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The Copper-Catalyzed Reaction of 2-(1-Hydroxyprop-2-yn-1-yl)phenols with Sulfonyl Azides Leading to C3-Unsubstituted *N*-Sulfonyl-2-iminocoumarins

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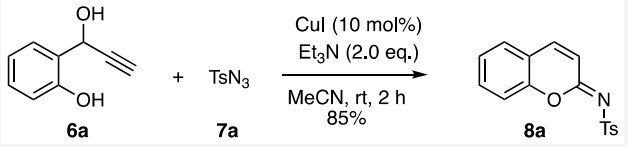
ABSTRACT: An operationally simple synthesis of *Z*-configured and C3-unsubstituted *N*-sulfonyl-2-iminocoumarins (e.g., **8a**) that proceeds under mild conditions is achieved by reacting 2-(1-hydroxyprop-2-yn-1-yl)phenols (e.g., **6a**) with sulfonyl azides (e.g., **7a**). The cascade process involved likely starts with a copper-catalyzed alkyne−azide cycloaddition (CuAAC) reaction. This is followed by ring-opening of the resulting metalated triazole (with accompanying loss of nitrogen), reaction of the ensuing ketenimine with the pendant phenolic hydroxyl group, and finally dehydration of the (*Z*)-*N*-(4-hydroxychroman-2-ylidene)-sulfonamide so formed.



Coumarin and its derivatives display broadly useful properties[1] including by virtue of their acting as antibacterial,[2] antifungal,[3] antiviral,[4] and/or anticancer agents.[5] Indeed, a number of them have considerable therapeutic potential. One subset of such compounds are the C3-unsubstituted iminocoumarins (Figure 1) that have been explored as enzyme inhibitors (e.g., **1**)[6] including, potentially, of acetylcholine esterase (AChE) (**2**),[7] as antimicrobial agents (**3**),[8] as antitumor agents (**4**),[9] and as antifungals (**5**).[10] Consequently, there is an attendant interest in the development of flexible and concise new routes to such systems. Previous studies have detailed multicomponent reactions (MCRs) involving terminal alkynes, sulfonyl azides, and other species that are combined using a copper-catalyzed alkyne−azide cycloaddition (CuAAC)/triazole ring-opening protocol.[11] These have been used extensively in 3-component and 4-component MCRs to assemble *N*-containing heterocycles and related compounds (Scheme 1).[12]

The adaptation of such chemistry to the synthesis of *N*-arylsulfonyl-2-iminocoumarins has been the subject of a number of recent reports.[13−18] For example, the copper-catalyzed three-component reaction of terminal alkynes, sulfonyl azides and salicylaldehydes (Scheme 2, a),[13] 3-(2-hydroxyphenyl)-propiolates (Scheme 2, b),[14] 2-hydroxybenzonitriles (Scheme 2, c),[15] benzo[*d*]isoxazoles (Scheme 2, d),[16] or alcohols (Scheme 2, e) have provided such target compounds.[17] Kumar's group has described[18] a metal-free method for the synthesis of *N*-arylsulfonyl-2-iminocoumarin derivatives by treating mixtures of aryl aldehydes, nitriles and *p*-TsCl with DABCO (Scheme 2, f).[19] Each of these methods has considerable merit, including the use of mild reaction conditions and being highly effective in the assembly of multisubstituted iminocoumarins. However, they all lack a demonstrated capacity to generate the 3-unsubstituted *N*-sulfonyl-2-iminocoumarins that, as highlighted above (Figure 1), are notable for their therapeutic potential. Accordingly, we now describe a related but complementary 2-MCR-based approach that proceeds under mild conditions to deliver 3-unsubstituted *N*-sulfonyl-2-iminocoumarins **8** in high yield. This operationally simple protocol involves stirring a mixture of the appropriate (and readily prepared) 2-(1-hydroxy-2-propyn-1-yl)phenol **6** and sulfonyl azide **7** in the presence of a copper(I) catalyst.

Our investigations began with an examination of the synthesis of the parent and previously unreported system *N*-(2*H*-chromen-2-ylidene)-4-methylbenzene-sulfonamide (**8a**) from 2-(1-hydroxyprop-2-yn-1-yl)phenol (**6a**) and *p*-tosyl azide (TsN_3) (**7a**). Initial screenings involved using CuI as catalyst and Et_3N as base in a range of standard solvents. These revealed that the desired conversion could be effected in many solvents (Table 1, entries 1−8) with acetonitrile delivering product **8a** in highest yield (85%).

Encouraged by these outcomes, a variety of catalysts was then investigated (Table 1, entries 9−13). Among the copper catalysts, Cu^{I}-species such as CuI and CuBr afforded the highest yields (85% and 82%, respectively) while the Cu^{II}-systems $CuBr_2$ (74%) and $Cu(OAc)_2$ (70%) were not quite as effective

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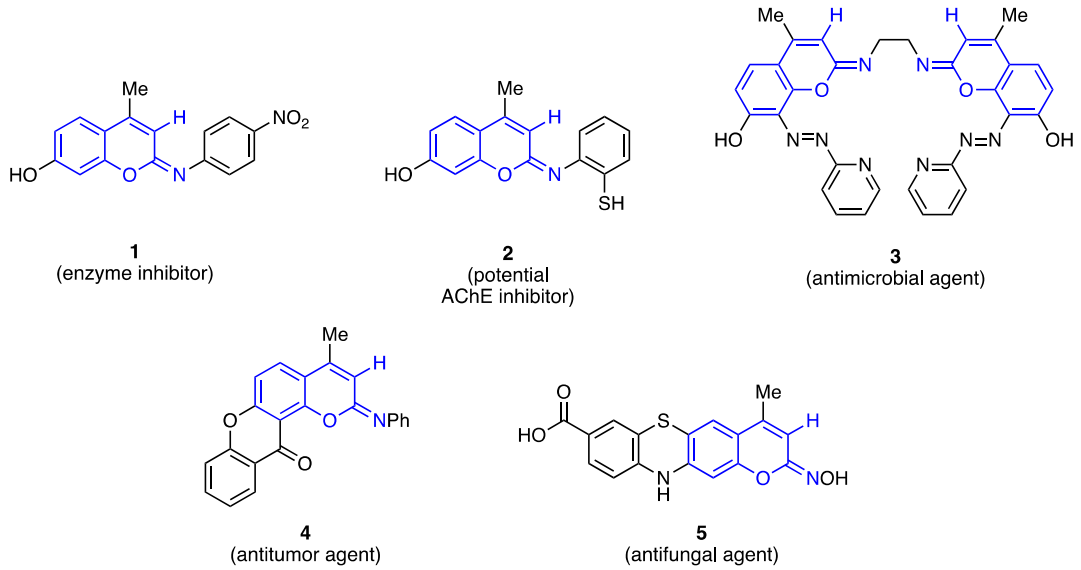
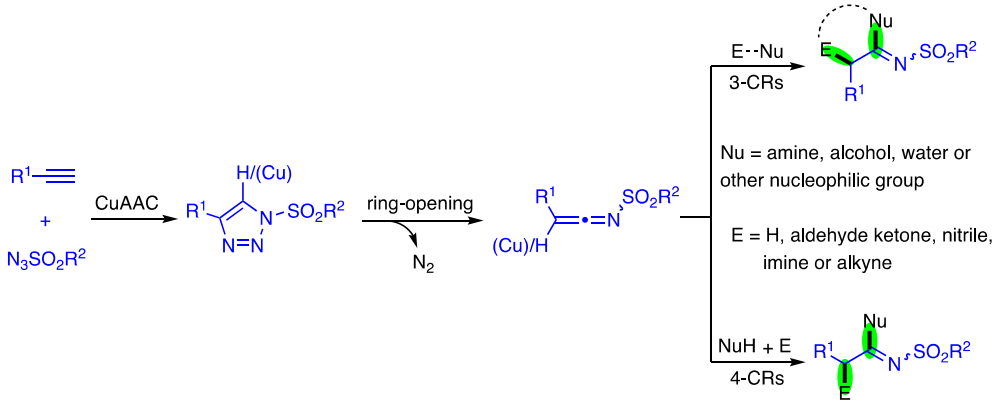


Figure 1. Examples of C3-unsubstituted iminocoumarins, **1**−**5**, that have been explored as drug candidates.

Scheme 1. Examples of the Copper-Catalyzed MCRs of Sulfonyl Azides and Terminal Alkynes with Other Components That Generate *N*-Heterocycles and Related Compounds



and $Cu(acac)_2$ was notably less so (42%). AgTFA failed to produce the desired product. The effect of different bases was also assessed (Table 1, entries 14−18) and revealed that the tertiary alkylamines Et_3N and *N*,*N*-di-isopropylethylamine (DIPEA) were superior to DMAP, pyridine, Cs_2CO_3, and sodium hydroxide.

With optimized reaction conditions for the formation of the "parent reaction" having been defined, the capacity of these to effect the coupling of a range of different substrates was investigated. As revealed in Table 2, various structurally and electronically distinct sulfonyl azides readily engaged in the desired reaction with the parent 2-(1-hydroxyprop-2-yn-1-yl)phenol (**6a**) to give the anticipated products (**8a**−**8l**) in modest to good yields.

Aryl sulfonyl azides proved more effective substrates than their simple alkyl counterparts (80−90% yield vs 58−78% yield) with the best "performing" member of the latter group being 3-chloropropane-1-sulfonyl azide and affording the anticipated product **8l**. Notably, the homochiral system **8k** could be obtained in 82% yield from camphorsulfonyl azide. The structure of the participating 2-(1-hydroxyprop-2-yn-1-yl)-phenols **6** can also be varied to a reasonable degree. Electron-donating as well as mildly electron-withdrawing substituents (R^1) attached to the aromatic ring of substrates of the general form **6** such as methyl and halogen are tolerated as evidenced by the formation of the anticipated products, **8m**−**8o** in serviceable yield but the introduction of a C4-nitro group (not shown) prevented any useful reaction from taking place. The successful formation of products **8p** and **8q** in yields of 61% and 52%, respectively, from the corresponding methyl-containing precursor **6** (R^2 = Me) shows that the present protocol allows for the formation of C4-substituted *N*-sulfonyl-2-iminocoumarins.

All of the product *N*-sulfonyl-2-iminocoumarins **8a**−**q**, none of which have been reported previously, were subject to full spectroscopic characterization (see SI for details), and the derived data were in complete accord with the assigned structures, and those of congeners **8a**, **8j**, and **8q** were confirmed by single-crystal X-ray analysis (see Experimental Section and Supporting Information for details). These analyses revealed that all three incorporate *Z*-configured imine residues, and so it has been assumed that all the other products formed during the course of this study possess the same geometry about the C═N bond. The only noteworthy feature among these data was the appearance, in the ^1H NMR spectra of all products, of the resonance due to H3 as a particularly broad signal, a feature attributed to the impact of the proximate sulfonyl residue.

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Scheme 2. Synthesis of 2-Iminocoumarins 8 via MCR Pathways a–f Reported Previously and the One Used in the Present Study

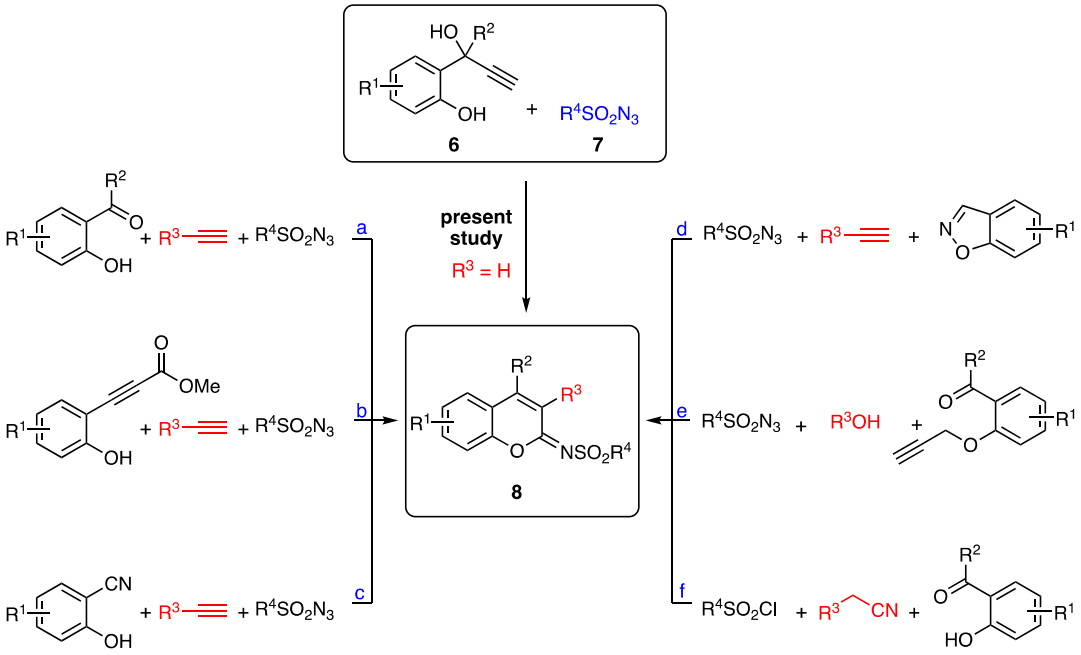
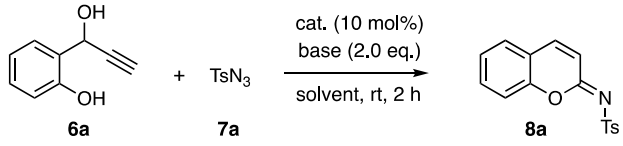


Table 1. Optimization of Reaction Conditions[a]



entry	cat.	base	solvent	yield[b] (%) **8a**
1	CuI	Et_3N	$CHCl_3$	76
2	CuI	Et_3N	$Cl(CH_2)_2Cl$	70
3	CuI	Et_3N	toluene	66
4	CuI	Et_3N	CH_2Cl_2	82
5	**CuI**	**Et_3N**	**MeCN**	**85**
6	CuI	Et_3N	THF	80
7	CuI	Et_3N	DMSO	80
8	CuI	Et_3N	1,4-dioxane	52
9	CuBr	Et_3N	CH_2Cl_2	82
10	$CuBr_2$	Et_3N	CH_2Cl_2	74
11	$Cu(OAc)_2$	Et_3N	CH_2Cl_2	70
12	$Cu(acac)_2$	Et_3N	CH_2Cl_2	42
13	AgTFA	Et_3N	CH_2Cl_2	nd[c]
14	CuI	DMAP	CH_2Cl_2	trace
15	CuI	DIPEA	CH_2Cl_2	82
16	CuI	pyridine	CH_2Cl_2	52
17	CuI	Cs_2CO_3	CH_2Cl_2	46
18	CuI	NaOH	CH_2Cl_2	13

[a]Reaction conditions: a solution of **6a** (0.5 mmol), cat. (10 mol %), and base (2.0 equiv) in the specified solvent (3 mL) was treated with **7a** (1.3 equiv) and stirred for 2 h at ambient temp. [b]Yield of isolated material. [c]nd = no product detected.

Specifically, and as shown in Figure 2, a zwitterionic resonance contributing form, **8B**, can be proposed for the sulfonyl-2-iminocoumarin framework that is both aromatic in character and allows for the opposing charges to exist in close spatial proximity to one another. As such, it might be expected to contribute significantly to the resonance hybrid and simultaneously allowing for some level of free rotation about the C2–N bond, a process resulting in structural change that, in turn, leads to broadening of the resonance due to H3.

Products **8a–8q** are all relatively stable species that survive chromatographic purification under conventional conditions. They do, however, undergo hydrolysis to the corresponding coumarins and sulfonamides, albeit under forcing conditions. For example, upon treatment with 1.5 equiv of *p*-TsOH in water under reflux for 12 h compound **8a** is converted into coumarin (83%).

A possible reaction pathway for the formation of *N*-(2*H*-chromen-2-ylidene)-4-methylbenzenesulfonamide (**8a**) from precursors **6a** and **7a** that is in keeping with earlier proposals[11,12] is provided in the SI.

In summary, we have developed an operationally simple and effective means for preparing C3-unsubstituted *N*-sulfonyl-2-iminocoumarins from a mixture of the corresponding 2-(1-hydroxyprop-2-yn-1-yl)phenol and sulfonyl azide in the presence of CuI. This methodology appears quite flexible and offers a capacity to generate forms of the title products that should be particularly useful in, for example, drug development studies.

EXPERIMENTAL SECTION

General Procedures. ^1H and $^{13}C\{^1H\}$ NMR spectra were recorded at ambient temperatures on a 400 MHz Bruker spectrometer using $CDCl_3$ or DMSO-d_6 as solvent and tetramethylsilane (TMS) as the internal standard. Chemical shifts are presented as δ values relative to TMS and $^1H–^1H$ coupling constants (J values) are given in Hz. IR spectra were recorded as KBr pellets on a Nicolet FT-IR 5DX spectrometer while HRMS measurements were carried out on a Bruker micrOTOF-Q II spectrometer. Melting points were determined on a Yanaco melting point apparatus and are uncorrected. The 2-(1-hydroxyprop-2-yn-1-yl)phenols and sulfonyl azides employed in this work were all known compounds and prepared by established and conventional procedures. So, in the case of the former substrates, this involved the addition of ethynylmagnesium bromide to the relevant *o*-hydroxybenzaldehyde or to *o*-hydroxyacetophenone[20] and, in the latter

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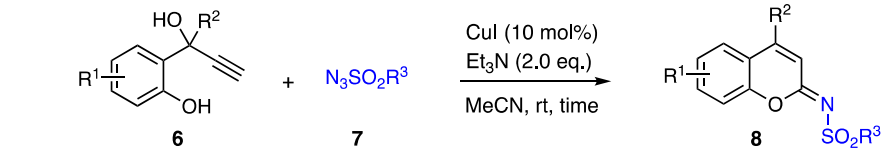
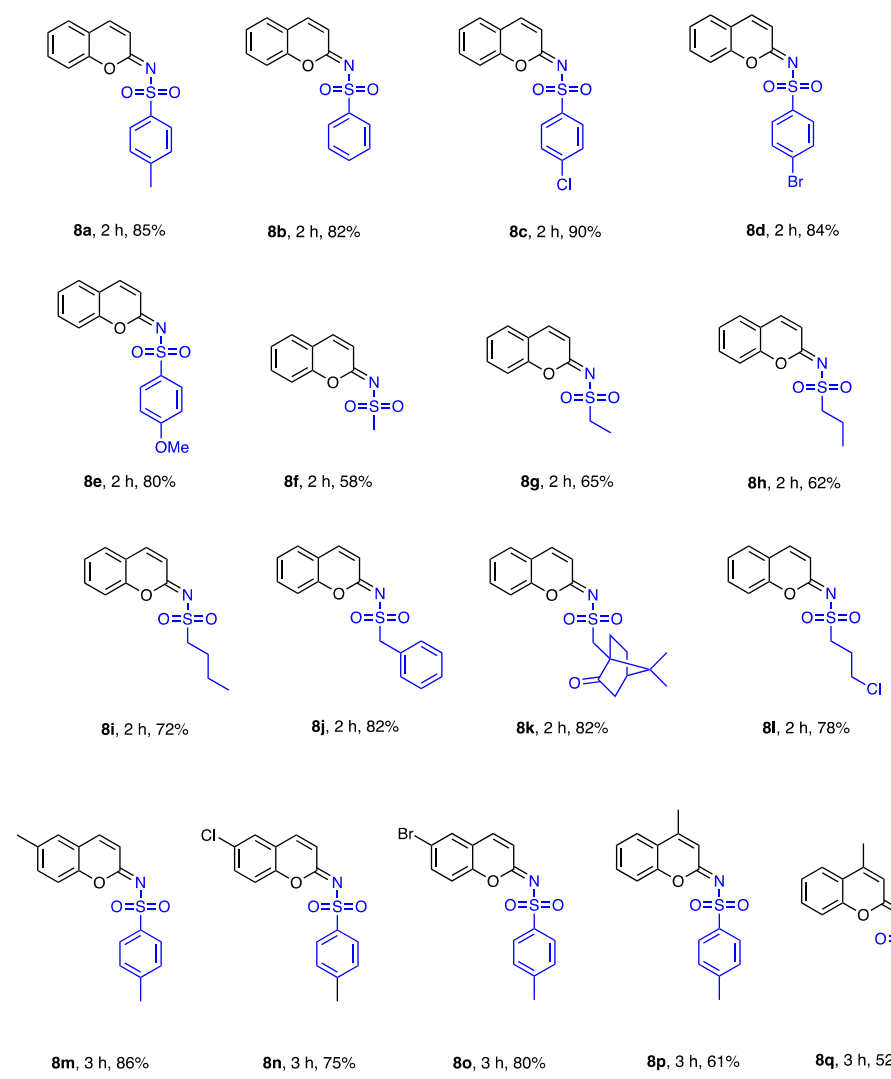
Table 2. Substrate Scope[a]





[a]Reactions were conducted as follows: a magnetically stirred solution of compound **6** (0.5 mmol), CuI (10 mol %), and Et_3N (2.0 equiv) in the MeCN (3 mL) was treated at room temperature (rt) with azide **7** (1.3 equiv) and stirring continued for the specified time.

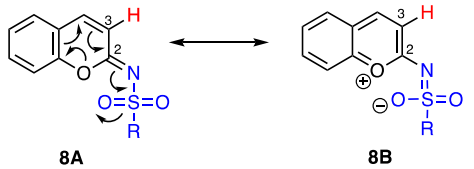


Figure 2. Key resonance contributing forms, **8A** and **8B**, associated with the *N*-sulfonyl-2-iminocoumarin framework.

case, reaction of the appropriate sulfonyl chloride with sodium azide in aqueous acetone.[21]

(*Z*)-*N*-(2*H*-Chromen-2-ylidene)-4-methylbenzenesulfonamide (8a). A magnetically stirred solution of 2-(1-hydroxyprop-2-yn-1-yl)phenol (**6a**, 74 mg, 0.5 mmol) and CuI (9.5 mg, 0.05 mmol) in MeCN (3 mL) was treated with TsN_3 (**7a**, 128 mg, 0.65 mmol) and Et_3N (101 mg, 1.0 mmol). The ensuing mixture was stirred at ambient temperatures for 2 h then concentrated under reduced pressure. The residue so obtained was subjected to flash chromatography (silica gel, 1:3 v/v ethyl acetate/60−90 petroleum ether elution) and providing, after concentration of the relevant fractions (R_f = 0.3 in 1:2 v/v ethyl acetate/60−90 petroleum ether), compound **8a** (127 mg, 85%) as a white, crystalline solid, mp = 177−180 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96 (d, J = 8.0 Hz, 2H), 7.69 (d, J = 13.6 Hz, 1H), 7.56−7.48 (complex m, 2H), 7.37−7.28 (complex m, 4H), 6.70 (broad s, 1H), 2.38 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 152.8, 143.5, 142.2, 138.8, 132.7, 129.4, 128.3, 127.4, 125.8, 119.1, 116.8, 21.6 (two signals obscured or overlapping); IR ν_{max} (KBr) 1632, 1577, 1510, 1485, 1446,

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1404, 1153, 1088, 830 cm^{-1}; HRMS (ESI-TOF) m/z $[M + H]^+$ calcd for $C_{16}H_{14}NO_3S$ 300.0694, found 300.0686.

Gram-Scale Synthesis of Compound 8a. A magnetically stirred solution of 1-(2-hydroxyphenyl)prop-2-yn-1-one (**6a**, 1.00 g, 6.76 mmol) and CuI (0.13 g, 0.68 mmol) in MeCN (20 mL) was treated with TsN_3 (1.73 g, 8.78 mmol) and Et_3N (1.36 g, 13.5 mmol). The resulting mixture was stirred at 25 °C for 2 h after which time TLC analysis indicated that all of the starting compound **6a** had been consumed. Accordingly, the reaction mixture was concentrated under reduced pressure and the residue subjected to flash chromatography in the manner detailed above. Concentration of the relevant fractions then gave compound **8a** (1.65 g, 82%) as a white, crystalline solid that was identical, in all respects, to that obtained at the smaller scale.

Synthesis of Compounds 8b–8q. The protocol described immediately above was employed, at the same scale, for the synthesis of compounds **8b–8q** by using the requisite combination of 2-(1-hydroxyprop-2-yn-1-yl)phenol and sulfonyl azide. Two or three hour reaction times were employed (see Table 2 for specific times) and the crude material obtained after extractive workup and drying was subjected to flash chromatography using 1:2–4 v/v ethyl acetate/60–90 petroleum ether.

(*Z*)-*N*-(2*H*-Chromen-2-ylidene)benzenesulfonamide (8b). The title compound (117 mg, 82%) was obtained as a white, crystalline solid, mp = 173.3–177.7 °C (R_f = 0.3 in 1:2 v/v ethyl acetate/60–90 petroleum ether). ^1H NMR (400 MHz, $CDCl_3$) δ 8.09 (d, J = 7.2 Hz, 2H), 7.02 (d, J = 9.6 Hz, 1H), 7.59–7.50 (complex m, 5H), 7.42–7.33 (complex m, 2H), 6.78 (broad s, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 153.0, 142.2, 141.9, 132.8, 128.9, 128.3, 127.4, 125.9, 119.2, 117.1 (three signals obscured or overlapping); IR ν_{max} (KBr) 1640, 1550, 1485, 1450, 1240, 1087, 830, 772, 733, 698 cm^{-1}; HRMS (ESI-TOF) m/z calcd for $C_{15}H_{12}NO_3S$, $[M + H]^+$ 286.0538, found 286.0537.

(*Z*)-4-Chloro-*N*-(2*H*-chromen-2-ylidene)-benzenesulfonamide (8c). The title compound (144 mg, 90%) was obtained as a white, crystalline solid, mp = 138.8–143.3 °C (R_f = 0.3 in 1:2 v/v ethyl acetate/60–90 petroleum ether). ^1H NMR (400 MHz, $CDCl_3$) δ 8.02 (d, J = 8.8 Hz, 2H), 7.74 (d, J = 9.6 Hz, 1H), 7.60 (m, 1H), 7.54–7.47 (complex m, 3H), 7.42 (d, J = 8.4 Hz, 1H), 7.36 (m, 1H), 6.85 (broad s, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 152.9, 142.6, 140.4, 139.2, 132.9, 129.2, 128.9, 128.4, 126.1, 119.2, 117.1 (two signals obscured or overlapping); IR ν_{max} (KBr) 1632, 1558, 1485, 1404, 1319, 1277, 1149, 1088, 837, 756, 682 cm^{-1}; HRMS (ESI-TOF) m/z calcd for $C_{15}H_{11}{}^{35}ClNO_3S$, $[M + H]^+$ 320.0148, found 320.0141.

(*Z*)-4-Bromo-*N*-(2*H*-chromen-2-ylidene)-benzenesulfonamide (8d). The title compound (149 mg, 84%) was obtained as a white, crystalline solid, mp = 159.2–161.6 °C [R_f = 0.2(6) in 1:2 v/v ethyl acetate/60–90 petroleum ether]. ^1H NMR (400 MHz, $CDCl_3$) δ 7.59 (d, J = 8.4 Hz, 2H), 7.75 (d, J = 9.6 Hz, 1H), 7.67–7.64 (complex m, 2H), 7.60 (m, 1H), 7.53 (m, 1H), 7.43 (d, J = 8.4 Hz, 1H), 7.37 (m, 1H), 6.82 (broad s, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 153.3, 142.9, 141.2, 133.3, 132.5, 129.3, 128.7, 128.0, 126.4, 119.5, 117.4 (two signals obscured or overlapping); IR ν_{max} (KBr) 1743, 1631, 1558, 1485, 1450, 1323, 1273, 1246, 1234, 1088, 1064, 999, 907, 710 cm^{-1}; HRMS (ESI-TOF) m/z calcd for $C_{15}H_{11}{}^{79}BrNO_3S$, $[M + H]^+$ 363.9643, found 363.9637.

(*Z*)-*N*-(2*H*-Chromen-2-ylidene)-4-methoxybenzenesulfonamide (8e). The title compound (126 mg, 80%) was obtained as a white, crystalline solid, mp = 147.6–149.8 °C [R_f = 0.1(6) in 1:2 v/v ethyl acetate/60–90 petroleum ether]. ^1H NMR (400 MHz, $CDCl_3$) δ 8.03 (d, J = 9.6 Hz, 2H), 7.69 (d, J = 9.6 Hz, 1H), 7.58 (m, 1H), 7.50 (m, 1H), 7.43 (d, J = 8.4 Hz, 1H), 7.34 (m, 1H), 7.00 (m, 2H), 6.66 (broad s, 1H), 3.86 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 163.1, 153.0, 141.9, 133.6, 132.7, 129.6, 128.8, 128.3, 125.8, 119.2, 117.1, 114.4, 114.1, 55.8; IR ν_{max} (KBr) 3074, 2825, 1640, 1550, 1493, 1404, 1258, 1150, 1088, 1015, 972, 903, 800, 756 cm^{-1}; HRMS (ESI-TOF) m/z calcd for $C_{16}H_{14}NO_4S$, $[M + H]^+$ 316.0644, found 316.0634.

(*Z*)-*N*-(2*H*-Chromen-2-ylidene)methanesulfonamide (8f). The title compound (65 mg 58%) was obtained as a white, crystalline solid, mp = 140.2–140.9 °C [R_f = 0.1(6) in 1:2 v/v ethyl acetate/60–90 petroleum ether]. ^1H NMR (400 MHz, $CDCl_3$) δ 7.73 (d, J = 9.6 Hz, 1H), 7.62–7.48 (complex m, 3H), 7.36 (m, 1H), 6.59 (broad s, 1H), 3.17 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 153.0, 142.1, 132.9, 128.4, 125.9, 119.1, 117.3, 43.1 (two signals obscured or overlapping); IR ν_{max} (KBr) 2910, 1639, 1577, 1485, 1446, 1296, 1199, 1123 cm^{-1}; HRMS (ESI-TOF) m/z calcd for $C_{10}H_{10}NO_3S$, $[M + H]^+$ 224.0381, found 224.0377.

(*Z*)-*N*-(2*H*-Chromen-2-ylidene)ethanesulfonamide (8g). The title compound (77 mg, 65%), was obtained as a white, crystalline solid, mp = 92.8–94.5 °C (R_f = 0.4 in 1:2 v/v ethyl acetate/60–90 petroleum ether). ^1H NMR (400 MHz, $CDCl_3$) δ 7.70 (d, J = 9.6 Hz, 1H), 7.60–7.47 (complex m, 3H), 7.35 (t, J = 8.4 Hz, 1H), 6.59 (broad s, 1H), 3.22 (q, J = 7.2 Hz, 2H), 1.48 (t, J = 7.2 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 153.0, 141.9, 132.8, 128.2, 125.7, 119.1, 117.4, 49.5, 8.3 (two signals obscured or overlapping); IR ν_{max} (KBr) 2930, 1639, 1578, 1450, 1404, 1300, 1199, 1003, 907, 772, 737, 698 cm^{-1}; HRMS (ESI-TOF) m/z calcd for $C_{11}H_{12}NO_3S$, $[M + H]^+$ 238.0538, found 238.0530.

(*Z*)-*N*-(2*H*-Chromen-2-ylidene)propane-1-sulfonamide (8h). The title compound (78 mg, 62%) was obtained as a white, crystalline solid, mp = 97.0–100.2 °C (R_f = 0.4 in 1:2 v/v ethyl acetate/60–90 petroleum ether). ^1H NMR (400 MHz, $CDCl_3$) δ 7.70 (d, J = 9.6 Hz, 1H), 7.60–7.47 (complex m, 3H), 7.35 (m, 1H), 6.59 (broad s, 1H), 3.17 (m, 2H), 1.99 (m, 2H), 1.09 (t, J = 8.4 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 153.0, 141.9, 132.8, 128.2, 125.7, 119.1, 117.3, 56.8, 17.4, 13.1 (two signals obscured or overlapping); IR ν_{max} (KBr) 2882, 1620, 1574, 1480, 1460, 1130, 999, 860, 826 cm^{-1}; HRMS (ESI-TOF) m/z calcd for $C_{12}H_{14}NO_3S$, $[M + H]^+$ 252.0694, found 252.0687.

(*Z*)-*N*-(2*H*-Chromen-2-ylidene)butane-1-sulfonamide (8i). The title compound (95 mg, 72%) was obtained as a white, crystalline solid, mp = 73.6–74.2 °C (R_f = 0.4 in 1:2 v/v ethyl acetate/60–90 petroleum ether). ^1H NMR (400 MHz, $CDCl_3$) δ 7.70 (d, J = 9.6 Hz, 1H), 7.61–7.48 (complex m, 3H), 7.35 (m, 1H), 6.58 (broad s, 1H), 3.20 (m, 2H), 1.94 (m, 2H), 1.51 (m, 2H), 0.97 (t, J = 7.2 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 153.1, 141.8, 132.8, 128.2, 125.7, 119.2, 117.4, 54.9, 25.6, 21.7, 13.8 (two signals obscured or overlapping); IR ν_{max} (KBr) 2950, 1625, 1578, 1485, 1296 1126, 829, 756, 595 cm^{-1}; HRMS (ESI-TOF) m/z calcd for $C_{13}H_{16}NO_3S$, $[M + H]^+$ 266.0851, found 266.0842.

(*Z*)-*N*-(2*H*-Chromen-2-ylidene)-1-phenylmethanesulfonamide (8j). The title compound (123 mg, 82%) was obtained as a white, crystalline solid, mp = 142.5–146.2 °C (R_f = 0.3 in 1:2 v/v ethyl acetate/60–90 petroleum ether). ^1H NMR (400 MHz, $CDCl_3$) δ 7.62 (d, J = 9.6 Hz, 1H), 7.56 (m, 1H), 7.52–7.44 (complex m, 3H), 7.43 (d, J = 8.4 Hz, 1H), 7.38–7.31 (complex m, 4H), 6.69 (broad s, 1H), 4.44 (s, 2H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 152.8, 141.9, 132.7, 131.2, 129.4, 128.7, 128.6, 128.2, 125.7, 119.1, 117.3, 60.8 (two signals obscured or overlapping); HRMS (ESI-TOF) m/z calcd for $C_{16}H_{14}NO_3S$, $[M + H]^+$ 300.0694, found 300.0686. Satisfactory IR data could not be obtained on this compound.

(*Z*)-*N*-(2*H*-Chromen-2-ylidene)-1-((1*R*,4*R*)-7,7-dimethyl-2-oxobicyclo[2.2.1]heptan-1-yl)methanesulfonamide (8k). The title compound (140 mg, 82%) was obtained as a white, crystalline solid, mp = 106.1–112.4 °C (R_f = 0.3 in 1:2 v/v ethyl acetate/60–90 petroleum ether). ^1H NMR (400 MHz, $CDCl_3$) δ 7.74 (d, J = 9.6 Hz, 1H), 7.61–7.49 (complex m, 3H), 7.36 (m, 1H), 6.57 (broad s, 1H), 3.86 (d, J = 14.8 Hz, 1H), 3.18 (d, J = 14.8 Hz, 1H), 2.69 (m, 1H), 2.38 (m, 1H), 2.12–2.03 (complex m, 2H), 1.94 (d, J = 18.4 Hz, 1H), 1.79 (m, 1H), 1.44 (m, 1H), 1.17 (s, 3H), 0.90 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 215.1, 152.9, 141.9, 132.6, 128.2, 125.7, 119.1, 117.2, 58.4, 51.0, 48.1, 42.7, 42.7, 27.0, 24.6, 20.1, 19.8 (two signals obscured or overlapping); IR ν_{max} (KBr) 2970, 1740, 1640, 1520, 1280, 1211, 1134, 826, 756, 645 cm^{-1}; HRMS (ESI-TOF) m/z calcd for $C_{19}H_{22}NO_4S$, $[M + H]^+$ 360.1270, found 360.1259.

(*Z*)-3-Chloro-*N*-(2*H*-chromen-2-ylidene)propane-1-sulfonamide (8l). The title compound (117 mg, 78%) was obtained as a white, crystalline solid, mp = 113.4–115.0 °C (R_f = 0.3 in 1:2 v/v ethyl acetate/60–90 petroleum ether). ^1H NMR (400 MHz, $CDCl_3$) δ 7.74 (d, J = 9.6 Hz, 1H), 7.61–7.47 (complex m, 3H), 7.36 (m, 1H), 6.78 (broad s, 1H), 3.75 (m, 2H), 3.37 (m, 2H), 2.43 (m, 2H); $^{13}C\{^1H\}$

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NMR (100 MHz, $CDCl_3$) δ 152.9, 142.3, 132.9, 128.3, 125.9, 119.1, 117.3, 52.2, 43.1, 27.0 (two signals obscured or overlapping); IR ν_{max} (KBr) 2953, 1639, 1570, 1450, 1400, 1118, 825, 756 cm^{-1}; HRMS (ESI-TOF) m/z calcd for $C_{12}H_{13}ClNO_3S$, $[M + H]^+$ 286.0305, found 286.0299.

(*Z*)-4-Methyl-*N*-(6-methyl-2*H*-chromen-2-ylidene)-benzenesulfonamide (8m). The title compound (135 mg, 86%) was obtained as a white, crystalline solid, mp = 170.3−175.1 °C (R_f = 0.3 in 1:2 v/v ethyl acetate/60−90 petroleum ether). ^1H NMR (400 MHz, $CDCl_3$) δ 7.97 (d, J = 8.4 Hz, 2H), 7.64 (d, J = 9.6 Hz, 1H), 7.37 (m, 1H), 7.31−7.28 (complex m, 4H), 6.68 (broad s, 1H), 2.40 (s, 6H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 151.2, 143.4, 142.1, 139.0, 135.8, 133.8, 129.4, 128.1, 127.5, 119.0, 116.7, 21.7, 20.9 (two signals obscured or overlapping); IR ν_{max} (KBr) 2910, 1640, 1565, 1365, 1288, 1230, 1150, 1088, 999, 868 745, 660 cm^{-1}; HRMS (ESI-TOF) m/z calcd for $C_{17}H_{16}NO_3S$, $[M + H]^+$ 314.0851, found 314.0846.

(*Z*)-*N*-(6-Chloro-2*H*-chromen-2-ylidene)-4-methylbenzenesulfonamide (8n). The title compound (125 mg, 75%) was obtained as a white, crystalline solid, mp = 210.9−216.8 °C [R_f = 0.4(5) in 1:2 v/v ethyl acetate/60−90 petroleum ether]. ^1H NMR (400 MHz, DMSO-d_6) δ 8.08 (d, J = 9.6 Hz, 1H), 7.93−7.89 (complex m, 3H), 7.72 (m, 1H), 7.56 (d, J = 9.6 Hz, 1H), 7.41 (d, J = 8.4 Hz, 2H), 6.94 (broad s, 1H), 2.37 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d_6) δ 151.3, 143.9, 142.9, 138.9, 132.9, 130.2, 130.0, 128.6, 127.6, 121.0, 118.7, 21.5 (two signals obscured or overlapping); IR ν_{max} (KBr) 3020, 1650, 1580, 1285, 1240, 1180, 814, 775, 698 cm^{-1}; HRMS (ESI-TOF) m/z calcd for $C_{16}H_{13}{}^{35}ClNO_3S$, $[M + H]^+$ 334.0305, found 334.0301.

(*Z*)-*N*-(6-Bromo-2*H*-chromen-2-ylidene)-4-methylbenzenesulfonamide (8o). The title compound (148 mg, 80%) was obtained as a white, crystalline solid, mp = 194.8−197.8 °C (R_f = 0.4 in 1:2 v/v ethyl acetate/60−90 petroleum ether). ^1H NMR (400 MHz, DMSO-d_6) δ 8.07 (m, 2H), 7.90 (d, J = 4.0 Hz, 2H), 7.83 (m, 1H), 7.49 (d, J = 4.4 Hz, 1H), 7.41 (d, J = 8.4 Hz, 2H), 6.94 (broad s, 1H), 2.37 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d_6) δ 151.7, 143.9, 142.8, 138.9, 135.7, 131.5, 130.0, 127.6, 121.5, 118.9, 118.1, 21.5 (two signals obscured or overlapping); IR ν_{max} (KBr) 1632, 1550, 1390, 1285, 903, 683 cm^{-1}; HRMS (ESI-TOF) m/z calcd for $C_{16}H_{13}{}^{79}BrNO_3S$, $[M + H]^+$ 377.9800, found 377.9797.

(*Z*)-4-Methyl-*N*-(4-methyl-2*H*-chromen-2-ylidene)-benzenesulfonamide (8p). The title compound (95 mg, 61%) was obtained as a white, crystalline solid, mp = 190−191 °C [R_f = 0.3(5) in 1:2 v/v ethyl acetate/60−90 petroleum ether]. ^1H NMR (400 MHz, $CDCl_3$) δ 7.96 (d, J = 7.6 Hz, 2H), 7.64−7.56 (complex m, 2H), 7.43−7.25 (complex m, 4H), 6.84 (broad s, 1H), 2.48 (s, 3H), 2.40 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 152.6, 152.1, 143.4, 139.3, 132.7, 129.5, 127.4, 125.7, 126.4, 120.4, 117.4, 21.8, 19.1 (two signals obscured or overlapping); IR ν_{max} (KBr) 2921, 1632, 1570, 1485, 1451, 1400, 1234, 1207, 1184, 972, 764 cm^{-1}; HRMS (ESI-TOF) m/z calcd for $C_{17}H_{16}NO_3S$, $[M + H]^+$ 314.0851, found 314.0847.

(*Z*)-*N*-(4-Methyl-2*H*-chromen-2-ylidene)-methanesulfonamide (8q). The title compound (62 mg, 52%), was obtained as a white, crystalline solid, mp = 142−144 °C (R_f = 0.3 in 1:3 v/v ethyl acetate/60−90 petroleum ether). ^1H NMR (400 MHz, $CDCl_3$) δ 7.66 (d, J = 8.0 Hz, 1H), 7.60 (t, J = 8.0 Hz, 1H), 7.48 (d, J = 7.6 Hz, 1H), 7.39 (d, J = 7.6 Hz, 1H), 6.84 (broad s, 1H), 3.15 (s, 3H), 2.51 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 152.6, 152.2, 132.9, 125.7, 124.9, 120.3, 117.6, 43.2, 19.1 (two signals obscured or overlapping); IR ν_{max} (KBr) 2903, 1635, 1572, 1482, 1283, 1194, 1075, 830 cm^{-1}; HRMS (ESI-TOF) m/z calcd for $C_{11}H_{12}NO_3S$, $[M + H]^+$ 238.0538, found 238.0531.

Hydrolysis of (*Z*)-*N*-(2*H*-chromen-2-ylidene)-4-methylbenzenesulfonamide (8a). Formation of 2*H*-Chromen-2-one. A magnetically stirred solution of *N*-(2*H*-chromen-2-ylidene)-4-methylbenzenesulfonamide (**8a**) (149.5 mg, 0.5 mmol) and $TsOH{\cdot}H_2O$ (258 mg, 1.35 mmol) in water (3 mL) was heated under reflux for 12 h then cooled and diluted with water (30 mL). The resulting mixture was extracted with ethyl acetate (3 × 20 mL) and the combined organic phases then dried (Na_2SO_4) and filtered before being concentrated under reduced pressure. The residue thus obtained was subjected flash chromatography (silica gel, 1:3 v/v ethyl acetate/60−90 petroleum ether) to give 2*H*-chromen-2-one (coumarin) (121 mg, 83%) as a white, crystalline solid, mp = 67−69 °C (lit.[1d] mp = 70−72 °C). ^1H NMR (400 MHz, $CDCl_3$) δ 7.72 (d, J = 9.6 Hz, 1H), 7.54−7.48 (complex m, 2H), 7.35−7.27 (complex m, 2H), 6.43 (d, J = 9.6 Hz, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 160.9, 154.2, 143.6, 132.0, 128.0, 124.6, 119.0, 117.1, 116.9. This material was identical, in all respects, with an authentic sample.

Crystallographic Data. *Compound **8a**.* $C_{16}H_{13}NO_3S$, M = 299.33, T = 296 K, monoclinic, space group $P2_1/c$, Z = 12, a = 10.721(3) Å, b = 8.754(2) Å, c = 45.493(12) Å; β = 90.004(5); V = 4270(2) $Å^3$, D_x = 1.397 Mg m^{-3}, 9705 unique data ($2\theta_{max}$ = 55.432°), R = 0.0579 [for 4055 reflections with $I > 2.0\sigma(I)$]; Rw = 0.1616 (all data), S = 0.995.

*Compound **8j**.* $C_{16}H_{13}NO_3S$, M = 299.33, T = 150 K, triclinic, space group $P\bar{1}$, Z = 2, a = 7.6011(4) Å, b = 8.6114(5) Å, c = 11.7562(6) Å; α = 95.672(5)°, β = 97.474(5)°, γ = 111.982(5)°; V = 698.34(7) $Å^3$, D_x = 1.424 Mg m^{-3}, 3225 unique data ($2\theta_{max}$ = 58.774°), R = 0.0414 [for 2696 reflections with $I > 2.0\sigma(I)$]; Rw = 0.1007 (all data), S = 1.034.

*Compound **8q**.* $C_{11}H_{11}NO_3S$, M = 237.27, T = 153 K, monoclinic, space group $P2_1/n$, Z = 4, a = 6.8798(3) Å, b = 8.0785(5) Å, c = 19.1741(13) Å; β = 94.770(5); V = 1061.98(11) $Å^3$, D_x = 1.484 Mg m^{-3}, 2734 unique data ($2\theta_{max}$ = 148.23°), R = 0.0340 [for 2577 reflections with $I > 2.0\sigma(I)$]; Rw = 0.0926 (all data), S = 1.079.

Structure Determination. Data for compounds **8a**, **8j** and **8q** were collected on a Bruker APEX-II CCD or a Rigaku Super Nova X-ray diffractometer employing either Mo Kα or Cu Kα radiation and a graphite monochromator (λ = 0.71073 Å or 1.54184, respectively). Using OLEX2,[22] structures were solved by dual-space with the ShelXT[23] program and refined, using least-squares minimization, with the ShelXL[24] package. Atomic coordinates, bond lengths and angles, and displacement parameters have been deposited at the Cambridge Crystallographic Data Centre (CCDC 2043700, 2060954, and 2060955).

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.joc.1c00331.

Plots derived from the single-crystal X-ray analyses of compound **8a**, **8j**, and **8q** together with copies of the ^1H and $^{13}C\{^1H\}$ NMR spectra of compounds **8a**−**8q** (PDF)

FAIR data, including the primary NMR FID files, for compounds **8a**−**8q** (ZIP)

Accession Codes

CCDC 2043700 and 2060954−2060955 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif, or by emailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033.

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Notes

The authors declare no competing financial interest.

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