Access to 1H-indazoles, 1H-benzoindazoles and 1H-azaindazoles from (het)aryl azides: a Staudinger-aza-Wittig tandem reaction leading to N-N bond formation?

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SUPPORTING INFORMATION

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Page 2-8 : General procedures and characterization data for all reaction products
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General Comments.

The reactions were monitored by thin-layer chromatography (TLC) analysis using silica gel (60 F254) plates. Compounds were visualized by UV irradiation. Flash column chromatography was performed on silica gel 60 (230−400.13 mesh, 0.040 0.063 mm). Melting points (mp [°C]) were taken on samples in open capillary tubes and are uncorrected. The infrared spectra of compounds are given in cm\(^{-1}\). \(^1\)H and \(^13\)C NMR spectra were recorded at 250 MHz (\(^13\)C, 62.9MHz) or at 400 MHz (\(^13\)C, 100.62 MHz). Chemical shifts are given in parts per million using tetramethylsilane (TMS) as internal standard. Coupling constants (J) are reported in Hertz (Hz). High-resolution mass spectra (HRMS) were performed on a quadrupole analyzer.

Dry acetonitrile was obtained from a dry station GT S100 immediately prior to use. The amount of water in acetonitrile is regularly checked (Karl Fisher) and is below 20 ppm.

Kornblum’s solution: To prepare 50mL, dissolve 15g of urea in 40mL of water and add 10mL of acetic acid.

The azido precursors 1a, 1b, 1f, 1g, 4, 13 were synthesized according to the following literature.\(^17,18\).

**FORMATION of 1c-1e, 1h-1l**

Formation of 1d

2-(2-Azidophenyl)-N,N-diethylacetamide (1d). The procedure\(^1\) with 2-(2-azidophenyl)acetic acid\(^2\) (200 mg) was followed to provide after purification with column chromatography (eluents = 1:1 ethyl acetate/pentane) 223mg (85 %) 1d as an orange oil; IR \(^ν\) (cm\(^{-1}\)) 2973, 2119, 1639, 1451, 1283, 748; \(^1\)H NMR (250 MHz, \(\text{CDCl}_3\)) δ 7.34 – 7.24 (m, 2H), 7.18 – 7.06 (m, 2H), 3.62 (s, 2H), 3.37 (dq, \(J\) = 14.4, 7.1 Hz, 4H), 1.15 (dt, \(J\) = 10.1, 7.1 Hz, 6H); \(^13\)C NMR (101 MHz, \(\text{CDCl}_3\)) δ 169.7 (C), 138.1 (C), 131.1 (CH), 128.3 (CH), 127.4 (C), 125.0 (CH), 118.1 (CH), 42.4 (CH\(_2\)), 40.5 (CH\(_2\)), 35.5 (CH\(_2\)), 14.4 (CH\(_3\)), 13.1 (CH\(_3\)); HRMS (ESI) : [M+H]\(^+\) calcd. 233.1396 for C\(_{12}\)H\(_{17}\)N\(_4\)O, found 233.1397.

Formation of 1e

Methyl 2-(2-azidophenyl)acetate (1e). To a solution of 2-azidophenylacetic acid\(^2\) (2.110 g, 1equiv.) in methanol (0.32M) at 0°C, under argon, was slowly added thionyl chloride (1.5equiv.). The mixture was then allowed to react at room temperature overnight. After concentration under reduced pressure, the residue was dissolved in dichloromethane, washed with water and brine, dried over MgSO\(_4\) and concentrated under reduced pressure. The desired compound 1e was obtained without any further purification with 94% yield (2.140 g) as a brown oil; IR \(^ν\) (cm\(^{-1}\)) 2118, 1736, 1490, 1258, 1158, 745; \(^1\)H NMR (250 MHz, \(\text{CDCl}_3\)) δ 7.33 (ddd, \(J\) = 8.0, 7.5, 1.7 Hz, 1H), 7.23 (dd, \(J\) = 7.5, 1.7 Hz, 1H), 7.17 (dd, \(J\) = 8.0, 1.2 Hz, 1H), 7.11 (td, \(J\) = 7.5, 1.2 Hz, 1H), 3.71 (s, 3H, CH\(_3\)), 3.62 (s, 2H, CH\(_2\)); \(^13\)C NMR (101 MHz, \(\text{CDCl}_3\)) δ 171.5, 138.6, 131.4, 128.7, 125.0, 118.1, 124.8, 118.1, 52.1, 36.4.

General procedure for the preparation of 1j″ 1l″ and 1k.

Ar/HetAr —NH\(_2\) → Ar/HetAr —N\(_3\)

1) HCl (2M), NaNO\(_2\), 0°C
2) NaN\(_3\), 0°C to 20°C

H\(_2\)O

1j″, 1l″ and 1k
To a solution of the aromatic amine (1 equiv.; 0.7 M) in hydrochloric acid (2 M) at 0°C was slowly added a solution of sodium nitrite (1.2 equiv.) in water (4.2 M). After 5 min of stirring, a solution of sodium azide (2.0 equiv.) and sodium acetate (3.0 equiv.) in water (2 M) was slowly added. The mixture was then allowed to react at room temperature for 4 h. The mixture was extracted three times with dichloromethane and the combined organic phase was washed with water and brine, dried over MgSO₄. After concentration under reduced pressure, the product was purified by flash chromatography on silica gel.

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\text{(2-Azido-4-nitrophenyl)methanol (1j\textsuperscript{''})}. \quad \text{The general procedure with commercial (2-amine-4-nitrophenyl)methanol (2.940 g) was followed to provide after purification with column chromatography (eluent = 1:1 ethyl acetate/pentane) 2.390 g (71%) of 1j\textsuperscript{''} as a beige solid; }{}^1\text{H NMR (250 MHz, CDCl}_3\text{) }\delta 8.02-8.04 (m, 2H), 7.66 (d, }J = 8.7 \text{ Hz, 1H), 4.74 (s, 2H, CH}_2\text{), 2.00 (br s, 1H, OH); }{}^{13}\text{C NMR (101 MHz, CDCl}_3\text{) }\delta 148.5, 139.3, 130.5, 129.3, 120.3, 113.3, 61.1 (CH}_2\text{).}
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\text{(3-Azidonaphthalen-2-yl)methanol (1l\textsuperscript{''})}. \quad \text{The general procedure with (3-aminonaphthalen-2-yl)methanol (900 mg) was followed to provide after purification with column chromatography (eluent = 1:1 ethyl acetate/pentane) 858 mg (83%) of 1l\textsuperscript{''} as a beige solid; mp= 95-96 °C; IR }\nu \text{ (cm}^{-1}\text{)3234; 2101; 1501; 1285; 1005; 864; 735; }{}^{13}\text{C NMR (63 MHz, CDCl}_3\text{) }\delta 136.5 (q), 133.5 (q), 131.4 (q), 131.1 (q), 128.3 (CH), 127.9 (CH), 127.0 (CH), 126.5 (CH), 125.8 (CH), 115.5 (CH), 62.2 (CH}_2\text{).}
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\text{2-(3-Azido-6-methoxypyridin-2-yl)acetonitrile (1k)}. \quad \text{The general procedure with 2-(3-amino-6-methoxypyridin-2-yl)acetonitrile (500mg) was followed to provide 152mg (27%) of 1k as a beige solid; mp= 92-93°C; }{}^1\text{H NMR (250 MHz, CDCl}_3\text{) }\delta 7.39 (d, }J = 8.8 \text{ Hz, 1H), 6.77 (d, }J = 8.8 \text{ Hz, 1H), 3.93 (s, 3H, CH}_3\text{), 3.76 (s, 2H, CH}_2\text{); }{}^{13}\text{C NMR (101 MHz, CDCl}_3\text{) }\delta 159.8, 136.7, 128.1, 126.5, 115.3, 111.0, 53.0, 21.3; \text{HRMS (ESI): [M+H]+ calcd. 190.0723 for C}_8\text{H}_8\text{N}_5\text{O, found 190.0723.}
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\text{General procedure for the preparation of 1c, 1h, 1i, 1j and 1l.}
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\text{1h\textsuperscript{"}, 1i\textsuperscript{"}, 1j\textsuperscript{"} and 1l\textsuperscript{"}} \quad \text{AgNO}_2, \text{Et}_2\text{O} \quad 1\text{c\textsuperscript{'}, 1h\textsuperscript{'}, 1i\textsuperscript{'}, 1j\textsuperscript{'} and 1l\textsuperscript{'}} \quad 1\text{c, 1h, 1i, 1j and 1l}
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The corresponding alcohol derivative (1.0 equiv.) was dissolved in anhydrous dichloromethane (0.2M) at 0°C before the slow addition of thionyl chloride (1.2equiv.). After 3 h at 0°C, the reaction was concentrated under reduced pressure and the residue was dissolved in anhydrous acetone (0.75M). Sodium iodide (1.5 equiv.) was added and the reaction was left at room temperature for 12h under inert atmosphere. Then, the reaction was filtered through celite pad, which was rinsed twice with acetone. After concentration under reduced pressure, the residue was dissolved in dichloromethane and filtered a second time through celite pad rinsed twice with dichloromethane. The filtrate is washed with a saturated solution of thiosulfate sodium and brine, dried over MgSO₄ and concentrated under reduced pressure to yield to the corresponding iodinated products 1h\textsuperscript{'}, 1i\textsuperscript{'} 1j\textsuperscript{'} and 1l\textsuperscript{'} without further purification.

In a flask coated with aluminum foil, a suspension of silver nitrite (1.5equiv. 0.22M) in Et₂O was made and cooled to 0°C before slowly adding a solution of the benzylic iodide compound (0.22 M). The
reaction mixture was kept at 0°C for 3h and then allowed to return at room temperature for 20h. After filtration over a celite pad, a solution of sodium methanolate in methanol (1.1 equiv., 1M) is added at 10°C. The resulted precipitate was filtered and dissolved in a minimum volume of water. The pH of the solution was corrected to 4 by using a Kornblum solution (6M) at 0°C. The resulted precipitate was filtered, washed with water and dried under vacuum to yield to the corresponding products 1c, 1h, 1i, 1j and 1l.

1-Azido-2-(nitromethyl)benzene (1c).

The general procedure with 1c (1.000 g) was followed to provide 290 mg (42 %) of 1c as a yellow solid; mp= 47-48 °C; IR ν (cm⁻¹) 2132, 1557, 1540, 1300, 763; ¹H NMR (250 MHz, Chloroform-d) δ 7.52 (t, J = 7.5 Hz, 1H), 7.38 (d, J = 7.5 Hz, 1H), 7.20-7.27 (m, 2H), 5.46 (s, 2H, CH₂); NMR (101 MHz, DMSO-d₆) δ (ppm) 140.1 (C), 132.6 (CH), 131.8 (CH), 125.2 (CH), 120.9 (C), 118.6 (C), 74.70 (CH₂).

1-Azido-4-bromo-2-(iodomethyl)benzene (1h).

The general procedure with (2-azido-5-bromophenyl)methanol (3.54 g) was followed to provide 3.460 g (87 %) of 1h as a yellow solid; mp= 66-67 °C; IR ν (cm⁻¹) 2115, 2078, 1486, 1473, 1299, 807; ¹H NMR (250 MHz, CDCl₃) δ 7.47 (d, J = 2.3 Hz, 1H), 7.41 (dd, J = 8.5, 2.3 Hz, 1H), 6.99 (d, J = 8.5 Hz, 1H), 4.32 (s, 2H); ¹³C NMR (101 MHz, CDCl₃) δ 137.4 (C), 133.4 (CH), 132.4 (CH), 132.3 (CH), 120.3 (CH), 117.6 (C), -1.5 (CH₂).

1-Azido-4-bromo-2-(nitromethyl)benzene (1h).

The general procedure with 1h' (1.920 g) was followed to provide 575 mg (40 %) of 1h as a yellow solid; mp= 63-64 °C; IR ν (cm⁻¹) 2124, 2087, 1550, 1289, 820; ¹H NMR (250 MHz, CDCl₃) δ 7.62 (dd, J = 2.1, 8.0 Hz, 1H), 7.52 (d, J = 2.1 Hz, 1H), 7.13 (d, J = 8.0 Hz, 1H), 5.40 (s, 2H, CH₂); ¹³C NMR (101 MHz, CDCl₃) δ 139.4 (C), 135.4 (CH), 134.7 (CH), 122.6 (C), 120.2 (CH), 117.8 (C), 20.8 (CH₃), 0.57 (CH₂).

1-Azido-2-(iodomethyl)-4-methylbenzene (1i').

The general procedure with (2-azido-5-methylphenyl)methanol (1.000 g) was followed to provide 1.650 g (99 %) of 1i' as a brown oil; IR ν (cm⁻¹) 2918, 2115, 2078, 1496, 1293, 1158, 806; ¹H NMR (250 MHz, CDCl₃) δ 7.13-7.16 (m, 1H), 7.10-7.11 (m, 1H), 7.00-7.02 (m, 1H), 4.38 (s, 2H, CH₂), 2.32 (s, 3H, CH₃); ¹³C NMR (101 MHz, CDCl₃) δ 135.5 (C), 135.0 (C), 131.3 (CH), 130.4 (CH), 130.2 (C), 118.7 (CH), 20.8 (CH₃), 0.57 (CH₂).

1-Azido-4-methyl-2-(nitromethyl) benzene (1i).

The general procedure with 1i' (137 mg) was followed to provide 57 mg (57 %) of 1i as a yellow solid; mp= 61-62 °C; IR ν (cm⁻¹) 2927, 2128, 2101, 1549, 1537, 1302, 823; ¹H NMR (250 MHz, CDCl₃) δ 7.51 (d, J = 3.0 Hz, 1H), 7.42 (dd, J = 2.2, 8.5 Hz, 1H), 7.10 (d, J = 8.5 Hz, 1H), 5.38 (s, 2H); ¹³C NMR (101 MHz, CDCl₃) δ 137.3 (C), 135.2 (C), 133.1 (CH), 132.4 (CH), 120.7 (C), 118.5 (CH), 74.8 (CH₂), 20.8 (CH₃).

2-Azido-1-(iodomethyl)-4-nitrobenzene (1j').

The general procedure with 1j" (1.200 g) was followed to provide 1.230 g (66%) of 1j' as a yellow solid; mp= 78-79 °C; IR ν (cm⁻¹) 2118, 1512, 1342, 1288, 1137, 870, 812, 743, 724; ¹H NMR (250 MHz, CDCl₃) δ 7.99 (d, J = 2.1 Hz, 1H), 7.92 (dd, J = 2.1 Hz, 8.4 Hz, 1H),
7.50 (d, J = 8.4 Hz, 1H), 4.41 (s, 2H, CH₂); ¹³C NMR (101 MHz, CDCl₃) δ 148.0, 139.7, 137.3, 131.1, 119.9, 113.6, -2.8 (CH₂).

2-Azido-4-nitro-1-(nitromethyl)benzene (1j).

The general procedure with 1j' (137 mg) was followed to provide 59% yield (57 mg) of 1j as a white solid; mp = 90–91°C; IR (cm⁻¹): 3071, 2125, 1553, 1520, 1345, 1275, 1150, 881, 814; ¹H NMR (250 MHz, CDCl₃) δ 8.10 (d, J = 2.2 Hz, 1H), 8.06 (dd, J = 8.3, 2.2 Hz, 1H), 7.57 (d, J = 8.3 Hz, 1H), 5.52 (s, 2H); ¹³C NMR (101 MHz, CDCl₃) δ 149.9 (C), 142.1 (C), 133.6 (CH), 126.6 (C), 119.9 (CH), 113.6 (CH), 73.8 (CH₂).

2-Azido-3-(nitromethyl)naphthalene (1l).

The general procedure with 1l' (300 mg) was followed to provide 103 mg (30% over the two steps) of 1l as a beige solid; mp = 71–72°C; IR (cm⁻¹): 2111, 1549, 1363, 1287, 875, 753, 697; ¹H NMR (250 MHz, CDCl₃) δ 7.88 – 7.78 (m, 3H), 7.63 – 7.54 (m, 2H), 7.53 – 7.45 (m, 1H), 5.59 (s, 2H); ¹³C NMR (101 MHz, CDCl₃) δ 137.31 (q), 134.74 (q), 133.17 (CH), 132.06 (q), 128.45 (CH), 128.33 (CH), 126.71 (CH), 126.41 (CH), 120.54 (q), 116.07 (CH), 75.2 (CH₂).

Preparation of 8

1-Nitro-2-(1-tosylethyl)benzene (8'').

The procedure with 1-nitro-2-(tosylmethyl)benzene (1,634 g) was followed to provide after purification with column chromatography (eluent = 2:8 ethyl acetate/pentane) 1,410 g (82%) of 8'' as a light pink solid; mp = 96-97°C; IR (cm⁻¹): 2105, 1530, 1226, 734; ¹H NMR (250 MHz, DMSO-d₆) δ 7.99 – 7.85 (m, 1H), 7.85 – 7.58 (m, 3H), 7.53 – 7.32 (m, 4H), 5.32 (q, J = 7.0 Hz, 1H), 2.39 (s, 3H), 1.65 (d, J = 7.0 Hz, 3H); ¹³C NMR (63 MHz, DMSO-d₆) δ 150.0 (C), 145.0 (C), 134.2 (C), 130.1 (CH), 129.9 (CH), 128.5 (CH), 127.1 (C), 124.9 (CH), 57.9 (CH), 21.1 (CH₃), 14.0 (CH₃); HRMS (ESI): [M+H]^+ calcd. 306.0794 for C₁₅H₁₆NO₄S, found 309.791.

1-Azido-2-(1-tosylethyl)benzene (8).

The procedure with 8'' (1,347 g) was followed to provide the amino intermediate which was directly used in the general procedure for the formation of azido compound to provide after purification with column chromatography (eluent = 3:2 ethyl acetate/pentane) 543 mg (41% 2 steps) of 8 as a pale orange solid; mp = 107-108°C; IR (cm⁻¹): 2116, 1492, 1299, 1141, 761; ¹H NMR (250 MHz, DMSO-d₆) δ 7.50 – 7.26 (m, 6H), 7.20 (td, J = 7.7, 1.3 Hz, 1H), 7.08 (dd, J = 7.7, 1.3 Hz, 1H), 4.66 (q, J = 7.1 Hz, 1H), 2.33 (s, 3H), 1.55 (d, J = 7.2 Hz, 3H); ¹³C NMR (63 MHz, DMSO) δ 144.5 (C), 138.5 (C), 134.2 (C), 130.3 (CH), 129.3 (CH), 129.2 (CH), 128.6 (CH), 125.1 (CH), 125.1 (C), 118.5 (CH), 57.7 (CH), 21.0 (CH₃), 13.0 (CH₃); HRMS (ESI): [M+Na]^+ calcd. 324.0777 for C₁₅H₁₄N₃NaO₄S, found 324.0777.
General procedure for the preparation of 3a-l. In a dry flask under argon, 1a-l (1.0 equiv.) was dissolved in anhydrous acetonitrile (0.12M) before adding triphenylphosphine (1.1 equiv.). The resulting mixture was stirred at room temperature up to total consumption of the starting material (3-4h). tert-Butylnitrite (4.0 equiv.) was then added and the mixture was left at room temperature for 20 h. After concentration under reduced pressure, the product was purified by flash chromatography on silica gel.

3-Tosyl-1H-indazole (3a). The general procedure with 1a (70 mg) was followed to provide after purification with column chromatography (eluent = 3:7 ethyl acetate/pentane) 45 mg (69%) of 3a as a white solid. mp = 167 °C; IR (cm⁻¹) 3263, 2924, 1594, 1369, 1312, 1300, 1289, 1141, 1084, 721, 684; ¹H NMR (250 MHz, DMSO-d₆) δ 14.20 (br s, 1H, NH), 8.04 (d, J = 8.4 Hz, 1H), 7.68 (d, J = 8.4 Hz, 2H), 7.50 (d, J = 8.4 Hz, 2H), 7.34 (t, J = 7.6 Hz, 1H), 7.19 (t, J = 7.6 Hz, 1H), 7.05 (t; J = 7.6 Hz, 1H), 6.79 (d, J = 7.7 Hz, 1H), 7.55 – 7.30 (m, 4H), 2.35 (s, 3H, CH₃); ¹³C NMR (101 MHz, DMSO-d₆) δ 144.5 (C), 143.3 (C), 140.9 (C), 138.1 (q), 130.1 (2xCH), 127.4 (CH), 127.1 (2xCH), 123.53 (CH), 119.7 (q), 119.5 (CH), 111.5 (CH), 21.02 (CH₃); HRMS (ESI) : [M+H]+ calcd 273.0692 for C₁₄H₁₄N₂O₅, found 273.0693.

3-Cyano-1H-indazole (3b). The general procedure with 1b (70 mg) was followed to provide after purification with column chromatography (eluent = 4:6 ethyl acetate/pentane) 51 mg (92%) of 3b as a white solid; mp=129-130 °C (lit. 140-141°C); ¹H NMR (250 MHz, CDCl₃) δ 11.21 (br s, 1H, NH), 8.15 (d, J = 8.4 Hz, 1H), 7.98 (d, J = 8.4 Hz, 1H, 7.69 (d, J = 7.7 Hz, 1H), 7.55 (t; J = 7.6 Hz, 1H), 7.39 (t; J = 7.6 Hz, 1H).

3-Nitro-1H-indazole (3c). The general procedure with 1c (35 mg) was followed to provide after purification with column chromatography (eluent = 4:6 ethyl acetate/pentane) 28 mg (87%) of 3c as a white solid; mp= 205°C (lit. 205°C); IR (cm⁻¹) 3195, 1531, 1478, 1381, 1321, 1249, 1065, 831, 743; ¹H NMR (250 MHz, DMSO-d₆) δ 14.05 (br s, 1H, NH), 8.15 (d, J = 8.4 Hz, 1H), 7.78 (d, J = 8.4 Hz, 1H), 7.60 (t; J = 7.6 Hz, 1H), 7.51 (t; J = 7.6 Hz, 1H); ¹³C NMR (101 MHz, DMSO-d₆) δ 148.0, 141.3, 127.9, 125.2, 119.8, 115.1, 111.8; HRMS (ESI) : [M+H]+ calcd 164.0454 for C₁₀H₆N₂O₂, found 164.0454.

N,N-Diethyl-1H-indazole-3-carboxamide (3d). The general procedure with 1d (220 mg) was followed to provide after purification with column chromatography (eluent = 3:7 ethyl acetate/pentane) 145 mg (71%) of 3d as a yellow solid (145mg). mp= 174-174.5°C (lit. 172.5-174°C); IR (cm⁻¹) 3147, 3107, 3063, 2989, 2972, 2927, 1594, 1579, 1493, 1454, 1434, 746; ¹H NMR (250 MHz, DMSO-d₆) δ 13.42 (br s, 1H, NH), 7.97 (dd, J = 8.1, 0.9 Hz, 1H), 7.58 (dt, J = 8.4, 1.0 Hz, 1H), 7.40 (ddd, J = 8.3, 6.8, 1.1 Hz, 1H), 7.19 (ddd, J = 8.0, 6.8, 1.0 Hz, 1H), 3.74 (d, J = 7.0 Hz, 2H, CH₂), 3.51 (d, J = 7.5 Hz, 2H, CH₂), 1.19 (t; J = 7.0 Hz, 6H, 2xCH₃); ¹³C NMR (101 MHz, DMSO-d₆) δ 162.7 (q), 140.1 (q), 139.3 (q), 126.4 (CH), 122.8 (q), 121.6 (CH), 121.4 (CH), 110.3 (CH), 42.5 (CH₂), 40.0 (CH₂), 14.7 (CH₂), 12.9 (CH₂); HRMS (ESI) : [M+H]+ calcd 218.1287 for C₁₄H₁₆N₂O₂, found 218.1288.

Methyl 1H-indazole-3-carboxylate (3e). The general procedure with 1e (76 mg) was followed to provide after purification with column chromatography (eluent = 2:8 ethyl acetate/pentane) 53 mg (77%) yield of 3e as a white solid; mp= 169°C (lit. 170-171°C); IR (cm⁻¹) 3159, 2106, 1783, 1462, 1230, 1148, 1128, 1067, 745, 734; ¹H NMR (250 MHz, DMSO-d₆) δ 13.93 (br s, 1H, NH), 8.08 (d, J = 8.2 Hz, 1H), 7.66 (d, J = 8.2 Hz, 1H), 7.45 (dd, J = 8.2, 6.8 Hz, 1H), 7.31 (dd, J = 8.2, 6.8 Hz, 1H), 3.08 (s, 3H); ¹³C NMR (101 MHz, DMSO-d₆) δ 163.0, 141.1, 135.2, 126.9, 123.1, 122.3, 121.2, 111.3, 51.8.
**1H-Indazole (3f)**: The general procedure with 1f (62 mg) was followed to provide after purification with column chromatography (elucent = 2:8 ethyl acetate/pentane) 24 mg (51 %) of 3f as a white solid; mp= 145-146°C (lit. 145-146°C); IR ν (cm⁻¹) 3178, 1622, 1504, 1367, 1004, 952; ¹H NMR (250 MHz, CDCl₃) δ 13.04 (br s, 1H, NH), 8.35 (d, J = 9.0 Hz, 1H), 8.30 (s, 1H), 8.06 (s, 1H), 7.78 (d, J = 8.3 Hz, 1H), 7.54 (d, J = 8.3 Hz, 1H), 7.33 (t, J = 7.3 Hz, 1H), 7.10 (t, J = 7.3 Hz, 1H); ¹³C NMR (101 MHz, CDCl₃) 140.0, 133.5, 126.0, 122.9, 120.6, 120.3, 110.2.

**5-Bromo-3-nitro-1H-indazole (3h)**: The general procedure with 1h (50 mg) was followed to provide after purification with column chromatography (elucent = 4:6 ethyl acetate/pentane) 41 mg (87 %) of 3h as a white solid; mp= 236°C (decomp.); IR ν (cm⁻¹) 3233, 1584, 1532, 1490, 1386, 1289, 915, 787; ¹H NMR (250 MHz, DMSO-d₆) δ 14.62 (br s, 1H, NH), 8.86 (s, 1H), 8.37 (s, 1H), 8.27 – 8.20 (m, 1H), 8.19 – 8.12 (m, 1H), 7.68 – 7.47 (m, 2H); ¹³C NMR (101 MHz, DMSO-d₆) δ 140.3, 131.1, 122.2, 118.2, 116.8, 114.3; HRMS (ESI) : [M+H]⁺ calcd. 214.9596 for C₉H₆BrN₂O₂, found 214.9959.

**5-Methyl-3-nitro-1H-indazole (3i)**: The general procedure with 1i (75 mg) was followed to provide after purification with column chromatography (elucent = 2:8 ethyl acetate/pentane) 58 mg (84 %) of 3i as a yellow solid; mp= 190°C (decomp.); IR ν (cm⁻¹) 3255, 1588, 1504, 1384, 1307, 1248, 1178, 941, 852, 797, 729; ¹H NMR (250 MHz, DMSO-d₆) δ 14.65 (s, 1H), 8.28 (dd, J = 9.0, 0.8 Hz, 1H), 7.71 (dd, J = 9.0, 1.8 Hz, 1H); ¹³C NMR (101 MHz, DMSO-d₆) δ 148.2, 140.7, 135.7, 130.7, 119.3, 116.2, 112.3, 21.7; HRMS (ESI) : [M+H]⁺ calcd. 178.0611 for C₈H₆N₂O₂, found 178.0612.

**3,6-Dinitro-1H-indazole (3j)**: The general procedure with 1j (40 mg) was followed to provide after purification with column chromatography (elucent = 2:8 ethyl acetate/pentane) 21 mg (57 %) of 3j as a white solid; mp= 251-252°C (decomp.) (lit.241 - 243 °C); IR ν (cm⁻¹) 1514, 1394, 1348, 1321, 1055, 887, 822, 791, 739; ¹H NMR (250 MHz, CDCl₃) δ 11.19 (br s, 1H, NH), 7.94 (s, 1H), 7.68 (d, J = 8.6 Hz, 1H), 7.43 (d, J = 8.6 Hz, 1H), 2.50 (s, 3H, CH₃); ¹³C NMR (101 MHz, CDCl₃) δ 148.2, 140.7, 135.7, 130.7, 119.3, 116.2, 112.3, 21.7; HRMS (ESI) : [M+H]⁺ calcd. 178.0611 for C₉H₆N₂O₂, found 178.0612.

**5-Methoxy-1H-pyrazolo[4,3-b]pyridine-3-carbonitrile (3k)**: The general procedure with 1k (98 mg) was followed to provide after purification with column chromatography (elucent = 2:8 ethyl acetate/pentane) 72 mg (80 %) of 3k as a pale orange solid; mp= 220°C (decomp.); IR ν (cm⁻¹) 3267, 2250, 1584, 1514, 1510, 1452, 1372, 1278, 1084,1010, 954, 817, 757; ¹H NMR (250 MHz, CDCl₃) δ 7.80 (d, J = 9.1 Hz, 1H), 6.94 (d, J = 9.1 Hz, 1H), 4.06 (s, 3H, CH₃); ¹³C NMR (101 MHz, CDCl₃) δ 162.5, 138.6, 130.9, 124.4, 116.9, 114.2, 114.1, 54.1; HRMS (ESI) : [M+H]⁺ calcd. 175.0614 for C₉H₇N₂O₂, found 175.0614.

**3-Nitro-1H-benzo[f]indazole (3l)**: The general procedure with 1l (50 mg) was followed to provide after purification with column chromatography (elucent = 1:1 ethyl acetate/pentane) 21 mg (40 %) of 3l as an orange solid. mp=269-270°C (decomp.); IR ν (cm⁻¹) 3192, 3056, 1533, 1502, 1486, 1377, 1298, 853, 734; ¹H NMR (250 MHz, DMSO-d₆) 14.62 (br s, 1H, NH), 8.86 (s, 1H), 8.37 (s, 1H), 8.27 – 8.20 (m, 1H), 8.19 – 8.12 (m, 1H), 7.68 – 7.44 (m, 2H); ¹³C NMR (101 MHz, DMSO-d₆) δ 139.9 (q), 132.5 (q), 130.9 (q), 129.1 (CH), 128.1 (CH), 126.8 (CH), 125.4 (CH), 119.1 (CH), 115.6 (q), 108.2 (CH); HRMS (ESI) : [M+H]⁺ calcd. 214.0611 for C₁₀H₇N₂O₂, found 214.0611.
General procedure for the preparation of 2a, 5 and 14. Azide (1.0 equiv.) was dissolved in anhydrous acetonitrile (0.12M) under argon. Then triphenylphosphine (1.1 equiv.) was added and the resulting mixture was stirred at room temperature until total consumption of starting material (3-4h). For compound 5 a precipitate appeared. This precipitate was filtered and triturated with 5mL of cold acetonitrile to yield the corresponding iminophosphorane without any further purification. For compounds 2a and 14 the solvent was evaporated and the crude mixture purified on flash chromatography to yield the corresponding product.

1,1,1-Triphenyl-N-(2-(tosylmethyl)phenyl)-l5-phosphanimine (2a). The general procedure with 1a (210 mg) was followed to provide after purification with column chromatography (eluent = 3:7 ethyl acetate/pentane) 310 mg (83%) of 2a as a white solid; mp= 171-172°C , IR ν (cm⁻¹) 3063, 2907, 1482, 1351, 1124, 733; ¹H NMR (250 MHz, DMSO-δ) δ 7.76 – 7.41 (m, 17H), 7.30 – 7.19 (m, 1H), 7.19 – 7.03 (m, 2H), 6.73 (ddd, J = 8.0, 7.3, 1.8 Hz, 1H), 6.52 (td, J = 7.4, 1.2 Hz, 1H), 6.19 – 6.06 (m, 1H), 4.91 (s, 2H), 2.22 (s, 3H).; ¹³C NMR (63 MHz, DMSO-δ) δ 150.3, 143.6, 137.0, 132.1, 131.9, 131.6, 130.6, 129.2, 129.1, 128.9, 128.7, 128.5, 128.0, 121.6, 121.2, 120.0, 116.2, 57.2 (CH₂), 21.02 (CH₃); HRMS (ESI) : [M+H]+ calcd. 522.1651 for C₃₂H₂₉NO₂PS found 522.1648.

1-(2-((Triphenyl-l5-phosphanylidene)amino)phenyl)ethan-1-one (5). The general procedure with 4 (210 mg) was followed, the resulted precipitate was filtered and triturated with cold acetonitrile (5 mL) to provide 360 mg (70%) of 5 as a white solid; mp= 120°C; IR ν (cm⁻¹) 1645, 1585, 1436, 1260, 1106, 744; ¹H NMR (250 MHz, DMSO-δ) δ 7.84 – 7.49 (m, 15H), 7.35 – 7.23 (m, 1H), 6.89 (ddd, J = 8.2, 1.2 Hz, 1H); ¹³C NMR (101 MHz, DMSO-δ) δ 203.29, 150.85, 134.97, 134.59, 132.23, 132.19, 132.13, 131.97, 131.23, 130.47, 129.15, 128.96, 128.89, 128.71, 128.67, 122.35, 122.15, 116.22, 31.36 (CH₃); HRMS (ESI): [M+H]+ calcd. 396.1511 for C₂₆H₂₃NOP, found 396.1512.

2-Methyl-1H-benzo[d]imidazole (14). The general procedure with 13 (132 mg) was followed in refluxing acetonitrile for 48h to provide after purification with column chromatography (eluent = 6:4 ethyl acetate/pentane) 79 mg (71%) of 14 as a white solid; mp = 174-175°C (lit. 175-176°C); IR ν (cm⁻¹) 3062, 2784, 2536, 1500, 1385, 1269, 1027, 729; ¹H NMR (250 MHz, DMSO-δ) δ 12.15 (s, 1H), 7.52 – 7.35 (m, 2H), 7.14 – 7.05 (m, 2H), 2.47 (s, 3H); HRMS (ESI): [M+H]+ calcd. 133.0760 for C₈H₉N₂, found 133.0757.

3-Methyl-2H-indazol-2-ol (15). The reaction was performed with 13 (100 mg) in refluxing toluene for 24h to provide after purification with column chromatography (eluent = 5% methanol in dichloromethane) 71mg (93%) of 15 as a light brown solid; mp = 174-175°C (lit. 173-175°C); IR ν (cm⁻¹) 3432, 1004, 758; ¹H NMR (250 MHz, DMSO-δ) δ 13.22 (br s, 1H, OH), 7.62 (dt, J = 8.3, 1.2 Hz, 1H), 7.45 (dt, J = 8.6, 1.0 Hz, 1H), 7.22 (ddd, J = 8.6, 6.8, 1.2 Hz, 1H), 7.02 (ddd, J = 8.3, 6.8, 1.0 Hz, 1H), 2.51 (s, 3H); ¹³C NMR (101 MHz, DMSO-δ) δ 140.1 (C), 124.9 (CH), 122.1 (C), 119.8 (CH), 119.3 (CH), 118.8 (C), 115.1 (CH), 8.3 (CH₃); HRMS (ESI): [M+H]+ calcd. 149.0709 for C₈H₉N₂O, found 149.0709.

Preparation of 10 and 11:
2-Chloro-3-(nitromethyl)pyrazine (10). In a dry flask was added to a solution of tBuOK (1.57 g; 14 mmol; 2 equiv.) in DMSO (10 mL) the nitromethane (0.80 mL; 14 mmol; 2 equiv.). Then the commercially available 2,3-Dichloropyrazine (1.00 g; 7 mmol; 1 equiv.) was slowly added and the resulting mixture was stirred for 3 hours at 20 °C. The reaction mixture was poured into 20 mL of iced water, the aqueous phase was washed three times with 20 mL of Et2O, acidified with a Kornblum solution (6 M) to pH = 4 and extracted three times with 20 mL of Et2O. The organic phase was dried under MgSO4 and concentrated under reduced pressure to provide 720 mg (62%) of 10 as a red oil without further purification; 1H NMR (250 MHz, CDCl3) δ 8.58 (d, J = 2.5 Hz, 1H), 8.48 (d, J = 2.5 Hz, 1H), 5.81 (s, 2H).

3-Chloropyrazin-2-yl(nitro)methanone oxime (11). In a dry flask under argon was added 10 (96 mg; 0.55 mmol; 1 equiv.) and dry MeCN (2 mL). Then tBuONO (0.27 mL; 2.21 mmol; 4 equiv.) was added and the mixture stirred at 20 °C for 20 h. The mixture was filtrated on celite pad and purified with column chromatography (eluent = 8:2 pentane/ethyl acetate) to provide 39 mg (35%) of 11 as a pale yellow solid; mp = 121-123 °C; 1H NMR (250 MHz, DMSO-d6) δ 8.67 (d, J = 2.4 Hz, 1H), 8.74 (d, J = 2.4 Hz, 1H), 8.81 (d, J = 2.4 Hz, 1H); 13C NMR (101 MHz, DMSO-d6) δ 152.8 (C), 147.9 (C), 146.8 (CH), 146.7 (CH), 143.8 (CH), 143.3 (CH), 139.0 (C), 138.0 (C), 111.8 (C); HRMS (ESI): [M+H-HNO2]+ calcd. 155.9959 for C5H3ClN3O, found 155.9959; [2M+H-2HNO2] calcd. 310.9846 for C10H5Cl2N6O2, found 310.9844.

Preparation of 12:

2-(2-Azidophenyl)-N,N-diethyl-2-oxoacetamide (12’). The reaction was performed with 12’’ (840 mg) following the general procedure for the generation of azido compound. The product appeared to precipitate in the reaction medium and was directly filtrated and washed with water to provide 830 mg (88%) of 12’ as a red solid; mp = 78-79 °C; IR ν (cm⁻¹) 2975, 2145 2126, 2106, 1666, 1634, 1472, 758; 1H NMR (250 MHz, DMSO-d6) δ 8.08 – 7.77 (m, 1H), 7.69 – 7.51 (m, 1H), 7.32 – 7.12 (m, 2H), 3.53 (q, J = 7.1 Hz, 2H), 3.29 (q, J = 7.1 Hz, 2H), 1.27 (t, J = 7.1 Hz, 3H), 1.23 (t, J = 7.1 Hz, 3H); 13C NMR (101 MHz, DMSO-d6) 189.6 (C), 167.3 (C), 140.7 (C), 135.2 (CH), 131.9 (CH), 126.2 (C), 125.3 (CH), 119.3 (CH), 42.1 (CH2), 38.9 (CH3), 13.8 (CH3), 12.2 (CH3); HRMS (ESI): [M+H]+ calcd. 247.1189 for C12H15N4O2, found 247.1190.
2-(2-Azidophenyl)-N,N-diethyl-2-(hydroxyimino)acetamide (12). The procedure with 12’ (750mg) was followed to provide after purification with column chromatography (eluent = 3:7 ethyl acetate/pentane) 406 mg (52%) of 12 as an orange solid; mp = 110-111 °C (decomp.); IR (cm⁻¹) 3148, 2989, 2937, 1624, 1596, 1435, 1116, 719; ¹H NMR (250 MHz, CDCl₃) δ 8.76 (s, 1H, OH), 7.65 (dd, J = 7.9, 1.6 Hz, 1H), 7.49 – 7.35 (m, 1H), 7.24 – 7.08 (m, 2H), 3.56 (q, J = 7.1 Hz, 2H, CH₂), 3.36 (q, J = 7.1 Hz, 2H, CH₂), 1.23 (t, J = 7.1 Hz, 3H, CH₃), 1.17 (t, J = 7.1 Hz, 3H, CH₃),; ¹³C NMR (63 MHz, CDCl₃) δ 163.5 (C), 152.3 (C), 137.8 (C), 131.3 (C), 123.5 (C), 119.3 (C), 42.5 (CH₂), 38.3 (CH₂), 13.7 (CH₃), 12.4 (CH₃); HRMS (ESI): [M+H]+ calcd. 262.1298 for C₁₂H₁₆N₅O₂, found 262.1301.

References:

15. Wrzeciono; U; Linkowska, E. Pharmazie, 1980, 35, 593.
$^{1}H$ NMR spectrum of 11 (250 MHz, CDCl$_3$)
$^{13}$C NMR spectrum 11$^\prime\prime$ (101 MHz, CDCl$_3$)
$^1$H NMR spectrum $1c$ (250 MHz, CDCl$_3$)
$^{13}$C NMR spectrum 1c (101 MHz, CDCl$_3$)

\[ 74.70, 76.65, 77.16, 77.67, 118.60, 120.94, 125.20, 131.77, 132.60, 140.12 \]
$^1$H NMR spectrum 1d (250 MHz, DMSO-$d_6$)
$^{13}$C NMR spectrum $\textbf{1d}$ (101 MHz, CDCl$_3$)
$^1$H NMR spectrum 1e (250 MHz, CDCl$_3$)
$^{13}$C NMR spectrum 1e (101 MHz, CDCl$_3$)
$^1$H NMR spectrum 1h' (250 MHz, CDCl$_3$)
$^{13}$C NMR spectrum 1h' (101 MHz, CDCl$_3$)
$^1$H NMR spectrum $1h$ (250 MHz, CDCl$_3$)
$^{13}$C NMR spectrum 1h (101 MHz, CDCl$_3$)
$^1$H NMR spectrum II$^*$ (250 MHz, CDCl$_3$)
$^{13}$C NMR spectrum 1i’ (101 MHz, CDCl$_3$)
$^1$H NMR spectrum 1i (250 MHz, CDCl$_3$)
$^{13}$C NMR spectrum 1i (101 MHz, CDCl$_3$)
$^1$H NMR spectrum 1j$^*$ (250 MHz, CDCl$_3$)
$^{13}$C NMR spectrum 1J" (101 MHz, CDCl$_3$)
$^1$H NMR spectrum 1j$^*$ (250 MHz, CDCl$_3$)
$^{13}$C NMR spectrum of 1j' (101 MHz, CDCl$_3$)
$^1$H NMR spectrum 1j (250 MHz, CDCl₃)
$^{13}$C NMR spectrum 1j (101 MHz, CDCl$_3$)

![13C NMR spectrum of 1j](image-url)
$^1$H NMR spectrum 1k (250 MHz, CDCl$_3$)
$^{13}$C NMR spectrum 1k (101 MHz, CDCl$_3$)

![C NMR spectrum](image)
$^1$H NMR spectrum of compound II (250 MHz, CDCl₃)
$^{13}$C NMR spectrum II (101 MHz, CDCl$_3$)
$^1$H NMR spectrum 2a (250 MHz, DMSO-$d_6$)
$^{13}$C NMR spectrum 2a (101 MHz, DMSO-$d_6$)
$^1$H NMR spectrum 3a (250 MHz, DMSO-$d_6$)
$^{13}$C NMR spectrum 3a (101 MHz, DMSO-$d_6$)
$^1$H NMR spectrum 3d (250 MHz, DMSO-$d_6$)
$^{13}$C NMR spectrum 3d (101 MHz, DMSO-$d_6$)
$^1$H NMR spectrum 3e (250 MHz, DMSO-$d_6$)
$^{13}$C NMR spectrum 3e (101 MHz, DMSO-$d_6$)

Chemical shifts:
- 39.52 ppm
- 51.61 ppm
- 111.09 ppm
- 120.94 ppm
- 122.12 ppm
- 122.88 ppm
- 126.69 ppm
- 134.97 ppm
- 140.88 ppm
- 162.75 ppm

Structural formula:

Chemical structures and functional groups:
- CO$_2$Me
- NH
- N
$^1$H NMR spectrum 3h (250 MHz, DMSO-$d_6$)
$^{13}$C NMR spectrum 3h (101 MHz, DMSO-$d_6$)
$^1$H NMR spectrum 3i (250 MHz, DMSO-$d_6$)
$^{13}$C NMR spectrum 3i (101 MHz, DMSO-$d_6$)

![NMR Spectrum Image]

- 57.72 ppm
- 40.38 ppm
- 135.28 ppm
- 130.28 ppm
- 118.28 ppm
- 113.79 ppm
- 111.79 ppm

![Chemical Structure Image]

- Me
- NO2
- NH

Functional groups and chemical shifts are marked in the spectrum.
$^1$H NMR spectrum 3j (250 MHz, CDCl$_3$)
$^1$H NMR spectrum 3k (250 MHz, CDCl$_3$)
$^{13}$C NMR spectrum 3k (101 MHz, CDCl$_3$)
$^1$H NMR spectrum 3l (250 MHz, DMSO-$d_6$)
$^{13}$C NMR spectrum 3i (101 MHz, DMSO-$d_6$)
$^1$H NMR spectrum 5 (250 MHz, DMSO-$d_6$)
$^{13}$C NMR spectrum 5 (101 MHz, DMSO-$d_6$)
$^1$H NMR spectrum 8 (250 MHz, DMSO-$d_6$)
\(^{13}\)C NMR spectrum 8 (101 MHz, DMSO-\(d_6\))
$^1$H NMR spectrum 10 (250 MHz, DMSO-$d_6$)
$^{13}$C NMR spectrum 10 (101 MHz, DMSO-$d_6$)
\(^1\)H NMR spectrum 11 (250 MHz, DMSO-\(d_6\))

Z and E mixture
\(^{13}\)C NMR spectrum 11 (101 MHz, DMSO-\(d_6\))

Z and E mixture
$^1$H NMR spectrum 12$^*$ (250 MHz, DMSO-$d_6$)

![NMR spectrum image]
$^{13}$C NMR spectrum 12' (101 MHz, DMSO-$d_6$)
$^1\text{H NMR spectrum 12 (250 MHz, CDCl}_3\text{)}$
$^{13}$C NMR spectrum 12 (101 MHz, CDCl$_3$)

![NMR Spectrum Image]

- 163.50
- 152.25
- 137.81
- 131.29
- 130.48
- 129.24
- 122.47
- 121.50
- 77.65
- 77.16
- 76.65
- 42.46
- 38.29
- 12.35
- 0.13

Chemical Structure:

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N
O

C
H
3
C
H
3
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N3
$^1$H NMR spectrum 14 (250 MHz, DMSO-$d_6$)
$^1$H NMR spectrum 15 (250 MHz, DMSO-$_d_6$)
$^{13}$C NMR spectrum 15 (63 MHz, DMSO-$d_6$)