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One-Pot Synthesis of 1,2-Dihydropyridines: Expanding the Diverse Reactivity of Propargyl Vinyl Ethers

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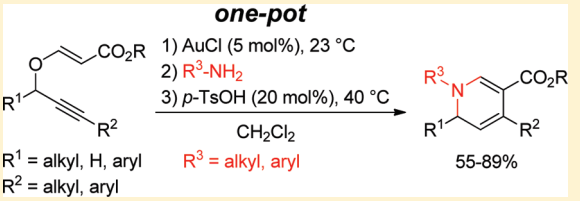
Supporting Information

ABSTRACT: The catalyzed synthesis of 1,2-dihydropyridines starting from easily accessible propargyl vinyl ethers was realized. The reaction sequence involving a transition metal-catalyzed propargyl-Claisen rearrangement, a condensation step, and a Brønsted acid-catalyzed heterocyclization furnishes the highly substituted heterocycles in moderate to excellent yields. Additionally, a practical one-pot protocol toward 1,2-dihydropyridines and 2*H*-pyrans starting from propargylic alcohols was developed.

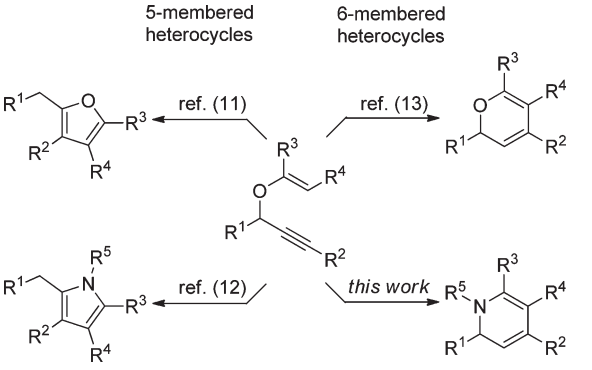


INTRODUCTION

Heterocyclic structures are abundant in natural products as well as pharmaceutically active substances.[1] They can be found as core structures of a variety of therapeutics against a broad spectrum of diseases reaching from hypercholesterolemia (Lipitor)[2] to peptic ulcer desease (Zantac)[3] and hypertension (Amlodipine).[4] Heterocycles are also important intermediates in organic synthesis[5] and gained importance as building blocks for the development of new materials.[6] Their ubiquity in various fields of chemical science contributed to an ongoing major interest in the synthesis of all classes of heterocyclic compounds. In this context, transition metal-catalyzed approaches have become a widely used tool[7−9] that is nowadays a valuable alternative to the more classical condensation approaches.[10]

Over the last five years we demonstrated that propargyl vinyl ethers are viable substrates for the synthesis of a broad variety of heterocyclic compounds by use of transition metal catalysts. Easily accessible, the ethers can3 conveniently be converted into furans,[11] pyrroles,[12] and pyrans[13] as outlined in Scheme 1. For all classes of heterocycles, our highly efficient and atom-economic domino approach[14] consists of rearrangement and subsequent cyclization. In 2005 for example, we reported the first direct conversion of propargyl vinyl ethers into highly substituted furans.[11] This reaction was believed to proceed through a gold-catalyzed propargyl-Claisen rearrangement, followed by a 5-*exo*-heterocyclization onto the gold-activated allene intermediate (Scheme 2).[15] When an additional condensation step with a primary amine was implemented into the reaction cascade, the corresponding pyrroles were obtained via a convenient one-pot sequence.[12,16,17] Both the synthesis of furans and pyrroles remained limited to 5-methyl-substituted heterocycles derived from primary propargylic alcohols. This drawback could be partially overcome by selective IBX-oxidation in the benzylic position as shown in Scheme 3.[12,18,19] Following our domino approach to furans and pyrroles, Jiang et al. very recently reported a few elegant methods for the direct synthesis of furan carbaldehydes

Scheme 1. Synthetic Variability of Propargyl Vinyl Ethers



through in situ oxidation in the presence of several transition metals.[20]

Further development of the methodology allowed the catalyzed formation of 6-membered heterocycles. Despite extensive screening, we never succeeded in finding an appropriate transition metal catalyst for the direct 6-*endo*-cyclization. To surmount this problem, the allenyl carbonyl intermediates were isomerized to 1-oxatrienes, which then underwent 6π-electrocyclization[21] to achieve the product of a formal 6-*endo*-cyclization.[22] We have also been first to synthesize 1,2-dihydropyridines from propargyl vinyl ethers[23] through a sequence of propargyl-Claisen rearrangement, condensation, and heterocyclization in the course of our studies toward the synthesis of pyrroles (Scheme 4).[12] The scope of the original protocol was quite limited yielding only four examples of dihydropyridines with low to moderate yields. Since 1,2-dihydropyridines are of great value as core structures in complex molecules[24] and play an important role as synthetic

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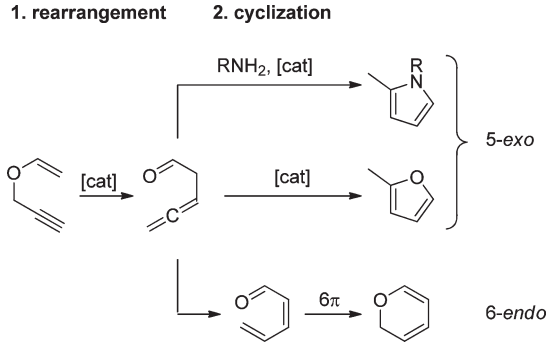
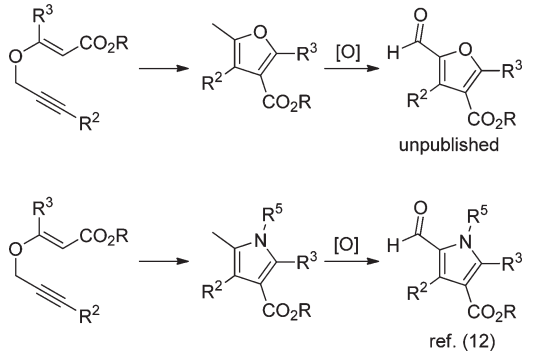
Scheme 2. Our Synthetic Strategies to 5- and 6-Membered Heterocycles



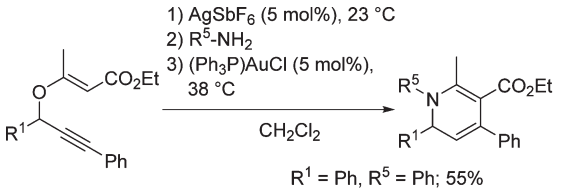
Scheme 3. Oxidative Functionalization of 5-Methyl Furans and Pyrroles



intermediates on the route to pyridines via oxidation and piperidines via reduction,[25] we felt it is of importance to continue our studies in the field with the goal to develop a broadly applicable protocol for the catalyzed transformation of propargyl vinyl ethers into 1,2-dihydropyridines. In the meantime, Tejedor, Méndez-Abt, and García-Tellado showed in an independent study that 1,2-dihydropyridines can be obtained from propargyl vinyl ethers and primary amines when using microwave irradiation at 120 °C in the absence of transition metal catalysts.[26] In 2010, Xu et al. reported a related sequence to 1,2-dihydropyridines catalyzed by gold and silver salts; therein, tosyl amide and propargyl vinyl ethers with mostly terminal alkynes were reacted.[27]

Herein, we now present our full results on the synthesis of 1,2-dihydropyridines from propargyl vinyl ethers. The heterocyclic products are formed in an efficient and easy to perform reaction cascade, which proceeds via a metal-catalyzed propargyl-Claisen rearrangement and a subsequent condensation step, and is terminated by an acid-induced 6π-electrocyclization. The excellent scope of the reaction is defined including its limitations. We also report full details on the transition metal-catalyzed propargyl-Claisen rearrangement that is key for our heterocycle syntheses. The focus is put on the influence of the substrate substitution pattern on their behavior in the catalytic reaction. In addition, an extended one-pot procedure is introduced, which provides access to 1,2-dihydropyridines and pyrans starting from propargylic alcohols rather than propargyl vinyl ethers.

Scheme 4. First Results on the Synthesis of 1,2-Dihydropyridines Starting from Propargyl Vinyl Ethers[12]



R^1 = Ph, R^5 = Ph; 55%
R^1 = Ph, R^5 = 3-Cl-(C_6H_4); 39%
R^1 = Et, R^5 = Ph; 40%
R^1 = Et, R^5 = 2-*i*-Pr-(C_6H_4); 13%

RESULTS AND DISCUSSION

Synthesis of the Propargyl Vinyl Ethers. The propargyl vinyl ethers **2a**−**k** were synthesized in a phosphine-catalyzed 1,4-addition of propargylic alcohols to ynoic acid esters.[28] A broad variety of substrates are accessible in good to excellent yields facing very few limitations (Scheme 5). Furthermore, ethyl ester **2j** was subjected to reduction and subsequent methylation of the alcohol to give **2*l***.

Transition Metal-Catalyzed Propargyl-Claisen Rearrangement. Earlier work in our group on the transition metal-catalyzed propargyl-Claisen rearrangement showed that but-2-enoate derivatives are converted to the corresponding allenes in a very clean and fast reaction by use of several silver salts. Among them, $AgSbF_6$ provides the best results.[12] Another single example of a silver-catalyzed propargyl-Claisen rearrangement was reported by Grissom et al. in 1997.[29] Toste et al. investigated the rearrangement of propargyl vinyl ethers with terminal alkenes and found $[(PPh_3Au)_3O]BF_4$ to be the most efficient catalyst for this class of substrates.[30,31] Since our own results and the results reported in the literature[32,33] give a somewhat unclear picture of the efficiency of catalysts, we decided to reinvestigate this rearrangement step with the focus on subtle changes in the vinylic moiety. To this end, we started the investigation with propargyl vinyl ether **2j** bearing an electron-withdrawing ester moiety (R^4 = CO_2Et) and a methyl donor group (R^3 = Me). Reaction with 0.7 mol % of $AgSbF_6$ proceeded as expected and provided the product in quantitative yield. Indeed, AuCl and $[(PPh_3Au)_3O]BF_4$ containing three atoms gold per molecule catalyst also turned out to be efficient catalysts for this transformation (Table 1, entries 1−4). The former, however, stands out due to its low costs and catalyst loadings as low as 0.1 mol % which are sufficient to reach full conversion. For example, conversion of **2j** with 0.1 mol % of $AgSbF_6$ provided allene **3j** as a mixture of tautomers in quantitative yield after 24 h in CH_2Cl_2 at room temperature (entry 4). Changing the electronic properties of the double bond by replacing the electron-withdrawing group with a donating group leads to a markedly increased reactivity of the substrate. (*E*)-(3-(4-Methoxybut-2-en-2-yloxy)pent-1-ynyl)benzene (**2*l***) is converted into the corresponding allene by use of both silver and gold catalysts. We feel, nevertheless, that also in this case $AgSbF_6$ should be the catalyst of choice due to its excellent efficacy at a low catalyst loading of 0.01 mol % (entry 8). Surprisingly, when acrylate derivate **2a** lacking the additional donor substituent (R^3 = H) was used in the reaction, $AgSbF_6$ only gave poor conversion even after 24 h as did $[(PPh_3Au)_3O]BF_4$. However, AuCl smoothly transformed the propargyl vinyl ether into the allene product. When using a

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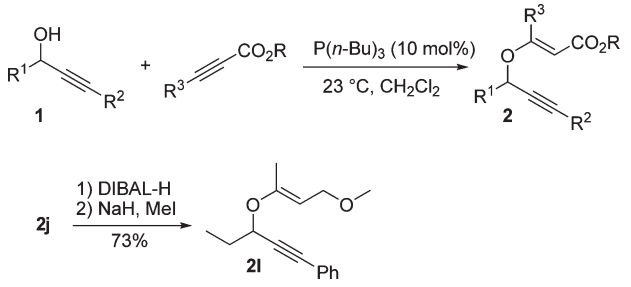
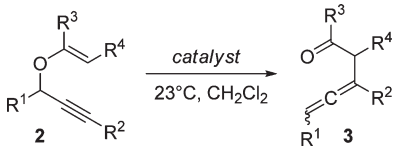
Scheme 5. Synthesis of Propargyl Vinyl Ethers 2a−*l*



2a R^1 = Et, R^2 = Ph, R^3 = H, R = Et; 96%
2b R^1 = Et, R^2 = Ph, R^3 = H, R = Me; 85%
2c R^1 = Me, R^2 = Ph, R^3 = H, R = Et; 93%
2d R^1 = *i*-Pr, R^2 = Ph, R^3 = H, R = Et; 71%
2e R^1 = Ph, R^2 = Ph, R^3 = H, R = Et; 70%
2f R^1 = H, R^2 = Ph, R^3 = H, R = Et; 90%
2g R^1 = CH_2CH_2Ph, R^2 = *n*-Pent, R^3 = H, R = Et; 90%
2h R^1 = Et, R^2 = 4-MeO_2C-C_6H_4, R^3 = H, R = Et; 58%
2i R^1 = Et, R^2 = 4-MeO-C_6H_4, R^3 = H, R = Et; 92%
2j R^1 = Et , R^2 = Ph, R^3 = Me, R = Et; 77%
2k R^1 = H, R^2 = Ph, R^3 = Me, R = Et; 71%

Table 1. Catalyst Screening for the Conversion of 2 into 3[a]



entry	2	R^1	R^2	R^3	R^4	catalyst (mol %)	time (h)	conversion to 3[b,c] (%)
1	j	Et	Ph	Me	CO_2Et	$AgSbF_6$ (0.7)	1.25	100
2						$[(PPh_3Au)_3O]$-BF_4 (0.7)	1.25	100
3						AuCl (0.7)	1.25	75
4						$AgSbF_6$ (0.1)	24	100
5	*l*	Et	Ph	Me	CH_2OMe	$AgSbF_6$ (0.1)	3.5	100
6						$[(PPh_3Au)_3O]$-BF_4 (0.1)	3.5	88
7						AuCl (0.1)	3.5	100
8						$AgSbF_6$ (0.01)	24	100
9	a	Et	Ph	H	CO_2Et	$AgSbF_6$ (3)	4	8
10						$[(PPh_3Au)_3O]$-BF_4 (3)	4	48
11						AuCl (3)	4	100
12						AuCl (0.5)	22	100

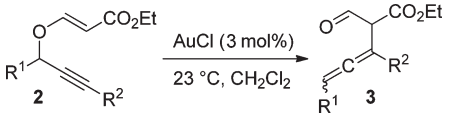
[a] Conditions: substrate **2**, catalyst (mol %), 23 °C, CH_2Cl_2. [b] Conversion was determined by ^{1}H NMR. [c] **3** was detected as the sole product.

minimum of 0.5 mol % of AuCl, allene **3a** was still obtained in quantitative yield after 22 h (Table 1, entry 12).

Subsequently, the substrate scope of the propargyl-Claisen rearrangement catalyzed by AuCl was investigated for substrates with R^3 = H and R^4 = CO_2R since these substrates proved best for the envisaged synthesis of 1,2-dihydropyridines (vide infra) (Table 2). In all cases, the rearrangement furnished a clean aldehyde product according to ^{1}H NMR. It should be noted that only after elongated reaction times the allene products were obtained as mixtures of tautomers. Isolation of the products was indeed possible, though problematic, as the allenes partially reacted to 2*H*-pyrans (<25%) under various workup and purification methods.[34]

Synthesis of 5-Methyl-1,2-dihydropyridines. With these optimized conditions for the rearrangement of different substrate classes, we attempted to complete the envisioned cascade by a condensation step and subsequent heterocyclization. As well as in the propargyl-Claisen rearrangement the substitution pattern

Table 2. Substrate Scope of the Propargyl-Claisen Rearrangement[a]



entry	3	R^1	R^2	conversion[b,c] (%)
1	i	Et	4-MeO-C_4H_6	100
2	d	*i*-Pr	Ph	100
3	g	CH_2CH_2Ph	*n*-Pent	100
4	c	Me	Ph	100
6	e	Ph	Ph	100[d]

[a] Conditions: 60 μmol of **2**, 3 mol % of AuCl, 23 °C, $CDCl_3$ (0.1 M). [b] Conversion was determined by ^{1}H NMR. [c] **3** was detected as the sole product. [d] **3e** was formed as a 1:1 mixture of diastereoisomers.

played a key role in the reaction outcome. Despite the fact that reaction of **2j** (R^3 = Me) using 5 mol % of $AgSbF_6$ provided a clean allenylcarbonyl compound, subsequent conversion with 1.5 equiv of aniline at 23 °C furnished the 1,2-dihydropyridine **4ja** after 16 h in only 27% yield (Scheme 6). As the major side product the corresponding 2*H*-pyran **5j** was formed due to the fast base-mediated heterocyclization prior to the condensation reaction.[13] This drawback could not be overcome by any investigated alteration in the reaction procedure. However, the scope of the reaction was determined and in all cases the desired 6-methyl-1,2-dihydropyridines **4jb**−**jf** were isolated. Unfortunately, only reactions with aniline derivatives provided the desired products. The use of aliphatic amines (R^5 = *i*-Pr, Bn) exclusively led to formation of 2*H*-pyrans. Reaction of propargyl vinyl ether **2k** (R^1 = H) with 3-chloroaniline provided the pyrrole **6kc** in a very slow but clean reaction (72% after 24 h).

Synthesis of Tetrasubstituted Dihydropyridines. In contrast to but-2-enoate **2j**, acrylate **2a** (R^3 = H) was converted into the expected allene intermediate by use of 5 mol % of AuCl and reacted with 1.5 equiv of aniline resulting in a mixture of enamine **7aa** (28%) and dihydropyridine **8aa** (65%) without giving any traces of the pyran side product (Scheme 7). Elaboration of the final cyclization step revealed *p*-toluenesulfonic acid as an efficient additive to catalyze the cyclization event. Consequently, addition of 0.2 equiv of *p*-TsOH led to completion of the reaction, and **8aa** was provided in 88% yield after 15 h at 40 °C.[35] Without the Brønsted acid, the reaction was slowed markedly and in our hands never did reach full conversion even after elongated reaction times.

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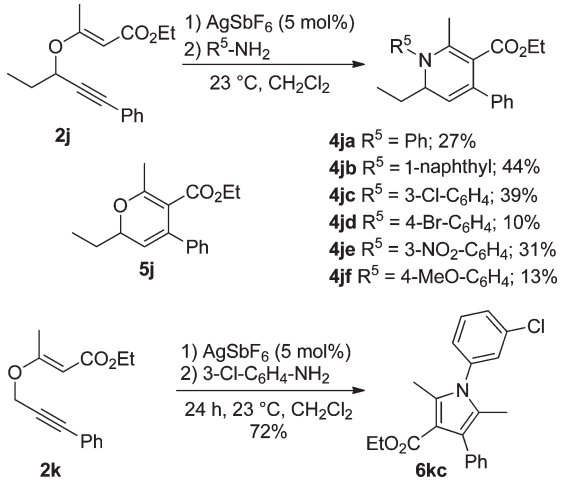
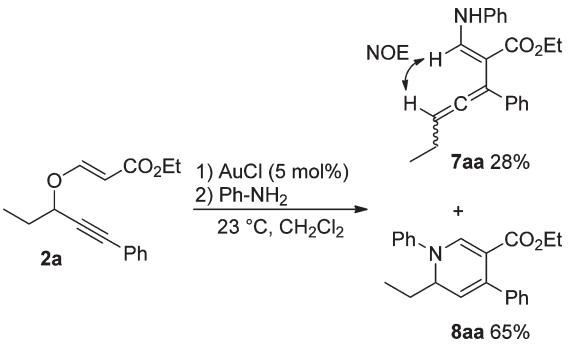
Scheme 6. Reactions of But-2-enoates 2j and 2k



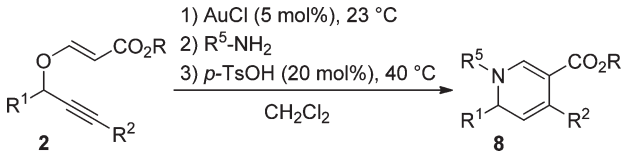
Scheme 7. Conversion of 2a to Enamine 7aa and Dihydropyridine 8aa



As a standardized protocol, we performed the dihydropyridine formation with internal alkynes and used a sequential addition of reagents and catalysts to obtain reproducibly high yields [(1) AuCl (5 mol %), 23 °C; (2) R^5-NH_2; (3) *p*-TsOH (20 mol %), 40 °C, CH_2Cl_2]. Under these conditions, and in contrast to the metal-free protocol developed by Tejedor et al.,[26] terminal alkynes unfortunately did not give the 1,2-dihydropyridines but reacted to inseparable mixtures of unknown products.[36] Nevertheless, a broad variety of previously unknown tetrasubstituted 1,2-dihydropyridines were synthesized in good to excellent yields by using standard conditions. Reaction with anilines as well as aliphatic amines furnished the corresponding products (Table 3, entries 1−8). The formation of 1,2-dihydropyridines also tolerated substitution of R^1 and R^2 with both aryl and alkyl groups (Table 3, entries 9−15). Compound **8fa** bearing no substituent in the 2-position (R^1 = H) was obtained in only moderate yield.

One-Pot Procedures Starting from Propargylic Alcohols. Next, we expanded this one-pot procedure by an additional step that is the formation of the propargyl vinyl ethers. When propargylic alcohols **1** were reacted with 1 equiv of ethyl propiolate and 5 mol % of P(*n*-Bu)$_3$, the Michael-addition remained an efficient process.[28] Subsequent addition of both AuCl and $AgSbF_6$ (5 mol % each) furnished the allenylcarbonyl compounds. Notably, only the use of both catalysts together provided good and reproducible results; neither one was able to catalyze the reaction on its own. The sequence was terminated by condensation with 1.5 equiv of an amine and 0.2 equiv of *p*-TsOH at 40 °C for 15 h to give the desired products in good yields (Scheme 8). It is of particular note that this one-pot procedure presents the possibility to access 1,2-dihydropyridines even in cases when the required propargyl vinyl ether is not accessible due to poor stability. Accordingly, **8ma** was obtained in a reasonable yield although the direct propargyl vinyl ether precursor decomposed upon purification via column chromatography.

Table 3. Substrate Scope of the Conversion of 2 in 1,2-Dihydropyridines 8[a]



	8					
entry	R^1	R^2	R	R^5	no.	yield (%)[b]
1	Et	Ph	Et	Ph	**aa**	88
2	Et	Ph	Et	PMB	**ag**	62
3	Et	Ph	Et	*i*-Pr	**ah**	75
4	Et	Ph	Et	(*S*)-PhCHMe	**ai**	67[c]
5	Et	Ph	Me	4-Br-C_6H_4	**bd**	69
6	Et	Ph	Me	3-NO_2-C_6H_4	**be**	78
7	Et	Ph	Me	4-MeO-C_6H_4	**bf**	85
8	Et	Ph	Me	Bn	**bj**	81
9	Me	Ph	Et	Ph	**ca**	84
10	*i*-Pr	Ph	Et	Ph	**da**	77
11	Ph	Ph	Et	Ph	**ea**	72
12	H	Ph	Et	Ph	**fa**	55
13	CH_2CH_2Ph	*n*-C_5H_9	Et	Ph	**ga**	55
14	Et	4-MeO_2C-C_6H_4	Et	Ph	**ha**	74
15	Et	4-MeO-C_6H_4	Et	Ph	**ia**	89

[a] Conditions: (1) 50 mg of **2**, 5 mol % of AuCl, 23 °C, CH_2Cl_2 (0.1 M), 1 h; (2) R^5-NH_2 (1.5 equiv), 23 °C, 30 min; (3) *p*-TsOH (20 mol %), 40 °C, 15 h. [b] Yield of pure product after column chromatography. [c] The product was isolated as a 1:1.3 mixture of diastereoisomers.

Having demonstrated the efficient generation of 1,2-dihydropyridines directly from propargyl alcohols, the developed sequence was also applied to the synthesis of 2*H*-pyrans. In the case of internal alkynes, PMe_3 proved the better catalyst for the Michael-type addition reaction. However, this step of the sequence remained the crucial one, since complete consumption of the starting material was never observed. Conversion of propargylic alcohols **1** with 1 equiv of ethyl but-2-ynoate in the presence of 0.2 equiv of PMe_3, subsequent addition of AuCl (10 mol %) and $AgSbF_6$ (5 mol %), and finally base-catalyzed 6π-oxaelectrocyclization with 10 mol % of DBU led to the oxygen-containing 6-membered heterocycles in moderate yields (Scheme 9).

Studies on Stereochemical and Mechanistic Details. Mechanistically, the cascade reaction to 1,2-dihydropyridine may proceed via two different pathways delineated in Scheme 10. After rearrangement and condensation, the imine (or enamine) moiety could perform a 6-*endo*-cyclization onto the allene when

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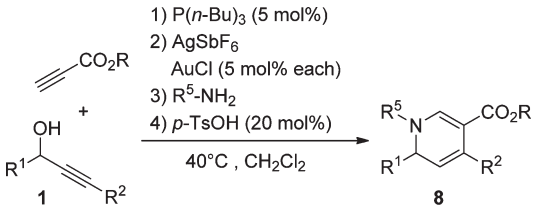
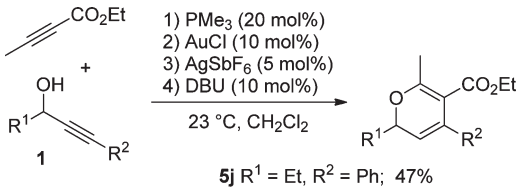
Scheme 8. One-Pot Synthesis of 1,2-Dihydropyridines 8 Starting from Propargylic Alcohols 1



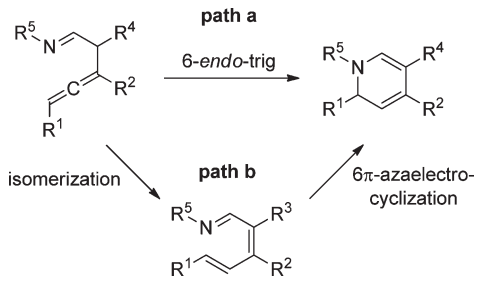
8aa R^1 = Et, R^2 = Ph, R = Et, R^5 = Ph; 66%
8da R^1 = *i*-Pr R^2 = Ph, R = Et, R^5 = Ph; 63%
8bf R^1 = Et, R^2 = Ph, R = Me R^5 = 4-MeO-C_6H_4; 75%
8ma R^1 = Ph, R^2 = *n*-C_5H_9, R = Et, R^5 = Ph; 41%

Scheme 9. One-Pot Synthesis of 2*H*-Pyrans 5 Starting from Propargylic Alcohols 1



5j R^1 = Et, R^2 = Ph; 47%
5n R^1 = Et, R^2 = 4-*t*-Bu-C_6H_4; 42%
5o R^1 = Et, R^2 = 3-thienyl; 42%
5p R^1 = Et, R^2 = 4-PhO-C_6H_4; 39%

Scheme 10. Two Possible Pathways of the 1,2-Dihydropyridine Formation

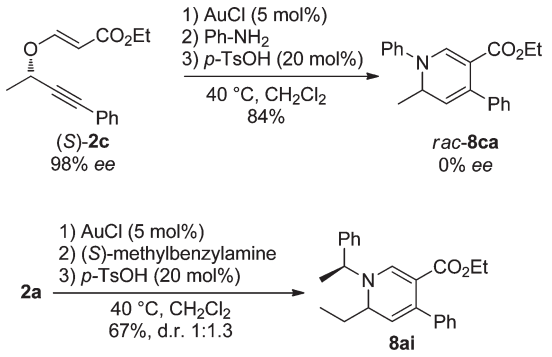


combined with a proton shift (path a).[37] On the other hand, isomerization to the azatriene system could take place, which then would undergo a 6π-azaelectrocyclization (path b).[38]

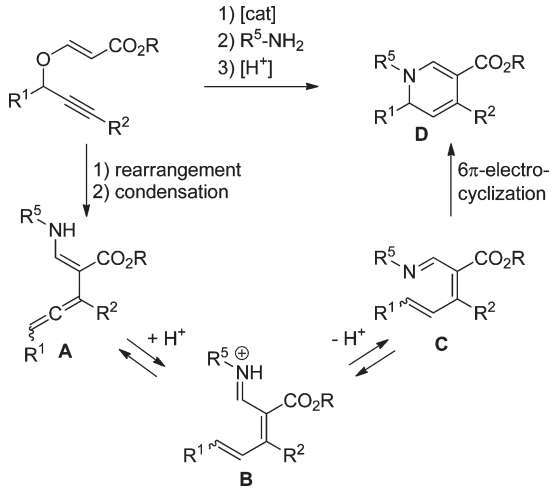
To conclusively determine mechanistic details, we took a deeper insight into the stereochemical course of the reaction. When enantiomerically pure propargyl vinyl ether (*S*)-**2c** (98% ee) was submitted to the standard reaction conditions, the product **8ca** was formed as a racemic mixture with complete loss of enatiopurity. This observation might point to a mechanism proceeding through an achiral intermediate (i.e., path b). In contrast, the reaction of **2a** with (*S*)-1-methylbenzylamine gave 1,2-dihydropyridine **8ai** with a slight diastereoselectivity as a 1:1.3 mixture of diastereoisomers (Scheme 11).

On the basis of these results and the isolation of the enamine intermediate **7aa** (Scheme 7), we propose a plausible mechanism

Scheme 11. Stereochemical Course of the 1,2-Dihydropyridine Formation



Scheme 12. Mechanistic Proposal



for the presented domino approach to 1,2-dihydropyridines outlined in Scheme 12: After Au-catalyzed rearrangement that most likely proceeds through a cyclization-induced rearrangement mechanism (CIR),[39,30] enamine **A** is formed in a classical condensation reaction. Protonation of **A** might lead to achiral iminium ion **B**, which is further converted to azatriene **C** resulting in a net tautomerization of **A** into **C**. Subsequent 6π-electrocyclization to 1,2-dihydropyridine **D** then terminates the reaction sequence.

CONCLUSION

In conclusion, we developed an independently catalyzed reaction cascade for the convenient synthesis of 1,2-dihydropyridines starting from propargyl vinyl ethers. We also presented a practical one-pot procedure that includes the in situ formation of these precursors and provides the nitrogen, as well as the oxygen, containing 6-membered heterocycles. These results once again emphasize the value of propargyl vinyl ethers as easily accessible starting materials for the synthesis of a broad variety of heterocyclic compounds. Further use of this concept in the library construction of heterocycles is currently under investigation.

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EXPERIMENTAL SECTION

General. All reactions were carried out in sealed reaction vials. CH_2Cl_2 was passed through activated alumina columns prior to use. All other commercial reagents were used as received. (*S*)-4-Phenylbut-3-yn-2-ol was synthesized following the procedure of Knochel et al.[40] Thin-layer chromatography (TLC) was conducted with precoated glass-backed plates (silica gel 60 F_{254}) and visualized by exposure to UV light (254 nm) or stained with ceric ammonium molybdate. Flash chromatography was performed with silica gel. The eluent used is reported in parentheses. ^{1}H NMR spectra were recorded on 500, 360, or 250 MHz spectrometers. ^{13}C NMR spectra were recorded at 126, 90.6, or 63 MHz. Chemical shifts are reported in ppm relative to solvent signal. Multiplicity is indicated as follows: s (singlet); d (doublet); t (triplet); q (quartet); m (multiplet); dd (doublet of doublets); sep (septet). *J* values are given in hertz. Low resolution mass spectra were recorded applying GC-MS, EI, or ESI technique. High-resolution mass spectra were obtained by using the EI or ESI ionization method.

General Procedure A for the Formation of Propargyl Vinyl Ethers 2 Starting from Propargylic Alcohols 1. (*E*)-Methyl 3-(1-phenylpent-1-yn-3-yloxy)acrylate (2a): To a solution of 800 mg of 1-phenylpent-1-yn-3-ol (4.99 mmol) and 0.51 mL of ethyl propiolate (498 mg, 4.99 mmol, 1 equiv) in 40 mL of dry CH_2Cl_2 was added 0.13 mL of P(*n*-Bu)$_3$ (101 mg, 0.50 mmol, 10 mol %) dropwise. The solution was stirred at room temperature until TLC indicated full conversion. The solvent was removed and the residue was purified by flash chromatography on silica gel (pentane/EtOAc 98:2). The product was obtained as a colorless oil (1.24 g, 4.78 mmol, 96%): R_f 0.84 (pentane/EtOAc 95:5) [UV], [CAM]; ^{1}H NMR (250 MHz, $CDCl_3$) δ 1.10 (t, J = 7.4, 3H), 1.28 (t, J = 7.1, 3H), 1.89−2.03 (m, 2H), 4.18 (q, J = 7.3, 2H), 4.68−4.77 (m, 1H), 5.43 (d, J = 12.5, 1H), 7.28−7.37 (m, 3H), 7.41−7.49 (m, 2H), 7.70 (d, J = 12.5, 1H); ^{13}C NMR (63 MHz, $CDCl_3$) δ 9.6, 14.5, 28.9, 60.0, 73.4, 85.4, 88.0, 98.9, 122.1, 128.5, 129.0, 132.0, 160.6, 167.9; LRMS (EI) *m*/*z* 258 (6%) [M^+], 228 (5%), 185 (9%), 143 (100%), 128 (74%), 115 (16%), 103 (5%), 43 (8%); HRMS (EI) *m*/*z* 258.1238 [258.1256 calculated for $C_{16}H_{18}O_3$ (M^+)].

(*E*)-Methyl 3-(1-phenylpent-1-yn-3-yloxy)acrylate (2b): Following general procedure A, **2b** was obtained as a colorless oil (85%) after flash chromatography on silica gel (pentane/EtOAc 95:5): R_f 0.29 (pentane/EtOAc 95:5) [UV] [CAM] [$KMnO_4$]; ^{1}H NMR (360 MHz, $CDCl_3$) δ 1.10 (t, J = 7.4, 1H), 1.96 (quint, J = 6.9, 1H), 3.71 (s, 3H), 4.72 (t, J = 6.4, 1H), 5.44 (d, J = 12.5, 1H), 7.29−7.37 (m, 3H), 7.42−7.47 (m, 2H), 7.70 (d, J = 12.5, 1H); ^{13}C NMR (90.6 MHz, $CDCl_3$) δ 9.6, 28.9, 51.3, 73.4, 85.3, 88.0, 98.6, 122.0, 128.5, 129.0, 132.0, 160.8, 168.3; LRMS (EI) *m*/*z* 244 (1%) [M^+], 212 (3%), 185 (16%), 143 (100%), 128 (93%), 115 (18%), 103 (17%), 77 (5%); HRMS (EI) *m*/*z* 185.0963 [185.0966 calculated for $C_{13}H_{13}O$ (M^+ − CO_2Me)].

(*E*)-Ethyl 3-(4-phenylbut-3-yn-2-yloxy)acrylate (2c): Following general procedure A, **2c** was obtained as a pale yellow oil (93%) after flash chromatography on silica gel (pentane/EtOAc 95:5). The enatiomerically pure (*S*)-(*E*)-ethyl 3-(4-phenylbut-3-yn-2-yloxy)acrylate was synthesized starting from (*S*)-4-phenylbut-3-yn-2-ol:[40] R_f 0.46 (pentane/EtOAc 90:10) [UV] [CAM]; ^{1}H NMR (250 MHz, $CDCl_3$) δ 1.28 (t, J = 7.1, 3H), 1.65 (d, J = 6.6, 2H), 4.17 (q, J = 7.1, 2H), 4.90 (q, J = 6.6, 1H), 5.42 (d, J = 12.5, 1H), 7.29−7.35 (m, 3H), 7.42−7.45 (m, 2H), 7.68 (d, J = 12.5, 1H); ^{13}C NMR (63 MHz, $CDCl_3$) δ 14.5, 22.0, 60.0, 68.1, 86.3, 87.2, 99.1, 122.0, 128.5, 129.0, 132.0, 160.3, 167.8; LRMS (EI) *m*/*z* 244(3%) [M^+], 229 (6%), 215 (18%), 171 (63%), 129 (100%); HRMS (EI) *m*/*z* 244.1096 [244.1099 calculated for $C_{15}H_{16}O_3$ (M^+)].

(*E*)-Ethyl 3-(4-methyl-1-phenylpent-1-yn-3-yloxy)acrylate (2d): Following general procedure A, **2d** was obtained as a pale yellow oil (71%) after flash chromatography on silica gel (pentane/EtOAc 95:5): R_f 0.29 (pentane/EtOAc 95:5) [UV] [CAM] [$KMnO_4$]; ^{1}H NMR (250 MHz, $CDCl_3$) δ 1.09 (t, J = 6.8, 6H), 1.27 (t, J = 7.1, 3H), 2.15 (qd, J = 13.4, 6.7, 1H), 4.17 (q, J = 7.1, 2H), 4.56 (d, J = 5.8, 1H), 5.42 (d, J = 12.5, 1H), 7.29−2.37 (m, 3H), 7.41−7.49 (m, 2H), 7.69 (d, J = 12.5, 1H); ^{13}C NMR (63 MHz, $CDCl_3$) δ 14.5, 7.8, 18.4, 33.4, 59.9, 77.6, 84.4, 88.5, 98.8, 122.1, 128.5, 128.9, 132.0, 160.9, 167.9 LRMS (EI) *m*/*z* 272.1 (1%), 199.1 (15%) [M^+ − $C_3H_5O_2$], 157.1 (100%), 142.1 (78%), 129.0 (46%), 115.0 (28%); HRMS (EI) *m*/*z* 229.0863 [229.0847 calculated for $C_{14}H_{13}O_3$ (M^+ − C_3H_7)].

(*E*)-Ethyl 3-(1,3-diphenylprop-2-ynyloxy)acrylate (2e): Following general procedure A, **2e** was obtained as a yellow oil (70%) after flash chromatography on silica gel (pentane/EtOAc 95:5): R_f 0.52 (pentane/EtOAc 90:10) [UV] [CAM]; ^{1}H NMR (360 MHz, $CDCl_3$) δ 1.28 (t, J = 7.1, 3H), 4.17 (q, J = 7.1, 2H), 5.51 (d, J = 12.5, 1H), 5.87 (s, 1H), 7.31−7.37 (m, 3H), 7.40−7.45 (m, 3H), 7.48−7.51 (m, 2H), 7.57−7.60 (m, 2H), 7.76 (d, J = 12.5, 1H); ^{13}C NMR (91 MHz, $CDCl_3$) δ 14.5, 60.0, 73.9, 84.5, 89.9, 99.9, 121.8, 127.7, 128.5, 129.0, 129.2, 129.4, 132.1, 136.6, 160.0, 167.7; LRMS (ESI) *m*/*z* 329 (19%) [M^+ + Na], 307 (30%) [M^+ + H], 282 (100%), 261 (14%), 191 (73%); HRMS (ESI) *m*/*z* 307.1329 [307.1334 calculated for $C_{20}H_{19}O_3$ (M^+ + H)].

(*E*)-Ethyl 3-(3-phenylprop-2-ynyloxy)acrylate (2f): Following general procedure A, **2f** was obtained as a light yellow oil (90%) after flash chromatography on silica gel (pentane/EtOAc 95:5): R_f 0.50 (pentane/EtOAc 90:10) [UV] [CAM]; ^{1}H NMR (250 MHz, $CDCl_3$) δ 1.28 (t, J = 7.1, 1H), 4.18 (q, J = 7.1, 1H), 4.75 (s, 1H), 5.38 (d, J = 12.6, 1H), 7.30−7.36 (m, 3H), 7.40−7.48 (m, 2H), 7.64 (d, J = 12.6, 1H); ^{13}C NMR (63 MHz, $CDCl_3$) δ 14.5, 59.2, 59.5, 60.1, 82.1, 88.6, 98.5, 121.9, 128.4, 128.5, 129.2, 132.0, 160.9, 167.5; LRMS (EI) *m*/*z* 230 (1%) [M^+], 201 (4%), 157 (9%), 115 (100%), 105 (3%), 89 (5%); HRMS (EI) *m*/*z* 230.0944 [230.0943 calculated for $C_{14}H_{14}O_3$ (M^+)].

(*E*)-Ethyl 3-(1-phenyldec-4-yn-3-yloxy)acrylate (2g): Following general procedure A, **2g** was obtained as a colorless oil (90%) after flash chromatography on silica gel (pentane/EtOAc 95:5): R_f 0.35 (pentane/EtOAc 95:5) [UV] [CAM] [$KMnO_4$]; ^{1}H NMR (250 MHz, $CDCl_3$) δ 0.89 (t, J = 7.1, 3H), 1.27 (t, J = 7.1, 3H), 1.32−1.42 (m, 4H), 1.46 − 1.58 (m, 2H), 2.02−2.17 (m, 2H), 2.23 (td, J = 7.0, 2.0, 2H), 2.78 (t, J = 7.6, 2H), 4.16 (q, J = 7.1, 2H), 4.49 (tt J = 6.5, 1.7, 1H), 5.35 (d, J = 12.5, 1H), 7.16−7.32 (m, 5H), 7.62 (d, J = 12.5, 1H); ^{13}C NMR (63 MHz, $CDCl_3$) δ 14.1, 14.5, 18.8, 22.3, 28.2, 31.1, 31.3, 37.4, 59.9, 71.2, 89.6, 98.8, 126.3, 128.6, 128.7, 140.8, 160.6, 167.9; LRMS (EI) *m*/*z* 328.2 (1%) [M^+], 143.1 (23%), 117.0 (27%), 91.0 (100%); HRMS (EI) *m*/*z* 328.2041 [328.2038 calculated for $C_{21}H_{28}O_3$ (M^+)].

(*E*)-Methyl 4-(3-(3-ethoxy-3-oxoprop-1-enyloxy)pent-1-ynyl)-benzoate (2h): Following general procedure A, **2h** was obtained as a colorless oil (58%) after flash chromatography on silica gel (pentane/EtOAc 95:5 → 90:10): R_f 0.36 (pentane/EtOAc 90:10) [UV] [CAM]; ^{1}H NMR (250 MHz, $CDCl_3$) δ 1.10 (t, J = 7.4, 3H), 1.27 (t, J = 7.1, 3H), 1.90−2.02 (m, 2H), 3.92 (s, 3H), 4.17 (q, J = 7.1, 2H), 4.72 (t, J = 6.4, 1H), 5.42 (d, J = 12.5, 1H), 7.50 (d, J = 8.6, 2H), 7.67 (d, J = 12.5, 1H), 7.99 (d, J = 8.6, 2H); ^{13}C NMR (63 MHz, $CDCl_3$) δ 9.5, 14.5, 28.8, 52.4, 60.0, 73.1, 87.1, 88.3, 99.1, 126.7, 129.6, 130.3, 131.9, 160.5, 166.5, 167.8; LRMS (EI) *m*/*z* 316 (4%) [M^+], 287 (8%), 243 (14%), 201 (100%), 169 (17%), 142 (62%), 59 (14%); HRMS (EI) *m*/*z* 316.1309 [316.1311 calculated for $C_{18}H_{20}O_5$ (M^+)].

(*E*)-Ethyl 3-(1-(4-methoxyphenyl)pent-1-yn-3-yloxy)-acrylate (2i): Following general procedure A, **2i** was obtained as a colorless oil (92%) after flash chromatography on silica gel (pentane/EtOAc 95:5): R_f 0.48 (pentane/EtOAc 90:10) [UV] [CAM]; ^{1}H NMR (360 MHz, $CDCl_3$) δ 1.09 (t, J = 7.4, 3H), 1.27 (t, J = 7.1, 3H), 1.90−1.98 (m, 2H), 3.81 (s, 3H), 4.17 (qd, J = 7.1, 0.7, 2H), 4.71 (t, J = 6.4, 1H), 5.41 (d, J = 12.5, 1H), 6.84 (d, J = 8.9, 2H), 7.38 (d, J = 8.9, 2H), 7.69 (d, J = 12.5, 1H); ^{13}C NMR (91 MHz, $CDCl_3$) δ 9.6, 14.5, 29.0, 55.4, 59.9, 73.6, 84.0, 88.0, 98.8, 114.1, 114.1, 133.5, 160.1, 160.7, 167.9; LRMS (EI) *m*/*z* 288 (3%) [M^+], 215 (31%), 173 (100%), 158 (34%); HRMS (EI) *m*/*z* 288.1361 [288.1362 calculated for $C_{17}H_{20}O_4$ (M^+)].

(*E*)-Ethyl 3-(1-phenylpent-1-yn-3-yloxy)but-2-enoate (2j): Following general procedure A, **2j** was obtained as a colorless oil (77%) after flash chromatography on silica gel (pentane/EtOAc 98:2): R_f 0.73 (pentane/EtOAc 95:5) [UV] [CAM]; ^{1}H NMR (250 MHz, $CDCl_3$) δ 1.04 (t, J = 7.4, 3H), 1.22 (t, J = 7.1, 3H), 1.83−1.97 (m, 2H), 2.27 (s, 3H), 3.98−4.19 (m, 2H), 4.71 (t, J = 6.3, 1H), 5.26 (s, 1H), 7.17−7.30 (m, 3H), 7.33−7.42 (m, 2H); ^{13}C NMR (63 MHz, $CDCl_3$) δ 9.7, 15.0, 19.2, 28.9, 59.5, 69.4, 85.9, 87.1, 93.4, 122.4, 128.4 (2C), 128.8, 132.0 (2C), 168.1, 170.7; LRMS (EI) m/z 272 (3%) [M^+], 243 (16%), 229 (18%), 199 (36%), 143 (79%), 128 (100%), 115 (24%), 43 (14%); HRMS (EI) m/z 272.1399 [272.1412 calculated for $C_{17}H_{20}O_3$ (M^+)].

(*E*)-Ethyl 3-(3-phenylprop-2-ynyloxy)but-2-enoate (2k): Following general procedure A, **2k** was obtained as a light yellow solid (71%) after flash chromatography on silica gel (pentane/EtOAc 95:5): R_f 0.43 (pentane/EtOAc 95:5) [UV] [CAM]; ^{1}H NMR (250 MHz, $CDCl_3$) δ 1.28 (t, J = 7.1, 3H), 2.35 (s, 3H), 4.15 (q, J = 7.1, 2H), 4.71 (s, 2H), 5.18 (s, 1H), 7.29−7.35 (m, 3H), 7.44−7.48 (m, 2H); ^{13}C NMR (63 MHz, $CDCl_3$) δ 14.6, 19.1, 56.8, 59.7, 82.5, 87.8, 92.7, 122.2, 128.5, 129.0, 132.0, 167.8, 171.1.; LRMS (GC-MS) m/z 244 (32%) [M^+], 215 (55%), 198 (75%), 171 (45%), 1555 (72%), 128 (100%), 115 (42%); HRMS (ESI) m/z 245.1173 [245.1172 calculated for $C_{15}H_{17}O_3$ ($M^+ + H$)].

(*E*)-(3-(4-Methoxybut-2-en-2-yloxy)pent-1-ynyl)benzene (2*l*): **2j** (480 mg, 1.76 mmol) was dissolved in 18 mL of dry CH_2Cl_2 and 4.4 mL of DIBAL-H (1 M in hexane; 4.41 mmol, 2.5 equiv) was added at −78 °C. The reaction mixture was stirred at the same temperature for 2 h. The Reaction was quenched by the addition of 20 mL of K-Na-tartrate solution (20% w/w in water) and 0.88 mL of glycerine (0.2 mL/mmol DIBAL-H) was added. The mixture was stirred at room temperature for 1 h. The phases were separated and the aqueous layer was extracted with 2 × 20 mL of CH_2Cl_2. The combined organic phases were washed with brine and dried over $MgSO_4$. The solvent was evaporated and the residue was purified by flash chromatography on silica gel (pentane/EtOAc 80:20). The primary alcohol was obtained as a colorless oil (368 mg, 1.68 mmol, 95%): R_f 0.46 (pentane/EtOAc 70:30) [UV] [CAM]; ^{1}H NMR (360 MHz, $CDCl_3$) δ 1.09 (t, J = 7.42, 3H), 1.56 (s, 1H), 1.90 (s, 3H), 1.87−1.97 (m, 2H), 4.18 (t, 2H), 4.64 (t, J = 6.4, 1H), 5.06 (t, J = 7.7, 1H), 7.27−7.33 (m, 3H), 7.39−7.46 (m, 2H); ^{13}C NMR (91 MHz, $CDCl_3$) δ 9.6, 31.2, 45.5, 58.0, 64.4, 85.1, 90.2, 122.9, 128.42, 128.5, 128.9, 131.9, 133.6, 137.6; LRMS (EI) m/z 230 (1%) [M^+], 211 (4%), 199 (12%), 183 (14%), 143 (33%), 131 (100%), 128 (78%), 115 (31%), 103 (30%); HRMS (EI) m/z 199.1114 [199.1123 calculated for $C_{14}H_{15}O$ (M^+CH_2OH)].

To a stirred suspension of 235 mg of NaH (5.88 mmol, 2 equiv) in 1.5 mL of dry DMF was added a solution of 676 mg of the above alcohol (2.94 mmol) in 1.5 mL of dry DMF dropwise at 0 °C. The mixture was stirred for 15 min and 0.46 mL of MeI (1.04 g, 7.35 mmol, 2.5 equiv) was added. The reaction mixture was warmed to room temperature and stirred for 2 h. The reaction was quenched by the addition of 10 mL of saturated NH_4Cl solution. The mixture was extracted with 3 × 10 mL of Et_2O. The combined organic phases were washed with brine and dried over $MgSO_4$. The solvent was evaporated and the residue was purified by flash chromatography on silica gel (pentane/EtOAc 95:5). Methyl ether **2*l*** was obtained as a colorless oil (555 mg, 2.27 mmol, 77%): R_f 0.69 (pentane/EtOAc 85:15) [UV] [CAM]; ^{1}H NMR (360 MHz, $CDCl_3$) δ 1.09 (t, J = 7.4, 3H), 1.89 (s, 3H), 1.85−1.97 (m, 2H), 3.32 (s, 3H), 3.98 (dd, J = 2.5, 7.6, 2H), 4.65 (t, 1H), 4.94 (t, J = 7.6, 1H), 7.27−7.34 (m, 3H), 7.39−7.45 (m, 2H); ^{13}C NMR (91 MHz, $CDCl_3$) δ 9.8, 16.7, 29.1, 57.2, 68.2, 68.9, 86.0, 87.7, 96.3, 123.0, 128.3, 128.4, 131.9, 156.2; LRMS (EI) m/z 230.13 (2%) [M − CH_3], 199 (36%), 183 (30%), 141 (65%), 128 (100%), 115 (47%), 105 (26%); HRMS (EI) m/z 245.1554 [245.1536 calculated for $C_{16}H_{21}O_2$ ($M^+ + H$)].

Synthesis of Allenyl Carbonyl Compounds 3. Ethyl 2-acetyl-3-phenylhepta-3,4-dienoate (3j): **2j** (15 mg, 55.1 μmol) was dissolved in 0.4 mL of CD_2Cl_2 and 14 μL of a 10 mg/mL stock solution of $AgSbF_6$ in CD_2Cl_2 (0.14 mg, 0.39 μmol, 0.7 mol %) was added. The reaction mixture was stirred until TLC indicated complete consumption of the starting material. Allene **3j** was formed in quantitative yield according to ^{1}H NMR: R_f 0.80 (P/EtOAc 95:5) [UV] [CAM]; ^{1}H NMR (250 MHz, $CDCl_3$) δ 1.09 (t, J = 7.4, 3H), 1.26 (t, J = 7.1, 3H), 2.12−2.23 (m, 2H), 2.26 (s, 3H), 4.11−4.27 (m, 2H), 4.57 (d, J = 1.8, 1H), 5.78 (td, J = 6.1, 1.8, 1H), 7.18−7.36 (m, 5H); ^{13}C NMR (63 MHz, $CDCl_3$) δ 13.2, 14.2, 22.1, 28.5, 61.7, 61.9, 99.2, 101.7, 125.7, 127.3, 128.8, 135.6, 168.6, 202.4, 204.7.

3-(Methoxymethyl)-4-phenylocta-4,5-dien-2-one (3*l*): To a solution of 15 mg of **2*l*** (61.4 μmol) in 0.5 mL of CD_2Cl_2 was added 11 μL of a 2 mg/mL stock solution of $AgSbF_6$ in CD_2Cl_2 (0.022 mg, 0.06 μmol, 0.1 mol %). The reaction mixture was stirred until TLC indicated complete conversion. Allene **3*l*** was formed in quantitative yield according to ^{1}H NMR: R_f 0.52 (P/EtOAc 95:5) [UV] [CAM]; ^{1}H NMR (250 MHz, $CDCl_3$) δ 1.07 (t, J = 7.4, 3H), 2.09−2.20 (m, 2H), 2.16 (s, 3H), 3.36 (s, 3H), 3.52−3.64 (m, 1H), 3.81−3.92 (m, 2H), 5.72 (t, J = 6.1, 1H), 7.19−7.26 (m, 1H), 7.30−7.36 (m, 2H), 7.42−7.45 (m, 2H); ^{13}C NMR (63 MHz, $CDCl_3$) δ 13.3, 22.1, 28.1, 53.9, 59.1, 72.6, 98.5, 103.0, 126.2, 127.2, 128.7, 136.1, 203.9, 206.6.

General Procedure B for the Formation of Allenyl Carbonyl Compounds 3a,c,d,e,g,i. Ethyl 2-formyl-3-phenylhepta-3,4-dienoate (3a): **2a** (15.0 mg, 58.1 μmol) was dissolved in 0.4 mL of $CDCl_3$ and 20 μL of a 20 mg/mL stock solution of AuCl in $CDCl_3$ (0.41 mg, 1.74 μmol, 3 mol %) was added. The reaction was stirred at room temperature until TLC indicated full conversion. Allene **3a** was formed in quantitative yield according to ^{1}H NMR: R_f 0.42 (P/EtOAc 93:7) [UV] [CAM]; ^{1}H NMR (250 MHz, $CDCl_3$) δ 1.10 (t, J = 7.4, 3H), 1.26 (t, J = 7.1, 3H), 2.14−2.25 (m, 1H), 4.22 (qd, J = 7.1, 1.2, 1H), 4.35 (dd, J = 3.0, 1.7, 1H), 5.85 (td, J = 6.2, 1.6, 1H), 7.20−7.40 (m, 5H), 9.67 (d, J = 3.0, 1H); ^{13}C NMR (63 MHz, $CDCl_3$) δ 13.1, 14.2, 22.1, 58.7, 61.9, 99.9, 100.1, 125.9, 127.5, 128.8, 135.2, 168.3, 195.0, 205.3.

Ethyl 2-formyl-3-(4-methoxyphenyl)hepta-3,4-dienoate (3i:). Following general procedure B, **3i** was furnished in quantitative yield according to ^{1}H NMR: R_f 0.43 (P/EtOAc 95:5) [UV] [CAM]; ^{1}H NMR (250 MHz, $CDCl_3$) δ 1.08 (t, J = 7.4, 3H), 1.26 (t, J = 7.1, 3H), 2.12−2.23 (m, 1H), 3.80 (s, 3H), 4.17−4.26 (m, 2H), 4.29−4.32 (m, 1H), 5.81 (td, J = 6.1, 1.4, 1H), 6.87 (d, J = 8.9, 2H), 7.29 (d, J = 8.9, 2H), 9.65 (d, J = 3.2, 1H); ^{13}C NMR (63 MHz, $CDCl_3$) δ 13.1, 13.3, 14.2, 22.2, 55.5, 58.9, 61.8, 99.8, 99.8, 114.3, 127.1, 127.3, 159.2, 168.3, 195.2, 204.6.

Ethyl 2-formyl-6-methyl-3-phenylhepta-3,4-dienoate (3d): Following general procedure B, **3d** was furnished in quantitative yield according to ^{1}H NMR: R_f 0.58 (P/EtOAc 95:5) [UV] [CAM]; ^{1}H NMR (250 MHz, $CDCl_3$) δ 1.11 (d, J = 6.8, 3H), 1.11 (d, J = 6.8, 3H), 1.25 (t, J = 7.1, 3H), 2.43−2.56 (m, 1H), 4.22 (qd, J = 7.2, 0.7, 2H), 4.36 (dd, J = 3.0, 1.8, 1H), 5.80 (dd, J = 5.8, 1.7, 1H), 7.20−7.40 (m, 5H), 9.67 (d, J = 3.0, 1H); ^{13}C NMR (63 MHz, $CDCl_3$) δ 14.2, 22.4, 22.4, 28.9, 58.7, 61.9, 100.5, 105.5, 125.8, 127.5, 128.8, 135.1, 168.2, 195.0, 204.0.

Ethyl 2-formyl-3-(4-phenylbut-1-enylidene)octanoate (3g): Following general procedure B, **3g** was furnished in quantitative yield according to ^{1}H NMR: R_f 0.62 (P/EtOAc 95:5) [UV] [CAM]; ^{1}H NMR (250 MHz, $CDCl_3$) δ 0.88 (t, J = 6.6, 3H), 1.24−1.40 (m, 6H), 1.29 (t, J = 7.1, 3H), 1.93−2.00 (m, 2H), 2.31−2.40 (m, 2H), 2.70−2.76 (m, 2H), 3.59 (dd, J = 3.6, 1.7, 1H), 4.22 (qd, J = 7.1, 1.6, 2H), 5.36−5.45 (m, 1H), 7.15−7.32 (m, 2H), 9.54 (d, J = 3.6, 1H); ^{13}C NMR (63 MHz, $CDCl_3$) δ 14.2, 14.3, 22.6, 27.0, 30.6, 31.4, 32.2, 35.3, 60.8, 61.6, 95.1, 98.2, 126.1, 128.5, 128.6, 141.6, 168.3, 195.4, 203.2.

Ethyl 2-formyl-3-phenylhexa-3,4-dienoate (3c): Following general procedure B, **3c** was furnished in quantitative yield according to ^{1}H NMR: R_f 0.39 (P/EtOAc 95:5) [UV] [CAM]; ^{1}H NMR (250 MHz, $CDCl_3$) δ 1.28 (t, J = 7.1, 3H), 1.83 (d, J = 7.2, 3H), 4.24 (q, J = 7.1, 2H), 4.33 (dd, J = 3.1, 1.6, 1H), 5.75 (qd, J = 7.3, 1.6, 1H), 7.20−7.38 (m,

5H), 9.70−9.70 (m, 1H); ^{13}C NMR (63 MHz, $CDCl_3$) δ 13.9, 14.2, 58.8, 61.9, 92.8, 98.9, 126.1, 127.5, 128.8, 135.1, 168.3, 194.9, 206.6.

Ethyl 2-formyl-3,5-diphenylpenta-3,4-dienoate (3e): Following general procedure B, **3e** was furnished in quantitative yield according to ^{1}H NMR: R_f 0.30 (P/EtOAc 95:5) [UV] [CAM]; ^{1}H NMR (250 MHz, $CDCl_3$) δ 1.16−1.27 (m, 6H), 4.09−4.29 (m, 4H), 4.50−4.53 (m, 2H), 6.77 (d, J = 1.3, 1H), 6.79 (d, J = 1.4, 1H), 7.25−7.47 (m, 20H), 9.75 (d, J = 2.5, 1H), 9.76 (d, J = 2.4, 1H); ^{13}C NMR (63 MHz, $CDCl_3$) δ 14.1, 14.2, 59.0, 59.6, 62.2, 62.2, 100.8, 101.1, 103.5, 103.5, 126.2, 126.2, 127.4, 127.6, 128.1, 128.2, 128.2, 129.0, 129.0, 129.1, 132.5, 132.7, 133.9, 133.9, 167.9, 168.0, 194.5, 194.6, 207.8, 208.1.

General Procedure C for the Synthesis of Dihydropyridines 4. Ethyl 6-ethyl-2-methyl-1,4-diphenyl-1,6-dihydropyridine-3-carboxylate (4ja): Propargyl vinyl ether **2j** (50.0 mg, 184 μmol) was dissolved in 1.8 mL of CH_2Cl_2 and 3 mg of $AgSbF_6$ (9.2 μmol, 5 mol %) was added. The solution was stirred at room temperature until TLC indicated the completion of the rearrangement. Aniline (25.2 μL, 25.7 mg, 276 μmol, 1.5 equiv) was added and the reaction mixture was stirred 16 h at room temperature. The solvent was evaporated and the residue was purified by flash chromatography (pentane/EtOAc 98:2). The product was obtained as a dark yellow solid (17.0 mg, 48.7 μmol, 27%): R_f 0.43 (pentane/EtOAc 95:5) [UV] [CAM]; ^{1}H NMR (250 MHz, $CDCl_3$) δ 0.68 (t, J = 7.1, 3H), 1.04 (t, J = 7.4, 3H), 1.59−175 (m, 1H), 1.83−1.97 (m, 1H), 2.29 (s, 3H), 3.69−3.93 (m, 2H), 4.13−4.22 (m, 1H), 5.33 (d, J = 6.6, 1H), 7.14−7.38 (m, 10H); ^{13}C NMR (63 MHz, $CDCl_3$) δ 9.7, 13.6, 20.2, 26.4, 59.4, 62.7, 108.3, 114.0, 125.5, 125.6, 126.6, 127.0, 127.9, 129.2, 137.3, 142.7, 145.4, 150.2, 168.3; LRMS (EI) m/z 347 (4%) [M^+], 318 (11%), 243 (100%), 215 (26%), 43 (45%); HRMS (EI) m/z 318.1491 [318.1494 calculated for $C_{21}H_{20}NO_2$ ($M^+ - C_2H_5$)]

Ethyl 6-ethyl-2-methyl-1-(naphthalen-1-yl)-4-phenyl-1,6-dihydropyridine-3-carboxylate (4jb): Following general procedure C, **4jb** was obtained as a white solid (44%) after flash chromatography on silica gel (pentane/EtOAc 99:1): R_f 0.28 (pentane/EtOAc 95:5): [UV] [CAM]; ^{1}H NMR (250 MHz, $CDCl_3$) δ 0.68 (t, J = 7.1, 3H), 1.01 (t, J = 7.4, 3H), 1.64−1.74 (m, 1H), 2.01−2.10 (m, 1H), 2.14 (s, 3H), 3.70−3.88 (m, 2H), 4.99−4.11 (m, 1H), 5.32 (d, J = 6.6, 1H), 7.25−7.44 (m, 5H), 7.45−7.56 (m, 4H), 7.76−7.91 (m, 3H); ^{13}C NMR (63 MHz, $CDCl_3$) δ 9.2, 13.6, 18.8, 26.7, 59.1, 63.1, 76.7, 77.2, 77.7, 102.9, 112.1, 123.1, 125.4, 126.5, 126.8, 127.1, 127.5, 127.7, 127.9, 128.2, 128.4, 131.1, 134.9, 138.6, 141.5, 143.6, 154.1, 168.5; LRMS (EI) m/z 397 (3%) [M^+], 368 (53%), 84 (34%), 43 (100%); HRMS (EI) m/z 368.1657 [368.1650 calculated for $C_{25}H_{22}NO_2$ ($M^+ - C_2H_5$)].

Ethyl 1-(3-chlorophenyl)-6-ethyl-2-methyl-4-phenyl-1,6-dihydropyridine-3-carboxylate (4jc): Following general procedure C, **4jc** was obtained as a dark yellow solid (39%) after flash chromatography on silica gel (pentane/EtOAc 99:1): R_f 0.45 (pentane/EtOAc 95:5) [UV] [CAM]; ^{1}H NMR (360 MHz, $CDCl_3$) δ 0.68 (t, J = 7.1, 3H), 1.05 (t, J = 7.5, 3H), 1.60−1.72 (m, 1H), 1.82−1.94 (m, 1H), 2.28 (s, 3H), 3.72−3.81 (m, 1H), 3.83−3.92 (m, 1H), 4.12−4.18 (m, 1H), 5.39 (d, J = 6.6, 1H), 7.00 (ddd, J = 8.0, 2.1, 1.0, 1H), 7.10−7.15 (m, 2H), 7.20−7.28 (m, 7H); ^{13}C NMR (63 MHz, $CDCl_3$) δ 9.8, 13.5, 20.1, 26.3, 59.6, 62.4, 110.9, 115.1, 123.0, 124.9, 125.0, 126.8, 126.9, 128.0, 130.0, 134.7, 137.0, 142.0, 146.7, 148.2, 168.1; LRMS (EI) m/z 382 (1%) [M^+], 352 (48%), 243 (100%), 43 (34%); HRMS (EI) m/z 352.1100 [352.1104 calculated for $C_{21}H_{19}ClNO_2$ ($M^+ - C_2H_5$)].

Ethyl 1-(4-bromophenyl)-6-ethyl-2-methyl-4-phenyl-1,6-dihydropyridine-3-carboxylate (4jd): Following general procedure C, **4jd** was obtained as a white solid (10%) after flash chromatography on silica gel (pentane/EtOAc 99:1): R_f 0.38 (pentane/EtOAc 95:5) [UV] [CAM]; ^{1}H NMR (250 MHz, $CDCl_3$) δ 0.68 (t, J = 7.1, 3H), 1.04 (t, J = 7.4, 3H), 1.60−1.69 (m, 1H), 1.82−1.93 (m, 1H), 2.27 (s, 3H), 2.72−3.80 (m, 1H), 3.82−3.91 (m, 1H), 4.09−4.15 (m, 1H), 5.36 (d, J = 6.6, 1H), 7.00 (d, J = 8.7, 1H), 7.20−7.30 (m, 2H), 7.44 (d, J = 8.7, 1H); ^{13}C NMR (63 MHz, $CDCl_3$) δ 9.8, 13.6, 20.1, 26.4, 59.6, 62.6, 110.0, 114.6, 118.4, 126.7, 126.8, 127.0, 128.0, 132.2, 137.1, 142.2, 144.5, 148.7, 168.2; LRMS (EI) m/z 426 (4%) [M^+], 398 (100%), 368 (30%), 121 (38%), 43 (27%); HRMS (EI) m/z 396.0594 [396.0599 calculated for $C_{21}H_{19}BrNO_2$ (M^+)].

Ethyl 6-ethyl-2-methyl-1-(3-nitrophenyl)-4-phenyl-1,6-dihydropyridine-3-carboxylate (4je): Following general procedure C, **4je** was obtained as an orange solid (31%) after flash chromatography on silica gel (pentane/EtOAc 95:5): R_f 0.26 (pentane/EtOAc 95:5) [UV] [CAM]; ^{1}H NMR (360 MHz, $CDCl_3$) δ 0.69 (t, J = 7.1, 3H), 1.08 (t, J = 7.5, 3H), 1.67−1.79 (m, 1H), 1.81−1.95 (m, 1H), 2.29 (s, 1H), 3.74−3.82 (m, 1H), 3.85−3.94 (m, 1H), 4.29−4.25 (m, 1H), 5.49 (d, J = 6.6, 1H), 7.19−7.30 (m, 5H), 7.38 (ddd, J = 8.1, 2.2, 1.0, 1H), 7.44−7.49 (m, 1H), 7.92−7.97 (m, 2H); ^{13}C NMR (91 MHz, $CDCl_3$) δ 9.6, 9.9, 13.6, 20.0, 26.3, 59.9, 62.3, 113.9, 116.2, 118.2, 118.8, 127.0, 127.0, 128.1, 129.7, 129.7, 136.9, 141.5, 146.2, 146.7, 149.0, 167.9; LRMS (EI) m/z 392 (4%) [M^+], 363 (100%) [M^+], 131 (27%); HRMS (EI) m/z 363.1346 [363.1345 calculated for $C_{21}H_{19}N_2O_4$ ($M^+ - C_2H_5$)].

Ethyl 6-ethyl-1-(4-methoxyphenyl)-2-methyl-4-phenyl-1,6-dihydropyridine-3-carboxylate (4jf): Following general procedure C, **4jf** was obtained as a yellow solid (13%) after flash chromatography on silica gel (pentane/EtOAc 95:5): R_f 0.20 (pentane/EtOAc 95:5) [UV] [CAM]; ^{1}H NMR (360 MHz, $CDCl_3$) δ 0.65 (t, J = 7.1, 3H), 1.00 (t, J = 7.4, 3H), 1.56−1.67 (m, 1H), 1.82−1.94 (m, 1H), 2.23 (s, 1H), 3.69−3.77 (m, 1H), 3.80 (s, 3H), 3.80−3.87 (m, 1H), 4.03−4.12 (m, 1H), 5.23 (d, J = 6.5, 1H), 6.86 (d, J = 9.0, 2H), 7.09 (d, J = 9.0, 2H), 7.22−7.28 (m, 5H); ^{13}C NMR (91 MHz, $CDCl_3$) δ 9.5, 13.6, 19.8, 26.6, 30.5, 55.7, 59.2, 63.3, 76.8, 77.2, 77.5, 105.9, 113.0, 114.5, 126.5, 127.1, 127.9, 137.8, 138.6, 143.1, 151.6, 158.0, 168.5; LRMS (EI) m/z 377 (8%) [M^+], 348 (100%), 320 (26%); HRMS (EI) m/z 377.1991 [377.1991 calculated for $C_{24}H_{27}NO_3$ (M^+)].

Ethyl 1-(3-chlorophenyl)-2,5-dimethyl-4-phenyl-1*H*-pyrrole-3-carboxylate (6kc): Following general procedure C, **6kc** was obtained as a white solid (72%) after flash chromatography on silica gel (pentane/EtOAc 95:5): R_f 0.22 (pentane/EtOAc 95:5) [UV] [CAM]; ^{1}H NMR (250 MHz, $CDCl_3$) δ 1.02 (t, J = 7.1, 3H), 1.90 (s, 3H), 2.33 (s, 3H), 4.08 (q, J = 7.1, 2H), 7.15−7.19 (m, 1H), 7.23−7.38 (m, 6H), 7.45−7.47 (m, 2H); ^{13}C NMR (63 MHz, $CDCl_3$) δ 11.3, 12.7, 14.1, 59.4, 111.7, 122.9, 126.2, 126.7, 126.8, 127.6, 128.8, 129.1, 130.5, 135.2, 135.7, 136.4, 139.2, 165.9; LRMS (EI) m/z 353 (5%) [M^+], 244 (61%), 215 (26%), 198 (68%), 171 (41%), 139 (46%), 128 (43%), 115 (41%), 105 (33%), 84 (100%); HRMS (EI) m/z 353.1173 [353.1183 calculated for $C_{21}H_{20}ClNO_2$ (M^+)].

General Procedure D for the Synthesis of Dihydropyridines 8. Ethyl 6-ethyl-1,4-diphenyl-1,6-dihydropyridine-3-carboxylate (8aa): Propargyl vinyl ether **2a** (50.0 mg, 194 μmol) was dissolved in 1.9 mL of CH_2Cl_2 and 2.2 mg of AuCl (9.7 μmol, 5 mol %) was added. The mixture was stirred at room temperature until TLC showed completion of the rearrangement. Aniline (26.5 μL, 27.0 mg, 290 μmol, 1.5 equiv) was added and the mixture was stirred for another 30 min at room temperature. After addition of 7.4 mg of *p*-TsOH (38.7 μmol, 20 mol %) the reaction mixture was heated to 40 °C and stirred for 15 h. The solvent was evaporated and the residue was purified by flash chromatography on silica gel (pentane/EtOAc 95:5). The product was obtained as a yellow solid (56.7 mg, 170 μmol, 88%): R_f 0.19 (pentane/EtOAc 95:5) [UV] [CAM]; ^{1}H NMR (250 MHz, $CDCl_3$) δ 0.99 (t, J = 7.1, 3H), 1.04 (t, J = 7.5, 3H), 1.59−1.75 (m, 1H), 1.88−2.05 (m, 1H), 3.89−4.13 (m, 2H), 4.55−4.64 (m, 1H), 5.30 (d, J = 6.4, 1H), 7.13−7.31 (m, 8H), 7.34−7.43 (m, 2H), 7.90 (d, J = 1.6, 1H); ^{13}C NMR (63 MHz, $CDCl_3$) δ 8.9, 14.1, 26.1, 58.8, 59.5, 106.3, 114.9, 118.7, 124.2, 126.9, 127.6, 127.7, 129.7, 136.6, 141.3, 141.5, 144.2, 166.5; LRMS (EI) m/z 333 (6%) [M^+], 304 (100%), 276 (40%), 230 (12%), 77 (15%); HRMS (EI m/z 333.1723 [333.1729 calculated for $C_{22}H_{23}NO_2$ (M^+)].

Ethyl 6-ethyl-1-(4-methoxybenzyl)-4-phenyl-1,6-dihydropyridine-3-carboxylate (8ag): Following general procedure D, **8ag** was obtained as a brown oil (62%) after flash chromatography on silica gel (pentane/EtOAc 90:10): R_f 0.13 (pentane/EtOAc 90:10) [UV] [CAM]; ^{1}H NMR (250 MHz, $CDCl_3$) δ 0.98 (vq, J = 7.3, 6H), 1.42−1.57 (m, 1H), 1.74−1.92 (m, 1H), 3.83 (s, 3H), 3.89−4.08 (m, 3H), 4.44 (s, 2H), 4.86 (d, J = 5.7, 1H), 6.92 (d, J = 8.7, 2H), 7.20−7.30 (m, 7H), 7.68 (d, J = 1.0, 1H); ^{13}C NMR (63 MHz, $CDCl_3$) δ 8.4, 14.2, 26.1, 55.5, 57.3, 57.8, 58.9, 98.7, 113.0, 114.5, 126.6, 127.4, 127.8, 128.2, 128.6, 129.1, 137.3, 142.1, 148.9, 159.6, 166.8, 195.4; LRMS (ESI) m/z 378 (26%) [$M^+ + H$], 348 (1%), 256 (3%), 121 (100%); HRMS (ESI) m/z 378.2054 [378.2069 calculated for $C_{24}H_{28}NO_3$ ($M^+ + H$)].

Ethyl 6-ethyl-1-isopropyl-4-phenyl-1,6-dihydropyridine-3-carboxylate (8ah): Following general procedure D, **8ah** was obtained as a brown oil (75%) after flash chromatography on silica gel (pentane/EtOAc 95:5): R_f 0.18 (pentane/EtOAc 90:10) [UV] [CAM]; ^{1}H NMR (250 MHz, $CDCl_3$) δ 0.92 (t, J = 7.1, 3H), 0.96 (t, J = 7.4, 3H), 1.29 (d, J = 6.6, 3H), 1.38 (d, J = 6.7, 3H), 1.69−187 (m, 1H), 3.42−3.54 (m, 1H), 3.82−4.01 (m, 2H), 4.03−4.11 (m, 1H), 4.87 (d, J = 6.0, 1H), 7.17−7.31 (m, 5H), 7.68 (d, J = 1.5, 1H); ^{13}C NMR (63 MHz, $CDCl_3$) δ 8.4, 14.2, 22.1, 23.6, 27.7, 46.2, 54.3, 58.8, 59.3, 98.6, 112.0, 126.5, 127.4, 127.8, 137.6, 142.3, 144.6, 166.9; LRMS (EI) m/z 299 (9%) [M^+], 270 (100%), 228 (23%), 205 (40%), 57 (39%), 43 (31%); HRMS (EI) m/z 270.1499 [270.1494 calculated for $C_{17}H_{20}NO_2$ ($M^+ - C_2H_5$)].

Ethyl 6-ethyl-4-phenyl-1-((*S*)-1-phenylethyl)-1,6-dihydropyridine-3-carboxylate (8ai): Following general procedure D, **8ai** was obtained as an orange oil (67%, dr 1:1.3) after flash chromatography on silica gel (pentane/EtOAc 95:5): R_f 0.33 (pentane/EtOAc 95:5) [UV] [CAM]; ^{1}H NMR (250 MHz, $CDCl_3$) δ 0.87−0.98 (m, 13.8H), 1.25−1.47 (m, 2.3H), 1.69 (d, J = 2.7, 1.3H), 1.72 (d, J = 2.8, 1H), 1.77−1.87 (m, 2.6H), 3.83−4.12 (m, 6.9H), 4.49−4.64 (m, 2.3H), 4.82 (d, J = 6.1, 1.3H), 4.92 (d, J = 6.1, 1H), 7.20−7.38 (m, 23H), 7.65 (d, J = 1.5, 1H), 7.94 (d, J = 1.4, 1.3H); ^{13}C NMR (63 MHz, $CDCl_3$) δ 8.4, 8.6, 14.1, 14.1, 21.1, 21.6, 26.3, 27.8, 58.7, 58.9, 58.9, 59.3, 60.9, 62.5, 99.3, 99.8, 112.2, 112.4, 126.1, 126.5, 126.5, 127.1, 127.4, 127.8, 127.8, 127.9, 128.1, 128.9, 129.0, 131.8, 137.4, 137.4, 141.1, 142.1, 142.2, 142.9, 144.0, 146.2, 166.8, 167.1; LRMS (GC-MS) m/z 361 (5%) [M^+], 332 (46%), 255 (13%), 228 (65%), 105 (100%); HRMS (ESI) m/z 362.2110 [362.2120 calculated for $C_{24}H_{28}NO_2$ ($M^+ + H$)].

Methyl 1-(4-bromophenyl)-6-ethyl-4-phenyl-1,6-dihydropyridine-3-carboxylate (8bd): Following general procedure D, **8bd** was obtained as a yellow oil (69%) after flash chromatography on silica gel (pentane/EtOAc 92:8): R_f 0.17 (pentane/EtOAc 90:10) [UV] [CAM]; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.03 (t, J = 7.5, 3H), 1.60−1.68 (m, 1H), 1.89−1.98 (m, 1H), 3.56 (s, 3H), 4.52−4.56 (m, 1H), 5.34 (d, J = 6.4, 1H), 7.06 (d, J = 9.0, 2H), 7.22−7.22 (m, 5H), 7.49 (d, J = 9.0, 2H), 7.81 (d, J = 1.7, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 8.9, 25.9, 51.0, 58.6, 106.8, 115.4, 117.0, 120.0, 127.1, 127.6, 127.7, 132.6, 136.4, 140.7, 140.8, 143.2, 166.6; LRMS (EI) m/z 397 (7%) [M^+], 370 (100%), 105 (28%), 83 (98%); HRMS (EI) m/z 397.0690 [397.0678 calculated for $C_{21}H_{20}NO_2Br$ (M^+)].

Methyl 6-ethyl-1-(3-nitrophenyl)-4-phenyl-1,6-dihydropyridine-3-carboxylate (8be): Following general procedure D, **8be** was obtained as a yellow solid (78%) after flash chromatography on silica gel (pentane/EtOAc 90:10 → 80:20): R_f 0.21 (pentane/EtOAc 80:20) [UV] [CAM]; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.08 (t, J = 7.4, 3H), 1.67−1.75 (m, 1H), 1.94−2.03 (m, 1H), 3.59 (s, 3H), 4.60−4.64 (m, 1H), 5.46 (d, J = 6.3, 1H), 7.23−7.26 (m, 2H), 7.29−7.34 (m, 3H), 7.48−7.49 (m, 1H), 7.29−7.34 (m, 1H), 7.85 (s, 1H), 7.98 (d, J = 8.1, 1H), 8.01 (s, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 9.0, 25.7, 51.2, 58.3, 76.9, 77.2, 77.4, 109.2, 112.3, 116.5, 118.0, 123.3, 127.3, 127.5, 127.8, 127.8, 130.5, 136.3, 139.2, 140.3, 145.0, 149.4, 166.3; LRMS (GC-MS) m/z 364 (7%) [M^+], 335 (100%), 289 (36%), 216 (29%), 184 (63%), 57 (29%); HRMS (ESI) m/z 364.1424 [364.1423 calculated for $C_{21}H_{20}N_2O_4$ (M^+)].

Methyl 6-ethyl-1-(4-methoxyphenyl)-4-phenyl-1,6-dihydropyridine-3-carboxylate (8bf): Following general procedure D, **8bf** was obtained after flash chromatography on silica gel (pentane/EtOAc 90:10) as an orange solid (85%): R_f 0.51 (pentane/EtOAc 85:15) [UV] [CAM]; ^{1}H NMR (360 MHz, $CDCl_3$) δ 1.02 (t, J = 7.5, 3H), 1.56−1.67 (m, 1H), 1.85−1.99 (m, 1H), 3.54 (s, 3H), 3.82 (s, 3H), 4.52−4.58 (m, 1H), 5.20 (d, J = 6.1, 1H), 6.92 (d, J = 9.0, 2H), 7.16 (d, J = 9.0, 2H), 7.23−7.33 (m, 2H), 7.81 (d, J = 1.6, 1H); ^{13}C NMR (91 MHz, $CDCl_3$) δ 8.8, 26.4, 50.7, 55.7, 59.7, 103.8, 114.2, 114.8, 121.2, 126.9, 127.6, 127.7, 136.6, 138.0, 141.2, 143.1, 157.0, 166.8; LRMS (EI) m/z 349 (8%) [M^+], 320 (100%), 207 (15%), 175 (22%), 84 (46%); HRMS (EI) m/z 349.1684 [349.1678 calculated for $C_{22}H_{23}NO_3$ (M^+)].

Methyl 1-benzyl-6-ethyl-4-phenyl-1,6-dihydropyridine-3-carboxylate (8bj): Following general procedure D, **8bj** was obtained as a yellow oil (81%) after flash chromatography on silica gel (pentane/EtOAc 85:15): R_f 0.36 (pentane/EtOAc 85:15) [UV] [CAM]; ^{1}H NMR (250 MHz, $CDCl_3$) δ 0.98 (t, J = 7.4, 3H), 1.44−1.58 (m, 1H), 1.73−1.90 (m, 1H), 3.49 (s, 3H), 4.00−4.07 (m, 1H), 4.48 (s, 2H), 4.88 (d, J = 5.7, 1H), 7.42−7.42 (m, 10H), 7.66 (d, J = 1.1, 1H); ^{13}C NMR (91 MHz, $CDCl_3$) δ 8.4, 26.1, 50.4, 57.8, 58.0, 98.5, 113.3, 126.7, 127.4, 127.6, 127.7, 128.2, 129.1, 136.3, 137.1, 141.7, 149.2, 166.7; LRMS (EI) m/z 333 5%) [M^+], 304 (68%), 91 (100%); HRMS (EI) m/z 333.1729 [333.1729 calculated for $C_{22}H_{23}NO_2$ (M^+)].

Ethyl 6-methyl-1,4-diphenyl-1,6-dihydropyridine-3-carboxylate (8ca): Following general procedure D, **8ca** was obtained as a yellow solid (84%) after flash chromatography on silica gel (pentane/EtOAc 95:5): R_f 0.18 (P/EtOAc 95:5) [UV] [CAM]; ^{1}H NMR (250 MHz, $CDCl_3$) δ 1.00 (t, J = 7.1, 3H), 1.39 (d, J = 6.4, 3H), 3.91−4.14 (m, 2H), 4.73−4.84 (m, 1H), 5.28 (d, J = 6.4, 1H), 7.13−7.31 (m, 8H), 7.35−7.43 (m, 2H), 7.86 (d, J = 1.6, 1H); ^{13}C NMR (63 MHz, $CDCl_3$) δ 14.1, 18.8, 53.3, 59.5, 106.2, 116.7, 118.4, 124.1, 126.8, 127.6, 127.7, 129.7, 135.8, 140.7, 141.1, 144.1, 166.6; LRMS (EI) m/z 319 (8%) [M^+], 304 (100%), 276 (57%), 242 (14%), 230 (12%), 77 (20%); HRMS (EI) m/z 320.1652 [320.1645 calculated for $C_{21}H_{22}NO_2$ ($M^+ - C_2H_5$)].

Ethyl 6-isopropyl-1,4-diphenyl-1,6-dihydropyridine-3-carboxylate (8da): Following general procedure D, **8da** was obtained as an orange oil (77%) after flash chromatography on silica gel (pentane/EtOAc 95:5): R_f 0.77 (pentane/EtOAc 90:10) [UV] [CAM]; ^{1}H NMR (360 MHz, $CDCl_3$) δ 0.95−0.99 (m, 6H), 1.08 (d, J = 6.7, 3H), 2.08−2.17 (m, 1H), 3.91−4.07 (m, 2H), 4.68 (td, J = 5.9, 1.5, 1H), 5.18 (d, J = 6.0, 1H), 7.13−7.18 (m, 1H), 7.23−7.26 (m, 3H), 7.27−7.32 (m, 4H), 7.36−7.41 (m, 2H), 7.94 (d, J = 1.4, 1H); ^{13}C NMR (91 MHz, $CDCl_3$) δ 14.1, 17.0, 18.6, 32.9, 59.4, 63.4, 105.7, 113.3, 119.7, 124.4, 126.8, 127.6, 127.7, 129.7, 137.5, 141.6, 142.6, 145.0, 166.5; LRMS (EI) m/z 347 (13%) [M^+], 333 (33%), 318 (38%), 304 (28%), 205 (61%), 131 (80%), 93 (91%), 83 (100%); HRMS (EI) m/z 347.1886 [347.1885 calculated for $C_{23}H_{25}NO_2$ (M^+)].

Ethyl 1,4,6-triphenyl-1,6-dihydropyridine-3-carboxylate (8ea): Following general procedure D, **8da** was obtained as a yellow solid (72%) after flash chromatography on silica gel (pentane/EtOAc 93:7): R_f 0.38 (P/EtOAc 90:10) [UV] [CAM]; ^{1}H NMR (360 MHz, $CDCl_3$) δ 0.98 (t, J = 7.1, 3H), 5.48 (dd, J = 6.5, 0.4 1H), 3.92−4.10, 5.70 (dd, J = 6.5, 1.5, 1H), 7.12−7.16 (m, 3H), 7.19−7.22 (m, 2H), 7.24−7.41 (m, 10H), 8.15 (dd, J = 1.5, 0.4, 1H); ^{13}C NMR (91 MHz, $CDCl_3$) δ 14.1, 59.6, 62.1, 105.8, 116.5, 119.4, 124.6, 125.4, 126.9, 127.6, 127.7, 127.9, 129.1, 129.5, 134.9, 141.0, 142.2, 142.3, 122.7, 166.4; LRMS (EI) m/z 381 (17%) [M^+], 304 (95%), 292 (100%), 219 (87%), 191 (48%), 149 (47%), 105 (74%), 57 (63%), 44 (53%); HRMS (EI) m/z 381.1721 [381.1729 calculated for $C_{26}H_{23}NO_2$ (M^+)].

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Ethyl 1,4-diphenyl-1,6-dihydropyridine-3-carboxylate (8fa): Following general procedure D, **8fa** was obtained as a red oil (55%) after flash chromatography on silica gel (pentane/EtOAc 95:5 → 90:10): R_f 0.19 (pentane/EtOAc 95:5) [UV] [CAM]; ^{1}H NMR (250 MHz, $CDCl_3$) δ 0.97 (t, J = 7.1, 3H), 4.00 (q, J = 7.1, 2H), 4.51 (d, J = 4.4, 2H), 5.26 (t, J = 4.4, 1H), 7.13−7.17 (m, 2H), 7.21−7.31 (m, 5H), 7.37−7.45 (m, 3H), 7.89 (d, J = 0.5, 1H).; ^{13}C NMR (63 MHz, $CDCl_3$) δ 14.1, 47.7, 59.5, 105.9, 111.9, 117.8, 124.1, 126.9, 127.4, 127.7, 129.5, 137.4, 141.1, 143.8, 144.4, 166.5; LRMS (ESI) m/z 306 (100%) [$M^+ + H$], 290 (63%), 276 (7%), 226 (10%), 182 (3%); HRMS (ESI) m/z 306.1497 [306.1494 calculated for $C_{20}H_{20}NO_2$ ($M^+ + H$)].

Ethyl 4-pentyl-6-phenethyl-1-phenyl-1,6-dihydropyridine-3-carboxylate (8ga): Following general procedure D, **8ga** was obtained as a light yellow oil (55%) after flash chromatography on silica gel (pentane/EtOAc 95:5): R_f 0.75 (pentane/EtOAc 90:10) [UV] [CAM]; ^{1}H NMR (250 MHz, $CDCl_3$) δ 0.93 (t, J = 7.1, 3H), 1.32 (t, J = 7.1, 3H), 1.40−1.53 (m, 4H), 1.76−2.05 (m, 2H), 2.21−2.31 (m, 3H), 2.49−2.61 (m, 1H), 2.66−2.78 (m, 1H), 3.00 (dd, J = 14.5, 2.3, 1H), 3.99−4.07 (m, 1H), 4.16−4.29 (m, 2H), 6.50−6.50 (m, 1H), 6.99−7.03 (m, 2H), 7.06−7.09 (m, 1H), 7.13−7.17 (m, 2H), 7.19−7.23 (m, 1H), 7.26−7.34 (m, 4H), 7.81 (s, 1H); ^{13}C NMR (91 MHz, $CDCl_3$) δ 14.2, 14.7, 22.8, 27.0, 27.9, 32.3, 32.4, 32.6, 55.3, 59.6, 103.2, 118.4, 123.4, 123.5, 126.3, 126.9, 128.5, 128.6, 129.6, 138.9, 141.2, 144.8, 167.3; LRMS (ESI) m/z 807 (3%) [$2M^+ + H$], 426 (4%) [$M^+ + Na$], 404 (100%) [$M^+ + H$], 358 (4%), 242 (6%), 167 (3%); HRMS (ESI) m/z 404.2585 [404.2584 calculated for $C_{27}H_{34}NO_2$ ($M^+ + H$)].

Ethyl 6-ethyl-4-(4-(methoxycarbonyl)phenyl)-1-phenyl-1,6-dihydropyridine-3-carboxylate (8ha): Following general procedure D, **8ha** was obtained as a dark yellow solid (74%) after flash chromatography on silica gel (pentane/EtOAc 90:10): R_f 0.31 (pentane/EtOAc 85:15) [UV] [CAM]; ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.99 (t, J = 7.1, 3H), 1.04 (t, J = 7.5, 3H), 1.64−1.73 (m, 1H), 1.92−2.01 (m, 1H), 3.91 (s, 3H), 3.95−4.07 (m, 2H), 4.60−4.63 (m, 1H), 5.33 (d, J = 6.3, 1H), 7.16−7.21 (m, 2H), 7.31 (d, J = 8.1, 1H), 7.39−7.42 (m, 2H), 7.91 (d, J = 1.5, 1H), 7.98 (d, J = 8.5, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 8.9, 14.2, 26.1, 52.1, 58.8, 59.6, 105.7, 115.9, 118.9, 124.5, 127.8, 128.6, 129.1, 129.7, 136.0, 141.9, 144.1, 146.3, 166.3, 167.3; LRMS (EI) m/z 391 (7%) [M^+], 362 (83%), 334 (26%), 84 (100%); HRMS (EI) m/z 391.1782 [391.1783 calculated for $C_{24}H_{25}NO_4$ (M^+)].

Ethyl 6-ethyl-4-(4-methoxyphenyl)-1-phenyl-1,6-dihydropyridine-3-carboxylate (8ia): Following general procedure D, **8ia** was obtained as a yellow oil (89%) after flash chromatography on silica gel (pentane/EtOAc 95:5): R_f 0.22 (pentane/EtOAc 90:10) [UV] [CAM]; ^{1}H NMR (250 MHz, $CDCl_3$) δ 1.04 (q, J = 7.3, 6H), 1.62−1.72 (m, 1H), 1.86−2.04 (m, 1H), 3.81 (s, 3H), 3.93−4.16 (m, 2H), 4.53−4.61 (m, 1H), 5.27 (d, J = 6.4, 1H), 6.84 (d, J = 8.8, 2H), 7.12−7.21 (m, 5H), 7.35−7.42 (m, 2H), 7.88 (d, J = 1.5, 1H); ^{13}C NMR (63 MHz, $CDCl_3$) δ 8.9, 14.3, 26.0, 55.4, 58.7, 59.5, 106.3, 113.1, 114.2, 118.7, 124.1, 128.8, 129.6, 133.7, 136.1, 141.4, 144.2, 158.8, 166.5; LRMS (GC-MS) m/z 363 (9%) [M^+], 334 (100%), 306 (38%), 256 (13%), 207 (10%), 77 (11%); HRMS (ESI) m/z 364.1913 [364.1907 calculated for $C_{23}H_{26}NO_3$ ($M^+ + H$].

One-Pot Procedures for the Synthesis of 6-Membered Heterocycles Starting from Propargylic Alcohols 1. General Procedure E for the Formation of 1,6-dihydropyridine-3-carboxylates 8 Starting from Propargylic Alcohols 1. Ethyl 6-ethyl-1,4-diphenyl-1,6-dihydropyridine-3-carboxylate (8aa): To a solution of 100 mg of 1-phenylpent-1-yn-3-ol (624 μmol) and 63.3 μL of ethyl propiolate (61.2 mg, 624 μmol, 1 equiv) in 6.2 mL of CH_2Cl_2 was added 7.8 μL of P(n-Bu)$_3$ (6.3 mg, 31.2 μmol, 5 mol %). The mixture was stirred at room temperature until TLC indicated full consumption of the propargylic alcohol. $AgSbF_6$ (9.08 mg, 25.0 μmol, 4 mol %) and 5.80 mg of AuCl (25.0 μmol, 4 mol %) were added and the solution was stirred for another hour at room temperature. Aniline (85.5 μL, 87.2 mg, 963 μmol, 1.5 equiv) was added and the solution was stirred for 30 min before adding 23.1 mg of p-TsOH (125 μmol, 20 mol %). The reaction mixture was heated to 40 °C and was kept at this temperature for 16 h. The solvent was evaporated and the residue was purified by flash chromatography on silica gel (pentane/EtOAc 95:5). The product was obtained as a yellow solid (66%). The analytical data were in good accordance to those reported above.

Ethyl 6-isopropyl-1,4-diphenyl-1,6-dihydropyridine-3-carboxylate (8da): Following general procedure E, **8da** was obtained after flash chromatography on silica gel (pentane/EtOAc 95:5) as an orange solid (63%). The analytical data were in good accordance to those reported above.

Methyl 6-ethyl-1-(4-methoxyphenyl)-4-phenyl-1,6-dihydropyridine-3-carboxylate (8bf): Following general procedure E, **8bf** was obtained after flash chromatography on silica gel (pentane/EtOAc 90:10) as an orange solid (75%). The analytical data were in good accordance to those reported above.

Ethyl 4-pentyl-1,6-diphenyl-1,6-dihydropyridine-3-carboxylate (8ma): Following general procedure E, **8ma** was obtained as a yellow oil (41%) after flash chromatography on silica gel (pentane/EtOAc 98:2 → 95:5): R_f 0.19 (pentane/EtOAc 93:7) [UV] [CAM]; ^{1}H NMR (250 MHz, $CDCl_3$) δ 0.71 (t, J = 6.9, 3H), 0.78−0.90 (m, 1H), 0.94−1.10 (m, 3H), 1.34 (t, J = 7.1, 1H), 1.74−1.98 (m, 2H), 2.61 (dd, J = 13.9, 4.7, 1H), 3.00 (dd, J = 13.9, 2.2, 1H), 4.17−4.30 (m, 2H), 5.08−5.11 (m, 1H), 6.23 (t, J = 7.6, 1H), 7.00−7.07 (m, 3H), 7.17−7.33 (m, 7H), 8.11 (s, 1H); ^{13}C NMR (63 MHz, $CDCl_3$) δ 14.1, 14.7, 22.3, 27.4, 32.0, 59.7, 61.0, 104.5, 118.3, 122.5, 123.5, 125.9, 127.4, 127.7, 128.7, 129.5, 139.3, 141.0, 145.4, 167.2; LRMS (GC-MS) m/z 375 (64%) [M^+], 346 (20%), 332 (100%), 298 (96%), 207 (22%), 141 (21%), 77 (33%); HRMS (ESI) m/z 376.2269 [376.2271 calculated for $C_{25}H_{30}NO_2$ ($M^+ + H$)].

General Procedure F for the Formation of 2*H*-Pyrans 5 Starting from Propargylic Alcohols 1. Ethyl 2-ethyl-6-methyl-4-phenyl-2*H*-pyran-5-carboxylate (5j): 1-Phenylpent-1-yn-3-ol (50 mg, 312 μmol) was dissolved in 3.1 mL of dry CH_2Cl_2. Ethyl butynoate (36.2 μL, 35.0 mg, 312 μmol, 1 equiv) and 62.4 μL of PMe_3 1 M in toluene (62.4 μmol, 20 mol %) were added. The reaction was stirred at room temperature until TLC indicated full consumption of the propargylic alcohol. AuCl (3.6 mg, 15.6 μmol, 5 mol %) and 11.3 mg of $AgSbF_6$ (31.2 μmol, 10 mol %) were added and the mixture was stirred for another hour at room temperature. DBU (4.7 μL, 4.8 mg, 31.2 μmol, 10 mol %) was added to the solution. After 1 h of stirring the solvent was evaporated and the residue was purified by flash chromatography in silica gel (pentane/EtOAc 95:5). The product was isolated as a colorless oil (40.1 mg, 147 μmol, 47%). ^{1}H and ^{13}C NMR spectra were in accordance with those reported before:[13] R_f 0.65 (pentane/EtOAc 80:20) [UV] [CAM]; ^{1}H NMR (360 MHz, $CDCl_3$) δ 0.72 (t, J = 7.1, 3 H), 1.04 (t, J = 7.4, 3 H), 1.74−1.96 (m, 2 H), 2.35 (s, 3 H), 3.81−3.87 (m, 2 H), 4.63 (dt, J = 3.8, 6.4, 1 H), 5.29 (d, J = 3.8, 1 H), 7.31−7.34 (m, 3 H), 7.44−7.48 (m, 2 H); ^{13}C NMR (91 MHz, $CDCl_3$) δ 9.4, 13.6, 18.8, 27.1, 59.8, 77.7, 108.3, 116.1, 126.6, 127.1, 128.1, 137.2, 140.9, 165.8, 167.4.

Ethyl 4-(4-*tert*-butylphenyl)-2-ethyl-6-methyl-2*H*-pyran-5-carboxylate (5n): Following general procedure F, **5n** was isolated after flash chromatography on silica (pentane/EtOAc 95:5) as a colorless oil (42%). ^{1}H and ^{13}C NMR spectra were in accordance with those reported before:[13] R_f 0.78 (pentane/EtOAc 80:20) [UV] [CAM]; ^{1}H NMR (360 MHz, $CDCl_3$) δ 1.02 (t, J = 7.4, 3 H), 1.30 (s, 9 H), 1.73−1.94 (m, 2 H), 2.33 (s, 3 H), 3.76−3.90 (m, 2 H), 4.61 (dt, J = 3.8, 6.4, 1 H), 5.28 (d, J = 3.8, 1 H), 7.11 (d, J = 8.5, 2 H), 7.29 (d, J = 8.5, 2 H); ^{13}C NMR (91 MHz, $CDCl_3$) δ 9.4, 13.4, 18.8, 27.1, 31.5, 34.6, 59.8, 77.7, 108.4, 115.5, 124.7, 125.0, 126.3, 129.8, 136.9, 137.9, 150.2, 165.6, 167.5.

Ethyl 2-ethyl-6-methyl-4-(thiophen-3-yl)-2*H*-pyran-5-carboxylate (5o): Following general procedure F, **5o** was isolated after flash chromatography on silica (pentane/EtOAc 95:5) as a colorless oil

(42%). ^{1}H and ^{13}C NMR spectra were in accordance with those reported before:[13] R_f 0.54 (pentane/EtOAc 80:20) [UV] [CAM]; ^{1}H NMR (360 MHz, $CDCl_3$) δ 0.88 (t, J = 7.1, 3 H), 1.02 (t, J = 7.4, 3 H), 1.73−1.91 (m, 2 H), 2.30 (s, 3 H), 3.93 (dq, J = 1.9, 7.1, 2 H), 4.58 (dt, J = 3.7, 6.8, 1 H), 5.35 (d, J = 3.6, 1 H), 6.93 (dd, J = 1.4, 5.0, 1 H), 7.07 (dd, J = 1.4, 3.0, 1 H), 7.21 (dd, J = 3.0, 5.0, 1 H); ^{13}C NMR (91 MHz, $CDCl_3$) δ 9.4, 13.8, 18.8, 27.0, 60.0, 77.5, 108.4, 115.5, 120.5, 125.0, 127.0, 131.9, 141.2, 165.2, 167.5.

Ethyl 2-ethyl-6-methyl-4-(4-phenoxyphenyl)-2*H*-pyran-5-carboxylate (5p): Following general procedure F, **5p** was isolated after flash chromatography on silica (pentane/EtOAc 95:5) as a colorless oil (39%). ^{1}H and ^{13}C NMR spectra were in accordance with those reported before:[13] R_f 0.59 (pentane/EtOAc 95:5) [UV] [CAM]; ^{1}H NMR (360 MHz, $CDCl_3$) δ 0.85 (t, J = 7.2, 3 H), 1.04 (t, J = 7.4, 3 H), 1.74−1.96 (m, 2 H), 2.34 (s, 3 H), 3.87−3.94 (m, 2 H), 4.61 (dt, J = 3.6, 6.6, 1 H), 5.28 (d, J = 3.6, 1 H), 6.93 (d, J = 8.6, 2 H), 6.99 (d, J = 7.5, 2 H), 7.09 (t. J = 7.5, 1 H), 7.17 (d, J = 8.6, 2 H), 7.32 (t, J = 7.5, 2 H); ^{13}C NMR (91 MHz, $CDCl_3$) δ 9.4, 13.8, 18.9, 27.0, 59.9, 77.7, 108.3, 115.8, 118.7, 118.8, 123.3, 128.0, 129.8, 136.1, 136.5, 156.5, 157.5, 165.8, 167.3.

■ ASSOCIATED CONTENT

Supporting Information. Copies of ^{1}H and ^{13}C NMR spectra of **2**, **3**, **4**, **5**, **6**, and **8**. This material is available free of charge via the Internet at http://pubs.acs.org.

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