Preparation of 2-(1*H*-Pyrazol-5-yl)Benzenesulfonamides from Polylithiated C(α),N-Carbo-*tert*-Butoxyhydrazones and Methyl 2-(Aminosulfonyl)benzoate

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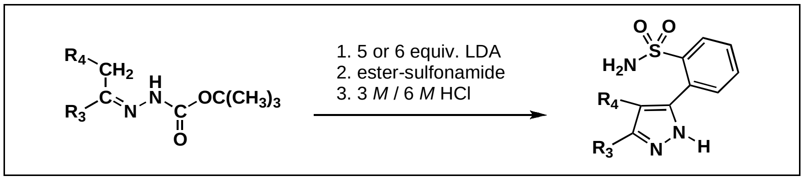

Select C(α), *N*-carbo-*tert*-butoxyhydrazones were dilithiated with excess lithium diisopropylamide followed by condensation with methyl 2-(aminosulfonyl)benzoate, acid cyclization, hydrolysis, and decarboxylation to afford new 2-(1*H*-pyrazol-5-yl)benzenesulfonamides, [*NH*-pyrazolyl-*ortho*-benzene-sulfonamides].

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INTRODUCTION

A distinct group of heterocyclic compounds with biological and agricultural potential and use are substituted 1*H*-pyrazoles and related compounds with a pyrazole component such as indazoles and dihydrobenz-indazoles [1]. In addition to the general characteristics of pyrazoles, their properties and uses may be modified based on the nature of the atoms or pendant groups bonded to the carbons or nitrogen of the pyrazole ring system. Specifically, several reports deal with the benzenesulfonamide pendant group bonded to a 1*H*-pyrazole; *para*-benzenesulfonamides are documented as herbicidal sulfonamides [2]; *ortho*-benzenesulfonamides have potential as chymase inhibitors [3]. The methods of preparation for these specific compounds, however, are rather limited.

Pyrazoles in general, especially 1*H*-pyrazoles, have been prepared by several key procedures such as the condensation-cyclization of β-dicarbonyl compounds with hydrazines or the 1,3-dipolar addition of nitrilimines with alkynes [1]. One of our synthetic interests and endeavors has been the condensation-cyclization of polylithiated C(α),*N*-hydrazones with aromatic esters and related reagents [4-6] for the preparation of pyrazoles. A part of our developing studies has been the condensation of these 1,4-dilithiated hydrazone intermediates with routine or challenging anionic electrophilic reagents such as lithiated ethyl benzoylacetate (dilithiated phenylhydrazones give phenacylpyrazoles) [7], lithiated methyl salicylates (dilithiated carboalkoxyhydrazones give pyrazolobenz-oxazinones) [8], or lithiated ethyl oxanilate (dilithiated phenylhydrazones gives pyrazolecarboxamides) [9]. Our continuing efforts have demonstrated the large potential for the 1,4-multiple anion synthesis of pyrazoles, especially N*H*-pyrazoles [10] and other heterocyclic compounds.

Methyl 2-(aminosulfonyl)benzoate **1** is well documented for the preparation of important compounds used in agriculture [11]. The vast majority of the reactions involving this compound take advantage of the synthetic potential of the sulfonamide group. One major use for the carbomethoxy ester group has been for its reaction with the *ortho*-substituted sulfonamide group to afford saccharin-related compounds, whose synthetic, biological, and agricultural potentials are documented [12].

In two introductory investigations, we explored the synthetic potential for the condensation of lithiated ester-sulfonamide **1'** (from **1**), an anionic electrophile, with polylithiated nucleophiles such as dilithiated β-ketoesters or dilithiated *ortho*-toluic acids, which are anionic nucleophiles, for the preparation of new heterocyclic compounds, benzoisothiazole dioxides [13] and fused ring benzoisothiazole dioxide-isoquinolinones [14].

The initially planned preparation of isoxazole-*ortho*-benzenesulfonamides **4** and pyrazole-*ortho*-benzene-sulfonamides **5** by the condensation-cyclization of 1,4-dilithiated oximes **2'** (from oxime **2**) or 1,4-dilithiated phenylhydrazones **3'** (from phenyl hydrazone **3**) with **1'** was expected to offer a challenge (Figure 1). The anticipated *C*-acylated intermediates could be more difficult to cyclize to **4** or **5** as a result of the *ortho*-benzenesulfonamide moiety bonded to the carbonyl

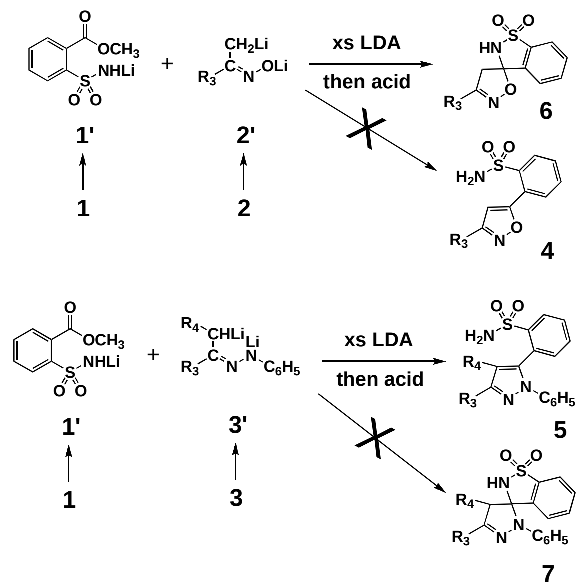

Figure 1. Methyl 2-(aminosulfonylbenzoate) and azole-*ortho*-benzenesulfonamides or spiro(benzisothiazole-azole)dioxides.

carbon. Unexpectedly, spiro(benzoisothiazole-isoxazole)-dioxides **6** [15] resulted and not the projected isoxazole-*ortho*-benzenesulfonamides **4**. Intermediates resulting from condensation-cyclization of dilithiated phenylhydrazones **3'** with lithiated ester-sulfonamide **1'** (from **1**) resulted in *N*-phenylpyrazolyl-*ortho*-benzenesulfonamides **5** [16]. Products **5** and **6** may be explained with plausible intermediates resulting from inductive and/or resonance effect arguments.

In comparison to the 1,4-dilithiated *N*-phenylhydrazone **3'** system, the condensation of **1'** and 1,4-dilthiatiated *N*-carbo-*tert*-butoxyhydrazones (BOC-hydrazones) **8'** (from BOC hydrazone **8**) have the potential to go to either

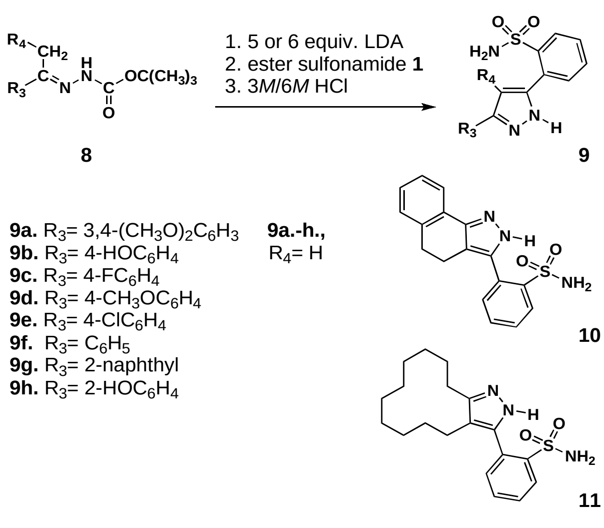

Figure 2. Overall reaction summary.

substituted N*H*-pyrazoles or spiro(BID-pyrazoles) analogous to **5** and/or **7**. This is due to the bonding location and restrictive properties/features of the sulfonamide group and the BOC group.

Also, we have been successful in preparing other BOC-pyrazoles by acid cyclization of the appropriate *C*-

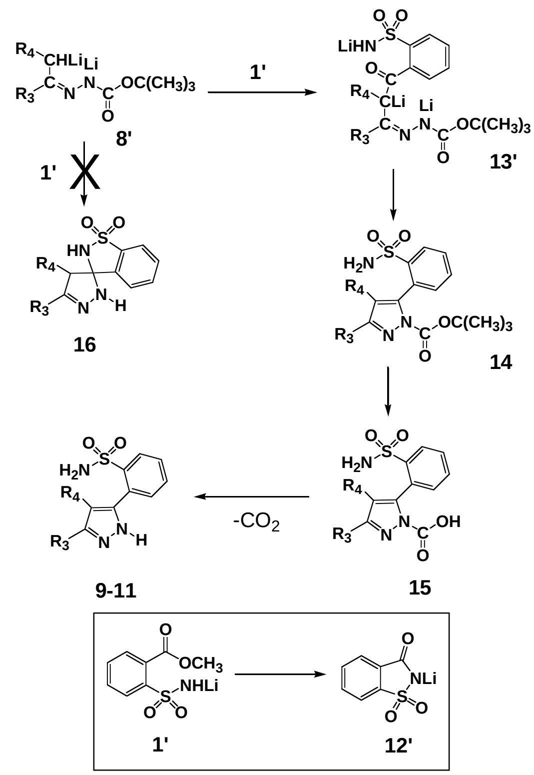

Figure 3. Reaction details.

acylated intermediates usually possessing an *ortho-* or *para-* electron donating phenyl substituents and not a sulfonamide group [17]. Initial attempts to affect a general procedure for acid hydrolysis-decarboxylation of BOC pyrazoles gave inconsistent results.

While all of the targeted new N*H*-pyrazoles **9-11** would have considerable developmental potential, their preparation is additionally challenging as a result of all of these steric, inductive and resonance factors.

RESULTS AND DISCUSSION

BOC-hydrazones **8** and ester-sulfonamide **1** were used in this investigation; **8** is easily prepared [18] as needed in multi-gram quantities by the straightforward 1:1 condensation of *C*(α)-ketones with *tert*-butyl carbazate (BOC-hydrazine), and **1** is readily available. The BOC-hydrazones **8** were easily purified by recrystallization from methanol (new: **8a**, 95%; **8b**, 56%; **8c**, 95%; **8d**, 92%) and chromatographic separations were unnecessary [19].

During the current study, *NH*-pyrazolyl-*ortho*-benzenesulfonamides **9a-h**, **10**, and **11** were prepared (Figure 2). BOC-hydrazones **8** were dilithiated to **8'** with excess lithium diisopropylamide (LDA) [hydrazone:LDA: ester-sulfonamide 1:6:1 for **9b** and **9h,** 1:5:1 for others] [20], condensed with **1**, which was presumed to be at least monolithiated to **1'** [21], or cyclized to the lithiated saccharin salt **12'** [22]. The presumed *C*-acylated intermediates **13** (from acification of **13'**), resulting from the condensation of **8'** with **1'**, were not isolated but acid-cyclized directly with 3 *M* hydrochloric acid to BOC-pyrazole **14** [17]. This was followed by the addition of concentrated hydrochloric acid until the total concentration of acid was brought to 6 *M*. The mixture was stirred at room temperature and under no other special conditions [12a]. Cyclodehydration to **14** would be followed by hydrolysis to cleave the *tert*-butyl ester group to *N*-carboxylic acid **15**, and then decarboxylation, resulting in the targeted N*H*-pyrazoles, **9-11**. It is likely that cyclization would occur before the hydrolysis and decarboxylation of the ester [16].

We established that **9a-h** (**10** is a dihydrobenzindazole) and **11** are pyrazoles and not potential isomeric spiro-(benzoisothiazole-pyrazole) dioxides **16** using absorption spectra, including DEPT, and liquid chromatography mass spectrometry (LCMS). The IR of the products indicated several NH/NH_2 absorptions, 3257-3387 cm^{-1}, with the lack of absorptions for the carboxyl group. The ^{1}H-NMR usually displayed the N*H*-pyrazole from δ 12.67-13.94 ppm. Also, DEPT, ^{1}H, and ^{13} C-NMR immediately ruled out the spiro isomer **16** with the absence of methylene carbon **9a-h**, or methyne carbon absorptions in **10** and **11**. Many of the analytical samples contained incorporated water and other solvent molecules (*e.g.*, for product **9c**, $C_{16}H_{15}N_3O_3S{\cdot}\frac{1}{4}\ H_2O$) [23]. Since this occurrence was higher than normal for us, Liquid Chromatography Mass Spectroscopy (LCMS) was used for all samples to verify the $[M+H]^+$ molecular ion for each compound (and $[M-H]^-$ for **9b** and **9h**) without incorporated solvent molecules interfering.

The current procedure affords examples for a regioselective multi-gram preparation of N*H*-pyrazolyl-*ortho*-benzenesulfonamides, **9-11**, starting with readily prepared carbo-*tert*-butoxyhydrazones **8**, using the straightforward application of a well documented earlier procedure for **8**, including rapid purification [18]. All of the products **9-11** are new, and it may difficult to prepare them by traditional procedures or even by a simple adaptation of the developed procedure for *N*-phenyl-pyrazolyl-benzenesulfonamides **5** [16]. The use of 3 and 6 *M* hydrochloric acid to bring about cyclization, hydrolysis [12a], and decarboxylation proved to be a simple yet effective choice where other acid procedures have given less consistent results because of side reactions. The yields of products ranged from 36-89 %; **9b** and **9h** were prepared from trilithiated and not dilithiated intermediates. The yields obtained for these products [50% and 44%] are relatively good when compared to other hydroxyphenyl-containing compounds in strong-base preparations. Since **9-11** were prepared by a general procedure, the yields reported here may not be the optimum possible for a particular compound. While all N*H*-pyrazoles are gaining in importance, it further demonstrates the use of methyl 2-(aminosulfonyl)-benzoate **1** for Claisen-type condensations with polylithiated systems and subsequent cyclization to new products of varying structure that have agricultural, other biological, synthetic, spectral studies, and other developmental potential.

EXPERIMENTAL

Melting points were obtained with a Mel-Temp II melting point apparatus in open capillary tubes and are uncorrected. Fourier Transform infrared spectra were obtained with a Nicolet Impact 410 FT-IR and a Mattson Genesis II FT-IR with Specac Golden Gate Accessory. ^{1}H, ^{13}C and ^{19}F (for **8c** and **9c**) magnetic resonance spectra were obtained with a Varian Associates Mercury Oxford 300 MHz nuclear magnetic resonance spectrometer, and chemical shifts are recorded in δ ppm downfield from an internal tetramethylsilane (TMS) standard. Combustion analyses were performed by Quantitative Technologies, Inc., P.O. Box 470, Salem Industrial Park, Bldg. 5, Whitehouse, NJ 08888.

LCMS analyses were measured on a Thermo-Finnigan LCQ Advantage system with the Surveyor autosampler, Surveyor pump, and LCQ Advantage Max mass spectral detector using electrospray ionization; 2-4 mg samples were prepared in 2 mL/L of acetonitrile; 10 μL injections were pumped at 1.00 mL/min isocratically with 70% acetonitrile and 30% water, each buffered with 0.1% formic acid by volume; 15 min runs were reproduced in both the positive and negative MS modes. Data were collected at full scan from 100 to 650 amu.

1,1-Dimethylethyl 2-[1-(3,4-Dimethoxyphenyl)ethylidene]-hydrazinecarboxylate (8a). To a 250 mL Erlenmeyer flask containing a magnetic stirrer was added 10.0 g (0.0555 mol) of 3',4'-dimethoxyacetophenone and 7.70 g (0.0568 mol) of *tert*-butyl carbazate followed by 100-150 mL of methanol and 8-10 drops of formic acid. Stirring was initiated to dissolve the ketone and hydrazide, and the solution was slowly brought to the boiling point. It was allowed to continue boiling slowly until approximately 50 mL of methanol remained in the flask. The flask was cooled, and the resulting solid was filtered to give 15.54 g (95%) of hydrazone **8a**, mp 149-152 °C (methanol), as white crystals. IR: 3207, 1727, and 1694 cm^{-1}. ^{1}H NMR: (deuteriochloroform): δ 1.55 (s, 9H), 2.18 (s, 3H), 3.88 (s, 3H), 3.93 (s, 3H), 6.82 (d, 1H, J = 9.0 Hz), 7.19 (d, 2H, J = 9.0 Hz), 7.55 (s, 1H), and 7.97 (s, NH). ^{13}C NMR (DMSO-d_6): δ 12.5, 28.3, 55.8, 81.1, 108.8, 110.2, 119.3, 131.1, 147.2, 148.9, 150.1, 153.1. LCMS, mw, 294.4; exact mass, 294.2: $(M+H)^+$, 295.0. *Anal.* Calcd for $C_{15}H_{22}N_2O_4$: C, 61.21; H, 7.53; N, 9.52. Found: C, 61.27; H, 7.54; N, 9.46.

1,1-Dimethylethyl 2-[1-(4-Hydroxyphenyl)ethylidene]-hydrazinecarboxylate (8b). Hydrazone **8b** was prepared in the same manner as **8a** using 8.80 g (0.0646 mol) of 4'-hydroxyacetophenone and 8.99 g (0.0681 mol) of *tert*-butyl carbazate, and yielded 9.03 g (56%) of product, mp 128-129 °C (methanol), as white crystals. IR: 3341, 3196, 1727, and 1693 cm^{-1}. ^{1}H NMR (DMSO-d_6): δ 1.45 (s, 9H), 2.11 (s, 3H), 6.80 (d, 2H, J = 9.0 Hz), 7.55 (d, 2H, J = 9.0 Hz), 7.56 (s, 1H), 9.60 (s, NH), and 9.66 (s, OH). ^{13}C NMR (DMSO-d_6): δ 14.3, 28.8, 79.8, 115.6, 128.1, 130.1, 149.3, 153.9, 158.9. LCMS, mw, 250.3; exact mass, 250.1: $(M+H)^+$, 250.7, $(M-H)^-$, 249.7. *Anal.* Calcd for $C_{13}H_{18}N_2O_3$: C, 62.37; H, 7.25; N, 11.19. Found: C, 62.19; H, 7.20; N, 11.18.

1,1-Dimethylethyl 2-[1-(4-Fluorophenyl)ethylidene]hydrazinecarboxylate (8c). Hydrazone **8c** was prepared in the same manner as **8a** using 10.0 g (0.0724 mol) of 4'-fluoroacetophenone and 10.04 g (0.0760 mol) of *tert*-butyl carbazate, and yielded 17.36 g (95%) of product, mp 168-171 °C (methanol), as white crystals. IR: 3280, 1733 cm^{-1}. ^{1}H NMR (deuteriochloroform): δ 1.46 (s, 9H), 2.16 (s, 3H), 7.14-7.21 (m, 1H), 7.73-7.78 (m, 2H), and 9.82 (s, NH). ^{13}C NMR (deuteriochloroform): δ 12.8, 28.3, 81.4, 115.2 (d, J_{CF} = 21.7 Hz), 128.1 (d, J_{CF} = 8.3 Hz), 134.4 (d, J_{CF} = 3.1 Hz), 147.8, 153.8, 163.4 (d, J_{CF} = 247.1 Hz). ^{19}F NMR (deuteriochloroform): δ -113.8 (b, m). LCMS, mw, 252.3; exact mass, 252.1: $(M+H)^+$, 252.9. *Anal.* Calcd for $C_{13}H_{17}FN_2O_2$: C, 61.89; H, 6.79; N, 11.10. Found: C, 61.77; H, 6.76; N, 10.99.

1,1-Dimethylethyl 2-Cyclododecylidenehydrazinecarboxylate (11d). Hydrazone **8d** was prepared in the same manner as **8a** using 3.0 g (0.0165 mol) of cyclododecanone and 2.25 g (0.0173 mol) of *tert*-butyl carbazate, and yielded 4.55 g (92%) of product, mp 155-157 °C (methanol), as white crystals. IR: 3241, 1677 cm^{-1}. ^{1}H NMR (deuteriochloroform): δ 1.35 (s, 9H), 1.50 (s broad, 14H), 1.61 (m, 2H), 1.70 (m, 2H), 2.22 (t, 2H, J = 6.8 Hz), 2.33 (t, 2H, J = 6.9 Hz), and 7.85 (s, NH). ^{13}C NMR (deuteriochloroform): δ 22.4, 23.1, 23.6, 24.5, 24.8, 25.0, 25.1, 26.9, 28.2, 28.3, 32.9, 80.5, 153.4, 155.9. LCMS, mw, 296.5; exact mass, 296.3: $(M+H)^+$, 296.9. *Anal.* Calcd for $C_{17}H_{32}N_2O_2$: C, 68.88; H, 10.88; N, 9.45. Found: C, 68.50; H, 10.86; N, 9.54.

General Procedure for the Preparation of 2-(1*H*-Pyrazol-5-yl)benzenesulfonamides). (Ratio of reagents – BOC hydrazone: LDA: ester, 1:5-6:1) In a typical reaction sequence, LDA was prepared by the addition of 49-50 mL (60 mL for **9b** and **9h**) of 1.60 *M* n-butyllithium (0.0788 mol/0.0945 mol for **9b** and **9h**) in hexanes to a three-neck round-bottomed flask (*e.g.*, 500 mL), equipped with a nitrogen inlet tube, a side-arm addition funnel (*e.g.*, 125 mL), and a magnetic stir bar. The flask was cooled in an ice water bath, and 8.01 g (0.0791 mol) or 9.76 g (0.0961 mol for **9b** and **9h**) of diisopropylamine (99.5% - Aldrich Chem. Co.), dissolved in 25-35 mL of dry THF (freshly distilled from sodium-benzophenone ketyl) was added from the addition funnel at a fast drop wise rate during a 5 min (0 °C, N_2) period. The solution was stirred for an additional 15-20 min, and then treated *via* the addition funnel, during 5 min, with BOC hydrazone [17] (0.015 mol) dissolved in 40-60 mL of THF. After 45-60 min [or 2-2.5 hr for **9b** and **9h**], a solution of 3.47 g (0.0158 mol – 5% molar excess) of methyl 2-(aminosulfonyl)-benzoate **1** dissolved in 50 mL of THF, was added, during 5 min, to the dilithiated or trilithiated intermediate, and the solution was stirred overnight (N_2) at room temp. Finally, 100 mL of 3 *M* hydrochloric acid was added all at once, followed by an additional 100 mL of reagent grade THF, and the two-phase mixture was well-stirred and heated under reflux for approximately 30-40 min. The mixture was cooled to room temp. and was followed by the addition of 50 mL of conc. hydrochloric acid. Vigorous stirring was conducted at room temp. for 24 hr. At the end of this period, the mixture was poured into a large flask (*ca.* 1 or 2 L) containing 100 mL of reagent grade ethyl ether. The mixture was then neutralized with solid sodium bicarbonate, and the layers separated. If a solid appeared at this point, reagent grade THF could be added to induce dissolution, or the precipitate could be filtered. The aqueous layer was extracted with ethyl ether (2 x 50 mL), and the organic fractions were combined, not dried, evaporated under reduced pressure, and recrystallized from common solvents to afford products **9-11**.

2-(3-(3,4-Dimethoxyphenyl)-1*H*-pyrazol-5-yl))benzenesulfonamide (9a). This compound was obtained as pale yellow crystals, mp 135-139 °C (benzene/methanol), in 65% yield (3.56 g) using the general procedure from the condensation-cyclization of dilithiated 3',4'-dimethoxyacetophenone BOC-hydrazone **8a** and ester-sulfonamide **1**. IR: 3277, 3250 cm^{-1}. ^{1}H NMR (DMSO-d_6): δ 3.78 (s, 3H), 3.85 (s, 3H), 7.03 (s, 1H), 7.05 (s, 1H), 7.37-7.82 (m, 5H), 8.10 (d, 1H, J = 7.8 Hz), and 13.59 (s, NH). ^{13}C NMR (DMSO-d_6): δ 56.2, 56.3, 103.2, 109.9, 112.8, 118.7, 122.3, 128.3, 128.7, 132.3, 132.7, 132.8, 141.7, 143.9, 149.8, and 152.3. LCMS, mw, 359.4; exact mass, 359.1: $(M+H)^+$, 360.0. *Anal.* Calcd for $C_{17}H_{17}N_3O_4S$•1/4 H_2O: C, 56.11; H, 4.85; N, 11.55. Found: C, 56.11; H, 4.54; N, 11.27.

2-(3-(4-Hydroxyphenyl)-1*H*-pyrazol-5-yl))benzenesulfonamide (9b). This compound was obtained as pale yellow crystals, mp 278 °C (xylenes/DMF), in 50% yield (2.38 g) using the general procedure from the condensation-cyclization of trilithiated 4'-hydroxyacetophenone BOC-hydrazone **8b** and ester-sulfonamide **1**. IR: 3382, 3351 cm^{-1}. ^{1}H NMR (DMSO-d_6): δ 6.95 (s, 1H), 6.93 (d, 1H, J = 6.3 Hz), 7.54-7.83 (m. 5H), 8.10 (d, 1H, J = 7.5 Hz), 9.82 (s, OH), and 13.50 (s, NH). ^{13}C NMR (DMSO-d_6): δ 102.7, 116.6, 120.6, 127.6, 128.3, 128.7, 132.3, 132.7, 141.7, 144.1, 151.3, and 158.5. LCMS, mw, 315.4; exact mass, 315.1: $(M+H)^+$, 316.0; $(M-H)^-$ 314.0. *Anal.* Calcd for C_{15} $H_{12}N_3O_3S$: C, 57.13; H, 4.16; N, 13.33. Found: C, 56.86; H, 3.84; N, 13.12.

2-(3-(4-Fluorophenyl)-1*H*-pyrazol-5-yl))benzenesulfonamide (9c). This compound was obtained as dark yellow crystals, mp 214-216 °C (xylenes), in 68% yield (3.25 g) using the general procedure from the condensation-cyclization of dilithiated 4'-fluoroacetophenone BOC-hydrazone **8c** and ester-sulfonamide **1**. IR: 3300 sh, 3284, 3275 sh cm^{-1}. ^{1}H NMR (DMSO-d_6): δ 7.09 (s, 1H), 7.34 (d, 2H, J = 8.7 Hz), 7.58-7.73 (m. 3H), and 7.92- 7.94 (m, 2H), and 8.11 (d, 1H, J = 7.5 Hz). ^{13}C NMR (DMSO-d_6): δ 104.1, 116.7 (d, J_{CF} = 21.6 Hz), 126.0, 128.2 (d, J_{CF} = 7.5 Hz), 128.3, 128.9, 129.6, 129.7, 131.5, 132.8 (d, J_{CF} = 7.5 Hz), 142.0, 144.1, 149.3, and 162.7 (d, J_{CF} = 245.5 Hz). ^{19}F NMR (DMSO-d_6): δ -113.6 (m, b). LCMS, mw, 317.3; exact mass, 317.1: $(M+H)^+$, 318.0. *Anal.* Calcd for $C_{15}H_{12}$ FN_3O_2S•1/8 C_8H_{10} [23]: C, 58.13; H, 4.04; N 12.71. Found: C. 58.17; H, 4.02; N, 12.54.

2-(3-(4-Methoxyphenyl)-1*H*-pyrazol-5-yl))benzenesulfonamide (9d). This compound was obtained as pale white crystals, mp 212 °C (benzene/methanol), in 64% yield (3.19 g) using the general procedure from the condensation-cyclization of dilithiated 4'-methoxyacetophenone BOC-hydrazone **8** and ester-sulfonamide **1**. IR: 3363, 3302 cm^{-1}. ^{1}H NMR (DMSO-d_6): δ 3.79 (s, 3H), 6.96 (s, 1H), 7.05 (d, 2H, J = 8.6 Hz), 7.66-7.73 (m, 5H), 8.06 (d, 1H, J = 7.5 Hz), and 13.59 (s, NH). ^{13}C NMR (DMSO-d_6): δ 55.9, 103.0, 115.2, 122.1, 127.5, 128.3, 128.7, 132.3, 132.7, 132.8, 141.7, 143.6, 151.3, and 160.1. LCMS, mw, 329.4; exact mass, 329.1: $(M+H)^+$, 329.9. *Anal.*

Calcd for $C_{16}H_{15}N_3O_3S$•1/4 H_2O: C, 57.56; H, 4.68; N, 12.59. Found: C, 57.70; H, 4.59; N, 12.28.

2-(3-(4-Chlorophenyl)-1*H*-pyrazol-5-yl))benzenesulfonamide (9e). This compound was obtained as pale orange crystals, mp 216 °C (xylenes/DMF), in 46% yield (2.30 g) using the general procedure from the condensation-cyclization of dilithiated 4'-chloroacetophenone BOC-hydrazone **8** and ester-sulfonamide **1**. IR: 3289 sh cm^{-1}. ^{1}H NMR (DMSO-d$_6$): δ 7.21 (s, 1H), 7.34 (d, 2H, *J* = 8.6 Hz), 7.58-7.84 (m. 5H), and 7.97-7.99 (m, 2H), and 8.17 (d, 1H, *J* = 7.8 Hz). ^{13}C NMR (DMSO-d$_6$): δ 104.0, 125.7, 127.4, 128.1, 128.5, 129.2, 129.4, 130.6, 132.4, 133.5, 142.0 and 151.4. LCMS, mw, 333.3; exact mass, 333.0: (M+H)$^+$, 333.9. *Anal.* Calcd for $C_{15}H_{12}ClN_3O_2S$•1/8 C_8H_{10} [23]: C, 55.37; H, 3.85; N 12.11. Found: C, 55.23; H, 3.64; N, 11.96.

2-(3-(Phenyl-1*H*-pyrazol-5-yl))benzenesulfonamide (9f). This compound was obtained as yellow crystals, mp 197-200 °C (benzene/methanol), in 63% yield (2.80 g) using the general procedure from the condensation-cyclization of dilithiated acetophenone BOC-hydrazone **8** and ester-sulfonamide **1**. IR: 3308 sh cm$^{\pm1}$. ^{1}H NMR (DMSO-d$_6$): δ 3.79 (s, 3H), 6.99 (s, 1H), 7.08 (d, 2H, *J* = 8.6 Hz), 7.38-7.84 (m. 8H), 8.07 (d, 1H, *J* = 7.8 Hz), and 13.69 (s, NH). ^{13}C NMR (DMSO-d$_6$): δ 103.3, 125.3, 127.5, 128.1, 128.6, 128.8, 129.2, 131.5, 132.1, 132.2, 141.1, 143.0, and 150.7. LCMS, mw, 299.4; exact mass, 299.1: (M+H)$^+$, 300.0. *Anal.* Calcd for $C_{15}H_{13}N_3O_2S$: C, 60.18; H, 4.38; N, 14.04. Found: C, 60.19; H, 4.21; N, 13.93.

2-(3-(2-Naphthyl)-1*H*-pyrazol-5-yl))benzenesulfonamide (9g). This compound was obtained as white crystals, mp 241-243 °C (xylenes/isobutanol), in 89% yield (4.65 g) using the general procedure from the condensation-cyclization of dilithiated 2-acetonaphthone BOC-hydrazone **8** and ester-sulfonamide **1**. IR: 3281 sh cm^{-1}. ^{1}H NMR (DMSO-d$_6$): δ 7.28 (s, 1H), 7.55-8.17 (m, 11H), 8.46 (s, 1H) and 13.94 (s, NH). ^{13} C NMR (DMSO-d$_6$): δ 104.0, 123.6, 124.0, 126.5, 126.8, 127.9, 127.8, 128.1, 128.3, 128.7, 132.1, 132.2, 132.7, 133.1, and 141.3. LCMS, mw, 349.4; exact mass, 349.1: (M+H)$^+$, 350.0. *Anal.* Calcd for $C_{15}H_{13}N_3O_2S$•1/3 H_2O: C, 64.32; H, 4.14; N, 11.82. Found: C, 64.48; H, 4.21; N, 11.87.

2-(3-(2-Hydroxyphenyl)-1*H*-pyrazol-5-yl))benzenesulfonamide (9h). This compound, was obtained as pale yellow crystals, mp 178-179 °C (toluene/1-propanol), in 44% yield (2.10 g) using the general procedure from the condensation-cyclization of dilithiated 2'-hydroxyacetophenone BOC-hydrazone **8** and ester-sulfonamide **1**. IR: 3375, 3277 cm^{-1}. ^{1}H NMR (DMSO-d$_6$): δ 6.87-7.02 (m, 2H), 7.14-7.25 (m, 1H), 7.47-7.67 (m, 5H), 8.13 (d, 1H, *J* = 7.5 Hz), 10.3 (s, OH), 12.7 (s, NH). ^{13}C NMR (DMSO-d$_6$): δ 103.9, 115.5, 116.2, 119.2, 126.9, 127.5, 128.8, 131.5, 131.6, 141.0, 148.6 and 154.1. LCMS, mw, 315.3; exact mass, 315.1: (M+H)$^+$, 316.0; (M-H)$^-$, 314.0. *Anal.* Calcd for $C_{15}H_{12}N_3O_3S$•1 H_2O: C, 54.04; H, 4.54; N, 12.60. Found: C, 54.05; H, 4.42; N, 12.48.

2-(4,5-Dihydro-2*H*-benz[*g*]indazol-3-yl)benzenesulfonamide (10). This compound was obtained as light orange crystals, mp 266-268 °C (toluene/1-propanol), in 66% yield (3.24 g) using the general procedure from the condensation-cyclization of dilithiated 1-tetralone BOC-hydrazone **8** and ester-sulfonamide **1**. IR: 3338, 3357 sh cm^{-1}. ^{1}H NMR (DMF-d$_7$): δ 2.94-2.99 (m, 2H), 3.15-3.20 (m, 2H), 7.30-7.39 (m, 3H), 7.65-7.77 (m, 3H), 7.86-7.90 (m, 1H), 8.20-8.23 (m, 1H), and 13.90 (s, NH). ^{13}C NMR (DMSO-d$_6$): δ 19.6, 29.8, 115.2, 122.0, 125.7, 127.2, 128.2, 128.4, 129.0, 131.6, 132.4, 132.7, 134.7, 140.2, 142.7, 147.3, and 162.2 [24]. LCMS, mw, 325.4; exact mass, 325.1: (M+H)$^+$, 326.0. *Anal.* Calcd for $C_{17}H_{13}N_3O_2S$: C, 62.75; H, 4.65; N, 12.91. Found: C, 62.69; H, 4.46; N, 12.69.

2-(4,5-(Decamethylene)-1*H*-pyrazol-3-yl))benzenesulfonamide (11). This compound was obtained as pale yellow crystals, mp 231-233 °C (benzene/methanol), in 36% yield (2.13 g) using the general procedure from the condensation-cyclization of dilithiated 1-cyclododecaone BOC-hydrazone **8d** and ester-sulfonamide **1**. IR: 3272, 3372 sh cm^{-1}. ^{1}H NMR (DMSO-d$_6$): δ 1.07-1.41 (m, 13H), 1.76 (s broad, 2H), 2.42-2.64 (m, 4H), 3.40 (s, 1H), 7.39-7.64 (m, 3H), 8.01(d. 1H, *J* = 7.86 Hz) and 12.67 (s, 1H). ^{13}C NMR: (DMSO-d$_6$): δ 19.2, 20.5, 22.0, 22.2, 24.0, 24.2, 24.5, 26.9, 27.2, 115.8, 127.1, 127.8, 131.8, 132.9, 141.1, 142.0, and 148.1. LCMS, mw, 361.5; exact mass, 361.2: (M+H)$^+$, 362.1. *Anal.* Calcd for $C_{19}H_{27}N_3O_2S$: C, 63.13; H, 7.53; N, 11.62. Found: C, 62.98; H, 7.60; N, 11.43.

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[23] During previous investigations, several analytical samples incorporated water, alcohols such as *tert*-butyl alcohol, acetonitrile or benzene [unpublished result]; Compounds **9c** and **9e** in this study incorporated xylenes. See also: ref. 9.

[24] The ^{13}C spectrum was taken at a frequency of 75 MHz, which does not provide a high enough resolution to distinguish several of the aromatic carbons in this molecule.