Functionalized Carbodiimide Mediated Synthesis of 2,3-Disubstituted Quinazolin-4(3*H*)-ones via the Tandem Strategy of C-Nucleophilic Addition and Intramolecular NH-Substitution Cyclization

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Abstract: A facile synthesis of quinazolin-4(3*H*)-ones possessing carbon substituents at positions 2 and 3 has been developed. Key to the synthesis is a tandem strategy involving introduction of a 2-substituent and construction of the quinazolinone framework via C-nucleophilic addition to the carbodiimide cumulenic carbon followed by intramolecular nucleophilic substitution by the newly formed NH moiety at the proximal ester group.

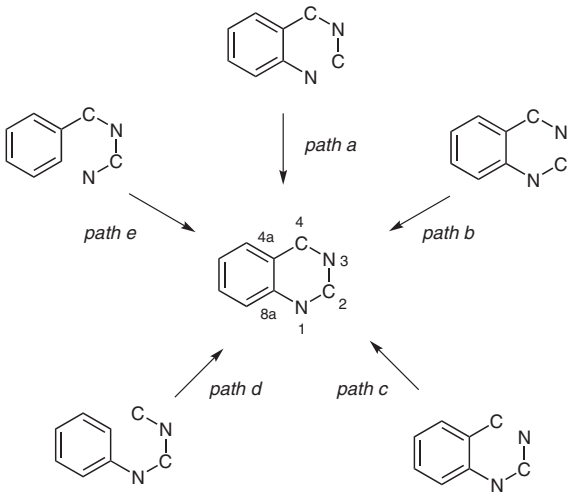
Key words: quinazolines, carbodiimides, organometallic reagents, tandem reaction, cyclization

Quinazolinone and quinazoline derivatives are among the most important six-membered nitrogen-containing heterocycles. They appear widely in both natural products and synthetic pharmaceuticals,[1] and have been shown to exhibit a wide range of biological activities;[1,2] for example, they act as central nervous system depressant and stimulant,[2] antiparkinsonian,[2] anticancer,[3] antidiabetic,[4] anti-inflammatory,[5] antimicrobial,[6] anticonvulsant,[7] antibacterial,[8] antimalarial,[9] antiallergy,[10] and analgesic[11] agents.

To date, considerable progress has been made in the synthesis of quinazoline and quinazolinone derivatives.[1] Conceptually, methods of constructing the quinazoline framework by bond-forming ring closure from benzene derivatives involve one of five paths: 1,2-, 2,3-, 3,4-, 4,4a-, and 1,8a-bond-forming paths, denoted *paths a–e* (Scheme 1).

Examples of 1,2-bond-forming *path a* include the intramolecular aza-Wittig reaction of an *ortho*-RCO–NMe–CO-group-bearing *N*-phenyliminophosphorane generated by the Staudinger reaction from the corresponding azide and phosphine,[12] and the reaction of anthranilic acids with N-unsubstituted imidates.[13] The latter one-pot synthesis possibly may involve 3,4-bond-forming cyclization at the final stage. Moreover, the synthesis of 2,4-diaminoquinazolines and tricyclic quinazolines by cascade reductive cyclization of methyl *N*-cyano-2-nitrobenzimidates has recently been reported.[14]

Examples of 2,3-bond-forming *path b* include cascade reductive cyclization,[15] copper-,[15a–d] ruthenium-,[15e] and iridium[15f]-catalyzed dehydrogenation (oxidation) or dehydration from *N*-cyano-2-nitrobenzimidates and *o*-halo- or *o*-aminobenzamides, and other related reactions.[1,16] In addition, Lygin and de Meijere[17] reported the synthesis of quinazolin-4-one by reaction of generated *o*-lithiated phenyl isocyanide with an isocyanate and an electrophile.



Scheme 1 Possible approaches to the quinazoline core via cyclization

Examples of 3,4-bond-forming *path c* include the Niementowski quinazoline synthesis,[18] which has been known since 1895. This path involves the reaction between anthranilic acid and carboxamide (or its equivalent), with 3,4-bond-forming cyclization occurring at the final stage; however, this traditional method often suffers from harsh conditions and low yields when the carboxamide bears one or more substituents. A microwave technique gives improved yields but is still limited to 2,3-unsubstituted quinazolin-4-ones.[18e] Alper and co-workers developed palladium-catalyzed cyclocarbonylation for the synthesis of 2,3-disubstituted quinazolin-4-one or quinazoline-2,4-dione derivatives by reaction of *o*-iodoanilines with heterocumulenes such as carbodiimides, isocyanates, and ketenimines, or with imidoyl chlorides.[19] Recently, the same group extended this palladium-catalyzed cyclocarbonylation methodology to tandem reactions using mono- or bis(iodoaryl)carbodiimides for quinazolinone synthesis.[20] Tandem reaction of various functionalized carbodiimides[21] has also been applied to the synthesis of quinazoline derivatives.[22]

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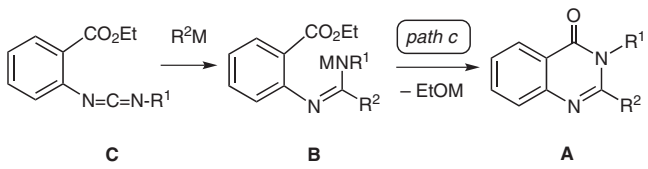
Examples of 4,4a-bond-forming *path d* include the 6π-electrocyclic ring closure undergone by *N*-aryl-1,3-diazabuta-1,3-dienes upon heating or electrophilic cyclization in the presence of an acid. Subsequent aromatization gives 2-monosubstituted or 2,3-disubstituted quinazolines.[23]

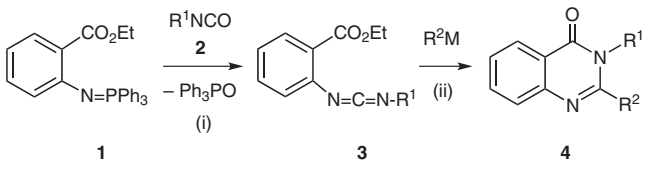
Reported examples of 1,8a-bond-forming *path e* are rare. 2-Substituted quinazolines were synthesized by intramolecular aromatic substitution of fluorobenzene derivatives with an inner NH-nucleophile formed from the reaction between 2-fluorobenzaldehydes and amidines or guanidines.[24]

Our approach to the synthesis of quinazolin-4(3*H*)-ones **A** involves an addition–cyclization methodology: specifically, intramolecular amidation via *path c* (3,4-bond formation) of intermediary amidinylbenzoates **B** generated from the reaction of *N*-[2-(ethoxycarbonyl)phenyl]carbodiimides **C** with organometallic C-nucleophiles R^2M (Scheme 2). This synthetic route is novel, simple, and facile, and enables production of a variety of quinazolin-4(3*H*)-ones having a wide range of carbon substituents at positions 2 and 3.



Scheme 2

The prerequisite carbodiimides **3** were prepared by the aza-Wittig reaction of iminophosphorane **1** with various isocyanates **2**.[21] As the majority of the formed carbodiimides **3** was lost during silica gel column chromatography, triphenylphosphane oxide was removed by filtration with solvent exchange (CH_2Cl_2 → hexane), and then the carbodiimides **3** in tetrahydrofuran solution were used for the subsequent reaction with organometallic reagents (Scheme 3).



Scheme 3 *Reagents and conditions*: (i) CH_2Cl_2, r.t., 5–19 h; (ii) THF, –78 °C → r.t.

We began by using carbodiimide **3a** (R^1 = Ph) for the model reaction with methyl Grignard, copper, and lithium reagents (R^2 = Me). The results are shown in Table 1. Addition of methyl Grignard reagent (1.0 equiv) to a tetrahydrofuran solution of **3a** at –78 °C, and then warming to room temperature for three hours, gave quinazolinone **4a** (R^1 = Ph, R^2 = Me) in 81% yield (Table 1, entry 1). Two equivalents of Gilman reagent (Me_2CuLi) were necessary to obtain a high yield (94%) of **4a** (Table 1, entries 2–4). Without warming to room temperature, ring closure of intermediate **B** hardly appeared to occur in reactions with the Grignard and Gilman reagents, whereas reaction with the higher-order organocuprate, $Me_2Cu(CN)Li_2$, at –78 °C for one hour produced **4a** in 84% yield (Table 1, entry 5). Reactions with methyllithium or phenyllithium gave low yields of **4a** (R^1 = Ph, R^2 = Me) or **4l** (R^1 = R^2 = Ph) along with several byproducts (Table 1, entries 6–8); these poor results are probably due to the low reactivity of the lithium reagent with a relatively harder nucleophilicity toward the softer cumulene carbon rather than toward the harder ester carbonyl on the basis of the hard and soft acids and bases (HSAB) theory.[25] For comparison, the one-pot tandem three-step reaction via the aza-Wittig reaction and nucleophilic addition with methyl Grignard reagent followed by cyclization (**1** → **3** → **B** → **4**) performed under similar reaction conditions in tetrahydrofuran solution (Table 1, entry 9) gave quinazolinone **4a** in 72% yield, which is 9% lower than that for entry 1.

Table 1 Model Reaction of **3a** (R^1 = Ph) with Methyl Grignard, Copper, and Lithium Reagents To Afford Quinazolinone **4a** (R^1 = Ph, R^2 = Me) or **4l** (R^1 = R^2 = Ph)

Entry	Reagent (equiv)	Temp	Time (h)	Yield[a] (%)
1	MeMgBr (1.0)	–78 °C → r.t.	3.0	81
2	Me_2CuLi (1.0)	–78 °C → r.t.	4.0	16
3	Me_2CuLi (1.5)	–78 °C → r.t.	3.0	64
4	Me_2CuLi (2.0)	–78 °C → r.t.	2.5	94
5	$Me_2Cu(CN)Li_2$ (2.0)	–78 °C	1.0	84
6	MeLi (1.1)	–78 °C → r.t.	29	49
7	MeLi (2.0)	–78 °C → r.t.	5.0	18
8	PhLi (1.0)	–78 °C → r.t.	9.0	35
9[b]	MeMgBr (1.0)	–78 °C → r.t.	3.0	72

[a] Isolated yield from iminophosphorane **1**.
[b] In one pot, in THF, at r.t. for 7 h for the aza-Wittig reaction.

With guaranteed Grignard and organocopper reagents and optimal conditions in hand, we next performed the reaction of carbodiimides **3** having diverse substituents R^1 with various Grignard and organocopper reagents R^2M to determine the generality of this reaction for the synthesis of a wide variety of 2,3-disubstituted quinazolinones **4**. The results are shown in Tables 2–4. Reactions with Grignard reagents (Table 2) gave good to excellent yields of **4**, indicating that aliphatic, aromatic, and vinyl Grignard reagents (R^2MgBr) are tolerant to the reactions of carbodiimides **3** with various substituents R^1. In addition, reactions with organocopper reagents gave good to excellent yields of **4**. An exception is the reaction of *p*-chlorophenyl-substituted carbodiimide **3c** (R^1 = *p*-ClC_6H_4), which gave relatively lower yields of **4c** and **4C** (Table 3, entries 3 and 8; Table 4, entries 3 and 8) than obtained otherwise.

Table 2 Reaction of Carbodiimides **3** with Grignard Reagents To Afford a Variety of Quinazolinones **4**[a]

Entry	R^1	R^2	Time (h)	Product	Yield[b] (%)
1	Ph	Me	3	**4a**	81
2	*p*-Tol	Me	3	**4b**	60
3	*p*-ClC_6H_4	Me	3	**4c**	93
4	*p*-$MeOC_6H_4$	Me	3	**4d**	60
5	*n*-Pr	Me	3.5	**4e**	81
6	Bn	Me	3	**4f**	60
7	Ph	Et	3	**4g**	69
8	*p*-Tol	Et	4	**4h**	79
9	*p*-ClC_6H_4	Et	3.5	**4i**	98
10	*n*-Pr	Et	2.5	**4j**	70
11	Bn	Et	4	**4k**	77
12	Ph	Ph	3	**4l**	96
13	*p*-Tol	Ph	3	**4m**	76
14	*p*-ClC_6H_4	Ph	3	**4n**	90
15	*p*-$MeOC_6H_4$	Ph	3	**4o**	50
16	*n*-Pr	Ph	3.5	**4p**	86
17	Bn	Ph	3	**4q**	87
18	Ph	Cy	3	**4r**	80
19	*p*-Tol	Cy	3	**4s**	84
20	*p*-ClC_6H_4	Cy	4	**4t**	76
21	Ph	$CH=CH_2$	3	**4u**	73
22	*p*-Tol	$CH=CH_2$	4	**4v**	77
23	*p*-ClC_6H_4	$CH=CH_2$	5	**4w**	92
24	*n*-Pr	$CH=CH_2$	4	**4x**	92
25	Bn	$CH=CH_2$	3	**4y**	68

[a] Reaction of **3** with R^2MgBr (1.1 equiv) was carried out in THF at –78 °C → r.t.
[b] Isolated yield.

Table 3 Reaction of Carbodiimides **3** with Gilman Reagents To Afford a Variety of Quinazolinones **4**[a]

Entry	R^1	R^2	Time (h)	Product	Yield[b] (%)
1	Ph	Me	2.5	**4a**	94
2	*p*-Tol	Me	2.5	**4b**	78
3	*p*-ClC_6H_4	Me	3	**4c**	54
4	*n*-Pr	Me	3	**4e**	86
5	Bn	Me	2.5	**4f**	77
6	Ph	*n*-Bu	3	**4A**	80
7	*p*-Tol	*n*-Bu	2.5	**4B**	86
8	*p*-ClC_6H_4	*n*-Bu	5	**4C**	50
9	*n*-Pr	*n*-Bu	2.5	**4D**	56
10	Bn	*n*-Bu	3	**4E**	74

[a] Reaction of **3** with $R^2{}_2CuLi$ (2.0 equiv) was carried out in THF at –78 °C → r.t.
[b] Isolated yield.

Table 4 Reaction of Carbodiimides **3** with Lipshutz Cuprates To Afford a Variety of Quinazolinones **4**[a]

Entry	R^1	R^2	Time (h)	Product	Yield[b] (%)
1	Ph	Me	1.0	**4a**	84
2	*p*-Tol	Me	1.2	**4b**	94
3	*p*-ClC_6H_4	Me	1.0	**4c**	67
4	*n*-Pr	Me	1.0	**4e**	86
5	Bn	Me	1.5	**4f**	62
6	Ph	*n*-Bu	1.2	**4A**	98
7	*p*-Tol	*n*-Bu	1.2	**4B**	70
8	*p*-ClC_6H_4	*n*-Bu	1.2	**4C**	50
9	*n*-Pr	*n*-Bu	1.0	**4D**	77
10	Bn	*n*-Bu	1.2	**4E**	96

[a] Reaction of **3** with $R^2{}_2Cu(CN)Li_2$ (2.0 equiv) was carried out in THF at –78 °C.
[b] Isolated yield.

Thus, our tandem methodology gives various alkyl-, benzyl-, vinyl-, and aryl-substituted quinazolinones **4** in fairly good to excellent yield. Simple, high-yield preparation of a broad range of functionalized Grignard reagents by lithium chloride promoted Br–Mg exchange has already been established,[26] so further practical extension of this quinazolinone synthesis using such Grignard reagents can be expected.

In conclusion, we have developed a simple new synthetic method that gives 2,3-di-C-substituted quinazolin-4(3*H*)-ones via a tandem methodology involving nucleophilic addition followed by intramolecular substitution of *N*-[2-(ethoxycarbonyl)phenyl]carbodiimides starting from the three building blocks of anthranilic acid esters, isocyanates, and organometallic C-nucleophiles.

All melting points were determined on a Yanaco MP melting point apparatus and are uncorrected. Infrared spectra were recorded on a Horiba FT-710 spectrophotometer. ^{1}H and ^{13}C NMR spectroscopic data were obtained with a Bruker Avance 600, a Jeol JNM-LA 500, a Bruker BioSpin AVANCE DPX-400 or a Jeol JNM-AL 300 instrument. Chemical shifts (δ) are quoted in ppm using tetramethylsilane (δ = 0) as the reference for ^{1}H NMR spectroscopy and $CDCl_3$ (δ = 77.0) for ^{13}C NMR spectroscopy. Mass spectra were measured on a Bruker Daltonics microTOF-NR focus spectrometer.

2,3-Diphenylquinazolin-4(3*H*)-one (4l, $R^1 = R^2 = Ph$);[19b] Typical Procedure for the Synthesis of 2,3-Disubstituted Quinazolin-4(3*H*)-ones 4 via the Reaction of *N*-[2-(Ethoxycarbonyl)phenyl]carbodiimides 3 with Organometallic Reagents

Phenyl isocyanate (**2a**, R^1 = Ph; 0.055 mL, 0.508 mmol, 1.09 equiv) was added to a soln of iminophosphorane **1** (197.8 mg, 0.465 mmol) in anhyd CH_2Cl_2 (4 mL) at 0 °C while stirring. The reaction mixture was warmed to r.t. with stirring for 5 h and then concentrated by evaporation. The oily residue was triturated by adding hexane and the resulting solid of triphenylphosphane oxide was removed by filtration. The filtrate was concentrated, and the resulting carbodiimide **3a** (R^1 = Ph) was dissolved in THF (4 mL) and cooled to –78 °C. A 1.08 M soln of PhMgBr in THF (0.47 mL, 0.507 mmol, 1.1 equiv) was added dropwise at –78 °C with stirring and the mixture was warmed to r.t. with stirring for 3 h (reaction progress was checked by TLC). The reaction was quenched by adding sat. aq NH_4Cl (6 mL), and the reaction mixture was extracted with EtOAc (3 × 15 mL), washed with sat. aq NaCl (10 mL), dried (Na_2SO_4), concentrated under reduced pressure, purified by silica gel column chromatography (hexane–EtOAc, 4:1), and crystallized to afford quinazolinone **4l** ($R^1 = R^2$ = Ph); yield: 133 mg (96%); colorless crystals; mp 158–159 °C (Lit.[19b] 158–159 °C).

^{1}H NMR (500.00 MHz, $CDCl_3$): δ = 7.13–7.17 (m, 2 H), 7.19–7.36 (m, 8 H), 7.54 (dd, *J* = 7.9, 7.9 Hz, 1 H), 7.79–7.85 (m, 2 H), 8.36 (d, *J* = 7.9 Hz, 1 H).

^{13}C NMR (125.65 MHz, $CDCl_3$): δ = 120.9 (C), 127.2 (CH), 127.3 (CH), 127.7 (CH), 128.0 (2 × CH), 128.4 (CH), 129.0 (4 × CH), 129.1 (2 × CH), 129.3 (CH), 134.7 (CH), 135.4 (C), 137.6 (C), 147.5 (C), 155.2 (C), 162.3 (C).

HRMS-ESI: *m*/*z* $[M + H]^+$ calcd for $C_{20}H_{15}N_2O$: 299.1179; found: 299.1179.

2-Methyl-3-phenylquinazolin-4(3*H*)-one (4a; R^1 = Ph, R^2 = Me)[15c,16d]

Yield: 89 mg (81%); colorless crystals; mp 146.8–148.2 °C (Lit.[16d] 145–146 °C).

^{1}H NMR (500.00 MHz, $CDCl_3$): δ = 2.24 (s, 3 H), 7.24–7.30 (m, 2 H), 7.46 (dd, *J* = 7.5, 7.5 Hz, 1 H), 7.48–7.59 (m, 3 H), 7.68 (d, *J* = 8.0 Hz, 1 H), 7.76 (dd, *J* = 8.0, 8.0 Hz, 1 H), 8.27 (d, *J* = 8.0 Hz, 1 H).

^{13}C NMR (125.65 MHz, $CDCl_3$): δ = 24.3 (CH_3), 120.7 (C), 126.6 (CH), 126.7 (CH), 127.0 (CH), 128.0 (2 × CH), 129.2 (CH), 129.9 (2 × CH), 134.5 (CH), 137.7 (C), 147.4 (C), 154.2 (C), 162.2 (C).

HRMS-ESI: *m*/*z* $[M + Na]^+$ calcd for $C_{15}H_{12}N_2ONa$: 259.0842; found: 259.0842.

3-(4-Chlorophenyl)-2-ethylquinazolin-4(3*H*)-one (4i; R^1 = *p*-ClC_6H_4, R^2 = Et)

Yield: 129 mg (98%); colorless crystals; mp 186.7–188.8 °C.

IR (KBr): 3070, 2985, 2908, 1689, 1597, 1257, 1080, 764 cm^{-1}.

^{1}H NMR (500.00 MHz, $CDCl_3$): δ = 1.23 (t, *J* = 7.3 Hz, 3 H), 2.43 (q, *J* = 7.3 Hz, 2 H), 7.21 (d, *J* = 8.6 Hz, 2 H), 7.46 (dd, *J* = 8.0, 8.0 Hz, 1 H), 7.53 (d, *J* = 8.6 Hz, 2 H), 7.71 (d, *J* = 8.2 Hz, 1 H), 7.76 (dd, *J* = 8.2, 8.2 Hz, 1 H), 8.24 (d, *J* = 8.0 Hz, 1 H).

^{13}C NMR (125.65 MHz, $CDCl_3$): δ = 11.1 (CH_3), 29.3 (CH_2), 120.5 (C), 126.6 (CH), 126.9 (CH), 127.1 (CH), 129.7 (2 × CH), 130.1 (2 × CH), 134.5 (CH), 135.2 (C), 135.8 (C), 147.4 (C), 157.2 (C), 162.3 (C).

HRMS-ESI: *m*/*z* $[M + Na]^+$ calcd for $C_{16}H_{13}ClN_2ONa$: 307.0609; found: 307.0609.

2-Ethyl-3-propylquinazolin-4(3*H*)-one (4j; R^1 = *n*-Pr, R^2 = Et)[27]

Yield: 71 mg (70%); colorless crystals; mp 95.1–95.9 °C (Lit.[27] 102 °C).

IR (KBr): 3062, 2970, 2924, 1674, 1589, 1458, 1134, 771 cm^{-1}.

^{1}H NMR (500.00 MHz, $CDCl_3$): δ = 1.04 (t, *J* = 7.3 Hz, 3 H), 1.42 (t, *J* = 7.3 Hz, 3 H), 1.77 (dt, *J* = 7.4, 7.3 Hz, 2 H), 2.87 (q, *J* = 7.3 Hz, 2 H), 4.06 (dd, *J* = 7.4, 7.4 Hz, 2 H), 7.42 (dd, *J* = 8.0, 8.0 Hz, 1 H), 7.64 (d, *J* = 8.0 Hz, 1 H), 7.71 (dd, *J* = 8.3, 8.3 Hz, 1 H), 8.25 (d, *J* = 8.3 Hz, 1 H).

^{13}C NMR (125.65 MHz, $CDCl_3$): δ = 11.4 (CH_3), 11.7 (CH_3), 22.3 (CH_2), 28.3 (CH_2), 45.2 (CH_2), 120.5 (C), 126.2 (CH), 126.7 (CH), 126.8 (CH), 134.0 (CH), 147.4 (C), 157.7 (C), 162.2 (C).

HRMS-ESI: *m*/*z* $[M + H]^+$ calcd for $C_{13}H_{17}N_2O$: 217.1135; found: 217.1132.

3-(4-Tolyl)-2-vinylquinazolin-4(3*H*)-one (4v; R^1 = *p*-Tol, R^2 = CH=CH_2)

Yield: 94 mg (77%); colorless crystals; mp 133.9–135.2 °C.

IR (KBr): 3032, 2916, 2862, 1682, 1558, 949, 771 cm^{-1}.

^{1}H NMR (500.00 MHz, $CDCl_3$): δ = 2.45 (s, 3 H), 5.52 (dd, *J* = 10.7, 1.7 Hz, 1 H), 6.16 (dd, *J* = 16.8, 10.7 Hz, 1 H), 6.58 (dd, *J* = 16.8, 1.7 Hz, 1 H), 7.14 (d, *J* = 8.2 Hz, 2 H), 7.34 (d, *J* = 8.2 Hz, 2 H), 7.47 (m, 1 H), 7.73–7.78 (m, 2 H), 8.29 (d, *J* = 7.9 Hz, 1 H).

^{13}C NMR (125.65 MHz, $CDCl_3$): δ = 21.2 (CH_3), 121.1 (C), 125.4 (CH_2), 126.8 (CH), 127.1 (CH), 127.5 (CH), 128.2 (2 × CH), 129.8 (CH), 130.5 (2 × CH), 134.1 (C), 134.5 (CH), 139.3 (C), 147.6 (C), 151.5 (C), 162.3 (C).

HRMS-ESI: *m*/*z* $[M + H]^+$ calcd for $C_{17}H_{15}N_2O$: 263.1179; found: 263.1185.

2-Butyl-3-phenylquinazolin-4(3*H*)-one (4A; R^1 = Ph, R^2 = *n*-Bu)

Yield: 127 mg (98%); colorless needles; mp 108.8–109.9 °C.

IR (KBr): 3062, 2939, 1682, 1589, 1273, 763 cm^{-1}.

^{1}H NMR (500.00 MHz, $CDCl_3$): δ = 0.79 (t, *J* = 7.4 Hz, 3 H), 1.25 (sextet, *J* = 7.4 Hz, 2 H), 1.63–1.71 (m, 2 H), 2.43 (dd, *J* = 7.9, 7.9 Hz, 2 H), 7.23–7.29 (m, 2 H), 7.42–7.58 (m, 4 H), 7.71 (d, *J* = 8.2 Hz, 1 H), 7.76 (dd, *J* = 8.2, 8.2 Hz, 1 H), 8.27 (d, *J* = 8.0 Hz, 1 H).

^{13}C NMR (125.65 MHz, $CDCl_3$): δ = 13.6 (CH_3), 22.3 (CH_2), 29.2 (CH_2), 35.5 (CH_2), 120.7 (C), 126.5 (CH), 127.0 (2 × CH), 128.3 (2 × CH), 129.2 (CH), 129.8 (2 × CH), 134.4 (CH), 137.4 (C), 147.6 (C), 157.1 (C), 162.5 (C).

HRMS-ESI: *m*/*z* $[M + Na]^+$ calcd for $C_{18}H_{18}N_2ONa$: 301.1311; found: 301.1309.

3-Benzyl-2-butylquinazolin-4(3*H*)-one (4E; R^1 = Bn, R^2 = *n*-Bu)

Yield: 130 mg (96%); colorless crystals; mp 79.2–80.3 °C.

IR (KBr): 3062, 2954, 2870, 1666, 1604, 1466, 1389, 717 cm^{-1}.

^{1}H NMR (500.00 MHz, $CDCl_3$): δ = 0.91 (t, *J* = 7.4 Hz, 3 H), 1.40 (sextet, *J* = 7.4 Hz, 2 H), 1.70–1.79 (m, 2 H), 2.71–2.76 (m, 2 H), 5.42 (s, 2 H), 7.18 (d, *J* = 7.4 Hz, 2 H), 7.24–7.35 (m, 3 H), 7.46 (dd, *J* = 8.0, 8.0 Hz, 1 H), 7.66 (d, *J* = 8.2 Hz, 1 H), 7.74 (dd, *J* = 8.2, 8.2 Hz, 1 H), 8.31 (d, *J* = 8.0 Hz, 1 H).

^{13}C NMR (125.65 MHz, $CDCl_3$): δ = 13.8 (CH_3), 22.4 (CH_2), 29.4 (CH_2), 35.0 (CH_2), 46.4 (CH_2), 120.3 (C), 126.4 (2 × CH), 126.4 (CH), 127.0 (CH), 127.1 (CH), 127.6 (CH), 128.9 (2 × CH), 134.3 (CH), 136.3 (C), 147.4 (C), 157.4 (C), 162.6 (C).

HRMS-ESI: *m*/*z* $[M + Na]^+$ calcd for $C_{19}H_{20}N_2ONa$: 315.1468; found: 315.1467.

Supporting Information for this article is available online at http://www.thieme-connect.com/ejournals/toc/synthesis.

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