**) or 98:2 hexane−AcOEt (for **5g**).

*1-(5-Butyl-2-methylfuran-3-yl)-hexan-1-one (**5f**).* Yield: 199 mg, starting from 236 mg of **1f** (84%) (Table 2, entry 1). Colorless oil: IR (film) ν = 2960 (m), 2931 (m), 2874 (m), 1713 (s), 1600 (m), 1467 (w), 1380 (m), 1217 (m), 759 (s) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ = 6.19 (s, 1 H), 2.65 (t, J = 7.3, 2 H), 2.56 (t, J = 7.7, 2 H), 2.54 (s, 3 H), 1.73−1.55 (m, 4 H), 1.45−1.26 (m, 6 H), 0.99−0.85 (m, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 196.9, 156.7, 154.4, 121.8, 105.0, 41.3, 31.7, 30.1, 27.5, 23.9, 22.6, 22.3, 14.3, 13.9, 13.8; GC−MS m/z = 236 (M$^+$, 21), 221 (2), 193 (22), 180 (78), 165 (100), 147 (3), 137 (41), 123 (16), 108 (4), 95 (8), 81 (10). Anal. calcd for $C_{15}H_{24}O_2$ (236.35): C, 76.23; H, 10.24. Found: C, 76.11; H, 10.24.

*1-(5-Butyl-2-phenylfuran-3-yl)-hexan-1-one (**5g**).* Yield: 266 mg, starting from 298 mg of **1g** (89%) (Table 2, entry 2). Yellow oil: IR (film) ν = 2957 (m), 2932 (m), 2872 (m), 1682 (s), 1541 (m), 1489 (m), 1386 (w), 1264 (w), 1169 (w), 768 (m), 692 (m) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ = 7.94−7.86 (m, 2 H), 7.47−7.33 (m, 3 H), 6.38 (s, 1 H), 2.70 (t, J = 7.3, 2 H), 2.66 (t, J = 7.6, 2 H), 1.74−1.58 (m, 4 H), 1.49−1.34 (m, 2 H), 1.34−1.23 (m, 4 H), 0.95 (t, J = 7.3, 3 H), 0.88 (t, J = 6.9, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 197.1, 155.6, 154.6, 130.5, 129.2, 128.2, 128.1, 122.6, 107.2, 41.8, 31.4, 29.9, 27.5, 24.0, 22.5, 22.2, 13.9, 13.8; GC−MS m/z = 298 (M$^+$, 35), 255 (21), 242 (47), 241 (41), 227 (100), 213 (5), 199 (9), 185 (9), 157 (8), 141 (3), 128 (12), 115 (8), 105 (51), 77 (26). Anal. calcd for $C_{20}H_{26}O_2$ (298.42): C, 80.50; H, 8.78. Found: C, 80.45; H, 8.76.

*1-(5-tert-Butyl-2-methylfuran-3-yl)-3,3-dimethylbutan-1-one (**5h**).* Yield: 184 mg, starting from 236 mg of **1h** (78%) (Table 2, entry 3). Colorless oil: IR (film) ν = 2957 (m), 2869 (w), 1668 (s), 1565 (m), 1464 (m), 1393 (m), 1364 (m), 1230 (m), 1108 (w), 1000 (w), 902 (m), 799 (m) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ = 6.13 (s, 1 H), 2.56 (s, 2 H), 2.55 (s, 3 H), 1.26 (s, 9 H), 1.06 (s, 9 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 196.3, 161.0, 156.1, 122.0, 102.0, 52.2, 31.7, 30.7, 29.3, 28.2, 13.9; GC−MS m/z = 236 (M$^+$, 35), 221 (80), 180 (61), 165 (100), 137 (7), 122 (5), 79 (9). Anal. calcd for $C_{15}H_{24}O_2$ (236.35): C, 76.23; H, 10.24. Found: C, 76.31; H, 10.26.

*1-(2-Methyl-5-phenylfuran-3-yl)-2-phenyl-ethanone (**5i**).* Yield: 207 mg, starting from 276 mg of **1i** (75%) (Table 2, entry 4). Yellow solid: mp 60−62 °C; IR (KBr) ν = 1680 (s), 1385 (m), 1360 (m), 1308 (m), 1198 (w), 1053 (w), 958 (m), 737 (m) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ = 7.65−7.59 (m, 2 H), 7.40−7.19 (m, 8 H), 6.86 (s, 1 H), 4.03 (s, 2 H), 2.63 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 193.8, 158.9, 151.7, 134.3, 129.9, 129.5, 128.7, 128.6, 127.8, 126.9, 123.7, 122.4, 104.8, 48.0, 14.5; GC−MS m/z = 276 (M$^+$, 21), 185 (100), 157 (22), 129 (8), 115 (26), 105 (6), 91 (6), 77 (11). Anal. calcd for $C_{19}H_{16}O_2$ (276.33): C, 82.58; H, 5.84. Found: C, 82.51; H, 5.83.

Synthesis of 2-Benzyl-5-phenylpyrrole 6f by $CuCl_2$-Catalyzed Heterocyclodehydration of *N*-Boc-4-amino-1,5-diphenylpent-1-yn-3-ol 3f, Followed by Basic Treatment (Scheme 2). A solution of *N*-Boc-4-amino-1,5-diphenylpent-1-yn-3-ol **3f** (351 mg, 1 mmol) in anyhydrous MeOH (5.0 mL) was added to $CuCl_2$ (2.7 mg, 6.8 mg, 5 × 10^{-2} mmol) under nitrogen in a Schlenk flask. The resulting mixture was stirred under nitrogen at 100 °C for 24 h. After cooling to room temperature, MeONa (162 mg, 3 mmol) was added under nitrogen, and the resulting mixture was heated at 100 °C for 15 h. After cooling, solvent was evaporated, and the crude product was purified by column chromatography on silica gel using 95:5 hexane−AcOEt as eluent. Yield: 124 mg, starting from 351 mg of **3f** (53%) (Scheme 2). Colorless solid: mp 91−92 °C; IR (KBr) ν = 3434 (m, br), 1603 (m), 1513 (m), 1453 (w), 1214 (w), 1041 (m), 783 (w), 760 (m), 721 (s), 690 (m) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ = 8.02 (s, br, 1 H); 7.43−7.22 (m, 9 H); 7.17−7.12 (m, 1 H), 6.46−6.41 (m, 1 H), 6.07−6.02 (m, 1 H), 4.02 (s, 2 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ = 139.3, 132.8, 132.0, 131.5, 128.8, 128.69, 128.67, 126.6, 125.8, 123.5, 108.6, 106.1, 34.3; GC−MS m/z = 233 (M$^+$, 99), 232 (47), 156 (100), 128 (16), 115 (13), 104 (7), 89 (6), 77 (18). Anal. calcd for $C_{17}H_{15}N$ (233.31): C, 87.52; H, 6.48; N, 6.00. Found: C, 87.65; H, 6.47; N 6.01.

General Procedure for the Synthesis of 3-Acylpyrroles 7g−i, 7k, 7m−o and 9 by $CuCl_2$-Catalyzed Heterocyclodehydration/Acid- and CO_2-Promoted Water Addition of *N*-Boc-2-alkynyl-1-amino-3-yn-2-ols 3g−i, 3k, 3m−o, and of (*S*)-7-(Pyrrolidin-2-yl)trideca-5,8-diyn-7-ol 8. A 250 mL stainless steel autoclave was charged in the presence of air with $CuCl_2$ (4.0 mg, 2.98 × 10^{-2} mmol), anhydrous MeOH (7.4 mL), (*S*)-7-(pyrrolidin-2-yl)trideca-5,8-diyn-7-ol **8** (389 mg, 1.49 mmol) or *N*-Boc-2-alkynyl-1-amino-3-yn-2-ols [**3g** (500 mg), **3h** (613 mg), **3i** (563 mg), **3k** (559 mg), **3m** (500 mg), **3n** (542 mg), **3o** (563 mg), 1.49 mmol], TsOH monohydrate (56.6 mg, 0.3 mmol) and H_2O (26.8 mg,1.49 mmol). The autoclave was sealed, and while the mixture was stirred, the autoclave was pressurized with CO_2 (40 atm). After being stirred at 100 °C for 15 h, the autoclave was cooled, degassed and opened. The crude products were purified by column chromatography on silica gel (8:2 hexane−AcOEt for **7g−i**, **7k**, **7m**, **7n**, **9**; 99:1 hexane−acetone for **7o**).

*1-(5-Butyl-2-methyl-1H-pyrrol-3-yl)-hexan-1-one (**7g**).* Yield: 245 mg, starting from 500 mg of **3g** (70%) (Table 5, entry 1). Yellow solid: mp 48−49 °C; IR (KBr) ν = 3266 (m), 2952 (m), 2929 (m), 2860 (w), 1636 (s), 1585 (m), 1522 (m), 1468 (m), 1384 (m), 1193 (m), 961 (m), 788 (m), 728 (w) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ = 8.84 (s, br, 1 H), 6.20−6.14 (m, 1 H), 2.71 (t, J = 7.6, 2 H), 2.56−2.48 (m, 5 H), 1.75−1.52 (m, 4 H), 1.41−1.25 (m, 6 H), 0.95−0.85 (m, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 198.1, 134.0, 130.8, 120.6, 106.5, 40.6, 31.9, 31.6, 27.1, 24.7, 22.6, 22.4, 13.95, 13.91, 13.8; GC−MS m/z

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= 235 (M^+, 7), 192 (14), 179 (22), 164 (100), 150 (7), 136 (34), 122 (15), 107 (24), 93 (44). Anal. calcd for $C_{15}H_{25}NO$ (235.37): C, 76.55; H, 10.71; N, 5.95. Found: C, 76.58; H, 10.68; N, 5.96.

*1-(2-Benzyl-5-butyl-1H-pyrrol-3-yl)-hexan-1-one (**7h**).* Yield: 381 mg, starting from 613 mg of **3h** (82%) (Table 5, entry 2). Yellow oil: IR (film) ν = 3375 (m, br), 2956 (m), 2930 (m), 2859 (m), 1635 (s), 1587 (m), 1516 (m), 1461 (s), 1396 (m), 1191 (m), 959 (m), 794 (m), 725 (m) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ = 8.97 (s, br, 1 H), 7.23−7.16 (m, 5 H), 6.22−6.18 (m, 1 H), 2.68 (t, J = 7.6, 2 H), 2.44 (t, J = 7.6, 2 H), 1.71−1.46 (m, 4 H), 1.37−1.20 (m, 6 H), 0.92−0.83 (m, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 198.1, 138.9, 136.1, 131.6, 128.9, 128.6, 126.4, 120.5, 106.6, 40.6, 33.7, 31.8, 31.5, 27.1, 24.7, 22.6, 22.3, 13.9, 13.8; GC−MS m/z = 311 (M^+, 36), 268 (38), 255 (25), 240 (100), 212 (47), 196 (19), 183 (89), 168 (92), 164 (53), 154 (21), 141 (11), 115 (14), 91 (46). Anal. calcd for $C_{21}H_{29}NO$ (311.46): C, 80.98; H, 9.38; N, 4.50. Found: C, 81.0; H, 9.35; N, 4.49.

*1-(5-Butyl-2-isobutyl-1H-pyrrol-3-yl)-hexan-1-one (**7i**).* Yield: 281 mg, starting from 563 mg of **3i** (68%) (Table 5, entry 3). Yellow oil: IR (film) ν = 3281 (m), 2957 (s), 2925 (s), 2868 (m), 1631 (s), 1588 (w), 1517 (m), 1466 (s), 1394 (m), 1288 (w), 961 (w), 795 (m) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ = 9.26 (s, br, 1 H), 6.22−6.16 (m, 1 H), 2.81 (d, J = 6.9, 2 H), 2.72 (t, J = 7.6, 2 H), 2.54 (t, J = 7.6, 2 H), 1.99 (nonuplet, J = 6.9, 1 H), 1.75−1.53 (m, 4 H), 1.42−1.23 (m, 6 H), 0.94−0.85 (m, 12 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 198.0, 138.2, 130.9, 120.3, 106.6, 40.7, 36.8, 31.8, 31.6, 28.9, 27.1, 24.9, 22.6, 22.5, 22.4, 13.9, 13.8; GC−MS m/z = 277 (M^+, 25), 234 (93), 221 (20), 206 (76), 178 (88), 164 (100), 136 (32), 120 (23), 107 (27), 93 (69). Anal. calcd for $C_{18}H_{31}NO$ (277.44): C, 77.92; H, 11.26; N, 5.05. Found: C, 77.94; H, 11.29; N, 5.03.

*1-(2-Methyl-5-phenyl-1H-pyrrol-3-yl)-2-phenyl-ethanone (**7k**).* Yield: 328 mg, starting from 559 mg of **3k** (80%) (Table 5, entry 4). Yellow solid: mp 176 −178 °C; IR (KBr) ν = 3273 (m), 1623 (s), 1475 (m), 1448 (m), 1197 (m), 1144 (w), 1071 (w), 988 (w), 815 (m), 765 (m), 729 (m), 693 (m) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ = 9.04 (s, br, 1 H), 7.48−7.42 (m, 2 H), 7.38−7.15 (m, 8 H), 6.86−6.83 (m, 1 H), 4.10 (s, 2 H), 2.53 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 194.8, 137.3, 135.5, 131.7, 130.0, 129.5, 129.0, 128.5, 126.7, 126.6, 123.8, 121.4, 107.1, 47.2, 14.1; GC−MS m/z = 275 (M^+, 8), 184 (100), 156 (5), 129 (17), 115 (7), 104 (8), 91 (10), 77 (7). Anal. calcd for $C_{19}H_{17}NO$ (275.34): C, 82.88; H, 6.22; N, 5.09. Found: C, 82.90; H, 6.27; N, 5.08.

*1-(5-tert-Butyl-2-methyl-1H-pyrrol-3-yl)-3,3-dimethylbutan-1-one (**7m**).* Yield: 305 mg, starting from 500 mg of **3m** (87%) (Table 5, entry 5). Yellow solid: mp 202−204 °C; IR (KBr) ν = 3283 (m, br), 2959 (m), 2867 (w), 1628 (s), 1576 (m), 1515 (m), 1474 (m), 1385 (m), 1362 (m), 1241 (m), 974 (m), 794 (m) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ = 8.51 (s, br), 6.16−6.13 (m, 1 H); 2.23 (s, 2 H), 3.16 (s, 3 H), 1.29 (s, 9 H), 1.06 (s, 9 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 197.6, 139.3, 133.8, 121.8, 104.7, 52.3, 31.1, 30.4, 30.3, 28.4, 14.1; GC−MS m/z = 235 (25), 220 (43), 179 (23), 164 (100), 148 (7), 121 (15). Anal. calcd for $C_{15}H_{25}NO$ (235.37): C, 76.55; H, 10.71; N, 5.95. Found: C, 76.54; H, 10.69; N, 5.96.

*1-(5-Butyl-2-isopropyl-1H-pyrrol-3-yl)-hexan-1-one (**7n**).* Yield: 279 mg, starting from 542 mg of **3n** (71%) (Table 5, entry 6). Yellow oil: IR (film) ν = 3297 (m, br), 2957 (m), 2930 (s), 2869 (m), 1630 (s), 1591 (m), 1514 (m), 1467 (s), 1402 (m), 1293 (m), 1191 (w), 1164 (w), 1074 (w), 953 (m), 796 (m) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ = 9.32 (s, br, 1 H), 6.22−6.16 (m, 1 H), 3.89 (heptuplet, J = 6.9, 1 H, 1 H), 2.74 (t, J = 7.5, 2 H), 2.55 (t, J = 7.6, 2 H), 1.77−1.54 (m, 4 H), 1.44−1.29 (m, 6 H), 1.25 (d, J = 6.9, 6 H), 0.95−0.84 (m, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 198.0, 144.3, 130.9, 118.9, 106.6, 40.9, 31.9, 31.6, 27.2, 26.4, 24.9, 22.6, 22.5, 21.8, 14.0, 13.8; GC−MS m/z = 263 (M^+, 17), 248 (6), 220 (21), 207 (20), 192 (100), 178 (8), 164 (21), 150 (12), 120 (16), 106 (35). Anal. calcd for $C_{17}H_{29}NO$ (263.42): C, 77.51; H, 11.10; N, 5.32. Found: C, 77.49; H, 11.07; N, 5.31.

*1-(5-tert-Butyl-2-isobutyl-1H-pyrrol-3-yl)-3,3-dimethyl-butan-1-one (**7o**).* Yield: 322 mg, starting from 563 mg of **3o** (78%) (Table 5, entry 7). Yellow solid: mp 126−128 °C; IR (KBr) ν = 3287 (m, br), 2958 (m), 2868 (w), 1628 (s), 1580 (m), 1470 (m), 1365 (m), 1232 (m), 1003 (w), 975 (w), 794 (m) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ = 8.27 (s, br), 6.17−6.12 (m, 1 H), 2.81 (d, J = 6.8, 2 H), 2.60 (s, 2 H), 1.97 (nonuplet, J = 6.8, 1 H), 1.29 (s, 9 H), 1.05 (s, 9 H), 0.88 (d, J = 6.8, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 197.4, 139.0, 137.8, 121.5, 104.9, 52.4, 36.9, 31.4, 31.0, 30.31, 30.27, 28.8, 22.4; GC−MS m/z = 277 (M^+, 49), 262 (50), 234 (100), 221 (27), 220 (45), 206 (76), 190 (7), 178 (72), 164 (14), 148 (8), 135 (13), 120 (14). Anal. calcd for $C_{18}H_{31}NO$ (277.44): C, 77.92; H, 11.26; N, 5.05. Found: C, 77.90; H, 11.29; N, 5.04.

*1-(3-Butyl-6,7-dihydro-5H-pyrrolizin-1-yl)-hexan-1-one (**9**).* Yield: 265 mg, starting from 389 mg of **8** (68%) (eq 2). Yellow oil: IR (film) ν = 2957 (m), 2931 (s), 2872 (m), 1652 (s), 1520 (m), 1431 (m), 1299 (w), 754 (m) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ = 6.30−6.26 (m, 1 H), 3.85 (t, J = 7.2, 2 H), 3.09 (t, J = 7.5, 2 H), 2.64 (t, J = 7.5, 2 H), 2.56−2.46 (m, 4 H), 1.75−1.52 (m, 4 H), 1.46−1.28 (m, 6 H), 0.98−0.84 (m, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 196.2, 142.0, 129.4, 116.9, 109.1, 44.9, 39.9, 31.9, 31.1, 27.0, 26.5, 26.2, 24.8, 22.6, 22.4, 14.0, 13.8; MS (ESI$^+$, direct infusion) m/z = 284 [$(M + Na)^+$]. Anal. calcd for $C_{17}H_{27}NO$ (261.40): C, 78.11; H, 10.41; N, 5.36. Found: C, 78.13; H, 10.43; N, 5.35.

Synthesis of 3-Acylpyrrole 7p by $CuCl_2$-Catalyzed Heterocyclodehydration/Acid- and CO_2-Promoted Water addition of (*S*)-*N*-Boc-4-amino-3-ethynyl-6-methylhept-1-yn-3-ol 3p. (*S*)-*N*-Boc-4-Amino-6-methyl-1-trimethylsilanyl-3-trimethylsilanylethynyl-hept-1-yn-3-ol **3p′** (5.87 g, 14.3 mmol) was dissolved in 50 mL of anhydrous methanol. To the solution was added anhydrous K_2CO_3 (0.36 g, 2.86 mmol), and the resulting mixture was stirred under nitrogen at room temperature for 15 h. Methanol was evaporated in order to remove ca. three-fourths of the initial volume, and successively to the crude product were added diethyl ether (50 mL) and water (50 mL). The two phases were separated, and the aqueous phase was extracted with diethyl ether (2 × 50 mL). The collected organic layers were dried over Na_2SO_4. Filtration and evaporation of the solvent led to crude (*S*)-*N*-Boc-4-amino-3-ethynyl-6-methylhept-1-yn-3-ol **3p**, which was used as such without further purification for the next step. A 250 mL stainless steel autoclave was charged in the presence of air with $CuCl_2$ (4.0 mg, 2.98 × 10^{-2} mmol), anhydrous MeOH (7.4 mL), crude **3p** (395 mg, formally deriving from 500 mg of **3p′**, 1.49 mmol], TsOH monohydrate (56.6 mg, 0.3 mmol) and H_2O (26.8 mg, 1.49 mmol). The autoclave was sealed, and while the mixture was stirred, the autoclave was pressurized with CO_2 (40 atm). After being stirred at 100 °C for 15 h, the autoclave was cooled, degassed and opened. The crude product 1-(2-isobutyl-furan-3-yl)-ethanone **7p** was purified by column chromatography on silica gel using 8:2 hexane−AcOEt as eluent. Yield: 202 mg, starting from 500 mg of **3p′** (82%). Colorless oil: IR (KBr) ν = 3264 (m, br), 2957 (m), 1637 (s), 1560 (m), 1464 (m), 1389 (m), 938 (m), 896 (w), 719 (w) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ = 9.95 (s, br, 1 H), 6.62−6.57 (m, 1 H), 6.56−6.51 (m, 1 H), 2.86 (d, J = 6.8, 2 H), 2.44 (s, 3 H), 2.03 (nonuplet, J = 6.8, 1 H), 0.90 (d, J = 6.8, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 195.7, 139.5, 120.4, 116.0, 110.8, 36.7, 28.8, 28.5, 22.5; GC−MS m/z = 165 (M^+, 41), 150 (19), 132 (3), 122 (100), 108 (26), 94 (9), 79 (9). Anal. calcd for $C_{10}H_{15}NO$ (165.23): C, 72.69; H, 9.15; N, 8.48. Found: C, 72.80; H, 9.17; N, 8.46.

■ ASSOCIATED CONTENT

Supporting Information

Copies of ^1H and ^{13}C NMR spectra for all products. 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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