A facile route to $1H$- and $2H$-indazoles from readily accessed acyl hydrazides by exploiting a novel aryne-based molecular rearrangement

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Determining carbamate group feasibility

To determine the optimal carbamate group for the reaction of an acyl hydrazide and a benzene, acyl hydrazides analogous to acyl hydrazide 1a with methyl-, ethyl- and tert-butyl (Boc) carbamate groups were synthesised, 1ab-1ad, and subjected to the developed reaction conditions (Table S1). It was observed that the methyl- and ethyl-carbamate containing acyl hydrazides afforded their respective desired 2-hydrazobenzophenone in low yield (Table S1, Entries 1&2). Analysis of the reaction mixture when using methyl-carbamate 1ab revealed the formation of a significant amount, 49% yield, of compound 10 (where R=Me). This accounted for a significant portion of the mass balance as the reaction did show complete conversion of acyl hydrazide starting material. The formation of by-product 10 (where R=Me) can be rationalised by competing attack of the intermediate carbanionic species on the carbamate carbonyl (see Scheme 4 (path C) of manuscript for more detail on the carbanion intermediate). NMR analysis of the crude mixture when employing ethyl-carbamate 1ac as the acyl hydrazide component also showed the presence of a substantial amount of by-product species 10 (where R=Et). It was thus rationalised that the high yield observed when using an isopropyl group was due to the increased steric hindrance about the carbamate-carbonyl. In line with this, it was anticipated that the use of a bulkier Boc-protected acyl hydrazide 1ad would result in a more efficient reaction (Table S1, Entry 4). However, under the reaction conditions, the Boc-protected acyl hydrazide resulted in incomplete conversion of acyl hydrazide 1ad. Increasing the equivalents of benzene precursor 2 and TBAT, had minimal impact on conversion and resulted in an even lower yield. Analysis of the reaction showed formation of various unidentifiable side-products despite several attempts to isolate each species, but the formation of a by-product of the form of compound 10 was not observed by crude NMR. In conclusion, it appears that the isopropyl groups strike a good balance of offering high conversion of 1a and yield of 3a with minimal byproduct formation (Table S1, Entry 3), and compounds of the form of 1a were chosen for further studies.

Table S1. Carbamate group feasibility

<table>
<thead>
<tr>
<th>Entry</th>
<th>R</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Me 3ab</td>
<td>26</td>
</tr>
<tr>
<td>2</td>
<td>Et 3ac</td>
<td>41</td>
</tr>
<tr>
<td>3</td>
<td>iPr 3a</td>
<td>86</td>
</tr>
<tr>
<td>4</td>
<td>Bu 3ad</td>
<td>65% ± 2%</td>
</tr>
</tbody>
</table>

Reaction conditions: acyl hydrazide 1a, 1ab-1ad (0.5 mmol, 1 eq.), benzene precursor 2 (0.75 mmol, 1.5 eq.) and TBAT (1 mmol, 2 eq.) in toluene (6 mL); 50 °C for 16 h. \(^a\) 80% conversion of starting material. \(^b\) 2 eq. of 2 and 3 eq. of TBAT was added, 82% conversion of starting material.
General Experimental

Chemicals

All reagents were purchased from Aldrich or AlfaAesar and were used as received without further purification unless otherwise stated.

Solvents

Where described below, Petrol refers to petroleum ether (b.p. 40-60 °C).

Chromatography

All reactions were monitored by thin-layer chromatography (TLC) on pre-coated silica gel plates. Silica gel plates were initially examined under short wave UV light and then developed using aqueous potassium permanganate stain. Flash column chromatography was carried out with pre-loaded GraceResolv™ flash cartridges on a Biotage® Isolera Spektra One flash chromatography system.

Spectroscopy

Quoted yields refer to chromatographically and spectroscopically pure compounds unless otherwise stated. $^1$H NMR spectra were recorded at 600 MHz or 700 MHz and $^{13}$C NMR at 150 MHz or 175 MHz on a Bruker Avance III 600 or Bruker Avance Neo 700 spectrometer. The chemical shifts (δ) for $^1$H and $^{13}$C are quoted relative to residual signals of the solvent on the parts per million (ppm) scale. In the case of multiple rotamers, only the major has been assigned. Coupling constants ($J$ values) are reported in Hertz (Hz) and are reported as $J_{H-H}$ unless otherwise stated. Signal multiplicities in $^{13}$C NMR were determined using the distortionless enhancement by polarisation transfer (DEPT) spectral editing technique. Where applicable, only the peaks for the major rotamer of 2-hydrazobenzophenones are assigned in the $^1$H and $^{13}$C spectra.

Miscellaneous

Melting points were measured with a Gallenkamp apparatus and are uncorrected.
General experimental for the formation of acyl hydrazides – Method A

To a solution of azodicarboxylate (6.00 mmol, 1.2 eq.) in H₂O (1 mL) was added aldehyde (5.00 mmol, 1.0 eq.) and the reaction mixture stirred at 21 °C for 48 h. The resulting solution was extracted with EtOAc (3 × 15 mL). The combined extracts were dried (MgSO₄), filtered and the solvent was evaporated in vacuo. The resultant crude residue was purified as described below.
Diisopropyl 1-(4-fluorobenzoyl)hydrazine-1,2-dicarboxylate\textsuperscript{1a}

Compound prepared according to method A. Purification by column chromatography (10%-50% EtOAc/Petrol) afforded diisopropyl 1-(4-fluorobenzoyl)hydrazine-1,2-dicarboxylate as a white solid (1.21 g, 3.70 mmol, 74\%). \textsuperscript{1}H NMR (600 MHz, CDCl\textsubscript{3}) \( \delta \) 7.80-7.62 (m, 2H), 7.11 (t, \( J = 8.5 \) Hz, 2H), 6.95-6.70 (m, NH, 1H), 5.02 (septet, \( J = 6.1 \) Hz, 1H), 4.92 (septet, \( J = 6.1 \) Hz, 1H), 1.30 (d, \( J = 5.2 \) Hz, 6H), 1.12 (d, \( J = 5.0 \) Hz, 6H); \textsuperscript{13}C NMR (150 MHz, CDCl\textsubscript{3}) \( \delta \) 170.3 (C), 165.2 (d, \( J_{C-F} = 253.4 \) Hz, C), 155.4 (C), 152.9 (C), 131.3 (d, \( J_{C-F} = 2.7 \) Hz, CH), 131.1 (d, \( J_{C-F} = 9.8 \) Hz, CH), 115.5 (d, \( J_{C-F} = 22.1 \) Hz, CH), 72.8 (CH), 70.9 (CH), 22.0 (CH\textsubscript{3}), 21.5 (CH\textsubscript{3}); IR (solid) 3306, 2984, 2939, 1704, 1602, 1507 cm\textsuperscript{-1}. 
Diisopropyl 1-benzoylhydrazine-1,2-dicarboxylate\textsuperscript{2} 1b

Compound prepared according to method A. Purification by column chromatography (10%-50% EtOAc/Petrol) afforded diisopropyl 1-benzoylhydrazine-1,2-dicarboxylate as a white solid (1.02 g, 3.30 mmol, 66%). \textsuperscript{1}H NMR (600 MHz, CDCl\textsubscript{3}) \(\delta\) 7.72-7.58 (m, 2H), 7.50 (t, \(J = 7.4\) Hz, 1H), 7.40 (t, \(J = 7.6\) Hz, 2H), 7.15-6.99 (m, NH, 1H), 5.00 (septet, \(J = 6.3\) Hz, 1H), 4.87 (septet, \(J = 5.9\) Hz, 1H), 1.28 (d, \(J = 5.5\) Hz, 6H), 1.04 (d, \(J = 4.7\) Hz, 6H); \textsuperscript{13}C NMR (150 MHz, CDCl\textsubscript{3}) \(\delta\) 171.4 (C), 155.5 (C), 153.0 (C), 135.3 (CH), 132.0 (CH), 128.2 (CH), 72.6 (CH), 70.7 (CH), 22.0 (CH\textsubscript{3}), 21.4 (CH\textsubscript{3}); IR (solid) 3308, 2983, 2938, 1705, 1601 cm\textsuperscript{-1}. 

\[\text{\includegraphics{diagram}}\]
Diisopropyl 1-(4-methoxybenzoyl)hydrazine-1,2-dicarboxylate\textsuperscript{3} 1c

\[
\begin{align*}
\text{MeO} & \quad \text{N} \\
\text{O} & \quad \text{N} \\
& \quad \text{CO}_2\text{Pr}
\end{align*}
\]

Compound prepared according to method A. Purification by column chromatography (10%-50% EtOAc/Petrol) afforded diisopropyl 1-(4-methoxybenzoyl)hydrazine-1,2-dicarboxylate as a white solid (1.03 g, 3.05 mmol, 61%). \textsuperscript{1}H NMR (600 MHz, CDCl\textsubscript{3}) δ 7.76-7.62 (m, 2H), 6.98-6.64 (m, 3H), 5.00 (septet, \(J = 6.2\) Hz, 1H), 4.92 (septet, \(J = 6.2\) Hz, 1H), 3.86 (s, 3H), 1.29 (d, \(J = 4.5\) Hz, 6H), 1.13 (d, \(J = 4.5\) Hz, 6H); \textsuperscript{13}C NMR (150 MHz, CDCl\textsubscript{3}) δ 170.8 (C), 163.1 (C), 155.5 (C), 153.3 (C), 131.2 (CH), 127.0 (C), 113.5 (CH), 72.4 (CH), 70.7 (CH), 55.6 (CH\textsubscript{3}), 22.1 (CH\textsubscript{3}), 21.6 (CH\textsubscript{3}); IR (solid) 3310, 2982, 2938, 1733, 1699, 1604, 1510 cm\textsuperscript{-1}. 

Diisopropyl 1-(4-(trifluoromethyl)benzoyl)hydrazine-1,2-dicarboxylate

Compound prepared according to method A. Purification by column chromatography (10%-50% EtOAc/Petrol) afforded diisopropyl 1-(4-(trifluoromethyl)benzoyl)hydrazine-1,2-dicarboxylate as a white solid (1.17 g, 3.10 mmol, 62%). $^1$H NMR (600 MHz, CDCl$_3$) $\delta$ 7.82-7.74 (m, 2H), 7.73-7.67 (m, 2H), 6.95-6.70 (m, NH, 1H), 5.03 (septet, $J = 6.1$ Hz, 1H), 4.91 (septet, $J = 6.1$ Hz, 1H), 1.31 (d, $J = 5.8$ Hz, 6H), 1.10 (d, $J = 5.1$ Hz, 6H); $^{13}$C NMR (150 MHz, CDCl$_3$) $\delta$ 170.2 (C), 155.3 (C), 152.6 (C), 138.8 (C), 133.4 (q, $J_{C-F} = 31.9$ Hz, C), 128.3 (CH), 125.3 (q, $J_{C-F} = 3.0$ Hz, CH), 123.7 (q, $J_{C-F} = 272.6$ Hz, CH), 73.1 (CH), 71.1 (CH), 22.0 (CH$_3$), 21.5 (CH$_3$); IR (solid) 3308, 2985, 2941, 1709, 1619, 1514 cm$^{-1}$. 
Diisopropyl 1-(4-(methoxycarbonyl)benzoyl)hydrazine-1,2-dicarboxylate 1e

Compound prepared according to method A. Purification by column chromatography (10%-50% EtOAc/Petrol) afforded diisopropyl 1-(4-(methoxycarbonyl)benzoyl)hydrazine-1,2-dicarboxylate as a white solid (898 mg, 2.45 mmol, 49%). m.p. 106-108 °C; $^1$H NMR (600 MHz, CDCl$_3$) $\delta$ 8.08 (d, 2H, $J = 8.1$ Hz), 7.75-7.62 (m, 2H), 7.00-6.76 (m, NH, 1H), 5.03 (septet, $J = 6.2$ Hz, 1H), 4.89 (septet, $J = 6.0$ Hz, 1H), 3.94 (s, 3H), 1.33-1.24 (m, 6H), 1.13-1.05 (m, 6H); $^{13}$C NMR (150 MHz, CDCl$_3$) $\delta$ 170.6 (C), 166.3 (C), 155.3 (C), 152.6 (C), 139.5 (C), 132.8 (C), 129.5 (CH), 127.9 (CH), 73.0 (CH), 71.0 (CH), 52.6 (CH$_3$), 22.0 (CH$_3$), 21.5 (CH$_3$); IR (solid) 3301, 2980, 2936, 1706, 1571 cm$^{-1}$; LRMS (ESI) 367 (100, [M+H]$^+$); HRMS (ESI) calcd for C$_{17}$H$_{23}$N$_2$O$_7$ [M+H]$^+$ 367.1500; observed 367.1503.
Diisopropyl 1-(4-iodobenzoyl)hydrazine-1,2-dicarboxylate$^5$ 1f

Compound prepared according to method A. Purification by column chromatography (10%-50% EtOAc/Petrol) afforded diisopropyl 1-(4-iodobenzoyl)hydrazine-1,2-dicarboxylate as a white solid (1.28 g, 2.95 mmol, 59%). $^1$H NMR (600 MHz, CDCl$_3$) δ 7.76 (d, 2H, $J = 8.2$ Hz), 7.43-7.30 (m, 2H), 7.11-7.03 (m, NH, 1H), 4.98 (septet, $J = 6.2$ Hz, 1H), 4.89 (septet, $J = 6.0$ Hz, 1H), 1.30-1.21 (m, 6H), 1.17-1.08 (m, 6H); $^{13}$C NMR (150 MHz, CDCl$_3$) δ 170.7 (C), 155.4 (C), 152.8 (C), 137.5 (CH), 134.7 (C), 129.8 (CH), 99.1 (C), 72.9 (CH), 70.9 (CH), 22.0 (CH$_3$), 21.5 (CH$_3$); IR (solid) 3302, 2982, 2937, 1705, 1585 cm$^{-1}$.
Diisopropyl 1-(3-bromobenzoyl)hydrazine-1,2-dicarboxylate \(^4\) \(1g\)

Compound prepared according to method A. Purification by column chromatography (10%-50% EtOAc/Petrol) afforded diisopropyl 1-(3-bromobenzoyl)hydrazine-1,2-dicarboxylate as a white solid (1.20 g, 3.10 mmol, 62%). \(^1\)H NMR (600 MHz, CDCl\(_3\)) \(\delta\) 7.84-7.73 (m, 1H), 7.67-7.52 (m, 2H), 7.30 (t, \(J = 7.8\) Hz, 1H), 6.99-6.80 (m, NH, 1H), 5.01 (septet, \(J = 6.0\) Hz, 1H), 4.91 (septet, \(J = 6.0\) Hz, 1H), 1.30 (d, \(J = 5.8\) Hz, 6H), 1.10 (d, \(J = 5.1\) Hz, 6H); \(^1^3\)C NMR (150 MHz, CDCl\(_3\)) \(\delta\) 169.8 (C), 155.3 (C), 152.6 (C), 137.2 (C), 134.8 (CH), 131.0 (CH), 129.9 (CH), 126.7 (CH), 122.2 (C), 73.0 (CH), 71.0 (CH), 22.0 (CH\(_3\)), 21.5 (CH\(_3\)); IR (solid) 3303, 2983, 2938, 1707, 1568 cm\(^{-1}\).
**Diisopropyl 1-(3-chlorobenzoyl)hydrazine-1,2-dicarboxylate**

Compound prepared according to method A. Purification by column chromatography (10%-50% EtOAc/Petrol) afforded diisopropyl 1-(3-chlorobenzoyl)hydrazine-1,2-dicarboxylate as a white solid (1.35 g, 3.95 mmol, 79%). $^1$H NMR (700 MHz, CDCl$_3$) $\delta$ 7.76-7.50 (m, 2H), 7.48 (d, $J = 7.9$ Hz, 1H), 7.36 (d, $J = 7.9$ Hz, 1H), 6.96-6.75 (m, NH, 1H), 5.01 (septet, $J = 6.2$ Hz, 1H), 4.91 (septet, $J = 5.6$ Hz, 1H), 1.29 (d, $J = 5.8$ Hz, 6H), 1.14-1.08 (m, 6H); $^{13}$C NMR (175 MHz, CDCl$_3$) $\delta$ 170.0 (C), 155.3 (C), 152.7 (C), 137.0 (C), 134.4 (CH), 131.9 (CH), 129.6 (CH), 128.2 (CH), 126.3 (C), 73.0 (CH), 71.0 (CH), 22.0 (CH$_3$), 21.5 (CH$_3$); IR (solid) 3287, 2981, 2940, 2921, 1710, 1560 cm$^{-1}$. 

![NMR spectrum](image_url)
Diisopropyl 1-(3-nitrobenzoyl)hydrazine-1,2-dicarboxylate 1i

Compound prepared according to method A. Purification by column chromatography (10%-50% EtOAc/Petrol) afforded diisopropyl 1-(3-nitrobenzoyl)hydrazine-1,2-dicarboxylate as a white solid (1.01 g, 2.85 mmol, 57%). m.p. 114-116 °C; \(^1\)H NMR (600 MHz, CDCl\(_3\)) \(\delta\) 8.54-8.43 (m, 1H), 8.40-8.36 (m, 1H), 8.05-7.91 (m, 1H), 7.65-7.60 (m, 1H), 6.87-6.62 (br s, NH, 1H), 5.08-4.99 (m, 1H), 4.98-4.91 (m, 1H), 1.34-1.12 (m, 12H); \(^{13}\)C NMR (150 MHz, CDCl\(_3\)) \(\delta\) 169.0 (C), 155.2 (C), 152.5 (C), 148.0 (C), 136.9 (C), 133.9 (CH), 129.5 (CH), 126.3 (CH), 123.2 (CH), 73.3 (CH), 71.3 (CH), 22.0 (CH\(_3\)), 21.6 (CH\(_3\)); IR (thin film) 3310, 2984, 1715, 1534, 1350, 1258, 1102 cm\(^{-1}\); LRMS (ESI) 354 (100, [M+H]\(^{+}\)); HRMS (ESI) calcd for C\(_{15}\)H\(_{20}\)N\(_3\)O\(_7\) [M+H]\(^{+}\) 354.1301, observed 354.1319.
Diisopropyl 1-(2-fluorobenzoyl)hydrazine-1,2-dicarboxylate$^4$ 1j

Compound prepared according to method A. Purification by column chromatography (10%-50% EtOAc/Petrol) afforded diisopropyl 1-(2-fluorobenzoyl)hydrazine-1,2-dicarboxylate as a white solid (979 mg, 3.00 mmol, 60%). $^1$H NMR (600 MHz, CDCl$_3$) δ 7.64-7.50 (m, 1H), 7.48 (q, $J = 6.6$ Hz, 1H), 7.22 (t, $J = 7.5$ Hz, 1H), 7.11-7.06 (m, 1H), 6.82-6.52 (m, NH, 1H), 5.04-4.92 (m, 2H), 1.32-1.11 (m, 12H); $^{13}$C NMR (150 MHz, CDCl$_3$) δ 166.2 (C), 159.1 (d, $J_{C-F} = 251.1$ Hz, C), 155.1 (C), 152.1 (C), 133.0 (d, $J_{C-F} = 7.7$ Hz, CH), 129.9 (CH), 124.4 (d, $J_{C-F} = 3.3$ Hz, CH), 124.2 (d, $J_{C-F} = 15.6$ Hz, C), 115.6 (d, $J_{C-F} = 21.0$ Hz, CH), 72.9 (CH), 70.9 (CH), 22.0 (CH$_3$), 21.5 (CH$_3$); IR (solid) 3306, 2984, 2943, 2857, 1739, 1714, 1614, 1581, 1563 cm$^{-1}$. 

![NMR spectrum](image-url)
Diisopropyl 1-(2-methylbenzoyl)hydrazine-1,2-dicarboxylate 4k

Compound prepared according to method A. Purification by column chromatography (10%-50% EtOAc/Petrol) afforded diisopropyl 1-(2-methylbenzoyl)hydrazine-1,2-dicarboxylate as a white solid (887 mg, 2.75 mmol, 55%). $^1$H NMR (600 MHz, CDCl$_3$) $\delta$ 7.43-7.34 (m, 1H), 7.32 (t, $J = 7.5$ Hz 1H), 7.23-7.16 (m, 2H), 7.06-6.86 (m, NH, 1H), 5.02 (septet, $J = 5.7$ Hz, 1H), 4.82 (septet, $J = 5.9$ Hz, 1H), 2.39 (s, 3H), 1.30 (d, $J = 5.7$ Hz, 6H), 1.05-0.95 (m, 6H); $^{13}$C NMR (150 MHz, CDCl$_3$) $\delta$ 171.0 (C), 155.3 (C), 152.4 (C), 136.3 (C), 135.4 (C), 130.4 (CH), 130.1 (CH), 126.4 (CH), 125.5 (CH), 72.5 (CH), 70.8 (CH), 22.1 (CH$_3$), 21.3 (CH$_3$), 19.3 (CH$_3$); IR (solid) 3308, 2983, 2938, 1705, 1602 cm$^{-1}$. 
Diisopropyl 1-(2-methoxybenzoyl)hydrazine-1,2-dicarboxylate 1l

Compound prepared according to method A. Purification by column chromatography (10%-50% EtOAc/Petrol) afforded diisopropyl 1-(2-methoxybenzoyl)hydrazine-1,2-dicarboxylate as a clear oil (1.08 g, 3.20 mmol, 64%). $^1$H NMR (600 MHz, CDCl$_3$) $\delta$ 7.44-7.11 (m, NH, 1H), 7.33-7.27 (m, 2H), 6.87 (t, $J = 7.5$ Hz, 1H), 6.79 (d, $J = 8.3$ Hz, 1H), 4.88 (septet, $J = 6.3$ Hz, 1H), 4.84-4.74 (m, 1H), 3.70 (s, 3H), 1.15 (d, $J = 6.8$ Hz, 6H), 1.10-0.92 (m, 6H); $^{13}$C NMR (150 MHz, CDCl$_3$) $\delta$ 168.4 (C), 156.2 (C), 155.3 (C), 152.4 (C), 131.9 (CH), 128.8 (CH), 125.7 (C), 110.8 (CH), 72.1 (CH), 70.2 (CH), 55.7 (CH$_3$), 21.9 (CH$_3$), 21.4 (CH$_3$); IR (thin film) 3308, 2970, 2932, 1731, 1699, 1601, 1517 cm$^{-1}$; LRMS (ESI) 361 (25, [M+Na]$^+$), 339 (100, [M+H]$^+$), 135 (70, [M-C$_8$H$_{13}$N$_2$O$_4$+H]$^+$); HRMS (ESI) calcd for C$_{16}$H$_{23}$N$_2$O$_6$ [M+H]$^+$ 339.1551; observed 339.1554.
Dimethyl 1-(4-fluorobenzoyl)hydrazine-1,2-dicarboxylate 1ab

Compound prepared according to method A. Purification by column chromatography (10%-40% EtOAc/Petrol) afforded dimethyl 1-(4-fluorobenzoyl)hydrazine-1,2-dicarboxylate as a white solid (918 mg, 3.40 mmol, 68%). m.p. 148-152 °C; $^1$H NMR (600 MHz, CDCl$_3$) δ 7.77-7.62 (m, 2H), 7.30 (br s, NH, 1H), 7.10 (t, $J = 8.6$ Hz, 2H), 3.80 (s, 3H) 3.75 (s, 3H); $^{13}$C NMR (150 MHz, CDCl$_3$) δ 170.0 (C), 165.5 (d, $J_{C-F} = 253.9$ Hz, C), 156.2 (C), 154.1 (C), 131.2 (d, $J_{C-F} = 23.5$ Hz, CH), 130.4 (C), 115.7 (d, $J_{C-F} = 9.1$ Hz, CH), 54.7 (CH$_3$), 53.6 (CH$_3$); IR (thin film) 3271, 3070, 3023 2959, 1748, 1718, 1699, 1602, 1559 cm$^{-1}$; LRMS (ESI) 293 (65, [M+Na]$^+$), 271 (20, [M+H]$^+$); HRMS (ESI) calcd for C$_{11}$H$_{12}$FN$_2$O$_5$ [M+H]$^+$ 271.0725; observed 271.0728.
Diethyl 1-(4-fluorobenzoyl)hydrazine-1,2-dicarboxylate\textsuperscript{7} 1ac

Compound prepared according to method A. Purification by column chromatography (10%-50% EtOAc/Petrol) afforded diethyl 1-(4-fluorobenzoyl)hydrazine-1,2-dicarboxylate as a white solid (1.07 g, 3.60 mmol, 72%). \textsuperscript{1}H NMR (600 MHz, CDCl\textsubscript{3}) \( \delta \) 7.73-7.70 (m, 2H), 7.29-7.20 (m, NH, 1H), 7.08 (t, \( J = 8.6 \) Hz, 2H), 4.22 (q, \( J = 7.1 \) Hz, 2H), 4.16 (q, \( J = 7.0 \) Hz, 6H), 1.30-1.21 (m, 3H), 1.19-1.10 (m, 3H); \textsuperscript{13}C NMR (150 MHz, CDCl\textsubscript{3}) \( \delta \) 170.2 (C), 165.2 (d, \( J_{\text{C-F}} = 253.5 \) Hz, C), 155.8 (C), 153.5 (C), 131.1 (d, \( J_{\text{C-F}} = 8.9 \) Hz, CH), 130.9 (C), 115.5 (d, \( J_{\text{C-F}} = 22.2 \) Hz, CH), 64.2 (CH\textsubscript{2}), 62.8 (CH\textsubscript{2}), 14.4 (CH\textsubscript{3}), 13.9 (CH\textsubscript{3}); IR (solid) 3302, 2985, 2940, 1737, 1706, 1603, 1507 cm\textsuperscript{-1}. 

\begin{align*}
\text{F} & \quad \text{N}^+ \text{CO}_2\text{Et} \\
& \quad \text{N}^+ \text{CO}_2\text{Et}
\end{align*}
Di-tert-butyl 1-(4-fluorobenzoyl)hydrazine-1,2-dicarboxylate 1ad

Compound prepared according to method A except in that the reaction duration was 120 h. Purification by column chromatography (10%-50% EtOAc/Petrol) afforded di-tert-butyl 1-(4-fluorobenzoyl)hydrazine-1,2-dicarboxylate as a white solid (921 mg, 2.60 mmol, 52%). m.p. 104-106 °C; $^1$H NMR (600 MHz, CDCl$_3$) δ 7.78-7.61 (m, 2H), 7.09 (t, $J = 8.6$ Hz, 2H), 6.90-6.60 (s, NH, 1H), 1.48 (s, 9H), 1.34-1.24 (m, 9H); $^{13}$C NMR (150 MHz, CDCl$_3$) δ 170.7 (C), 165.0 (d, $J_{C-F} = 253.1$ Hz, C), 154.7 (C), 151.8 (C), 131.9 (C), 131.0 (d, $J_{C-F} = 8.9$ Hz, CH), 115.4 (d, $J_{C-F} = 22.1$ Hz, CH), 84.7 (C), 82.4 (C), 28.2 (CH$_3$), 27.6 (CH$_3$); IR (solid) 3335, 3007, 2974, 2937 1756, 1702, 1603, 1506 cm$^{-1}$; LRMS (ESI) 377 (100, [M+Na]$^+$), 355 (15, [M+H]$^+$); HRMS (ESI) calcd for C$_{17}$H$_{24}$FN$_2$O$_5$ [M+H]$^+$ 355.1664; observed 355.1664.
Synthesis of benzyne precursor

(2-Bromophenoxy)trimethylsilane

To a solution of 2-bromophenol (603 μL, 5.70 mmol) in THF (10 mL) was added hexamethyldisilazane (1.57 mL, 7.50 mmol). The solution was refluxed for 2 h and then allowed to cool to room temperature. The solvent was then removed in vacuo to afford (2-bromophenoxy)trimethylsilane as an orange oil (1.24 g, 5.10 mmol, 89%). $^1$H NMR (600 MHz, CDCl$_3$) $\delta$ 7.53 (dd, $J = 7.9$, 1.6 Hz, 1H), 7.18 (td, $J = 8.0$, 1.6 Hz, 1H), 6.88 (dd, $J = 8.0$, 1.5 Hz, 1H), 6.85 (td, $J = 7.8$, 1.5 Hz, 1H), 0.31 (s, 9H); $^{13}$C NMR (150 MHz, CDCl$_3$) $\delta$ 152.6 (C), 133.4 (CH), 128.4 (CH), 122.8 (CH), 120.9 (CH), 115.7 (C), -0.5 (CH$_3$); IR (thin film) 3056, 2986, 1584 cm$^{-1}$. 

2-(Trimethylsilyl)phenyl trifluoromethanesulfonate

To a solution of (2-bromophenoxy)trimethylsilane (2.00 g, 8.60 mmol) in THF (20 mL) at -78 °C was added dropwise n-BuLi (2.5 M, 3.91 mL, 12.2 mmol). The reaction mixture was stirred for 20 mins. After this time, to the solution was added dropwise Tf₂O (1.90 mL, 12.2 mmol). The reaction was allowed to warm slowly to room temperature and stirred for a further 30 mins. The solution was quenched with NaHCO₃ and extracted with EtOAc. The combined organic extracts were dried (MgSO₄), filtered and the solvent removed in vacuo. Purification by column chromatography (10%-80% EtOAc/Petrol) afforded 2-(trimethylsilyl)phenyl trifluoromethanesulfonate as a yellow oil (1.46 g, 4.90 mmol, 57%).

¹H NMR (600 MHz, CDCl₃) δ 7.54 (d, J = 7.3 Hz, 1H), 7.45 (td, J = 7.8, 1.5 Hz, 1H), 7.36-7.33 (m, 2H), 0.37 (s, 9H); ¹³C NMR (150 MHz, CDCl₃) δ 155.2 (C), 136.4 (CH), 132.7 (CH), 131.4 (CH), 127.6 (CH), 119.6 (CH), 118.6 (q, J_C-F = 319.9 Hz, C), -0.7 (CH₃); IR (thin film) 3054, 2987 cm⁻¹.
General experimental for the formation of ortho-hydrazobenzophenones – Method B

To a solution of acyl hydrazide (500 μmol, 1.0 eq.) and TBAT (1.00 mmol, 540 mg, 2.0 eq.) in toluene (6 mL) was added 2-(trimethylsilyl)phenyl trifluoromethanesulfonate (750 μmol, 182 μL, 1.5 eq.). The reaction mixture was stirred at 50 °C for 16 h. The resulting solution was then allowed to cool to room temperature and the solvent evaporated in vacuo. The resultant crude residue was purified as described below.
Diisopropyl 1-(2-(4-fluorobenzoyl)phenyl)hydrazine-1,2-dicarboxylate 3a

Compound prepared according to method B. Purification by column chromatography (10%-50% EtOAc/Petrol) afforded diisopropyl 1-(2-(4-fluorobenzoyl)phenyl)hydrazine-1,2-dicarboxylate as a pale-yellow oil (173 mg, 430 μmol, 86%). $^1$H NMR (700 MHz, CDCl$_3$) δ 7.83-7.81 (m, 2H), 7.77-7.76 (m, 1H), 7.57-7.54 (m, 1H), 7.42-7.35 (m, 2H), 7.12 (t, $J = 7.6$ Hz, 2H), 7.12 (br s, 1H, NH), 5.00-4.93 (m, 1H), 4.79 (septet, $J = 6.1$ Hz, 1H), 1.31-1.22 (m, 6H), 1.16-0.90 (m, 6H); $^{13}$C NMR (175 MHz, CDCl$_3$) δ 195.1 (C), 194.5 (C), 166.1 (d, $J_{C:F} = 253.8$ Hz, C), 165.9 (d, $J_{C:F} = 253.7$ Hz, C), 156.1 (C), 155.8 (C), 155.0 (C), 154.5 (C), 141.0 (C), 135.4 (C), 133.5 (C), 133.4 (C), 133.1 (CH), 132.4 (CH), 130.1 (CH), 129.8 (CH), 129.4 (CH), 128.9 (CH), 127.7 (CH), 127.4 (CH), 115.7 (d, $J_{C:F} = 21.7$ Hz), 71.2 (CH), 70.8 (CH), 70.0 (CH), 22.1 (CH$_3$), 22.0 (CH$_3$), 21.8 (CH$_3$); IR (thin film) 3323, 2921, 2834, 1711, 1666, 1622, 1599, 1574 cm$^{-1}$; LRMS (ESI) 403 (100, [M+H]$^+$); HRMS (ESI) calcd for C$_{21}$H$_{24}$FN$_2$O$_5$ [M+H]$^+$ 403.1664; observed 403.1658.
Diisopropyl 1-(2-benzoylphenyl)hydrazine-1,2-dicarboxylate 3b

Compound prepared according to method B. Purification by column chromatography (10%-50% EtOAc/Petrol) afforded diisopropyl 1-(2-benzoylphenyl)hydrazine-1,2-dicarboxylate as a pale brown oil (161 mg, 420 μmol, 84%). ¹H NMR (700 MHz, CDCl₃) δ 7.83-7.81 (m, 2H), 7.80-7.49 (m, 5H), 7.46-7.35 (m, 4H), 7.10-6.87 (m, 1H, NH), 5.06-4.92 (m, 1H), 4.92-4.76 (m, 1H), 1.32-1.22 (m, 6H), 1.18-0.92 (m, 6H); ¹³C NMR (175 MHz, CDCl₃) δ 196.7 (C), 196.1 (C), 156.1 (C), 155.8 (C), 154.9 (C), 154.5 (C), 153.0 (C), 141.0 (C), 137.3 (C), 137.1 (C), 135.6 (C), 133.6 (CH), 133.2 (C), 132.3 (CH), 132.0 (CH), 130.4 (CH), 130.3 (CH), 129.7 (CH), 129.5 (CH), 128.5 (CH), 128.3 (CH), 127.6 (CH), 127.4 (CH), 120.8 (CH), 72.6 (CH), 71.2 (CH), 70.8 (CH), 70.0 (CH), 69.9 (CH), 22.1 (CH₃), 22.1 (CH₃), 22.0 (CH₃), 21.7 (CH₃), 21.5 (CH₃); IR (thin film) 3301, 2981, 2937, 1883, 1716, 1659, 1598, 1579 cm⁻¹, LRMS (ESI) 385 (100, [M+H]⁺); HRMS (ESI) calcd for C₂₁H₂₅N₂O₅ [M+H]⁺ 385.1758; observed 385.1755.
Diisopropyl 1-(2-(4-methoxybenzoyl)phenyl)hydrazine-1,2-dicarboxylate 3c

Compound prepared according to method B. Purification by column chromatography (10%-50% EtOAc/Petrol) afforded diisopropyl 1-(2-(4-methoxybenzoyl)phenyl)hydrazine-1,2-dicarboxylate as a pale brown oil (151 mg, 365 μmol, 73%). $^1$H NMR (700 MHz, CDCl$_3$) δ 7.77-7.57 (m, 3H), 7.57 (t, $J = 7.5$ Hz, 1H), 7.41-7.35 (m, 2H), 7.17-7.04 (m, 1H, NH), 6.92 (d, $J = 8.6$ Hz, 1H), 5.02-4.93 (m, 1H), 4.90-4.75 (m, 1H), 3.87-3.82 (m, 3H), 1.31-1.20 (m, 6H), 1.16-0.90 (m, 6H); $^{13}$C NMR (175 MHz, CDCl$_3$) δ 195.4 (C), 194.7 (C), 164.0 (C), 163.9 (C), 163.1 (C), 156.0 (C), 156.1 (C), 155.7 (C), 155.0 (C), 154.6 (C), 140.8 (C), 136.3 (C), 132.9 (C), 131.9 (CH), 131.1 (CH), 131.1 (CH), 129.8 (CH), 129.6 (CH), 128.9 (CH), 127.6 (CH), 127.4 (CH), 120.8 (CH), 113.8 (CH), 113.5 (CH), 72.6 (CH), 72.3 (CH), 70.7 (CH), 70.6 (CH), 69.9 (CH), 55.7 (CH$_3$), 55.6 (CH$_3$), 55.6 (CH$_3$), 22.1 (CH$_3$), 22.1 (CH$_3$), 22.0 (CH$_3$), 21.7 (CH$_3$), 21.6 (CH$_3$); IR (thin film) 3302, 2981, 2937, 2842, 1717, 1652, 1597, 1577 cm$^{-1}$; LRMS (ESI) 437 (30, [M+Na]$^+$), 415 (100, [M+H]$^+$); HRMS (ESI) calcd for C$_{22}$H$_{27}$N$_2$O$_6$ [M+H]$^+$ 415.1864; observed 415.1862.
Diisopropyl 1-(2-(4-(trifluoromethyl)benzoyl)phenyl)hydrazine-1,2-dicarboxylate 3d

Compound prepared according to method B. Purification by column chromatography (10%-50% EtOAc/Petrol) afforded diisopropyl 1-(2-(4-(trifluoromethyl)benzoyl)phenyl)hydrazine-1,2-dicarboxylate as a clear oil (161 mg, 355 μmol, 71%). $^1$H NMR (600 MHz, CDCl$_3$) $\delta$ 7.94-7.85 (m, 2H), 7.83-7.63 (m, 3H), 7.62-7.57 (m, 1H), 7.42-7.34 (m, 2H), 7.09-6.84 (m, NH, 1H), 5.03-4.94 (m, 1H), 4.85-4.75 (m, 1H), 1.30-1.23 (m, 6H), 1.18-0.92 (m, 6H); $^{13}$C NMR (150 MHz, CDCl$_3$) $\delta$ 195.4 (C), 194.9 (C), 155.9 (C), 154.9 (C), 141.1 (C), 140.2 (C), 134.7 (C), 132.9 (CH), 130.6 (CH), 130.0 (CH), 129.9 (CH), 129.2 (CH), 128.7 (CH), 127.7 (CH), 127.4 (CH), 125.6 (CH), 123.7 (q, $J_{C:F}$ = 272.2 Hz, C), 119.0 (CH), 71.3 (CH), 71.0 (CH), 70.1 (CH), 22.1 (CH$_3$), 21.9 (CH$_3$); IR (thin film) 3323, 2921, 2834, 1711, 1666, 1622, 1599, 1574 cm$^{-1}$; LRMS (ESI) 453 (100, [M+H]$^+$); HRMS (ESI) calcd for C$_{22}$H$_{24}$F$_3$N$_2$O$_5$ [M+H]$^+$ 453.1632; observed 453.1630.
Diisopropyl 1-(2-(4-(methoxycarbonyl)benzoyl)phenyl)hydrazine-1,2-dicarboxylate 3e

Compound prepared according to method B. Purification by column chromatography (10%-50% EtOAc/Petrol) afforded diisopropyl 1-(2-(4-(methoxycarbonyl)benzoyl)phenyl)hydrazine-1,2-dicarboxylate as a clear oil (150 mg, 340 μmol, 68%). $^1$H NMR (600 MHz, CDCl$_3$) δ 8.11 (d, $J = 8.3$, 1.5 Hz, 2H), 7.98-7.65 (m, 3H), 7.59 (td, $J = 7.9$, 2.0 Hz, 1H), 7.53-7.27 (m, 2H), 7.09-6.62 (m, NH, 1H), 5.03-4.76 (m, 2H), 3.96-3.93 (m, 3H), 1.31-0.94 (m, 12H); $^{13}$C NMR (150 MHz, CDCl$_3$) δ 195.9 (C), 195.4 (C), 168.6 (C), 166.2 (C), 155.9 (C), 154.7 (C), 151.4 (C), 141.1 (C), 140.9 (C), 140.5 (C), 138.8 (C), 134.9 (C), 134.2 (CH), 133.9 (CH), 133.1 (CH), 132.8 (CH), 130.1 (CH), 129.7 (CH), 129.6 (CH), 128.0 (CH), 127.7 (CH), 127.4 (CH), 120.8 (CH), 73.5 (CH), 71.0 (CH), 70.1 (CH), 52.6 (CH$_3$), 52.6 (CH$_3$), 22.1 (CH$_3$), 21.8 (CH$_3$), 21.4 (CH$_3$); IR (thin film) 3302, 2910, 2836, 1723, 1660, 1620, 1602, 1570 cm$^{-1}$; LRMS (ESI) 465 (25, [M+Na]$^+$), 443 (100, [M+H]$^+$); HRMS (ESI) calcd for C$_{23}$H$_{27}$N$_2$O$_7$ [M+H]$^+$ 443.1813; observed 443.1809.
Diisopropyl 1-(2-(4-iodobenzoyl)phenyl)hydrazine-1,2-dicarboxylate 3f

![Chemical structure](image)

Compound prepared according to method B. Purification by column chromatography (10%-50% EtOAc/Petrol) afforded diisopropyl 1-(2-(4-iodobenzoyl)phenyl)hydrazine-1,2-dicarboxylate as a clear oil (189 mg, 370 μmol, 74%). $^1$H NMR (600 MHz, CDCl$_3$) δ 7.88-7.73 (m, 2H), 7.58 (t, $J = 7.2$ Hz, 1H), 7.55-7.29 (m, 4H), 7.25-6.94 (m, 1H), 5.04-4.79 (m, 2H), 1.29-0.94 (m, 12H); $^{13}$C NMR (150 MHz, CDCl$_3$) δ 195.9 (C), 195.3 (C), 155.9 (C), 154.9 (C), 152.2 (C), 150.1 (C), 141.1 (C), 137.9 (CH), 136.5 (C), 135.1 (CH), 132.6 (CH), 131.7 (CH), 129.9 (CH), 128.7 (CH), 127.4 (CH), 120.8 (CH), 101.3 (C), 71.2 (CH), 71.1 (CH), 70.2 (CH), 70.1 (CH), 22.8 (CH$_3$), 21.1 (CH$_3$), 22.0 (CH$_3$) 21.9 (CH$_3$); IR (thin film) 3314, 2919, 2835, 1709, 1666, 1620, 1599 cm$^{-1}$; LRMS (ESI) 511 (100, [M+H]$^+$); HRMS (ESI) calcd for C$_{21}$H$_{24}$IN$_2$O$_5$ [M+H]$^+$ 511.0724; observed 511.0719.
Diisopropyl 1-(2-(3-bromobenzoyl)phenyl)hydrazine-1,2-dicarboxylate 3g

Compound prepared according to method B. Purification by column chromatography (10%-50% EtOAc/Petrol) afforded diisopropyl 1-(2-(3-bromobenzoyl)phenyl)hydrazine-1,2-dicarboxylate as a clear oil (183 mg, 395 μmol, 79%). $^1$H NMR (600 MHz, CDCl$_3$) δ 8.08-7.09 (m, 8H), 7.08-6.65 (m, NH, 1H), 5.06-4.77 (m, 2H), 3.96-3.93 (m, 3H), 1.31-0.94 (m, 12H); $^{13}$C NMR (150 MHz, CDCl$_3$) δ 195.0 (C), 194.6 (C), 156.2 (C), 155.8 (C), 154.9 (C), 154.5 (C), 142.0 (C), 141.1 (C), 139.1 (C), 136.4 (CH), 136.1 (CH), 134.8 (CH), 133.3 (CH), 132.7 (CH), 130.1 (CH), 128.9 (CH), 128.7 (CH), 127.7 (CH), 127.4 (CH), 126.1 (C), 122.8 (C), 71.3 (CH), 71.0 (CH), 70.1 (CH), 22.2 (CH$_3$), 22.1 (CH$_3$), 22.0 (CH$_3$), 21.8 (CH$_3$); IR (thin film) 3312, 2980, 2880, 1715, 1660, 1622, 1595, 1575 cm$^{-1}$; LRMS (ESI) 487 (30, [M$^{81}$Br+Na$^+$]), 485 (31, [M$^{79}$Br+Na$^+$]), 465 (100, [M$^{79}$Br+H$^+$]), 463 (98, [M$^{79}$Br+H$^+$]); HRMS (ESI) calcd for C$_{21}$H$_{24}$BrN$_2$O$_5$ [M$^{79}$Br+H$^+$] 463.0863; observed 463.0858.
Diisopropyl 1-(2-(3-chlorobenzoyl)phenyl)hydrazine-1,2-dicarboxylate 3h

Compound prepared according to method B. Purification by column chromatography (10%-50% EtOAc/Petrol) afforded diisopropyl 1-(2-(3-chlorobenzoyl)phenyl)hydrazine-1,2-dicarboxylate as a pale-yellow oil (170 mg, 405 μmol, 81%). $^1$H NMR (700 MHz, CDCl$_3$) δ 8.00-7.11 (m, 8H), 7.10-6.73 (m, 1H, NH), 5.07-4.80 (m, 2H), 1.30-0.94 (m, 12H); $^{13}$C NMR (175 MHz, CDCl$_3$) δ 195.1 (C), 194.7 (C), 156.2 (C), 156.1 (C), 155.9 (C), 154.9 (C), 154.5 (C), 142.0 (C), 141.0 (C), 138.9 (C), 138.7 (C), 134.8 (C), 133.5 (CH), 133.2 (CH), 132.7 (CH), 130.4 (CH), 130.0 (CH), 129.9 (CH), 129.2 (CH), 128.7 (CH), 128.4 (CH), 127.8 (CH), 127.4 (CH), 126.2 (CH), 120.8 (CH), 71.3 (CH), 71.0 (CH), 70.1 (CH), 22.1 (CH$_3$), 22.1 (CH$_3$), 22.0 (CH$_3$), 22.0 (CH$_3$), 21.8 (CH$_3$); IR (thin film) 3305, 2985, 2884, 1718, 1658, 1619, 1599, 1580 cm$^{-1}$; LRMS (ESI) 443 (8, [M$^{37}$Cl+Na$^+$/]), 441 (25, [M$^{35}$Cl+Na$^+$]), 421 (30, [M$^{37}$Cl+H$^+$]), 419 (100, [M$^{35}$Cl+H$^+$]); HRMS (ESI) calcd for C$_{21}$H$_{24}$ClN$_2$O$_5$ [M$^{35}$Cl+H$^+$] 419.1368; observed 419.1367.
Diisopropyl 1-(2-(3-nitrobenzoyl)phenyl)hydrazine-1,2-dicarboxylate 3i

Compound prepared according to method B. Purification by column chromatography (10%-50% EtOAc/Petrol) afforded diisopropyl 1-(2-(3-nitrobenzoyl)phenyl)hydrazine-1,2-dicarboxylate as a yellow oil (155 mg, 360 μmol, 72%). $^1$H NMR (600 MHz, CDCl$_3$) δ 8.70-8.34 (m, 2H), 8.18-7.97 (m, 1H), 7.96-7.28 (m, 4H), 7.12-6.78 (m, NH, 1H), 5.08-4.76 (m, 2H), 3.96-3.93 (m, 3H), 1.31-0.95 (m, 12H); $^{13}$C NMR (150 MHz, CDCl$_3$) δ 195.6 (C), 193.8 (C), 193.8 (C), 156.5 (C), 156.0 (C), 155.3 (C), 152.5 (C), 148.4 (C), 147.9 (C), 141.1 (C), 138.6 (C), 136.9 (C), 135.8 (C), 133.8 (C), 133.0 (C), 129.7 (CH), 127.9 (CH), 127.4 (CH), 126.2 (CH), 125.0 (CH), 123.2 (CH), 73.2 (CH), 71.1 (CH), 70.2 (CH), 22.1 (CH$_3$), 22.0 (CH$_3$), 22.0 (CH$_3$), 21.6 (CH$_3$); IR (thin film) 3313, 2914, 2830, 1715, 1664, 1619, 1593, 1574 cm$^{-1}$; LRMS (ESI) 452 (30, [M+Na]$^+$), 430 (100, [M+H]$^+$); HRMS (ESI) calcd for C$_{21}$H$_{24}$N$_3$O$_7$ [M+H]$^+$ 430.1609; observed 430.1606.
**Diisopropyl 1-(2-(2-fluorobenzoyl)phenyl)hydrazine-1,2-dicarboxylate 3j**

Compound prepared according to method B. Purification by column chromatography (10%-50% EtOAc/Petrol) afforded diisopropyl 1-(2-(2-fluorobenzoyl)phenyl)hydrazine-1,2-dicarboxylate as a clear oil (141 mg, 350 μmol, 70%). $^1$H NMR (600 MHz, CDCl$_3$) δ 7.85-7.13 (m, 8H), 5.02-4.83 (m, 2H), 1.28-1.03 (m, 12H); $^{13}$C NMR (150 MHz, CDCl$_3$) δ 193.4 (C), 193.0 (C), 166.2 (C), 166.2 (C), 160.9 (d, $J_{\text{C-F}}$ = 253.2 Hz, C), 159.1 (d, $J_{\text{C-F}}$ = 253.2 Hz, C), 156.1 (C), 155.8 (C), 155.2 (C), 155.0 (C), 154.6 (C), 140.6 (C), 135.4 (C), 140.6 (C), 135.4 (CH), 134.6 (CH), 133.0 (CH), 131.7 (CH), 130.7 (CH), 129.7 (CH), 128.0 (C), 127.8 (C), 126.6 (d, $J_{\text{C-F}}$ = 10.8 Hz, CH), 124.5 (CH), 124.3 (CH), 116.7 (d, $J_{\text{C-F}}$ = 20.8 Hz, CH), 115.6 (C), 73.5 (CH), 71.0 (CH), 70.1 (CH), 52.6 (CH$_3$), 52.6 (CH$_3$), 22.1 (CH$_3$), 21.8 (CH$_3$), 21.4 (CH$_3$); IR (thin film) 3320, 2919, 2835, 1711, 1667, 1620, 1570 cm$^{-1}$; LRMS (ESI) 425 (25, [M+Na]$^+$), 403 (100, [M+H]$^+$); HRMS (ESI) calcd for C$_{21}$H$_{24}$FN$_2$O$_5$ [M+H]$^+$ 403.1664; observed 403.1661.
Diisopropyl 1-(2-(2-methylbenzoyl)phenyl)hydrazine-1,2-dicarboxylate 3k

Compound prepared according to method B. Purification by column chromatography (10%-50% EtOAc/Petrol) afforded diisopropyl 1-(2-(2-methylbenzoyl)phenyl)hydrazine-1,2-dicarboxylate as a clear oil (104 mg, 260 μmol, 52%). $^1$H NMR (600 MHz, CDCl$_3$) δ 7.79-7.19 (m, 9H), 5.14-4.77 (m, 2H), 2.55-2.33 (m, 3H), 1.33-1.01 (m, 12H); $^{13}$C NMR (150 MHz, CDCl$_3$) δ 198.8 (C), 198.3 (C), 156.0 (C), 155.8 (C), 155.1 (C), 154.7 (C), 140.9 (C), 140.9 (C), 138.9 (C), 138.3 (CH), 138.1 (CH), 137.6 (C), 136.2 (CH), 135.6 (CH), 133.0 (CH), 131.4 (CH), 130.6 (CH), 128.0 (CH), 125.5 (CH), 125.3 (CH), 109.2 (C), 71.1 (CH), 70.8 (CH), 69.9 (CH), 69.7 (CH), 24.0 (CH$_3$), 22.1 (CH$_3$), 21.9 (CH$_3$), 20.7 (CH$_3$), 20.5 (CH$_3$); IR (thin film) 3314, 2924, 2830, 1710, 1656, 1621, 1599, 1573 cm$^{-1}$; LRMS (ESI) 421 (20, [M+Na$^+$]), 399 (100, [M+H$^+$]); HRMS (ESI) calcd for C$_{22}$H$_{27}$N$_2$O$_5$ [M+H$^+$] 399.1914; observed 399.1910.
Diisopropyl 1-(2-(2-methoxybenzoyl)phenyl)hydrazine-1,2-dicarboxylate 3l

Compound prepared according to method B. Purification by column chromatography (10%-50% EtOAc/Petrol) afforded diisopropyl 1-(2-(2-methoxybenzoyl)phenyl)hydrazine-1,2-dicarboxylate as a clear oil (99.5 mg, 240 μmol, 48%). \(^1\)H NMR (600 MHz, CDCl\(_3\)) δ 7.75-6.76 (m, 8H), 5.03-4.83 (m, 2H), 3.83-3.71 (m, 3H), 1.30-1.03 (m, 12H); \(^1^3\)C NMR (150 MHz, CDCl\(_3\)) δ 196.5 (C), 195.9 (C), 168.4 (C), 158.4 (C), 156.1 (C), 155.2 (C), 152.3 (C), 140.6 (C), 133.5 (CH), 133.2 (CH), 132.9 (CH), 132.7 (CH), 132.0 (CH), 131.6 (C), 131.3 (C), 130.9 (CH), 130.3 (CH), 130.2 (CH), 129.6 (CH), 129.0 (CH), 128.5 (C), 127.8 (CH), 125.7 (C), 120.8 (CH), 120.4 (CH), 111.9 (CH), 111.8 (CH), 100.8 (CH), 72.2 (CH), 70.8 (CH), 70.6 (CH), 70.5 (CH), 70.0 (CH), 69.8 (CH), 69.6 (CH), 55.9 (CH\(_3\)), 55.8 (CH\(_3\)), 55.7 (CH\(_3\)), 22.1 (CH\(_3\)), 22.0 (CH\(_3\)), 21.9 (CH\(_3\)), 21.5 (CH\(_3\)); IR (thin film) 3300, 2979, 2937, 2912, 2845, 1721, 1650, 1591 cm\(^{-1}\); LRMS (ESI) 415 (100, [M+H]\(^+\)), 339 (95, [M+H]\(^+\)); HRMS (ESI) calcd for C\(_{22}\)H\(_{27}\)N\(_2\)O\(_6\) [M+H]\(^+\) 415.1864; observed 415.1863.
Dimethyl 1-(2-(4-fluorobenzoyl)phenyl)hydrazine-1,2-dicarboxylate 3ab

Compound prepared according to method B. Purification by column chromatography (10%-30% EtOAc/Petrol) afforded dimethyl 1-(2-(4-fluorobenzoyl)phenyl)hydrazine-1,2-dicarboxylate as a brown-orange oil (45.0 mg, 130 μmol, 26%). $^1$H NMR (600 MHz, CDCl$_3$) δ 7.84-7.82 (m, 2H), 7.63-7.54 (m, 1H), 7.44-7.38 (m, 2H), 7.37-7.33 (m, 1H), 7.12 (t, $J$ = 7.6 Hz, 2H), 3.83-3.45 (m, 6H); $^{13}$C NMR (150 MHz, CDCl$_3$) δ 195.5 (C), 194.6 (C), 166.9 (d, $J_{C,F}$ = 255.8 Hz, C), 164.1 (d, $J_{C,F}$ = 255.8 Hz, C), 156.8 (C), 156.3 (C), 156.1 (C), 155.3 (C), 140.6 (C), 135.5 (C), 133.1 (C), 132.8 (CH), 132.5 (CH), 131.5 (d, $J_{C,F}$ = 8.6 Hz, CH), 130.4 (CH), 130.2 (CH), 130.1 (d, $J_{C,F}$ = 8.6 Hz, CH), 129.7 (CH), 129.2 (CH), 128.9 (CH), 127.9 (CH), 127.4 (C), 115.8 (d, $J_{C,F}$ = 22.2 Hz), 115.3 (d, $J_{C,F}$ = 21.9 Hz), 54.0 (CH$_3$), 53.7 (CH$_3$), 53.1 (CH$_3$); IR (thin film) 3308, 3020, 2957, 1722, 1659, 1598 cm$^{-1}$; LRMS (ESI) 347 (100, [M+H]$^+$); HRMS (ESI) calcd for C$_{17}$H$_{16}$FN$_2$O$_5$ [M+H]$^+$ 347.1038; observed 347.1043.
Diethyl 1-(2-(4-fluorobenzoyl)phenyl)hydrazine-1,2-dicarboxylate 3ac

Compound prepared according to method B. Purification by column chromatography (10%-30% EtOAc/Petrol) afforded diethyl 1-(2-(4-fluorobenzoyl)phenyl)hydrazine-1,2-dicarboxylate as a brown-orange oil (77.0 mg, 210 μmol, 41%). $^1$H NMR (600 MHz, CDCl$_3$) $\delta$ 7.84-7.76 (m, 2H), 7.60-7.55 (m, 1H), 7.44-7.38 (m, 2H), 7.33-7.22 (m, 1H), 7.15-7.05 (m, 2H), 4.26-3.94 (m, 4H), 1.30-0.91 (m, 6H); $^{13}$C NMR (150 MHz, CDCl$_3$) $\delta$ 195.4 (C), 194.6 (C), 166.0 (d, $J_{C:F} = 254.5$ Hz, C), 156.4 (C), 156.0 (C), 155.5 (C), 154.9 (C), 153.3 (C), 141.8 (C), 140.8 (C), 135.4 (C), 133.1 (d, $J_{C:F} = 8.6$ Hz, CH), 132.4 (CH), 131.1 (CH), 131.0 (CH), 130.1 (CH), 129.8 (CH), 127.8 (CH), 127.6 (CH), 115.8 (d, $J_{C:F} = 21.8$ Hz), 64.2 (CH$_2$), 63.1 (CH$_2$), 62.8 (CH$_2$), 62.4 (CH$_2$), 62.2 (CH$_2$), 14.6 (CH$_3$), 14.5 (CH$_3$), 14.3 (CH$_3$); IR (thin film) 3310, 3019, 2984, 1720, 1659, 1598 cm$^{-1}$; LRMS (ESI) 375 (100, [M+H]$^+$); HRMS (ESI) calcd for C$_{19}$H$_{20}$FN$_2$O$_5$ [M+H]$^+$ 375.1351; observed 375.1345.
Di-tert-butyl 1-(2-(4-fluorobenzoyl)phenyl)hydrazine-1,2-dicarboxylate 3ad

Compound prepared according to method B. Purification by column chromatography (10%-25% EtOAc/Petrol) afforded di-tert-butyl 1-(2-(4-fluorobenzoyl)phenyl)hydrazine-1,2-dicarboxylate as a brown-orange oil (140 mg, 330 μmol, 65%). \(^1\)H NMR (600 MHz, CDCl\(_3\)) \(\delta 7.85-7.82\) (m, 2H), \(7.77-7.72\) (m, 1H), \(7.56\) (td, \(J = 7.7, 1.6\) Hz, 1H), \(7.43-7.36\) (m, 2H), \(7.15-7.07\) (m, 2H), \(6.88-6.75\) (br s, NH, 1H), \(1.54-1.44\) (m, 9H), \(1.36-1.20\) (m, 9H); \(^{13}\)C NMR (150 MHz, CDCl\(_3\)) \(\delta 195.2\) (C), \(194.2\) (C), \(165.8\) (d, \(J_{C-F} = 254.1\) Hz, C), \(155.2\) (C), \(154.3\) (C), \(141.2\) (C), \(140.8\) (C), \(135.5\) (C), \(133.4\) (C), \(133.0\) (d, \(J_{C-F} = 9.1\) Hz, CH), \(132.2\) (CH), \(131.9\) (CH), \(129.5\) (CH), \(129.2\) (CH), \(128.5\) (CH) \(127.3\) (CH), \(127.1\) (CH), \(115.6\) (d, \(J_{C-F} = 20.4\) Hz), \(82.3\) (C), \(81.3\) (C), \(28.3\) (CH\(_3\)), \(28.0\) (CH\(_3\)); IR (thin film) 3307, 2981, 2932, 1716, 1661, 1505 cm\(^{-1}\); LRMS (ESI) 431 (100, [M+H]\(^{+}\)); HRMS (ESI) calcd for C\(_{19}\)H\(_{20}\)F\(_2\)N\(_2\)O\(_5\) [M+H]\(^{+}\) 431.1977; observed 431.1968.
General experimental for the formation of 1H-indazoles – Method C

To a stirring solution of 2-hydrazobenzophenone (250 μmol, 1 eq.) in dimethylacetamide (5 mL) was added KOH (56.1 mg, 1.00 mmol, 4 eq.) pre-dissolved in distilled H₂O (3 mL) under an atmosphere of argon. The reaction mixture was stirred at 60 °C for 16 h and then poured over distilled H₂O (20 mL). The resulting mixture was extracted with EtOAc (3 × 15 mL). The combined extracts were then dried (MgSO₄), filtered and the solvent evaporated in vacuo. The resultant crude residue was purified as described below.
3-(4-Fluorophenyl)-1H-indazole 4a

Compound prepared according to method C. Purification by column chromatography (10%-50% EtOAc/Petrol) afforded 3-(4-fluorophenyl)-1H-indazole as a white solid (48.8 mg, 0.230 mmol, 92%). m.p. 116-118 °C; $^1$H NMR (600 MHz, CDCl$_3$) δ 8.01-7.95 (m, 3H), 7.45-7.38 (m, 2H), 7.27-7.21 (m, 3H); $^{13}$C NMR (150 MHz, CDCl$_3$) δ 162.9 (d, $J_{C-F}$ = 247.5 Hz, C), 145.0 (C), 141.8 (C), 129.8 (d, $J_{C-F}$ = 3.3 Hz, C), 129.4 (d, $J_{C-F}$ = 8.1 Hz, CH), 127.1 (CH), 121.7 (CH), 121.0 (CH), 121.0 (C), 116.0 (d, $J_{C-F}$ = 21.6 Hz, CH), 110.2 (CH); IR (thin film) 3420, 3098, 2918, 2858, 1590 cm$^{-1}$; LRMS (ESI) 213 (100, [M+H]$^+$); HRMS (ESI) calcd for C$_{13}$H$_{10}$FN$_2$ [M+H]$^+$ 213.0823; observed 213.0822.
3-Phenyl-1H-indazole 4b

Compound prepared according to method C. Purification by column chromatography (10%-50% EtOAc/Petrol) afforded 3-phenyl-1H-indazole as a white solid (42.7 mg, 0.220 mmol, 88%). m.p. 113-115 °C; $^1$H NMR (600 MHz, CDCl$_3$) δ 8.05 (dt, $J$ = 8.2, 0.8 Hz, 1H), 8.01-7.98 (m, 2H), 7.53 (tt, $J$ = 7.7, 1.6 Hz, 2H), 7.48-7.45 (m, 1H), 7.45-7.40 (m, 2H), 7.24 (ddd, $J$ = 7.9, 6.8, 1.0 Hz, 1H); $^{13}$C NMR (150 MHz, CDCl$_3$) δ 146.0 (C), 141.8 (C), 133.6 (C), 129.0 (CH), 128.3 (CH), 127.7 (CH), 127.0 (CH), 121.6 (CH), 121.4 (C), 121.2 (C), 110.2 (CH); IR (solid) 3150, 2935, 1622 cm$^{-1}$; LRMS (ESI) 195 (100, [M+H]$^+$); HRMS (ESI) calcd for C$_{13}$H$_{11}$N$_2$ [M+H]$^+$ 195.0917; observed 195.0916.
3-(4-Methoxyphenyl)-1H-indazole 4c

Compound prepared according to method C except reaction temperature was 100 °C. Purification by column chromatography (10%-50% EtOAc/Petrol) afforded 3-(4-methoxyphenyl)-1H-indazole as a white solid (44.9 mg, 0.200 mmol, 80%). m.p. 84-86 °C; $^1$H NMR (600 MHz, CDCl$_3$) δ 8.01 (dt, $J = 8.2, 0.9$ Hz, 1H), 7.94-7.91 (m, 2H), 7.45 (dt, $J = 8.4, 0.9$ Hz, 1H), 7.42-7.39 (m, 1H), 7.22 (ddd, $J = 7.9, 6.7, 1.0$ Hz, 1H), 7.07-7.04 (m, 2H); $^{13}$C NMR (150 MHz, CDCl$_3$) δ 159.8 (C), 145.7 (C), 141.8 (C), 129.0 (CH), 127.0 (CH), 126.2 (C), 121.4 (CH), 121.4 (CH), 121.0 (C), 114.5 (CH), 110.2 (CH), 55.5 (CH$_3$); IR (solid) 3454, 3163, 2940, 1614 cm$^{-1}$; LRMS (ESI) 225 (100, [M+H]$^+$); HRMS (ESI) calcd for C$_{14}$H$_{13}$N$_2$O [M+H]$^+$ 225.1022; observed 225.1024.
3-(4-(Trifluoromethyl)phenyl)-1H-indazole 4d

Compound prepared according to method C. Purification by column chromatography (10%-50% EtOAc/Petrol) afforded 3-(4-(trifluoromethyl)phenyl)-1H-indazole as a white solid (54.4 mg, 0.208 mmol, 83%). m.p. 82-84 °C; \(^1\)H NMR (600 MHz, CDCl\(_3\)) \(\delta\) 10.51 (br s, NH, 1H), 8.12 (d, \(J = 8.1\) Hz, 2H), 8.03 (d, \(J = 8.2\) Hz, 1H), 7.78 (d, \(J = 8.2\) Hz, 2H), 7.52-7.48 (m, 1H), 7.47-7.43 (m, 1H), 7.28 (ddd, \(J = 7.8, 6.8, 0.8\) Hz, 1H); \(^1^3\)C NMR (150 MHz, CDCl\(_3\)) \(\delta\) 144.5 (C), 141.8 (C), 137.2 (C), 130.1 (q, \(J_{\text{C-F}} = 32.9\) Hz, C), 127.8 (CH), 127.3 (CH), 125.9 (q, \(J_{\text{C-F}} = 3.5\) Hz, CH), 124.4 (q, \(J_{\text{C-F}} = 271.9\) Hz, C), 122.1 (CH), 121.1 (C), 120.9 (CH), 110.3 (CH); IR (solid) 3468, 3242, 2943, 1619 cm\(^{-1}\); LRMS (ESI) 263 (100, [M+H]+); HRMS (ESI) calcd for C\(_{14}\)H\(_{10}\)F\(_3\)N\(_2\) [M+H]+ 263.0791; observed 263.0795.
4-(1H-Indazol-3-yl)benzoic acid 4e

Compound prepared according to method C except that the reaction was poured over HCl (1 M, 20 mL) prior to extraction with EtOAc. Purification by column chromatography (10%-50% EtOAc/Petrol) afforded 4-(1H-indazol-3-yl)benzoic acid as a white solid (47.7 mg, 0.200 mmol, 80%). m.p. 196-202 °C; \(^1\)H NMR (600 MHz, DMSO-\(d_6\)) \(\delta\) 13.44 (br s, NH, 1H), 13.00 (br s, CO\(_2\)H, 1H), 8.16-8.14 (m, 3H), 8.10-8.07 (m, 2H), 7.63 (dt, \(J = 8.4, 0.8\) Hz, 1H), 7.44 (ddd, \(J = 7.6, 6.8, 1.0\) Hz, 1H), 7.26 (ddd, \(J = 7.6, 6.8, 1.0\) Hz, 1H); \(^1^3\)C NMR (150 MHz, DMSO-\(d_6\)) \(\delta\) 167.2 (C), 142.1 (C), 141.7 (C), 138.0 (C), 130.0 (CH), 129.6 (C), 126.6 (CH), 126.3 (CH), 121.5 (CH), 120.6 (C), 120.2 (CH), 110.9 (CH); IR (solid) 3470, 3223, 2970, 2799, 1737, 1565 cm\(^{-1}\); LRMS (ESI) 239 (100, [M+H]\(^+\)); HRMS (ESI) calcd for C\(_{14}\)H\(_{11}\)N\(_2\)O\(_2\) [M+H]\(^+\) 239.0815; observed 239.0815.
3-(4-Iodophenyl)-1H-indazole 4f

Compound prepared according to method C. Purification by column chromatography (10%-50% EtOAc/Petrol) afforded 3-(4-iodophenyl)-1H-indazole as a white solid (66.4 mg, 0.208 mmol, 83%). m.p. 154-157 °C; \(^1\)H NMR (600 MHz, CDCl\(_3\)) \(\delta\) 10.17 (br s, NH, 1H), 7.99 (d, \(J = 8.2\) Hz, 1H), 7.86-7.83 (m, 2H), 7.75-7.71 (m, 2H), 7.52 (d, \(J = 8.4\) Hz, 1H), 7.45-7.43 (m, 1H), 7.27-7.25 (m, 1H); \(^{13}\)C NMR (150 MHz, CDCl\(_3\)) \(\delta\) 145.0 (C), 141.8 (C), 138.1 (CH), 133.2 (C), 129.3 (CH), 128.7 (CH), 127.2 (CH), 121.9 (CH), 121.1 (C), 110.2 (CH), 94.0 (C); 3425, 3179, 2922, 1621 cm\(^{-1}\); LRMS (ESI) 321 (100, [M+H]\(^+\)); HRMS (ESI) calcd for C\(_{13}\)H\(_{10}\)N\(_2\) [M+H]\(^+\) 320.9883; observed 320.9887.
Compound prepared according to method C. Purification by column chromatography (10%-50% EtOAc/Petrol) afforded 3-(3-bromophenyl)-1H-indazole as a white solid (57.4 mg, 0.210 mmol, 84%). m.p. 125-128 °C; $^1$H NMR (700 MHz, CDCl$_3$) δ 10.17 (br s, NH, 1H), 8.15 (s, 1H), 8.02 (d, $J = 8.2$ Hz, 1H), 7.92 (d, $J = 7.7$ Hz, 1H), 7.54 (t, $J = 8.0$ Hz, 2H), 7.45 (t, $J = 7.6$ Hz, 1H), 7.39 (t, $J = 8.0$ Hz, 1H) 7.28 (t. $J = 7.5$ Hz, 1H); $^{13}$C NMR (175 MHz, CDCl$_3$) δ 144.5 (C), 141.8 (C), 133.7 (C), 131.2 (CH), 130.5 (CH), 130.5 (CH), 127.2 (CH), 126.1 (CH), 123.1 (C), 122.0 (CH), 121.0 (CH), 121.0 (C), 110.2 (CH); IR (solid) 3120, 2938, 1619 cm$^{-1}$; LRMS (ESI) 275 (96, [M$^{81}$Br+H]$^+$) 273 (100, [M$^{79}$Br+H]$^+$); HRMS (ESI) calcd for C$_{13}$H$_{10}$BrN$_2$ [M$^{81}$Br+H]$^+$ 273.0022; observed 273.0025.
3-(3-Chlorophenyl)-1H-indazole 4h

Compound prepared according to method C. Purification by column chromatography (10%-50% EtOAc/Petrol) afforded 3-(3-chlorophenyl)-1H-indazole as a white solid (48.6 mg, 0.213 mmol, 85%). m.p. 136-137 °C; 

\(^1\)H NMR (600 MHz, CDCl\(_3\)) \(\delta\) 8.02 (dt, \(J = 8.2, 0.9\) Hz, 1H), 7.99 (t, \(J = 1.8\) Hz, 1H), 7.88 (ddd, \(J = 7.7, 1.5, 1.2\) Hz, 1H), 7.52 (dt, \(J = 8.4, 0.9\) Hz, 1H), 7.46-7.43 (m, 2H), 7.39 (ddd, \(J = 8.0, 2.1, 1.1\) Hz, 1H) 7.29-7.26 (m, 1H); 

\(^1\)^3\)C NMR (150 MHz, CDCl\(_3\)) \(\delta\) 144.6 (C), 141.8 (C), 133.5 (C), 134.9 (C), 130.2 (CH), 128.3 (CH), 127.7 (CH), 127.6 (CH), 127.2 (CH), 125.7 (CH), 121.9 (CH), 121.0 (C), 110.2 (CH); IR (solid) 3425, 3179, 2922, 1621 cm\(^{-1}\); LRMS (ESI) 231 (30, [M\(^{37}\)Cl+H]\(^+\)), 229 (100, [M\(^{35}\)Cl+H]\(^+\)); HRMS (ESI) calcd for C\(_{13}\)H\(_{10}\)ClN\(_2\) [M\(^{35}\)Cl+H]\(^+\) 229.0527; observed 229.0528.
3-(3-Nitrophenyl)-1H-indazole 4i

Compound prepared according to method C. Purification by column chromatography (10%-50% EtOAc/Petrol) afforded 3-(3-nitrophenyl)-1H-indazole as a white solid (11.4 mg, 0.0475 mmol, 19%). m.p. 182-185 °C; \(^{1}\)H NMR (700 MHz, CDCl\(_3\)) \(\delta\) 10.31 (br s, NH, 1H), 8.87 (t, \(J = 1.9\) Hz, 1H), 8.35 (ddd, \(J = 7.7, 1.6, 1.1\) Hz, 1H), 8.26 (ddd, \(J = 8.2, 2.3, 1.0\) Hz, 1H), 8.08-8.06 (m, 1H), 7.71-7.66 (m, 1H), 7.57 (d, \(J = 8.4, 0.9\) Hz, 1H), 7.48 (ddd, \(J = 8.4, 6.9, 1.0\) Hz, 1H), 7.34-7.30 (m, 1H); \(^{13}\)C NMR (175 MHz, CDCl\(_3\)) \(\delta\) 146.0 (C), 143.5 (C), 141.9 (C), 135.5 (C), 133.2, 129.9 (CH), 127.4 (CH), 122.8 (CH), 122.4 (CH), 122.3 (CH), 120.9 (C), 120.7 (CH), 110.4 (CH); IR (solid) 3419, 3120, 2941, 1621 cm\(^{-1}\); LRMS (ESI) 240 (100, [M+H]+); HRMS (ESI) calcd for C\(_{13}\)H\(_{10}\)N\(_3\)O\(_2\) [M+H]+ 240.0768; observed 240.0768.
3-(2-fluorophenyl)-1H-indazole 4j

Compound prepared according to method C. Purification by column chromatography (10%-50% EtOAc/Petrol) afforded 3-(2-fluorophenyl)-1H-indazole as a white solid (41.4 mg, 0.195 mmol, 78%). m.p. 114-116 °C; ¹H NMR (600 MHz, CDCl₃) δ 7.88-7.83 (m, 2H), 7.46-7.38 (m, 3H), 7.32-7.26 (m, 2H), 7.24-7.20 (m, 1H); ¹³C NMR (150 MHz, CDCl₃) δ 160.3 (d, J_C-F = 249.6 Hz, C), 141.5 (C), 141.3 (C), 131.3 (d, J_C-F = 4.1 Hz, CH), 130.2 (d, J_C-F = 8.1 Hz, C), 127.1 (CH), 124.6 (d, J_C-F = 3.3 Hz, C), 122.0 (C), 121.7 (d, J_C-F = 6.2 Hz, C), 121.5 (CH), 121.2 (d, J_C-F = 14.3 Hz, C), 116.4 (d, J_C-F = 22.0 Hz, C), 110.1 (CH); 3418, 3054, 2926, 2870, 1594 cm⁻¹; LRMS (ESI) 213 (100, [M+H]⁺); HRMS (ESI) calcd for C₁₃H₁₀FN₂ [M+H]⁺ 213.0823; observed 213.0822.
3-(o-Tolyl)-1H-indazole 4k

Compound prepared according to method C except reaction temperature was 100 ºC. Purification by column chromatography (10%-50% EtOAc/Petrol) afforded 3-(o-tolyl)-1H-indazole as a white solid (44.3 mg, 0.213 mmol, 85%). m.p. 89-92 ºC; ¹H NMR (600 MHz, CDCl₃) δ 10.35 (br s, NH, 1H), 7.67 (d, J = 8.1 Hz, 1H), 7.54 (d, J = 7.4 Hz, 1H), 7.47 (d, J = 8.4, Hz, 1H), 7.41 (t, J = 7.6 Hz, 1H), 7.38-7.35 (m, 2H), 7.32 (t, J = 7.1 Hz, 1H), 7.19 (t, J = 7.4 Hz, 1H); ¹³C NMR (150 MHz, CDCl₃) δ 146.6 (C), 141.0 (C), 137.5 (C), 133.2 (CH), 130.9 (CH), 130.6 (CH), 128.4 (CH), 126.9 (CH), 125.8 (CH), 122.6 (C), 121.4 (C), 121.2 (CH), 110.0 (CH); IR (solid) 3420, 3103, 2949, 1616 cm⁻¹; LRMS (ESI) 209 (100, [M+H]⁺); HRMS (ESI) calcd for C₁₄H₁₃N₂ [M+H]⁺ 209.1073; observed 209.1074.
3-(2-Methoxyphenyl)-1H-indazole 4l

Compound prepared according to method C except reaction temperature was at 100 °C. Purification by column chromatography (10%-50% EtOAc/Petrol) afforded 3-(2-methoxyphenyl)-1H-indazole as a white solid (44.3 mg, 0.198 mmol, 79%). m.p. 78-80 °C; \(^1\)H NMR (600 MHz, CDCl\(_3\)) \(\delta\) 7.78 (d, \(J = 8.2\) Hz, 1H), 7.69 (dd, \(J = 8.2, 1.7\) Hz, 1H), 7.45-7.42 (m, 2H), 7.39-7.36 (m, 1H), 7.18-7.15 (m, 1H), 7.13-7.06 (m, 2H); \(^13\)C NMR (150 MHz, CDCl\(_3\)) \(\delta\) 157.4 (C), 143.5 (C), 131.5 (C), 129.9 (CH), 126.7 (CH), 122.4 (CH), 122.2 (C), 121.0 (CH), 120.9 (CH), 111.5 (CH), 110.4 (CH); IR (solid) 3454, 3163, 2940, 1614 cm\(^{-1}\); LRMS (ESI) 225 (100, [M+H]\(^+\)); HRMS (ESI) calcd for C\(_{14}\)H\(_{13}\)N\(_2\)O [M+H]\(^+\) 225.1022; observed 225.1022.
Formation of carbamate-protected 1H-indazole

Isopropyl 3-(4-fluorophenyl)-1H-indazole-1-carboxylate 5

To a solution of diisopropyl 1-(2-(4-fluorobenzoyl)phenyl)hydrazine-1,2-dicarboxylate 3a (163 mg, 0.400 mmol) in EtOAc (2.4 mL) was added HCl (3 M, 0.5 mL). The reaction mixture was refluxed for 16 h. The resulting solution was allowed to cool to room temperature before distilled H2O (15 mL) was added. The organic layer was then extracted with EtOAc (3 × 15 mL), dried (MgSO4), filtered and the solvent removed in vacuo. Purification of the crude residue by column chromatography (10%-40% EtOAc/Petrol) afforded isopropyl 3-(4-fluorophenyl)-1H-indazole-1-carboxylate as a clear oil (74.2 mg, 0.260 mmol, 65%). 1H NMR (600 MHz, CDCl3) δ 8.27 (d, J = 8.4 Hz, 1H), 7.99-7.97 (m, 2H), 7.93 (d, J = 8.1 Hz, 1H), 7.59 (ddd, J = 8.3, 7.1, 1.0 Hz, 1H), 7.41-7.38 (m, 1H), 7.41-7.21 (m, 2H), 5.40 (septet, J = 6.3 Hz, 1H), 1.54 (d, J = 6.3 Hz, 6H); 13C NMR (150 MHz, CDCl3) δ 163.6 (d, JCF = 249.2 Hz, C), 150.6 (C), 149.5 (C), 141.3 (C), 130.4 (d, JCF = 8.4 Hz, CH), 129.2 (CH), 128.1 (d, JCF = 3.3 Hz, C), 124.3 (CH), 124.3 (C), 121.3 (CH), 116.1 (d, JCF = 21.8 Hz, C) 115.1 (CH), 72.7 (CH), 22.1 (CH3); IR (thin film) 3077, 2983, 2937, 1754, 1731, 1608, 1529 cm⁻¹; LRMS (ESI) 597 (60, [2M+H]+), 299 (100, [M+H]+); HRMS (ESI) calcd for C15H16FN2O2 [M+H]+ 299.1190; observed 299.1188.
Synthesis of $2H$-indazoles

Diisopropyl 1-(2-(4-fluorobenzoyl)phenyl)-2-methylhydrazine-1,2-dicarboxylate 6

![Chemical structure](image)

To a solution of diisopropyl 1-(2-(4-fluorobenzoyl)phenyl)hydrazine-1,2-dicarboxylate 3a (201 mg, 0.500 mmol, 1 eq.) in DMF (20 mL) were added caesium carbonate (179 mg, 0.55 mmol, 1.1 eq.) and iodomethane (34.0 µL, 0.550 mmol, 1.1 eq.). The heterogeneous mixture was stirred at 21 °C for 24 h. After this time, DMF was removed in vacuo with toluene co-evaporation (3 × 50 mL as an azeotrope). The crude reaction mixture was then dissolved in ethyl acetate (50 mL), and then washed with H$_2$O (3 × 15 mL) and sat. aq. LiCl solution (3 × 15 mL). The organic layer was dried (MgSO$_4$), filtered and concentrated in vacuo. Purification by column chromatography (10%-30% EtOAc/Petrol) afforded diisopropyl 1-(2-(4-fluorobenzoyl)phenyl)-2-methylhydrazine-1,2-dicarboxylate as a clear oil (192 mg, 0.460 mmol, 92%). $^1$H NMR (600 MHz, CDCl$_3$) δ 7.98-7.72 (m, 2H), 7.72-7.35 (m, 2H), 7.34-7.21 (m, 2H), 7.18-7.06 (m, 2H), 5.09-4.98 (m, 1H), 4.86-4.68 (m, 2H), 3.21 (s, 3H), 1.34-1.23 (m, 6H), 1.19-0.63 (m, 6H); $^{13}$C NMR (150 MHz, CDCl$_3$) δ 194.1 (C), 193.6 (C), 165.7 (d, $J_{C\text{-}F} = 253.2$ Hz, C), 157.1 (C), 156.4 (C), 153.9 (C), 139.1 (C), 138.7 (C), 134.8 (C), 134.5 (C), 129.1 (CH), 128.7 (C), 128.5 (CH), 125.9 (CH), 125.8 (CH), 125.0 (CH), 115.5 (d, $J_{C\text{-}F} = 21.8$ Hz, CH), 72.4 (CH), 71.5 (CH), 70.9 (CH), 70.4 (CH), 36.6 (CH$_3$), 35.5 (CH$_3$), 22.4 (CH$_3$), 22.3 (CH$_3$) 22.3 (CH$_3$), 22.3 (CH$_3$), 22.1 (CH$_3$); IR (thin film) 3008, 2957, 1712, 1660, 1597 cm$^{-1}$; LRMS (ESI) 439 (40, [M+Na]$^+$), 417 (100, [M+H]$^+$); HRMS (ESI) calcd for C$_{22}$H$_{26}$FN$_2$O$_5$ [M+H]$^+$ 417.1820; observed 417.1817.
3-(4-Fluorophenyl)-2-methyl-2H-indazole 7a

A solution of diisopropyl 1-(2-(4-fluorobenzoyl)phenyl)-2-methylhydrazine-1,2-dicarboxylate 6 (104 mg, 250 µmol) in concentrated HCl (35%, 5 mL) was refluxed for 24 h and then poured over sat. aq. NaHCO₃ (20 mL). The resulting mixture was then extracted with EtOAc (3 × 15 mL). The combined extracts were dried (MgSO₄), filtered and the solvent evaporated in vacuo. Purification by column chromatography (10%-50% EtOAc/Petrol) afforded 3-(4-fluorophenyl)-2-methyl-2H-indazole as a pale yellow oil (94.7 mg, 228 µmol, 91%). ¹H NMR (600 MHz, CDCl₃) δ 7.71 (td, J = 8.7, 0.9 Hz, 1H), 7.55-7.49 (m, 3H), 7.31 (ddd, J = 8.7, 6.6, 1.1 Hz, 1H), 7.29-7.24 (m, 2H), 7.09 (ddd, J = 8.4, 6.6, 0.8 Hz, 1H), 4.16 (s, 3H); ¹³C NMR (150 MHz, CDCl₃) δ 163.9 (d, J_C-F = 249.4 Hz, C), 148.1 (C), 135.1 (C), 131.6 (d, J_C-F = 8.0 Hz, CH), 126.5 (CH), 125.9 (d, J_C-F = 3.3 Hz, C) 122.1 (CH), 121.4 (CH), 120.0 (CH), 117.2 (CH), 116.4 (d, J_C-F = 21.8 Hz, CH), 38.6 (CH₃); IR (thin film) 3087, 2935, 2902, 2858, 1600 cm⁻¹; LRMS (ESI) 227 (100, [M+H]⁺); HRMS (ESI) calcd for C₁₄H₁₂FN₂ [M+H]⁺ 227.0979; observed 227.0980.
Isopropyl 2-(2-(4-fluorobenzoyl)phenyl)-1-methylhydrazine-1-carboxylate 8

A solution of diisopropyl 1-(2-(4-fluorobenzoyl)phenyl)-2-methylhydrazine-1,2-dicarboxylate 6 (104 mg, 250 µmol) in AcOH (5 mL) was refluxed for 24 h and then poured over sat. aq. NaHCO₃ (20 mL). The resulting mixture was extracted with EtOAc (3 × 15 mL). The combined extracts were dried (MgSO₄), filtered and the solvent evaporated in vacuo. Purification by column chromatography (10%-30% EtOAc/Petrol) afforded isopropyl 2-(2-(4-fluorobenzoyl)phenyl)-1-methylhydrazine-1-carboxylate as a lime-green oil (57.8 mg, 175 µmol, 70%). ¹H NMR (600 MHz, CDCl₃) δ 9.43 (br s, NH, 1H), 7.71-7.66 (m, 2H), 7.49 (dd, J = 7.9, 1.5 Hz, 1H), 7.46-7.41 (m, 1H), 7.17-7.12 (m, 2H), 6.88 (d, J = 8.4 Hz, 1H), 6.78-6.74 (m, 1H), 4.92-4.90 (m, 1H), 3.27 (s, 3H), 1.28-1.05 (m, 6H); ¹³C NMR (150 MHz, CDCl₃) δ 197.5 (C), 164.9 (d, J_C-F = 252.9 Hz, C), 156.6 (C), 150.9 (C), 135.9 (d, J_C-F = 3.2 Hz, C), 134.9 (CH), 134.5 (CH), 132.0 (d, J_C-F = 8.9 Hz, CH), 118.9 (C), 117.5 (CH), 115.4 (d, J_C-F = 21.6 Hz, CH), 112.3 (CH), 70.0 (CH), 37.7 (CH₃), 22.2 (CH₃); IR (thin film) 3401, 2989, 2946, 1720, 1651, 1580 cm⁻¹; LRMS (ESI) 331 (100, [M+H]⁺); HRMS (ESI) calcd for C₁₈H₂₀FN₂O₃ [M+H]⁺ 331.1452; observed 331.1457.
2-(3-(4-Fluorophenyl)-2H-indazol-2-yl)ethan-1-ol 7b

To a solution of diisopropyl 1-(2-(4-fluorobenzoyl)phenyl)hydrazine-1,2-dicarboxylate 3a (201 mg, 0.500 mmol, 1 eq.) in DMF (20 mL) were added caesium carbonate (179 mg, 0.550 mmol, 1.1 eq.) and 2-bromoethanol (39.0 µL, 0.550 mmol, 1.1 eq.). The heterogeneous mixture was stirred at 21 °C for 24 h. After this time, DMF was removed in vacuo with toluene co-evaporation (3 × 50 mL as an azeotrope). The crude reaction mixture was then dissolved in ethyl acetate (50 mL), and then washed with distilled H2O (3 × 15 mL) and sat. aq. LiCl solution (3 × 15 mL). The organic layer was dried (MgSO4), filtered and concentrated in vacuo. To the resultant crude residue was then added concentrated HCl (35%, 5 mL). The reaction mixture was refluxed for 24 h and then poured over sat. aq. NaHCO3 (20 mL) and the resulting mixture was extracted with EtOAc (3 × 15 mL). The combined extracts were dried (MgSO4), filtered and the solvent evaporated in vacuo. Purification by column chromatography (10%-70% EtOAc/Petrol) afforded 2-(3-(4-Fluorophenyl)-2H-indazol-2-yl)ethan-1-ol (101 mg, 395 µmol, 79%) as a pale yellow oil. \(^1\)H NMR (600 MHz, CDCl3) δ 7.71 (d, J = 8.8 Hz, 1H), 7.56-7.51 (m, 3H), 7.35 (ddd, J = 8.7, 6.6, 1.0 Hz, 1H), 7.29-7.24 (m, 2H), 7.11 (ddd, J = 8.4, 6.6, 0.7 Hz, 1H) 4.49 (dd, J = 5.3, 4.2 Hz, 2H), 4.14-4.11 (m, 2H); \(^13\)C NMR (150 MHz, CDCl3) δ 163.2 (d, \(J_{\text{C-F}} = 250.1\) Hz, C), 148.3 (C), 135.9 (C), 132.0 (d, \(J_{\text{C-F}} = 8.3\) Hz, C), 127.0 (CH), 125.5 (d, \(J_{\text{C-F}} = 3.5\) Hz, C), 122.3 (CH), 121.2 (C), 120.2 (CH), 117.2 (C), 116.5 (d, \(J_{\text{C-F}} = 21.8\) Hz, CH), 62.0 (CH2), 52.1 (CH2); IR (thin film) 3201, 2921, 2905, 2834, 1641, 1569 cm\(^{-1}\). LRMS (ESI) 257 (100, [M+H]+).
Mechanistic Study

Diisopropyl 1-(4-fluorobenzoyl)-2-methylhydrazine-1,2-dicarboxylate 9

To a solution of diisopropyl 1-(4-fluorobenzoyl)hydrazine-1,2-dicarboxylate 1a (163 mg, 0.500 mmol) and TBAT (594 mg, 0.550 mmol) in toluene (6 mL) was added iodomethane (31.0 µL, 0.500 mmol) and the reaction mixture stirred at 60 °C for 16 h. After this time, to the crude reaction mixture was added distilled H₂O (15 mL). The organic layer was then extracted with EtOAc (3 × 15 mL), dried (MgSO₄), filtered and the solvent removed in vacuo. Purification by column chromatography (10%-40% EtOAc/Petrol) afforded diisopropyl 1-(4-fluorobenzoyl)-2-methylhydrazine-1,2-dicarboxylate as a clear oil (153 mg, 0.450 mmol, 90%). ¹H NMR (600 MHz, CDCl₃) δ 7.71-7.60 (m, 2H), 7.10-7.06 (m, 2H), 4.96-4.89 (m, 2H), 3.25-3.21 (m, 3H), 1.30-1.09 (m, 12H); ¹³C NMR (150 MHz, CDCl₃) δ 169.7 (C), 169.0 (C), 165.0 (d, J_C,F = 253.2 Hz, C), 155.4 (C), 155.0 (C), 152.4 (C), 152.3 (C), 131.7 (d, J_C,F = 3.3 Hz, CH), 131.4 (d, J_C,F = 3.2 Hz, CH), 130.7 (d, J_C,F = 9.5 Hz, CH), 130.5 (d, J_C,F = 8.9 Hz, CH), 115.5 (d, J_C,F = 22.2 Hz, CH), 115.4 (d, J_C,F = 22.2 Hz, CH), 72.5 (CH), 72.4 (CH), 71.0 (CH), 71.0 (CH), 70.6 (CH), 70.6 (CH), 37.5 (CH), 36.7 (CH), 22.2 (CH₃), 22.2 (CH₃), 22.1 (CH₃), 21.6 (CH₃); IR (thin film) 2983, 2937, 1744, 1599 cm⁻¹; LRMS (ESI) 341 (100, [M+H]⁺); HRMS (ESI) calcd for C₁₆H₂₂FN₃O₅ [M+H]⁺ 341.1507; observed 341.1503.
By-product formed upon aryl anion attack on carbamate-carbonyl

Methyl 2-(4-fluorobenzoyl)-1-(2-(methoxycarbonyl)phenyl)hydrazine-1-carboxylate 10

Compound observed upon utilization of method B and dimethyl 1-(4-fluorobenzoyl)hydrazine-1,2-dicarboxylate 1ab as acyl hydrazide starting material. Purification by column chromatography (10%-30% EtOAc/Petrol) afforded methyl 2-(4-fluorobenzoyl)-1-(2-(methoxycarbonyl)phenyl)hydrazine-1-carboxylate as a brown-orange oil (85.0 mg, 0.250 mmol, 49%). \(^1\)H NMR (600 MHz, CDCl\(_3\)) \(\delta\) 9.25-8.97 (m, NH, 1H), 8.03 (t, \(J = 6.2\) Hz, 1H), 7.90-7.81 (m, 3H), 7.67-7.61 (m, 1H), 7.45 (t, \(J = 6.6\) Hz, 1H), 7.12 (q, \(J = 8.1\) Hz, 2H), 3.97-3.93 (m, 3H), 3.83-3.69 (m, 3H); \(^1\)C NMR (150 MHz, CDCl\(_3\)) \(\delta\) 166.9 (C), 166.5 (C), 165.4 (C), 165.3 (d, \(J_{C-F} = 254.5\) Hz, C), 164.6 (C), 156.0 (C), 155.4 (C), 141.1 (C), 140.8 (C), 134.2 (CH), 134.0 (CH), 132.0 (CH), 131.7 (CH), 131.5 (CH), 131.3 (CH), 130.0 (d, \(J_{C-F} = 9.0\) Hz, CH), 129.9 (d, \(J_{C-F} = 9.0\) Hz, CH), 128.8 (CH), 128.5 (C), 126.9 (C), 126.7 (C), 116.0 (d, \(J_{C-F} = 22.0\) Hz), 115.9 (d, \(J_{C-F} = 22.0\) Hz), 54.0 (CH\(_3\)), 54.0 (CH\(_3\)), 52.8 (CH\(_3\)), 52.7 (CH\(_3\)); IR (thin film) 3295, 2957, 1718, 1602 cm\(^{-1}\); LRMS (ESI) 347 (100, [M+H]\(^+\)); HRMS (ESI) calcd for C\(_{17}\)H\(_{16}\)F\(_2\)O\(_5\) [M+H]\(^+\) 347.1042; observed 347.1038.
References


