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A Palladium Iodide-Catalyzed Carbonylative Approach to Functionalized Pyrrole Derivatives

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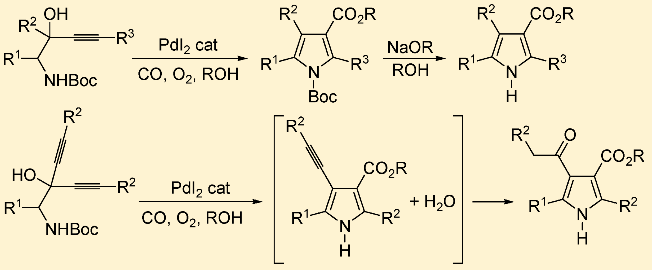
S *Supporting Information*



ABSTRACT: A novel and convenient approach to functionalized pyrroles is presented, based on Pd-catalyzed oxidative heterocyclization–alkoxycarbonylation of readily available *N*-Boc-1-amino-3-yn-2-ols. Reactions were carried out in alcoholic solvents at 80–100 °C and under 20 atm (at 25 °C) of a 4:1 mixture of CO–air, in the presence of the PdI_2–KI catalytic system (2–5 mol % of PdI_2, KI/PdI_2 molar ratio = 10). In the case of *N*-Boc-1-amino-3-yn-2-ols **3**, bearing alkyl or aryl substituents, the carbonylation reaction led to a mixture of Boc-protected and *N*-unsubstituted pyrrole-3-carboxylic esters **4** and **5**, respectively. This mixture could be conveniently and quantitatively converted into deprotected pyrrole-3-carboxylic esters **5** by a simple basic treatment. In the case of diastereomeric (3*RS*,4*RS*)- and (3*RS*,4*SR*)-*N*-Boc-3-amino-2-methyldec-5-yn-4-ol (*syn*-**3f** and *anti*-**3f**, respectively, whose relative configuration was determined by X-ray crystallographic analysis), no particular difference was observed in the reactivity of the two diastereomers between them and with respect to the diastereomeric mixture (3*S*,4*S*) + (3*S*,4*R*). Interestingly, *N*-Boc-2-alkynyl-1-amino-3-yn-2-ols **6**, bearing an additional alkynyl substituent α to the hydroxyl group, spontaneously underwent *N*-deprotection under the reaction conditions and regioselective water addition to the alkynyl group at C-3 of the corresponding pyrrole-3-carboxylic ester derivative, thus directly affording highly functionalized pyrrole derivatives **7** in one step. In a similar manner, a novel functionalized dihydropyrrolizine derivative **9** was directly synthesized starting from (*S*)-7-(pyrrolidin-2-yl)trideca-5,8-diyn-7-ol **8**.

INTRODUCTION

The PdI_2–KI catalytic system, introduced by our research group about 20 years ago,[1] is now established as one of the most efficient and versatile catalysts for the oxidative carbonylation of simple and functionalized alkynes[1−3] as well as of amines,[4] amino alcohols,[5] and diols,[6] with only oxygen as oxidizing agent. The main success of this system is due to the very efficient mechanism for the reoxidation of the Pd(0) species ensuing from the oxidative carbonylation process, which occurs through oxidative addition of I_2, formed in its turn by oxidation of the HI also ensuing from the process (Scheme 1; anionic iodide ligands are omitted for clarity; SH_2 = substrate).[1−3]

Scheme 1. Mechanism of Pd(0) Reoxidation in PdI_2-Catalyzed Oxidative Carbonylation Reactions[a]

$$SH_2 + CO + PdI_2 \longrightarrow \text{carbonylated product(s)} + Pd(0) + 2\,HI$$

$$2\,HI + (1/2)\,O_2 \longrightarrow I_2 + H_2O$$

$$Pd(0) + I_2 \longrightarrow PdI_2$$

[a]SH_2 = organic substrate(s).

In particular, the PdI_2/KI catalytic system has proved valuable for the direct synthesis of a variety of carbonylated heterocyclic derivatives starting from suitably functionalized alkynes, by either a cyclocarbonylation or a cyclization–carbonylation pathway.[2−6] Very recently, we have reported that furan-3-carboxylic esters **2** can be obtained in good yields (56–72%) by PdI_2/KI-catalyzed 5-*endo-dig* heterocyclodehydration-alkoxycarbonylation of 3-yne-1,2-diols **1** (Scheme 2, Y = O).[2c] Reactions were carried out in alcoholic solvents at 100 °C and under 40 atm of a 4:1 mixture of CO–air.

In this study, we have investigated the reactivity of *N*-Boc-1-amino-3-yn-2-ols **3** under similar conditions, to verify if the methodology could be also applied to the synthesis of *N*-Boc-pyrrole-3-carboxylic esters **4** and, after deprotection, of *N*-unsubstituted pyrrole-3-carboxylic esters **5**. Pyrrole-3-carboxylic ester derivatives represent, in fact, a particularly important subclass of pyrrole derivatives,[7] which have been so far obtained by synthetic methods not involving a direct carbonylation approach.[8]

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Scheme 2. PdI_2/KI-Catalyzed Formation of Furan-3-carboxylic Esters 2 and Pyrrole-3-carboxylic Esters 4 and 5 by Oxidative Carbonylation of 3-Yne-1,2-diols 1 or *N*-Boc-1-amino-3-yn-2-ols 3, Respectively

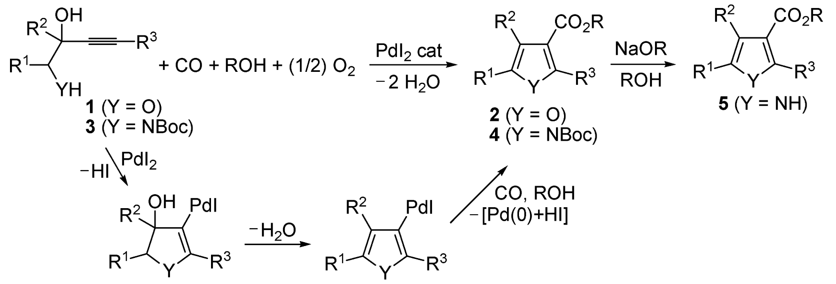
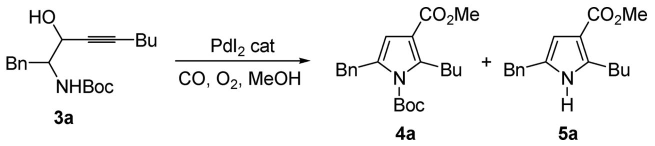


Table 1. PdI_2/KI-Catalyzed Oxidative Carbonylation Reactions of *N*-Boc-2-amino-1-phenylnon-4-yn-3-ol 3a Under Different Conditions[a]



entry	KI:PdI_2 molar ratio	*T* (°C)	substrate concentration[b]	time (h)	yield of **4a**[c] (%)	yield of **5a**[c] (%)	total yield (%)
1	10	80	0.20	3	4	66	70
2	10	80	0.20	2	4	47	51[d]
3	10	100	0.20	3	18	14	32
4	10	60	0.20	3		38	38[d]
5	10	80	0.05	3		57	57
6	10	80	0.50	3	5	49	54
7	50	80	0.20	3	15	42	57
8	5	80	0.20	3	10	55	65
9	2	80	0.20	3	18	47	65
10[e]	10	80	0.20	3		60	60[f]

[a] Substrate **3a** was directly used as a (2*S*,3*S*) and (2*S*,3*R*) mixture of diastereoisomers (see the Experimental Section for details). Unless otherwise noted, all reactions were carried out in MeOH in the presence of 2 mol % of PdI_2 under 20 atm (at 25 °C) of a 4:1 mixture CO−air. Unless otherwise noted, substrate conversion was quantitative. [b] mmol of starting **3a** per mL of MeOH. [c] Isolated yield based on starting **3a**. The formation of unidentified heavy products (chromatographically immobile materials) accounted for the difference between the substrate conversion and the product yield. [d] Substrate conversion was 70%. [e] The reaction was carried out under 40 atm of a 4:1 mixture (at 25 °C) of CO−air. [f] Substrate conversion was 79%.

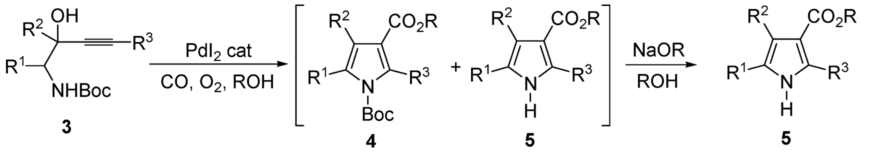
■ RESULTS AND DISCUSSION

PdI_2/KI-Catalyzed Oxidative Carbonylation of *N*-Boc-1-amino-3-yn-2-ols Bearing Alkyl or Aryl Substituents (3a−g). The reactivity of *N*-Boc-2-amino-1-phenylnon-4-yn-3-ol **3a**, easily obtained from Boc-protected L-phenylalaninal by alkynylation with 1-hexynylmagnesium bromide (see the Experimental Section for details), was investigated first. This substrate, directly employed as a mixture of diastereoisomers (2*S*,3*S*) and (2*S*,3*R*), was initially let to react at 80 °C in MeOH (substrate concentration = 0.2 mmol per mL of MeOH) under 20 atm of a 4:1 mixture CO−air,[9] in the presence of PdI_2 (2 mol %) and KI (KI/PdI_2 molar ratio = 10). After 3 h, analysis of the reaction mixture revealed a total substrate conversion and the formation of two products, which were separated and identified as methyl *N*-Boc-5-benzyl-2-butylpyrrole-3-carboxylate **4a** (4% yield) and methyl 5-benzyl-2-butyl-1*H*-pyrrole-3-carboxylate **5a** (66% yield) (Table 1, entry 1), thus confirming the validity of our initial work hypothesis. In fact, formation of **4a** can be rationalized by 5-*endo-dig* intramolecular nucleophilic attack by nitrogen to the triple bond coordinated to the metal center, followed by dehydration, carbon monoxide insertion, and nucleophilic displacement by MeOH (Scheme 2, Y = NBoc, R = Me), while *N*-unsubstitued pyrrole **5a** is clearly formed by deprotection of the nitrogen of **4a** under the reaction conditions.

With reference to the total yield of the carbonylated products (**4a** + **5a**), this initial result did not improve by changing the reaction parameters, such as the reaction time (Table 1, entry 2), temperature (Table 1, entries 3 and 4), substrate concentration (Table 1, entries 5 and 6), KI:PdI_2 molar ratio (Table 1, entries 7−9), and total pressure (Table 1, entry 10), even though the reaction allowed the predominant formation of product **5a** under some conditions (Table 1, entries 4, 5, and 10). In any case, a total conversion of **4a** into **5a**, with selective formation of unprotected pyrrole-3-carboxylic ester **5a**, could be achieved by treating the crude reaction mixture with NaOMe at 60 °C for 8 h.[10] In this way, a 68% isolated yield of **5a** was achieved by carrying out the carbonylation reaction under the conditions reported in entry 1 (Table 1) followed by basic treatment (Table 2, entry 1).

Having established a simple and efficient two-step protocol for the synthesis of *N*-unprotected pyrrole-3-carboxylic ester **5a** starting from *N*-Boc-2-amino-1-phenylnon-4-yn-3-ol **3a**, we next assessed the generality of the process by applying this procedure to other *N*-Boc-1-amino-3-yn-2-ols, variously substituted with different alkyl or aryl groups. The results obtained, shown in Table 2, demonstrate that the process is quite general, with the corresponding pyrrole-3-carboxylic esters being consistently obtained in satisfactory yields (61−89%). In some cases, better results were observed by carrying out the

Table 2. Synthesis of *N*-Unsubstituted Pyrrole-3-carboxylic Esters **5** by PdI_2/KI-Catalyzed Oxidative Carbonylation of *N*-Boc-1-amino-3-yn-2-ols **3** Followed by Basic Treatment[a,b]



entry	3	R^1	R^2	R^3	R	PdI_2 (mol %)	*T* (°C)	*t* (h)	yield of **4**[c] (%)	yield of **5**[c] (%)	overall yield of **5**[d] (%)
1	**3a**	Bn	H	Bu	Me	2	80	3	4	66	68
2	**3b**	Bn	Me	Bu	Me	2	80	3	71	20	89
3	**3c**	H	H	Bu	Me	5	80	3	44	18	61[e]
4	**3d**	Me	H	Bu	Me	2	100	2	54	16	70[e]
5	**3e**	Me	H	Ph	Me	2	100	2	47	34	80[e]
6	**3f**	*i*-Pr	H	Bu	Me	2	100	2	15	44	58[f]
7	**3f**	*i*-Pr	H	Bu	Me	5	100	2	31	49	79[f]
8[g]	*syn*-**3f**	*i*-Pr	H	Bu	Me	5	100	2	31	50	80[f]
9[h]	*anti*-**3f**	*i*-Pr	H	Bu	Me	5	100	2	29	53	81[f]
10	**3g**	Bn	H	Ph	Et	2	100	2	53	12	65[i]

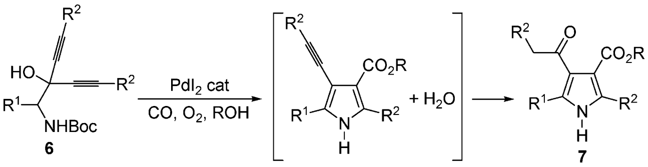
[a] All carbonylation reactions were carried out in ROH (0.20 mmol of starting **3** per mL of solvent) with a KI:PdI_2 molar ratio = 10. With the exception of entries 3, 8, and 9, all the starting **3** employed were (*SS*) + (*SR*) diastereomeric mixtures (see the Experimental Section for details). Conversion of **3** was quantitative in all cases. [b] Unless otherwise noted, the basic treatment was carried out on the carbonylation reaction crude by adding to the mixture 4 equiv of NaOMe (with respect to starting **3**) and allowing the resulting mixture to react at 60 °C for 8 h (see the Experimental Section for details). [c] Isolated yield based on starting **3**, referred to the oxidative carbonylation step. [d] Overall isolated yield based on starting **3**, referred to the oxidative carbonylation step followed by the one-pot basic treatment. [e] The basic treatment was carried out by adding, to the carbonylation crude, 4 equiv of NaOMe (with respect to starting **3**) and allowing the resulting mixture to react at 25 °C for 15 h. [f] The basic treatment was carried out by adding, to the carbonylation crude, 16 equiv of NaOMe (with respect to starting **3f**) and allowing the resulting mixture to react at 25 °C for 72 h. [g] The substrate employed was a racemic mixture of the *syn*-diastereomer, or (3*RS*,4*RS*)-diastereomer. [h] The substrate employed was a racemic mixture of the *anti*-diastereomer, or (3*RS*,4*SR*)-diastereomer. [i] The basic treatment was carried out on the carbonylation reaction crude by adding to the mixture 4 equiv of NaOEt (with respect to starting **3g**) and allowing the resulting mixture to react at 60 °C for 8 h.

carbonylation step at 100 °C (Table 2, entries 4−10) or with a higher catalyst loading (Table 2, entries 3, 7−9) and the deprotection step at 25 °C rather than 60 °C (Table 2, entries 3−9). The process could also be carried out successfully in EtOH rather than MeOH as reactant and solvent, as shown by entry 10 (Table 2).

The influence of the substrate stereochemistry on the reaction outcome was also investigated by reacting separately the two racemic *syn* and *anti* diastereomers (3*RS*,4*RS*) and (3*RS*,4*SR*) of *N*-Boc-3-amino-2-methyldec-5-yn-4-ol **3f** (whose relative configuration was established by X-ray diffraction analysis; see the Supporting Information for details), obtained from racemic valinal. As shown in Table 2, entries 8 and 9, the two diastereomers gave practically the same results, which were also comparable with that obtained starting directly from the diastereomeric mixture (3*S*,4*S*) + (3*S*,4*R*) (Table 2, entry 7), so it can be concluded that the stereochemistry of the substrate does not significantly affect the reaction outcome.

PdI_2/KI-Catalyzed Oxidative Carbonylation of *N*-Boc-2-alkynyl-1-amino-3-yn-2-ols (6a−g) and (*S*)-7-(Pyrrolidin-2-yl)trideca-5,8-diyn-7-ol (8). Very interestingly, when the oxidative carbonylation reaction was carried out on *N*-Boc-2-alkynyl-1-amino-3-yn-2-ols **6**, bearing an additional alkynyl substituent α to the hydroxyl group, *N*-deprotection occurred spontaneously under the reaction conditions, together with regioselective water addition to the triple bond of the alkynyl substituent, with direct formation of polysubstituted and multifunctionalized pyrrole derivatives **7** in one step (Scheme 3). The regioselectivity of the water addition to the triple bond may be due to the higher stability of the products obtained, in which the carbonyl group is conjugated with the aromatic pyrrole ring. Regarding the spontaneous *N*-deprotection, we refrain to suggest a possible explanation, which would require additional investigation.

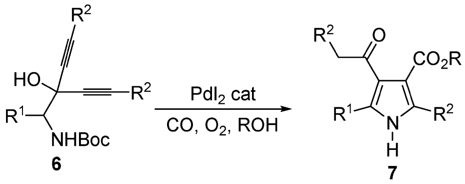
Scheme 3. PdI_2/KI-Catalyzed Formation of 4-Acylpyrrole-3-carboxylic Esters **7** by Oxidative Carbonylation of *N*-Boc-2-alkynyl-1-amino-3-yn-2-ols **6**



Thus, when (*S*)-*N*-Boc-7-(1-aminoethyl)-trideca-5,8-diyn-7-ol **6a** was allowed to react under conditions similar to those previously employed for **3a** (see Table 2, entry 1) (2 mol % of PdI_2 in conjunction with 10 equiv of KI, at 100 °C and in MeOH with a substrate concentration of 0.2 mmol of **6a** per mL of MeOH, under a 4:1 mixture of CO−air), after 15 h the substrate conversion was complete, with selective formation of 2-butyl-4-hexanoyl-5-methyl-1*H*-pyrrole-3-carboxylate **7a** in 70% isolated yield (Table 3, entry 1). Under the same conditions, other differently substituted *N*-Boc-2-alkynyl-1-amino-3-yn-2-ols, including highly hindered substrates such as **6g** and **6h**, behaved similarly (Table 3, entries 2−7), thus confirming the general applicability of the process. The reaction could also be carried out in EtOH rather than MeOH as the solvent, even though a higher catalyst loading was required to achieve satisfactory results (Table 3, entry 8).

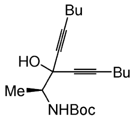
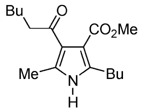
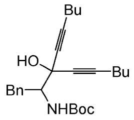
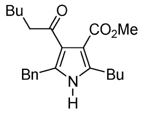
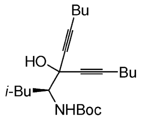
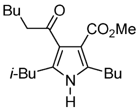
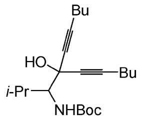
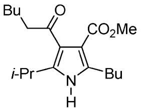
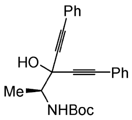
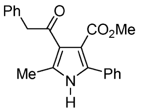
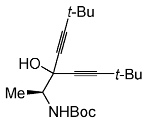
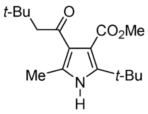
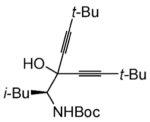
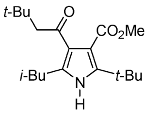
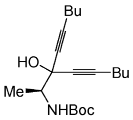
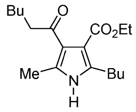
Our methodology could also be successfully applied to unprotected (*S*)-7-(pyrrolidin-2-yl)trideca-5,8-diyn-7-ol **8**, deriving from L-proline methyl ester, which, under the same

Table 3. Synthesis of 4-Acylpyrrole-3-carboxylic Esters 7 by PdI_2/KI-Catalyzed Oxidative Carbonylation of 2-Alkynyl-1-amino-3-yn-2-ols 6[a]



6

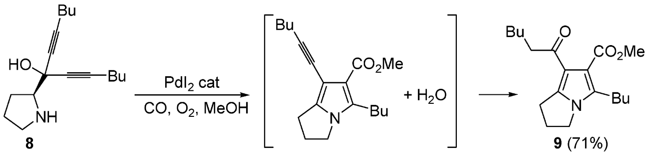
7

entry	substrate 6	ROH	product 7	yield of 7[b] (%)
1	 6a	MeOH	 7a	70
2	 6b	MeOH	 7b	73
3	 6c	MeOH	 7c	75
4	 6d	MeOH	 7d	68
5	 6e	MeOH	 7e	56
6	 6f	MeOH	 7f	66
7	 6g	MeOH	 7g	70
8[c]	 6a	EtOH	 7a'	55

[a] Unless otherwise noted, all reactions were carried out in ROH (0.20 mmol of starting **6** per mL of solvent) in the presence of 2 mol % of PdI_2 and with a KI:PdI_2 molar ratio = 10. Conversion of **6** was quantitative in all cases. [b] Isolated yield based on starting **6**. [c] The reaction was carried out with 5 mol % of PdI_2, with a KI:PdI_2 molar ratio = 10.

conditions as those of Table 3, entries 1−7, was directly converted into the corresponding bicyclic derivative, methyl 2-butyl-1-hexanoyl-6,7-dihydro-5*H*-pyrrolizine-2-carboxylate **9**, in 71% yield (Scheme 4).

Scheme 4. PdI_2/KI-Catalyzed Synthesis of Methyl 2-Butyl-1-hexanoyl-6,7-dihydro-5*H*-pyrrolizine-2-carboxylate 9 by Oxidative Carbonylation of (*S*)-7-(pyrrolidin-2-yl)trideca-5,8-diyn-7-ol 8



8 **9** (71%)

CONCLUSIONS

In conclusion, we have developed a novel and general synthesis of pyrrole-3-carboxylic ester derivatives **5** in good to high yields (61−89%), starting from readily available building blocks, by a simple two-step synthetic approach involving PdI_2-catalyzed oxidative carbonylation of *N*-Boc-1-amino-3-yn-2-ols **3** followed by basic treatment. In the case of *N*-Boc-2-alkynyl-1-amino-3-yn-2-ols **6**, bearing an additional alkynyl substituent α to the hydroxyl group, *N*-deprotection and water addition to the triple bond occurred spontaneously under the carbonylation conditions, thus allowing a direct synthesis of multifunctionalized polysubstituted pyrroles (alkyl 4-acylpyrrole-3-carboxylates **7**) in one step in satisfactory yields (55−75%). In a similar manner, (*S*)-7-(pyrrolidin-2-yl)trideca-5,8-diyin-7-ol **8** was directly converted into the corresponding bicyclic derivative, methyl 2-butyl-1-hexanoyl-6,7-dihydro-5*H*-pyrrolizine-2-carboxylate **9**, in 71% yield.

EXPERIMENTAL SECTION

General Experimental Methods. Melting points are uncorrected. ^{1}H NMR and ^{13}C NMR spectra were recorded at 25 °C in $CDCl_3$ 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]. 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 or using a gas chromatograph and a capillary column with diethyl *tert*-butylsilyl-β-cyclodextrin 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. Boc-protected α-alkynyl-β-amino alcohols **3a**−**g**, Boc-protected α,α'-dialkynyl-β-amino alcohols **6a**−**g**, and (*S*)-7-(pyrrolidin-2-yl)trideca-5,8-diyn-7-ol **8** were prepared as described below. All other materials were commercially available and were used without further purification.

General Procedure for the Preparation of *N*-Boc-1-amino-3-yn-2-ols 3a and 3c−g. *First Step: Preparation of N-Boc-2-amino Aldehydes.* The method of Verkade[11] was employed. To a cold (−78 °C), mechanically stirred solution of methyl *N*-Boc-amino esters (18.3 mmol) [*N*-Boc-L-phenylalanine methyl ester: 5.1 g; *N*-Boc-L-alanine methyl ester: 3.7 g; *N*-Boc-D/L-valine methyl ester: 4.2 g; *N*-Boc-glycine methyl ester: 3.5 g] in CH_2Cl_2 (60 mL) was added dropwise a 1.0 M solution of DIBAL-H in hexane (40 mL, 40 mmol) under nitrogen over 1 h. After additional stirring at −78 °C for 2 h, a 5 M solution of AcOH in benzene (34 mL) was added dropwise at −78 °C. The resulting mixture was allowed to warm to room temperature, and then it was poured into 10% aqueous tartaric acid (100 mL) and extracted with hexane−AcOEt (1:1) (3× 60 mL). The combined organic layers were washed with brine and dried over Na_2SO_4. The solvent was removed, and the crude products were used as such for the next step.

*Second Step: Preparation of N-Boc-1-amino-3-yn-2-ols **3a** and **3c**−**g**.* To a stirred suspension of Mg turnings (1.0 g, 41.1 mmol) in anhydrous THF (6 mL), maintained under nitrogen and under reflux, was added pure ethyl bromide (0.7 mL) to start the formation of the Grignard reagent. The remaining bromide was added dropwise in THF solution (2 mL of EtBr in 22 mL of THF; total amount of EtBr added: 3.94 g, 36.2 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-alkyne (36.2 mmol) (1-hexyne: 2.97 g; phenylacetylene: 3.69 g) in anhydrous THF (11 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 it was heated at 45 °C and stirred for 2 h. To the hot solution of 1-alkynylmagnesium bromide thus obtained was added dropwise and under nitrogen a solution of the crude *N*-Boc-2-amino aldehyde, obtained as described in the first step, in anhydrous THF (13 mL). The resulting mixture was allowed to stir at 35 °C overnight. Saturated NH_4Cl (100 mL) and AcOEt (100 mL) were sequentially added, the 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, products were purified by column chromatography on silica gel using 7:3 hexane−AcOEt (**3a**, **3d**−**g**), 1:1 hexane−AcOEt (**3c**) as the eluent. With the exception of *N*-Boc-1-aminooct-3-yn-2-ol **3c**, all products were obtained as mixtures of *syn* and *anti* diastereomers. In the case of *N*-Boc-3-amino-2-methyldec-5-yn-4-ol **3f**, separation of the *syn*-**3f** and *anti*-**3f** diastereosiomers was possible using hexane−AcOEt from 8:2 to 7:3 as eluent, to give pure *syn*-**3f** (936 mg, 18% based on starting *N*-Boc-D/L-valine methyl ester) and pure *anti*-**3f** (672 mg, 13% based on starting *N*-Boc-D/L-valine methyl ester) together with some fractions containing the mixture of the two diastereomers (1.01 g, 19% based on starting *N*-Boc-D/L-valine methyl ester).

*N-Boc-2-amino-1-phenylnon-4-yn-3-ol (**3a**).* (Mixture of diastereomers A + B, A:B ratio = 1.6:1, determined by GLC). Yield: 2.4 g, starting from 5.1 g of *N*-Boc-L-phenylalanine methyl ester (40%). Colorless amorphous solid: IR (KBr) ν = 3379 (m), 2933 (m), 2230 (vw), 1675 (s), 1531 (m), 1391 (w), 1367 (m), 1250 (w), 1172 (m), 1041 (w), 759 (w), 705 (m) cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.32−7.16 [A (m, 5 H) + B (m, 5 H)], 4.92−4.79 [A (m, 1 H) + B (m, 1 H)], 4.42−4.37 [B (m, br, 1 H)], 4.34 [A (dt, J = 4.5, 2.0, 1 H], 4.11−3.99 [B (m, 1 H)], 3.99−3.86 [A (m, 1 H)], 3.08−2.98 [A (m, 1 H) + B (m, 1 H)], 2.96−2.77 [A (m, 2 H) + B (m, 2 H)], 2.26 [A (td, J = 7.0, 2.0, 2 H)], 2.20 [B (td, J = 7.0, 2.0, 2 H)], 1.60−1.25 [A (m, 4 H) + B (m, 4 H)], 1.38 [A (s, 9 H) + B (s, 9 H)], 0.94 [A (t, J = 7.2, 3 H)], 0.90 [B (t, J = 7.2, 3 H)]; ^{13}C NMR (75 MHz, $CDCl_3$) δ = 156.3 (A or B), 156.1 (B or A), 138.2 (A or B), 137.8 (B or A), 129.5 (A or B), 129.3 (B or A), 128.53 (A or B), 128.48 (B or A), 126.6 (A or B), 126.4 (B or A), 87.8 (A or B), 86.9 (B or A), 79.9 (A or B), 79.6 (B or A), 78.9 (A or B), 77.8 (B or A), 64.9 (A or B), 64.0 (B or A), 56.9 (A or B), 56.7 (B or A), 37.6 (A or B), 37.1 (B or A), 30.8 (A or B), 30.7 (B or A), 28.3 (A + B), 22.04 (A or B), 21.98 (B or A), 18.5 (A or B), 18.4 (B or A), 13.6 (A + B); MS (ESI+, direct infusion) m/z = 354 [$(M + Na)^+$]. Anal. calcd for $C_{20}H_{29}NO_3$ (331.45): C, 72.47; H, 8.82; N, 4.23. Found: C, 72.58; H, 8.83; N, 4.24.

*N-Boc-1-aminooct-3-yn-2-ol (**3c**).* Yield: 1.7 g, starting from 3.5 g of *N*-Boc-glycine methyl ester (38%). Colorless oil: IR (film) ν = 3396 (m, br), 2965 (m), 2934 (m), 2236 (vw), 1695 (s), 1512 (s), 1367 (w), 1251 (m), 1171 (s), 1073 (m) cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 5.26−5.06 (m, br, 1 H), 4.41 (s, br, 1 H), 3.63−3.33 (m, 2 H), 3.32−3.16 (m, 1 H), 2.21 (td, J = 7.1, 2.0, 2 H), 1.55−1.33 (m, 4 H), 1.45 (s, 9 H), 0.91 (t, J = 7.2, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 156.5, 86.4, 79.7, 78.9, 62.2, 47.1, 30.6, 28.4, 21.9, 18.4, 13.6; MS (ESI+, direct infusion) m/z = 364 [$(M + Na)^+$]. Anal. calcd for $C_{13}H_{23}NO_3$ (241.33): C, 64.70; H, 9.61; N, 5.80. Found: C, 64.60; H, 9.63; N, 5.81.

*N-Boc-2-aminonon-4-yn-3-ol (**3d**).* (Mixture of diastereomers A + B, A:B ratio = 1.9:1, determined by ^{1}H NMR). Yield: 2.6 g, starting from 3.7 g of *N*-Boc-L-alanine methyl ester (56%). Colorless oil: IR (film) ν = 3404 (m, br), 2964 (m), 2934 (m), 2212 (w), 1695 (s), 1506 (m), 1455 (w), 1384 (m), 1367 (m), 1250 (w), 1169 (m), 1051 (m), 1029 (m) cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 4.94 [B (d, br, J = 8.6, 1 H)], 4.86 [A (d, br, J = 9.1, 1 H)], 4.43−4.38 [B (m, 1 H)], 4.34 [A (dt, J = 5.1, 2.0, 1 H)], 3.93−3.73 [A (m, 1 H) + B (m, 1 H)], 3.61 [A (s, br, 1 H) + B (s, br, 1 H)], 2.26−2.17 [A (m, 2 H) + B (m, 2 H)], 1.55−1.32 [A (m, 4 H) + B (m, 4 H)], 1.45 [A (s, 9 H) + B (s, 9 H)], 1.22 [A (d, J = 6.9, 3 H)], 1.18 [B (d, J = 6.9, 3 H)], 0.91 [A (t, J = 7.2, 3 H + B (t, J = 7.2, 3 H)]; ^{13}C NMR (75 MHz, $CDCl_3$) δ = 156.2 (B), 156.0 (A), 87.0 (B), 86.6 (A), 79.8 (B), 79.6 (A), 78.5 (A), 78.0 (B), 66.2 (B), 66.0 (A), 51.3 (B), 51.1 (A), 30.7 (A + B), 28.4 (A + B), 21.9 (A + B), 18.4 (A + B), 16.3 (A), 16.1 (B), 13.6 (A + B); MS (ESI+, direct infusion) m/z = 278 [(M + Na)$^+$]. Anal. calcd for $C_{14}H_{25}NO_3$ (255.35): C, 65.85; H, 9.87; N, 5.49. Found: C, 65.96; H, 9.84; N, 5.50.

N-Boc-4-amino-1-phenylpent-1-yn-3-ol (***3e***). (Mixture of diastereoisomers A + B, A:B ratio = 1.6:1 by ^{1}H NMR). Yield: 3.4 g, starting from 3.7 g of *N*-Boc-L-alanine methyl ester (67%). Colorless oil: IR (film) ν = 3353 (m, br), 2978 (m), 2932 (w), 2226 (vw), 1688 (s), 1504 (m), 1367 (m), 1249 (m), 1166 (m), 1047 (m), 757 (m), 691 (m) cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.47−7.41 [B (m, 5 H)], 7.34−7.27 [A (m, 5 H)], 4.86 [B (d, br, J = 9.0, 1 H)], 4.79 [A (d, br, J = 8.1, 1 H)], 4.64 [B (d, br, J = 2.4, 1 H)], 4.57 [A (d, J = 5.3, 1 H)], 4.10−3.86 [A (m, 1 H) + B (m, 1 H)], 1.46 [B (s, 9 H)], 1.45 [A (s, 9 H)], 1.31 [A (d, J = 6.5, 3 H)], 1.27 [B (d, J = 6.9, 3 H)]; ^{13}C NMR (75 MHz, $CDCl_3$) δ = 156.0 (A + B), 131.83 (A), 131.77 (B), 128.5 (B), 128.32 (A), 128.28 (A + B), 122.4 (A + B), 87.5 (A), 86.9 (B), 86.0 (A + B), 80.1 (B), 79.9 (A), 66.9 (B), 66.6 (A), 51.4 (B), 51.1 (A), 28.4 (A + B), 16.4 (A + B) (*Note: the −OH signals were too broad to be detected*); MS (ESI+, direct infusion) m/z = 298 [(M + Na)$^+$]. Anal. calcd for $C_{16}H_{21}NO_3$ (275.34): C, 69.79; H, 7.69; N, 5.09. Found: C, 69.85; H, 7.70; N, 5.08.

syn-N-Boc-3-amino-2-methyldec-5-yn-4-ol (*syn-**3f***). Yield: 934 mg, starting from 4.2 g of *N*-Boc-D/L-valine methyl ester (18%). Colorless crystalline solid: mp 52−54 °C; IR (KBr) ν = 3403 (m, br), 2962 (m), 2933 (m), 2873 (w), 2230 (vw), 1696 (s), 1508 (m), 1390 (w), 1366 (w), 1248 (m), 1172 (m), 1047 (m), 1018 (w) cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 4.86 (d, br, J = 9.7, 1 H), 4.46−4.38 (m, 1 H), 3.49−3.36 (m, 1 H), 2.94 (d, br, J = 5.7, 1 H), 2.19 (td, J = 6.9, 2.0, 2 H), 2.11−1.98 (m, 1 H), 1.54−1.32 (m, 4 H), 1.45 (s, 9 H), 0.98 (d, J = 6.9, 3 H), 0.92 (d, J = 6.9, 3 H), 0.90 (t, J = 7.3, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 156.9, 86.4, 79.4, 79.2, 63.9, 61.0, 30.6, 29.1, 28.4, 21.9, 20.2, 18.4, 18.1, 13.6; MS (ESI+, direct infusion) m/z = 306 [(M + Na)$^+$]. Anal. calcd for $C_{16}H_{29}NO_3$ (283.41): C 67.81, H 10.31, N 4.94. Found: C 67.89, H, 10.28, N 4.93.

anti-N-Boc-3-amino-2-methyldec-5-yn-4-ol (*anti-**3f***). Yield: 674 mg, starting from 4.2 g of *N*-Boc-D/L-valine methyl ester (13%). Colorless crystalline solid: mp 42−44 °C; IR (KBr) ν = 3323 (m, br), 2962 (m), 2236 (v w), 1683 (s), 1541 (m), 1387 (m), 1366 (m), 1261 (m), 1176 (m), 1096 (m), 1028 (m), 802 (w) cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 4.67 (d, br, J = 9.2, 1 H), 4.57−4.49 (m, 1 H), 3.53 (td, J = 9.2, 3.2, 1 H), 2.99 (d, br, J = 7.3, 1 H), 2.22 (td, J = 6.9, 1.6, 2 H), 1.82−1.66 (m, 1 H), 1.56−1.32 (m, 4 H), 1.46 (s, 9 H), 0.98 (d, J = 6.9, 3 H), 0.97 (d, J = 6.9, 3 H), 0.91 (t, J = 7.3, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 157.1, 87.2, 79.7, 77.7, 64.5, 61.2, 30.7, 28.4, 22.0, 19.9, 19.2, 18.4, 13.6; MS (ESI+, direct infusion) m/z = 306 [(M + Na)$^+$]. Anal. calcd for $C_{16}H_{29}NO_3$ (283.41): C 67.81, H 10.31, N 4.94. Found: C 67.89, H, 10.28, N 4.93.

N-Boc-2-amino-1,5-diphenylpent-4-yn-3-ol (***3g***). (Mixture of diastereoisomers A + B, A:B ratio = 2:1, determined by ^{1}H NMR). Yield: 4.9 g, starting from 5.1 g of *N*-Boc-L-phenylalanine methyl ester (76%). Colorless amorphous solid: IR (KBr) ν = 3444 (m, br), 3370 (m), 2978 (m), 2225 (vw), 1679 (s), 1527 (m), 1490 (w), 1444 (w), 1390 (w), 1367 (m), 1249 (m), 1171 (m), 1066 (m), 1041 (m), 756 (m), 704 (m); ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.49−7.45 [B (m, 2 H)], 7.44−7.39 [A (m, 2 H)], 7.35−7.15 [A (m, 8 H) + B (m, 8 H)], 5.05−4.82 [A (m, 1 H) + B (m, 1 H)], 4.68−4.62 [B (m, 1 H)], 4.59 [A (d, J = 4.4, 1 H)], 4.25−3.95 [A (m, 1 H) + B (m, 1 H)], 3.17−2.75 [A (m, 2 H) + B (m, 2 H)], 1.38 [A (s, 9 H) + B (s, 9 H)] (*Note: the OH signal was too broad to be detected*); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 156.1 (A + B), 137.8 (A + B), 132.0 (B), 131.8 (A), 129.4 (A), 129.2 (B), 128.7 (B), 128.55 (A), 128.49 (A + B), 128.3 (B), 128.2 (A), 126.6 (B), 126.5 (A), 122.4 (A + B) 87.8 (A + B), 85.9 (A + B), 80.1 (A), 79.8 (B), 65.3 (B), 64.2 (A), 56.8 (B), 56.5 (A), 37.5 (A), 36.9 (B), 28.3 (A + B); MS (ESI+, direct infusion) m/z = 374 [(M + Na)$^+$], 352 [(M + H)$^+$]. Anal. calcd for $C_{22}H_{25}NO_3$ (351.44): C, 75.19; H, 7.17; N, 3.99. Found: C, 75.27; H, 7.15; N, 3.98.

Preparation of *N*-Boc-2-Amino-3-methyl-1-phenylnon-4-yn-3-ol 3b. *First Step: Preparation of (S)-N-Boc-3-amino-4-phenyl-2-butanone.* To a cold (−78 °C), mechanically stirred solution of *N*-Boc-L-phenylalanine (4.0 g, 15.1 mmol) in anhydrous THF (15 mL) was added dropwise a 1.6 M solution of methyllithium in Et_2O (30.2 mL, 48.3 mmol) under nitrogen over 0.5 h. The reaction mixture was allowed to warm to room temperature, stirred for additional 2 h, and then quenched with a 1 N aqueous solution of HCl (66 mL). Et_2O (50 mL) was added, and the aqueous layer was separated and extracted with Et_2O (3 × 25 mL). The combined organic extracts were dried over anhydrous Na_2SO_4. After filtration, the solvent was removed by rotary evaporation. Purification by chromatography on silica gel (1:1 hexane−AcOEt) gave (*S*)-*N*-Boc-3-amino-4-phenyl-2-butanone as a colorless solid (mp 74−76 °C, lit.[12] 75−76 °C), whose spectroscopic data agreed with those reported in the literature[12] (yield: 2.58 g, 65% based on starting *N*-Boc-L-phenylalanine).

*Second Step: Preparation of N-Boc-2-amino-3-methyl-1-phenylnon-4-yn-3-ol **3b**.* To a suspension of Mg turnings (0.4 g, 16.8 mmol) in anhydrous THF (2 mL), maintained under nitrogen and under reflux, was added pure ethyl bromide (0.2 mL) to start the formation of the Grignard reagent. The remaining bromide was added dropwise in THF solution (1 mL of EtBr in 9 mL of THF; total amount of EtBr added: 1.9 g, 16.1 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 (1.3 g, 16.1 mmol) in anhydrous THF (4 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 it 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 (*S*)-3-*N*-Boc-3-amino-4-phenyl-2-butanone (obtained as described above, 2.13 g, 8.1 mmol) in anhydrous THF (5 mL). The resulting mixture was allowed to stir at 35 °C overnight. Saturated NH_4Cl (50 mL) and AcOEt (50 mL) were sequentially added, the 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, *N*-Boc-2-amino-3-methyl-1-phenylnon-4-yn-3-ol **3b** (as a diastereomeric mixture A + B, A:B ratio = 2.4:1, determined by GLC) was purified by column chromatography on silica gel using 7:3 hexane−AcOEt as the eluent. Yield: 2.24 g, starting from 2.13 g of (*S*)-*N*-Boc-3-amino-4-phenyl-2-butanone (80%). Colorless amorphous solid: IR (KBr) ν = 3444 (m, br), 3377 (m), 2967 (m), 2933 (m), 2241 (vw), 1676 (s), 1530 (m), 1455 (w), 1366 (m), 1250 (m), 1171 (m), 753 (w), 700 (m) cm^{-1} ; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.32−7.13 [A (m, 5 H) + B (m, 5 H)], 4.64 [B (d, br, J = 9.7, 1 H)], 4.54 [A (d, br, J = 8.9, 1 H)], 3.98−3.84 [A (m, 1 H) + B (m, 1 H)], 3.36−3.22 [A (m, 1 H) + B (m, 1 H)], 2.89 [A (s, br, 1 H)], 2.72 [B (s, br, 1 H)], 2.70−2.54 [A (m, 1 H) + B (m, 1 H)], 2.25 [B (t, J = 6.9, 2 H)], 2.24 [A (t, J = 6.9, 2 H)], 1.58−1.38 [A (m, 4 H) + B (m, 4 H)], 1.30 [A (s, 9 H)], 1.29 [B (s, 9 H)], 1.25 [A (s, 3 H) + B (s, 3 H)], 0.97−0.82 [A (m, 3 H) + B (m, 3 H)]; ^{13}C NMR (75 MHz, $CDCl_3$) δ = 156.1 (A + B), 138.6 (A + B), 129.3 (B), 129.2 (A), 128.3 (A + B), 126.3 (B), 126.2 (A), 85.6 (A + B), 81.9 (A + B), 79.5 (A + B), 71.4 (A), 70.8 (B), 60.3 (B), 60.0 (A), 37.4 (B), 36.7 (A), 30.8 (A + B), 29.7 (A + B), 28.2 (A + B), 22.0 (A + B), 18.4 (A + B), 13.6 (A + B); MS (ESI+, direct infusion) m/z = 368 [(M + Na)$^+$], 346 [(M + H)$^+$]. Anal. calcd for $C_{21}H_{31}NO_3$ (345.48): C, 73.01; H, 9.04; N, 4.05. Found: C, 73.10; H, 9.01; N, 4.05.

General Procedure for the Preparation of *N*-Boc-2-alkynyl-1-amino-3-yn-2-ols 6a−g. 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-alkyne (24.1 mmol) (1-hexyne: 1.98 g; phenylacetylene: 2.46 g; *tert*-butylacetylene: 1.98) 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 it was heated at 45 °C and stirred for 2 h. To the hot solution of the 1-alkynylmagnesium bromide thus obtained was added, dropwise and under nitrogen, a solution of the methyl Boc-protected-L-amino ester (6.21 mmol) (*N*-Boc-L-alanine methyl ester: 1.26 g; *N*-Boc-L-leucine methyl ester: 1.52 g; *N*-Boc-D/L-phenylalanine methyl ester: 1.73 g ; *N*-Boc-D/L-valine methyl ester: 1.44 g) 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, the 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, products **6a–g** were purified by column chromatography on silica gel using 8:2 hexane–AcOEt as the eluent.

*(S)-N-Boc-7-(1-aminoethyl)-trideca-5,8-diyn-7-ol (**6a**).* Yield: 1.46 g, starting from 1.26 g of *N*-Boc-L-alanine methyl ester (70%). Yellow oil: $[\alpha]^{25}_{D}$ (MeOH, $c = 1.04 \times 10^{-2}$ g mL^{-1}) = −46°; IR (film) ν = 3436 (m, br), 2960 (m), 2935 (m), 2874 (s), 2236 (w), 1701 (s), 1508 (s), 1507 (m), 1455 (m), 1367 (m), 1247 (m), 1165 (m), 1052 (m), 1019 (m), 861 (w), 756 (s) cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 4.76 (d, br, J = 6.8, 1 H), 4.04−3.87 (m, 1 H), 3.30 (s, br, 1 H), 2.24 (t, J = 7.0, 2 H), 2.23 (t, J = 7.0, 2 H), 1.57−1.34 (m, 8 H), 1.46 (s, 9 H), 1.31 (d, J = 6.8, 3 H), 0.915 (t, J = 7.1, 3 H), 0.906 (t, J = 7.1, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 156.1, 85.1, 84.9, 79.7, 79.6, 78.9, 67.5, 55.7, 30.6, 30.5, 28.4, 22.0, 18.4, 17.0, 13.5; MS (ESI+, direct infusion) m/z = 358 [(M + Na)$^+$]. Anal. calcd for $C_{20}H_{33}NO_3$ (335.48): C, 71.60; H, 9.91; N, 4.18. Found: C, 71.71; H, 9.89; N, 4.16.

*N-Boc-7-(1-amino-2-phenylethyl)-trideca-5,8-diyn-7-ol (**6b**).* Yield: 1.76 g, starting from 1.73 g of *N*-Boc-D/L-phenylalanine methyl ester (69%). Yellow amorphous solid: mp = 61−65 °C; IR (KBr) ν = 3380 (m), 3291 (m, br), 2959 (m), 2935 (m), 2873 (w), 2230 (w), 1687 (s), 1493 (w), 1453 (w), 1394 (m), 1366 (m), 1256 (w), 1170 (m), 1128 (m), 1061 (m), 1022 (w), 848 (w), 745 (m), 699 (m) cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.32−7.16 (m, 5 H), 4.70 (d, J = 10.3, 1 H), 4.20−4.07 (m, 1 H), 3.52 (s, br, 1 H), 3.41 (dd, J = 13.9, 2.4, 1 H), 2.70 (dd, J = 13.9, 11.5, 1 H), 2.30−2.20 (m, 4 H), 1.60−1.35 (m, 8 H), 1.31 (s, 9 H,), 0.92 (t, J = 7.0), 0.91 (t, J = 7.0, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 156.1, 138.3, 129.2, 128.3, 126.2, 85.50, 85.45, 79.6, 79.5, 78.8, 67.2, 60.9, 37.1, 30.5, 30.4, 28.2, 22.0, 18.4, 13.6; m/z = 434 [(M + Na)$^+$]. Anal. calcd for $C_{26}H_{37}NO_3$ (411.58): C, 75.87; H, 9.06; N, 3.40. Found: C, 75.89; H, 9.04; N, 3.41.

*(S)-N-Boc-7-(1-amino-3-methylbutyl)-trideca-5,8-diyn-7-ol (**6c**).* Yield: 1.76 g, starting from 1.52 g of *N*-Boc-L-leucine methyl ester (75%). Yellow oil: $[\alpha]^{25}_{D}$ (MeOH, $c = 1.05 \times 10^{-2}$ g mL^{-1}) −55°; IR (film) ν = 3379 (m, br), 2958 (m), 2234 (m), 2872 (w), 2223 (vw), 1716 (s), 1505 (m), 1436 (w), 1391 (w), 1367 (m), 1251 (w), 1166 (m), 1049 (w), 1025 (w) cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 4.69 (d, br, J = 10.3, 1 H), 3.90 (t, br, J = 10.3, 1 H), 3.51 (s, br, 1 H), 2.27−2.18 (m, 4 H), 1.78−1.63 (m, 2 H), 1.58−1.33 (m, 9 H), 1.45 (s, 9 H), 1.00−0.88 (m, 12 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 156.5, 85.0, 84.8, 79.9, 79.5, 79.0, 67.6, 58.2, 40.1, 30.54, 30.50, 28.4, 25.1, 23.9, 22.0, 18.5, 13.6; MS (ESI+, direct infusion) m/z = 400 [(M + Na)$^+$]. Anal. calcd for $C_{23}H_{39}NO_3$ (377.56): C, 73.17; H, 10.41; N, 3.71. Found: C, 73.25; H, 10.39; N, 3.70.

*N-Boc-7-(1-amino-2-methylpropyl)-trideca-5,8-diyn-7-ol (**6d**).* Yield: 1.58 g, starting from 1.44 g of *N*-Boc-D/L-valine methyl ester (70%). Yellow oil: IR (film) ν = 3440 (m, br), 2960 (m), 2930 (m), 2874 (m), 2234 (w), 1700 (s), 1505 (m), 1467 (w), 1392 (m), 1311 (m), 1239 (m), 1171 (m), 1094 (w), 1057 (m), 1000 (w), 872 (w), 761 (w) cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 4.84 (d, br, J = 10.8, 1 H), 3.77 (dd, J = 10.8, 2.9, 1 H), 3.19 (s, br, 1 H), 2.46−2.32 (m, 1 H), 2.27−2.18 (m, 4 H), 1.57−1.33 (m, 8 H), 1.46 (s, 9 H), 1.00 (d, J = 6.6, 3 H), 0.97 (d, J = 6.6, 3 H), 0.91 (t, J = 7.3, 3 H), 0.90 (t, J = 7.3, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 156.9, 85.6, 85.1, 79.9, 79.5, 79.4, 67.0, 63.4, 30.4, 29.2, 28.4, 22.2, 22.0, 18.5, 17.0, 13.6; MS (ESI+, direct infusion) m/z = 386 [(M + Na)$^+$]. Anal. calcd for $C_{22}H_{37}NO_3$ (363.53): C, 72.69; H, 10.26; N, 3.85. Found: C, 72.72; H, 10.25; N, 3.83.

*(S)-N-Boc-3-(1-aminoethyl)-1,5-diphenylpenta-1,4-diyn-3-ol (**6e**).* Yield: 1.61 g, starting from 1.26 g of *N*-Boc-L-alanine methyl ester (69%). Colorless amorphous solid: mp = 127−129 °C; $[\alpha]^{25}_{D}$ (MeOH, $c = 9.0 \times 10^{-3}$ g mL^{-1}) −44°; IR (KBr) ν = 3308 (m, br), 2230 (w), 1664 (s), 1537 (s), 1490 (m), 1456 (m), 1384 (m), 1315 (m), 1257 (w), 1159 (s), 1112 (m), 1009 (m), 856 (w), 756 (m), 692 (m) cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.51−7.43 (m, 4 H), 7.35−7.25 (m, 6 H), 4.97 (d, J = 9.3, 1 H), 4.34−4.20 (m, 1 H), 4.10 (s, 1 H), 1.47 (d, J = 6.9, 1 H), 1.44 (s, 9 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 156.3, 132.0, 128.8, 128.3, 128.2, 122.2, 87.8, 87.0, 84.9, 84.7, 80.1, 68.6, 55.8, 28.4, 17.1; MS (ESI+, direct infusion) m/z = 398 [(M + Na)$^+$]. Anal. calcd for $C_{24}H_{25}NO_3$ (375.46): C, 76.77; H, 6.71; N, 3.73. Found: C, 76.81; H, 6.70; N, 3.71.

*(S)-N-Boc-5-(1-aminoethyl)-2,2,8,8-tetramethylnona-3,6-diyn-5-ol (**6f**).* Yield: 1.48 g, starting from 1.26 g of *N*-Boc-L-alanine methyl ester (71%). Colorless amorphous solid: mp = 63−66 °C; $[\alpha]^{25}_{D}$ (MeOH, $c = 7.3 \times 10^{-3}$ g mL^{-1}) −44°; IR (KBr) ν = 3439 (m, br), 2972 (m), 2932 (w), 868 (w), 2247 (vw), 1675 (s), 1513 (m), 1455 (m), 1384 (s), 1267 (m), 1165 (m), 1054 (m), 979 (w), 858 (w) cm^{-1} ; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 4.80−4.67 (m, 1 H), 4.03−3.88 (m, 1 H), 3.10 (s, br, 1 H), 1.46 (s, 9 H), 1.45 (d, J = 3.0, 3 H), 1.23 (s, 9 H), 1.22 (s, 9 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 156.0, 93.0, 92.8, 79.6, 78.2, 67.3, 55.6, 30.75, 30.66, 28.4, 27.4, 27.3, 17.2; MS (ESI+, direct infusion) m/z = 358 [(M + Na)$^+$]. Anal. calcd for $C_{20}H_{33}NO_3$ (335.48): C, 71.60; H, 9.91; N, 4.18. Found: C, 71.56; H, 9.90; N, 4.17.

*(S)-N-Boc-5-(1-amino-3-methyl-butyl)-2,2,8,8-tetramethylnona-3,6-diyn-5-ol (**6g**).* Yield: 1.36 g, starting from 1.52 g of *N*-Boc-L-leucine methyl ester (58%). Colorless amorphous solid: mp = 92−93 °C; $[\alpha]^{25}_{D}$ (MeOH, $c = 8.5 \times 10^{-3}$ g mL^{-1}) −41°; IR (KBr) ν = 3449 (m, br), 2971 (m), 2930 (w), 2867 (w), 2244 (vw), 1701 (s), 1511 (m), 1367 (m), 1267 (w), 1175 (m), 1015 (w), 871 (w) cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 4.59 (d, J = 10.3, 1 H), 3.88 (t, br, J = 10.3, 1 H), 2.91 (s, br, 1 H), 1.74−1.62 (m, 2 H), 1.46 (s, 9 H), 1.42−1.30 (m, 1 H), 1.23 (s, 9 H), 1.22 (s, 9 H), 0.98−0.92 (m, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 156.4, 93.0, 92.6, 79.5, 78.5, 77.4, 67.3, 58.3, 40.5, 30.75, 30.67, 28.4, 27.4, 27.3, 23.9, 21.7; MS (ESI+, direct infusion) m/z = 400 [(M + Na)$^+$]. Anal. calcd for $C_{23}H_{39}NO_3$ (377.56): C, 73.17; H, 10.41; N, 3.71. Found: C, 73.25; H, 10.40; N, 3.70.

Preparation of (*S*)-7-(Pyrrolidin-2-yl)trideca-5,8-diyn-7-ol 8. *First Step: Preparation of L-Proline Methyl Ester.* A solution of L-proline methyl ester hydrochloride (3.64 g, 22 mmol) in 0.2 M aqueous NaOH solution (120 mL) was extracted with diethyl ether (2 × 100 mL). The collected organic layers were dried over Na_2SO_4. After filtration and evaporation of the solvent, the crude L-proline methyl ester thus obtained was immediately used as such for the next step.

*Second Step: Preparation of (S)-7-(Pyrrolidin-2-yl)trideca-5,8-diyn-7-ol **8**.* To a suspension of Mg turnings (2.1 g, 86.4 mmol) in anhydrous THF (9 mL), maintained under nitrogen and under reflux, was added pure ethyl bromide (1.8 mL) to start the formation of the Grignard reagent. The remaining bromide was added dropwise in THF solution (4.5 mL of EtBr in 48 mL of THF; total amount of EtBr added: 9.2 g, 84.2 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 (7.23 g, 88 mmol) in anhydrous THF (24 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 it was heated at 45 °C and stirred for 2 h. To the hot solution of 1-hexynylmagnesium bromide thus obtained was added, dropwise and under nitrogen, a solution of crude L-proline methyl ester (obtained as described above) in anhydrous THF (7 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, the 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, (*S*)-7-(pyrrolidin-2-yl)trideca-5,8-diyn-7-ol **8** was purified by column chromatography on silica gel using 8:2 hexane−AcOEt as the eluent. Yield: 3.22 g, starting from 22 mmol of L-proline methyl ester (56%). Brown oil: $[\alpha]^{25}_{D}$ (MeOH, $c = 1.05 \times 10^{-2}$ g mL^{-1}) −54°; IR (film) ν = 3436 (m, br), 2956 (m), 2930 (m), 2871 (w), 2345 (vw), 1648 (s), 1560 (w), 1522 (m), 1458 (m), 1430 (w), 1385 (m), 1299 (w) cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 5.88 (s, 1 H), 3.77 (t, *J* = 7.1, 2H), 2.82 (t, *J* = 7.1, 2 H), 2.51−2.32 (m, 6 H), 1.60−1.29 (m, 10 H), 0.93 (t, *J* = 7.4, 3 H), 0.91 (t, *J* = 7.4, 3 H); GC−MS *m*/*z* = 261 (M^+, 35), 218 (48), 205 (57), 191 (15), 190 (100), 163 (12), 162 (34), 148 (7), 120 (10), 119 (18). Anal. calcd for $C_{17}H_{27}NO$ (261.40): C, 78.11; H, 10.41; N, 5.36. Found: C, 78.12; H, 10.44, N, 5.33.

General Procedure for the Synthesis of *N*-Protected Pyrrole-3-carboxylic Esters 4a−g and *N*-Unsubstituted Pyrrole-3-carboxylic Esters 5a−g. A 250 mL stainless steel autoclave was charged in the presence of air with PdI_2 (9.5 mg, 2.64×10^{-2} mmol or 23.7 mg, 6.58×10^{-2} mmol, see Table 2), KI (43.8 mg, 0.26 mmol or 109.2 mg, 0.66 mmol, see Table 2), anhydrous ROH (R = Me or Et, 6.6 mL), and *N*-Boc-1-amino-3-yn-2-ols (1.32 mmol) (*N*-Boc-2-amino-1-phenylnon-4-yn-3-ol **3a**: 437 mg; *N*-Boc-2-amino-3-methyl-1-phenylnon-4-yn-3-ol **3b**: 456 mg; *N*-Boc-1-aminooct-3-yn-2-ol **3c**: 318 mg; *N*-Boc-2-aminonon-4-yn-3-ol **3d**: 337 mg; *N*-Boc-4-amino-1-phenylpent-1-yn-3-ol **3e**: 363 mg; *N*-Boc-3-amino-2-methyl-dec-5-yn-4-ol **3f**: 374 mg; *N*-Boc-2-amino-1,5-diphenylpent-4-yn-3-ol **3g**: 464 mg). The autoclave was sealed, and while the mixture was stirred, the autoclave was pressurized with CO (16 atm) and air (up to 20 atm). After being stirred at 80 °C for 3 h (**3a−c**) or 100 °C for 2 h (**3d−g**), the autoclave was cooled, degassed and opened. The mixture was diluted with ROH (R = Me or Et) in a volumetric flask (50 mL) to a total volume of 50 mL. Evaporation of 25 mL of this solution (formally deriving from 0.66 mmol of substrate) followed by column chromatography on silica gel (95:5 to 9:1 hexane−AcOEt as eluent) afforded pure products **4** and **5** (the order of elution was **5a**, **4a** and **4b−g**, **5b−g**). To the remaining 25 mL was added ROH (2 mL) and a 6.5 N solution of NaOR in ROH (0.80 mL, 5.2 mmol, for products deriving from **3a−e** and **3g**; 3.15 mL, 20.5 mmol, for products deriving from **3f**). The mixture was allowed to stir in a Schlenk flask at 60 °C for 8 h (for products deriving from **3a**, **3b**, **3g**), 25 °C for 15 h (for products deriving from **3c**, **3d**, **3e**), or 25 °C for 72 h (for products deriving from **3f**). Three-fourths of the initial solvent volume were evaporated, and the mixture was diluted with 10 mL of Et_2O and 10 mL of water. The phases were separated, and the organic layer was dried over Na_2SO_4. After filtration and elimination of the solvent by rotary evaporation, crude products **5a−g** were purified by column chromatography on silica gel using 9:1 hexane−AcOEt as eluent.

Methyl N-Boc-5-benzyl-2-butylpyrrole-3-carboxylate (***4a***). Yield: 10 mg (4%, based on 0.66 mmol of starting **3a**) (Table 2, entry 1). Yellow oil: IR (film) ν = 2955 (m), 2871 (w), 1751 (s), 1710 (s), 1541 (m), 1454 (m), 1370 (m), 1303 (m), 1213 (m), 1127 (m), 1055 (m), 848 (m), 784 (m), 701 (m) cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.31−7.13 (m, 3 H), 7.13−7.04 (m, 2 H), 6.17 (s, 1 H), 4.11 (s, 2 H), 3.76 (s, 3 H), 3.27−3.16 (m, 2 H), 1.64−1.48 (m, 2 H), 1.48−1.31 (m, 2 H), 1.41 (s, 9 H), 0.93 (t, *J* = 7.2, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 165.2, 149.7, 143.3, 139.3, 132.5, 128.6, 128.4, 126.3, 113.6, 112.2, 84.9, 50.8, 34.9, 32.5, 27.6, 26.3, 22.8, 13.9; MS (ESI+, direct infusion) *m*/*z* = 394 [$(M + Na)^+$]. Anal. calcd for $C_{22}H_{29}NO_4$ (371.47): C 71.13, H 7.87, N 3.77. Found: C 71.18, H, 7.87, N 3.78.

Methyl N-Boc-5-benzyl-2-butyl-4-methylpyrrole-3-carboxylate (***4b***). Yield: 181 mg (71%, based on 0.66 mmol of starting **3b**) (Table 2, entry 2). Colorless oil: IR (film) ν = 2956 (m), 1748 (s), 1707 (s), 1604 (w), 1533 (w), 1437 (m), 1383 (m), 1300 (m), 1250 (m), 1133 (s), 1105 (m), 844 (w), 758 (m), 704 (w) cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.27−7.19 (m, 2 H), 7.17−7.10 (m, 1 H), 7.02−6.95 (m, 2 H), 4.15 (s, 2 H), 3.83 (s, 3 H), 3.16−3.08 (m, 2 H), 2.18 (s, 3 H), 1.59−1.47 (m, 2 H), 1.45−1.31 (m, 2 H), 1.30 (s, 9 H), 0.92 (t, *J* = 7.3, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 166.3, 149.7, 142.1, 139.9, 128.3, 127.8, 127.5, 125.9, 119.7, 113.8, 84.6, 50.8, 32.5, 30.8, 27.4, 26.4, 22.8, 13.9, 11.2; MS (ESI+, direct infusion) *m*/*z* = 408 [$(M + Na)^+$], 386 [$(M + H)^+$]. Anal. calcd for $C_{23}H_{31}NO_4$ (385.50): C 71.66, H 8.11, N 3.63. Found: C 71.70, H, 8.09, N 3.64.

Methyl N-Boc-2-butylpyrrole-3-carboxylate (***4c***). Yield: 82 mg (44%, based on 0.66 mmol of starting **3c**) (Table 2, entry 3). Colorless oil: IR (film) ν = 2987 (w), 2923 (w), 1752 (s), 1699 (s), 1500 (w), 1423 (m), 1375 (m), 1340 (m), 1289 (m), 1230 (m), 1185 (m), 1095 (m), 846 (m), 782 (w), 754 (m), 700 (m) cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.12 (d, *J* = 3.6, 1 H), 6.49 (d, *J* = 3.6, 1 H), 3.81 (s, 3 H), 3.35−3.27 (m, 2 H), 1.64−1.50 (m, 2 H), 1.61 (s, 9 H), 1.49−1.34 (m, 2 H), 0.94 (t, *J* = 7.1, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 165.2, 148.8, 143.5, 120.3, 115.8, 110.9, 84.5, 51.0, 32.1, 27.9, 26.1, 22.7, 14.0; MS (ESI+, direct infusion) *m*/*z* = 304 [$(M + Na)^+$], 386 [$(M + H)^+$]. Anal. calcd for $C_{15}H_{23}NO_4$ (281.35): C 64.03, H 8.24, N 4.98. Found: C 64.09, H, 8.27, N 4.97.

Methyl N-Boc-2-butyl-5-methylpyrrole-3-carboxylate (***4d***). Yield: 105 mg (54%, based on 0.66 mmol of starting **3d**) (Table 2, entry 4). Colorless amorphous solid: mp 34−36 °C; IR (KBr) ν = 2953 (m), 2931 (m), 1748 (s), 1712 (s), 1545 (m), 1466 (m), 1437 (m), 1396 (m), 1288 (m), 1217 (m), 1168 (m), 1128 (m), 1059 (m), 1000 (w), 783 (m) cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 6.23−6.20 (m, 1 H), 3.78 (s, 3 H), 3.25−3.17 (m, 2 H), 2.32 (d, *J* = 1.2, 3 H), 1.61 (s, 9 H), 1.60−1.48 (m, 2 H), 1.46−1.32 (m, 2 H), 0.93 (t, *J* = 7.3, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 165.3, 149.8, 142.9, 130.0, 113.5, 110.7, 84.6, 51.0, 32.5, 27.9, 26.4, 22.8, 15.7, 14.0; MS (ESI+, direct infusion) *m*/*z* = 318 [$(M + Na)^+$]. Anal. calcd for $C_{16}H_{25}NO_4$ (295.37): C 65.06, H 8.53, N 4.74. Found: C 65.17, H, 8.55, N 4.73.

Methyl N-Boc-5-methyl-2-phenylpyrrole-3-carboxylate (***4e***). Yield: 98 mg (47%, based on 0.66 mmol of starting **3e**) (Table 2, entry 5). Colorless amorphous solid: mp 112−114 °C; IR (KBr) ν = 2969 (m), 1742 (s), 1721 (s), 1544 (m), 1433 (w), 1371 (m), 1346 (m), 1283 (m), 1237 (m), 1178 (m), 1153 (m), 1091 (m), 782 (m), 725 (m), 699 (m) cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.42−7.28 (m, 5 H), 6.37 (q, *J* = 1.0, 1 H), 3.63 (s, 3 H), 2.42 (d, *J* = 1.0, 3 H), 1.67 (s, 9 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 164.5, 149.6, 138.1, 133.7, 131.6, 130.0, 127.9, 127.5, 115.3, 110.7, 84.5, 51.0, 27.2, 14.7; MS (ESI+, direct infusion) *m*/*z* = 316 [$(M + H)^+$]. Anal. calcd for $C_{18}H_{21}NO_4$ (315.36): C 68.55, H 6.71, N 4.44. Found: C 68.47, H, 6.72, N 4.43.

Methyl N-Boc-2-butyl-5-isopropylpyrrole-3-carboxylate (***4f***). Yield: 66 mg (31%, based on 0.66 mmol of starting **3f**) (Table 2, entry 7). Colorless oil: IR (film) ν = 2957 (m), 2919 (m), 1750 (s), 1712 (s), 1547 (m), 1437 (m), 1395 (m), 1370 (m), 1304 (m), 1216 (m), 1149 (m), 1061 (m), 1003 (w), 850 (w), 783 (m) cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 6.27 (d, *J* = 0.8, 1 H), 3.79 (s, 3 H), 3.28 (heptuplet of doublets, *J* = 6.7, 0.8, 1 H), 3.20−3.11 (m, 2 H), 1.62 (s, 9 H), 1.60−1.47 (m, 2 H), 1.45−1.31 (m, 2 H), 1.20 (d, *J* = 6.7, 6 H), 0.92 (t, *J* = 7.3, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 165.4, 150.1, 142.4, 140.9, 112.9, 107.0, 84.9, 50.9, 32.4, 27.8, 26.4, 26.2, 22.9, 13.9; MS (ESI+, direct infusion) *m*/*z* = 324 [$(M + H)^+$]. Anal. calcd for $C_{18}H_{29}NO_4$ (323.43): C 66.84, H 9.04, N 4.33. Found: C 66.77, H, 9.06, N 4.33.

Ethyl N-Boc-5-benzyl-2-phenylpyrrole-3-carboxylate (***4g***). Yield: 142 mg (53%, based on 0.66 mmol of starting **3g**) (Table 2, entry 10). Colorless amorphous solid: mp 74−76 °C; IR (KBr) ν = 2957 (m), 2936 (m), 2873 (w), 1754 (s), 1717 (s), 1570 (w), 1508 (w), 1438 (m), 1371 (m), 1293 (m), 1269 (m), 1205 (m), 1161 (m), 1103 (m), 1002 (m), 849 (m), 737 (m) cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.39−7.16 (m, 10 H), 6.35 (s, 1 H), 4.19 (s, 2 H), 4.07 (q, *J* = 7.2, 2 H), 1.09 (t, *J* = 7.2, 3 H), 1.0 (s, 9 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 164.2, 149.4, 138.7, 138.4, 134.1, 133.4, 130.0, 128.9, 128.4, 127.9, 127.4, 126.3, 115.4, 111.7, 84.5, 59.7, 34.2, 26.9, 14.0; MS (ESI+, direct infusion) *m*/*z* = 428 [$(M + Na)^+$]. Anal. calcd for $C_{25}H_{27}NO_4$ (405.49): C 74.05, H 6.71, N 3.45. Found: C 74.15, H, 6.72, N 3.46.

Methyl 5-Benzyl-2-butyl-1H-pyrrole-3-carboxylate (***5a***). Yield: 122 mg (68% based on 0.66 mmol of starting **3a**) (Table 2, entry 1). Colorless oil: IR (film) ν = 3312 (m, br), 2956 (m), 2930 (m), 1677 (s), 1524 (w), 1495 (w), 1456 (m), 1367 (m), 1224 (m), 1096 (m), 1075 (m), 782 (m), 701 (m) cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.17 (s, br, 1 H), 7.34−7.11 (m, 5 H), 6.27 (d, *J* = 2.7, 1 H), 3.87

(s, 2 H), 3.73 (s, 3 H), 2.85 (t, J = 7.7, 2 H), 1.61−1.46 (m, 2 H), 1.38−1.24 (m, 2 H), 0.88 (t, J = 7.2, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 166.0, 140.0, 139.0, 128.69, 128.68, 128.64, 126.6, 110.9, 108.5, 50.5, 33.8, 31.7, 27.0, 22.5, 13.8; GC−MS m/z = 271 (M^+, 27), 240 (7), 228 (100), 212 (11), 196 (8), 169 (13), 141 (4), 120 (7), 105 (8), 91 (31), 78 (8), 65 (10). Anal. calcd for $C_{17}H_{21}NO_2$ (271.35): C 75.25, H 7.80, N 5.16. Found: C 75.19, H, 7.82, N 5.15.

*Methyl 5-Benzyl-2-butyl-4-methyl-1H-pyrrole-3-carboxylate (**5b**).* Yield: 167 mg (89%, based on 0.66 mmol of starting **3b**) (Table 2, entry 2). Colorless amorphous solid: mp 80−82 °C; IR (KBr) ν = 3289 (m, br), 2956 (m), 2929 (m), 1659 (s), 1470 (m), 1455 (m), 1364 (w), 1260 (m), 1121 (m), 1082 (m), 1029 (m), 756 (w), 702 (w) cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.81 (s, br, 1 H), 7.33−7.16 (m, 3 H), 7.16−7.09 (m, 2 H), 3.86 (s, 2 H), 3.77 (s, 3 H), 2.86−2.77 (m, 2 H), 2.22 (s, 3 H), 1.58−1.45 (m, 2 H), 1.39−1.23 (m, 2 H), 0.88 (t, J = 7.3, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 166.7, 139.4, 128.7, 128.4, 126.4, 124.8, 117.1, 110.2, 50.3, 31.8, 31.4, 27.6, 22.5, 13.8, 11.1; GC−MS m/z = 285 (M^+, 36), 270 (2), 254 (7), 243 (18), 242 (100), 226 (6), 210 (3), 183 (4), 167 (3), 107 (2), 91 (8). Anal. calcd for $C_{18}H_{23}NO_2$ (285.38): C 75.76, H 8.12, N 4.91. Found: C 75.70, H, 8.10, N 4.92.

*Methyl 2-Butyl-1H-pyrrole-3-carboxylate (**5c**).* Yield: 73 mg (61% based on 0.66 mmol of starting **3c**) (Table 2, entry 3). Colorless oil: IR (film) ν = 3356 (m, br), 2956 (m), 1678 (s), 1574 (m), 1466 (m), 1340 (m), 1264 (m), 1199 (m), 1129 (m), 1041 (m), 899 (m), 722 (m) cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.78 (s, br, 1 H), 6.58−6.53 (m, 2 H), 3.80 (s, 3 H), 2.98−2.91 (m, 2 H), 1.68−1.55 (m, 2 H), 1.43−1.28 (m, 2 H), 0.91 (t, J = 7.3, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 165.9, 140.1, 115.7, 111.1, 110.6, 50.7, 31.5, 27.0, 22.5, 13.9; GC−MS m/z = 181 (M^+, 27), 166 (4), 150 (19), 139 (31), 138 (100), 124 (25), 120 (41), 108 (49), 106 (89), 93 (14), 80 (49), 79 (39), 78 (19), 65 (11). Anal. calcd for $C_{10}H_{15}NO_2$ (181.23): C 66.27, H 8.34, N 7.73. Found: C 66.39, H, 8.32, N 7.72.

*Methyl 2-Butyl-5-methyl-1H-pyrrole-3-carboxylate (**5d**).* Yield: 90 mg (70% based on 0.66 mmol of starting **3d**) (Table 2, entry 4). Colorless oil: IR (film) ν = 3319 (m, br), 2955 (m), 2930 (m), 2872 (w), 1676 (s), 1601 (w), 1530 (w), 1460 (m), 1400 (w), 1367 (w), 1224 (m), 1097 (m), 1075 (m), 781 (m), cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.11 (s, br, 1 H), 6.20−6.16 (m, 1 H), 3.77 (s, 3 H), 2.93−2.85 (m, 2 H), 2.20 (s, 3 H), 1.65−1.53 (m, 2 H), 1.43−1.29 (m, 2 H), 0.92 (t, J = 7.3, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 166.1, 139.3, 125.6, 110.8, 107.5, 50.6, 31.8, 26.9, 22.5, 13.9, 12.7; GC−MS m/z = 195 (M^+, 31), 180 (2), 164 (9), 152 (100), 138 (7), 134 (7), 122 (10), 120 (19), 106 (3), 94 (7), 93 (8). Anal. calcd for $C_{11}H_{17}NO_2$ (195.26): C 67.66, H 8.78, N 7.17. Found: C 67.60, H, 8.80, N 7.15.

*Methyl 5-Methyl-2-phenyl-1H-pyrrole-3-carboxylate (**5e**).* Yield: 113 mg (80% based on 0.66 mmol of starting **3e**) (Table 2, entry 5). Yellow oil: IR (film) ν = 3309 (m, br), 2948 (m), 1681 (s), 1593 (m), 1467 (m), 1333 (w), 1283 (m), 1233 (m), 1167 (m), 1117 (m), 943 (m), 782 (m), 696 (m) cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.49 (s, br, 1 H), 7.58−7.49 (m, 2 H), 7.40−7.27 (m, 3 H), 6.37−6.33 (m, 1 H), 3.68 (s, 3 H), 2.22 (d, J = 1.0, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 165.6, 136.2, 132.3, 128.8, 128.1, 127.9, 127.8, 111.7, 109.6, 50.8, 12.6; GC−MS m/z = 215 (M^+, 78), 199 (4), 184 (100), 170 (3), 156 (13), 141 (4), 128 (13), 115 (7), 104 (7), 92 (7), 77 (17), 63 (8). Anal. calcd for $C_{13}H_{13}NO_2$ (215.25): C 72.54, H 6.09, N 6.51. Found: C 72.70, H, 6.10, N 6.50.

*Methyl 2-Butyl-5-isopropyl-1H-pyrrole-3-carboxylate (**5f**).* Yield: 116 mg (79% based on 0.66 mmol of starting **3f**) (Table 2, entry 7). Colorless oil: IR (film) ν = 3333 (m, br), 2959 (m), 2932 (m), 2871 (w), 1671 (s), 1523 (w), 1457 (m), 1384 (w), 1285 (w), 1200 (w), 1113 (m), 757 (m) cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.03 (s, br, 1 H), 6.22 (dd, J = 3.0, 1.0, 1 H), 3.78 (s, 3 H), 2.95−2.87 (m, 2 H), 2.83 (heptuplet of doublets, J = 6.9, 1.0, 1 H), 1.67−1.54 (m, 2 H), 1.44−1.30 (m, 2 H), 1.23 (d, J = 6.9, 6 H), 0.92 (t, J = 7.3, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 166.0, 139.1, 136.9, 110.3, 104.6, 50.6, 31.7, 27.0, 26.8, 22.6, 22.4, 13.9; GC−MS m/z = 223 (M^+, 40), 208 (70), 192 (11), 180 (100), 164 (14), 148 (7), 120 (8), 107 (18). Anal. calcd for $C_{13}H_{21}NO_2$ (223.16): C 69.92, H 9.48, N 6.27. Found: C 69.87, H, 9.46, N 6.28.

*Ethyl 5-Benzyl-2-phenyl-1H-pyrrole-3-carboxylate (**5g**).* Yield: 131 mg (65% based on 0.66 mmol of starting **3g**) (Table 2, entry 10). Colorless amorphous solid: mp 95−97 °C; IR (KBr) ν = 3298 (m), 1662 (s), 1482 (m), 1438 (m), 1385 (m), 1284 (w), 1263 (m), 1227 (m), 1179 (m), 1107 (m), 1019 (w), 766 (s), 698 (m) cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.71 (s, br, 1 H), 7.48−7.40 (m, 2 H), 7.30−7.12 (m, 8 H), 6.41−6.37 (m, 1 H), 4.06 (q, J = 7.2, 2 H), 3.84 (s, 2 H), 1.15 (t, J = 7.2, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 165.3, 138.8, 136.7, 132.2, 131.1, 128.9, 128.6, 127.9, 127.8, 126.5, 111.8, 110.0, 59.6, 33.6, 14.2; GC−MS m/z = 305 (M^+, 100), 276 (19), 260 (38), 232 (56), 230 (17), 228 (12), 200 (11), 182 (20), 170 (4), 154 (8), 127 (9), 115 (11), 91 (20), 77 (10). Anal. calcd for $C_{20}H_{19}NO_2$ (305.37): C 78.66, H 6.27, N 4.59. Found: C 78.78, H, 6.26, N 4.60.

General Procedure for the Synthesis of Pyrrole-3-carboxylic Esters 7a−g and 9. A 35 mL stainless steel autoclave was charged in the presence of air with PdI_2 (5.0 mg, 1.39 × 10^{-2} mmol), KI (23 mg, 13.9 × 10^{-2} mmol) and a solution of **6** (0.69 mmol) [(*S*)-*N*-Boc-7-(1-aminoethyl)-trideca-5,8-diyn-7-ol **6a**: 232 mg; *N*-Boc-7-(1-amino-2-phenylethyl)-trideca-5,8-diyn-7-ol **6b**: 285 mg; (*S*)-*N*-Boc-7-(1-amino-3-methylbutyl)-trideca-5,8-diyn-7-ol **6c**: 261 mg; *N*-Boc-7-(1-amino-2-methylpropyl)-trideca-5,8-diyn-7-ol **6d**: 252 mg; (*S*)-*N*-Boc-3-(1-aminoethyl)-1,5-diphenylpenta-1,4-diyn-3-ol **6e**: 260 mg; (*S*)-*N*-Boc-5-(1-aminoethyl)-2,2,8,8-tetramethylnona-3,6-diyn-5-ol **6f**: 232 mg; (*S*)-*N*-Boc-5-(1-amino-3-methyl-butyl)-2,2,8,8-tetramethylnona-3,6-diyn-5-ol **6g**: 261 mg; (*S*)-7-(pyrrolidin-2-yl)trideca-5,8-diyn-7-ol **8**: 181 mg] in ROH (R = Me or Et, 3.5 mL). The autoclave was sealed, and while the mixture was stirred, the autoclave was pressurized with CO (16 atm) and air (up to 20 atm). After being stirred at 100 °C for 15 h, the autoclave was cooled, degassed, and opened. The solvent was evaporated, and the products were purified by column chromatography on silica gel: **7a** was a yellow oil (8:2 hexane−AcOEt, 142 mg, 70% based on **6a**); **7a′** was a colorless oil (8:2 hexane−AcOEt, 117 mg, 55% based on **6a**); **7b** was a colorless oil (8:2 hexane−AcOEt, 186 mg, 73% based on **6b**); **7c** was a yellow oil (8:2 hexane−AcOEt, 173 mg, 75% based on **6c**); **7d** was a yellow solid, mp 27−28 °C (8:2 hexane−AcOEt, 150 mg, 68% based on **6d**); **7e** was a yellow oil (8:2 hexane−AcOEt, 129 mg, 56% based on **6e**); **7f** was a colorless oil (8:2 hexane−AcOEt, 134 mg, 66% based on **6f**); **7g** was a yellow oil (7:3 hexane−AcOEt, 162 mg, 70% based on **6g**); **9** was a yellow oil (8:2 hexane−AcOEt, 156 mg, 71% based on **8**).

*Methyl 2-Butyl-4-hexanoyl-5-methyl-1H-pyrrole-3-carboxylate (**7a**).* Yield: 142 mg, starting from 232 mg of (*S*)-*N*-Boc-7-(1-aminoethyl)-trideca-5,8-diyn-7-ol **6a** (70%) (Table 3, entry 1). Yellow oil: IR (film) ν = 3289 (s), 2957 (w), 2928 (m), 2872 (m), 1705 (s), 1646 (m), 1528 (m), 1448 (m), 1169 (m), 1110 (m), 1072 (m), 787 (w), 736 (w) cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 9.28 (s, br, 1 H), 3.78 (s, 3 H), 2.77 (t, J = 7.7, 2 H), 2.70 (t, J = 7.7, 2 H), 2.17 (s, 3 H), 1.71−1.48 (m, 4 H), 1.40−1.20 (m, 6 H), 0.89 (t, J = 7.3, 3 H), 0.87 (t, J = 7.3, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 202.9, 165.8, 138.7, 129.9, 123.3, 110.5, 51.0, 43.5, 31.8, 31.7, 26.6, 24.7, 22.5, 22.4, 13.9, 13.8, 12.1; GC−MS m/z = 293 (M^+, 10), 278 (3), 262 (6), 261 (7), 250 (6), 232 (11), 223 (12), 222 (100), 218 (16), 205 (26), 192 (13), 176 (7), 163 (10), 162 (9), 134 (7), 121 (11), 107 (9), 93 (30). Anal. calcd for $C_{17}H_{27}NO_3$ (293.40): C, 69.59; H, 9.28; N, 4.77. Found: C, 69.65; H, 9.30; N, 4.76.

*Ethyl 2-Butyl-4-hexanoyl-5-methyl-1H-pyrrole-3-carboxylate (**7a′**).* Yield: 117 mg, starting from 232 mg of (*S*)-*N*-Boc-7-(1-aminoethyl)-trideca-5,8-diyn-7-ol **6a** (55%) (Table 3, entry 8). Yellow oil: IR (film) ν = 3300 (s), 2957 (m), 2927 (m), 2872 (w), 1709 (s), 1652 (s), 1525 (m), 1435 (m), 1174 (m), 1108 (m), 1070 (m) cm^{-1}; δ = 8.93 (s, br, 1 H), 4.26 (q, J = 7.3, 2 H), 2.79 (t, J = 7.7, 2 H), 2.73 (t, J = 7.7, 2 H), 2.20 (s, 3 H), 1.70−1.50 (m, 4 H), 1.40−1.20 (m, 6 H), 1.32 (t, J = 7.3, 3 H), 0.96−0.82 (m, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 203.1, 165.4, 138.5, 129.9, 123.0, 110.5, 60.0, 43.6, 31.8, 31.6, 26.7, 24.7, 22.55, 22.46, 14.3, 14.0, 13.8, 12.2; GC−MS m/z = 307 (M^+, 28), 292 (6), 264 (14), 262 (18), 261 (21), 251 (11), 236 (100), 232 (31), 218 (33), 208 (98), 205 (45), 192 (13), 190 (10), 163 (21), 148 (6), 134 (10), 120 (8), 107 (10), 93 (26). Anal. calcd for $C_{18}H_{29}NO_3$ (307.43): C, 70.32; H, 9.51; N, 4.56. Found: C, 70.44; H, 9.49, N, 4.57.

*Methyl 5-Benzyl-2-butyl-4-hexanoyl-1H-pyrrole-3-carboxylate (**7b**)*. Yield: 186 mg, starting from 285 mg of *N*-Boc-7-(1-amino-2-phenylethyl)-trideca-5,8-diyn-7-ol **6b** (73%) (Table 3, entry 2). Yellow amorphous solid: mp = 94−96 °C; IR (KBr) ν = 3287 (m, br), 2956 (m), 2930 (m), 2872 (w), 1704 (s), 1673 (s), 1525 (m), 1495 (w), 1456 (s), 1367 (w), 1199 (m), 1160 (w), 1110 (m), 1076 (m), 755 (m), 728 (m), 696 (m) cm^{-1}; ^{1}H NMR (300 MHz, CDCl$_3$) δ = 8.83 (s, br, 1 H), 7.29−7.08 (m, 5 H), 3.94 (s, 2 H), 3.75 (s, 3 H), 2.75 (t, J = 7.3, 2 H), 2.67 (t, J = 7.3, 2 H), 1.65−1.42 (m, 4 H), 1.37−1.18 (m, 6 H), 0.92−0.81 (m, 6 H); ^{13}C NMR (75 MHz, CDCl$_3$) δ = 203.0, 165.6, 139.4, 138.4, 131.8, 128.7, 128.6, 126.6, 123.7, 110.2, 51.0, 43.7, 32.2, 31.7, 31.6, 26.7, 24.6, 22.5, 22.4, 13.9, 13.8; GC−MS m/z = 369 (M^+, 37), 338 (35), 337 (100), 308 (15), 298 (34), 295 (22), 294 (50), 281 (30), 279 (23), 278 (39), 266 (57), 252 (13), 239 (21), 196 (17), 168 (34), 167 (21), 115 (8), 91 (23), 73 (19). Anal. calcd for $C_{23}H_{31}NO_3$ (369.50): C, 74.76; H, 8.46; N, 3.79. Found: C, 74.85; H, 8.44; N, 3.78.

*Methyl 2-Butyl-4-hexanoyl-5-isobutyl-1H-pyrrole-3-carboxylate (**7c**)*. Yield: 173 mg, starting from 261 mg of (*S*)-*N*-Boc-7-(1-amino-3-methylbutyl)-trideca-5,8-diyn-7-ol **6c** (75%) (Table 3, entry 3). Yellow amorphous solid: mp = 40−42 °C; IR (KBr) ν = 3295 (m, br), 2957 (m), 2927 (m), 2871 (w), 1708 (s), 1675 (s), 1525 (m), 1449 (m), 1368 (m), 1193 (m), 1166 (m), 1091 (m), 1066 (w), 787 (w), 750 (w) cm^{-1}; ^{1}H NMR (300 MHz, CDCl$_3$) δ = 9.14 (s, br, 1 H), 3.76 (s, 3 H), 2.81 (t, J = 7.7, 2 H), 2.69 (t, J = 7.7, 2 H), 2.40 (d, J = 7.7, 2 H), 1.92−1.74 (m, 1 H), 1.71−1.50 (m, 4 H), 1.40−1.23 (m, 6 H), 0.93−0.83 (m, 6 H), 0.82 (d, J = 6.5, 6 H); ^{13}C NMR (75 MHz, CDCl$_3$) δ = 203.0, 165.7, 138.8, 133.1, 123.9, 110.2, 50.9, 43.9, 35.3, 31.8, 31.7, 29.3, 26.7, 24.6, 22.6, 22.44, 22.36, 13.9, 13.8; GC−MS m/z = 335 (M^+, 21), 304 (15), 303 (36), 292 (17), 288 (22), 274 (10), 265 (16), 264 (100), 260 (50), 247 (18), 246 (11), 232 (17), 93 (27). Anal. calcd for $C_{20}H_{33}NO_3$ (335.48): C, 71.60; H, 9.91; N, 4.18. Found: C, 71.65; H, 9.90; N, 4.17.

*Methyl 2-Butyl-4-hexanoyl-5-isopropyl-1H-pyrrole-3-carboxylate (**7d**)*. Yield: 150 mg, starting from 252 mg of *N*-Boc-7-(1-amino-2-methylpropyl)-trideca-5,8-diyn-7-ol **6d** (68%) (Table 3, entry 4). Yellow amorphous solid: mp = 68−71 °C; IR (KBr) ν = 3217 (m, br), 2962 (m), 2934 (m), 2873 (w), 1711 (s), 1647 (s), 1529 (m), 1464 (m), 1384 (m), 1362 (m), 1206 (m), 1110 (m), 1077 (w), 792 (m) cm^{-1}; ^{1}H NMR (300 MHz, CDCl$_3$) δ = 9.05 (s, br, 1 H), 3.77 (s, 3 H), 3.27−3.12 (m, 1 H), 2.88−2.78 (m, 2 H), 2.74−2.65 (m, 2 H), 1.71−1.50 (m, 4 H), 1.40−1.24 (m, 6 H), 1.20 (d, J = 7.3, 6 H), 0.95−0.84 (m, 6 H); ^{13}C NMR (75 MHz, CDCl$_3$) δ = 203.9, 165.7, 139.2, 138.7, 121.9, 109.6, 51.0, 44.2, 31.9, 31.6, 26.8, 25.5, 24.8, 22.6, 22.51, 22.48, 14.0, 13.8; GC−MS m/z = 321 (M^+, 20), 290 (15), 289 (39), 278 (9), 260 (11), 251 (17), 250 (100), 246 (38), 233 (25), 232 (14), 218 (16), 204 (9), 191 (9), 176 (8), 164 (8), 148 (10), 132 (11), 120 (17), 107 (17), 106 (24), 79 (10). Anal. calcd for $C_{19}H_{31}NO_3$ (321.45): C, 70.99; H, 9.72; N, 4.36. Found: C, 71.12; H, 9.70; N, 4.35.

*Methyl 5-Methyl-2-phenyl-4-phenylacetyl-1H-pyrrole-3-carboxylate (**7e**)*. Yield: 129 mg, starting from 260 mg of (*S*)-*N*-Boc-3-(1-aminoethyl)-1,5-diphenylpenta-1,4-diyn-3-ol **6e** (56%) (Table 3, entry 5). Yellow oil: IR (film) ν = 3426 (m, br), 1701 (s), 1641 (s), 1525 (w), 1493 (w), 1437 (s), 1263 (m), 1194 (w), 1170 (w), 1127 (m), 1040 (w), 761 (m) cm^{-1}; ^{1}H NMR (300 MHz, CDCl$_3$) δ = 9.28 (s, br, 1 H), 7.43−7.36 (m, 2 H), 7.32−7.10 (m, 8 H), 4.01 (s, 2 H), 3.68 (s, 3 H), 2.14 (s, 3 H); ^{13}C NMR (75 MHz, CDCl$_3$) δ = 197.6, 166.6, 135.1, 134.0, 133.6, 131.0, 129.6, 128.4, 128.3, 128.23, 128.16, 126.6, 122.6, 112.0, 51.7, 49.2, 12.7; GC−MS m/z = 333 (M^+, 5), 301 (4), 243 (16), 242 (100), 212 (16), 128 (4), 115 (3), 104 (5), 91 (5). Anal. calcd for $C_{21}H_{19}NO_3$ (333.38): C, 75.66; H, 5.74; N, 4.20. Found: C, 75.52; H, 5.75; N, 4.19.

*Methyl 2-tert-Butyl-4-(3,3-dimethylbutanoyl)-5-methyl-1H-pyrrole-3-carboxylate (**7f**)*. Yield: 134 mg, starting from 232 mg of (*S*)-*N*-Boc-5-(1-aminoethyl)-2,2,8,8-tetramethylnona-3,6-diyn-5-ol **6f** (66%) (Table 3, entry 6). Yellow oil: IR (film) ν = 3334 (m, br), 2956 (m), 1711 (s), 1647 (m), 1522 (w), 1432 (m), 1366 (w), 1270 (m), 1218 (m), 1165 (m), 1065 (m), 756 (s) cm^{-1}; ^{1}H NMR (500 MHz, CDCl$_3$) δ = 8.93 (s, br, 1 H), 3.79, (s, 3 H), 2.51 (s, 2 H), 2.35 (s, 3 H), 1.34 (s, 9 H), 1.00 (s, 9 H); ^{13}C NMR (126 MHz, CDCl$_3$) δ = 198.9, 168.5, 140.2, 129.3, 124.2, 111.3, 54.1, 51.7, 32.5, 31.5, 29.9, 29.6, 13.3; GC−MS m/z = 293 (M^+, 14), 278 (2), 261 (8), 246 (26), 222 (100), 205 (42), 190 (58), 172 (9), 121 (20). Anal. calcd for $C_{17}H_{27}NO_3$ (293.40): C, 69.59; H, 9.28; N, 4.77. Found: C, 69.65; H, 9.30; N, 4.76.

*Methyl 2-tert-Butyl-4-(3,3-dimethylbutanoyl)-5-isobutyl-1H-pyrrole-3-carboxylate (**7g**)*. Yield: 162 mg, starting from 261 mg of (*S*)-*N*-Boc-5-(1-amino-3-methyl-butyl)-2,2,8,8-tetramethylnona-3,6-diyn-5-ol **6g** (70%) (Table 3, entry 7). Yellow amorphous solid: mp 127−129 °C; IR (KBr) ν = 3369 (m, br), 2963 (m), 1712 (s), 1652 (s), 1513 (w), 1438 (m), 1366 (m), 1271 (w), 1222 (m), 1168 (m), 1062 (m), 710 (w) cm^{-1}; ^{1}H NMR (300 MHz, CDCl$_3$) δ = 7.99 (s, br, 1 H), 3.80 (s, 3 H), 2.56 (d, J = 7.3, 2 H), 2.50 (s, 2 H), 2.02−1.82 (m, 1 H), 1.37 (s, 9 H), 1.01 (s, 9 H); 0.93 (d, J = 6.6, 6 H); ^{13}C NMR (75 MHz, CDCl$_3$) δ = 199.1, 167.8, 140.5, 131.9, 124.9, 111.1, 54.5, 51.6, 35.9, 31.4, 29.9, 29.5, 29.4, 22.5; GC−MS m/z = 335 (M^+, 28), 304 (15), 303 (44), 288 (43), 274 (10), 264 (83), 247 (37), 246 (100), 236 (28), 232 (36), 204 (9), 120 (10). Anal. calcd for $C_{20}H_{33}NO_3$ (335.48): C, 71.60; H, 9.91; N, 4.18. Found: C, 71.67; H, 9.90; N, 4.20.

*Methyl 2-Butyl-1-hexanoyl-6,7-dihydro-5H-pyrrolizine-2-carboxylate (**9**)*. Yield: 156 mg, starting from 181 mg of (*S*)-7-pyrrolidin-2-yl-trideca-5,8-diyn-7-ol **8** (71%) (Scheme 4). Yellow amorphous solid: mp = 59−62 °C; IR (KBr) ν = 3447 (m, br), 2983 (w), 2928 (w), 1744 (s), 1384 (s), 1327 (s), 1291 (w), 1153 (m), 1136 (m), 756 (m), 691 (m) cm^{-1}; ^{1}H NMR (300 MHz, CDCl$_3$) δ = 3.89 (t, J = 7.3, 2 H), 3.80 (s, 3 H), 3.02 (t, J = 7.4, 2 H), 2.76−2.66 (m, 4 H), 2.58−2.46 (m, 2 H), 1.69−1.25 (m, 10 H), 1.00−0.83 (m, 6 H); ^{13}C NMR (75 MHz, CDCl$_3$) δ = 197.8, 166.1, 141.6, 134.9, 117.3, 114.4, 51.2, 45.1, 41.7, 31.76, 31.72, 26.5, 26.0, 25.7, 24.4, 22.6, 22.4, 14.0, 13.8; GC−MS m/z = 319 (M^+, 19), 288 (11), 287 (13), 276 (14), 263 (18), 258 (14), 258 (14), 249 (16), 248 (100), 231 (17), 218 (10), 189 (26), 178 (8), 160 (11), 147 (9), 119 (28), 91 (11). Anal. calcd for $C_{19}H_{29}NO_3$ (319.44): C, 71.44; H, 9.15; N, 4.38. Found: C, 71.38; H, 9.17; N, 4.40.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

X-ray crystallographic data for product *syn*-**3f** and copies of ^{1}H 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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