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Microwave-Assisted Diversity-Oriented Domino Synthesis of Functionalized Nicotinic Acid Derivatives

David Tejedor,*[a,b] Gabriela Méndez-Abt,[a,b] and Fernando García-Tellado*[a,b]

Dedicated to Professor Carmen Nájera on the occasion of her 60th birthday

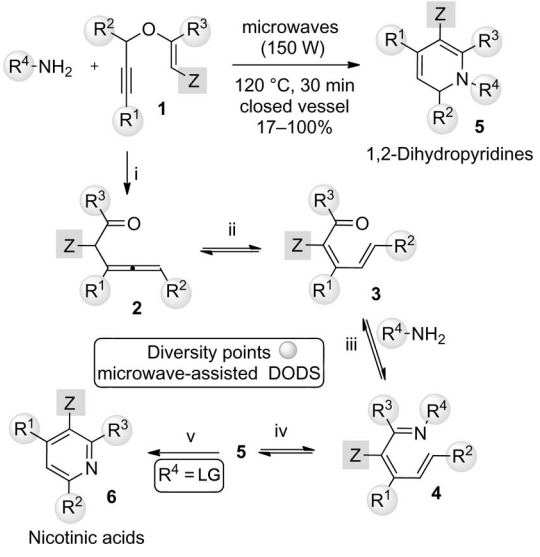
Keywords: Domino reactions / Electrocyclic reactions / Microwave chemistry / Nitrogen heterocycles / Nicotinic acid

The microwave-assisted diversity-oriented domino synthesis of functionalized alkyl nicotinates from propargyl vinyl ethers is described. The domino manifold comprises a complex network of reactions involving at least five distinct chemical steps. The obtained alkyl nicotinates incorporate two diversity points at the ring and one ester functionality as convenient handles for further elaboration.

Introduction

Functionalized pyridines with one carboxylic acid derived function (e.g., amide, ester, oxazoline) at the C-3 position (nicotinic acid derivatives), constitute an important group of biologically and pharmaceutically relevant molecules.[1] A survey of the methodologies for general access to functionalized pyridine rings has been published.[2] Among the approaches described, modern (catalyzed) versions of the Bohlmann–Rahtz heteroannulation reaction[3] with combinatorial[4] and multicomponent[4a,5] extensions, involving β-amino acrylates (conjugated enamines) and conjugated alkynes, have proven to be synthetically convenient and general processes for the construction of substituted nicotinic derivatives.[2c] Recently, Rodriguez and co-workers have reported a regioselective, multicomponent synthesis of functionalized nicotinic acid derivatives through the H^+-catalyzed reaction of 1,3-dicarbonyl compounds with β,γ-unsaturated α-oxo carbonyl compounds and ammonium acetate under oxidative conditions.[6] In spite of these advances, there is still a need for synthetic methodologies that enable controlled access to these heterocycles with structural (functional) diversity and a wide range of ring substitution patterns.[7] The use of commercially available or readily accessible, simple starting materials, together with bench-friendly and environmentally benign reaction conditions are important factors that should be taken into account in these strategies.[8]

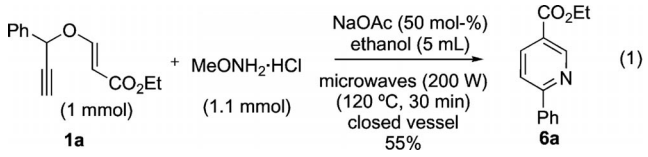
In a recent communication,[9] we reported the formation of substituted alkyl 1,2-dihydropyridine-3-carboxylates **5** from propargyl enol ethers **1** and primary amines through a microwave-assisted domino reaction (Scheme 1). Therein, we proposed that azatrienes **4** could be conveniently transformed into substituted alkyl nicotinates **6** if a primary amine armed with a good leaving group was used in this



Scheme 1. Microwave-assisted diversity-oriented domino synthesis (DODS) of 1,2-dihydropyridines **5** and nicotinic acid derivatives **6** from propargyl vinyl ethers **1**. Domino sequence: (i) [3,3] propargyl enol ether rearrangement; (ii) 1,3-protropic isomerization; (iii) condensation; (iv) 6π-aza-electrocyclization; (v) elimination. Z = CO_2R; LG = leaving group.

[a] Instituto de Productos Naturales y Agrobiología, Consejo Superior de Investigaciones Científicas,
Astrofísico Francisco Sánchez 3, 38206 La Laguna, Tenerife, Canary Islands, Spain
Fax: +34-922-260135
E-mail: fgarcia@ipna.csic.es
dtejedor@ipna.csic.es
http://www.ipna.csic.es/departamentos/qbb/qb/
[b] Instituto Canario de Investigación del Cáncer, Canary Islands, Spain

manifold [R^4 = leaving group (LG); Scheme 1]. In this scenario, the 1,2-dihydropyridine intermediate **5**, which would be formed from the corresponding azatriene **4** through a thermally allowed 6π-aza electrocyclization reaction,[10] would generate the corresponding pyridine derivative **6** by elimination of a neutral molecule (H-LG). As a proof of concept, we reported therein the microwave-assisted domino synthesis of ethyl 6-phenylnicotinate (**6a**) from the propargyl derivative **1a** and methoxyamine hydrochloride [Equation (1)]. In this paper, we have extended this protocol to the diversity-oriented domino synthesis (DODS) of functionalized alkyl nicotinates **6** from propargyl vinyl ethers **1** and methoxyamine hydrochloride under microwave irradiation. Nicotinates **6** are obtained in good yields, incorporating three points for diversity and a wide range of aryl-based substitution patterns on the ring.[11]

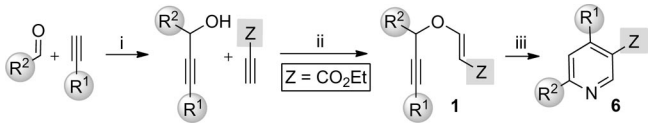


Results and Discussion

Propargyl vinyl ethers **1** (Scheme 1) constitute densely functionalized platforms with three diversity points and a reactivity-directing carboxylic ester group.[9] These scaffolds can be conveniently assembled from commercial sources (aldehydes, alkynes, and alkyl propiolates) in one or two straightforward synthetic steps (some propargyl alcohols are commercially available) (Table 1).[12] Because libraries of these scaffolds can be prepared in a very simple and direct way with a certain degree of functional (structural) diversity, they constitute versatile building blocks for use in DODS. We started our study by optimizing the previously reported reaction of propargyl vinyl ether **1a** and methoxyamine hydrochloride to generate ethyl nicotinate **6a** [Equation (1)]; the reaction was assessed by careful variation of the reaction conditions (microwave potency, temperature, time, solvent, stoichiometry, and buffer). It was found that performing the reaction in ethanol, in the presence of sodium acetate (0.55 equiv.), under microwave irradiation (200 W, 100 °C, closed vessel)[13] for 60 min, increased the initially reported 55% yield for product **6a**[9] to 65%. The use of 2-propanol instead of ethanol as the reaction solvent allowed the yield to be further increased to 77% (Table 1, Entry 1). Once a set of optimized conditions was established, we next studied the scope of this process by using the set of propargyl vinyl ethers **1a**–**n** outlined in Table 1. Under the standardized conditions, the majority of propargyl vinyl ethers assayed afforded the corresponding alkyl nicotinates **6** in good yields, although we observed that changing the solvent from ethanol to 2-propanol was not beneficial in all cases (small differences were observed). Therefore, we routinely performed the reactions in both solvents to determine the optimal solvent for each entry.

With regard to the functionalities decorating the propargylic platform **1**, the reaction tolerated a diverse range of alkyl/aryl substitution patterns. As a general tendency, aromatic substituents at the propargylic sp^3-position (R^2) and the sp^3-alkyne position (R^1) were more productive than alkyl substituents (compare Table 1, Entries 1 and 9 with Entries 2–4). A bulky *tert*-butyl group located at the pro-

Table 1. Microwave-assisted diversity-oriented domino synthesis of functionalized alkyl nicotinates **6** from propargyl vinyl ethers **1**.[a]



Entry	R^1	R^2	**1** (yield [%])[b]	Solvent	Microwave power [W][c]	Temperature [°C]	Time [min]	**6**	Yield [%][d]
1	H	Ph	**1a** (95)	*i*PrOH	200	100	60	**6a**	77
2	H	*n*Pent	**1b** (87)	EtOH	300	150	180	**6b**	54
3	H	Me	**1c** (98)[e]	EtOH	300	150	180	**6c**	14
4	*n*Bu	Ph	**1d** (96)	EtOH	200	100	60	**6d**	45
5	*p*-$MeOC_6H_4$	Ph	**1e** (78)[f]	*i*PrOH	200	100	60	**6e**	78
6	3,4-$Cl_2C_6H_3$	Ph	**1f** (79)	EtOH	200	100	60	**6f**	61
7	*p*-ClC_6H_4	Ph	**1g** (84)	EtOH	200	100	60	**6g**	60
8	*p*-MeC_6H_4	Ph	**1h** (81)[f]	EtOH	200	100	60	**6h**	61
9	Ph	Ph	**1i** (89)	EtOH	200	100	60	**6i**	67
10	Ph	*t*Bu	**1j** (99)	*i*PrOH	300	150	180	**6j**	13
11	Ph	*p*-ClC_6H_4	**1k** (79)[f]	EtOH	200	100	60	**6k**	62
12	Ph	*p*-$MeOC_6H_4$	**1l** (76)[f]	*i*PrOH	200	100	60	**6l**	72
13	Ph	2-furyl	**1m** (48)	*i*PrOH	200	100	60	**6m**	60
14	Me_3Si	Ph	**1n** (77)	*i*PrOH	200	100	60	**6n**	35

[a] Reagents and conditions: (i) BuLi, THF, –78 °C (30 min), then –30 °C (30 min), then –78 °C, R^2CHO, 1 h; (ii) Et_3N (10 mol-%), CH_2Cl_2, room temp., 2 h; (iii) propargyl vinyl ether **1** (1 mmol), $MeONH_2$·HCl (1.1 mmol), NaOAc (0.55 mmol), EtOH or *i*PrOH (5 mL), microwave irradiation. [b] Yields of isolated compounds **1** from the corresponding propargyl alcohols. [c] Microwave irradiation of specialized closed vessels. [d] Yield of isolated compounds **6**. [e] Methyl propiolate was used as alkynoate. [f] These substrates spontaneously rearranged partially to the corresponding dienals **3** (combined yield of **1** and **3**).

pargylic sp^3-position (**1j**; R^2 = *t*Bu) reduced the efficiency of the reaction significantly (Table 1, Entry 10). Release of steric congestion at this position (**1b**; R^2 = *n*Pent) increased the yield to 54% (Table 1, Entry 2). Intriguingly, methyl-substituted **1c** (R^2 = Me) afforded nicotinate **6c** in very low yield (14%; Table 1, Entry 3). Remarkably, when no substituents were present in the propargylic scaffold (R^1 = R^2 = H), none of the desired product was formed (data not shown). These results could point to the existence of a certain degree of conformational control (a substituent-biased conformational control) in the intermediate azatriene **4**, which drives the process toward pyridine ring formation. Substitution at the sp^3-propargylic position (R^2) was found to be dependent on the nature of substituent R^1.[9] Whereas R^2 could be aliphatic or aromatic for terminal alkynes (R^1 = H) (Table 1, Entries 1, 2, and 3) and aromatic for internal alkynes (R^1 = *n*Bu, Ar, or Me_3Si) (Entries 4–9 and Entries 11–14), the combination of R^2 = alkyl and an internal alkyne, was detrimental for the transformation of these propargyl derivatives into the corresponding functionalized pyridines (data not shown). The electronic nature of the aryl substituents at either the propargylic sp^3-position or at the alkyne sp-position did not significantly influence the global efficiency of the reaction (compare Table 1, Entries 5–8 and 11–13 with Entry 9), although the *para*-methoxy group proved to be the most convenient (compare Table 1, Entries 5 and 12 with Entries 6–8 and 11). Propargylic scaffold **1m**, bearing a furan ring at the propargylic sp^3-position, was efficiently converted into the corresponding nicotinate derivative **6m**, which is a very interesting biheterocyclic scaffold (Table 1, Entry 13). Remarkably, even the silyl-containing propargylic vinyl ether **1n** was able to give, in reasonable yield (35%), the corresponding alkyl nicotinate **6n**, which bears an important trimethylsilyl group at the ring.

Conclusions

We have described the microwave-assisted diversity-oriented synthesis of functionalized alkyl nicotinates **6** from propargyl vinyl ethers **1** through a complex and efficient domino manifold involving at least five discrete chemical steps. The propargylic platforms **1** are rapidly and easily assembled from commercially available or readily available materials. The obtained alkyl nicotinates **6** feature a maximum of two diversity points at the ring and one appended chemical handle for further elaboration (ester functionality). The reaction is fast, economical, bench-friendly (it does not require special care with solvent and protective reaction atmospheres) and environmentally benign. These practical advantages make this approach a good alternative to other well-known methods, and can be used to rapidly generate libraries of functionalized nicotinate derivatives **6** for use in drug discovery programs.[11]

Experimental Section

General Remarks: ^1H and ^{13}C NMR spectra of the samples as $CDCl_3$ solutions were recorded either at 400 and 100 MHz or at 500 and 125 MHz (Bruker AC200 or AMX2-500), respectively. Microwave reactions were conducted in sealed glass vessels (capacity 10 mL) with a CEM Discover microwave reactor. FTIR spectra were measured in chloroform solutions with a Perkin–Elmer FTIR Spectrum BX spectrophotometer. Mass spectra (low-resolution) (EI/CI) were obtained with a Hewlett–Packard 5995 gas chromatograph/mass spectrometer. High-resolution mass spectra (HRMS) were recorded with a Micromass Autospec mass spectrometer. Microanalyses were performed with a Fisons Instruments EA 1108 carbon, hydrogen, and nitrogen analyzer. Analytical thin-layer chromatography (TLC) plates used were E. Merck Brinkman UV-active silica gel (Kieselgel 60 F254) on aluminum. Flash column chromatography was carried out with E. Merck silica gel 60 (particle size less than 0.020 mm) by using appropriate mixtures of ethyl acetate and hexanes as eluent. All reactions were performed in oven-dried glassware under nitrogen unless otherwise stated. Dichloromethane was distilled from CaH_2. All other materials were obtained from commercial suppliers and used as received. Products **1a**,[9] **6a**,[14] and **6c**[15] have been previously reported, and all data are in accordance with those reported in the literature.

Representative Procedure for the Synthesis of Propargyl Vinyl Ethers 1a–n: Triethylamine (0.30 mmol) was added to a solution of ethyl propiolate (3.0 mmol) and 1-phenylprop-2-yn-1-ol (3.0 mmol) in anhydrous CH_2Cl_2 (10 mL). The reaction mixture was stirred for 2 h; then, after removing the solvent under reduced pressure, the products were purified by flash column chromatography (silica gel; *n*-hexane/EtOAc, 90:10) to yield **1a** (656 mg, 95%).[9]

(±)-Ethyl (*E*)-3-(Oct-1-yn-3-yloxy)acrylate (1b): Yield: 584.6 mg (2.61 mmol, 87%). ^1H NMR ($CDCl_3$, 400 MHz): δ = 0.89 (t, $^3J_{H,H}$ = 6.9 Hz, 3 H, Me), 1.26 (t, $^3J_{H,H}$ = 6.9 Hz, 3 H, Me), 1.29–1.33 (m, 4 H, 2 × 5′-H and 2 × 6′-H), 1.42–1.50 (m, 2 H, 2 × 7′-H), 1.76–1.90 (m, 2 H, 2 × 4′-H), 2.57 (d, $^3J_{H,H}$ = 2.1 Hz, 1 H, 1′-H), 4.12–4.20 (q, $^3J_{H,H}$ = 6.9 Hz, 2 H, OCH_2Me), 4.52 (dt, $^3J_{H,H}$ = 6.6, 2.1 Hz, 1 H, 3′-H), 5.37 (d, $^3J_{H,H}$ = 12.5 Hz, 1 H, 2-H), 7.59 (d, $^3J_{H,H}$ = 12.5 Hz, 1 H, 3-H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 13.9, 14.3, 22.4, 24.4, 31.2, 35.1, 59.8, 71.2, 75.9, 80.2, 99.0, 160.1, 167.5 ppm. IR ($CHCl_3$): $\tilde{\nu}$ = 3305.6, 2957.8, 2122.7, 1701.0, 1640.3, 1464.7, 1371.3, 1289.6, 1222.8, 1191.7, 1136.5 cm^{-1}. MS (70 eV): *m*/*z* (%) = 225 (22) [M^+ + 1], 195 (12.7), 179 (22), 151 (9.4), 139 (9.1), 125 (8.5), 117 (40), 109 (35), 93 (49), 89 (22), 81 (54), 79 (56), 71 (66), 67 (100), 55 (75). $C_{13}H_{20}O_3$ (224.14): calcd. C 69.61, H 8.99; found C 69.52, H 8.69.

(±)-Methyl (*E*)-3-(But-3-yn-2-yloxy)acrylate (1c): Yield: 452.8 mg (2.94 mmol, 98%). ^1H NMR ($CDCl_3$, 400 MHz): δ = 1.56 (d, $^3J_{H,H}$ = 6.6 Hz, 3 H, Me), 2.57 (d, $^3J_{H,H}$ = 2.1 Hz, 1 H, 4′-H), 3.69 (s, 3 H, OMe), 4.66 (dq, $^3J_{H,H}$ = 6.6, 2.1 Hz, 1 H, 2′-H), 5.37 (d, $^3J_{H,H}$ = 12.5 Hz, 1 H, 2-H), 7.59 (d, $^3J_{H,H}$ = 12.5 Hz, 1 H, 3-H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 21.6, 51.2, 67.0, 75.4, 80.9, 98.8, 160.0, 167.9 ppm. IR ($CHCl_3$): $\tilde{\nu}$ = 3306.9, 3024.2, 2952.9, 2122.0, 1706.4, 1645.7, 1625.6, 1438.4, 1333.4, 1293.9, 1224.5, 1194.1, 1145.3, 1120.8, 1035.2 cm^{-1}. MS (70 eV): *m*/*z* (%) = 154 (3.8) $[M]^+$, 123 (20), 111 (16), 102 (13), 95 (30), 71 (76), 53 (100). $C_8H_{10}O_3$ (154.06): calcd. C 62.33, H 6.54; found C 62.20, H 6.56.

(±)-Ethyl (*E*)-3-(1-Phenylhept-2-ynyloxy)acrylate (1d): Yield: 823.7 mg (2.88 mmol, 96%). ^1H NMR ($CDCl_3$, 400 MHz): δ = 0.91 (t, $^3J_{H,H}$ = 7.2 Hz, 3 H, Me), 1.26 (t, $^3J_{H,H}$ = 7.2 Hz, 3 H, Me), 1.37–1.46 (m, 2 H, 2 × 6′-H), 1.50–1.57 (m, 2 H, 2 × 5′-H), 2.30 (dt, $^3J_{H,H}$ = 6.9, 2.1 Hz, 2 H, 2 × 4′-H), 4.16 (q, $^3J_{H,H}$ = 7.2 Hz, 2 H, OCH_2Me), 5.43 (d, $^3J_{H,H}$ = 12.5 Hz, 1 H, 2-H), 5.62 (t, $^3J_{H,H}$ = 2.1 Hz, 1 H, 1′-H), 7.35–7.41 (m, 3 H, Ph), 7.48–7.51 (m, 2 H, Ph), 7.69 (d, $^3J_{H,H}$ = 12.5 Hz, 1 H, 3-H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 13.5, 14.3, 18.5, 21.9, 30.4, 59.7, 73.7, 75.7, 91.4,

99.4, 127.4, 128.7, 129.0, 137.0, 159.9, 167.6 ppm. IR ($CHCl_3$): $\tilde{\nu}$ = 3018.8, 2936.1, 2871.1, 2232.5, 1701.2, 1641.4, 1324.4, 1289.0, 1216.8, 1179.0, 1131.5 cm^{-1}. MS (70 eV): *m*/*z* (%) = 286 (1.4) $[M]^+$, 257 (1.7), 229 (2.9), 213 (4.8), 171 (100), 141 (9.9), 128 (30), 115 (23), 91 (36), 77 (10). $C_{18}H_{22}O_3$ (286.16): calcd. C 75.50, H 7.74; found C 75.15, H 7.39.

Ethyl (2*Z*,4*E*)-2-Formyl-3-(4-methoxyphenyl)-5-phenylpenta-2,4-dienoate (1e): Yield: 786.2 mg (2.34 mmol, 78%). ^1H NMR ($CDCl_3$, 400 MHz): δ = 1.42 (t, $^3J_{H,H}$ = 7.2 Hz, 3 H, Me), 3.88 (s, 3 H, OMe), 4.44 (q, $^3J_{H,H}$ = 7.2 Hz, 2 H, OCH_2Me), 6.68 (d, $^3J_{H,H}$ = 15.9 Hz, 1 H, 5-H), 6.98–7.02 (m, 2 H, ArH), 7.26–7.41 (m, 8 H, 4-H and ArH), 9.33 (s, 1 H, CHO) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 14.3, 55.3, 61.6, 113.9, 125.6, 127.2, 127.8, 128.8, 129.9, 131.8, 132.8, 135.6, 143.3, 157.7, 160.7, 166.4, 189.6 ppm. MS (70 eV): *m*/*z* (%) = 336 (32) $[M]^+$, 318 (25), 290 (100), 262 (81), 247 (33), 234 (29), 231 (32), 219 (42), 202 (32), 191 (37), 165 (22), 159 (11), 135 (17), 115 (19), 105 (16), 91 (28), 77 (20). HRMS: calcd. for $C_{21}H_{20}O_4$ $[M]^+$ 336.1362; found 336.1354.

(±)-Ethyl (*E*)-3-[3-(3,4-Dichlorophenyl)-1-phenylprop-2-ynyloxy]-acrylate (1f): Yield: 886.4 mg (2.37 mmol, 79% yield). ^1H NMR ($CDCl_3$, 400 MHz): δ = 1.23–1.28 (m, 3 H, Me), 4.08–4.19 (m, 2 H, OCH_2Me), 5.48 (d, $^3J_{H,H}$ = 12.7 Hz, 1 H, 2-H), 5.82 (s, 1 H, 1′-H), 7.29 (dd, $^3J_{H,H}$ = 8.5 and 2.1 Hz, 1 H, ArH), 7.38–7.43 (m, 4 H, ArH), 7.53–7.55 (m, 3 H, ArH), 7.69 (d, $^3J_{H,H}$ = 12.7 Hz, 3-H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 14.3, 59.9, 73.4, 86.4, 87.2, 99.9, 121.5, 127.4, 128.9, 129.4, 130.4, 131.0, 132.7, 133.5, 133.7, 136.0, 159.6, 167.3 ppm. IR ($CHCl_3$): $\tilde{\nu}$ = 3025.1, 2231.8, 1703.3, 1653.0, 1466.9, 1288.3, 1177.1, 1131.9 cm^{-1}. MS (70 eV): *m*/*z* (%) = 374 (8.0) $[M]^+$, 328 (16), 301 (13), 259 (100), 236 (10), 202 (26), 189 (20), 105 (13), 91 (13), 77 (11). $C_{20}H_{16}O_3Cl_2$ (374.05): calcd. C 64.02, H 4.30; found C 63.90, H 4.51.

(±)-Ethyl (*E*)-3-[3-(4-Chlorophenyl)-1-phenylprop-2-ynyloxy]acrylate (1g): Yield: 856.8 mg (2.52 mmol, 84%). ^1H NMR ($CDCl_3$, 400 MHz): δ = 1.26 (t, $^3J_{H,H}$ = 7.2 Hz, 3 H, Me), 4.16 (q, $^3J_{H,H}$ = 7.2 Hz, 2 H, OCH_2Me), 5.51 (d, $^3J_{H,H}$ = 12.5 Hz, 1 H, 2-H), 5.84 (s, 1 H, 1′-H), 7.28–7.31 (m, 2 H, ArH), 7.39–7.45 (m, 5 H, ArH), 7.55–7.58 (m, 2 H, ArH), 7.74 (d, $^3J_{H,H}$ = 12.5 Hz, 1 H, 3-H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 14.3, 59.8, 73.5, 85.3, 88.5, 99.7, 120.1, 127.4, 128.7, 128.8, 129.3, 133.1, 135.2, 136.2, 159.7, 167.6 ppm. MS (70 eV): *m*/*z* (%) = 340 (3.0) $[M]^+$, 225 (56), 188 (4.9), 138 (9.2), 105 (13), 91 (100), 65 (9.2). HRMS: calcd. for $C_{20}H_{17}ClO_3$ $[M]^+$ 340.0866; found 340.0854.

(±)-Ethyl (*E*)-3-[1-Phenyl-3-(*p*-tolyl)prop-2-ynyloxy]acrylate (1h): Yield: 777.6 mg (2.43 mmol, 81%). ^1H NMR ($CDCl_3$, 400 MHz): δ = 1.27 (t, $^3J_{H,H}$ = 7.2 Hz, 3 H, Me), 2.35 (s, 3 H, Me), 4.17 (q, $^3J_{H,H}$ = 7.2 Hz, 2 H, OCH_2Me), 5.50 (d, $^3J_{H,H}$ = 12.5 Hz, 1 H, 2-H), 5.86 (s, 1 H, 1′-H), 7.13 (d, $^3J_{H,H}$ = 7.9 Hz, 2 H, ArH), 7.36–7.45 (m, 5 H, ArH), 7.57–7.60 (m, 2 H, ArH), 7.76 (d, $^3J_{H,H}$ = 12.5 Hz, 1 H, 3-H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 14.3, 21.5, 59.9, 73.8, 83.6, 90.0, 99.6, 118.6, 127.5, 128.8, 129.1, 129.2, 131.8, 136.6, 139.4, 159.9, 167.6 ppm. IR ($CHCl_3$): $\tilde{\nu}$ = 3027.0, 2227.6, 1701.9, 1642.7, 1511.6, 1287.8, 1177.8, 1131.6 cm^{-1}. MS (70 eV): *m*/*z* (%) = 320 (3.5) $[M]^+$, 247 (7.7), 205 (100), 143 (6.8), 119 (8.1), 77 (5.1). $C_{21}H_{20}O_3$ (320.38): calcd. C 78.73, H 6.29; found C 78.83, H 6.25.

(±)-Ethyl (*E*)-3-(1,3-Diphenylprop-2-ynyloxy)acrylate (1i): Yield: 817.0 mg (2.67 mmol, 89%). ^1H NMR ($CDCl_3$, 400 MHz): δ = 1.27 (t, $^3J_{H,H}$ = 7.2 Hz, 3 H, Me), 4.17 (q, $^3J_{H,H}$ = 7.2 Hz, 2 H, OCH_2Me), 5.51 (d, $^3J_{H,H}$ = 12.5 Hz, 1 H, 2-H), 5.86 (s, 1 H, 1′-H), 7.30–7.38 (m, 3 H, PhH), 7.39–7.45 (m, 3 H, PhH), 7.48–7.50 (m, 2 H, PhH), 7.57–7.59 (m, 2 H, PhH), 7.75 (d, $^3J_{H,H}$ = 12.5 Hz, 1 H, 3-H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 14.3, 59.9, 73.7, 84.3, 89.8, 99.7, 121.7, 127.5, 128.4, 128.8, 129.1, 129.3, 131.9, 136.5, 159.9, 167.5 ppm. IR ($CHCl_3$): $\tilde{\nu}$ = 3020.2, 2228.4, 1701.8, 1642.4, 1323.7, 1289.5, 1177.1, 1132.3 cm^{-1}. MS (70 eV): *m*/*z* (%) = 306 (2.9) $[M]^+$, 260 (3.9), 231 (4.4), 202 (4.5), 191 (100), 189 (14.7), 165 (5.4), 129 (3.0), 105 (5.2), 89 (2.7), 77 (4.8). $C_{20}H_{18}O_3$ (306.13): calcd. C 78.41, H 5.92; found C 78.23, H 6.00.

(±)-Ethyl (*E*)-3-(4,4-Dimethyl-1-phenylpent-1-yn-3-yloxy)acrylate (1j): Yield: 849.4 mg (2.97 mmol, 99%). ^1H NMR ($CDCl_3$, 400 MHz): δ = 1.08 (s, 9 H, *t*Bu), 1.26 (t, $^3J_{H,H}$ = 7.2 Hz, 3 H, Me), 4.16 (q, $^3J_{H,H}$ = 7.2 Hz, 2 H, OCH_2Me), 4.38 (s, 1 H, 3′-H), 5.42 (d, $^3J_{H,H}$ = 12.5 Hz, 1 H, 2-H), 7.28–7.34 (m, 3 H, PhH), 7.42–7.45 (m, 2 H, PhH), 7.69 (d, $^3J_{H,H}$ = 12.5 Hz, 1 H, 3-H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 14.3, 25.6, 36.0, 59.7, 80.8, 84.3, 88.5, 98.4, 122.1, 128.3, 128.7, 131.8, 161.2, 167.8 ppm. IR ($CHCl_3$): $\tilde{\nu}$ = 3017.7, 2976.7, 2226.7, 1699.4, 1626.0, 1323.4, 1221.9, 1186.5, 1135.6 cm^{-1}. MS (70 eV): *m*/*z* (%) = 286 (0.8) $[M]^+$, 229 (6.4), 213 (8.7), 171 (100), 156 (54), 143 (25), 129 (21), 115 (26), 102 (3.6), 91 (18), 77 (8.6), 57 (12). $C_{18}H_{22}O_3$ (286.16): calcd. C 75.50, H 7.74; found C 75.66, H 7.45.

(±)-Ethyl (*E*)-3-[1-(4-Chlorophenyl)-3-phenylprop-2-ynyloxy]acrylate (1k): Yield: 805.8 mg (2.37 mmol, 79%). ^1H NMR ($CDCl_3$, 400 MHz): δ = 1.26 (t, $^3J_{H,H}$ = 7.2 Hz, 3 H, Me), 4.16 (q, $^3J_{H,H}$ = 7.2 Hz, 2 H, OCH_2Me), 5.49 (d, $^3J_{H,H}$ = 12.5 Hz, 1 H, 2-H), 5.82 (s, 1 H, 1′-H), 7.30–7.36 (m, 3 H, ArH), 7.37–7.40 (m, 2 H, ArH), 7.46–7.48 (m, 2 H, ArH), 7.49–7.52 (m, 2 H, ArH), 7.72 (d, $^3J_{H,H}$ = 12.5 Hz, 1 H, 3-H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 14.3, 59.9, 72.9, 83.8, 90.1, 99.9, 121.4, 128.4, 128.8, 129.0, 129.2, 131.9, 135.0, 135.2, 159.6, 167.4 ppm. IR ($CHCl_3$): $\tilde{\nu}$ = 3017.6, 2228.9, 1703.8, 1643.6, 1491.3, 1131.8, 1044.6 cm^{-1}. MS (70 eV): *m*/*z* (%) = 294 (11) $[M^+ - EtOH]$, 240 (11), 225 (100), 202 (15), 139 (13), 129 (19), 105 (19), 77 (12). $C_{20}H_{17}ClO_3$ (340.09): calcd. C 70.49, H 5.03; found C 70.25, H 5.00.

Ethyl (2*Z*,4*E*)-2-Formyl-5-(4-methoxyphenyl)-3-phenylpenta-2,4-dienoate (3l): Yield: 766.1 mg (2.28 mmol, 76%). ^1H NMR ($CDCl_3$, 400 MHz): δ = 1.42 (t, $^3J_{H,H}$ = 7.2 Hz, 3 H, Me), 3.81 (s, 3 H, OMe), 4.44 (q, $^3J_{H,H}$ = 7.2 Hz, 2 H, OCH_2Me), 6.55 (d, $^3J_{H,H}$ = 15.6 Hz, 1 H, 5-H), 6.83–6.87 (m, 2 H, ArH), 7.21 (d, $^3J_{H,H}$ = 15.6 Hz, 1 H, 4-H), 7.33–7.35 (m, 4 H, ArH), 7.46–7.48 (m, 3 H, ArH), 9.25 (s, 1 H, CHO) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 14.3, 55.4, 61.6, 114.4, 124.7, 128.0, 128.4, 129.2, 129.6, 130.1, 132.1, 133.8, 143.5, 158.4, 161.3, 166.4, 189.6 ppm. MS (70 eV): *m*/*z* (%) = 336 (48) $[M]^+$, 290 (100), 245 (12), 234 (68), 219 (24), 202 (21), 191 (46), 165 (17), 135 (22), 121 (20), 105 (11), 77 (15). HRMS: calcd. for $C_{21}H_{20}O_4$ $[M]^+$ 336.1362; found 336.1358.

Ethyl (2*Z*,4*E*)-2-Formyl-5-(furan-2-yl)-3-phenylpenta-2,4-dienoate (3m): Yield: 426.2 mg (1.44 mmol, 48%). ^1H NMR ($CDCl_3$, 400 MHz): δ = 1.42 (t, $^3J_{H,H}$ = 7.2 Hz, 3 H, Me), 4.44 (q, $^3J_{H,H}$ = 7.2 Hz, 2 H, OCH_2Me), 6.33 (d, $^3J_{H,H}$ = 15.4 Hz, 1 H, 5-H), 6.42 (m, 2 H, furan 3-H and 4-H), 7.22 (d, $^3J_{H,H}$ = 15.4 Hz, 1 H, 4-H), 7.31–7.33 (m, 2 H, PhH), 7.46–7.48 (m, 4 H, PhH and furan 5-H), 9.20 (s, 1 H, CHO) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 14.2, 61.6, 112.5, 114.5, 124.9, 128.1, 128.4, 129.3, 129.5, 130.0, 133.3, 144.8, 152.0, 157.4, 166.1, 189.4 ppm. IR ($CHCl_3$): $\tilde{\nu}$ = 3019.7, 1724.7, 1661.8, 1567.1, 1333.0, 1266.8, 1146.4, 1019.3 cm^{-1}. MS (70 eV): *m*/*z* (%) = 296 (32) $[M]^+$, 250 (65), 221 (28), 194 (83), 165 (100), 152 (27), 139 (16), 115 (27), 105 (14), 94 (12), 77 (19), 63 (14). $C_{18}H_{16}O_4$ (296.10): calcd. C 72.96, H 5.44; found C 73.09, H 5.48.

(±)-Ethyl (*E*)-3-[1-Phenyl-3-(trimethylsilyl)prop-2-ynyloxy]acrylate (1n): Yield: 697.6 mg (2.31 mmol, 77%). ^1H NMR ($CDCl_3$, 400 MHz): δ = 0.09 (s, 9 H, $SiMe_3$), 1.13 (t, $^3J_{H,H}$ = 7.2 Hz, 3 H, Me), 4.03 (q, $^3J_{H,H}$ = 7.2 Hz, 2 H, OCH_2Me), 5.33 (d, $^3J_{H,H}$ =

12.5 Hz, 1 H, 2-H), 5.50 (s, 1 H, 1′-H), 7.23–7.29 (m, 3 H, PhH), 7.36–7.39 (m, 2 H, PhH), 7.57 (d, $^3J_{H,H}$ = 12.5 Hz, 1 H, 3-H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = –0.45, 14.2, 59.7, 73.5, 95.7, 99.6, 100.0, 127.4, 128.7, 129.1, 136.1, 159.6, 167.3 ppm. IR ($CHCl_3$): $\tilde{\nu}$ = 3019.7, 2178.5, 1701.7, 1642.0, 1454.0, 1248.9, 1176.8, 1133.0, 849.9 cm^{-1}. MS (70 eV): *m*/*z* (%) = 302 (0.5) $[M]^+$, 213 (12), 187 (100), 172 (11), 83 (15). $C_{17}H_{22}O_3Si$ (302.13): calcd. C 67.51, H 7.33; found C 67.70, H 7.15.

Representative Procedure for the Microwave-Assisted Synthesis of Pyridines 6a–n: A solution of propargyl vinyl ether **1a** (1.0 mmol), methoxyamine hydrochloride (1.1 mmol), and NaOAc (0.55 mmol) in 2-propanol (5 mL) was placed in a microwave-specific closed vial, and the solution was irradiated in a single-mode microwave oven (200 W, 100 °C) for 60 min. The reaction mixture was filtered through Celite by using dichloromethane as solvent. After removing the solvent under reduced pressure, the products were purified by flash column chromatography (silica gel; *n*-hexane/EtOAc, 90:10, 1% Et_3N) to yield **6a** (175.0 mg, 77%).[14]

Ethyl 6-Pentylnicotinate (6b): Yield: 119.34 mg (0.54 mmol, 54%). ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 0.86 (t, $^3J_{H,H}$ = 7.2 Hz, 3 H, Me), 1.22–1.33 (m, 4 H, 2×3′-H and 2×4′-H), 1.37 (t, $^3J_{H,H}$ = 7.2 Hz, 3 H, Me), 1.69–1.73 (m, 2 H, 2×2′-H), 2.82 (pseudo t, $^3J_{H,H}$ = 7.7 Hz, 2 H, 2×1′-H), 4.36 (q, $^3J_{H,H}$ = 7.2 Hz, 2 H, OCH_2Me), 7.20 (d, $^3J_{H,H}$ = 8.0 Hz, 1 H, 5-H), 8.16 (dd, $^3J_{H,H}$ = 8.0, 2.4 Hz, 1 H, 4-H), 9.10 (d, $^3J_{H,H}$ = 2.4 Hz, 1 H, 2-H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 13.9, 14.2, 22.4, 29.3, 31.5, 38.4, 61.1, 122.3, 123.8, 137.3, 150.3, 165.4, 167.0 ppm. IR ($CHCl_3$): $\tilde{\nu}$ = 2933.2, 1715.8, 1600.8, 1377.7, 1289.9, 1121.9, 1030.7 cm^{-1}. MS (70 eV): *m*/*z* (%) = 221 (7.4) $[M]^+$, 192 (56), 178 (65), 165 (100), 150 (27), 137 (90), 92 (15), 65 (16). $C_{13}H_{19}NO_2$ (221.14): calcd. C 70.56, H 8.65, N 6.33; found C 70.19, H 8.61, N 5.92.

Ethyl 4-Butyl-6-phenylnicotinate (6d): Yield: 127.4 mg (0.45 mmol, 45%). ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 0.95 (t, $^3J_{H,H}$ = 7.4 Hz, 3 H, Me), 1.41 (t, $^3J_{H,H}$ = 7.2 Hz, 3 H, Me), 1.38–1.48 (m, 2 H, 2×3′-H), 1.59–1.67 (m, 2 H, 2×2′-H), 3.03 (pseudo t, $^3J_{H,H}$ = 8.0 Hz, 2 H, 2×1′-H), 4.40 (q, $^3J_{H,H}$ = 7.2 Hz, 2 H, OCH_2Me), 7.41–7.50 (m, 3 H, PhH), 7.58 (s, 1 H, 5-H), 8.01–8.03 (m, 2 H, PhH), 9.12 (s, 1 H, 2-H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 13.9, 14.2, 22.8, 33.1, 33.9, 61.0, 121.9, 124.1, 127.2, 128.8, 129.6, 138.5, 152.0, 154.4, 159.6, 166.2 ppm. IR ($CHCl_3$): $\tilde{\nu}$ = 2964.3, 1713.2, 1596.9, 1371.6, 1282.4, 1102.4 cm^{-1}. MS (70 eV): *m*/*z* (%) = 283 (100) $[M]^+$, 241 (33), 28 (72), 226 (45), 208 (36), 194 (13), 167 (17), 153 (14), 115 (10), 77 (13). $C_{18}H_{21}NO_2$ (283.16): calcd. C 76.29, H 7.47, N 4.94; found C 76.24, H 7.42, N 5.00.

Ethyl 4-(4-Methoxyphenyl)-6-phenylnicotinate (6e): Yield: 259.7 mg (0.78 mmol, 78%). ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 1.15 (t, $^3J_{H,H}$ = 7.2 Hz, 3 H, Me), 3.84 (s, 3 H, OMe), 4.21 (q, $^3J_{H,H}$ = 7.2 Hz, 2 H, OCH_2Me), 6.95–6.99 (m, 2 H, *p*-$MeOC_6H_4$, 3-H and 5 H), 7.31–7.33 (m, 2 H, *p*-$MeOC_6H_4$, 2-H and 6 H), 7.41–7.50 (m, 3 H, PhH), 7.69 (d, $^3J_{H,H}$ = 0.8 Hz, 1 H, 5-H), 8.04–8.07 (m, 2 H, PhH), 9.08 (d, $^3J_{H,H}$ = 0.8 Hz, 1 H, 2-H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 13.8, 55.2, 61.1, 113.7, 121.5, 124.7, 127.2, 128.7, 129.4, 129.6, 131.2, 138.2, 150.6, 151.0, 159.3, 159.9, 166.9 ppm. IR ($CHCl_3$): $\tilde{\nu}$ = 2984.6, 2840.6, 1715.9, 1598.1, 1513.7, 1291.7, 1246.1, 1111.6 cm^{-1}. MS (70 eV): *m*/*z* (%) = 333 (100) $[M]^+$, 304 (29), 288 (75), 233 (15), 189 (13), 77 (4.2). $C_{21}H_{19}NO_3$ (333.14): calcd. C 75.66, H 5.74, N 4.20; found C 75.62, H 5.80, N 3.92.

Ethyl 4-(3,4-Dichlorophenyl)-6-phenylnicotinate (6f): Yield: 226.3 mg (0.61 mmol, 61%). ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 1.17 (t, $^3J_{H,H}$ = 7.2 Hz, 3 H, Me), 4.22 (q, $^3J_{H,H}$ = 7.2 Hz, 2 H, OCH_2Me), 7.19 (dd, $^3J_{H,H}$ = 8.2, 2.1 Hz, 1 H, 3,4-Cl_2Ph 5-H), 7.46–7.52 (m, 5 H, ArH), 7.64 (s, 1 H, 5-H), 8.04–8.06 (m, 2 H, PhH), 9.18 (s, 1 H, 2-H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 13.9, 61.4, 121.3, 123.9, 127.3, 127.5, 128.9, 130.0, 130.1, 130.2, 132.5, 132.7, 137.8, 139.1, 148.8, 151.6, 159.9, 165.9 ppm. IR ($CHCl_3$): $\tilde{\nu}$ = 2986.7, 1717.2, 1591.7, 1466.4, 1290.3, 1120.1, 1038.2 cm^{-1}. MS (70 eV): *m*/*z* (%) = 371 (100) $[M]^+$, 342 (65), 326 (99), 273 (20), 236 (35), 200 (15), 160 (8.9), 77 (12). $C_{20}H_{15}Cl_2NO_2$ (371.05): calcd. C 64.53, H 4.06, N 3.76; found C 64.47, H 4.18, N 3.51.

Ethyl 4-(4-Chlorophenyl)-6-phenylnicotinate (6g): Yield: 202.2 mg (0.60 mmol, 60%). ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 1.14 (t, $^3J_{H,H}$ = 7.2 Hz, 3 H, Me), 4.20 (q, $^3J_{H,H}$ = 7.2 Hz, 2 H, OCH_2Me), 7.29–7.31 (m, 2 H, *p*-ClC_6H_4, 3-H and 5-H), 7.41–7.44 (m, 2 H, ArH), 7.45–7.50 (m, 3 H, ArH), 7.66 (d, $^3J_{H,H}$ = 0.8 Hz, 1 H, 5-H), 8.04–8.07 (m, 2 H, PhH), 9.15 (d, $^3J_{H,H}$ = 0.8 Hz, 1 H, 2-H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 13.8, 61.3, 121.5, 124.3, 127.3, 128.4, 128.9, 129.4, 129.9, 134.6, 137.6, 138.0, 150.1, 151.4, 159.7, 166.3 ppm. IR ($CHCl_3$): $\tilde{\nu}$ = 3021.2, 2084.1, 1715.6, 1641.2, 1473.0, 1285.0, 1218.7, 1115.3 cm^{-1}. MS (70 eV): *m*/*z* (%) = 337 (100) $[M]^+$, 308 (57), 292 (94), 237 (31), 202 (39), 126 (9.1), 77 (11). HRMS: calcd. for $C_{20}H_{16}ClNO_2$ $[M]^+$ 337.0870; found 337.0859.

Ethyl 6-Phenyl-4-*p*-tolylnicotinate (6h): Yield: 193.4 mg (0.61 mmol, 61%). ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 0.99 (t, $^3J_{H,H}$ = 7.2 Hz, 3 H, Me), 2.28 (s, 3 H, Me), 4.06 (q, $^3J_{H,H}$ = 7.2 Hz, 2 H, OCH_2Me), 7.10–7.15 (m, 4 H, tolyl), 7.29–7.36 (m, 3 H, PhH), 7.56 (s, 1 H, 5-H), 7.90–7.93 (m, 2 H, PhH), 8.97 (s, 1 H, 2-H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 13.8, 21.2, 61.2, 121.7, 124.9, 127.3, 128.0, 128.8, 129.0, 129.8, 136.1, 138.2, 138.4, 150.9, 151.2, 159.3, 166.8 ppm. IR ($CHCl_3$): $\tilde{\nu}$ = 2985.8, 1716.2, 1593.6, 1472.5, 1292.6, 1222.5, 1113.0 cm^{-1}. MS (70 eV): *m*/*z* (%) = 317 (90) $[M]^+$, 272 (100), 244 (15), 217 (16), 202 (18), 115 (10), 59 (17). $C_{21}H_{19}NO_2$ (317.14): calcd. C 79.47, H 6.03, N 4.41; found C 79.39, H 6.06, N 4.34.

Ethyl 4,6-Diphenylnicotinate (6i): Yield: 203.0 mg (0.67 mmol, 67%). ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 1.07 (t, $^3J_{H,H}$ = 7.2 Hz, 3 H, Me), 4.17 (q, $^3J_{H,H}$ = 7.2 Hz, 2 H, OCH_2Me), 7.36–7.51 (m, 8 H, PhH), 7.71 (d, $^3J_{H,H}$ = 0.5 Hz, 1 H, 5-H), 8.05–8.07 (m, 2 H, PhH), 9.13 (d, $^3J_{H,H}$ = 0.5 Hz, 1 H, 2-H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 13.7, 61.2, 121.7, 124.8, 127.3, 128.1, 128.2, 128.3, 128.9, 129.8, 138.3, 139.2, 151.13, 151.16, 159.5, 166.8 ppm. IR ($CHCl_3$): $\tilde{\nu}$ = 2987.6, 1716.1, 1590.7, 1296.3, 1221.3, 1115.8 cm^{-1}. MS (70 eV): *m*/*z* (%) = 303 (90) $[M]^+$, 274 (58), 258 (100), 230 (18), 202 (41), 77 (15). HRMS: calcd. for $C_{20}H_{17}NO_2$ $[M]^+$ 303.1260; found 303.1259.

Ethyl 6-*tert*-Butyl-4-phenylnicotinate (6j): Yield: 36.8 mg (0.13 mmol, 13%). ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 1.04 (t, $^3J_{H,H}$ = 7.2 Hz, 3 H, Me), 1.40 (s, 9 H, *t*Bu), 4.13 (q, $^3J_{H,H}$ = 7.2 Hz, 2 H, OCH_2Me), 7.30–7.33 (m, 3 H, PhH), 7.41–7.44 (m, 3 H, PhH and 5-H), 9.00 (s, 1 H, 2-H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 13.7, 30.0, 37.8, 61.1, 120.6, 123.9, 128.1, 128.2, 128.3, 131.9, 139.4, 149.7, 149.8, 166.8 ppm. IR ($CHCl_3$): $\tilde{\nu}$ = 2970.4, 1717.2, 1592.4, 1370.2, 1294.3, 1142.1 cm^{-1}. MS (70 eV): *m*/*z* (%) = 283 (69) $[M]^+$, 268 (100), 254 (17), 241 (62), 238 (18), 227 (13), 194 (14), 154 (12), 127 (12), 86 (15), 84 (21), 57 (23). HRMS: calcd. for $C_{18}H_{21}NO_2$ $[M]^+$ 283.1572; found 283.1570.

Ethyl 6-(4-Chlorophenyl)-4-phenylnicotinate (6k): Yield: 208.9 mg (0.62 mmol, 62%). ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 1.06 (t, $^3J_{H,H}$ = 7.2 Hz, 3 H, Me), 4.16 (q, $^3J_{H,H}$ = 7.2 Hz, 2 H, OCH_2Me), 7.34–7.37 (m, 2 H, PhH), 7.36–7.46 (m, 5 H, ArH), 7.67 (s, 1 H, 5-H), 8.00–8.02 (m, 2 H, *p*-ClC_6H_4, 2-H and 6-H), 9.10 (s, 1 H, 2-H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 13.7, 61.3, 121.4, 125.1, 128.0, 128.3, 128.5, 128.6, 129.1, 136.1, 136.6, 139.0, 151.1, 151.3, 158.2, 166.6 ppm. IR ($CHCl_3$): $\tilde{\nu}$ = 2979.8, 1717.8, 1592.9, 1469.7,

1296.5, 1220.6, 1100.1 cm^{-1}. MS (70 eV): *m/z* (%) = 337 (100) $[M]^+$, 292 (99), 265 (25), 237 (28), 202 (41), 127 (10), 105 (13), 77 (17). $C_{20}H_{16}ClNO_2$ (337.09): calcd. C 71.11, H 4.77, N 4.15; found C 71.00, H 5.09, N 4.11.

Ethyl 6-(4-Methoxyphenyl)-4-phenylnicotinate (6l): Yield: 239.8 mg (0.72 mmol, 72%). ^1H NMR ($CDCl_3$, 400 MHz): δ = 1.06 (t, $^3J_{H,H}$ = 7.2 Hz, 3 H, Me), 3.87 (s, 3 H, OMe), 4.15 (q, $^3J_{H,H}$ = 7.2 Hz, 2 H, OCH_2Me), 6.98–7.02 (m, 2 H, *p*-$MeOC_6H_4$, 3-H and 5-H), 7.35–7.37 (m, 2 H, PhH), 7.43–7.45 (m, 3 H, PhH), 7.64 (s, 1 H, 5-H), 8.02–8.06 (m, 2 H, *p*-$MeOC_6H_4$, 2-H and 6-H), 9.09 (s, 1 H, 2-H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 13.7, 55.4, 61.1, 114.3, 120.9, 124.0, 128.0, 128.2, 128.3, 128.5, 128.8, 139.4, 151.0 (2 signals), 159.0, 161.3, 166.7 ppm. IR ($CHCl_3$): $\tilde{\nu}$ = 2978.9, 2841.7, 1714.0, 1590.9, 1470.1, 1369.3, 1228.7, 1176.6, 1113.8 cm^{-1}. MS (70 eV): *m/z* (%) = 333 (100) $[M]^+$, 304 (16), 288 (43), 233 (15), 189 (11). $C_{21}H_{19}NO_3$ (333.14): calcd. C 75.66, H 5.74, N 4.20; found C 75.82, H 5.93, N 3.86.

Ethyl 6-(Furan-2-yl)-4-phenylnicotinate (6m): Yield: 175.8 mg (0.60 mmol, 60%). ^1H NMR ($CDCl_3$, 400 MHz): δ = 1.04 (t, $^3J_{H,H}$ = 7.2 Hz, 3 H, Me), 4.14 (q, $^3J_{H,H}$ = 7.2 Hz, 2 H, OCH_2Me), 6.55 (dd, $^3J_{H,H}$ = 3.5, 1.9 Hz, 1 H, furan 4-H), 7.19 (dd, $^3J_{H,H}$ = 3.5, 0.8 Hz, 1 H, furan 3-H), 7.33–7.35 (m, 2 H, PhH), 7.40–7.44 (m, 3 H, Ph and furan 5-H), 7.54 (dd, $^3J_{H,H}$ = 1.9, 0.8 Hz, 1 H, 5-H), 7.65 (d, $^3J_{H,H}$ = 0.8 Hz, 1 H, 2-H), 9.02 (s, 1 H, 2-H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 13.6, 61.1, 110.9, 112.4, 119.5, 124.3, 128.0, 128.2, 128.3, 139.0, 144.3, 151.0, 151.2, 151.3, 152.8, 166.5 ppm. IR ($CHCl_3$): $\tilde{\nu}$ = 2979.0, 1713.7, 1602.6, 1493.1, 1372.1, 1290.1, 1224.6, 1162.8, 1113.3, 1044.7 cm^{-1}. MS (70 eV): *m/z* (%) = 293 (96) $[M]^+$, 248 (100), 193 (15), 165 (36), 139 (10), 77 (5.0). $C_{18}H_{15}NO_3$ (293.11): calcd. C 73.71, H 5.15, N 4.78; found C 73.86, H 5.33, N 4.35.

Ethyl 4-(Trimethylsilyl)-6-phenylnicotinate (6n): Yield: 104.7 mg (0.35 mmol, 35%). ^1H NMR ($CDCl_3$, 400 MHz): δ = 0.39 (s, 9 H, $SiMe_3$), 1.42 (t, $^3J_{H,H}$ = 7.2 Hz, 3 H, Me), 4.42 (q, $^3J_{H,H}$ = 7.2 Hz, 2 H, OCH_2Me), 7.43–7.52 (m, 3 H, PhH), 7.98 (d, $^3J_{H,H}$ = 0.8 Hz, 1 H, 5-H), 8.02–8.04 (m, 2 H, PhH), 9.24 (d, $^3J_{H,H}$ = 0.8 Hz, 1 H, 2-H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = –0.37, 14.3, 61.3, 126.4, 127.4, 128.9, 129.5, 129.7, 138.7, 150.5, 153.3, 158.8, 167.0 ppm. IR ($CHCl_3$): $\tilde{\nu}$ = 2984.9, 1714.9, 1513.9, 1286.1, 1137.7 cm^{-1}. MS (70 eV): *m/z* (%) = 284 (18) $[M^+ – CH_3]$, 256 (61), 203 (19), 187 (27), 159 (33), 128 (17), 115 (13), 99 (28), 77 (18), 73 (100), 59 (11). HRMS: calcd. for $C_{17}H_{21}NO_2Si$ $[M – 15]^+$ 284.1107; found 284.1111.

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