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Synthesis of 3-(Tosylalkyl)indazoles and their Desulfonylation Reactions – A New Entry to 3-Substituted Indazoles by an Unprecedented Friedel–Crafts Process

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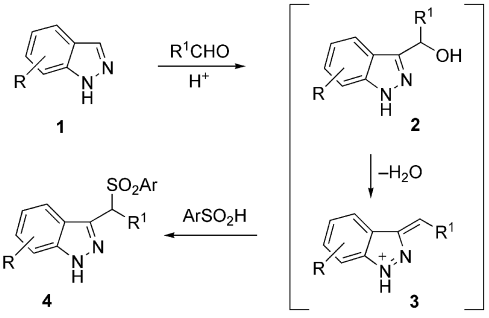
Reaction of indazoles with aldehydes in the presence of *p*-toluenesulfinic acid affords the corresponding sulfonyl indazoles in satisfactory yields. The reported Friedel–Crafts process is rather unusual on indazoles because of the reduced electronic density of the heterocycle. The obtained sulfonyl indazoles can be desulfonylated under reductive conditions, finally leading to 3-alkylated indazoles.

Introduction

Products of natural origin based on the indazole nucleus are rather uncommon and have been isolated from extracts of a limited number of plant species.[1] Conversely, a large amount of synthetically prepared compounds recognize a key structural feature in the indazole ring that is responsible for their enhanced biological activity.[2] Indazole-containing derivatives are known for their anti-aggregatory and vasorelaxant properties,[3] antimicrobial,[4] anti-inflammatory activities,[5] and anticancer effects.[6] From a synthetic standpoint, the indazole ring may be assembled by exploiting an intramolecular coupling of arenediazo groups with vicinal *o*-methyl groups or by reaction of hydrazines with functionalized arenecarbonyl derivatives.[7] Introduction of carbon frameworks into the indazole system can be carried out at the nitrogen atom as well as at 3-position in the pyrazole ring.

The latter process could be in principle correlated to the very popular Friedel–Crafts reaction, currently used to functionalize indoles at the same position.[8] However, the reduced electronic density of the pyrazole ring in indazoles sorely prevents the 3-position from attack by carbon electrophiles. As a matter of fact, because halogenation of indazoles occurs regioselectively at 3-C, the corresponding haloindazoles can be profitably involved in a Suzuki or Heck cross-coupling by using aryl or alkenyl reagents.[9] Recently, we reported that indoles react with aldehydes in the presence of arenesulfinic acids, leading to 3-(1-arylsulfonylalkyl)indoles.[10] These compounds behave similarly to gramine derivatives, as under basic conditions they eliminate arenesulfinic acid to give an alkylideneindolenine that may react with nucleophilic reagents.[11] In this paper, we demonstrate that indazoles **1** undergo a similar process in which a preliminary Friedel–Crafts reaction with an aldehyde leads to corresponding alcohol **2** (Scheme 1). Upon dehydration, under acidic conditions, indazolium salt **3** is formed, and this highly electrophilic species readily reacts with arenesulfinic acid to give sulfonyl indazole **4**. To the best of our knowledge, this process represents the first example of an intermolecular Friedel–Crafts reaction on these heterocyclic systems.[12]



Scheme 1. Synthesis of sulfonyl indazoles via indazolium salt intermediate.

Results and Discussion

A three-component coupling of indazoles **1** with aldehydes **5** and *p*-toluenesulfinic acid in dichloromethane at reflux affords the corresponding sulfonyl indazoles **6** in satisfactory yields (Table 1). *p*-Toluenesulfinic acid, besides being a reagent, is also able to provide a certain degree of acidity in the reaction medium. However, the acidity level brought by *p*-toluenesulfinic acid is not adequate to properly shift the equilibrium toward complete formation of sul-

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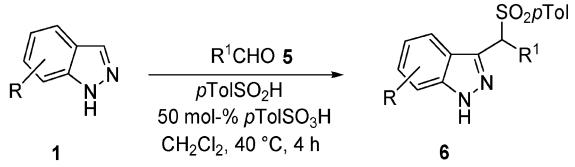
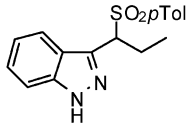
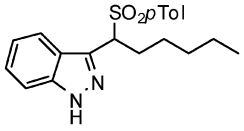
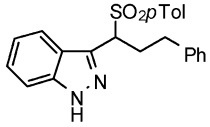
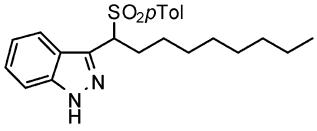
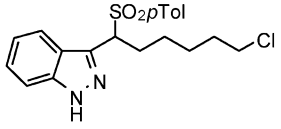
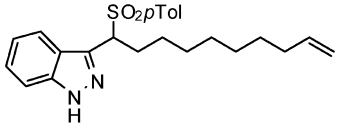
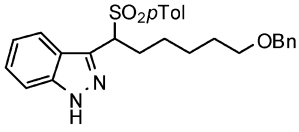
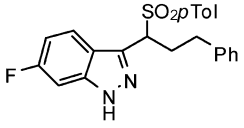
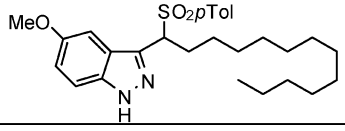
fonyl indazoles. Therefore, *p*-toluenesulfonic acid is added to the reaction mixture to provide the necessary acidity. The success of this procedure is closely related to the thermodynamic stability of compounds **6**, which provide the necessary driving force for their efficient formation.

Table 1. Synthesis of sulfonyl indazoles **6** by reaction of indazoles **1** with aldehydes **5** and *p*-toluenesulfinic acid.

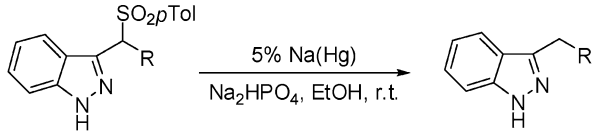


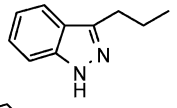
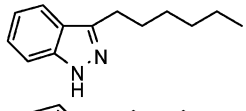
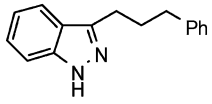
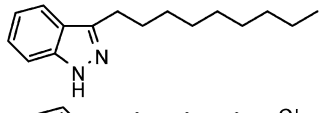
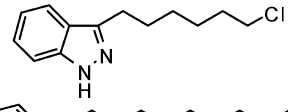
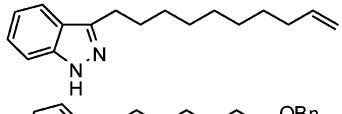
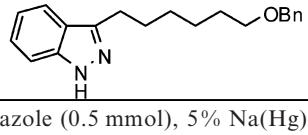
Entry		Sulfonyl Indazole **6**[a]	Yield [%][b]
1	**6a**		82
2	**6b**		71
3	**6c**		73
4	**6d**		70
5	**6e**		68
6	**6f**		63
7	**6g**		60
8	**6h**		30[c]
9	**6i**		32[d]

[a] Indazole (1.05 mmol), aldehyde (1 mmol), *p*-toluenesulfinic acid (1.2 mmol), *p*-toluenesulfonic acid (0.5 mmol) in dichloromethane (3 mL) at 40 °C for 4 h. [b] Yield of pure, isolated products. [c] Reaction carried out in 1,2-dichloroethane at reflux. [d] Reaction carried out in 1,4-dioxane at reflux.

Other nucleophiles (halides, nitro, etc.) could in principle be used to trap the intermediate vinylogous iminium ion, but none of them seem to be able to impart the necessary stability to the final product. The poor reactivity of the indazole system in Friedel–Crafts reactions obviously poses some limitations on the nature of aldehydes usable for this procedure. Straight-chain aldehydes react properly with indazole even when functional groups are present, provided that their position is far from the carbonyl group (Table 1, Entries 5–7). Ketones and aldehydes bearing substituents in close proximity to the carbonyl group react sluggishly with indazole under typical reaction conditions. Preliminary attempts to force the process by using high-boiling solvents (1,2-dichloroethane, toluene, dioxane) or by increasing the acidity of the mixture did not give any appreciable results. Arylaldehydes also give disappointing results, even though they contain electron-withdrawing groups such as in 4-nitrobenzaldehyde. Substitution of the aromatic ring in indazoles **1** is also troublesome. The presence of substituents at the 4-position prevents the formation of any product **6**, regardless of the electronic aptitude of the corresponding group. Concerning the 5- and 6-positions, iodo, chloro, and

Table 2. Desulfonylation of sulfonyl indazoles **6** by Na(Hg) amalgam.



Entry		Indazole **7**[a]	Yield [%][b]
1	**7a**		77
2	**7b**		88
3	**7c**		80
4	**7d**		92
5	**7e**		93
6	**7f**		94
7	**7g**		89

[a] Sulfonyl indazole (0.5 mmol), 5% Na(Hg) amalgam (0.9 g), Na_2HPO_4 (2 mmol) in dry ethanol (5 mL) at room temperature for 2 h. [b] Yield of pure, isolated products.

nitro groups make the corresponding indazoles **1** totally unreactive, whereas fluoro and methoxy groups react with aldehydes, although a consistently lower yield of obtained products **6** is observed (Table 1, Entries 8 and 9). These findings support the involvement of electronic and steric factors in our process, although the lack of reactivity of branched aldehydes clearly indicates a prevalence of steric effects. The importance of the sulfonyl group in synthesis mostly stems from its activating properties as a leaving group and its ability to stabilize carbanions.[13] Because the sulfonyl moiety is seldom present in final targets, different procedures directed to its removal are available.[14]

Substitution of the sulfonyl groups with hydrogen atoms can be readily performed by following a classical procedure that employs Na(Hg) amalgam in protic solvents (Table 2).[15] The desulfonylation reaction is operationally simple and occurs with an interesting degree of chemoselectivity, as evidenced in the retention of the chlorine atom in compound **7e** (Table 2, Entry 5). The whole two-step synthetic operation leading to compounds **7** from indazole is equivalent to an alkylation reaction that cannot be accomplished directly by using organometallic reagents or by sp^3-carbon electrophiles on indazole.

Conclusions

In summary, a three-component coupling of indazoles with aldehydes and *p*-toluenesulfinic acid leading to sulfonyl indazoles was described. The reduced electronic density of the indazole ring usually prevents its reaction with carbon electrophiles, making the corresponding Friedel–Crafts process hardly achievable. As for the parent indole derivatives, the mechanism involves electrophilic attack of the aldehyde to the indazole followed by loss of a water molecule. The resulting indazolium salt is intercepted by the *p*-toluenesulfinate anion, leading to the final product. Although limited to straight-chain aldehydes, to the best of our knowledge, this reaction represents the first successful substitution brought about by carbon electrophiles on the indazole ring. The obtained sulfonyl indazoles can undergo reductive desulfonylation to afford 3-alkylindazoles in good yields.

Experimental Section

General Remarks: ^{1}H NMR spectra were recorded at 400 MHz with a Varian Mercury Plus 400. ^{13}C NMR spectra were recorded at 100 MHz. Mass spectra were carried out by using the EI technique (70 eV) with a GC–MS Agilent Technologies 6850 SerieII/5973 Inert instrument. Microanalyses were performed with a CHNS-O analyzer Model EA 1108 from Fisons Instruments. IR spectra were recorded with a Perkin–Elmer Paragon 500 FTIR. All chemicals used were commercial.

General Procedure for the Synthesis of Sulfonylindazoles 6: To a stirred solution of indazole **1** (1.05 mmol), *p*-toluenesulfinic acid (1.2 mmol), and *p*-toluenesulfonic acid monohydrate (0.5 mmol) in CH_2Cl_2 (3 mL) was added carbonyl compound **5** (1 mmol) at room temperature. The resulting reaction mixture was stirred at reflux for 4 h and, after cooling, was then diluted with CH_2Cl_2 (12 mL). The organic solution was extracted with saturated $NaHCO_3$ (3×2 mL) and then dried with Na_2SO_4. Crude product **6** obtained after removal of the solvent at reduced pressure was purified by flash chromatography (hexanes/ethyl acetate, 9:1).

3-{1-[(4-Methylphenyl)sulfonyl]propyl}-1*H*-indazole (6a): Yield: 0.258 g, (82%). White solid. M.p. 83–85 °C. IR (nujol): $\tilde{\nu}$ = 739, 1147, 1595, 1614 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.87 (t, J = 7.3 Hz, 3 H), 2.32 (s, 3 H), 2.54–2.72 (m, 2 H), 5.43 (dd, J = 4.7, 10.3 Hz, 1 H), 7.09 (d, J = 8.5 Hz, 2 H), 7.15 (t, J = 8.1 Hz, 1 H), 7.29–7.41 (m, 4 H), 7.66 (d, J = 8.1 Hz, 1 H), 7.95 (br. s, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 10.5, 20.7, 21.9, 80.6, 109.9, 121.2, 121.9, 124.6, 127.3, 129.5, 129.8, 132.8, 135.8, 141.0, 145.5 ppm. MS (EI): *m*/*z* (%) = 159 (100), 131 (12), 117 (8), 91 (10), 77 (7). $C_{17}H_{18}N_2O_2S$ (314.40): calcd. C 64.94, H 5.77, N 8.91; found C 6.78, H 5.89, N 9.09.

3-{1-[(4-Methylphenyl)sulfonyl]hexyl}-1*H*-indazole (6b): Yield: 0.253 g (71%). White solid. M.p. 95–98 °C. IR (nujol): $\tilde{\nu}$ = 1145, 1594, 1614 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.77 (t, J = 7.3 Hz, 3 H), 1.09–1.33 (m, 6 H), 2.31 (s, 3 H), 2.45–2.57 (m, 1 H), 2.58–2.72 (m, 1 H), 5.51 (dd, J = 3.0, 11.5 Hz, 1 H), 7.08 (d, J = 8.5 Hz, 2 H), 7.14 (t, J = 8.1 Hz, 1 H), 7.28–7.36 (m, 4 H), 7.65 (d, J = 8.1 Hz, 1 H), 7.94 (br. s, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.1, 21.9, 22.5, 25.4, 26.7, 31.2, 79.2, 109.9, 121.2, 121.9, 124.6, 127.3, 129.5, 129.7, 132.8, 135.7, 140.8, 145.5 ppm. MS (EI): *m*/*z* (%) = 201 (6), 157 (10), 131 (12), 91 (7), 77 (6), 126 (100), 32 (18). $C_{20}H_{24}N_2O_2S$ (356.48): calcd. C 67.38, H 6.79, N 7.86; found C 67.50, H 6.95, N 7.99.

3-{1-[(4-Methylphenyl)sulfonyl]-3-phenylpropyl}-1*H*-indazole (6c): Yield: 0.285 g (73%). White solid. M.p. 124–126 °C. IR (nujol): $\tilde{\nu}$ = 742, 749, 1134, 1597, 1616 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.32 (s, 3 H), 2.33–2.43 (m, 1 H), 2.66–2.75 (m, 1 H), 2.79–2.90 (m, 1 H), 2.96–3.08 (m, 1 H), 5.40 (d, J = 10.7 Hz, 1 H), 6.92–6.97 (m, 2 H), 7.08 (d, J = 8.5 Hz, 2 H), 7.13–7.37 (m, 8 H), 7.70 (d, J = 8.1 Hz, 1 H), 8.01 (br. s, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.8, 28.5, 31.5, 77.5, 109.9, 121.2, 122.0, 124.6, 126.7, 127.3, 128.8, 129.5, 129.7, 132.7, 136.0, 139.3, 145.5 ppm. MS (EI): *m*/*z* (%) = 233 (100), 218 (26), 206 (10), 157 (16), 131 (75), 115 (46), 104 (60), 91 (20), 77 (24). $C_{23}H_{22}N_2O_2S$ (390.50): calcd. C 70.74, H 5.68, N 7.17; found C 70.88, H 5.51, N 7.31.

3-{1-[(4-Methylphenyl)sulfonyl]nonyl}-1*H*-indazole (6d): Yield: 0.279 g (70%). White solid. M.p. 83–85 °C. IR (nujol): $\tilde{\nu}$ = 663, 751, 907, 1153, 1597, 1615, 3057 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.82 (t, J = 7.3 Hz, 3 H), 1.07–1.35 (m, 12 H), 2.32 (s, 3 H), 2.47–2.58 (m, 1 H), 2.59–2.73 (m, 1 H), 5.51 (dd, J = 3.4, 11.5 Hz, 1 H), 7.10 (d, J = 8.1 Hz, 2 H), 7.16 (t, J = 7.7 Hz, 1 H), 7.29–7.42 (m, 4 H), 7.66 (dd, J = 0.9, 8.1 Hz, 1 H), 7.94 (br. s, 1 H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 14.2, 21.8, 22.8, 25.8, 26.8, 29.0, 29.2, 29.3, 31.9, 79.6, 110.0, 121.2, 121.9, 125.8, 127.3, 129.5, 129.7, 133.2, 135.7, 141.0, 145.4 ppm. MS (EI): *m*/*z* (%) = 242 (24), 171 (19), 157 (88), 131 (100), 118 (44), 105 (23), 91 (7), 77 (19), 32 (22). $C_{23}H_{30}N_2O_2S$ (398.56): calcd. C 69.31, H 7.59, N 7.03; found C 69.09, H 7.72, N 6.88.

3-{6-Chloro-1-[(4-methylphenyl)sulfonyl]hexyl}-1*H*-indazole (6e): Yield: 0.266 g (68%). Yellow oil. IR (neat): $\tilde{\nu}$ = 750, 814, 907, 1146, 1596, 1615, 3064 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.10–1.32 (m, 2 H), 1.35–1.52 (m, 2 H), 1.59–1.68 (m, 2 H), 2.31 (s, 3 H), 2.47–2.58 (m, 1 H), 2.61–2.73 (m, 1 H), 3.40 (dt, J = 1.7, 6.4 Hz, 2 H), 5.50 (dd, J = 3.4, 11.5 Hz, 1 H), 7.08 (d, J = 8.1 Hz, 2 H), 7.11–7.18 (m, 1 H), 7.25–7.36 (m, 4 H), 7.65 (dd, J = 0.9, 8.1 Hz, 1 H), 7.94 (br. s, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.8, 25.1, 26.3, 26.6, 32.2, 44.9, 78.9, 109.8, 121.3, 121.9, 124.6,

127.4, 129.5, 129.8, 132.7, 135.8, 140.9, 145.6 ppm. MS (EI): *m*/*z* (%) = 236 (10), 234 (32), 199 (10), 157 (97), 131 (100), 105 (31), 77 (25). $C_{20}H_{23}ClN_2O_2S$ (390.93): calcd. C 61.45, H 5.93, N 7.17; found C 61.57, H 5.76, N 7.25.

3-{1-[(4-Methylphenyl)sulfonyl]dec-9-enyl}-1*H*-indazole (6f): Yield: 0.258 g (63%). White solid. M.p. 70–73 °C. IR (nujol): $\tilde{\nu}$ = 752, 908, 1152, 1596, 1614, 1640, 3062 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 1.10–1.35 (m, 10 H), 1.96 (q, *J* = 7.7 Hz, 2 H), 2.33 (s, 3 H), 2.47–2.59 (m, 1 H), 2.60–2.73 (m, 1 H), 4.87–4.98 (m, 2 H), 5.51 (dd, *J* = 3.0, 11.1 Hz, 1 H), 5.69–5.81 (m, 1 H), 7.10 (d, *J* = 8.1 Hz, 2 H), 7.16 (t, *J* = 7.7 Hz, 1 H), 7.29–7.42 (m, 4 H), 7.67 (d, *J* = 8.1 Hz, 1 H), 7.94 (br. s, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.8, 25.7, 26.7, 28.8, 28.9, 29.0, 29.2, 33.9, 77.4, 110.0, 114.4, 121.2, 121.9, 124.6, 127.3, 129.5, 129.7, 132.8, 135.6, 135.7, 139.3, 145.5 ppm. MS (EI): *m*/*z* (%) = 254 (17), 211 (8), 171 (17), 157 (98), 131 (100), 118 (49), 105 (29), 91 (7), 77 (26), 32 (27). $C_{24}H_{30}N_2O_2S$ (410.57): calcd. C 70.21, H 7.36, N 6.82; found C 70.34, H 7.22, N 6.58.

3-{6-Benzyloxy-1-[(4-methylphenyl)sulfonyl]hexyl}-1*H*-indazole (6g): Yield: 0.277 g (60%). White solid. M.p. 85–87 °C. IR (nujol): $\tilde{\nu}$ = 662, 750, 907, 1085, 1117, 1150, 1596, 1614 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 1.10–1.30 (m, 2 H), 1.31–1.57 (m, 4 H), 2.31 (s, 3 H), 2.46–2.58 (m, 1 H), 2.60–2.73 (m, 1 H), 3.35 (t, *J* = 6.4 Hz, 2 H), 4.40 (s, 2 H), 5.50 (dd, *J* = 3.9, 11.5 Hz, 1 H), 7.08 (d, *J* = 8.1 Hz, 2 H), 7.14 (t, *J* = 7.7 Hz, 1 H), 7.23–7.36 (m, 9 H), 7.65 (d, *J* = 8.1 Hz, 1 H), 7.93 (br. s, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.8, 25.6, 25.7, 26.7, 29.5, 70.2, 73.0, 79.1, 109.9, 121.2, 121.9, 124.6, 127.3, 127.7, 127.8, 128.6, 129.5, 129.7, 132.9, 135.7, 138.7, 140.9, 145.5 ppm. MS (EI): *m*/*z* (%) = 306 (8), 215 (41), 157 (36), 131 (83), 118 (75), 91 (100), 77 (27), 65 (15). $C_{27}H_{30}N_2O_3S$ (462.60): calcd. C 70.10, H 6.54, N 6.06; found C 70.33, H 6.64, N 6.27.

6-Fluoro-3-{1-[(4-methylphenyl)sulfonyl]-3-phenylpropyl}-1*H*-indazole (6h): Yield: 0.122 g (30%). Brown viscous oil. IR (neat): $\tilde{\nu}$ = 736, 908, 1149, 1377, 1455, 1597, 1626, 3027 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 2.22–2.53 (m, 1 H), 2.34 (s, 3 H), 2.68–2.91 (m, 2 H), 2.94–3.06 (m, 1 H) 5.29 (d, *J* = 10.7 Hz, 1 H), 6.92–6.96 (m, 2 H), 7.10 (d, *J* = 8.1 Hz, 2 H), 7.13–7.37 (m, 7 H), 7.63 (dd, *J* = 5.1, 8.9 Hz, 1 H), 7.99 (br. s, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.8, 28.2, 31.4, 77.5, 96.2, 111.7, 112.0, 122.5, 122.6, 126.8, 129.5, 129.8, 130.6, 131.7, 132.7, 136.1, 139.2, 145.7, 161.4 ppm. $C_{23}H_{21}FN_2O_2S$ (408.49): calcd. C 67.63, H 5.18, N 6.86; found C 67.81, H 5.33, N 6.99.

5-Methoxy-3-{1-[(4-methylphenyl)sulfonyl]tridecyl}-1*H*-indazole (6i): Yield: 0.155 g (32%). Brown viscous oil. IR (neat): $\tilde{\nu}$ = 734, 912, 1152, 1374, 1460, 1601, 1629, 3033 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 0.87 (t, *J* = 7.3 Hz, 3 H), 1.10–1.38 (m, 20 H), 2.34 (s, 3 H), 2.47–2.68 (m, 2 H), 3.84 (s, 3 H), 5.47 (d, *J* = 9.0 Hz, 1 H), 6.97–7.08 (m, 2 H), 7.13 (d, *J* = 8.1 Hz, 2 H), 7.24–7.39 (m, 3 H), 7.82 (br. s, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.3, 21.8, 22.9, 25.7, 26.6, 29.0, 29.3, 29.5, 29.6, 29.7, 29.8, 29.9, 32.1, 55.9, 79.6, 100.5, 111.0, 119.2, 129.4, 129.7, 130.6, 131.7, 132.9, 134.9, 145.4, 155.3 ppm. $C_{28}H_{40}N_2O_3S$ (484.69): calcd. C 69.38, H 8.32, N 5.78; found C 69.12, H 8.15, N 5.91.

General Procedure for the Synthesis of 3-Alkylindazoles 7: 5% Na(Hg) amalgam (0.9 g) and Na_2HPO_4 (2 mmol) were added at room temperature to a stirred solution of sulfonyl indazole **6** (0.5 mmol) in dry EtOH (5 mL). After stirring for 2 h at room temperature, the mixture was filtered through a short pad of florisil, which was subsequently washed with CH_2Cl_2 (3 × 3 mL). Crude product **7** obtained after removal of the solvent was purified by column chromatography (hexanes/ethyl acetate, 95:5).

3-Propyl-1*H*-indazole (7a): Yield: 62 mg (77%). Yellow oil. IR (neat): $\tilde{\nu}$ = 740, 765, 911, 1466, 1499, 1616, 3060 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 0.93 (t, *J* = 7.3 Hz, 3 H), 1.90–2.01 (m, 2 H), 4.34 (t, *J* = 7.3 Hz, 2 H) 7.10–7.15 (m, 1 H), 7.32–7.44 (m, 2 H), 7.72 (dt, *J* = 0.9, 8.1 Hz, 1 H), 7.99 (s, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 11.7, 23.5, 50.7, 109.3, 120.5, 121.3, 124.2, 126.3, 132.9, 139.7 ppm. MS (EI): *m*/*z* (%) = 160 (28) $[M]^+$, 131 (100), 118 (23), 103 (20), 91 (9), 77 (36), 63 (10), 51 (12), 39 (8). $C_{10}H_{12}N_2$ (160.22): calcd. C 74.97, H 7.55, N 17.48; found C 75.24, H 7.31, N 17.59.

3-Hexyl-1*H*-indazole (7b): Yield: 89 mg (88%). Yellow oil. IR (neat): $\tilde{\nu}$ = 739, 764, 909, 1465, 1499, 1616, 3061 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 0.86 (t, *J* = 7.3 Hz, 3 H), 1.21–1.40 (m, 6 H), 1.87–2.00 (m, 2 H), 4.38 (t, *J* = 7.3 Hz, 2 H), 7.15 (dt, *J* = 1.3, 8.1 Hz, 1 H), 7.34–7.45 (m, 2 H), 7.74 (d, *J* = 8.1 Hz, 1 H), 8.00 (s, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.2, 22.7, 26.7, 30.0, 31.6, 49.1, 109.2, 120.5, 121.3, 124.1, 126.3, 132.8, 139.5 ppm. MS (EI): *m*/*z* (%) = 202 (16) $[M]^+$, 173 (14), 131 (100), 118 (33), 103 (9), 91 (5), 77 (17). $C_{13}H_{18}N_2$ (202.30): calcd. C 77.18, H 8.97, N 13.85; found C 77.37, H 9.12, N 13.09.

3-(3-Phenylpropyl)-1*H*-indazole (7c): Yield: 94 mg (80%). White waxy solid. IR (neat): $\tilde{\nu}$ = 740, 761, 909, 1008, 1460, 1498, 1602, 3059 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 2.25–2.36 (m, 2 H), 2.66 (t, *J* = 7.7 Hz, 2 H), 4.41 (t, *J* = 6.8 Hz, 2 H), 7.14–7.22 (m, 4 H), 7.27–7.38 (m, 4 H), 7.75 (d, *J* = 8.1 Hz, 1 H), 8.03 (s, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 31.4, 33.1, 48.3, 109.2, 120.7, 121.4, 124.2, 126.3, 126.4, 128.7, 133.1, 139.7, 141.3 ppm. MS (EI): *m*/*z* (%) = 236 (26) $[M]^+$, 131 (100), 118 (15), 104 (9), 91 (11), 77 (13). $C_{16}H_{16}N_2$ (236.31): calcd. C 81.32, H 6.82, N 11.85; found C 81.02, H 6.59, N 11.61.

3-Nonyl-1*H*-indazole (7d): Yield: 112 mg (92%). Yellow oil. IR (neat): $\tilde{\nu}$ = 739, 908, 1007, 1425, 1465, 1500, 1616, 3062 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 0.87 (t, *J* = 7.3 Hz, 3 H), 1.18–1.39 (m, 12 H), 1.86–1.99 (m, 2 H), 4.38 (t, *J* = 7.3 Hz, 2 H), 7.14 (t, *J* = 7.7 Hz, 1 H), 7.32–7.44 (m, 2 H), 7.73 (d, *J* = 8.1 Hz, 1 H), 8.00 (s, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.3, 22.8, 27.1, 29.4, 29.5, 29.6, 30.1, 32.0, 49.1, 109.2, 120.5, 121.3, 124.2, 126.2, 132.8, 139.6 ppm. MS (EI): *m*/*z* (%) = 244 (10) $[M]^+$, 187 (6), 173 (14), 131 (100), 118 (32), 103 (6), 77 (9). $C_{16}H_{24}N_2$ (244.38): calcd. C 78.64, H 9.90, N 11.46; found C 78.90, H 9.81, N 11.63.

3-(6-Chlorohexyl)-1*H*-indazole (7e): Yield: 110 mg (93%). Yellow oil. IR (neat): $\tilde{\nu}$ = 741, 908, 1425, 1465, 1499, 1616, 3061 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 1.25–1.38 (m, 2 H), 1.40–1.51 (m, 2 H), 1.68–1.77 (m, 2 H), 1.87–1.98 (m, 2 H), 3.48 (t, *J* = 6.8 Hz, 2 H), 4.38 (t, *J* = 6.8 Hz, 2 H), 7.10–7.15 (m, 1 H), 7.33–7.42 (m, 2 H), 7.72 (dt, *J* = 0.9, 8.1 Hz, 1 H), 7.98 (s, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 26.3, 26.6, 29.8, 32.5, 45.1, 48.8, 109.1, 120.5, 121.3, 124.1, 126.3, 132.9, 139.5 ppm. MS (EI): *m*/*z* (%) = 238 (10) $[M + 2]^+$, 236 (30) $[M]^+$, 201 (22), 187 (12), 173 (20), 131 (100), 118 (75), 103 (26), 91 (10), 77 (42), 41 (19). $C_{13}H_{17}ClN_2$ (236.74): calcd. C 65.95, H 7.24, N 11.83; found C 65.77, H 7.11, N 11.58.

3-Dec-9-enyl-1*H*-indazole (7f): Yield: 120 mg (94%). Yellow oil. IR (neat): $\tilde{\nu}$ = 740, 909, 1005, 1426, 1465, 1499, 1616, 1640, 3063 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 1.20–1.39 (m, 10 H), 1.86–1.97 (m, 2 H), 2.01 (q, *J* = 7.3 Hz, 2 H), 4.37 (t, *J* = 7.3 Hz, 2 H), 4.89–5.01 (m, 2 H), 5.73–5.85 (m, 1 H), 7.10–7.16 (m, 1 H), 7.33–7.43 (m, 2 H), 7.72 (d, *J* = 8.1 Hz, 1 H), 7.99 (s, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 27.0, 29.0, 29.2, 29.3, 29.5, 30.0, 33.9, 49.1, 109.2, 114.3, 120.5, 121.3, 124.1, 126.2, 132.8, 139.3, 139.5 ppm. MS (EI): *m*/*z* (%) = 256 (7) $[M]^+$, 173 (9), 131 (100), 118 (56), 103

(9), 77 (18), 55 (10), 41 (15). $C_{17}H_{24}N_2$ (256.39): calcd. C 79.64, H 9.44, N 10.93; found C 79.86, H 9.31, N 10.78.

3-[6-(Benzyloxy)hexyl]-1*H*-indazole (7g): Yield: 137 mg (89%). Yellow oil. IR (neat): $\tilde{\nu}$ = 739, 908, 1006, 1101, 1427, 1455, 1464, 1498, 1615, 3062 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 1.27–1.47 (m, 4 H), 1.54–1.66 (m, 2 H), 1.88–1.99 (m, 2 H), 3.43 (t, J = 6.8 Hz, 2 H), 4.37 (t, J = 7.3 Hz, 2 H), 4.47 (s, 2 H), 7.11–7.16 (m, 1 H), 7.24–7.43 (m, 7 H), 7.73 (dd, J = 0.9, 8.1 Hz, 1 H), 7.99 (s, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 25.9, 26.7, 29.6, 29.8, 48.9, 70.2, 72.9, 109.1, 120.4, 121.1, 124.0, 126.1, 127.5, 127.7, 128.4, 132.7, 138.7, 139.4 ppm. MS (EI): m/z (%) = 308 (4) $[M]^+$, 217 (20), 131 (100), 118 (53), 103 (5), 91 (28), 77 (11). $C_{20}H_{24}N_2O$ (308.42): calcd. C 77.89, H 7.84, N 9.08; found C 78.07, H 8.02, 9.27.

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