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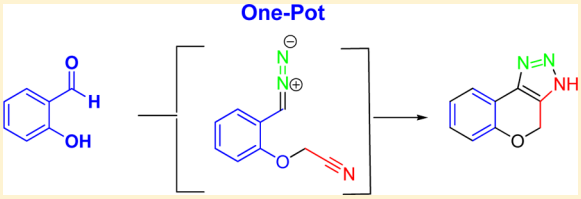
A Step-Economical Route to Fused 1,2,3-Triazoles via an Intramolecular 1,3-Dipolar Cycloaddition between a Nitrile and an in Situ Generated Aryldiazomethane

Neelakandha S. Mani* and Anne E. Fitzgerald

Janssen Research & Development, LLC, 3210 Merryfield Row, San Diego, California 92121, United States

Supporting Information

ABSTRACT: An intramolecular 1,3-dipolar cycloaddition strategy for rapid entry into triazole-fused heterocyclic compounds without recourse to the traditional Cu(1)-catalyzed azide−alkyne cycloadditions is described. Central to the strategy is the in situ generation of substituted diazomethanes in a two-step sequence from the corresponding aldehydes, which then undergo smooth cycloaddition with a cyano group to generate the desired fused 1,2,3-triazoles in good overall yields. The entire sequence can be carried out in a one-pot operation.

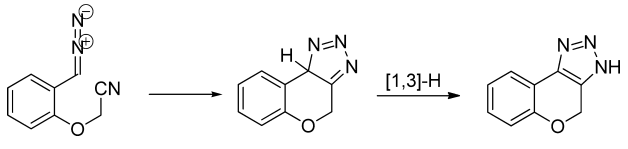


Fused 1,2,3-triazoles are structural motifs increasingly found in a wide array of bioactive molecules in medicinal chemistry.[1] As a result, there is considerable interest in developing synthetic methods for their facile construction. One of the most popular "click chemistry" reactions,[2a] the copper-catalyzed cycloaddition of azides with terminal alkynes (CuAAC), developed by Sharpless and Fokin and co-workers,[2b] and independently by Meldal et al.,[2c] is a powerful tool for the construction of 1,2,3-triazoles. However, due to the attenuated reactivity of disubstituted alkynes toward azides as well as the possibility of formation of regioisomers, this mode of assembly is not particularly suited for the synthesis of 4,5-disubstituted triazoles.[3] Thus, to take advantage of this facile dipolar cycloaddition for the synthesis of annulated 1,2,3-triazoles, one has to resort to additional substitution at the 4/5-position and cyclization manipulations. As a result, early methodologies were based on cycloaddition of azides with other reactive dipolarophiles, such as enolates,[4] enol ethers,[5] nitroalkenes,[6] and vinyl sulfones,[7] that function as disubstituted acetylene surrogates. Recently, Ackermann and colleagues reported a useful strategy to annulated 1,2,3-triazoles where a click reaction was employed to initially generate the 1,4-disubstituted triazole, which was then followed by an intramolecular dehydrogenative coupling sequence using a Pd^{2+}−Cu^{2+} catalytic system under ambient pressure of air to prepare a number of annulated triazoles.[8] More recently, Lautens et al.[9] followed up on this strategy to develop an elegant palladium-catalyzed, intramolecular cyclization of 5-iodotriazoles to form a number of benzopyranotriazoles. Using a related approach, Reddy and Swamy[10] recently reported a copper-catalyzed tandem, one-pot click-intramolecular arylation reaction sequence to prepare several benzopyran fused 1,2,3-triazoles.

Cycloaddition of diazomethane derivatives to substituted nitriles is another approach to triazoles, first reported by Huisgen.[11] However, poor reactivity of unactivated nitriles toward diazocompounds limited their wider utility in triazole synthesis.[11] We, however, speculated that an intramolecular variant of this reaction might still be feasible and, if successful, could provide a useful entry to a wide variety of annulated 1,2,3-triazoles. Padwa and Sakac and co-workers have shown that diazoalkanes generated from the decomposition of tosylhydrazones can indeed undergo intramolecular cycloadditions with unactivated olefinic and nitrile groups.[12] Recently, we reported a facile one-pot construction of fused pyrazoles based on an intramolecular cycloaddition of in situ generated aryl diazomethane and an internal dichlorovinyl ether.[13] On the basis of this work, we hypothesized that a similar intramolecular cycloaddition between a suitably placed nitrile and an in situ generated aryldiazomethane should form the triazoline adduct, which would then undergo a facile [1,3]-proton transfer, leading to a variety of annulated triazoles such as benzopyran fused 1,2,3-triazoles—one of the triazole skeletons keenly investigated by Ackermann, Lautens, and others (Scheme 1).[8−10]

Aryl diazomethanes can be generated under mild conditions by the base-mediated decomposition of the corresponding aryl sulfonyl hydrazones.[14] The hydrazones, in turn, are readily accessed from the corresponding aldehydes. We have shown that this sequence of reactions can be carried out in a one-pot

Scheme 1. Intramolecular Cycloaddition Strategy



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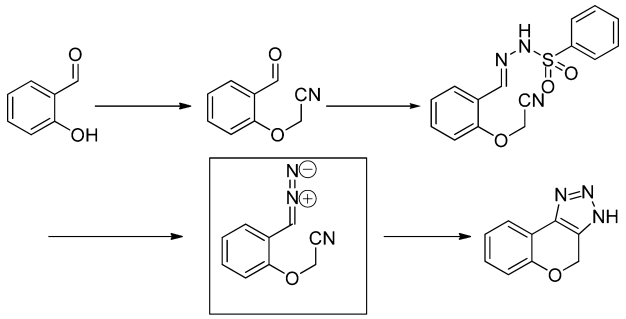
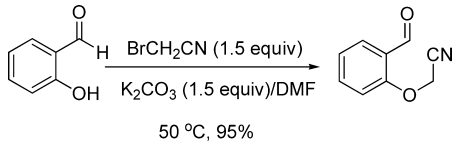
operation starting from the aldehyde under very mild conditions. To test the intramolecular cycloaddition reaction, we chose to introduce the nitrile group by reaction of bromoacetonitrile with a salicylaldehyde (Scheme 2).

Scheme 2. Proposed Route to Fused Triazoles



Thus, reacting salicyladehyde with bromoacetonitrile in DMF using potassium carbonate as the base at 50 °C furnished the desired *O*-alkylated benzaldehyde in very good yield (Scheme 3).

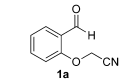
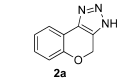
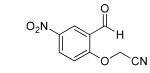
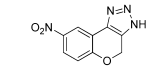
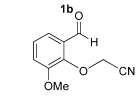
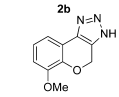
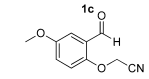
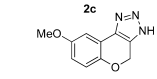
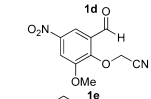
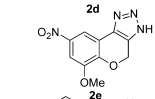
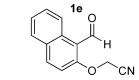
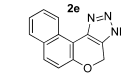
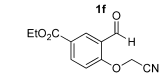
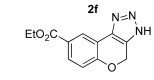
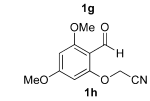
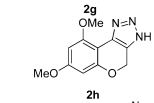
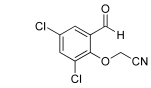
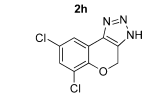
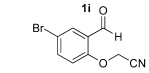
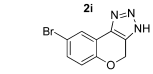
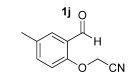
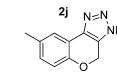
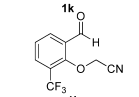
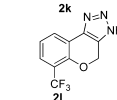
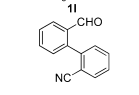
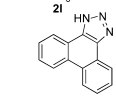
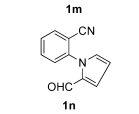
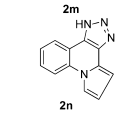
Scheme 3. Synthesis of 2-(2-Formylphenoxy) Acetonitrile



With the cyanomethoxy substituted benzaldehyde substrate in hand, we examined the intramolecular cycloaddition reaction by generating the aryl diazomethane. Thus, reaction of the aldehyde with phenylsulfonyl hydrazine in acetonitrile at room temperature resulted in the smooth conversion to the hydrazone, as indicated by TLC. Adding a slight excess of K_2CO_3 and heating the reaction mixture to about 50 °C resulted in the formation of a diazo compound and concomitant cyclization to form the 1,4-dihydrochromene-[3,4-*d*]-1,2,3-triazole in excellent yields (Scheme 4).

With this encouraging result, we examined the scope of the reaction sequence, and the results are outlined in Table 1. The needed substrates were easily prepared by the reaction of the corresponding salicylaldehyde derivatives with bromoacetonitrile.[15] Very good yields of the triazoles were obtained in all cases. In the case of a strongly electron-withdrawing substituent (entry 2), a slightly lower yield was observed. Among the various solvents examined, DMF and THF were found to be most ideal for this reaction. Protic solvents such as ethanol and isopropanol gave considerably diminished yields. In addition to benzopyranotriazoles, this methodology also appears to have considerable scope in preparing a variety of fused triazole derivatives, as exemplified by the successful synthesis of a triazolophenanthrene and triazoloquinoline (entries 13 and 14).

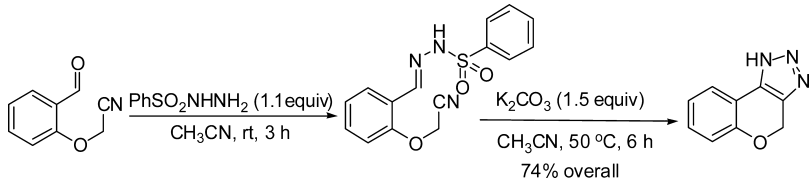
Table 1. Synthesis of Fused Triazoles

Entry	Substrate	Product	Yield (%)
1			74
2			60
3			99
4			96
5			82
6			95
7			85
8			99
9			84
10			81
11			93
12			93
13			95
14			75

derivatives, as exemplified by the successful synthesis of a triazolophenanthrene and triazoloquinoline (entries 13 and 14).

Since the cyanomethyl ether formation as well as the dipolar cycloadditions were carried out under basic conditions, we reasoned that, by optimizing the first step using just 1 equiv of

Scheme 4. Synthesis of 1,4-Dihydrochromene[3,4-*d*]-1,2,3-triazole



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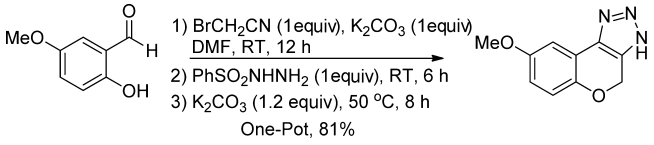
the bromoacetonitrile, we should be able to carry out the entire synthetic sequence in a one-pot operation. This indeed proved to be quite an efficient process in our test experiment, as outlined in Scheme 5

Scheme 5. One-Pot Synthesis of Benzopyran Fused Triazoles



Initial alkylation was carried out using 1 equiv of bromoacetonitrile in DMF. After the reaction was judged complete by TLC, benzenesulfonyl hydrazine was added to form the hydrazone, which, on heating with K_2CO_3, cleanly formed the desired triazole in excellent yield.

In conclusion, we have developed an efficient route to fused triazoles using an intramolecular 1,3-dipolar cycloaddition strategy. Our one-pot strategy employs mild conditions, starts from readily available starting materials, and does not involve toxic heavy metal catalysts. This concise, step-economical route should complement previously reported methods for this important class of compounds.

EXPERIMENTAL SECTION

General Experimental Methods. Reagents were purchased from commercial suppliers and used without purification unless otherwise noted. ^{1}H NMR (400, 500, 600 MHz) and ^{13}C NMR (101, 126, 150 MHz) spectra were acquired on a 400, 500, or 600 NMR spectrometer. Chemical shifts (δ) are reported in parts per million downfield from an internal tetramethylsilane standard. Spin multiplets are given as s (singlet), d (doublet), t (triplet), q (quartet), and m (multiplet). Coupling constants (J) are given in hertz (Hz). Mass spectra were recorded using electrospray ionization (ESI) or electron impact ionization (EI) in either positive or negative mode as indicated. Melting points were recorded on DSC (method: 10 °C/min to 275 °C), except for i, ii, iii, and iv were taken on an electrothermal melting point apparatus and are uncorrected. HPLC Conditions: 35 °C, 0.75 mL/min; Eclipse XDB-C8, 5 μm, 4.6 × 150 mm; Gradient: 5−99% CH_3CN (0.05% TFA) in H_2O (0.05% TFA) 3.8 min; then 99% CH_3CN (0.05% TFA) in H_2O (0.05% TFA) 0.6 min; then 99−5% CH_3CN (0.05% TFA) in H_2O (0.05% TFA) 0.6 min.

General Procedure for the *O*-Alkylation of Salicylaldehydes. The salicylaldehyde was dissolved in DMF. Bromoacetonitrile and potassium carbonate were added, and the reaction mixture was heated to 50 °C and stirred for 8 h. After cooling down to room temperature, the reaction mixture was concentrated under reduced pressure. The residue was treated with water and extracted with ethyl acetate. The combined organic layers were washed with brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. Subsequent flash column chromatography with ethyl acetate−hexanes yielded the corresponding *O*-alkylated salicylaldehydes.

*2-(2-Formylphenoxy)acetonitrile (**1a**).* According to the general procedure, the corresponding salicylaldehyde (400.0 mg, 3.28 mmol), bromoacetonitrile (370.9 mg, 4.91 mmol), and potassium carbonate (679.0 mg, 4.91 mmol) were reacted in DMF (5 mL) at 50 °C for 8 h. Subsequent workup and flash column chromatography yielded 310.0 mg of the title compound as a white solid in 59% yield. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 10.44 (d, J = 0.8 Hz, 1H), 7.91 (dd, J = 7.7, 1.8 Hz, 1H), 7.64 (ddd, J = 8.4, 7.4, 1.8 Hz, 1H), 7.22 (tt, J = 7.5, 0.9 Hz, 1H), 7.09 (dd, J = 8.4, 0.8 Hz, 1H), 4.93 (s, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 188.6, 158.3, 136.0, 129.5, 125.7, 123.3, 114.5, 112.7, 53.8; Mp 84.5 °C; HRMS (ESI-qTOF) Calcd for $C_9H_8NO_2$ [M + H]$^+$, 162.0550: found 162.0548; HPLC retention time: 2.45 min.

*2-(2-Formyl-4-nitrophenoxy)acetonitrile (**1b**).* According to the general procedure, the corresponding salicylaldehyde (250.0 mg, 1.50 mmol), bromoacetonitrile (269.2 mg, 2.24 mmol), and potassium carbonate (310.1 mg, 2.24 mmol) were reacted in DMF (5 mL) at 50 °C for 8 h. Subsequent workup and flash column chromatography yielded 300.0 mg of the title compound as a white solid in 97% yield. ^{1}H NMR (600 MHz, Chloroform-*d*) δ 10.44 (s, 1H), 8.77 (d, J = 2.9 Hz, 1H), 8.53 (dd, J = 9.1, 2.9 Hz, 1H), 7.24 (d, J = 9.1 Hz, 1H), 5.06 (s, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 186.1, 161.5, 143.4, 130.6, 125.7, 125.3, 113.2, 112.8, 54.0; Mp 117−118 °C (lit[15] Mp 115−117 °C); HPLC retention time: 2.58 min.

*2-(2-Formyl-6-methoxyphenoxy)acetonitrile (**1c**).* According to the general procedure, the corresponding salicylaldehyde (250.0 mg, 1.64 mmol), bromoacetonitrile (295.6 mg, 2.47 mmol), and potassium carbonate (340.6 mg, 2.47 mmol) were reacted in DMF (5 mL) at room temperature for 8 h. Subsequent workup and flash column chromatography yielded 270.0 mg of the title compound as a white solid in 86% yield. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 10.43 (d, J = 0.8 Hz, 1H), 7.48 (dd, J = 7.6, 1.8 Hz, 1H), 7.29−7.19 (m, 2H), 4.99 (s, 2H), 3.95 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 186.6, 152.6, 152.2, 145.1, 129.8, 115.7, 114.3, 112.1, 58.0, 57.0; Mp 121.0 °C; HRMS (ESI-qTOF) Calcd for $C_{10}H_{10}NO_3$ [M + H]$^+$, 192.0655: found 192.0640; HPLC retention time: 2.61 min.

*2-(2-Formyl-4-methoxyphenoxy)acetonitrile (**1d**).* According to the general procedure, the corresponding salicylaldehyde (250.0 mg, 1.64 mmol), bromoacetonitrile (295.6 mg, 2.47 mmol), and potassium carbonate (340.6 mg, 2.47 mmol) were reacted in DMF (5 mL) at room temperature for 8 h. Subsequent workup and flash column chromatography yielded 300.0 mg of the title compound as a white solid in 95% yield. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 10.38 (d, J = 1.4 Hz, 1H), 7.37 (dd, J = 3.3, 1.7 Hz, 1H), 7.18 (ddd, J = 9.1, 3.2, 1.4 Hz, 1H), 7.06 (dd, J = 9.1, 1.0 Hz, 1H), 4.89 (s, 2H), 3.83 (d, J = 1.4 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 188.4, 155.6, 152.8, 126.6, 122.8, 115.4, 114.7, 111.9, 55.9, 55.1; Mp 73.9 °C; HRMS (ESI-qTOF) Calcd for $C_{10}H_{10}NO_3$ [M + H]$^+$, 192.0655: found 192.0654; HPLC retention time: 2.59 min.

*2-(2-Formyl-6-methoxy-4-nitrophenoxy)acetonitrile (**1e**).* According to the general procedure, the corresponding salicylaldehyde (250.0 mg, 1.27 mmol), bromoacetonitrile (228.2 mg, 1.90 mmol), and potassium carbonate (262.9 mg, 1.90 mmol) were reacted in DMF (5 mL) at room temperature for 8 h. Subsequent workup and flash column chromatography yielded 270.0 mg of the title compound as a white solid in 90% yield. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 10.43 (s, 1H), 8.37 (d, J = 2.6 Hz, 1H), 8.04 (d, J = 2.7 Hz, 1H), 5.13 (s, 2H), 4.08 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 188.9, 152.2, 148.1, 130.2, 125.9, 120.2, 118.3, 115.0, 58.0, 56.3; Mp 127.4 °C; HRMS (ESI-qTOF) Calcd for $C_{10}H_9N_2O_5$ [M + H]$^+$, 237.0506: found 237.0501; HPLC retention time: 2.80 min.

*2-((1-Formylnaphthalen-2-yl)oxy)acetonitrile (**1f**).* According to the general procedure, the corresponding salicylaldehyde (250.0 mg, 1.45 mmol), bromoacetonitrile (261.2 mg, 2.18 mmol), and potassium carbonate (301.0 mg, 2.18 mmol) were reacted in DMF (5 mL) at room temperature for 8 h. Subsequent workup and flash column chromatography yielded 300.0 mg of the title compound as a white solid in 98% yield. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 10.88 (s, 1H), 9.24 (dd, J = 8.7, 1.0 Hz, 1H), 8.15 (d, J = 9.0 Hz, 1H), 7.88−7.81 (m, 1H), 7.69 (ddd, J = 8.6, 6.9, 1.4 Hz, 1H), 7.52 (ddd, J = 8.2, 6.9, 1.2 Hz, 1H), 7.33 (d, J = 9.0 Hz, 1H), 5.03 (s, 2H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 190.8, 160.1, 137.7, 131.5, 130.4, 130.0, 128.4, 126.0, 125.3, 119.0, 114.4, 113.1, 55.1; Mp 168.8 °C; HRMS (ESI-TOF) Calcd for $C_{13}H_{10}NO_2$ [M + H]$^+$, 212.0706: found 212.0706; HPLC retention time: 3.01 min.

*Ethyl 4-(Cyanomethoxy)-3-formylbenzoate (**1g**).* According to the general procedure, the corresponding salicylaldehyde (250.0 mg, 1.29 mmol), bromoacetonitrile (231.6 mg, 1.93 mmol), and potassium carbonate (266.9 mg, 1.93 mmol) were reacted in DMF (5 mL) at room temperature for 8 h. Subsequent workup and flash column chromatography yielded 260.0 mg of the title compound as a white solid in 87% yield. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 10.44 (s, 1H), 8.57 (d, J = 2.3 Hz, 1H), 8.33 (dd, J = 8.7, 2.3 Hz, 1H), 7.13 (d, J

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= 8.8 Hz, 1H), 5.00 (s, 2H), 4.40 (q, J = 7.1 Hz, 2H), 1.41 (t, J = 7.1 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 187.6, 164.9, 160.9, 137.1, 131.4, 126.1, 125.5, 113.8, 112.3, 61.5, 53.8, 14.3; Mp 99.2 °C; HRMS (ESI-TOF) Calcd for $C_{12}H_{12}NO_4$ $[M + H]^+$, 234.0761: found 234.0749; HPLC retention time: 2.82 min.

*2-(2-Formyl-3,5-dimethoxyphenoxy)acetonitrile (**1h**).* According to the general procedure, the corresponding salicylaldehyde (500.0 mg, 2.75 mmol), bromoacetonitrile (493.8 mg, 4.12 mmol), and potassium carbonate (569.0 mg, 4.12 mmol) were reacted in DMF (5 mL) at 50 °C for 8 h. Subsequent workup and flash column chromatography yielded 575.0 mg of the title compound as a white solid in 95% yield. ^{1}H NMR (400 MHz, Chloroform-d) δ 10.32 (s, 1H), 6.23 (dd, J = 13.2, 2.1 Hz, 2H), 4.86 (s, 2H), 3.91 (d, J = 5.6 Hz, 6H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 187.0, 166.1, 164.8, 160.0, 114.8, 110.3, 94.7, 93.5, 56.2, 55.8, 55.4; Mp 103−104 °C; HRMS (ESI-TOF) Calcd for $C_{11}H_{12}NO_4$ $[M + H]^+$, 222.0761: found 222.0745; HPLC retention time: 2.33 min.

*2-(2,4-Dichloro-6-formylphenoxy)acetonitrile (**1i**).* According to the general procedure, the corresponding salicylaldehyde (250.0 mg, 1.31 mmol), bromoacetonitrile (235.5 mg, 1.96 mmol), and potassium carbonate (271.3 mg, 1.96 mmol) were reacted in DMF (5 mL) at room temperature for 8 h. Subsequent workup and flash column chromatography yielded 280.0 mg of the title compound as a white solid in 93% yield. ^{1}H NMR (400 MHz, Chloroform-d) δ 10.31 (s, 1H), 7.80 (d, J = 2.6 Hz, 1H), 7.70 (d, J = 2.6 Hz, 1H), 4.97 (s, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 186.5, 153.0, 136.0, 132.7, 131.8, 129.4, 128.2, 114.0, 58.8; Mp 103.4 °C; HRMS (ESI-qTOF) Calcd for $C_9H_6Cl_2NO_2$ $[M + H]^+$, 229.9770: found 229.9767; HPLC retention time: 3.16 min.

*2-(4-Bromo-2-formylphenoxy)acetonitrile (**1j**).* According to the general procedure, the corresponding salicylaldehyde (400.0 mg, 1.99 mmol), bromoacetonitrile (225.3 mg, 2.99 mmol), and potassium carbonate (412.5 mg, 2.99 mmol) were reacted in DMF (5 mL) at 50 °C for 8 h. Subsequent workup and flash column chromatography yielded 350.0 mg of the title compound as a white solid in 73% yield. ^{1}H NMR (500 MHz, Chloroform-d) δ 10.36 (s, 1H), 8.01 (d, J = 2.6 Hz, 1H), 7.73 (dd, J = 8.8, 2.6 Hz, 1H), 6.99 (d, J = 8.8 Hz, 1H), 4.92 (s, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 187.0, 157.1, 138.4, 132.2, 127.0, 116.5, 114.6, 114.0, 54.0; Mp 92−93 °C; HRMS (ESI-qTOF) Calcd for $C_9H_7BrNO_2$ $[M + H]^+$, 239.9655: found 239.9652; HPLC retention time: 2.95 min.

*2-(2-Formyl-4-methylphenoxy)acetonitrile (**1k**).* According to the general procedure, the corresponding salicylaldehyde (250.0 mg, 1.84 mmol), bromoacetonitrile (330.4 mg, 2.75 mmol), and potassium carbonate (380.7 mg, 2.75 mmol) were reacted in DMF (5 mL) at 50 °C for 8 h. Subsequent workup and flash column chromatography yielded 310.0 mg of the title compound as a white solid in 96% yield. ^{1}H NMR (400 MHz, Chloroform-d) δ 10.40 (s, 1H), 7.70 (d, J = 2.3 Hz, 1H), 7.43 (dd, J = 8.6, 2.4 Hz, 1H), 6.98 (d, J = 8.4 Hz, 1H), 4.90 (s, 2H), 2.36 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 188.7, 156.4, 136.5, 133.3, 129.8, 125.7, 114.5, 113.2, 54.3, 20.4; Mp 70.2 °C; HRMS (ESI-TOF) Calcd for $C_{10}H_{10}NO_2$ $[M + H]^+$, 176.0706: found 176.0699; HPLC retention time: 2.75 min.

*2-(2-Formyl-6-(trifluoromethyl)phenoxy)acetonitrile (**1l**).* According to the general procedure, the corresponding salicylaldehyde (250.0 mg, 1.32 mmol), bromoacetonitrile (236.6 mg, 1.97 mmol), and potassium carbonate (272.6 mg, 1.97 mmol) were reacted in DMF (5 mL) at room temperature for 8 h. Subsequent workup and flash column chromatography yielded 275.0 mg of the title compound as a white solid in 91% yield. ^{1}H NMR (400 MHz, Chloroform-d) δ 10.29 (s, 1H), 8.11 (dd, J = 7.8, 1.8 Hz, 1H), 7.94 (dd, J = 7.8, 1.7 Hz, 1H), 7.54 (t, J = 7.8 Hz, 1H), 4.92 (s, 2H); ^{13}C NMR (151 MHz, Chloroform-d) δ 188.0, 156.0, 136.0, 133.2 (q, J = 4.8 Hz), 130.5, 126.3, 114.1, 60.7; Mp 116.5 °C; HRMS (ESI-qTOF) Calcd for $C_{10}H_7F_3NO_2$ $[M + H]^+$, 230.0423: found 230.0419; HPLC retention time: 2.95 min.

General Procedure for the Synthesis of Fused 1,2,3-Triazoles (Table 1). The aldehyde was dissolved in THF. Benzenesulfonyl hydrazine and potassium carbonate were added, and the mixture was stirred at room temperature for 3 h and then heated to 50 °C until complete transformation to the desired triazole. After cooling down to room temperature, water was added, and extracted with MTBE. The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified by flash column chromatography with ethyl acetate−hexanes to afford the corresponding annulated 1,2,3-triazoles.

*3,4-Dihydrochromeno[3,4-d][1,2,3]triazole (**2a**).* According to the general procedure, the corresponding aldehyde (100 mg, 0.621 mmol), benzenesufonyl hydrazide (122.9 mg, 0.714 mmol), and potassium carbonate (128.6 mg, 0.931 mmol) were reacted in acetonitrile (2 mL) at room temperature for 14 h and then heated to 50 °C for 4 h. Subsequent workup and flash chromatography yielded 80.0 mg of the title compound as a white solid in 74% yield. ^{1}H NMR (400 MHz, Methanol-d_4) δ 7.65 (d, J = 7.6 Hz, 1H), 7.27−7.20 (m, 1H), 7.06−6.95 (m, 2H), 5.44 (s, 2H); ^{13}C NMR (151 MHz, MeOD) δ 131.1, 123.8, 123.3, 118.4, 64.9; Mp 156.6 °C; HRMS (ESI-TOF) Calcd for $C_9H_8N_3O$ $[M + H]^+$, 174.0662: found 174.0678; HPLC retention time: 2.41 min.

*8-Nitro-3,4-dihydrochromeno[3,4-d][1,2,3]triazole (**2b**).* According to the general procedure, the corresponding aldehyde (174.4 mg, 0.846 mmol), benzenesufonyl hydrazide (174.8 mg, 1.01 mmol), and potassium carbonate (233.8 mg, 1.692 mmol) were reacted in THF (2 mL) at room temperature for 3 h and then heated to 50 °C overnight. Subsequent workup and flash chromatography yielded 111.3 mg of the title compound as a yellow solid in 60% yield. ^{1}H NMR (600 MHz, Methanol-d_4) δ 8.52 (t, J = 2.3 Hz, 1H), 8.14 (dt, J = 9.1, 2.4 Hz, 1H), 7.13 (dd, J = 9.1, 1.9 Hz, 1H), 5.65 (d, J = 3.7 Hz, 2H); Mp 266.0 °C; HRMS (ESI-TOF) Calcd for $C_9H_7N_4O_3$ $[M + H]^+$, 219.0513: found 219.0513; HPLC retention time: 2.51 min.

*6-Methoxy-3,4-dihydrochromeno[3,4-d][1,2,3]triazole (**2c**).* According to the general procedure, the corresponding aldehyde (100 mg, 0.523 mmol), benzenesufonyl hydrazide (108.1 mg, 0.628 mmol), and potassium carbonate (144.6 mg, 1.046 mmol) were reacted in THF (1 mL) at room temperature for 3 h and then heated to 50 °C overnight. Subsequent workup and flash chromatography yielded 105.4 mg of the title compound as a light yellow solid in 99% yield. ^{1}H NMR (500 MHz, Methanol-d_4) δ 7.28 (dd, J = 7.0, 2.1 Hz, 1H), 7.03−6.96 (m, 2H), 5.45 (s, 2H), 3.86 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 149.0, 143.0, 122.3, 116.8, 115.3, 112.7, 64.3, 56.1; Mp 203.3 °C; HRMS (ESI-qTOF) Calcd for $C_{10}H_{10}N_3O_2$ $[M + H]^+$, 204.0768: found 204.0774; HPLC retention time: 2.18 min.

*8-Methoxy-3,4-dihydrochromeno[3,4-d][1,2,3]triazole (**2d**).* According to the general procedure, the corresponding aldehyde (150 mg, 0.785 mmol), benzenesufonyl hydrazide (162.1 mg, 0.941 mmol), and potassium carbonate (216.9 mg, 1.569 mmol) were reacted in THF (1 mL) at room temperature for 3 h and then heated to 50 °C overnight. Subsequent workup and flash chromatography yielded 153.8 mg of the title compound as a white solid in 96% yield. ^{1}H NMR (400 MHz, Methanol-d_4) δ 7.20 (d, J = 3.0 Hz, 1H), 6.92−6.79 (m, 2H), 5.35 (s, 2H), 3.79 (s, 3H); ^{13}C NMR (151 MHz, MeOD) δ 156.4, 149.0, 119.2, 116.9, 108.2, 64.6, 56.1; Mp 175.6 °C; HRMS (ESI-TOF) Calcd for $C_{10}H_{10}N_3O_2$ $[M + H]^+$, 204.0768: found 204.0761; HPLC retention time: 2.45 min.

*6-Methoxy-8-nitro-3,4-dihydrochromeno[3,4-d][1,2,3]triazole (**2e**).* According to the general procedure, the corresponding aldehyde (100 mg, 0.423 mmol), benzenesufonyl hydrazide (87.5 mg, 0.508 mmol), and potassium carbonate (117.0 mg, 0.847 mmol) were reacted in THF (1 mL) at room temperature for 3 h and then heated to 50 °C overnight. Subsequent workup and flash chromatography yielded 86.4 mg of the title compound as a yellow solid in 82% yield. ^{1}H NMR (400 MHz, Methanol-d_4) δ 8.18 (d, J = 2.6 Hz, 1H), 7.80 (d, J = 2.6 Hz, 1H), 5.65 (s, 2H), 3.95 (s, 3H); Mp 236.3 °C; HRMS (ESI-TOF) Calcd for $C_{10}H_9N_4O_4$ $[M + H]^+$, 249.0618: found 249.0627; HPLC retention time: 2.45 min.

*3,4-Dihydrobenzo[5,6]chromeno[3,4-d][1,2,3]triazole (**2f**).* According to the general procedure, the corresponding aldehyde (150.0 mg, 0.710 mmol), benzenesufonyl hydrazide (146.8 mg, 0.852 mmol), and potassium carbonate (196.3 mg, 1.42 mmol) were reacted in THF (2 mL) at room temperature for 14 h and then heated to 50 °C for 4 h. Subsequent workup and flash chromatography

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yielded 150.0 mg of the title compound as a white solid in 95% yield. ^{1}H NMR (400 MHz, Methanol-d_4) δ 9.07 (d, J = 8.5 Hz, 1H), 7.85−7.73 (m, 2H), 7.49 (dddd, J = 62.1, 8.1, 6.8, 1.3 Hz, 2H), 7.19 (d, J = 8.9 Hz, 1H), 5.53 (s, 2H); ^{13}C NMR (151 MHz, MeOD) δ 64.8, 111.1, 119.4, 125.4, 126.5, 128.3, 129.3, 130.9, 131.3, 131.5, 154.0; Mp 183.9 °C; HRMS (ESI-TOF) Calcd for $C_{13}H_{10}N_3O$ [M + H]$^+$, 224.0818: found 224.0825; HPLC retention time: 3.04 min.

*Ethyl 3,4-Dihydrochromeno[3,4-d][1,2,3]triazole-8-carboxylate (**2g**).* According to the general procedure, the corresponding aldehyde (200.0 mg, 0.858 mmol), benzenesufonyl hydrazide (177.2 mg, 1.029 mmol), and potassium carbonate (237.0 mg, 1.715 mmol) were reacted in THF (2 mL) at room temperature for 3 h and then heated to 50 °C overnight. Subsequent workup and flash chromatography yielded 179.3 mg of the title compound as a light yellow solid in 85% yield. ^{1}H NMR (500 MHz, Methanol-d_4) δ 8.34 (d, J = 2.1 Hz, 1H), 7.91 (dd, J = 8.6, 2.2 Hz, 1H), 7.05 (d, J = 8.6 Hz, 1H), 5.57 (s, 2H), 4.36 (q, J = 7.1 Hz, 2H), 1.40 (t, J = 7.1 Hz, 3H); ^{13}C NMR (151 MHz, MeOD) δ 167.4, 158.9, 132.5, 125.4, 125.3, 118.4, 65.7, 62.1, 14.6; Mp 169.6 °C; HRMS (ESI-qTOF) Calcd for $C_{12}H_{11}N_3O_3$ [M$^+$], 245.0795: found 245.0785; HPLC retention time: 2.72 min.

*7,9-Dimethoxy-3,4-dihydrochromeno[3,4-d][1,2,3]triazole (**2h**).* According to the general procedure, the corresponding aldehyde (59.1 mg, 0.267 mmol), benzenesufonyl hydrazide (55.1 mg, 0.321 mmol), and potassium carbonate (73.8 mg, 0.534 mmol) were reacted in THF (1 mL) at room temperature for 3 h and then heated to 50 °C overnight. Subsequent workup and flash chromatography yielded 61.4 mg of the title compound as an orange solid in 99% yield. ^{1}H NMR (400 MHz, Methanol-d_4) δ 6.26 (dd, J = 21.0, 2.2 Hz, 1H), 5.43 (s, 1H), 3.80 (s, 2H), 3.31 (p, J = 1.6 Hz, 6H); Mp 248.0 °C; HRMS (ESI-TOF) Calcd for $C_{11}H_{12}N_3O_3$ [M + H]$^+$, 234.0873: found 234.0868; HPLC retention time: 2.37 min.

*6,8-Dichloro-3,4-dihydrochromeno[3,4-d][1,2,3]triazole (**2i**).* According to the general procedure, the corresponding aldehyde (100 mg, 0.435 mmol), benzenesufonyl hydrazide (89.8 mg, 0.522 mmol), and potassium carbonate (90.1 mg, 0.652 mmol) were reacted in THF (5 mL) at room temperature for 14 h and then heated to 50 °C for 4 h. Subsequent workup and flash chromatography yielded 88.0 mg of the title compound as a white solid in 84% yield. ^{1}H NMR (400 MHz, Methanol-d_4) δ 7.59 (d, J = 2.5 Hz, 1H), 7.36 (d, J = 2.5 Hz, 1H), 5.58 (s, 2H); ^{13}C NMR (151 MHz, MeOD) δ 149.5, 130.5, 128.1, 124.5, 122.0, 120.5, 65.9; Mp 253.3 °C; HRMS (ESI-qTOF) Calcd for $C_9H_6Cl_2N_3O$ [M + H]$^+$, 241.9882: found 241.9881; HPLC retention time: 3.12 min.

*8-Bromo-3,4-dihydrochromeno[3,4-d][1,2,3]triazole (**2j**).* According to the general procedure, the corresponding aldehyde (150.0 mg, 0.625 mmol), benzenesufonyl hydrazide (123.7 mg, 0.719 mmol), and potassium carbonate (129.5 mg, 0.937 mmol) were reacted in THF (5 mL) at room temperature for 14 h and then heated to 50 °C for 4 h. Subsequent workup and flash chromatography yielded 128.0 mg of the title compound as a white solid in 81% yield. ^{1}H NMR (400 MHz, Methanol-d_4) δ 7.76 (d, J = 2.4 Hz, 1H), 7.35 (dd, J = 8.7, 2.4 Hz, 1H), 6.91 (d, J = 8.7 Hz, 1H), 5.46 (s, 2H); ^{13}C NMR (151 MHz, MeOD) δ 154.2, 133.6, 126.3, 120.3, 115.2, 65.1; Mp 206.5 °C; HRMS (ESI-TOF) Calcd for $C_9H_7BrN_3O$ [M + H]$^+$, 251.9767: found 251.9756; HPLC retention time: 2.86 min.

*8-Methyl-3,4-dihydrochromeno[3,4-d][1,2,3]triazole (**2k**).* According to the general procedure, the corresponding aldehyde (150.0 mg, 0.856 mmol), benzenesufonyl hydrazide (176.9 mg, 1.027 mmol), and potassium carbonate (236.7 mg, 1.712 mmol) were reacted in THF (1 mL) at room temperature for 3 h and then heated to 50 °C overnight. Subsequent workup and flash chromatography yielded 149.3 mg of the title compound as a light yellow solid in 93% yield. ^{1}H NMR (500 MHz, Methanol-d_4) δ 7.48−7.46 (m, 1H), 7.05 (ddd, J = 8.4, 2.2, 0.8 Hz, 1H), 6.86 (d, J = 8.4 Hz, 1H), 5.39 (s, 2H), 2.31 (s, 3H); ^{13}C NMR (151 MHz, MeOD) δ 153.0, 132.9, 131.6, 124.0, 118.1, 64.7, 20.7; Mp 191.5 °C; HRMS (ESI-TOF) Calcd for $C_{10}H_{10}N_3O$ [M + H]$^+$, 188.0818: found 188.0834; HPLC retention time: 2.65 min.

*6-(Trifluoromethyl)-3,4-dihydrochromeno[3,4-d][1,2,3]triazole (**2l**).* According to the general procedure, the corresponding aldehyde (202.4 mg, 0.883 mmol), benzenesufonyl hydrazide (182.5 mg, 1.06 mmol), and potassium carbonate (244.1 mg, 1.766 mmol) were reacted in THF (2.5 mL) at room temperature for 3 h and then heated to 50 °C overnight. Subsequent workup yielded 209.3 mg of the title compound as a light yellow solid in 93% yield. ^{1}H NMR (400 MHz, Methanol-d_4) δ 7.91 (dd, J = 7.7, 1.5 Hz, 1H), 7.54 (dd, J = 8.0, 1.5 Hz, 1H), 7.16 (t, J = 7.8 Hz, 1H), 5.58 (s, 2H); ^{13}C NMR (151 MHz, Methanol-d_4) δ 152.7, 127.8 (q, J = 5.1 Hz), 127.6, 125.7, 123.9, 122.8, 120.4, 120.2, 119.4, 65.8; Mp 190.9 °C; HRMS (ESI-TOF) Calcd for $C_{10}H_7F_3N_3O$ [M + H]$^+$, 242.0536: found 242.0527; HPLC retention time: 2.93 min.

*1H-Phenanthro[9,10-d][1,2,3]triazole (**2m**).* According to the general procedure, commercially available 2′-formyl-[1,1′-biphenyl]-2-carbonitrile (200.0 mg, 0.965 mmol), benzenesufonyl hydrazide (166.2 mg, 0.965 mmol), and potassium carbonate (133.4 mg, 0.965 mmol) were reacted in DMF (3.0 mL) at room temperature for 6 h and then heated to 50 °C for 4 h. Subsequent workup yielded 200.0 mg of the title compound as a light tan solid in 95% yield. Mp 316 °C (lit[16] 315−316 °C). HRMS (ESI-qTOF) Calcd for $C_{14}H_9N_3$ [M + H]$^+$, 220.0869: found 220.0869.

*3H-Pyrrolo[1,2-a][1,2,3]triazolo[4,5-c]quinolone (**2n**).* According to the general procedure, commercially available 1-(2-formylphenyl)-1*H*-pyrrole-2-carbonitrile (25.0 mg, 0.127 mmol), benzenesufonyl hydrazide (21.9 mg, 0.127 mmol), and potassium carbonate (17.6 mg, 0.127 mmol) were reacted in DMF (0.5 mL) at room temperature for 4 h and then heated to 50 °C overnight. Subsequent workup yielded 20.0 mg of the title compound as a light tan solid in 75% yield. ^{1}H NMR (400 MHz, Methanol-d_4) δ 8.29 (dd, J = 7.9, 1.5 Hz, 1H), 8.11−8.07 (m, 1H), 8.03 (dd, J = 3.1, 1.4 Hz, 1H), 7.61 (ddd, J = 8.6, 7.3, 1.5 Hz, 1H), 7.45 (ddd, J = 8.2, 7.4, 1.0 Hz, 1H), 6.90 (dd, J = 3.8, 1.3 Hz, 1H), 6.73 (dd, J = 3.8, 3.0 Hz, 1H); ^{13}C NMR (101 MHz, MeOD) δ 130.6, 126.0, 125.1, 117.1, 116.7, 113.8, 104.4; HRMS (ESI-TOF) Calcd for $C_{12}H_9N_4$ [M + H]$^+$, 209.0822: found 209.0811; HPLC retention time: 2.61 min.

*One-Pot Procedure to 8-Methoxy-3,4-dihydrochromeno[3,4-d]-[1,2,3]triazole (**2d**).* The commercially available salicylaldehyde (500.0 mg, 3.29 mmol), bromoacetonitrile (394.2 mg, 3.29 mmol), and potassium carbonate (908.4 mg, 6.57 mmol) were reacted in DMF (6 mL) at room temperature for 12 h. Upon completion of the first step, benzenesufonyl hydrazide (565.9 mg, 3.29 mmol) was added, and the reaction was stirred at room temperature overnight. Potassium carbonate (454.2 mg, 3.29 mmol) was added, and the reaction was heated to 50 °C for 4 h. Subsequent workup yielded 540.0 mg of the title compound as a white crystalline solid in 81% yield. ^{1}H NMR (400 MHz, Methanol-d_4) δ 7.20 (d, J = 3.0 Hz, 1H), 6.92−6.79 (m, 2H), 5.35 (s, 2H), 3.79 (s, 3H); ^{13}C NMR (151 MHz, MeOD) δ 156.4, 149.0, 119.2, 116.9, 108.2, 64.6, 56.1; Mp 175.6 °C; HRMS (ESI-TOF) Calcd for $C_{10}H_{10}N_3O_2$ [M + H]$^+$, 204.0768: found 204.0761; HPLC retention time: 2.45 min.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Proton and carbon NMR spectra of all compounds in Table 1. This material is available free of charge via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

Corresponding Author

*E-mail: nmani@its.jnj.com (N.S.M.).

Notes

The authors declare no competing financial interests

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