DMSO arbitrated Oxidative Annulation Followed by Homologated N-Alkylation: Microwave-Assisted Efficient and Greener Approach to Access 3-(3-Oxo-3-arylpropyl) Quinazolinones

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Abstract

A convenient, time efficient, tandem approach for the synthesis of medicinally privileged 3-(3-oxo-3-arylpropyl) quinazolinones is developed from ubiquitously available acetophenones and anthranilamide via microwave irradiation. This transition-metal-free reaction is initiated by the oxidative annulation of anthranilamide and in situ generation of $\alpha,\beta$-unsaturated carbonyl compounds from aryl ketones in the presence of K$_2$S$_2$O$_8$ and dimethyl sulfoxide. The latter acts as a source of two carbons [methylene (=CH–) and methylene (–CH$_2$–)] apart from being the solvent. The reaction is carried out under microwave irradiation which has the advantage of homogenous heat distribution, reducing the reaction time drastically compared to the conventional heating reaction.

Keywords
anthranilamide, acetophenones, quinazolinones, oxidative annulation, Michael addition, transition-metal-free synthesis, microwave irradiation

In recent past, dimethyl sulfoxide (DMSO) has become a versatile entity in organic synthesis. The role of DMSO started as a low-toxic, aprotic, polar solvent. Its application is further extended to an oxidizing agent in many organic transformations such as Kornblum oxidation, Swern oxidation, Pfitzner–Moffatt oxidation, and Corey–Chaykovsky reaction. More recently, DMSO is employed as a source of several synthons such as $-\text{CH}_3$, $-\text{CH}_2$, $-\text{CN}$, $-\text{SMe}$, etc. Such transformations play a vital role in the synthesis of several pharmaceuticals, agrochemicals, and life science materials.

N-Containing heterocyclic compounds are the most profuse and integral scaffolds that occur ubiquitously in a variety of synthetic drugs, bioactive natural products, pharmaceuticals, and agrochemicals. The quinazolinone skeleton containing frameworks are one such class of biologically privileged scaffolds that occur in several natural alkaloids. Literature study reveals that quinazolinones are also functional in the construction of several medicinally active entities (Figure 1) such as antibacterial, analgesic, anti-inflammatory, antifungal, antimarial, antihypertensive, CNS inhibitors, and anticancer agents.
depressant, anticonvulsant, antihistaminic, antiparkinsonism, antiviral, and anticancer activities.9

Owing to their structural and biological importance quinazolinones have become the interest of several researchers. Synthesis of 3-(3-oxo-3-arylpropyl)-quinazolin-4(3H)-one was achieved by alkylation of 4(3H)-quinazolinone with 3-halo-1-phenylpropan-1-one.10 Another research group established its synthesis from N-heteroarenes, methyl ketones using DMPO as one carbon source using copper catalyst.11

Furthermore, a very recent report demonstrated the synthesis of 3-(3-oxo-3-phenylpropyl)quinazolin-4(3H)-one from readily available starting materials using a conventional synthetic method.12 All the above-mentioned methods have few drawbacks of preparation of reaction intermediates, use of metal catalyst, and long reaction time. To overcome all the aforesaid inadequacies, there is a need to develop a new synthetic strategy. Condensation of aryl methyl ketones with anthranilamide in the presence of a carbon source could be one such solution. In the literature two independent reports proposed iodine-13 and sulfur-promoted14 synthesis of 2-arylquinazolin-4(3H)-one from anthranilamide and acetoephonenes, respectively. More recently, iodine-mediated oxidative synthesis of 2-arylquinazolin-4(3H)-one,15 and Hf-zeolite-catalyzed synthesis of 2,3-dihydroquinazolin-4(1H)-ones16 were reported from the same starting materials. On the other hand, DMSO used as one carbon source for the K2S2O8-mediated oxidative annulation reaction of anthranilamides (Scheme 1a)17a and homologation of the acetoephonenes (Scheme 1a)17b is described in independent reports.

Since last three decades, many green protocols have been developed using microwave (MW) chemistry with significant benefits of drastically reduced reaction time, homogenous heat distribution, better yields, etc.18 In continuation to our research efforts in the development of a greener protocol for the organic synthesis19 coupled with the significance of microwave chemistry, we have developed an efficient protocol for the synthesis of 3-oxopropyl quinazoline-4(3H)-one. Herein, we report (Scheme 1) a one-pot microwave-assisted synthesis of 3-(3-oxo-3-arylpropyl) quinazolinones from readily available aryl methyl ketones and anthranilamide in the presence of DMSO, an oxidant, and an additive (Scheme 1b).

DMSO is utilized not only as a solvent but also as a source of two carbons (methine (–CH–) and methylene (–CH2–)), in which one carbon inserted between two nitrogen atoms of anthranilamide forming quinazolin-4(3H)-one and the other carbon participates in the homologation of aryl methyl ketones further forming a bridge between quinazolinone and aryl methyl ketones. It is noteworthy to mention that these reactions take very less time compared to conventional synthetic process without any catalyst loading thereby making this method highly valuable.

Considering the previous reports, it is evident that aryl methyl ketones upon reaction with K2S2O8 and CH3COONa would result in the formation of 4a.17b On the other hand anthranilamide resulted in the formation of 3a under similar reaction conditions.17b We started our investigation by reacting anthranilamide (1a) with readily available acetoephonene 2a as model substrates in the presence of K2S2O8 and CH3COONa in the presence of DMSO. The details are summarized in Table 1.

Conventional heating of this reaction was fruitful in delivering the product 5a after 16 h at 120 °C (Table 1, entry 1). With a vision to reduce the reaction time and make use of the microwave irradiation, we tried to perform the reaction at 100 °C for 0.5 h in a microwave reactor, which resulted in trace amount of intermediate 3a but no formation of required compound 5a (Table 1, entry 2). In an attempt to achieve the required results, we tried to increase the reaction temperature to 120 °C (Table 1, entry 3).

Unfortunately, these conditions also could not give us the required results. Further we increased the reaction time to 1 h simultaneously increasing the temperature to 140 °C which resulted in trace amount of 5a along with intermediates 3a and 4a (Table 1, entry 4). Leaving the reaction for one more hour gave us a considerable amount of 5a with traces of other intermediates (Table 1, entry 5). Delightfully, we could succeed in optimizing the reaction conditions when the temperature was raised to 160 °C for 2 h, with significant increase in the yield of 5a without any intermediate left unreacted (Table 1, entry 6). Furthermore, we tried to explore the reaction by using different base, such as DABCO (Table 1, entry 7), DBU (Table 1, entry 8), and Et3N (Table 1, entry 9), but none of these improved the results. Changing the oxidant (Table 1, entries 10, 11) gave 0% yield of 5a. All these reactions (Table 1, entries 2–12) were microwave assisted.

With the optimized reaction conditions to broaden the scope of this microwave-assisted one-pot tandem reaction, we performed the reaction with different aryl methyl ketones having both electron-donating (EDG) and electron-withdrawing (EWG) groups to study the electronic effect of various electron-rich and electron-deficient substituents.
Surprisingly, both the groups were well tolerated. As cited in Table 2, aryl methyl ketones containing various electron-donating groups such as alkyl (2b–f) and alkoxy (2g–h) readily delivered the corresponding 3-(3-oxo-3-arylpropyl) quinazolinones (5b–h) with very good yields (75–84%). Ketones with free hydroxy and phenoxy substitution (2j–k) also tolerated the reaction conditions smoothly and gave good yields. Furthermore, several halo-substituted aryl methyl ketones such as 4-chloro (2l), 3-chloro (2m), 4-bromo (2o), 3-bromo (2p), 4-fluoro (2q), and 3,4-dichloro (2n) provided the desired products (5l–q) with moderate to good yields (67–74%). To our delight, strong electron-withdrawing groups such as 3-CF₃ (2r) and 4-NO₂ (2s) also participated efficiently in the reaction and furnished the corresponding products (5r–s) in decent yields. Pleasantly, aryl methyl ketone with both EDG and EWG (2t) also provided the expected product 5t with a moderate yield. Aryl methyl ketones such as 4-phenyl acetophenone (2u) also furnished the expected product 5u with good yield. To examine the substitution on anthranilamide, we conducted reactions with 5-chloro anthranilamide (1b) and 5-fluoro anthranilamide (1c) also producing the products 5ba and 5ca, respectively, with moderate yields. This shows that the method can tolerate a wide range of substitutions.

The method was further explored with heteroaromatic methyl ketones (Figure 2) like 2-acetyl furan (2v) and 2-acetyl thiophene (2w); polyaromatic 2-acetyl naphthalene (2y) and 9-acetyl anthracene (2z), all of which contributed to the anticipated products 5v–z with good yields. Hence, it is unambiguous that the protocol is not affected by the substitutions of aryl methyl ketones, making the method ver-

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### Table 1 Preliminary Experiments and Optimization

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<th>Entry</th>
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<th>Base</th>
<th>Temp (°C)</th>
<th>Time (h)</th>
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<th>Yield (%) of 4a</th>
<th>Yield (%) of 5a</th>
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* Reaction was performed using 1a (1.0 mmol), 2a (1.1 mmol), DMSO (2.0 mL), oxidant (2.5 mmol), base (2.5 mmol) under microwave irradiation.

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### Table 2 Scope with Different Acetophenones

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* Reaction was performed using 1a (1.0 mmol), 2a (1.1 mmol), DMSO (2.0 mL), oxidant (2.5 mmol), base (2.5 mmol), microwave irradiation, 2 h, 160 °C.
Satellite. To expand the scope of ketone, we conducted a reaction with 3-methylbutan-2-one (2aa) and anthralinamide (1a) which unfortunately could not furnish the expected product 5aa.

In order to further understand the reaction mechanism, we carried out a series of control experiments (Scheme 2). Initially, when our desired product 5a was treated with a strong base like t-BuOK, it underwent β-elimination and furnished two reactive intermediates 3a and 4a with quantitative yields (Scheme 2, A). This indicates the generation of phenyl vinyl ketone (4a) from acetophenone and quinazolin-4(3H)-one (3a) from anthranilamide. On this basis, 3a was reacted with 4a in DMSO without any oxidant and additive (Scheme 2, B). Pleasingly, 5a was formed in good yield. Conducting a reaction between 1a and 2a under standard reaction conditions in the absence of CH3COONa (Scheme 2, D) resulted in a reduced yield, illustrating that CH3COONa affects product yield. The absence of K2S2O8 did not allow the reaction to proceed (Scheme 2, C). This evidently shows the essential role of K2S2O8. Furthermore, we carried out deuterium-labelling experiments to verify the carbon source by treating 1a with 2a in DMSO-d6 under standard reaction conditions which gave 5a-d3 in 75% yield (Scheme 2, E). 1H NMR analysis further revealed 100% deuteration at the C-2 position and at the terminal carbon of the phenyl vinyl ketone which justifies DMSO as two-carbon source.

Based on the literature and considering the mechanistic and control experiments, a plausible mechanism has been designed as shown in Scheme 3. Initially, K2S2O8 activates DMSO to form sulfonium ion A. Then anthranilamide (1a) condenses with A to furnish intermediate B, which on further elimination of methanethiol forms C, which upon intramolecular annulation gives D. This upon oxidation in the

\[ \text{Scheme 3} \quad \text{A plausible reaction pathway} \]
presence of K$_2$S$_2$O$_8$ affords 3a. Subsequently, aryl ketones react with sulfinium ion $A$ to form $E$, leading to the generation of $\alpha,\beta$-unsaturated carbonyl compound 4a by eliminating methanethiol. Finally, 3a undergoes Michael addition with 4a to deliver the desired product 5a.

In conclusion, we have expounded a microwave-irradiated transition-metal-free tandem approach for the synthesis of 3-(3-oxo-3-arylpropyl) quinazolinones from readily available anthranilamide and various substituted aryl methyl ketones in the presence of K$_2$S$_2$O$_8$ and DMSO via cyclization of anthranilamide followed byaza-Michael addition with homologated acetophenones. In this protocol, DMSO is acting as a carbon source to form the 3-(3-oxo-3-arylpropyl) quinazolinones. Microwave irradiation adds the benefit of reduced reaction time drastically and homogenous heat distribution. Notably, this method does not afford any side products. Considering the wide availability of the starting materials, broad substrate scopes, and operational simplicity, fast reaction, the present method provides an attractive protocol for the synthesis of the 3-(3-oxo-3-arylpropyl) quinazolinones.

All solvents were dried by a standard literature procedure. Crude products were purified by column chromatography on silica gel of EtOAc/hexane to afford the products. Pure products were visualized by exposure to ultraviolet light at 254 nm and by exposure to iodine vapors and/or by exposure to methanolic acidic solution.

**General Procedure for the Synthesis of 5**
A mixture of anthranilamides (1a–c, 1.0 mmol), acetophenones (2a–z, 1.1 mmol), DMSO (2 mL), K$_2$S$_2$O$_8$ (2.5 mmol), and sodium acetate (2.5 mmol) were added to a 5 mL microwave vial. The vial is sealed and stirred in the microwave reactor at 160 °C for 2 h. The reaction mixture was quenched with ice-cold water, extracted with EtOAc and water. Further, the organic layer was concentrated and purified by column chromatography on silica gel (EtOAc/hexane) to afford the pure products 5a–z, 5ba–ca.

**3-(3-Oxo-3-phenylpropyl)quinazolin-4(3H)-one (5a)**
Yield 0.165 g, 81%; off-white solid; mp 105–107 °C.

**1H NMR (400 MHz, CDCl$_3$):** $\delta = 7.94$ (s, 1 H), $8.29$ (dd, $J = 8.0, 0.9$ Hz, 1 H), $7.58$–$7.54$ (m, 1 H), $7.51$–$7.41$ (m, 3 H), $4.43$ (t, $J = 5.9$ Hz, 2 H), $3.60$ (t, $J = 5.9$ Hz, 2 H).

**13C NMR (101 MHz, CDCl$_3$):** $\delta = 197.52$, 161.46, 148.19, 147.72, 136.14, 134.29, 133.70, 128.74, 128.10, 127.55, 127.19, 126.42, 122.02, 42.84, 36.88.

**HRMS (ESI):** $m/z$ calcd for C$_{19}$H$_{19}$N$_2$O$_2$: [M+H]+; 307.1447; found: 307.1394.

**3-[3-Oxo-3-(p-tolyl)propyl]quinazolin-4(3H)-one (5b)**
Yield 0.168 g, 75%; white solid; mp 92–94 °C.

**1H NMR (400 MHz, CDCl$_3$):** $\delta = 7.80$ (d, $J = 8.0$ Hz, 1 H), $7.79$–$7.75$ (m, 2 H), $7.40$ (s, 1 H), $4.39$ (t, $J = 6.8$ Hz, 2 H), $4.38$ (t, $J = 5.9$ Hz, 2 H), $2.29$ (s, 3 H).

**13C NMR (101 MHz, CDCl$_3$):** $\delta = 197.37$, 161.46, 147.88, 144.59, 134.34, 133.70, 129.39, 128.21, 127.54, 127.14, 126.97, 124.99, 36.72, 21.69.

**HRMS (ESI):** $m/z$ calcd for C$_{19}$H$_{19}$N$_2$O$_2$: [M+H]+; 307.1447; found: 307.1394.

**3-[3-Oxo-3-(p-tolyl)propyl]quinazolin-4(3H)-one (5c)**
Yield 0.173 g, 77%; white solid; mp 125–128 °C.

**1H NMR (400 MHz, CDCl$_3$):** $\delta = 7.81$ (d, $J = 8.0$ Hz, 1 H), $7.40$ (s, 1 H), $7.25$ (d, $J = 7.6$ Hz, 2 H), $4.40$–$4.22$ (m, 2 H), $3.48$ (t, $J = 5.4$ Hz, 2 H), $2.29$ (s, 3 H).

**13C NMR (101 MHz, CDCl$_3$):** $\delta = 197.14$, 161.41, 147.96, 144.59, 134.34, 133.70, 129.39, 128.21, 127.26, 127.24, 126.44, 126.93, 42.99, 36.72, 21.69.

**HRMS (ESI):** $m/z$ calcd for C$_{19}$H$_{19}$N$_2$O$_2$: [M+H]+; 307.1447; found: 307.1394.

**3-[3-(4-Dimethylphenyl)-3-oxopropyl]quinazolin-4(3H)-one (5d)**
Yield 0.173 g, 77%; white solid; mp 125–128 °C.

**1H NMR (300 MHz, CDCl$_3$):** $\delta = 8.31$ (s, 1 H), $8.21$ (dd, $J = 8.0, 0.7$ Hz, 1 H), $7.69$–$7.57$ (m, 4 H), $7.41$ (dd, $J = 8.1, 6.6, 1.7$ Hz, 1 H), $7.11$ (d, $J = 7.8$ Hz, 1 H), $4.35$ (t, $J = 5.9$ Hz, 2 H), $3.49$ (t, $J = 5.9$ Hz, 2 H), $2.21$ (d, $J = 3.5$ Hz, 6 H).

**13C NMR (126 MHz, CDCl$_3$):** $\delta = 197.37$, 161.46, 148.20, 147.76, 143.34, 137.10, 134.25, 134.12, 129.94, 129.22, 127.54, 127.14, 126.40, 125.82, 122.03, 42.91, 36.76, 20.09, 19.76.

**HRMS (ESI):** $m/z$ calcd for C$_{18}$H$_{17}$N$_2$O$_2$: [M+H]+; 293.1290; found: 293.1287.

**3-[3-(4-Ethylphenyl)-3-oxopropyl]quinazolin-4(3H)-one (5e)**
Yield 0.168 g, 75%; white solid; mp 92–94 °C.

**1H NMR (500 MHz, CDCl$_3$):** $\delta = 8.30$ (s, 1 H), $8.19$ (dd, $J = 8.0$, 1.0 Hz, 1 H), $7.79$–$7.75$ (m, 2 H), $7.66$–$7.59$ (m, 2 H), $7.39$ (dd, $J = 8.2, 6.8, 1.5$ Hz, 1 H), $7.16$ (d, $J = 8.4$ Hz, 2 H), $4.33$ (s, 2 H), $3.48$ (t, $J = 6.0$ Hz, 2 H), $2.59$ (q, $J = 7.6$ Hz, 2 H), $1.14$ (t, $J = 7.6$ Hz, 3 H).

**13C NMR (101 MHz, CDCl$_3$):** $\delta = 197.14$, 161.41, 150.74, 148.12, 147.78, 134.25, 133.93, 128.32, 128.22, 127.49, 127.14, 126.40, 122.01, 42.89, 36.76, 28.97, 15.15.

**HRMS (ESI):** $m/z$ calcd for C$_{19}$H$_{19}$N$_2$O$_2$: [M+H]+; 307.1447; found: 307.1446.

**3-[3-(4-Tert-Butylphenyl)-3-oxopropyl]quinazolin-4(3H)-one (5f)**
Yield 0.194 g, 79%; pale yellow solid; mp 148–150 °C.
3-[3-(3-Methoxyphenyl)-3-oxopropyl]quinazolin-4(3H)-one (5g)
Yield 0.190 g, 84%; off-white solid; mp 103–105 °C.

1H NMR (400 MHz, CDCl3): δ = 8.38 (s, 1 H), 8.29 (dd, J = 8.0, 0.9 Hz, 1 H), 7.77–7.69 (m, 2 H), 7.54–7.48 (m, 2 H), 7.45–7.39 (m, 1 H), 7.35–7.29 (m, 2 H), 7.24 (t, J = 5.9 Hz, 2 H), 3.83 (s, 3 H), 3.58 (t, J = 5.9 Hz, 2 H).

13C NMR (101 MHz, CDCl3): δ = 197.37, 161.43, 159.89, 148.18, 147.71, 137.47, 134.29, 129.74, 127.54, 127.19, 126.42, 122.02, 120.78, 120.05, 114.98, 42.88, 37.01, 29.73.

HRMS (ESI): m/z calcd for C17H15N2O3 [M + H]: 295.1083; found: 295.1083.

1H NMR (500 MHz, CDCl3): δ = 8.39 (s, 1 H), 8.29 (d, J = 7.7 Hz, 1 H), 7.92 (d, J = 8.8 Hz, 2 H), 7.76–7.70 (m, 2 H), 7.51–7.46 (m, 1 H), 7.39 (t, J = 7.9 Hz, 2 H), 7.20 (t, J = 7.4 Hz, 1 H), 7.04 (d, J = 7.8 Hz, 2 H), 6.97 (d, J = 8.8 Hz, 2 H), 4.42 (t, J = 5.9 Hz, 2 H), 3.54 (t, J = 5.9 Hz, 2 H).

HRMS (ESI): m/z calcd for C17H15N2O3 [M + H]: 313.1396; found: 313.1394.

3-[3-Oxo-3-(4-Chlorophenyl)-3-oxopropyl]quinazolin-4(3H)-one (5i)
Yield 0.169 g, 74%; off-white solid; mp 130–133 °C.

1H NMR (400 MHz, CDCl3): δ = 8.37 (s, 1 H), 8.28 (dd, J = 8.0, 1.0 Hz, 1 H), 7.90–7.84 (m, 2 H), 7.77–7.68 (m, 2 H), 7.49 (ddd, J = 8.2, 6.8, 1.5 Hz, 1 H), 7.43–7.38 (m, 2 H), 4.42 (t, J = 5.9 Hz, 2 H), 3.56 (t, J = 5.9 Hz, 2 H).

13C NMR (101 MHz, CDCl3): δ = 196.33, 161.44, 148.15, 147.62, 140.20, 134.44, 134.34, 129.49, 129.07, 127.55, 127.24, 126.40, 121.97, 42.79, 36.84.

HRMS (ESI): m/z calcd for C17H14ClN2O2 [M + H]: 313.0712; found: 313.0739.

3-[3-(3-Hydroxyphenyl)-3-oxopropyl]quinazolin-4(3H)-one (5k)
Yield 0.165 g, 72%; white solid; mp 145–148 °C.

1H NMR (400 MHz, CDCl3): δ = 8.35 (s, 1 H), 7.98 (s, 1 H), 7.77 (d, J = 7.9 Hz, 1 H), 7.34 (dd, J = 21.7, 7.9 Hz, 3 H), 7.22 (d, J = 8.0 Hz, 1 H), 7.05 (t, J = 7.4 Hz, 1 H), 6.39 (d, J = 8.5 Hz, 2 H), 3.94 (t, J = 6.1 Hz, 2 H), 3.06 (t, J = 6.1 Hz, 2 H).

13C NMR (75 MHz, CDCl3 + DMSO): δ = 200.64, 167.49, 165.72, 153.04, 138.92, 135.31, 132.86, 132.17, 131.73, 131.02, 126.78, 120.31, 83.83, 83.39, 82.96, 47.67, 41.21.

HRMS (ESI): m/z calcd for C17H15N2O2 [M + H]: 291.1083; found: 291.1083.

3-[3-(3-Hydroxy-3-methylphenyl)-3-oxopropyl]quinazolin-4(3H)-one (5l)
Yield 0.172 g, 76%; off-white solid; mp 238–240 °C.

1H NMR (400 MHz, DMSO): δ = 9.98 (s, 1 H), 8.40 (s, 1 H), 8.21 (d, J = 7.9 Hz, 1 H), 7.75 (t, J = 7.6 Hz, 1 H), 7.69 (s, 1 H), 7.67–7.61 (m, 2 H), 7.49 (t, J = 7.5 Hz, 1 H), 6.83 (d, J = 8.3 Hz, 1 H), 4.37 (t, J = 6.0 Hz, 2 H), 3.48 (t, J = 6.0 Hz, 2 H), 2.17 (t, 3 H).

13C NMR (101 MHz, DMSO): δ = 196.08, 161.00, 148.29, 134.19, 131.30, 128.02, 127.96, 127.42, 127.00, 126.28, 124.66, 122.03, 114.64, 42.99, 36.44, 16.21.

HRMS (ESI): m/z calcd for C17H15N2O2 [M + H]: 291.1083; found: 291.1083.
Yield 0.188 g, 72%; white solid; mp 138–141 °C.

HRMS (ESI): m/z calcd for C_{18}H_{14}N_{2}O_{4} [M + H]: 323.1032; found: 323.1034.

3-[3-(4-Nitrophenyl)-3-oxopropyl]quinazolin-4(3H)-one (5q)

Yield 0.190 g, 75%; off-white solid; mp 160–162 °C.

1H NMR (500 MHz, CDCl3): δ = 8.33 (s, 1 H), 8.29 (dd, J = 8.0, 1.0 Hz, 1 H), 8.02 (d, J = 8.2 Hz, 2 H), 7.76–7.68 (m, 3 H), 6.74 (d, J = 8.9 Hz, 1 H), 7.51–7.48 (m, 1 H), 4.49 (t, J = 5.9 Hz, 2 H), 3.56 (t, J = 5.9 Hz, 2 H).

13C NMR (126 MHz, CDCl3): δ = 196.18, 161.42, 152.16, 148.32, 134.76, 132.87, 128.56, 127.83, 127.66, 126.42, 122.00, 115.91, 115.67, 42.85, 36.78.

HRMS (ESI): m/z calcd for C_{19}H_{15}N_{2}O_{5} [M + H]: 347.1007; found: 347.1003.

3-[3-(3-Methoxy-4-nitrophenyl)-3-oxopropyl]quinazolin-4(3H)-one (5r)

Yield 0.181 g, 70%; off-white solid; mp 156–158 °C.

1H NMR (500 MHz, CDCl3): δ = 8.16, 6.08, 6.05, (dd, J = 2.0 Hz, 1 H), 2.79, 7.78–7.74 (m, 1 H), 7.71 (d, J = 7.4 Hz, 1 H), 7.52–7.47 (m, 1 H), 4.45 (t, J = 5.9 Hz, 2 H), 3.66 (t, J = 6.0 Hz, 2 H), 3.45 (t, J = 6.0 Hz, 2 H).

13C NMR (126 MHz, CDCl3): δ = 196.19, 161.42, 152.16, 148.32, 134.76, 132.87, 128.56, 127.83, 127.66, 126.42, 122.00, 115.91, 115.67, 42.85, 36.78.

HRMS (ESI): m/z calcd for C_{19}H_{15}N_{2}O_{5} [M + H]: 347.1007; found: 347.1003.

3-[3-(3-Methoxy-4-nitrophenyl)-3-oxopropyl]quinazolin-4(3H)-one (5s)

Yield 0.190 g, 75%; off-white solid; mp 160–162 °C.

1H NMR (500 MHz, CDCl3): δ = 8.33 (s, 1 H), 8.29 (dd, J = 8.0, 1.0 Hz, 1 H), 8.02 (d, J = 8.2 Hz, 2 H), 7.76–7.68 (m, 3 H), 6.74 (d, J = 8.9 Hz, 1 H), 7.51–7.48 (m, 1 H), 4.49 (t, J = 5.9 Hz, 2 H), 3.56 (t, J = 5.9 Hz, 2 H).

13C NMR (126 MHz, CDCl3): δ = 196.18, 161.42, 152.16, 148.32, 134.76, 132.87, 128.56, 127.83, 127.66, 126.42, 122.00, 115.91, 115.67, 42.85, 36.78.

HRMS (ESI): m/z calcd for C_{19}H_{15}N_{2}O_{5} [M + H]: 347.1007; found: 347.1003.

3-[3-(3-Methoxy-4-nitrophenyl)-3-oxopropyl]quinazolin-4(3H)-one (5t)

Yield 0.181 g, 70%; off-white solid; mp 156–158 °C.

1H NMR (500 MHz, CDCl3): δ = 8.16, 6.08, 6.05, (dd, J = 2.0 Hz, 1 H), 2.79, 7.78–7.74 (m, 1 H), 7.71 (d, J = 7.4 Hz, 1 H), 7.52–7.47 (m, 1 H), 4.45 (t, J = 5.9 Hz, 2 H), 3.66 (t, J = 6.0 Hz, 2 H), 3.45 (t, J = 6.0 Hz, 2 H).

13C NMR (126 MHz, CDCl3): δ = 196.19, 161.42, 152.16, 148.32, 134.76, 132.87, 128.56, 127.83, 127.66, 126.42, 122.00, 115.91, 115.67, 42.85, 36.78.

HRMS (ESI): m/z calcd for C_{19}H_{15}N_{2}O_{5} [M + H]: 347.1007; found: 347.1003.
3-(Naphthalen-2-yl)-3-oxopropylquinazolin-4(3H)-one (5y)
Yield 0.176 g, 73%; pale white solid; mp 110–112 °C.
1H NMR (400 MHz, CDCl3): δ = 8.46 (s, 1 H), 8.43 (s, 1 H), 8.30 (d, J = 7.9 Hz, 1 H), 8.00 (dd, J = 8.6, 1.3 Hz, 1 H), 7.93 (d, J = 8.0 Hz, 1 H), 7.89–7.88 (m, 2 H), 7.72 (t, J = 8.2 Hz, 2 H), 7.59 (dd, J = 14.3, 7.2 Hz, 2 H), 7.53–7.46 (m, 1 H), 4.49 (t, J = 5.9 Hz, 2 H).
13C NMR (101 MHz, CDCl3): δ = 197.46, 196.23, 161.50, 161.32, 148.14, 147.78, 147.28, 141.69, 135.80, 135.36, 134.44, 134.32, 134.14, 133.48, 132.42, 132.16, 131.31, 130.45, 130.15, 129.64, 129.44, 128.80, 128.64, 128.52, 127.80, 127.61, 127.51, 127.39, 127.22, 126.96, 126.66, 126.42, 125.15, 123.47, 122.11, 122.02, 42.99, 42.69, 36.94.

6-Chloro-3-(3-oxo-3-phenylpropyl)quinazolin-4(3H)-one (5a)
Yield 0.131 g, 72%; off-white solid; mp 138–140 °C.
1H NMR (400 MHz, CDCl3): δ = 8.75 (s, 1 H), 8.24 (d, J = 13.8 Hz, 1 H), 7.92 (s, 1 H), 7.84 (d, J = 13.8 Hz, 1 H), 7.71 (s, 1 H), 7.56 (s, 1 H), 7.45 (d, J = 6.8 Hz, 2 H), 7.24 (d, J = 15.3 Hz, 1 H), 4.49 (s, 2 H), 3.61 (s, 2 H).
13C NMR (101 MHz, CDCl3): δ = 197.45, 162.28, 160.76, 159.81, 147.10, 144.86, 136.07, 133.74, 130.02, 129.94, 128.76, 128.09, 129.92, 129.74, 114.42, 111.18, 42.89, 36.74.

Conflict of Interest
The authors declare no conflict of interest.

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