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N-Alkylation and Aminohydroxylation of 2-Azidobenzenesulfonamide Gives a Pyrrolobenzothiadiazepine Precursor Whereas Attempted N-Alkylation of 2-Azidobenzamide Gives Benzotriazinones and Quinazolinones

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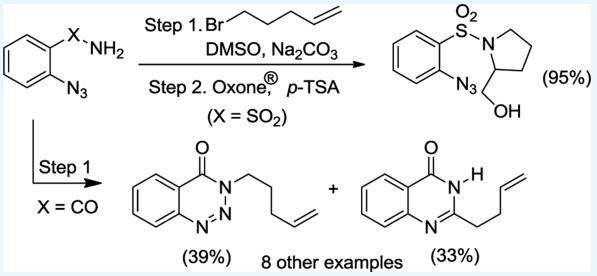
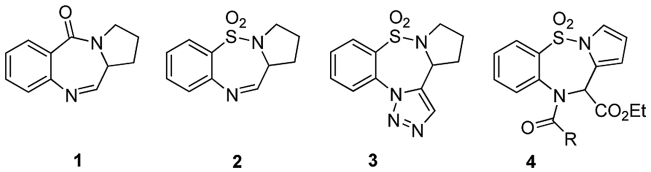
Supporting Information

ABSTRACT: N-Alkylation of 2-azidobenzenesulfonamide with 5-bromopent-1-ene gave an *N*-pentenyl sulfonamide, which underwent intramolecular aminohydroxylation to give an *N*-(2-azidoaryl)-sulfonyl prolinol, a precursor for the synthesis of a pyrrolobenzothiadiazepine. The attempted N-alkylation of 2-azidobenzamide gave a separable mixture (~1:1) of a benzotriazinone and a quinazolinone in a 72% combined yield. Other primary alkyl halides (3 examples) gave similar mixtures of benzotriazinones and quinazolinones. Benzylic, allylic, and secondary and tertiary alkyl halides (5 examples) gave only benzotriazinones in moderate yields. The results of mechanistic studies show the likely involvement of nitrene intermediates in the quinazolinone pathway and a second pathway involving a dimethylsulfoxide or dimethylsulfide-mediated conversion of 2-azidobenzamide into benzotriazinones.



INTRODUCTION

Pyrrolo[2,1-*c*][1,4]benzodiazepines (PBDs) **1** are a class of natural products that have attracted a great deal of interest[1] because of their ability to function as sequence-selective DNA-interactive molecules.[2−4] PBD derivatives have entered phase II clinical trials as antitumor compounds[5] and have also attracted attention as antibiotics with a novel mode of action.[6] Pyrrolo[1,2-*b*][1,2,5]benzothiadiazepines (PBTDs) **2** are attracting interest as PBD analogues,[7] non-nucleosidic reverse transcriptase inhibitors,[8] antischistosomals,[9] and Glut-1 transporter inhibitors (compound **3**)[10] and are emerging as a potential treatment for chronic leukemia (compound **4**).[11−13]



1 **2** **3** **4**

Almost all approaches toward the synthesis of PBDs and PBTDs use L-proline-derived starting materials, meaning that the de novo synthesis of the pyrrolidine ring is a rare approach to the PBDs and a very rare approach to the PBTDs. Metathesis,[14] intramolecular lactam formation,[15] reductive cyclization,[16,17] cyclization−elimination,[18] and ring contraction of 1,2-thiazines[10,19] are approaches to the PBDs that involve five-membered ring construction. Only the latter has been applied for the synthesis of PBTDs. With this in mind, we became interested in using intramolecular aminohydroxylation to construct a functionalized pyrrolidine derivative, which would then act as a precursor to the PBTDs or PBDs. Intramolecular aminohydroxylation of alkenes is an area of recent interest in heterocyclic synthesis and has been used to access simple prolinol derivatives.[20−22] Using this, our initial hypothesis (Figure 1) was that the *N*-(pent-4-en-1-yl)-azidobenzenesulfonamide **5** and *N*-(pent-4-en-1-yl)-azidobenzamide **6** would undergo aminohydroxylation to yield *N*-arylazido-substituted prolinols **7** and **8**, respectively, which could then be used to synthesize PBDs and PBTDs.

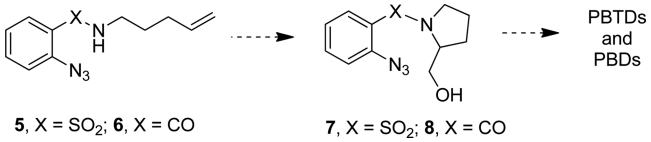


Figure 1. Initial aim of the current work.

RESULTS AND DISCUSSION

We synthesized *N*-(pent-4-en-1-yl)benzenesulfonamide **5** from the reaction of 2-azidobenzenesulfonamide **9** with 5-bromopentene (21%) or from the reaction of 2-azidobenzenesulfonyl chloride **10** with pent-4-en-1-amine (63%), as shown in Scheme 1. Pent-4-en-1-amine was synthesized from 5-

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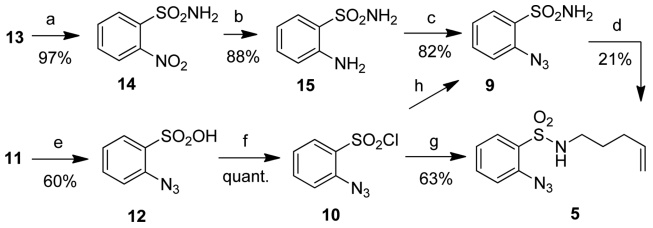
Scheme 1. Synthesis of Aminohydroxylation Precursor 5[a]

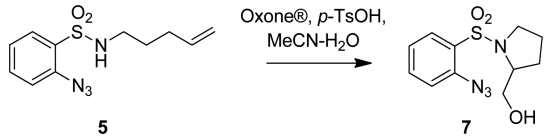


[a]Reagents and conditions: (a) NH_3 (aq); (b) Pd/C, NH_2NH_2; (c) (i) $NaNO_2$, HCl (aq) and (ii) NaN_3, NaOAc (aq); (d) 5-bromopentene, base, and dimethyl sulfoxide (DMSO); (e) (i) $NaNO_2$, HCl (aq) and (ii) NaN_3, NaOAc (aq); (f) $SOCl_2$, reflux; (g) pent-4-en-1-amine;[23] and (h) NH_3 (aq).

bromopentene.[23] The sulfonyl chloride **10** was synthesized using diazotization and azidation of 2-aminobenzenesulfonic acid **11** followed by the treatment of 2-azidobenzenesulfonic acid **12** with thionyl chloride.[10,24] 2-Azidobenzenesulfonamide **9** was synthesized by reacting the sulfonyl chloride **10** with ammonia or from the diazotization and azidation of 2-aminobenzenesulfonamide **15**, which was produced from 2-nitrobenzenesulfonyl chloride **13** via the sulfonamide **14**.[10,24]

For the intramolecular aminohydroxylation, we found that Oxone in the presence of tosic acid as an electrophilic oxidant system, as reported previously by Togo[20] for nonazido substrates, worked well for our azido substrate **5**. The desired prolinol **7** (Scheme 2) was produced over repeated attempts in

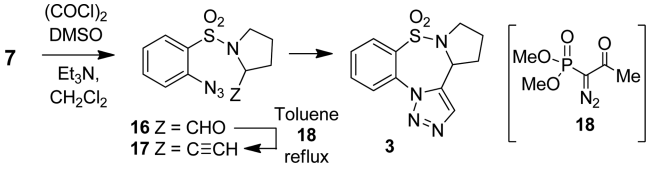
Scheme 2. Intramolecular Aminohydroxylation to Form PBTD Precursor 7



an 83−95% yield. As far as we are aware, this is the first reported example of such a reaction having been performed with an azide group present.

In our previous studies,[10,25] we reported the synthesis of the Glut-1 transporter-inhibiting triazolo-PBTD **3** as a single enantiomer from the enantiopure version of alcohol **7**, which we derived from L-prolinol. The formation of racemic alcohol **7** gave us the opportunity to provide a sample of racemic **3**. Thus, as shown in Scheme 3, alcohol **7** was oxidized to give aldehyde

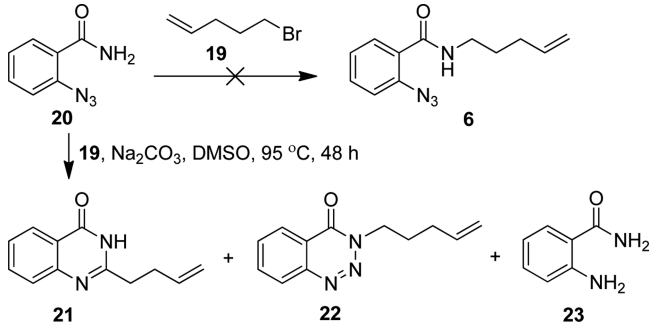
Scheme 3. Synthesis of Triazolo-PBTD 3



16 (96%), which was converted into alkyne **17** using the Bestmann−Ohira reagent **18**. Intramolecular 1,3-dipolar cycloaddition occurred spontaneously to furnish the racemic PBTD derivative **3** in a 70% yield from aldehyde **16**.

With a successful PBTD system in hand (Figure 1, X = SO_2), we next attempted to synthesize the analogous PBD system using the same approach (Figure 1, X = CO). 2-Azidobenzoyl chloride was prepared in two steps from anthranilic acid[26−28] and converted into secondary amide **6** by reaction with pent-4-en-1-amine.[23] Attempted intramolecular aminohydroxylation failed to deliver the desired *N*-arylazido substituted **8**. As shown in Scheme 4, we also attempted to form compound **6** by the

Scheme 4. Formation of Benzotriazinone 21 and Quinazolinone 22



reaction of 2-azidobenzamide **20** with 5-bromopentene **19** in DMSO in the presence of a base, a reaction that had worked with 2-azidobenzenesulfonamide (Scheme 1). This did not produce *N*-(pent-4-en-1-yl)benzamide **6** but instead led to some unexpected results (also shown in Scheme 4). Thus, under a variety of conditions, we observed the formation of a mixture of benzotriazinone **21** and quinazolinone **22**. The use of anhydrous DMSO as the solvent, sodium carbonate as the base, and a temperature of 95 °C allowed an optimized combined yield of 72% (isolated yields of 39% for compound **21** and 33% for compound **22**) with 4% recovery of the starting material **20** and the formation of 15% of the reduced product, 2-aminobenzamide **23**.

We decided to explore this process in more detail (Scheme 5) with respect to the substrate scope of the organohalide. The reaction of 2-azidobenzamide with 4-bromobutene gave benzotriazinone **26** (35%) and quinazolinone **24** (29%), whereby the expected quinazolinone **25** underwent a facile double-bond migration to give conjugated **24**. The recovered starting material **20** (8%) and 2-aminobenzamide **23** (14%) were also present and were also formed in all other reactions shown in Scheme 5. 1-Bromobutane and 1-bromopropane gave benzotriazinones **27** and **28**, respectively, again as mixtures with the respective quinazolinones. Benzyl bromide, 2-bromopropane, and bromocyclohexane did not form quinazolinones, giving only benzotriazinones **29**−**31**, respectively. 2-Bromo-2-methylpropane behaved unexpectedly and gave benzotriazinone **32** in a 30% yield, a reaction that is discussed later. The identical benzotriazinone **32** was formed in a 36% yield from the reaction of 2-azidobenzamide with 3-bromo-2-methylprop-1-ene. Attempts to optimize these reactions further were unsuccessful: other solvents (see below) did not react; other bases (Et_3N, DBU, DABCO, and pyridine) and/or reduced temperatures gave reduced yields; and increased temperatures gave increased degradation resulting in reduced yields of benzotriazinones and quinazolinones, together with higher yields of the reduced product 2-aminobenzamide **23**. (Bromomethylene)dibenzene was unreactive toward the azide but was converted into benzophenone **33**, whereas trityl bromide was unreactive and furnished triphenyl methanol **34**.

Scheme 6 shows our suggested mechanism for the formation of quinazolinones. We consider that nitrene **35** (path A) reacts

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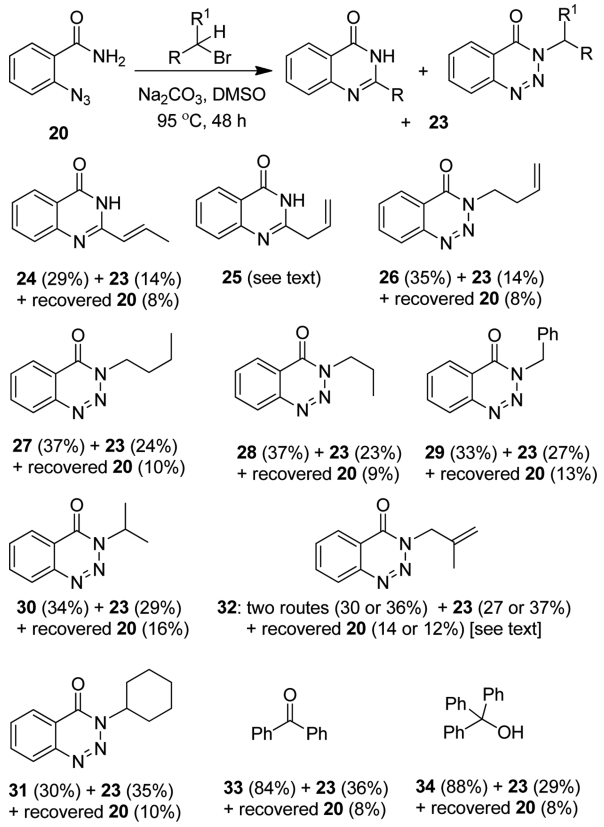
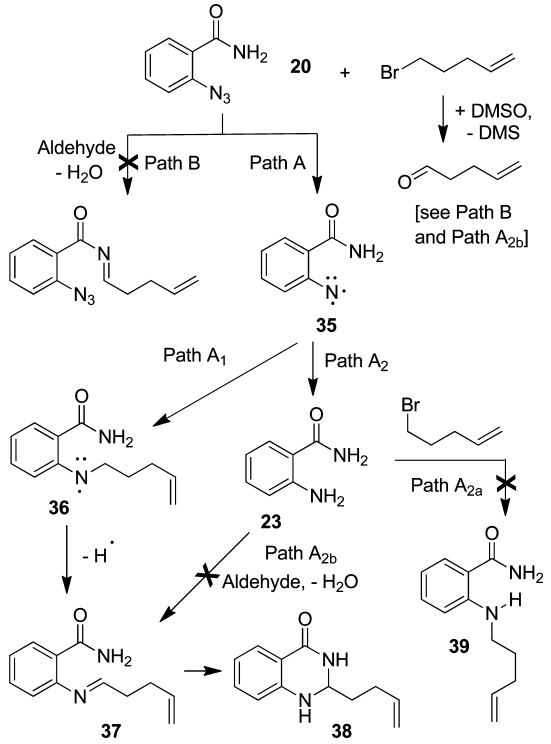
Scheme 5. Reaction of Alkyl Halides with 2-Azidobenzamide

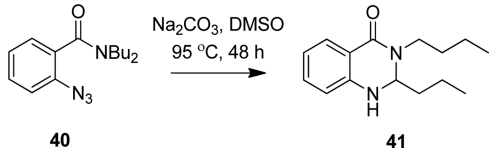


Scheme 6. Mechanisms to Explain Quinazolinone Formation



with the alkyl halide to form intermediate **36** (path A_1), which undergoes hydrogen radical extrusion to form imine **37**. Cyclization gives the dihydroquinazoline species **38**, and loss of hydrogen would form the final quinazolinone. This pathway also explains the formation of 2-aminobenzamide due to nitrene **35** abstracting hydrogen from the reaction medium (path A_2). Generation of nitrenes from aryl azides in solvents at temperatures below 100 °C,[29,30] including DMSO,[31] is known. There is an alternative route whereby nitrene formation is preceded by N-alkylation of the amide nitrogen to give compound **6** (see earlier for structure and synthesis). However, we saw no evidence for the formation of compound **6** using thin-layer chromatography (TLC). Compound **6** also failed to give quinazolinones under our reaction conditions. Quinazolinones are important and well-known heterocycles[32−36] that are synthesized by a variety of routes including an iron-catalyzed intramolecular C−N bond formation from N,N-disubstituted 2-azidobenzamides[36] and from dihydroquinazolinones formed from 2-aminobenzamides and aldehydes using DMSO as a mild oxidant,[37,38] providing some precedent for our suggested mechanism. We speculated that our process may occur via the formation of 2-aminobenzamide **23** from the azide and subsequent reaction with the alkyl halide to give intermediate **39**, which could then form species **36**. However, when 2-aminobenzamide was used as the starting material in the place of 2-azidobenzamide, the reaction was not seen. We also thought it was possible that DMSO could generate an aldehyde from the alkyl halide and that this aldehyde was reacting with either starting material **20** or with 2-aminobenzamide **23** (paths B and A_{2b} in Scheme 6). We exclude these two paths because (i) the introduction of the relevant aldehyde into the system had no influence and (ii) our reaction was very sensitive to water (anhydrous DMSO was necessary) and the paths B and A_{2b} both generate water. Path B also supposes the formation of an *N*-acyl imine by the reaction of 2-azidobenzamide with an aldehyde, a conversion that we have been unable to achieve. Thus, it appears that 2-azidobenzamide **20** forms nitrene **35** under our reaction conditions and goes on to form quinazolinones via path A_1 and 2-aminobenzamide **23** via path A_2. The secondary amide **6** did not react in this way. Interestingly, when we subjected a tertiary amide, compound **40** (Scheme 7), to the same reaction conditions, we isolated the disubstituted dihydroquinazolinone **41**, in line with the literature precedent for tertiary amides.[36]

Scheme 7. Formation of a Dihydroquinazolinone



Scheme 8 shows our mechanism for the formation of benzotriazinones **26**−**32**. 3-Substituted 1,2,3-benzotriazin-4-ones are useful targets in medicinal chemistry[39−41] and as synthetic intermediates.[42,43] The most common route to 3-substituted 1,2,3-benzotriazin-4-ones is diazotization of the relevant N-substituted anthranilamide.[39−42] For our mechanism, we suggest that compound **42** (Scheme 8) is an intermediate. When this readily available[44] compound was used as the starting material in our reaction, the same benzotriazinones could be isolated. N-Alkylation of benzotriazinone **42** is a known route to *N*-alkyl benzotriazinones.[45] 2-Azidobenzamide **20** has an azide group, which can be stabilized by an intramolecular hydrogen bond that renders the azide susceptible to nucleophilic attack followed by alkylation. Such

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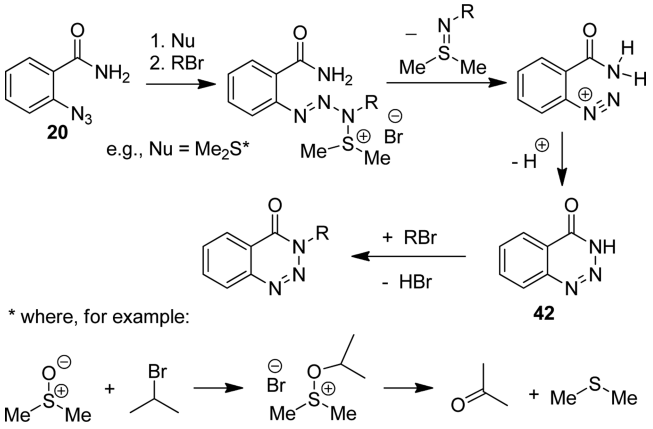
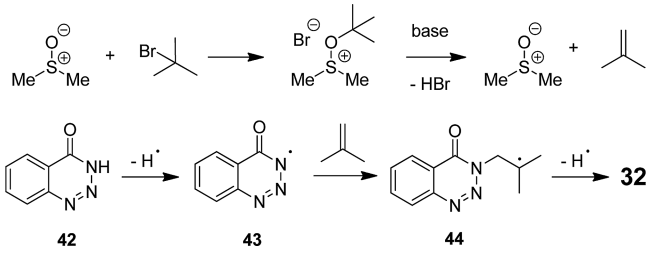
Scheme 8. Proposed Mechanism for Benzotriazinone Formation



processes have precedent in azide chemistry.[46−49] Loss of the azide terminal nitrogen is then facilitated, allowing the formation of a diazonium species, which can cyclize to give intermediate **42**. As discussed previously, we were able to isolate significant quantities of benzophenone **33** from the reaction mixture when (bromomethylene)dibenzene was used as the alkyl halide. We also isolated triphenyl methanol when trityl bromide was used. DMSO was the only solvent in which we observed a reaction [dimethylformamide (DMF), nitromethane, chloroform, and toluene gave no reaction]. This leads us to suggest that ketones or aldehydes plus dimethylsulfide form from the known reaction of alkyl halides and DMSO,[50] and so, we favor dimethylsulfide as the nucleophile, as shown in Scheme 8. This process consumes 2 equiv of alkyl halide, which is consistent with our observation that excess alkyl halide is needed (see Experimental Section). An alternative mechanism for benzotriazinone formation is for N-alkylation to precede the nucleophilic attack at the azide, but this would involve N-alkylation of the amide nitrogen as discussed and dismissed for the quinazolinone mechanism shown in Scheme 6.

The unexpected formation of benzotriazinone **32** (see Scheme 5) from 2-bromo-2-methylpropane can be explained by a combination of the mechanisms shown in Schemes 6 and 8. Thus, as shown in Scheme 9, alkoxysulfonium salt formation

Scheme 9. Proposed Mechanism to Account for the Formation of Benzotriazinone 32



and elimination would generate 2-methylpropene, a process that has precedent.[51,52] The interception of a free radical species by benzotriazinone **42** would generate the free radical intermediate **43**, which could then react with 2-methylpropene to form intermediate **44**, which would yield benzotriazinone **32** after the loss of a hydrogen radical.

CONCLUSIONS

A new approach to the synthesis of pyrrolobenzothiadiazepine nucleus has been presented that relies upon the formation of a racemic proline derivative using the previously unreported intramolecular aminohydroxylation of an N-alkenylated 2-azidobenzenesulfonamide. We are currently working to expand the scope of this process by applying it to other N-alkenylated 2-azidobenzenesulfonamide substrates. Attempts to form the corresponding N-alkenylated 2-azidobenzamides led to mixtures of benzotriazinones and benzoquinazolines, which were formed from an unusual process that allowed us to hypothesize a nitrene-based pathway to the benzoquinazolines and a pathway to the benzotriazinones that involves the conversion of an azide into a diazonium via nucleophilic attack on the azide. Our work offers some useful and interesting mechanistic insights into organoazide chemistry and organosulfur chemistry.

EXPERIMENTAL SECTION

Compounds (**9**) to (**15**)[10,24,53] and (**20**)[24,27,28] were synthesized as described in the literature. The methods that we used to access racemic (**16**) and (**3**) are methods that we developed previously to produce enantiopure (**16**) and (**3**).[10,25] Enantiopure compound (**7**) is also known[10,25] but was previously accessed using chemistry different from the new method that is reported for racemic (**7**) below. The synthesis of benzotriazinones (**28**),[54] (**29**),[44] and (**30**)[54] have been reported previously but with no data and via a different route. Other routes to 2-ethylquinazolin-4(3*H*)-one,[55] 2-propylquinazolin-4(3*H*)-one,[55] and 2-(1′-propen-1′-yl)-quinazolinone (**24**)[56] have been reported.

2-Azido-*N*-(pent-4-en-1-yl)benzamide (6). 2-Azidobenzoic acid (717 mg, 4.4 mmol) was heated at reflux in a 2 M solution of $(COCl)_2$ in dichloromethane (5.0 mL, 10.0 mmol) with a drop of DMF under an inert atmosphere of nitrogen for 5 h. The reaction was cooled to room temperature before the crude acid chloride was concentrated, and the residue was washed with dichloromethane (2 × 20 mL) to give crude 2-azidobenzoyl chloride as a dark brown solid. One portion of a solution of potassium carbonate (1.10 g, 8.00 mmol) in water (10 mL) was added to a stirring solution of 5-amino-1-pentene[23] (170 mg, 2.0 mmol) in dichloromethane (10 mL). 2-Azidobenzoyl chloride was dissolved in dichloromethane (5 mL) and was added slowly to this solution. The reaction mixture was stirred at room temperature for 18 h before the organic layer was separated, and the aqueous layer was washed with dichloromethane (2 × 20 mL). The combined organic phases were dried ($MgSO_4$), filtered, concentrated, and purified using silica column chromatography (petroleum ether/ethyl acetate 1:4, R_f = 0.25) to yield the product as a yellow oil (330 mg, 72%). IR (neat, ν_{max}) cm^{-1}: 1164, 1294, 1445, 1480, 1536, 1577, 1638, 1712, 2125, 2864, 2930, 3076, 3294. ^1H NMR (400 MHz, $CDCl_3$): δ 1.66 (2H, tt, J = 7.4, 7.4 Hz, $-CH_2CH_2CH_2-$), 2.09 (2H, dt, J = 7.4, 7.8 Hz, $CH_2CH=CH_2$), 3.37−3.42 (2H, m, $NHCH_2$), 4.88−4.97 (2H, m, $CH=CH_2$), 5.72−5.82 (1H, m, $CH=CH_2$), 7.10 (1H, dd, J^1 = 7.8 Hz, J^2 = 0.8 Hz, Ar**H**), 7.14 (1H, ddd, J^1 = 7.8 Hz, J^2 = 7.4 Hz, J^3 = 1.6 Hz, Ar**H**), 7.39−7.41 (2H, m, N**H** + Ar**H**), 8.04 (1H, dd, J^1 = 7.8 Hz, J^2 = 1.6 Hz, Ar**H**). ^{13}C NMR (100 MHz, $CDCl_3$): δ 28.64 (CH_2), 31.25 (CH_2), 39.54 (CH_2), 115.22 ($=CH_2$), 118.37 (CH), 125.17 (CH), 125.26 (qC), 132.17 (CH), 132.19 (CH), 136.82 (qC), 137.79 (CH), 164.58 (C=

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O). HRMS (ESI$^+$) m/z: found 231.1238 [M + H]$^+$, $C_{12}H_{15}N_4O$ requires 231.1240.

2-Azido-*N*-(pent-4-en-1-yl)benzenesulfonamide (5). 2-Azido-*N*-(pent-4-en-1-yl)benzenesulfonamide (**5**) was formed in the same manner using 2-azidobenzenesulfonic acid as the starting material. IR (neat, ν_{max}) cm^{-1}: 1125, 1162, 1291, 1329, 1415, 1471, 1575, 1641, 2133, 2854, 2926, 3074, 3300. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.52 (2H, tt, J = 7.1, 7.1 Hz, C**H**$_2$), 2.00 (2H, dt, J = 7.1, 7.1 Hz, C**H**$_2$), 2.83 (2H, dt, J = 6.8, 6.8 Hz, C**H**$_2$), 4.88−4.96 (3H, m, N−**H**, =C**H**$_2$), 5.59−5.70 (1H, m, =C**H**), 7.18−7.23 (2H, m, 2 × Ar**H**), 7.53 (1H, ddd, J = 7.8, 7.7, 1.3 Hz, Ar**H**), 7.91 (1H, dd, J^1 = 7.8 Hz, J^2 = 1.1 Hz, Ar**H**). ^{13}C NMR (100 MHz, $CDCl_3$): δ 28.66 (CH_2), 30.67 (CH_2), 42.79 (CH_2), 115.62 (CH_2), 119.36 (CH), 124.91 (CH), 129.92 (qC), 130.76 (CH), 133.96 (CH), 137.19 (CH), 137.47 (qC). HRMS (ESI$^+$) m/z: found 289.0730 [M + Na]$^+$, $C_{11}H_{14}N_4O_2SNa$ requires 289.0730.

(1-[(2-Azidophenyl)sulfonyl]pyrrolidin-2-yl)methanol (7). To a solution of 2-azido-*N*-(pent-4-en-1-yl)-benzenesulfonamide (**5**, 20 mg, 0.075 mmol) and Oxone (35 mg, 0.113 mmol) in a 1:1 mixture (5 mL) of acetonitrile and water was added *p*-toluenesulfonic acid monohydrate (2.9 mg, 0.015 mmol). The whole mixture was heated at reflux temperature for 12 h, while being monitored using TLC. To this solution, saturated aqueous $NaHCO_3$ solution (15 mL) was added, and the product was extracted with ethyl acetate (3 × 15 mL). The combined organic layer was washed with brine (15 mL) and dried over anhydrous $MgSO_4$, and the solvent was removed under vacuum. Purification using silica chromatography (eluent: petroleum ether/ethyl acetate 1:10, R_f = 0.2) yielded the product as a yellow oil (20 mg, 95%). IR (neat, ν_{max}) cm^{-1}: 1065, 1142, 1200, 1305, 1472, 1575, 1582, 2101, 2872, 2963, 3081, 3526. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.61−1.68 (1H, m, C***H***H), 1.72−1.80 (1H, m, CH***H***), 1.81−1.98 (2H, m, C**H**$_2$), 2.70 (1H, bs, CH_2O***H***), 3.28−3.34 (1H, m, NC***H***), 3.44−3.50 (1H, m, NCH***H***), 3.53−3.60 (1H, m, NC***H***H), 3.62−3.66 (1H, m, HOCH***H***), 3.94−4.00 (1H, m, HOC***H***H), 7.28 (1H, dd, J^1 = 8.1 Hz, J^2 = 7.0 Hz, Ar**H**), 7.33 (1H, dd, J = 8.0 Hz, Ar**H**), 7.62 (1H, ddd, J^1 = 8.1 Hz, J^2 = 7.0 Hz, J^3 = 1.1 Hz, Ar**H**), 8.04 (1H, dd, J = 8.0 Hz, J = 1.1 Hz, Ar**H**). ^{13}C NMR (100 MHz, $CDCl_3$): δ 24.67 (CH_2), 29.05 (CH_2), 49.52 (CH_2), 61.83 (CH), 65.48 (CH_2), 119.92 (CH), 124.81 (CH), 129.05 (qC), 132.58 (CH), 134.22 (CH), 138.20 (qC). HRMS (ESI$^+$) m/z: found 305.0674 [M + Na]$^+$, $C_{11}H_{14}N_5O_3SNa$ requires 305.0679.

(1-[2-Azidobenzenesulfonyl]pyrrolidin-2-yl)-carbaldehyde (16). A 2 M solution of oxalyl chloride in dichloromethane (0.94 mL, 1.68 mmol) was diluted with dichloromethane (5 mL) and cooled to −78 °C under nitrogen. DMSO (0.26 mL, 265 mg, 3.40 mmol) in dichloromethane (5 mL) and alcohol (**7**) (400 mg, 1.42 mmol) in dichloromethane (2.5 mL) were added separately, each over 10 min. The whole mixture was maintained at −78 °C for 30 min before the dropwise addition of triethylamine (1.09 mL, 0.78 g, 7.09 mmol), and then, it was allowed to reach room temperature. The reaction was quenched with a mixture of diethyl ether (5 mL) and water (5 mL). The organic layer was separated, and the aqueous phase was extracted with dichloromethane (3 × 10 mL). The combined organics were dried ($MgSO_4$), filtered, concentrated, and purified on silica (20 g) (petroleum ether/ethyl acetate 3:2, R_f = 0.2) to yield the product as a white solid (383 mg, 96%, mp = 103−105 °C). IR (neat, ν_{max}) cm^{-1}: 1151, 1323, 1435, 1467, 1572, 1732, 2122, 2887, 2977, 3101. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.81−1.95 (2H, m, C**H**$_2$), 2.00−2.09 (1H, m, C***H***H), 2.14−2.23 (1H, m, CH***H***), 3.38−3.44 (1H, m, NC***H***H), 3.55−3.60 (1H, m, CH***H***), 4.46−4.49 (1H, m, NC**H**), 7.28 (1H, ddd, J^1 = 7.5 Hz, J^2 = 7.1 Hz, J^3 = 1.5 Hz, Ar**H**), 7.34 (1H, d, J = 8.0 Hz, Ar**H**), 7.64 (1H, dd, J^1 = 7.8 Hz, J^2 = 7.5 Hz, Ar**H**), 8.04 (1H, d, J = 8.0 Hz, Ar**H**), 9.7 (1H, d, J = 9.8 Hz, C**H**O). ^{13}C NMR (100 MHz, $CDCl_3$): δ 24.99 (CH_2), 27.70 (CH_2), 48.80 (CH_2), 67.08 (CH), 119.88 (CH), 124.86 (CH), 128.97 (qC), 132.50 (CH), 134.38 (CH), 138.24 (qC), 200.42 (CH). HRMS (ESI$^+$) m/z: found 281.0697 [M + H]$^+$, $C_{11}H_{13}N_4O_3S$ requires 281.0703.

Pyrrolo[1,2-*b*][1,2,3]triazolo[5,1-*d*][1,2,5]-benzothiadiazepine 8,8-dioxide (3). Aldehyde (**16**) (300 mg, 1.07 mmol) was dissolved in dry methanol (5 mL); potassium carbonate (296 mg, 2.14 mmol) and the Bestmann−Ohira reagent (209 μL, 247 mg, 1.29 mmol) were added, and the whole mixture was stirred for 22 h under nitrogen. The reaction was quenched with saturated aqueous ammonium chloride (10 mL). The organic phase was separated, and the aqueous phase was extracted with dichloromethane (3 × 20 mL). The combined organic phases were dried ($MgSO_4$), filtered, and concentrated in vacuo to yield an orange solid. Purification using silica chromatography (20 g) (petroleum ether/ethyl acetate 1:3, R_f = 0.22) yielded the product as a yellow solid (207 mg, 70%, mp = 208−210 °C). IR (neat, ν_{max}) cm^{-1}: 1050, 1195, 1242, 1336, 1483, 1592, 2870, 2992, 3108. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.53−1.63 (1H, m, C***H***H), 1.77−1.85 (1H, m, CH***H***), 1.87−1.98 (1H, m, C***H***H), 2.14−2.21 (1H, m, CH***H***), 2.98−3.04 (1H, m, C***H***H), 3.54−3.59 (1H, m, CH***H***), 5.06−5.10 (1H, m, NCH), 7.51 (1H, dd, J^1 = 7.8 Hz, J^2 = 7.6 Hz, Ar**H**), 7.67 (1H, s, C***H***NN), 7.72 (1H, dd, J^1 = 7.8 Hz, J^2 = 7.6 Hz, Ar**H**), 7.99 (1H, d, J = 7.8 Hz, Ar**H**), 8.05 (1H, d, J = 7.8 Hz, Ar**H**) ppm. ^{13}C NMR (100 MHz, DMSO): δ 24.42 (CH_2), 35.45 (CH_2), 49.96 (CH_2), 55.09 (CH), 125.41 (CH), 128.61 (CH), 129.32 (CH), 130.94 (qC), 133.54 (qC), 134.03 (CH), 134.37 (CH), 136.77 (qC) ppm. HRMS (ESI$^+$) m/z: found 277.0754 [M + H]$^+$, $C_{12}H_{13}N_4O_2S$ requires 277.0754.

3-(Pent-4-en-1-yl)benzo[*d*][1,2,3]triazin-4-one (22) and 2-(But-3-en-1-yl)quinazolin-4-one (21). To a solution of 2-azidobenzamide (200 mg, 1.23 mmol) and sodium carbonate (392 mg, 3.70 mmol) in anhydrous DMSO (10 mL), 5-bromo-1-pentene (368 mg, 2.46 mmol) was added. The solution was heated at 95 °C for 48 h under a nitrogen atmosphere, and after the completion of the reaction, which was monitored using TLC, the resultant mixture was diluted with dichloromethane (30 mL) and washed with 0.1 M NaCl and water many times to remove DMSO. The mixture was dried with anhydrous magnesium sulfate and filtered under gravity, and the solvent was removed under vacuum. The residue was purified using column chromatography to give 3-(pent-4-en-1-yl)benzo[*d*][1,2,3]triazin-4-one (**22**) (eluent: petroleum ether/ethyl acetate 4:1, R_f = 0.2) as a dark orange oil (100 mg, 38%). IR (neat, ν_{max}) cm^{-1}: 1037, 1072, 1184, 1274, 1333, 1463, 1579, 1607, 1641, 1680, 2856, 2929, 3076. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.90−1.96 (2H, m, C**H**$_2$), 2.10−2.20 (2H, m, C**H**$_2$), 4.41 (2H, t, J = 7.3 Hz, C**H**$_2$), 4.92 (1H, d, J = 10.2 Hz, CH**H**), 5.00 (1H, d, J = 17.1 Hz, C**H**H), 5.71−5.82 (1H, m, C**H**), 7.72 (1H, dd, J^1 = 7.7 Hz, J^2 = 7.5 Hz, Ar**H**), 7.86 (1H, dd, J^1 = 7.7 Hz, J^2 = 7.3 Hz, Ar**H**), 8.07 (1H, d, J = 7.7 Hz, Ar**H**), 8.27 (1H, d, J = 7.7 Hz, Ar**H**). ^{13}C NMR (100 MHz, $CDCl_3$): δ 27.90 (CH_2), 30.72 (CH_2), 49.37 (CH_2), 115.56 (CH_2), 119.77 (qC), 125.01 (CH), 128.18 (CH),

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132.23 (CH), 134.69 (CH), 137.12 (CH), 144.27 (qC), 155.46 (C═O). HRMS (ESI$^+$) m/z: found 215.1059 [M]$^+$, $C_{12}H_{13}N_3O$ requires 215.1059. Also isolated was 2-(but-3-en-1-yl)quinazolin-4-one (**21**) (eluent: petroleum ether/ethyl acetate 1:1, R_f = 0.3) as a light yellow solid (80 mg, 33%, mp: 167−169 °C). IR (neat, ν_{max}) cm^{-1}: 1105, 1140, 1195, 1253, 1288, 1342, 1421, 1445, 1469, 1564, 1609, 1673, 2916, 2975, 3030, 3168. ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.59 (2H, m, C**H**$_2$), 2.84 (2H, t, J = 7.3 Hz, C**H**$_2$), 4.97 (1H, d, J = 10.1 Hz, ═C**H**H), 5.08 (1H, dd, J^1 = 17.1 Hz, J^2 = 1.0 Hz, ═CH**H**), 5.82−5.92 (1H, m, C**H**), 7.40 (1H, dd, J^1 = 7.8 Hz, J^2 = 7.2 Hz, Ar**H**), 7.63 (1H, d, J = 8.0 Hz, Ar**H**), 7.70 (1H, dd, J^1 = 8.0 Hz, J^2 = 7.1 Hz, Ar**H**), 8.21 (1H, d, J = 7.8 Hz, Ar**H**), 12.11 (1H, bs, N**H**). ^{13}C NMR (100 MHz, $CDCl_3$): δ 31.31 (CH_2), 35.19 (CH_2), 116.29 (CH_2), 120.53 (qC), 126.24 (CH), 126.44 (CH), 127.26 (CH), 134.82 (CH), 136.43 (CH), 149.45 (qC), 156.07 (qC), 164.39 (C═O) ppm. HRMS (ESI$^+$) m/z: found 201.1023 [M + H]$^+$, $C_{12}H_{13}N_2O$ requires 201.1022.

3-(But-3-en-1-yl)benzo[*d*][1,2,3]triazin-4-one (26) and 2-(1′-Propen-1′-yl)-quinazolinone (24). To a solution of 2-azidobenzamide (200 mg, 1.23 mmol) and sodium carbonate (392 mg, 3.70 mmol) in anhydrous DMSO (10 mL), 4-bromo-1-butene (333 mg, 2.47 mmol) was added. The solution was heated at 95 °C for 48 h under a nitrogen atmosphere, and after completion of the reaction, which was monitored using TLC, the resultant mixture was diluted with dichloromethane (30 mL) and washed with 0.1 M NaCl and water many times to remove DMSO. The mixture was dried with anhydrous magnesium sulfate and filtered under gravity, and the solvent was removed under vacuum. The residue was purified using column chromatography to give 3-(but-3-en-1-yl)benzo[*d*]-[1,2,3]triazin-4-one (**26**) (eluent: petroleum ether/ethyl acetate 4:1, R_f = 0.21) as a yellow oil (85 mg, 35%). IR (neat, ν_{max}) cm^{-1}: 1043, 1105, 1165, 1280, 1296, 1346, 1463, 1608, 1642, 1681, 2840, 2954, 3075. ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.61 (2H, dt, J = 7.1, 7.1 Hz, C**H**$_2$), 4.47 (2H, t, J = 7.1 Hz, C**H**$_2$), 4.95−5.05 (2H, m, ═C**H**$_2$), 5.71−5.84 (1H, m, ═C**H**), 7.72 (1H, dd, J^1 = 7.7 Hz, J^2 = 7.4 Hz, Ar**H**), 7.86 (1H, dd, J^1 = 8.1 Hz, J^2 = 8.0 Hz, Ar**H**), 8.06 (1H, d, J = 8.1 Hz, Ar**H**), 8.27 (1H, d, J = 7.7 Hz, Ar**H**). ^{13}C NMR (100 MHz, $CDCl_3$): δ 33.15 (CH_2), 49.03 (CH_2), 117.78 (CH_2), 119.77 (qC), 125.07 (CH), 128.24 (CH), 132.27 (CH), 133.97 (CH), 134.73 (CH), 144.27 (qC), 155.50 (C═O) ppm. HRMS (ESI$^+$) m/z: found 202.0970 [M + H]$^+$, $C_{11}H_{12}N_3O$ requires 202.0975. Also isolated was 2-(1′-propen-1′-yl)-quinazolinone (**24**) (eluent: petroleum ether/ethyl acetate 1:1, R_f = 0.29) as a yellow solid (65 mg, 29%, mp = 148−150 °C). IR (neat, ν_{max}) cm^{-1}: 1007, 1144, 1252, 1296, 1343, 1468, 1562, 1607, 1659, 2924, 3063, 3182. ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.08 (3H, dd, J^1 = 6.8 Hz, J^2 = 1.1 Hz, C**H**$_3$), 6.40 (1H, dd, J^1 = 15.9 Hz, J^2 = 1.3 Hz, ═C**H**), 7.19−7.26 (1H, m, ═C**H**), 7.47 (1H, dd, J^1 = 7.6 Hz, J^2 = 7.3 Hz, Ar**H**), 7.72 (1H, d, J = 7.8 Hz, Ar**H**), 7.78 (1H, dd, J^1 = 7.8 Hz, J^2 = 7.6 Hz, Ar**H**), 8.30 (1H, d, J = 7.6 Hz, Ar**H**), 11.98 (1H, s, N**H**). ^{13}C NMR (100 MHz, $CDCl_3$): δ 18.77 (CH_3), 120.75 (qC), 125.32 (CH), 126.28 (CH), 126.36 (CH), 127.51 (CH), 134.83 (CH), 138.47 (CH), 149.67 (qC), 150.89 (qC), 164.12 (C═O). HRMS (ESI$^+$) m/z: found 187.0860 [M + H]$^+$, $C_{11}H_{11}N_3O$ requires 187.0793. The data recorded for compound (**24**) are consistent with those published elsewhere.[56]

3-Butylbenzo[*d*][1,2,3]triazin-4(3*H*)-one (27) and 2-Propylquinazolin-4(3*H*)-one. To a solution of 2-azidobenzamide (200 mg, 1.23 mmol) and sodium carbonate (392 mg, 3.70 mmol) in anhydrous DMSO (10 mL), 1-bromobutane (338 mg, 2.47 mmol) was added. The solution was heated at 95 °C for 48 h under a nitrogen atmosphere, and after completion of the reaction, which was monitored using TLC, the resultant mixture was diluted with dichloromethane (30 mL) and washed with 0.1 M NaCl and water many times to remove DMSO. The mixture was dried with anhydrous magnesium sulfate and filtered under gravity, and the solvent was removed under vacuum. The residue was purified using column chromatography to give 3-butylbenzo[*d*][1,2,3]triazin-4(3*H*)-one (**27**) (eluent: petroleum ether/ethyl acetate 4:1, R_f = 0.2) as a light yellow oil (92 mg, 37%). IR (neat, ν_{max}) cm^{-1}: 1032, 1164, 1294, 1320, 1380, 1429, 1463, 1607, 1678, 2873, 2960. ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.91 (3H, t, J = 7.4 Hz, C**H**$_3$), 1.37 (2H, app. sextet, J = 7.6 Hz, C**H**$_2$), 1.86 (2H, app. pentet, J = 7.5 Hz, C**H**$_2$), 4.40 (2H, t, J = 7.1 Hz, C**H**$_2$), 7.71 (1H, dd, J^1 = 7.9 Hz, J^2 = 7.5 Hz, Ar**H**), 7.86 (1H, dd, J^1 = 7.9 Hz, J^2 = 7.5 Hz, Ar**H**), 8.07 (1H, d, J = 8.1 Hz, Ar**H**), 8.28 (1H, d, J = 8.1 Hz, Ar**H**). ^{13}C NMR (100 MHz, $CDCl_3$): δ 13.66 (CH_3), 19.89 (CH_2), 30.94 (CH_2), 49.67 (CH_2), 119.83 (qC), 125.05 (CH), 128.18 (CH), 132.20 (CH), 134.66 (CH), 144.33 (qC), 155.50 (C═O). HRMS (ESI$^+$) m/z: found 204.1127 [M + H]$^+$, $C_{11}H_{14}N_3O$ requires 204.1131. Also formed was 2-propylquinazolin-4(3*H*)-one (eluent: petroleum ether/ethyl acetate 1:1, R_f = 0.22) as a light yellow oil (∼20% by NMR), which could not be obtained free of 2-aminobenzamide. IR (neat, ν_{max}) cm^{-1}: 1082, 1161, 1265, 1293, 1394, 1449, 1478, 1565, 1615, 1650, 2962, 3173. ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.98 (3H, t, J = 7.5 Hz, C**H**$_3$), 1.69 (2H, app. sextet, J = 7.4 Hz, C**H**$_2$), 2.68 (2H, t, J = 7.8 Hz, C**H**$_2$), 7.37 (1H, dd, J^1 = 8.0 Hz, J^2 = 7.0 Hz, **H**Ar), 7.61 (1H, d, J = 8.0 Hz, **H**Ar), 7.68 (1H, dd, J^1 = 8.0 Hz, J^2 = 7.0 Hz, **H**Ar), 8.17 (1H, d, J = 8.0 Hz, **H**Ar), 11.12 (1H, s, N**H**). ^{13}C NMR (100 MHz, $CDCl_3$): δ 13.77 (CH_3), 18.99 (CH_2), 40.47 (CH_2), 121.46 (qC), 122.46 (CH), 125.18 (CH), 127.35 (CH), 132.96 (CH), 149.47 (qC), 157.17 (qC), 164.25 (C═O). HRMS (ESI$^+$) m/z: found 189.1023 [M + H]$^+$, $C_{11}H_{13}N_2O$ requires 189.1022. The data recorded for 2-propylquinazolin-4(3*H*)-one are consistent with those published elsewhere.[55]

3-Propylbenzo[*d*][1,2,3]triazin-4-one (28) and 2-Ethylquinazolin-4-one. To a solution of 2-azidobenzamide (200 mg, 1.23 mmol) and sodium carbonate (392 mg, 3.70 mmol) in anhydrous DMSO (10 mL), 1-bromo propane (304 mg, 2.47 mmol) was added. The solution was heated at 95 °C for 48 h under a nitrogen atmosphere, and after completion of the reaction, which was monitored using TLC, the resultant mixture was diluted with dichloromethane (30 mL) and washed with 0.1 M NaCl and water many times to remove DMSO. The mixture was dried with anhydrous magnesium sulfate and filtered under gravity, and the solvent was removed under vacuum. The residue was purified using column chromatography to give 3-propylbenzo[*d*][1,2,3]triazin-4-one (**28**) (eluent: petroleum ether/ethyl acetate 4:1, R_f = 0.21) as a light yellow solid (88 mg, 38%, mp = 49−51 °C). IR (neat, ν_{max}) cm^{-1}: 1024, 1143, 1175, 1226, 1281, 1294, 1320, 1334, 1458, 1497, 1578, 1606, 1641, 2879, 2964. ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.95 (3H, t, J = 7.4 Hz, C**H**$_3$), 1.88 (2H, app. sextet, J = 7.4 Hz, C**H**$_2$), 4.37 (2H, t, J = 7.4 Hz, C**H**$_2$), 7.72 (1H, dd, J^1 = 7.9 Hz, J^2 = 7.3 Hz, Ar**H**), 7.87 (1H, dd, J^1 = 8.1 Hz, J^2 = 7.5 Hz, Ar**H**), 8.07 (1H, d, J = 8.1 Hz, Ar**H**), 8.29 (1H, d, J = 7.9 Hz, Ar**H**). ^{13}C NMR (100 MHz, $CDCl_3$): δ 11.18 (CH_3), 22.29 (CH_2), 51.44 (CH_2), 119.85 (qC), 125.08 (CH),

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128.20 (CH), 132.21 (CH), 134.68 (CH), 144.33 (qC), 155.54 (C═O). HRMS (ESI$^+$) m/z: found 190.0973 $[M + H]^+$, $C_{10}H_{12}N_3O$ requires 190.0975. Also present was 2-ethylquinazolin-4-one (eluent: petroleum ether/ethyl acetate 1:1, R_f = 0.28) as a light yellow solid (~23% by NMR), which could not be obtained free of 2-aminobenzamide. IR (neat, ν_{max}) cm^{-1}: 1139, 1201, 1251, 1341, 1373, 1467, 1504, 1608, 1619, 1674, 2853, 2922, 3044, 3163. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.17−1.38 (2H, m, **CH$_3$**), 2.78 (2H, d, J = 6.9 Hz, C**H$_2$**), 7.18 (1H, bs, Ar**H**), 7.38−7.40 (1H, m, Ar**H**), 7.64−7.68 (2H, m, 2 × Ar**H**), 8.22 (1H, d, J = 6.8 Hz, Ar**H**), 12.17 (1H, s, N**H**). ^{13}C NMR (100 MHz, $CDCl_3$): δ 11.57 (CH_3), 29.71 (CH_2), 120.50 (qC), 126.23 (CH), 126.33 (CH), 127.22 (CH), 134.78 (CH), 149.54 (qC), 156.78 (qC), 164.57 (C═O). HRMS (ESI$^+$) m/z: found 175.0869 $[M + H]^+$, $C_{10}H_{11}N_2O$ requires 175.0866. The data recorded for 2-ethylquinazolin-4(3*H*)-one are consistent with those published elsewhere.[55]

3-Benzylbenzo[*d*][1,2,3]triazin-4-one (29). To a solution of 2-azidobenzamide (200 mg, 1.23 mmol) and sodium carbonate (392 mg, 3.70 mmol) in anhydrous DMSO (10 mL), benzyl bromide (422 mg, 2.47 mmol) was added. The solution was heated at 95 °C for 48 h under a nitrogen atmosphere, and after completion of the reaction, which was monitored using TLC, the resultant mixture was diluted with dichloromethane (30 mL) and washed with 0.1 M NaCl and water many times to remove DMSO. The mixture was dried with anhydrous magnesium sulfate and filtered under gravity, and the solvent was removed under vacuum. The residue was purified using column chromatography (eluent: petroleum ether/ethyl acetate 4:1, R_f = 0.2) to yield the product as a yellow solid (95 mg, 33%, mp = 110−112 °C; lit.[39] 114−116 °C). IR (neat, ν_{max}) cm^{-1}: 1049, 1086, 1179, 1205, 1295, 1349, 1454, 1492, 1581, 1605, 1682, 3033. ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.65 (2H, s, C**H$_2$**), 7.29−7.38 (3H, m, 3 × Ar**H**), 7.55 (2H, d, J = 6.9 Hz, 2 × Ar**H**), 7.79 (1H, dd, J^1 = 7.7 Hz, J^2 = 7.3 Hz, Ar**H**), 7.94 (1H, dd, J^1 = 8.0 Hz, J^2 = 7.3 Hz, Ar**H**), 8.16 (1H, d, J = 8.0 Hz, Ar**H**), 8.35 (1H, d, J = 7.7 Hz, Ar**H**) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 53.39 (CH_2), 120.10 (qC), 125.18 (qC), 128.23 (CH), 128.33 (CH), 128.73 (2 × CH), 128.87 (2 × CH), 132.36 (CH), 134.82 (CH), 135.76 (qC), 144.34 (qC), 155.39 (C═O) ppm. HRMS (ESI$^+$) m/z: found 238.0977 $[M + H]^+$, $C_{14}H_{12}N_3O$ requires 238.0975.

3-Isopropylbenzo[*d*][1,2,3]triazin-4-one (30). To a solution of 2-azidobenzamide (200 mg, 1.23 mmol) and sodium carbonate (392 mg, 3.70 mmol) in anhydrous DMSO (10 mL), 2-bromopropane (301 mg, 2.47 mmol) was added. The solution was heated at 95 °C for 48 h under a nitrogen atmosphere, and after completion of the reaction, which was monitored using TLC, the resultant mixture was diluted with dichloromethane (30 mL) and washed with 0.1 M NaCl and water many times to remove DMSO. The mixture was dried with anhydrous magnesium sulfate and filtered under gravity, and the solvent was removed under vacuum. The residue was purified using column chromatography (eluent: petroleum ether/ethyl acetate 4:1, R_f = 0.23) to yield the product as a light yellow solid (80 mg, 34%, mp = 47−49 °C). IR (neat, ν_{max}) cm^{-1}: 1016, 1131, 1195, 1266, 1290, 1338, 1386, 1462, 1494, 1608, 1677, 2875, 2976. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.60 (6H, d, J = 6.8 Hz, 2 × C**H$_3$**), 5.45 (1H, sept., J = 6.8 Hz, C**H**), 7.79 (1H, dd, J^1 = 7.8 Hz, J^2 = 7.5 Hz, Ar**H**), 7.94 (1H, dd, J^1 = 7.8 Hz, J^2 = 7.5 Hz, Ar**H**), 8.15 (1H, d, J = 8.1 Hz, Ar**H**), 8.36 (1H, d, J = 8.1 Hz, Ar**H**). ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.61 (2 × CH_3), 49.53 (CH), 119.61 (qC), 125.20 (CH), 128.05 (CH), 132.07 (CH), 134.66 (CH), 144.00 (qC), 155.09 (C═O). HRMS (ESI$^+$) m/z: found 190.0970 $[M + H]^+$, $C_{10}H_{12}N_3O$ requires 190.0975.

3-Cyclohexylbenzo[*d*][1,2,3]triazin-4-one (31). To a solution of 2-azidobenzamide (200 mg, 1.23 mmol) and sodium carbonate (392 mg, 3.70 mmol) in anhydrous DMSO (10 mL), bromocyclohexane (403 mg, 2.47 mmol) was added. The solution was heated at 95 °C for 48 h under a nitrogen atmosphere, and after completion of the reaction, which was monitored using TLC, the resultant mixture was diluted with dichloromethane (30 mL) and washed with 0.1 M NaCl and water many times to remove DMSO. The mixture was dried with anhydrous magnesium sulfate and filtered under gravity, and the solvent was removed under vacuum. The residue was purified using column chromatography (eluent: petroleum ether/ethyl acetate 4:1, R_f = 0.23) to yield the product as a light yellow solid (85 mg, 30%, mp = 137−139 °C). IR (neat, ν_{max}) cm^{-1}: 1064, 1164, 1161, 1181, 1221, 1267, 1292, 1331, 1376, 1460, 1607, 1681, 2851, 2928, 3073. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.17−1.30 (1H, m, CH**H**), 1.39−1.50 (2H, m, C**H$_2$**), 1.68−2.72 (1H, m, C**H**H), 1.86−2.01 (6H, m, 3 × C**H$_2$**), 4.96 (1H, p, J = 7.6 Hz, C**H**), 7.70 (1H, dd, J^1 = 8.0 Hz, J^2 = 7.3 Hz, Ar**H**), 7.85 (1H, ddd, J^1 = 8.1 Hz, J^2 = 8.0 Hz, J^3 = 1.1 Hz, Ar**H**), 8.06 (1H, d, J = 8.0 Hz, Ar**H**), 8.28 (1H, d, J = 8.1 Hz, Ar**H**). ^{13}C NMR (100 MHz, $CDCl_3$): δ 25.31 (CH_2), 25.80 (2 × CH_2), 56.64 (2 × CH_2), 119.60 (qC), 123.01 (qC), 125.27 (CH), 128.02 (CH), 132.00 (CH), 134.62 (CH), 143.88 (qC), 155.12 (C═O). HRMS (ESI$^+$) m/z: found 230.1285 $[M + H]^+$, $C_{13}H_{16}N_3O$ requires 230.1288.

3-(2-Methylallyl)benzo[*d*][1,2,3]triazin-4-one (32). To a solution of 2-azidobenzamide (200 mg, 1.23 mmol) and sodium carbonate (392 mg, 3.70 mmol) in anhydrous DMSO (10 mL), 3-bromo-2-methylpropene (333 mg, 2.47 mmol) was added. The solution was heated at 95 °C for 48 h under a nitrogen atmosphere, and after completion of the reaction, which was monitored using TLC, the resultant mixture was diluted with dichloromethane (30 mL) and washed with 0.1 M NaCl and water many times to remove DMSO. The mixture was dried with anhydrous magnesium sulfate and filtered under gravity, and the solvent was removed under vacuum. The residue was purified using column chromatography (eluent: petroleum ether/ethyl acetate 4:1, R_f = 0.21) to yield the product as a light orange solid (90 mg, 36%, mp = 69−71 °C). IR (neat, ν_{max}) cm^{-1}: 1089, 1153, 1223, 1276, 1297, 1333, 1463, 1580, 1609, 1684, 2930, 2973, 3083. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.84 (3H, s, C**H$_3$**), 4.85 (1H, s, ═CH**H**), 5.00 (H, s, ═CH**H**), 5.03 (2H, s, C**H$_2$**), 7.83 (1H, ddd, J^1 = 8.1 Hz, J^2 = 8.0 Hz, J^3 = 1.1 Hz, Ar**H**), 7.97 (1H, ddd, J^1 = 8.1 Hz, J^2 = 8.0 Hz, J^3 = 1.1 Hz, Ar**H**), 8.18 (1H, d, J = 8.1 Hz, Ar**H**), 8.38 (1H, dd, J^1 = 8.1 Hz, J^2 = 1.0 Hz, Ar**H**). ^{13}C NMR (100 MHz, $CDCl_3$): δ 20.45 (CH_3), 54.77 (CH_2), 113.54 (CH_2), 119.88 (qC), 125.22 (CH), 128.33 (CH), 132.38 (CH), 134.84 (CH), 139.51 (qC), 144.29 (qC), 155.43 (C═O). HRMS (ESI$^+$) m/z: found 202.0975 $[M + H]^+$, $C_{11}H_{12}N_3O$ requires 202.0975.

3-(2-Methylallyl)benzo[*d*][1,2,3]triazin-4-one (32): Method 2—from 2-Bromo-2-methylpropane. To a solution of 2-azidobenzamide (250 mg, 1.54 mmol) and sodium carbonate (490 mg, 4.63 mmol) in anhydrous DMSO (15 mL), 2-bromo-2-methylpropane (425 mg, 3.10 mmol) was added. The solution was heated at 95 °C for 45 h under a nitrogen atmosphere, and the resultant mixture was diluted with dichloromethane (50 mL) and washed with 0.1 M NaCl

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and water many times to remove DMSO. The mixture was dried with anhydrous magnesium sulfate and filtered under gravity, and the solvent was removed under vacuum. The residue was purified using column chromatography (eluent: petroleum ether/ethyl acetate 4:1, R_f = 0.21) to yield the product as a light yellow oil (94 mg, 30%) with identical spectroscopic data to those reported above.

2-Azido-*N*,*N*-dibutylbenzamide (40). 2-Azidobenzamide (98 mg, 0.60 mmol), KOH (50 mg, 0.90 mmol), and TBAB (58 mg, 0.18 mmol) were mixed and stirred for 15 min at room temperature, and then, 1-bromobutane (102 mg, 81 μL, 0.75 mmol) was added. The mixture was heated at 80 °C in an oil bath for 15 min. The crude mixture was diluted with water (10 mL) and then extracted with dichloromethane (3 × 10 mL). The organic layer was dried with anhydrous magnesium sulfate and filtered, and the solvent was removed in vacuo. Purification using silica chromatography (eluent: petroleum ether/ethyl acetate 2:1, R_f = 0.25) yielded the product as a yellow oil (115 mg, 70%). IR (neat, ν_{max}) cm^{-1}: 1081, 1118, 1201, 1289, 1425, 1444, 1577, 1598, 1633, 2091, 2873, 2931, 2957. ^1H NMR (400 MHz, $CDCl_3$): δ 0.68 (3H, t, J = 7.3 Hz, C***H***$_3$), 0.90 (3H, t, J = 7.3 Hz, C***H***$_3$), 1.04 (2H, app. Sextet, J = 7.3 Hz, C***H***$_2$), 1.29−1.38 (4H, m, 2 × C***H***$_2$), 1.57 (2H, app. Pentet, J = 7.6 Hz, C***H***$_2$), 2.96−2.98 (2H, m, C***H***$_2$), 3.29 (1H, br s, CH***H***), 3.54 (1H, br s, C***H***H), 7.06−7.14 (3H, m, 3 × Ar***H***), 7.31 (1H, ddd, J^1 = 8.2 Hz, J^2 = 8.0 Hz, J^3 = 1.4 Hz, Ar***H***). ^{13}C NMR (100 MHz, $CDCl_3$): δ 13.56 (CH_3), 13.93 (CH_3), 19.70 (CH_2), 20.25 (CH_2), 29.51 (CH_2), 30.55 (CH_2), 44.22 (CH_2), 48.18 (CH_2), 118.41 (CH), 124.93 (CH), 127.87 (CH), 129.44 (qC), 129.95 (CH), 136.17 (qC), 168.19 (C═O). HRMS (ESI^+) m/z: found 275.1860 $[M + H]^+$, $C_{15}H_{23}N_4O$ requires 275.1866.

3-Butyl-2-propyl-2,3-dihydroquinazolin-4-one (41). To a solution of 2-azido-*N*,*N*-dibutylbenzamide (98 mg, 0.36 mmol) and sodium carbonate (114 mg, 1.07 mmol) in anhydrous DMSO (8 mL), 2-bromopropane (88 mg, 67 μL, 0.72 mmol) was added. The solution was heated at 95 °C for 48 h under a nitrogen atmosphere, and after completion of the reaction, which was monitored using TLC, there was no product. The reaction mixture was heated at 120 °C for 48 h, and after completion of the reaction, which was monitored using TLC, the resultant mixture was diluted with dichloromethane (30 mL) and washed with 0.1 M NaCl and water many times to remove DMSO. The mixture was dried with anhydrous magnesium sulfate and filtered under gravity, and the solvent was removed under vacuum. The residue was purified using column chromatography (eluent: petroleum ether/ethyl acetate 2:1, R_f = 0.21) to yield the product as a yellow oil (55 mg, 63%). IR (neat, ν_{max}) cm^{-1}: 1028, 1153, 1169, 1322, 1464, 1509, 1580, 1610, 2872, 2930, 2957, 3284. ^1H NMR (400 MHz, $CDCl_3$): δ 0.84 (6H, 2 × t, J = 7.2 Hz, 2 × C***H***$_3$), 1.15−1.24 (1H, m, C***H***H), 1.29−1.36 (3H, m, C***H***$_2$ + CH***H***), 1.50−1.59 (3H, m, C***H***$_2$ + C***H***H), 1.74−1.84 (1H, m, C***H***H), 2.76 (1H, dt, J = 13.7, 7.1 Hz, NCH***H***), 4.04 (1H, dt, J = 13.7, 7.5 Hz, NC***H***H), 4.48−4.50 (2H, m, C***H*** + N***H***), 6.55 (1H, d, J = 8.0 Hz, Ar***H***), 6.75 (1H, ddd, J^1 = 7.8 Hz, J^2 = 7.6 Hz, J^3 = 1.2 Hz, Ar***H***), 7.16−7.20 (1H, m, Ar***H***), 7.81 (1H, dd, J^1 = 7.8 Hz, J^2 = 1.2 Hz, Ar***H***). ^{13}C NMR (100 MHz, $CDCl_3$): δ 13.68 (CH_3), 13.89 (CH_3), 18.64 (CH_2), 20.15 (CH_2), 30.48 (CH_2), 35.48 (CH_2), 44.88 (CH_2), 69.25 (CH), 114.81 (CH), 117.14 (qC), 118.41 (CH), 128.41 (CH), 133.06 (CH), 145.06 (qC), 162.34 (C═O). HRMS (ESI^+) m/z: found 247.1802 $[M + H]^+$, $C_{13}H_{16}N_3O$ requires 247.1805.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acsomega.7b00211.

Copies of ^1H and ^{13}C NMR spectra for the compounds **5**, **6**, **7**, **16**, **3**, **21**, **22**, **24**, **26**−**33**, **40**, and **41** (PDF)

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Notes

The authors declare no competing financial interest.

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