Furan Ring Opening – Pyridine Ring Closure: New Route to Quinolines under the Bischler–Napieralski Reaction Conditions

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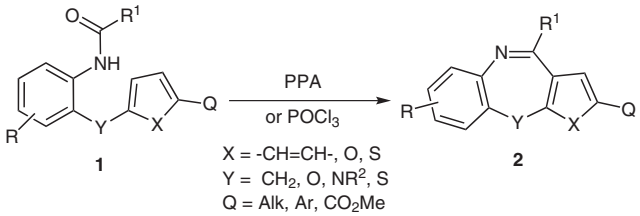
Abstract: A new approach to highly functionalized quinolines is proposed. This approach is based on the electrophilic recyclization of 2-[2-(acylamino)benzyl]furans under the Bischler–Napieralski reaction conditions.

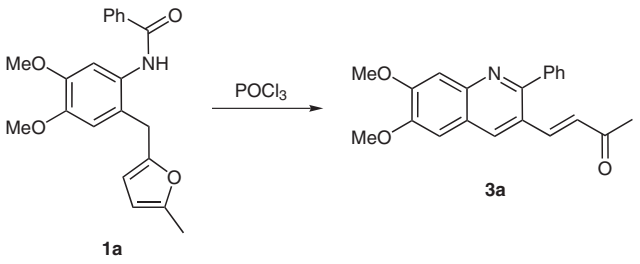
Key words: furans, ring opening, ring closure, fused-ring systems, quinolines, Bischler–Napieralski reaction

The Bischler–Napieralski reaction[1] is an efficient method for the transformation of phenethylamines into 3,4-dihydroisoquinolines,[2] and tryptamines into β-carbolines.[3] The Bischler–Napieralski reaction has also been applied in the annulation of the pyridine ring to other heterocyclic compounds, i.e. thiophene,[4] benzothiophene,[4,5] pyrrole,[6] thiazole,[7] and carbazole.[8] The appropriate choice of aromatic fragment and linker opens the way to a wide variety of nitrogen-containing heterocycles via Bischler–Napieralski-like reactions. For example, benzazepine derivatives were obtained using compounds with an amide group separated from the benzene ring by a propylene linker.[9] Similarly, *ortho*-acylamino-substituted diphenylmethanes, diphenyl ethers, diphenylamines, and diphenyl sulfides were transformed into dibenzazepines,[10–12] dibenzoxazepines,[11,12] dibenzodiazepines,[12,13] and dibenzothiazepines,[12,14] respectively (Scheme 1; X = –CH=CH–, Y = CH_2, O, NR^2, S). This transformation is also efficient for 2-[2-(carbamoylamino)benzyl]thiophenes (X = S, Y = CH_2).[15] In contrast, the Bischler–Napieralski reaction with 2-(2-aminoethyl)furans as a substrate affords the corresponding furopyridine derivatives in low to moderate yield only.[16] A single example of a high-yielding Bischler–Napieralski cyclization for furan derivatives was reported for 2-[2-(carbamoylamino)phenylthio]-5-methoxycarbonylfurans (Scheme 1; X = O, Y = S) wherein the substituents facilitate electrophilic attack at the C(3) atom of the furan ring and hinder attack at the C(2) atom.[17]

Taking these results into account, it might be expected that 2-[2-(acylamino)benzyl]furans **1** (X = O, Y = CH_2) should afford the corresponding furo[3,2-*c*][1]benzazepines **2** under the Bischler–Napieralski reaction conditions; however, we recently found that treatment of 2-[2-(benzoylamino)-4,5-dimethoxybenzyl]-5-methylfuran (**1a**) with phosphorus oxychloride yields the quinoline derivative **3a** (Scheme 2) instead of **2**.[18] Herein, we report our overall results of investigations of this unusual transformation.



Scheme 1 Bischler–Napieralski-like reaction of substrates **1**



Scheme 2 Phosphorus oxychloride induced transformation of **1a** into quinoline **3a**

To study the new reaction more carefully, we synthesized a series of substrates **1a–p** by acylation of 2-(2-furylmethyl)anilines **4** and 2-[di(2-furyl)methyl]anilines **5**, which were obtained according to Schemes 3 and 4, respectively. Thus, Friedel–Crafts acylation of veratrole (1,2-dimethoxybenzene, **6**) with acyl chlorides **7a–c** gave rise to 2-(3,4-dimethoxybenzoyl)furans **8a–c**. These ketones were nitrated using fuming nitric acid in acetic acid which afforded nitrobenzenes **9a–c**.[19] The obtained nitro ketones **9** were reduced with iron powder and acetic acid under reflux to the 2-furoylanilines **10a–c** which then further reduced with sodium borohydride in the presence of anhydrous aluminum chloride in tetrahydrofuran under heating to reflux to yield the 2-(2-furylmethyl)anilines **4a–c**.

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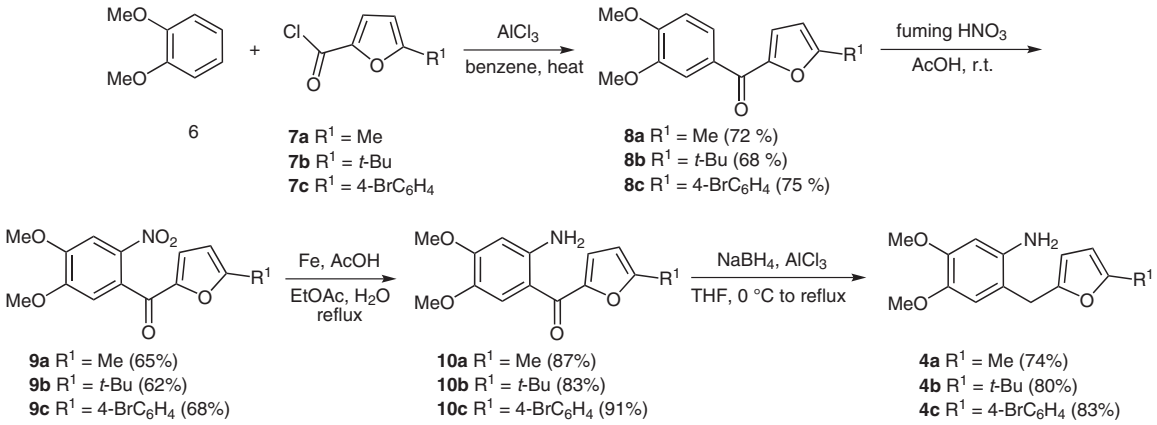
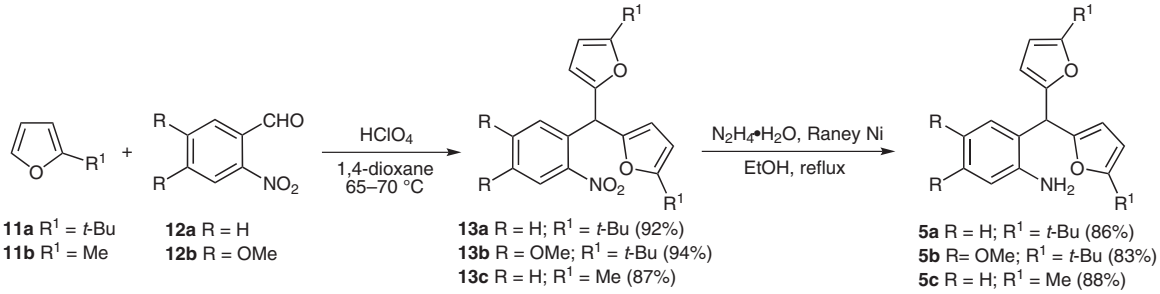


Scheme 3 Synthesis of 2-(2-furylmethyl)anilines **4a–c**



Scheme 4 Synthesis of 2-[di(2-furyl)methyl]anilines **5a–c**

Condensation of 2-(*tert*-butyl)furan (**11a**)[20] and 2-methylfuran (**11b**) with the commercially available 2-nitrobenzaldehydes **12a**,**b** in 1,4-dioxane in the presence of a catalytic quantity of perchloric acid, followed by reduction of the resulting bis(5-alkyl-2-furyl)(2-nitrophenyl)methanes **13a–c** with hydrazine hydrate in the presence of Raney nickel, yielded anilines **5a–c**.[21]

Treatment of anilines **4** and **5** with acyl chlorides in benzene afforded the goal amides **1a–p** (Table 1). When amides **1a–m** were refluxed in benzene or toluene in the presence of phosphorus oxychloride, quinolines **3a–m** were obtained in low to good yields (Table 1).

The structures of compounds **3** were determined by analysis of ^{1}H and ^{13}C NMR spectra, mass spectroscopic data, and elemental analysis, and proved unambiguously by single-crystal X-ray analysis for compound **3a** (Figure 1).[22] It needs to be pointed out that the exocyclic C=C bond in quinolines **3a–i** has the *E* configuration (^{3}J = 15.3–16.2 Hz), but the *Z* configuration for **3j–m** (^{3}J = 11.7–12.0 Hz). Possibly, this can be explained by a high-energy barrier for *cis-trans* isomerization due to large steric effects preventing rotation around this C=C bond in these compounds, even in protonated form.

Evidently, the formation of **3** proceeds via an electrophilic attack of the amide-derived iminium ion onto the α- but not the β-carbon atom of the furan. This attack is accompanied by furan ring opening and formation of the aromatic quinoline system (Scheme 5). There are a few examples of *ipso* attack by an electrophilic carbon atom in the Bischler–Napieralski reaction and related processes.[23] These reactions have been referred to as 'abnormal results'. On the other hand, electrophilic attack onto a substituted α-carbon atom of the furan ring is often preferable to the corresponding attack onto an unsubstituted β-position.[24] The preferable site of attack is under kinetic or thermodynamic control. In the case of **1a–m**, both factors result in preferential α-attack. Indeed, formation of the quinoline system conjugated to the enone moiety is, evidently, more preferable than the alternative creation of 10*H*-furo[3,2-*c*][1]benzazepines due to the low aromaticity energy of the furan ring and the nonaromatic nature of the central azepine cycle in **2** (X = O, Y = CHR[2]).

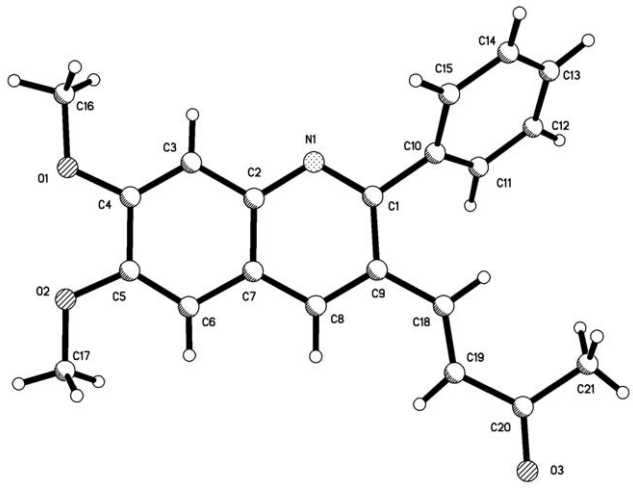
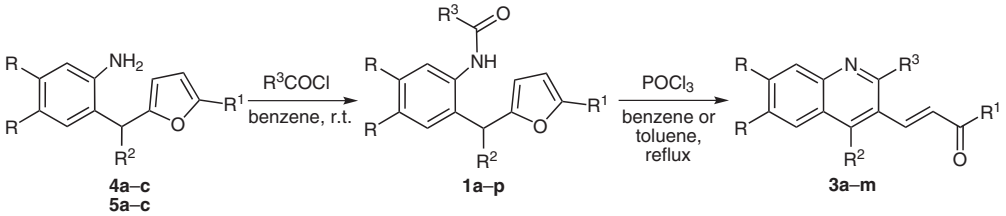


Figure 1 X-ray crystallographic structure of **3a**

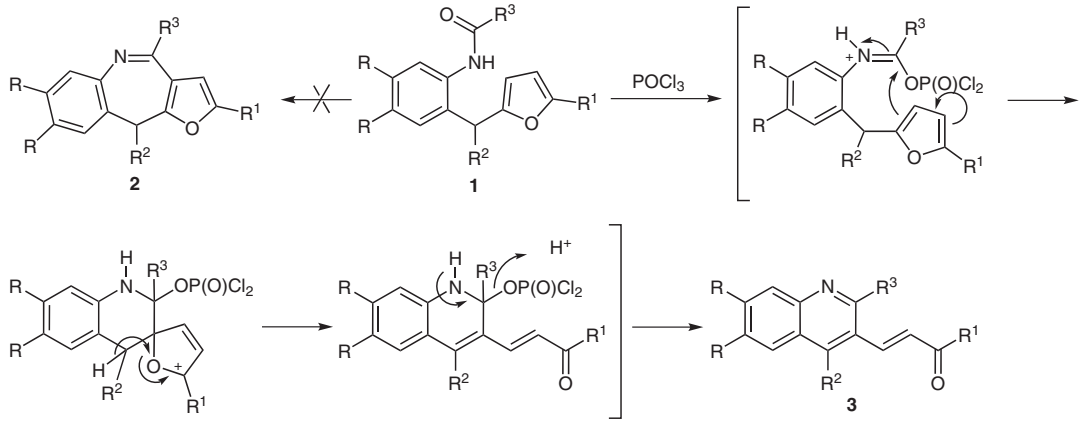
Table 1 Synthesis of Amides **1a–p** and Quinolines **3a–m**



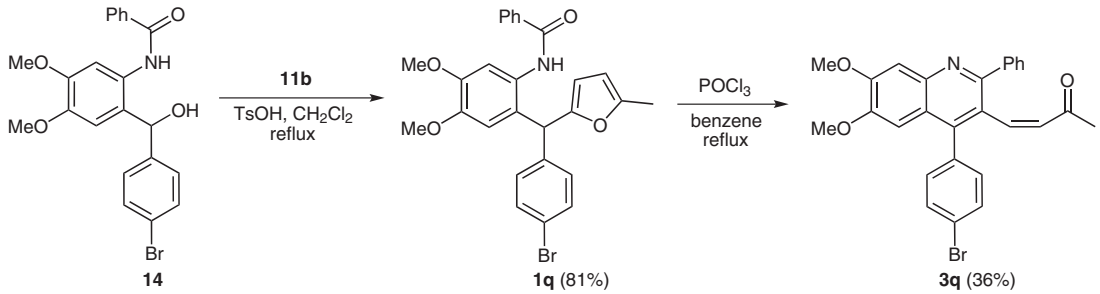
Entry	R	R^1	R^2	R^3	Yield (%) of **1**	Yield (%) of **3**
a	OMe	Me	H	Ph	72	61
b	OMe	Me	H	Me	65	34
c	OMe	Me	H	2-$O_2NC_6H_4$	76	68
d	OMe	Me	H	2-thienyl	80	56
e	OMe	*t*-Bu	H	Ph	68	82
f	OMe	*t*-Bu	H	Bn	87	42
g	OMe	*t*-Bu	H	CH_2Cl	63	45
h	OMe	4-BrC_6H_4	H	Ph	74	75
i	OMe	4-BrC_6H_4	H	$PhthNCH_2CH_2$	75	72
j	H	*t*-Bu	5-*t*-BuFur[a]	Ph	79	52
k	H	*t*-Bu	5-*t*-BuFur[a]	4-BrC_6H_4	87	69
l	H	*t*-Bu	5-*t*-BuFur[a]	4-$O_2NC_6H_4$	84	54
m	H	*t*-Bu	5-*t*-BuFur[a]	4-$MeOC_6H_4$	76	25
n	OMe	*t*-Bu	5-*t*-BuFur[a]	4-$O_2NC_6H_4$	85	–
o	OMe	*t*-Bu	5-*t*-BuFur[a]	4-Tol	90	–
p	H	Me	5-MeFur[a]	4-$O_2NC_6H_4$	73	–

[a] Fur = 2-furyl.

We have demonstrated the broad scope of this reaction. In general, transformation of furans **1e–g** with a *tert*-butyl group at the C(5) position, and **1h**,**i** with an aryl group, into quinolines **3** proceeds with better yields than that of furans **1a–d** containing a methyl group at this position. Both electron-enriched and electron-depleted benzamides could be employed in the reaction, giving similar yields of quinolines. At the same time, in some examples yields of quinolines **3** are low or moderate. In the case of **3b**,**f**,**g**, it is possibly explained by acid-catalyzed condensations with participation of the α-carbon atom in the alkyl group at the C(2) atom of the quinoline, leading to the formation



Scheme 5 The possible mechanism of quinoline **3** formation



Scheme 6 Synthesis of quinoline **3q**

of various byproducts. Recyclization of **1j–l** proceeds with satisfactory yield, accounting for the presence of the second furyl group prone to acid-catalyzed transformations. In contrast, **3m** was obtained in low yield only. We believe this is a result of further product transformation by intramolecular cyclizations with participation of the carbonyl group and the second furan ring, leading to salt-like products and tar. Such secondary cyclizations were observed previously in the recyclizations of other aryldifurylmethanes.[25] These byprocesses are especially efficient for electron-enriched compounds and for substrates with the small methyl group at the C(5) position of the furan ring. Indeed, substrates **1n–p** failed to give quinolines **3**.

To check this proposition, we synthesized diaryl(furyl)methane **1q** by the alkylation of 2-methylfuran (**11b**) with the corresponding benzhydrol **14**. Treatment of **1q** with phosphorus oxychloride in benzene under reflux affords quinoline **3q** in 36% yield (Scheme 6).

Thus, we have developed a principally new method for the synthesis of polyfunctionalized quinolines[26] by recyclization of 2-[2-(acylamino)benzyl]furans in the presence of phosphorus oxychloride. In contrast to our previous investigations[19,21,25a] wherein the same substrates were transformed into indoles in the presence of Brønsted acids via protonation of the furan ring followed by the interaction of the electrophilic intermediate with the amide moiety functioning as a nucleophile, in this novel approach the amide function reacts as an electrophile and the furan ring plays the role of nucleophile. Therefore, the appropriate choice of acidic catalyst allows either indoles or quinolines to be synthesized from the same 2-[2-(acylamino)benzyl]furans. Both kinds of products are interesting, both in themselves and as precursors for the preparation of various natural and non-natural physiologically active compounds.

NMR spectra were recorded with a Bruker DPX 300 spectrometer (300 MHz for ^{1}H and 75 MHz for ^{13}C NMR) at room temperature; the chemical shifts (δ) were measured in ppm with respect to the solvent ($CDCl_3$, ^{1}H: 7.26 ppm, ^{13}C: 77.13 ppm; DMSO-d_6, ^{1}H: 2.50 ppm, ^{13}C: 39.7 ppm). Coupling constants (*J*) are given in hertz (Hz). Multiplicities of signals are described as follows: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, dd = doublet of doublets, br = broadened. Abbreviations used for peak assignments are as follows: Py = pyridyl, Ar = aryl, Fur = furyl, Th = thienyl. IR spectra were measured as KBr plates on InfraLUM FT-02 and InfraLUM FT-801 instruments. Mass spectra were recorded on a Kratos MS-30 instrument with 70-eV electron-impact ionization at 200 °C. Crystallographic measurements were performed at 293 K on an Enraf Nonius CAD4 diffractometer. Melting points (uncorrected) were determined in capillaries with an Electrothermal 9100 capillary melting-point apparatus. Column chromatography was performed on silica gel KSK (50–160 μm, LTD Sorbpolymer). All reactions were carried out using freshly distilled and dried solvents.

(3,4-Dimethoxyphenyl)(2-furyl)methanones 8a–c

Ketone **8a** was synthesized according to a published method.[19] Compounds **8b**,**c** were obtained by a similar procedure.

(5-*tert*-Butyl-2-furyl)(3,4-dimethoxyphenyl)methanone (8b)

Yellow oil; yield: 68%. This compound was further used without additional purification.

[5-(4-Bromophenyl)-2-furyl](3,4-dimethoxyphenyl)methanone (8c)

Pale yellow needles; yield: 75%; mp 130–131 °C (EtOH).

IR (KBr): 1631, 1599, 1508, 1469, 1307, 1273, 1237, 1137, 1031, 806 cm^{-1}.

^{1}H NMR (300 MHz, DMSO-d_6): δ = 3.95 (s, 3 H, OCH_3), 3.96 (s, 3 H, OCH_3), 6.81 (d, *J* = 3.6 Hz, 1 H, H_{Fur}), 6.95 (d, *J* = 8.4 Hz, 1 H, H_{Ar}), 7.29 (d, *J* = 3.6 Hz, 1 H, H_{Fur}), 7.55 (d, *J* = 8.7 Hz, 2 H, H_{Ar}), 7.58 (d, *J* = 2.1 Hz, 1 H, H_{Ar}), 7.65 (d, *J* = 8.7 Hz, 2 H, H_{Ar}), 7.73 (dd, *J* = 2.1, 8.4 Hz, 1 H, H_{Ar}).

^{13}C NMR (75 MHz, DMSO-d_6): δ = 56.2, 56.3, 107.9, 110.3, 112.0, 122.0, 123.4, 124.1, 126.5 (2 C), 128.6, 130.2, 132.3 (2 C), 149.2, 152.1, 153.2, 156.8, 180.7.

MS (EI, 70 eV): *m*/*z* (%) = 388/386 (99/100) [M$^+$], 314/312 (17/16), 225 (17), 165 (21), 77 (18), 43 (27).

Anal. Calcd for $C_{19}H_{15}BrO_4$: C, 58.93; H, 3.90. Found: C, 58.61; H, 3.79.

(4,5-Dimethoxy-2-nitrophenyl)(2-furyl)methanones 9a–c; General Procedure

Fuming HNO_3 (5 mL) was added dropwise under efficient stirring to a soln of the corresponding ketone **8** (15 mmol) in AcOH (25 mL) at 3–5 °C. The reaction mixture was maintained at 5–7 °C for 20 min and at r.t. for 20 min (TLC monitoring). Then, it was poured onto ice and the separated residue was collected by filtration and washed with H_2O until pH ~7. Compounds **9a**,**c** were recrystallized from the specified solvents. Product **9b** was purified by column chromatography on silica gel (CH_2Cl_2–PE, 1:3).

(4,5-Dimethoxy-2-nitrophenyl)(5-methyl-2-furyl)methanone (9a)[19]

Yellow solid; yield: 2.84 g (65%); mp 128–129 °C (EtOH–acetone).

(5-*tert*-Butyl-2-furyl)(4,5-dimethoxy-2-nitrophenyl)methanone (9b)
Yellow oil; yield: 3.10 g (62%). This compound was used in the further transformations without additional purification.

[5-(4-Bromophenyl)-2-furyl](4,5-dimethoxy-2-nitrophenyl)methanone (9c)
Yellow solid; yield: 4.41 g (68%); mp 189–190 °C (CH_2Cl_2–PE).

IR (KBr): 1655, 1523, 1469, 1334, 1276, 1225, 1076, 1034, 868, 815, 789 cm^{-1}.

^1H NMR (300 MHz, DMSO-d_6): δ = 3.98 (s, 3 H, OCH_3), 4.04 (s, 3 H, OCH_3), 6.77 (d, *J* = 3.6 Hz, 1 H, H_{Fur}), 6.99 (s, 1 H, H_{Ar}), 7.14 (d, *J* = 3.6 Hz, 1 H, H_{Fur}), 7.52 (s, 4 H, H_{Ar}), 7.70 (s, 1 H, H_{Ar}).

^{13}C NMR (75 MHz, DMSO-d_6): δ = 57.0, 57.1, 107.4, 108.7, 111.2, 121.5, 124.1, 126.9 (2 C), 128.4, 128.9, 132.6 (2 C), 140.9, 150.6, 151.4, 154.0, 157.8, 180.4.

MS (EI, 70 eV): *m*/*z* (%) = 433/431 (1/1) [M^+], 239/237 (100/100), 194 (35), 164 (53), 136 (65), 63 (37), 43 (35).

Anal. Calcd for $C_{19}H_{14}BrNO_6$: C, 52.80; H, 3.26; N, 3.24. Found: C, 52.71; H, 3.35; N, 3.28.

(2-Amino-4,5-dimethoxyphenyl)(2-furyl)methanones 10a–c; General Procedure
A mixture of the corresponding nitro ketone **9** (15 mmol), iron powder (10 g), AcOH (35 mL), H_2O (50 mL), and EtOAc (10 mL) was stirred under reflux for 6 h. After completion of the reaction, the mixture was neutralized with $NaHCO_3$ until pH 7 and filtered. The residue was washed on the filter with EtOAc (3 × 150 mL). The organic layer was separated, and the aqueous layer was extracted with EtOAc (3 × 150 mL). The combined extracts were dried (Na_2SO_4) and concentrated under reduced pressure. The residue was recrystallized (CH_2Cl_2–PE) to afford compound **10**.

(2-Amino-4,5-dimethoxyphenyl)(5-methyl-2-furyl)methanone (10a)[19]
Yellow needles; yield: 3.41 g (87%); mp 120 °C.

(2-Amino-4,5-dimethoxyphenyl)(5-*tert*-butyl-2-furyl)methanone (10b)
Yellow needles; yield: 3.77 g (83%); mp 98–100 °C.

IR (KBr): 3417, 3305, 2939, 1630, 1584, 1570, 1524, 1502, 1465, 1402, 1322, 1250, 1143, 1021, 816 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 1.35 (s, 9 H, *t*-Bu), 3.84 (s, 3 H, OCH_3), 3.87 (s, 3 H, OCH_3), 6.16 (d, *J* = 3.6 Hz, 1 H, H_{Fur}), 6.17 (s, 1 H, H_{Ar}), 7.10 (d, *J* = 3.6 Hz, 1 H, H_{Fur}), 7.64 (s, 1 H, H_{Ar}).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 28.9 (3 C), 33.1, 55.7, 56.4, 99.3, 104.9, 109.9, 114.2, 119.4, 140.1, 148.4, 152.1, 154.8, 168.0, 181.5.

MS (EI, 70 eV): *m*/*z* (%) = 303 (100) [M^+], 288 (21), 247 (21), 218 (38), 164 (77), 43 (39).

Anal. Calcd for $C_{17}H_{21}NO_4$: C, 67.31; H, 6.98; N, 4.62. Found: C, 67.45; H, 7.08; N, 4.54.

(2-Amino-4,5-dimethoxyphenyl)[5-(4-bromophenyl)-2-furyl]methanone (10c)
Yellow needles; yield: 5.49 g (91%); mp 184–185 °C.

IR (KBr): 3444, 3334, 1620, 1589, 1554, 1509, 1469, 1252, 1138, 810 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 3.83 (s, 3 H, OCH_3), 3.89 (s, 3 H, OCH_3), 6.20 (s, 1 H, H_{Ar}), 6.79 (d, *J* = 3.6 Hz, 1 H, H_{Fur}), 7.21 (d, *J* = 3.6 Hz, 1 H, H_{Fur}), 7.53 (d, *J* = 9.0 Hz, 2 H, H_{Ar}), 7.59 (s, 1 H, H_{Ar}), 7.64 (d, *J* = 9.0 Hz, 2 H, H_{Ar}).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 56.0, 56.7, 99.6, 107.7, 110.1, 114.3, 120.4, 123.0, 126.2 (2 C), 128.8, 132.3 (2 C), 140.5, 148.6, 152.9, 155.5, 155.8, 181.4.

MS (EI, 70 eV): *m*/*z* (%) = 403/401 (99/100) [M^+], 388/386 (18/18), 218 (48), 164 (67), 136 (45), 43 (40).

Anal. Calcd for $C_{19}H_{16}BrNO_4$: C, 56.73; H, 4.01; N, 3.48. Found: C, 56.48; H, 4.00; N, 3.41.

2-(2-Furylmethyl)anilines 4a–c
Anilines **4a–c** were synthesized according to a procedure published previously.[19] These compounds were used in the further transformations without additional purification.

2-[Di(2-furyl)methyl]anilines 5
Compounds **13a**,**b** and **5a**,**b** were synthesized according to a published procedure,[21] as were compounds **13c** and **5c**.[25a]

Amides 1a–p; General Procedure
A soln of an acyl chloride (7 mmol) in benzene (20–30 mL) was added under stirring to a soln of an amine **4** or **5** (6 mmol) in benzene (15 mL). The mixture was stirred at r.t. for 30–60 min (TLC monitoring). Then, sat. aq $NaHCO_3$ (50 mL) was added, and the mixture was vigorously stirred for 30 min. The precipitate was collected by filtration. The organic fraction was separated from the aqueous fraction; the aqueous fraction was extracted with EtOAc (3 × 25 mL). The combined organic phases were washed with H_2O (2 × 30 mL) and dried (Na_2SO_4). The solvent was evaporated under reduced pressure. The residue and the precipitate were combined. The crude product was purified by flash chromatography on silica gel (CH_2Cl_2–PE, 1:8) and recrystallization (CH_2Cl_2–PE, 1:5).

***N*-{4,5-Dimethoxy-2-[(5-methyl-2-furyl)methyl]phenyl}benzamide (1a)**
White solid; yield: 1.52 g (72%); mp 115–116 °C.

IR (KBr): 3260, 1644, 1612, 1516, 1488, 1468, 1308, 1284, 1260, 1220, 1092, 712 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 2.25 (s, 3 H, CH_3), 3.87 (s, 2 H, CH_2), 3.88 (s, 3 H, OCH_3), 3.90 (s, 3 H, OCH_3), 5.89 (d, *J* = 3.3 Hz, 1 H, H_{Fur}), 5.94 (d, *J* = 3.3 Hz, 1 H, H_{Fur}), 6.75 (s, 1 H, H_{Ar}), 7.44–7.58 (m, 3 H, H_{Ar}), 7.61 (s, 1 H, H_{Ar}), 7.85–7.87 (m, 2 H, H_{Ar}), 8.38 (s, 1 H, NH).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.5, 31.2, 55.9, 56.0, 106.4, 106.9, 108.1, 112.9, 122.0, 127.0 (2 C), 128.6 (2 C), 129.0, 131.7, 134.7, 146.3, 147.8, 151.3, 151.5, 165.5.

MS (EI, 70 eV): *m*/*z* (%) = 351 (78) [M^+], 247 (24), 246 (76), 105 (95), 77 (100), 59 (48), 43 (55).

Anal. Calcd for $C_{21}H_{21}NO_4$: C, 71.78; H, 6.02; N, 3.99. Found: C, 71.61; H, 6.11; N, 3.81.

***N*-{4,5-Dimethoxy-2-[(5-methyl-2-furyl)methyl]phenyl}acetamide (1b)**
White solid; yield: 1.13 g (65%); mp 148–149 °C.

IR (KBr): 3272, 1656, 1536, 1516, 1408, 1340, 1260, 1216, 1020 cm^{-1}.

^1H NMR (300 MHz, DMSO-d_6): δ = 1.98 (s, 3 H, CH_3), 2.18 (s, 3 H, CH_3), 3.68 (s, 3 H, OCH_3), 3.69 (s, 3 H, OCH_3), 3.80 (s, 2 H, CH_2), 5.86 (d, *J* = 3.0 Hz, 1 H, H_{Fur}), 5.92 (d, *J* = 3.0 Hz, 1 H, H_{Fur}), 6.72 (s, 1 H, H_{Ar}), 6.91 (s, 1 H, H_{Ar}), 9.26 (s, 1 H, NH).

^{13}C NMR (75 MHz, DMSO-d_6): δ = 13.2, 23.0, 29.4, 55.5, 55.7, 106.2, 106.8, 110.5, 113.1, 124.7, 128.9, 146.3, 147.0, 149.9, 151.9, 168.2.

MS (EI, 70 eV): *m*/*z* (%) = 289 (66) [M^+], 247 (36), 246 (100), 231 (19), 204 (41), 189 (31).

Anal. Calcd for $C_{16}H_{19}NO_4$: C, 66.42; H, 6.62; N, 4.84. Found: C, 66.46; H, 6.66; N, 4.90.

***N*-{4,5-Dimethoxy-2-[(5-methyl-2-furyl)methyl]phenyl}-2-nitrobenzamide (1c)**

Pale yellow solid; yield: 1.81 g (76%); mp 136–137 °C.

IR (KBr): 3234, 1652, 1525, 1348, 1259, 1218, 1099, 1021, 1001, 859, 790 cm^{-1}.

^1H NMR (300 MHz, DMSO-d_6): δ = 2.20 (s, 3 H, CH_3), 3.71 (s, 3 H, OCH_3), 3.75 (s, 3 H, OCH_3), 3.91 (s, 2 H, CH_2), 5.91 (d, *J* = 3.0 Hz, 1 H, H_{Fur}), 5.95 (d, *J* = 3.0 Hz, 1 H, H_{Fur}), 6.79 (s, 1 H, H_{Ar}), 7.03 (s, 1 H, H_{Ar}), 7.67–7.70 (m, 1 H, H_{Ar}), 7.71–7.77 (m, 1 H, H_{Ar}), 7.83–7.89 (m, 1 H, H_{Ar}), 8.11–8.14 (m, 1 H, H_{Ar}), 10.13 (s, 1 H, NH).

^{13}C NMR (75 MHz, DMSO-d_6): δ = 13.3, 29.3, 55.7 (2 C), 106.3, 107.0, 110.6, 113.1, 124.2, 126.0, 127.9, 129.2, 130.8, 132.8, 133.8, 146.8, 147.1, 147.3, 150.0, 151.9, 164.5.

MS (EI, 70 eV): *m*/*z* (%) = 396 (9) [M^+], 379 (36), 319 (33), 281 (100), 247 (23), 246 (45), 120 (26), 95 (29), 43 (29).

Anal. Calcd for $C_{21}H_{20}N_2O_6$: C, 63.63; H, 5.09; N, 7.07. Found: C, 63.64; H, 5.25; N, 7.06.

***N*-{4,5-Dimethoxy-2-[(5-methyl-2-furyl)methyl]phenyl}thiophene-2-carboxamide (1d)**

Orange oil; yield: 1.71 g (80%). This compound was used in the further transformations without additional purification.

***N*-{2-[(5-*tert*-Butyl-2-furyl)methyl]-4,5-dimethoxyphenyl}benzamide (1e)**

White solid; yield: 1.60 g (68%); mp 119–120 °C.

IR (KBr): 3324, 1646, 1608, 1518, 1485, 1227, 1092, 1009, 854, 788 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 1.21 (s, 9 H, *t*-Bu), 3.86 (s, 3 H, OCH_3), 3.91 (s, 5 H, OCH_3 + CH_2), 5.86 (d, *J* = 3.0 Hz, 1 H, H_{Fur}), 5.88 (d, *J* = 3.0 Hz, 1 H, H_{Fur}), 6.75 (s, 1 H, H_{Ar}), 7.41–7.47 (m, 2 H, H_{Ar}), 7.50–7.56 (m, 1 H, H_{Ar}), 7.61 (s, 1 H, H_{Ar}), 7.78–7.81 (m, 2 H, H_{Ar}), 8.14 (s, 1 H, NH).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 29.0 (3 C), 31.1, 32.5, 55.9, 56.0, 102.7, 106.5, 108.2, 112.8, 122.0, 127.0 (2 C), 128.6 (2 C), 128.7, 131.7, 134.6, 146.4, 147.8, 151.1, 163.8, 165.5.

MS (EI, 70 eV): *m*/*z* (%) = 393 (54) [M^+], 289 (25), 288 (59), 232 (22), 121 (17), 105 (100), 76 (65), 57 (21).

Anal. Calcd for $C_{24}H_{27}NO_4$: C, 73.26; H, 6.92; N, 3.56. Found: C, 73.47; H, 6.90; N, 3.62.

***N*-{2-[(5-*tert*-Butyl-2-furyl)methyl]-4,5-dimethoxyphenyl}-2-phenylacetamide (1f)**

White solid; yield: 2.12 g (87%); mp 90–91 °C.

IR (KBr): 3480, 2956, 1680, 1608, 1592, 1496, 1464, 1448, 1384, 1256, 1228, 1208, 1156, 1076, 1012, 700 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 1.24 (s, 9 H, *t*-Bu), 3.59 (s, 2 H, CH_2), 3.69 (s, 2 H, CH_2), 3.79 (s, 3 H, OCH_3), 3.85 (s, 3 H, OCH_3), 5.55 (d, *J* = 3.0 Hz, 1 H, H_{Fur}), 5.77 (d, *J* = 3.0 Hz, 1 H, H_{Fur}), 6.63 (s, 1 H, H_{Ar}), 7.16 (br s, 1 H, NH), 7.25–7.37 (m, 6 H, H_{Ar}).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 29.1 (3 C), 30.4, 32.5, 44.7, 56.0 (2 C), 102.5, 106.2, 108.3, 112.9, 122.0, 127.5, 128.3, 129.1 (2 C), 129.4 (2 C), 134.6, 146.6, 147.8, 150.7, 163.5, 169.3.

MS (EI, 70 eV): *m*/*z* (%) = 407 (32) [M^+], 288 (100), 192 (69), 165 (45), 91 (61), 43 (49).

Anal. Calcd for $C_{25}H_{29}NO_4$: C, 73.69; H, 7.17; N, 3.44. Found: C, 73.52; H, 7.08; N, 3.48.

***N*-{2-[(5-*tert*-Butyl-2-furyl)methyl]-4,5-dimethoxyphenyl}-2-chloroacetamide (1g)**

Beige solid; yield: 1.38 g (63%); mp 96–97 °C.

IR (KBr): 3236, 2960, 1676, 1648, 1612, 1548, 1516, 1464, 1404, 1212, 1100, 1004, 856, 796 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 1.23 (s, 9 H, *t*-Bu), 3.84 (s, 5 H, OCH_3 + CH_2), 3.87 (s, 3 H, OCH_3), 4.17 (s, 2 H, CH_2), 5.83 (s, 2 H, H_{Fur}), 6.72 (s, 1 H, H_{Ar}), 7.35 (s, 1 H, H_{Ar}), 8.35 (br s, 1 H, NH).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 29.0 (3 C), 30.7, 32.5, 42.9, 56.0 (2 C), 102.5, 106.5, 108.1, 112.9, 122.7, 127.3, 147.0, 147.9, 150.6, 163.8, 164.3.

MS (EI, 70 eV): *m*/*z* (%) = 367/365 (33/100) [M^+], 314 (23), 288 (63), 272 (47), 244 (56), 242 (99), 192 (23), 137 (20), 121 (28), 57 (27), 43 (74).

Anal. Calcd for $C_{19}H_{24}ClNO_4$: C, 62.38; H, 6.61; N, 3.83. Found: C, 62.26; H, 6.63; N, 3.70.

***N*-(2-{[5-(4-Bromophenyl)-2-furyl]methyl}-4,5-dimethoxyphenyl)benzamide (1h)**

White solid; yield: 2.18 g (74%); mp 187–188 °C.

IR (KBr): 3284, 1640, 1612, 1528, 1476, 1448, 1404, 1216, 1204, 1072, 692 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 3.88 (s, 3 H, OCH_3), 3.90 (s, 3 H, OCH_3), 4.00 (s, 2 H, CH_2), 6.08 (d, *J* = 3.3 Hz, 1 H, H_{Fur}), 6.57 (d, *J* = 3.3 Hz, 1 H, H_{Fur}), 6.80 (s, 1 H, H_{Ar}), 7.36–7.44 (m, 6 H, H_{Ar}), 7.48–7.54 (m, 2 H, H_{Ar}), 7.76–7.79 (m, 2 H, H_{Ar}), 8.04 (br s, 1 H, NH).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 31.1, 56.0, 56.1, 106.6, 108.5, 108.8, 112.9, 120.9, 121.9, 124.9 (2 C), 126.9 (2 C), 128.6, 128.7 (2 C), 129.4, 131.7 (2 C), 131.8, 134.5, 146.6, 148.0, 152.2, 153.5, 165.7.

MS (EI, 70 eV): *m*/*z* (%) = 493/491 (16/16) [M^+], 388/386 (64/64), 183 (31), 105 (88), 76 (100), 45 (36).

Anal. Calcd for $C_{26}H_{22}BrNO_4$: C, 63.43; H, 4.50; N, 2.84. Found: C, 63.43; H, 4.29; N, 2.72.

***N*-(2-{[5-(4-Bromophenyl)-2-furyl]methyl}-4,5-dimethoxyphenyl)-3-(1,3-dioxo-1,3-dihydro-2*H*-isoindol-2-yl)propanamide (1i)**

White solid; yield: 2.65 g (75%); mp 209–210 °C.

IR (KBr): 3256, 1712, 1644, 1540, 1436, 1392, 1216, 924, 720 cm^{-1}.

^1H NMR (300 MHz, DMSO-d_6): δ = 2.64–2.68 (m, 2 H, CH_2), 3.68 (s, 3 H, OCH_3), 3.69 (s, 3 H, OCH_3), 3.86–3.91 (m, 2 H, CH_2), 3.87 (s, 2 H, CH_2), 6.09 (d, *J* = 3.3 Hz, 1 H, H_{Fur}), 6.80 (s, 1 H, H_{Ar}), 6.82 (d, *J* = 3.3 Hz, 1 H, H_{Fur}), 6.87 (s, 1 H, H_{Ar}), 7.50–7.57 (m, 4 H, H_{Ar}), 7.79–7.87 (m, 4 H, H_{Ar}), 9.48 (s, 1 H, NH).

^{13}C NMR (75 MHz, DMSO-d_6): δ = 29.4, 34.4, 34.5, 55.5, 55.7, 107.5, 108.7, 110.7, 113.0, 119.8, 123.0 (2 C), 124.6, 124.9 (2 C), 128.6, 129.6, 131.7 (2 C), 131.8 (2 C), 134.4 (2 C), 146.6, 147.2, 150.6, 154.4, 167.8 (2 C), 168.9.

MS (EI, 70 eV): *m*/*z* (%) = 590/588 (74/70) [M^+], 388/386 (96/100), 185 (19), 160 (46), 147 (33), 103 (19), 76 (37), 59 (67), 55 (70), 43 (42).

Anal. Calcd for $C_{30}H_{25}BrN_2O_6$: C, 61.13; H, 4.28; N, 4.75. Found: C, 61.10; H, 4.40; N, 4.88.

***N*-{2-[Bis(5-*tert*-butyl-2-furyl)methyl]phenyl}benzamide (1j)[27]**

Colorless needles; yield: 2.16 g (79%); mp 144–145 °C.

***N*-{2-[Bis(5-*tert*-butyl-2-furyl)methyl]phenyl}-4-bromobenzamide (1k)[27]**
Pale yellow cubes; yield: 2.79 g (87%); mp 155–156 °C.

***N*-{2-[Bis(5-*tert*-butyl-2-furyl)methyl]phenyl}-4-nitrobenzamide (1l)[27]**
Colorless needles; yield: 2.52 g (84%); mp 159–160 °C.

***N*-{2-[Bis(5-*tert*-butyl-2-furyl)methyl]phenyl}-4-methoxybenzamide (1m)[27]**
White solid; yield: 2.21 g (76%); mp 134–135 °C.

***N*-{2-[Bis(5-*tert*-butyl-2-furyl)methyl]-4,5-dimethoxyphenyl}-4-nitrobenzamide (1n)[21]**
White solid; yield: 2.86 g (85%); mp 199–200 °C.

***N*-{2-[Bis(5-*tert*-butyl-2-furyl)methyl]-4,5-dimethoxyphenyl}-4-methylbenzamide (1o)[21]**
White solid; yield: 2.85 g (90%); mp 149–151 °C.

***N*-{2-[Bis(5-methyl-2-furyl)methyl]phenyl}-4-nitrobenzamide (1p)**
White solid; yield: 1.82 g (73%); mp 181–182 °C.

IR (KBr): 3283, 1645, 1599, 1523, 1492, 1345, 1299, 1022, 851, 780, 753, 717 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 2.20 (s, 6 H, CH_3), 5.48 (s, 1 H, CH), 5.89 (d, *J* = 3.0 Hz, 2 H, H_{Fur}), 5.98 (d, *J* = 3.0 Hz, 2 H, H_{Fur}), 7.18–7.21 (m, 2 H, H_{Ar}), 7.33–7.39 (m, 1 H, H_{Ar}), 7.85 (d, *J* = 9.0 Hz, 2 H, H_{Ar}), 8.00–8.02 (m, 1 H, H_{Ar}), 8.26 (d, *J* = 9.0 Hz, 2 H, H_{Ar}), 8.43 (br s, 1 H, NH).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.7 (2 C), 43.2, 106.6 (2 C), 109.1 (2 C), 123.8 (2 C), 124.8, 126.2, 128.3, 128.4, 130.2 (2 C), 130.7, 135.4 (2 C), 140.5, 149.8, 150.7 (2 C), 152.3 (2 C).

Anal. Calcd for $C_{24}H_{20}N_2O_5$: C, 69.22; H, 4.84; N, 6.73. Found: C, 69.24; H, 4.94; N, 6.91.

Quinolines 3a–m; General Procedure
A mixture of an amide **1** (1.4 mmol), $POCl_3$ (7.5 mL), and benzene (for the synthesis of **3a**–**i**) or toluene (for the synthesis of **3j**–**m**) (25 mL) was refluxed for 1.5 h. The reaction mixture was poured into H_2O (800 mL) and neutralized with a soln of NaOH (50 g) in H_2O (200 mL). The product was extracted with CH_2Cl_2 (3 × 150 mL). The combined organic fractions were dried (Na_2SO_4), filtered, and concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, 50–160 mm; CH_2Cl_2–PE, 1:3) and recrystallization (CH_2Cl_2–PE, 1:4).

(3*E*)-4-(6,7-Dimethoxy-2-phenylquinolin-3-yl)but-3-en-2-one (3a)
Pale yellow needles; yield: 284 mg (61%); mp 200–201 °C.

IR (KBr): 1664, 1616, 1588, 1496, 1432, 1392, 1260, 1228, 1212, 1132, 1008, 704 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 2.28 (s, 3 H, CH_3), 4.03 (s, 3 H, OCH_3), 4.04 (s, 3 H, OCH_3), 6.73 (d, *J* = 16.2 Hz, 1 H, =CH), 7.10 (s, 1 H, H_{Ar}), 7.46–7.54 (m, 4 H, H_{Ar}), 7.58–7.62 (m, 2 H, H_{Ar}), 7.66 (d, *J* = 16.2 Hz, 1 H, =CH), 8.30 (s, 1 H, H_{Py}).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 26.9, 56.0, 56.2, 104.8, 107.9, 122.5, 124.8, 128.3 (3 C), 128.6, 129.7 (2 C), 132.8, 139.3, 142.0, 145.6, 150.2, 153.7, 157.1, 198.2.

MS (EI, 70 eV): *m*/*z* (%) = 333 (27) [M^+], 290 (100), 275 (31), 274 (38), 246 (30), 217 (26), 101 (29), 59 (55), 43 (57).

Anal. Calcd for $C_{21}H_{19}NO_3$: C, 75.66; H, 5.74; N, 4.20. Found: C, 75.37; H, 5.60; N, 4.19.

Crystal data: $C_{21}H_{19}NO_3$, monoclinic, space group $P2_1/n$; *a* = 8.536(2) Å, *b* = 8.566(2) Å, *c* = 24.213(5) Å, β = 90.44(3)°, *V* = 1770.4(6) $Å^3$, *Z* = 4, D_{calcd} = 1.251 g/cm^3, *F*(000) = 704; 2473 reflections collected, 2290 unique (R_{int} = 0.0265); final *R* indices (1180 observed collections, $I > 2\sigma I$): *R*1 = 0.0292, *wR*2 = 0.0743; final *R* indices (all data): *R*1 = 0.1012, *wR*2 = 0.0783.

(3*E*)-4-(6,7-Dimethoxy-2-methylquinolin-3-yl)but-3-en-2-one (3b)
Yellow needles; yield: 129 mg (34%); mp 179–180 °C.

IR (KBr): 1661, 1495, 1358, 1261, 1227, 1153, 1122, 1018, 969 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 2.42 (s, 3 H, CH_3), 2.79 (s, 3 H, CH_3), 4.00 (s, 3 H, OCH_3), 4.02 (s, 3 H, OCH_3), 6.74 (d, *J* = 16.2 Hz, 1 H, =CH), 7.02 (s, 1 H, H_{Ar}), 7.35 (s, 1 H, H_{Ar}), 7.85 (d, *J* = 16.2 Hz, 1 H, =CH), 8.16 (s, 1 H, H_{Py}).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 23.1, 27.8, 55.9, 56.1, 105.0, 107.0, 122.1, 125.3, 128.6, 132.0, 139.4, 145.2, 149.6, 153.5, 155.1, 197.7.

MS (EI, 70 eV): *m*/*z* (%) = 271 (60) [M^+], 257 (23), 256 (100), 228 (39), 212 (60), 184 (22), 101 (33), 59 (51), 45 (62).

Anal. Calcd for $C_{16}H_{17}NO_3$: C, 70.83; H, 6.32; N, 5.16. Found: C, 70.78; H, 6.15; N, 5.03.

(3*E*)-4-[6,7-Dimethoxy-2-(2-nitrophenyl)quinolin-3-yl]but-3-en-2-one (3c)
Yellow needles; yield: 360 mg (68%); mp 193–194 °C.

IR (KBr): 1666, 1523, 1499, 1347, 1252, 1231, 1217, 856 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 2.22 (s, 3 H, CH_3), 4.01 (s, 3 H, OCH_3), 4.04 (s, 3 H, OCH_3), 6.71 (d, *J* = 15.9 Hz, 1 H, =CH), 7.11 (s, 1 H, H_{Ar}), 7.34 (d, *J* = 15.9 Hz, 1 H, =CH), 7.36 (s, 1 H, H_{Ar}), 7.49–7.52 (m, 1 H, H_{Ar}), 7.62–7.68 (m, 1 H, H_{Ar}), 7.72–7.78 (m, 1 H, H_{Ar}), 8.15–8.19 (m, 1 H, H_{Ar}), 8.33 (s, 1 H, H_{Py}).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 27.7, 56.1, 56.2, 105.0, 107.7, 123.0, 124.8, 124.9, 128.8, 129.6, 132.0, 132.4, 133.2, 134.9, 138.8, 145.3, 148.8, 150.6, 153.9, 154.1, 197.5.

MS (EI, 70 eV): *m*/*z* (%) = 378 (97) [M^+], 346 (51), 335 (37), 307 (34), 289 (100), 274 (41), 246 (44), 204 (36), 110 (42).

Anal. Calcd for $C_{21}H_{18}N_2O_5$: C, 66.66; H, 4.79; N, 7.40. Found: C, 66.89; H, 4.71; N, 7.45.

(3*E*)-4-[6,7-Dimethoxy-2-(2-thienyl)quinolin-3-yl]but-3-en-2-one (3d)
Pale green-yellow needles; yield: 266 mg (56%); mp 210–211 °C.

IR (KBr): 1660, 1617, 1493, 1249, 1230, 1003, 887, 853, 745 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 2.40 (s, 3 H, CH_3), 4.02 (s, 3 H, OCH_3), 4.04 (s, 3 H, OCH_3), 6.75 (d, *J* = 16.2 Hz, 1 H, =CH), 7.05 (s, 1 H, H_{Ar}), 7.17 (dd, *J* = 3.6, 5.1 Hz, 1 H, H_{Th}), 7.32 (dd, *J* = 1.2, 3.6 Hz, 1 H, H_{Th}), 7.41 (s, 1 H, H_{Ar}), 7.51 (dd, *J* = 1.2, 5.1 Hz, 1 H, H_{Th}), 7.97 (d, *J* = 16.2 Hz, 1 H, =CH), 8.18 (s, 1 H, H_{Py}).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 27.3, 56.0, 56.2, 104.8, 107.5, 122.3, 124.5, 127.7, 128.3, 129.0, 129.2, 133.4, 141.9, 143.2, 145.5, 149.7, 150.2, 153.7, 198.0.

MS (EI, 70 eV): *m*/*z* (%) = 339 (37) [M^+], 296 (100), 281 (73), 264 (16), 252 (67), 236 (15), 222 (17), 209 (15), 45 (14).

Anal. Calcd for $C_{19}H_{17}NO_3S$: C, 67.24; H, 5.05; N, 4.13. Found: C, 67.24; H, 4.88; N, 4.01.

(1*E*)-1-(6,7-Dimethoxy-2-phenylquinolin-3-yl)-4,4-dimethylpent-1-en-3-one (3e)
Yellow solid; yield: 431 mg (82%); mp 114–115 °C.

IR (KBr): 1684, 1604, 1584, 1504, 1392, 1236, 1076, 1008 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 1.21 (s, 9 H, *t*-Bu), 4.05 (s, 3 H, OCH_3), 4.06 (s, 3 H, OCH_3), 7.07 (d, *J* = 15.6 Hz, 1 H, =CH), 7.14 (s, 1 H, H_{Ar}), 7.45–7.53 (m, 3 H, H_{Ar}), 7.56–7.60 (m, 3 H, H_{Ar}), 7.83 (d, *J* = 15.6 Hz, 1 H, =CH), 8.35 (s, 1 H, H_{Py}).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 26.2 (3 C), 43.2, 56.1, 56.3, 104.8, 108.0, 122.4, 122.6, 125.6, 128.5 (2 C), 128.6, 129.6 (2 C), 133.2, 139.5, 140.9, 145.4, 150.2, 153.6, 157.6, 203.7.

MS (EI, 70 eV): *m*/*z* (%) = 375 (13) [M^+], 318 (100), 290 (16), 274 (18), 57 (13), 45 (27).

Anal. Calcd for $C_{24}H_{25}NO_3$: C, 76.77; H, 6.71; N, 3.73. Found: C, 76.58; H, 6.76; N, 3.79.

(1*E*)-1-(2-Benzyl-6,7-dimethoxyquinolin-3-yl)-4,4-dimethylpent-1-en-3-one (3f)
White solid; yield: 229 mg (42%); mp 183–185 °C.

IR (KBr): 1680, 1608, 1592, 1496, 1256, 1228, 1208, 1156, 1076, 1012, 700 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 1.17 (s, 9 H, *t*-Bu), 3.99 (s, 3 H, OCH_3), 4.04 (s, 3 H, OCH_3), 4.43 (s, 2 H, CH_2), 6.98 (d, *J* = 15.3 Hz, 1 H, =CH), 7.04 (s, 1 H, H_{Ar}), 7.09–7.15 (m, 1 H, H_{Ar}), 7.18–7.24 (m, 4 H, H_{Ar}), 7.41 (s, 1 H, H_{Ar}), 8.02 (d, *J* = 15.3 Hz, 1 H, =CH), 8.14 (s, 1 H, H_{Py}).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 26.2 (3 C), 42.8, 43.1, 56.0, 56.2, 105.1, 107.8, 122.4, 123.1, 126.2, 126.6, 128.5 (2 C), 128.7 (2 C), 132.5, 139.0, 139.6, 145.5, 150.0, 153.4, 157.5, 203.5.

MS (EI, 70 eV): *m*/*z* (%) = 389 (33) [M^+], 332 (73), 304 (89), 298 (98), 91 (100), 57 (78), 43 (61).

Anal. Calcd for $C_{25}H_{27}NO_3$: C, 77.09; H, 6.99; N, 3.60. Found: C, 77.23; H, 7.17; N, 3.62.

(1*E*)-1-[2-(Chloromethyl)-6,7-dimethoxyquinolin-3-yl]-4,4-dimethylpent-1-en-3-one (3g)
Beige needles; yield: 219 mg (45%); mp 195–196 °C.

IR (KBr): 1680, 1608, 1592, 1500, 1432, 1392, 1256, 1228, 1208, 1164, 1080, 1008, 876 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 1.25 (s, 9 H, *t*-Bu), 4.01 (s, 3 H, OCH_3), 4.02 (s, 3 H, OCH_3), 4.90 (s, 2 H, CH_2), 7.06 (s, 1 H, H_{Ar}), 7.20 (d, *J* = 15.3 Hz, 1 H, =CH), 7.37 (s, 1 H, H_{Ar}), 8.07 (d, *J* = 15.3 Hz, 1 H, =CH), 8.24 (s, 1 H, H_{Py}).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 26.1 (3 C), 43.2, 45.4, 56.0, 56.2, 104.8, 107.5, 123.4, 123.7, 125.8, 132.9, 137.8, 145.0, 150.6, 152.7, 153.6, 203.5.

MS (EI, 70 eV): *m*/*z* (%) = 349/347 (7/21) [M^+], 292/290 (25/75), 262 (23), 256 (87), 227 (100), 212 (31), 59 (31), 57 (79), 45 (35), 43 (65).

Anal. Calcd for $C_{19}H_{22}ClNO_3$: C, 65.61; H, 6.38; N, 4.03. Found: C, 65.39; H, 6.48; N, 4.12.

(2*E*)-1-(4-Bromophenyl)-3-(6,7-dimethoxy-2-phenylquinolin-3-yl)prop-2-en-1-one (3h)
Yellow needles; yield: 498 mg (75%); mp 183–184 °C.

IR (KBr): 1659, 1585, 1497, 1393, 1299, 1236, 1206, 1104 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 4.05 (s, 3 H, OCH_3), 4.06 (s, 3 H, OCH_3), 7.14 (s, 1 H, H_{Ar}), 7.43 (d, *J* = 15.6 Hz, 1 H, =CH), 7.46–7.53 (m, 4 H, H_{Ar}), 7.59–7.63 (m, 4 H, H_{Ar}), 7.83 (d, *J* = 8.7 Hz, 2 H, H_{Ar}), 7.95 (d, *J* = 15.6 Hz, 1 H, =CH), 8.41 (s, 1 H, H_{Py}).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 56.1, 56.3, 104.9, 108.1, 122.5, 122.9, 125.4, 127.9, 128.5 (2 C), 128.7, 129.7 (2 C), 130.0 (2 C), 131.9 (2 C), 133.3, 136.6, 139.5, 143.7, 145.8, 150.3, 153.9, 157.7, 188.9.

MS (EI, 70 eV): *m*/*z* (%) = 475/473 (21/21) [M^+], 290 (100), 246 (28), 217 (32), 185/183 (33/33), 157/155 (29/29), 101 (35), 77 (40), 43 (32).

Anal. Calcd for $C_{26}H_{20}BrNO_3$: C, 65.83; H, 4.25; N, 2.95. Found: C, 66.07; H, 4.26; N, 3.19.

2-(2-{3-[(1*E*)-3-(4-Bromophenyl)-3-oxoprop-1-en-1-yl]-6,7-dimethoxyquinolin-2-yl}ethyl)-1*H*-isoindole-1,3(2*H*)-dione (3i)
Pale yellow solid; yield: 576 mg (72%); mp 228–229 °C.

IR (KBr): 1700, 1660, 1592, 1496, 1388, 1308, 1244, 1212, 1164, 1108, 1032, 1008, 720 cm^{-1}.

^1H NMR (300 MHz, DMSO-d_6): δ = 3.36–3.41 (m, 2 H, CH_2), 3.88 (s, 3 H, OCH_3), 3.92 (s, 3 H, OCH_3), 3.98–4.03 (m, 2 H, CH_2), 7.13 (s, 1 H, H_{Ar}), 7.26 (s, 1 H, H_{Ar}), 7.67–7.81 (m, 7 H, H_{Ar} + =CH), 7.99 (d, *J* = 8.7 Hz, 2 H, H_{Ar}), 8.03 (d, *J* = 15.3 Hz, 1 H, =CH), 8.75 (s, 1 H, H_{Py}).

^{13}C NMR (75 MHz, DMSO-d_6): δ = 33.1, 37.1, 55.6, 55.7, 105.5, 107.0, 121.9, 122.8 (2 C), 123.3, 125.2, 127.3, 130.4 (2 C), 131.6 (2 C), 131.7 (2 C), 132.8, 134.0 (2 C), 136.2, 139.9, 145.1, 149.5, 153.3, 155.3, 167.6 (2 C), 187.3.

MS (EI, 70 eV): *m*/*z* (%) = 572/570 (16/16) [M^+], 388 (25), 387 (100), 240 (22), 183 (22), 77 (18), 43 (47).

Anal. Calcd for $C_{30}H_{23}BrN_2O_5$: C, 63.06; H, 4.06; N, 4.90. Found: C, 63.02; H, 4.18; N, 4.89.

(1*Z*)-1-[4-(5-*tert*-Butyl-2-furyl)-2-phenylquinolin-3-yl]-4,4-dimethylpent-1-en-3-one (3j)
Beige needles; yield: 318 mg (52%); mp 158–159 °C.

IR (KBr): 2968, 1680, 1616, 1556, 1076, 1004, 816, 768, 700 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 0.77 (s, 9 H, *t*-Bu), 1.35 (s, 9 H, *t*-Bu), 6.14 (d, *J* = 3.3 Hz, 1 H, H_{Fur}), 6.37 (d, *J* = 11.7 Hz, 1 H, =CH), 6.50 (d, *J* = 3.3 Hz, 1 H, H_{Fur}), 7.18 (d, *J* = 11.7 Hz, 1 H, =CH), 7.32–7.37 (m, 3 H, H_{Ar}), 7.46–7.51 (m, 1 H, H_{Ar}), 7.55–7.59 (m, 2 H, H_{Ar}), 7.65–7.70 (m, 1 H, H_{Ar}), 8.07–8.10 (m, 1 H, H_{Ar}), 8.14–8.17 (m, 1 H, H_{Ar}).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 25.6 (3 C), 29.2 (3 C), 32.8, 42.9, 103.7, 114.7, 124.7, 125.1, 125.8, 126.5, 127.6 (2 C), 128.0, 129.0, 129.1, 129.9 (3 C), 134.5, 141.2, 141.6, 146.5, 147.4, 158.1, 165.4, 203.4.

MS (EI, 70 eV): *m*/*z* (%) = 437 (52) [M^+], 352 (37), 296 (100), 85 (16), 57 (92), 43 (76).

Anal. Calcd for $C_{30}H_{31}NO_2$: C, 82.35; H, 7.14; N, 3.20. Found: C, 82.34; H, 7.29; N, 3.18.

(1*Z*)-1-[2-(4-Bromophenyl)-4-(5-*tert*-butyl-2-furyl)quinolin-3-yl]-4,4-dimethylpent-1-en-3-one (3k)
Pale yellow solid; yield: 498 mg (69%); mp 196–197 °C.

IR (KBr): 2964, 1680, 1608, 1560, 1528, 1484, 1360, 1272, 1072, 1004, 808, 800, 792, 768 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 0.80 (s, 9 H, *t*-Bu), 1.34 (s, 9 H, *t*-Bu), 6.15 (d, *J* = 3.3 Hz, 1 H, H_{Fur}), 6.40 (d, *J* = 12.0 Hz, 1 H, =CH), 6.52 (d, *J* = 3.3 Hz, 1 H, H_{Fur}), 7.16 (d, *J* = 12.0 Hz, 1 H, =CH), 7.44–7.54 (m, 5 H, H_{Ar}), 7.67–7.73 (m, 1 H, H_{Ar}), 8.08–8.11 (m, 1 H, H_{Ar}), 8.16–8.19 (m, 1 H, H_{Ar}).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 25.6 (3 C), 29.1 (3 C), 32.9, 43.0, 103.8, 115.1, 122.5, 124.8, 125.1, 125.9, 126.9, 128.6, 129.5, 129.6, 130.7 (2 C), 131.6 (2 C), 135.0, 139.7, 141.2, 146.2, 147.0, 156.9, 165.6, 203.5.

MS (EI, 70 eV): *m*/*z* (%) = 517/515 (34/35) [M^+], 376/374 (96/100), 57 (77), 43 (32).

Anal. Calcd for $C_{30}H_{30}BrNO_2$: C, 69.77; H, 5.85; N, 2.71. Found: C, 69.66; H, 5.91; N, 2.59.

(1*Z*)-1-[4-(5-*tert*-Butyl-2-furyl)-2-(4-nitrophenyl)quinolin-3-yl]-4,4-dimethylpent-1-en-3-one (3l)

Yellow solid; yield: 364 mg (54%); mp 209–210 °C.

IR (KBr): 2964, 1680, 1604, 1516, 1344, 1272, 1072, 1008, 808, 792, 772, 716 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 0.77 (s, 9 H, *t*-Bu), 1.35 (s, 9 H, *t*-Bu), 6.17 (d, *J* = 3.3 Hz, 1 H, H_{Fur}), 6.42 (d, *J* = 12.0 Hz, 1 H, =CH), 6.53 (d, *J* = 3.3 Hz, 1 H, H_{Fur}), 7.22 (d, *J* = 12.0 Hz, 1 H, =CH), 7.52–7.58 (m, 1 H, H_{Ar}), 7.70–7.75 (m, 1 H, H_{Ar}), 7.78 (d, *J* = 9.0 Hz, 2 H, H_{Ar}), 8.12–8.17 (m, 2 H, H_{Ar}), 8.23 (d, *J* = 9.0 Hz, 2 H, H_{Ar}).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 25.5 (3 C), 29.1 (3 C), 32.9, 43.1, 103.9, 115.4, 122.7 (2 C), 125.0, 125.2, 125.9, 127.3, 128.1, 129.7, 129.8, 130.9 (2 C), 135.0, 141.0, 145.9, 147.2, 147.4, 147.5, 156.0, 165.8, 203.6.

MS (EI, 70 eV): *m*/*z* (%) = 482 (24) [M^+], 398 (24), 381 (18), 341 (53), 325 (18), 85 (24), 57 (100), 43 (42).

Anal. Calcd for $C_{30}H_{30}N_2O_4$: C, 74.67; H, 6.27; N, 5.80. Found: C, 74.52; H, 6.30; N, 5.69.

(1*Z*)-1-[4-(5-*tert*-Butyl-2-furyl)-2-(4-methoxyphenyl)quinolin-3-yl]-4,4-dimethylpent-1-en-3-one (3m)

Red-orange solid; yield: 163 mg (25%); mp 148–149 °C.

IR (KBr): 2966, 1684, 1607, 1514, 1249, 1182, 1073, 1005, 809, 758 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 0.79 (s, 9 H, *t*-Bu), 1.34 (s, 9 H, *t*-Bu), 3.82 (s, 3 H, OCH_3), 6.13 (d, *J* = 3.3 Hz, 1 H, H_{Fur}), 6.38 (d, *J* = 12.0 Hz, 1 H, =CH), 6.48 (d, *J* = 3.3 Hz, 1 H, H_{Fur}), 6.89 (d, *J* = 8.7 Hz, 2 H, H_{Ar}), 7.19 (d, *J* = 12.0 Hz, 1 H, =CH), 7.44–7.50 (m, 1 H, H_{Ar}), 7.52 (d, *J* = 8.7 Hz, 2 H, H_{Ar}), 7.63–7.68 (m, 1 H, H_{Ar}), 8.04–8.07 (m, 1 H, H_{Ar}), 8.11–8.14 (m, 1 H, H_{Ar}).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 25.7 (3 C), 29.1 (3 C), 32.8, 42.9, 55.4, 103.6, 113.1 (2 C), 114.6, 124.5, 124.9, 125.7, 126.3, 128.9, 129.0, 129.7, 131.2 (2 C), 133.7, 134.4, 141.7, 146.5, 147.3, 157.7, 159.7, 165.2, 203.5.

MS (EI, 70 eV): *m*/*z* (%) = 467 (42) [M^+], 410 (27), 382 (37), 326 (93), 85 (64), 69 (22), 57 (100), 43 (68).

Anal. Calcd for $C_{31}H_{33}NO_3$: C, 79.63; H, 7.11; N, 3.00. Found: C, 79.49; H, 7.24; N, 3.20.

***N*-{2-[(4-Bromophenyl)(hydroxy)methyl]-4,5-dimethoxyphenyl}benzamide (14)**

Benzhydrol **14** was synthesized according to a published procedure[19] and was used in the further transformations without additional purification.

White solid; mp 153–154 °C (EtOH–acetone).

^1H NMR (300 MHz, DMSO-d_6): δ = 3.75 (s, 6 H, OCH_3), 5.88 (s, 1 H, CH), 6.55 (br s, 1 H, OH), 7.05 (s, 1 H, H_{Ar}), 7.23 (d, *J* = 8.7 Hz, 2 H, H_{Ar}), 7.41 (s, 1 H, H_{Ar}), 7.43 (d, *J* = 8.7 Hz, 2 H, H_{Ar}), 7.49–7.61 (m, 3 H, H_{Ar}), 7.80–7.83 (m, 2 H, H_{Ar}), 10.05 (s, 1 H, NH).

***N*-{2-[(4-Bromophenyl)(5-methyl-2-furyl)methyl]-4,5-dimethoxyphenyl}benzamide (1q)**

A mixture of compound **14** (10 mmol), 2-methylfuran (**11b**; 20 mmol), *p*-TsOH (0.1 g, 0.6 mmol), and CH_2Cl_2 (70 mL) was refluxed for 2 h using a Dean–Stark trap (TLC monitoring). Then, the reaction mixture was neutralized with aq $NaHCO_3$ and dried (Na_2SO_4). The mixture was concentrated to a volume of ca. 5–10 mL, and hexane (50 mL) was added. The resulting solution was filtered through a pad of silica gel and kept until crystallization of the product.

White solid; yield: 4.10 g (81%); mp 194–195 °C.

IR (KBr): 3236, 1660, 1643, 1515, 1486, 1310, 1291, 1262, 1216, 1092, 1011, 714, 693 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 2.23 (s, 3 H, CH_3), 3.74 (s, 3 H, OCH_3), 3.89 (s, 3 H, OCH_3), 5.40 (s, 1 H, CH), 5.88 (d, *J* = 3.3 Hz, 1 H, H_{Fur}), 5.92 (d, *J* = 3.3 Hz, 1 H, H_{Fur}), 6.49 (s, 1 H, H_{Ar}), 7.00–7.02 (m, 2 H, H_{Ar}), 7.36–7.44 (m, 4 H, H_{Ar}), 7.46–7.55 (m, 4 H, H_{Ar}), 7.69 (br s, 1 H, NH).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.5, 46.6, 56.0, 56.1, 106.4, 109.0, 109.7, 113.0, 121.2, 125.4, 126.8 (2 C), 128.5, 128.6 (2 C), 130.2 (2 C), 131.7, 131.8 (2 C), 134.5, 139.3, 146.6, 148.3, 152.3, 152.5, 165.4.

MS (EI, 70 eV): *m*/*z* (%) = 507/505 (79/76) [M^+], 402/400 (79/76), 180 (30), 165 (78), 105 (100), 77 (50), 59 (56), 43 (58).

Anal. Calcd for $C_{27}H_{24}BrNO_4$: C, 64.04; H, 4.78; N, 2.77. Found: C, 64.23; H, 4.94; N, 2.96.

(3*Z*)-4-[4-(4-Bromophenyl)-6,7-dimethoxy-2-phenylquinolin-3-yl]but-3-en-2-one (3q)

A mixture of amide **1q** (0.5 g, 1 mmol), $POCl_3$ (5 mL), and benzene (50 mL) was refluxed for 1.5 h. The reaction mixture was poured into H_2O (800 mL) and neutralized with a soln of NaOH (50 g) in H_2O (200 mL). The product was extracted with CH_2Cl_2 (3 × 150 mL). The combined organic fractions were dried (Na_2SO_4), filtered, and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (CH_2Cl_2–PE, 1:3) and recrystallization (CH_2Cl_2–PE).

Beige solid; yield: 176 mg (36%); mp 157–159 °C.

IR (KBr): 1692, 1616, 1500, 1464, 1452, 1428, 1352, 1212, 1184, 1144, 1016, 840 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 1.61 (s, 3 H, CH_3), 3.78 (s, 3 H, OCH_3), 4.03 (s, 3 H, OCH_3), 5.94 (d, *J* = 12.0 Hz, 1 H, =CH), 6.64 (d, *J* = 12.0 Hz, 1 H, =CH), 6.68 (s, 1 H, H_{Ar}), 7.18–7.21 (m, 2 H, H_{Ar}), 7.34–7.42 (m, 3 H, H_{Ar}), 7.54–7.62 (m, 5 H, H_{Ar}).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 30.0, 55.8, 56.2, 103.1, 108.2, 121.1, 122.3, 126.1, 127.8 (3 C), 127.9 (2 C), 129.8 (2 C), 130.9, 131.6 (2 C), 135.9, 138.5, 140.5, 143.6, 144.2, 149.9, 152.5, 155.4, 198.3.

MS (EI, 70 eV): *m*/*z* (%) = 489/487 (25/26) [M^+], 446/444 (97/98), 430 (17), 257 (53), 105 (100), 77 (18), 43 (35).

Anal. Calcd for $C_{27}H_{22}BrNO_3$: C, 66.40; H, 4.54; N, 2.87. Found: C, 66.37; H, 4.60; N, 2.67.

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