Facile One-Pot Access to α-Diazo-β-ketosulfones from Sulfonyle Chlorides and α-Haloketones

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Abstract A convenient one-pot approach to the preparation of α-diazo-β-ketosulfones from sulfonyl chlorides is described. It involves the conversion of the sulfonyl chloride to sodium sulfinate, alkylolation of the latter with α-haloketones followed by diazo transfer using the ‘sulfonyl-azole-free’ (‘SAFE’) protocol in aqueous medium. The simple and expedient method relies on readily available starting materials and provides facile access to a wide variety of valuable diazo reagents for organic synthesis.

Key words aliphatic diazo compounds, diazo ketosulfones, diazo transfer, α-haloketones, Rh(II)-catalyzed cyclization, pyrazole synthesis

To date, the chemistry of α-diazo-carbonyl compounds is one of the most intensively developing and widely represented in the literature fields of chemical science. In recent years, there has been an exponential increase in the number of scientific papers devoted to this topic. One of the aspects that determine the high interest in the chemistry of diazo compounds is their unique and remarkably diverse reactivity, including transformations both with the loss of a nitrogen molecule (during their thermal, catalytic or photolytic decomposition), and with the incorporation of nitrogen atoms into the molecule of the reaction product.1

α-Diazo-β-ketosulfones (and diazo sulfones in general) are a very promising class of aliphatic diazo compounds for organic synthesis. Recently, reports on various transformations of these diazo substrates (cyclopropanation,2 insertion into C–H2 and heteroatom–H3 bonds, Wolff rearrangement,2 and others6) are increasingly appearing in the literature. Diazo sulfones manifested themselves as convenient precursors for the construction of various heterocyclic cores such as pyrazoles,7 azines,8 and other heterocycles.9 Of particular interest are enantioselective transformations of diazo sulfones10 and their use in key steps of the synthesis of complex molecules; total synthesis of exhibiting anticancer activity (+)-digitoxigenin11 and synthetic approach to daphniglaucin-type daphniphyllum alkaloids12 being notable examples. In connection with the high demand for this class of diazo compounds, development of a simple and convenient method for their preparation from available starting materials would be highly desirable. The most common method for producing diazo compounds containing electron-withdrawing groups is the diazo transfer reaction. Recently, we reported a fundamentally new modification of this general approach, which allows carrying out the reaction in aqueous medium and avoiding preparation, isolation, and handling of the sulfonyl azide diazo transfer reagent (an approach we dubbed the ‘Sulfonyl-Azide-Free’ protocol).13 The present work is devoted to the extension of this method to the synthesis of diazo ketosulfones derived from sulfonyl chlorides and α-haloketones via a sequence of one-pot transformations (RSO2Cl → RSO2N → RSO2CH2COR′ → RSO2CNHCOR′).

The conversion of a sulfonyl chloride to a sulfinic acid salt followed by its in situ alklylation is often carried out in water or in aqueous solvent mixtures.14 We reasoned that this aspect would make this two-step sequence a convenient preamble for the final synthetic step (diazo transfer). Since the earlier described ‘SAFE’ diazo transfer is also carried out in aqueous medium, the isolation of the final products (diazo ketosulfones) could, in principle, be reduced to filtration or simple extraction with an organic solvent.

Table 1 presents the results of the preparation of diazo ketosulfones by a three-step one-pot process. Commercially available or synthetically accessible sulfonyl chlorides and α-haloketones, both aromatic and aliphatic, were used as starting materials.
Formation of the sulfinate salt from a sulfonyl chloride and its subsequent alkylation with a chloromethyl ketone occurred under mild conditions and proceeded in high yields. To facilitate the initial sulfonyl chloride reduction step, the sulfonyl chloride was introduced into the reaction mixture as a solution in acetonitrile (which is rather critical for highly hydrophobic sulfonyl chlorides). Generally, in order to achieve maximum conversion, each step was carried out over 14–18 hours. Upon addition of the aqueous solution we termed as the ‘SAFE’ cocktail\(^1\) (i.e., a solution of 3-carboxybenzenesulfonyl chloride, sodium azide, and potassium carbonate in water) to the reaction mixture, the diazo transfer was complete within 6 hours. The solid reaction products were isolated by filtration and, if necessary, crystallized from an appropriate solvent. In some cases, the product was extracted and purified by flash chromatography on silica gel. The yields of the diazo ketosulfones thus obtained (over three steps starting from the sulfonyl chloride) range from moderate to high. In one case (Table 1, entry 2), it was possible to compare the yield over three steps (80%) with the yield of the final, SAFE diazotransfer step (86%) previously reported for the same active-methylene compound.\(^1\) In the case of sterically hindered mesitylene sulfonyl chloride (entry 12), the content of the desired diazo compound in the resulting reaction mixture was rather low (according to \(^1\)H NMR analysis, thus we failed to isolate the product in an appreciable amount. Sterically hindered tert-butyl ketone (entry 19) also gave a lower yield of the respective diazo compound 1s. A total of 26 diazo ketosulfones were synthesized, 15 of which have not been previously described. To illustrate the suitability of the diazo compounds obtained in this work for further transformations, some Rh(II)-catalyzed intramolecular cyclizations based on Csp\(^3\)–H insertion were carried out using diazo compounds 1i and 1z as starting materials (Scheme 1). As the result, cyclic acylsulfones were obtained under mild conditions in moderate (2) and high (3) yield.

\(^{4}\)Isolated yields.
\(^{5}\)Purified by flash column chromatography.
\(^{6}\)Double amount of K\(_2\)CO\(_3\) was used in diazo transfer step.
\(^{7}\)Diazo transfer step was run for 20 hours.

### Table 1 \(\alpha\)-Diazomethanesulfones 1 Prepared

<table>
<thead>
<tr>
<th>Entry</th>
<th>(R^1)</th>
<th>(R^2)</th>
<th>Product</th>
<th>Yield (%)(^{a})</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Ph</td>
<td>Me</td>
<td>1a</td>
<td>84(^{a})</td>
</tr>
<tr>
<td>2</td>
<td>4-MeC(_6)H(_4)</td>
<td>Me</td>
<td>1b</td>
<td>80(^{a}) (63)(^{a})</td>
</tr>
<tr>
<td>3</td>
<td>4-FC(_6)H(_4)</td>
<td>Me</td>
<td>1c</td>
<td>73(^{a}) (59)(^{a})</td>
</tr>
<tr>
<td>4</td>
<td>4-CIC(_6)H(_4)</td>
<td>Me</td>
<td>1d</td>
<td>81(^{a})</td>
</tr>
<tr>
<td>5</td>
<td>4-MeOC(_6)H(_4)</td>
<td>Me</td>
<td>1e</td>
<td>62(^{a})</td>
</tr>
<tr>
<td>6</td>
<td>4-O(_2)NC(_6)H(_4)</td>
<td>Me</td>
<td>1f</td>
<td>39(^{a})</td>
</tr>
<tr>
<td>7</td>
<td>4-(AcNH)C(_6)H(_4)</td>
<td>Me</td>
<td>1g</td>
<td>64(^{a})</td>
</tr>
<tr>
<td>8</td>
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<td>Me</td>
<td>1h</td>
<td>65(^{a})</td>
</tr>
<tr>
<td>9</td>
<td>2,5-(MeO)(_2)C(_6)H(_3)</td>
<td>Me</td>
<td>1i</td>
<td>68(^{a})</td>
</tr>
<tr>
<td>10</td>
<td>2,4,6-Me(_3)C(_6)H(_2)</td>
<td>Me</td>
<td>1j</td>
<td>67(^{a})</td>
</tr>
<tr>
<td>11</td>
<td>2-naphthyl</td>
<td>Me</td>
<td>1k</td>
<td>74(^{a}) (60)(^{a})</td>
</tr>
<tr>
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<td>Me</td>
<td>1l</td>
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<td>Me</td>
<td>Me</td>
<td>1m</td>
<td>72(^{a}) (51)(^{a})</td>
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<td>i-Pr</td>
<td>Me</td>
<td>1n</td>
<td>52(^{a})</td>
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<td>c-hexyl</td>
<td>Me</td>
<td>1o</td>
<td>82(^{a})</td>
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<tr>
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<td>Me</td>
<td>1r</td>
<td>71(^{a})</td>
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<tr>
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<td>4-MeC(_6)H(_4)</td>
<td>t-Bu</td>
<td>1s</td>
<td>47(^{a})</td>
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<tr>
<td>20</td>
<td>Me</td>
<td>Ph</td>
<td>1t</td>
<td>57(^{a})</td>
</tr>
<tr>
<td>21</td>
<td>c-hexyl</td>
<td>Me</td>
<td>1u</td>
<td>54(^{a})</td>
</tr>
<tr>
<td>22</td>
<td>3-Cl-4-MeOC(_6)H(_3)</td>
<td>4-CIC(_6)H(_4)</td>
<td>1v</td>
<td>81(^{a}) (62)(^{a})</td>
</tr>
<tr>
<td>23</td>
<td>4-MeC(_6)H(_4)</td>
<td>4-FC(_6)H(_4)</td>
<td>1w</td>
<td>61(^{a})</td>
</tr>
<tr>
<td>24</td>
<td>4-MeC(_6)H(_4)</td>
<td>4-O(_2)NC(_6)H(_4)</td>
<td>1x</td>
<td>78(^{a})</td>
</tr>
<tr>
<td>25</td>
<td>4-MeC(_6)H(_4)</td>
<td>3,4-(MeO)(_2)C(_6)H(_3)</td>
<td>1y</td>
<td>76(^{a})</td>
</tr>
<tr>
<td>26</td>
<td>Ph(CH(_3))(_2)</td>
<td>4-O(_2)NC(_6)H(_4)</td>
<td>1z</td>
<td>59(^{a})</td>
</tr>
<tr>
<td>27</td>
<td>Et</td>
<td>Me</td>
<td>1aa</td>
<td>46(^{a})</td>
</tr>
</tbody>
</table>

\(^{a}\)Isolated yields.

Also, a two-step pyrazole synthesis involving three acetyl diazocompounds 1b,j,q was performed (Scheme 2). In the first step, the starting diazo sulfones were de-acylated on treatment with alumina to give the terminal diazo sulfones which, without isolation, were introduced into a [3+2] cycloaddition step with acetylenic esters.
In conclusion, we have described a one-pot, facile, and flexible approach to α-diazo-β-ketosulfones from readily available sulfonyl chlorides and α-halo ketones. The method is convenient and practically simple while displaying a wide scope with respect to various substituents and deliver the target diazo compounds in good to high yields. The latter were shown to be directly employable in downstream heterocyclic systems.

All commercial reagents and solvents were used without further purification, unless otherwise noted. NMR spectroscopic data were recorded with a 400 MHz spectrometer (400.13 MHz for 1H and 100.61 MHz for 13C) in CDCl3, and in DMSO-d6, and were referenced to residual solvent proton signals (δH = 7.26 and δC = 25.0, respectively) and solvent carbon signals (δC = 77.0 and δC = 39.5, respectively). All chemical shifts are reported in parts per million (ppm). Standard abbreviations were used in the description of resonances. Coupling constants (J) are quoted to the nearest 0.1 Hz. Mass spectra were recorded with a HRMS-ESI-QTOF spectrometer (electrospray ionization mode). Melt points were determined with short-wavelength UV light. Flash column chromatography was performed using silica gel Merck grade 60 (0.040–0.063 mm) 230–400 mesh (isocratic or gradient elution as indicated).

**Caution!** The aqueous waste obtained in the SAFE diazotransfer reaction should be disposed of according to the general guidelines for aqueous solutions containing inorganic azides.15

**α-Diazo-β-ketosulfones 1; General Procedure 1 (GP1)**

To a stirred solution of Na2SO3 (1.51 g, 12 mmol) and NaHCO3 (2.02 g, 2.4 mmol) in H2O (20 mL) was added a solution of the corresponding sulfonyl chloride (10 mmol) in MeCN (5–10 mL) and the mixture was stirred at r.t. for 12–16 h. To the resulting solution were added the corresponding α-halo ketone (11 mmol) and KI (83 mg, 0.5 mmol) and the mixture was stirred for 16–20 h. ‘SAFE’ cocktail [prepared by the addition of 3-(chlorosulfonyl)benzoic acid (2.76 g, 12.5 mmol) to a solution of NaN3 (1.0 g, 15 mmol) and K2CO3 (2.1 g, 15.0 mmol) in H2O (20 mL) and stirring for 10 min] was added to the reaction mixture and stirring was continued for 6 h. If a solid precipitate was formed, the mixture was cooled to 5 °C, the product was filtered, washed with H2O (30 mL) and cold H2O/EtOH mixture (1:1, 25 mL), and dried in air.

Oil precipitates were extracted with DCM (3 × 25 mL), the combined organic phases were dried (CaCl2), and evaporated to dryness. Additional purification was used, if needed, by flash column chromatography on silica gel or by recrystallization (as indicated).

**1-Diazo-1-(phenylsulfonyl)propan-2-one (1a)**

The title compound was synthesized according to GP1 from commercially available benzenesulfonyl chloride and chloroacetone and purified by flash column chromatography on silica gel (n-hexane/EtOAc 4:1); yield: 1.88 g (84%); yellow solid; mp 70.2–72.6 °C.

| H NMR (400 MHz, CDCl3); δ = 8.07–7.92 (m, 2 H), 7.77–7.67 (m, 1 H), 7.62 (t, J = 7.7 Hz, 1 H), 2.32 (s, 3 H). |
| 13C NMR (101 MHz, CDCl3); δ = 185.7 (C=O), 142.1, 134.2, 129.6, 127.2, 85.9 (C=N), 27.0. |

**1-Diazo-1-tosylopropan-2-one (1b)**

The title compound was synthesized according to GP1 from commercially available p-TsCl and chloroacetone; yield: 1.91 g (80%). The product was additionally purified by crystallization from MeOH; yield: 1.50 g (63%); light yellow solid; mp 110.3–111.7 °C (dec.).

| H NMR (400 MHz, CDCl3); δ = 7.87 (d, J = 8.4 Hz, 2 H), 7.40 (d, J = 8.1 Hz, 2 H), 2.49 (s, 3 H), 2.31 (s, 3 H). |
| 13C NMR (101 MHz, CDCl3); δ = 185.9 (C=O), 145.5, 139.2, 130.1, 127.3, 86.1 (C=N), 27.0, 21.7. |

**1-Diazo-1-[(4-fluorophenyl)sulfonyl]propan-2-one (1c)**

The title compound was synthesized according to GP1 from commercially available 4-fluorobenzenesulfonyl chloride and chloroacetone; yield: 1.27 g (73%). The product was additionally purified by crystallization from MeOH; yield: 1.43 g (59%); light yellow solid; mp 111.7 °C (dec.).

| H NMR (400 MHz, CDCl3); δ = 8.03 (dd, J = 8.9, 4.9 Hz, 2 H), 7.28 (d, J = 8.5 Hz, 2 H), 2.31 (s, 3 H). |
| 13C NMR (101 MHz, CDCl3); δ = 185.3 (C=O), 166.0 (d, J = 257.9 Hz), 138.0 (d, J = 3.1 Hz), 130.4 (d, J = 9.7 Hz), 116.8 (d, J = 22.8 Hz), 85.6 (C=N), 27.0. |

**1-Diazo-1-[(4-chlorophenyl)sulfonyl]propan-2-one (1d)**

The title compound was synthesized according to GP1 from commercially available 4-chlorobenzenesulfonyl chloride and chloroacetone; yield: 2.09 g (81%); yellow liquid solid; mp 113.2–115.0 °C.

| H NMR (400 MHz, CDCl3); δ = 7.95 (d, J = 8.8 Hz, 2 H), 7.58 (d, J = 8.8 Hz, 2 H), 2.31 (s, 3 H). |
| 13C NMR (101 MHz, CDCl3); δ = 185.2 (C=O), 141.0, 140.3, 129.8, 128.9, 85.5 (C=N), 27.0. |

**HRMS (ESI +ve): m/z calcd for C9H7FN2O3SNa [M + Na]+: 265.0054; found: 265.0052.**

**1-Diazo-1-[(4-methoxyphenyl)sulfonyl]propan-2-one (1e)**

The title compound was synthesized according to GP1 from commercially available 4-methoxybenzenesulfonyl chloride and chloroacetone; yield: 1.8 g (61%); yellow solid; mp 78.8–80.5 °C.

| H NMR (400 MHz, CDCl3); δ = 7.92 (d, J = 9.0 Hz, 2 H), 7.04 (d, J = 9.0 Hz, 2 H), 3.91 (s, 3 H), 2.29 (s, 3 H). |
The title compound was synthesized according to GP1 from commercially available 2,5-dimethoxybenzenesulfonyl chloride and chloroacetone and purified by flash column chromatography on silica gel (4:1); yield: 1.57 g (65%); tan solid; mp 80.8–82.4 °C.

HRMS (ESI +ve): m/z calcd for C_{11}H_{12}N_{2}O_{5}SNa [M + Na]^+: 292.0011; found: 292.0011.

1-Diazo-1-[(3,4-dimethoxyphenyl)sulfonyl]propan-2-one (1j)

The title compound was synthesized according to GP1 from commercially available 3,4-dimethoxybenzenesulfonyl chloride and chloroacetone and purified by flash column chromatography on silica gel (hexane/EtOAc 4:1 to 2:1); yield: 1.93 g (68%); yellow solid; mp 105.5–107.1 °C (dec.).

1H NMR (400 MHz, CDCl₃): δ = 7.54 (d, J = 1.2 Hz, 1 H), 7.42 (d, J = 8.2 Hz, 1 H); 7.30 (dd, J = 7.0, 1.9 Hz, 1 H), 7.28 (s, 3 H). 13C NMR (101 MHz, CDCl₃): δ = 129.9 (s), 129.5 (d, J = 186.6 Hz), 129.1, 128.9, 128.6, 119.5, 85.8 (C=N₂), 27.0.

HRMS (ESI +ve): m/z calcd for C_{11}H_{12}N_{2}O_{5}SNa [M + Na]^+: 285.0543; found: 285.0538.

1-Diazo-1-[(naphthalen-2-ylsulfonyl)phenyl]acetamide (1g)

The title compound was synthesized according to GP1 from commercially available naphthlene-2-sulfonyl chloride and chloroacetone; yield: 1.64 g (60%); yellow solid; mp 101.1–104.4 °C (dec.).

HRMS (ESI +ve): m/z calcd for C_{16}H_{14}N_{2}O_{5}SNa [M + Na]^+: 291.0006; found: 291.0006.

1-Diazo-1-[2-(fluorophenyl)sulfonyl]propan-2-one (1h)

The title compound was synthesized according to GP1 from commercially available 2-fluorobenzenesulfonyl chloride and chloroacetone and purified by flash column chromatography on silica gel (n-hexane/EtOAc 4:1); yield: 1.57 g (65%); tan solid; mp 80.8–82.4 °C.

1H NMR (400 MHz, CDCl₃): δ = 7.51 (dd, J = 7.9, 6.2 Hz, 1 H), 7.78 (br s, 1 H), 7.74 (d, J = 8.9 Hz, 2 H), 2.30 (s, 3 H), 2.24 (s, 3 H). 13C NMR (101 MHz, CDCl₃): δ = 158.5 (C=O), 168.9 (CONH), 143.4, 136.3, 128.8, 119.5, 85.8 (C=N₂), 27.0, 24.7.

HRMS (ESI +ve): m/z calcd for C_{15}H_{11}NO_{5}SNa [M + Na]^+: 265.0054; found: 265.0057.

1-Diazo-1-[(2-fluorophenyl)sulfonyl]propan-2-one (1i)

The title compound was synthesized according to GP1 from commercially available 2-fluorobenzenesulfonyl chloride and chloroacetone and purified by flash column chromatography on silica gel (hexane/EtOAc 5:1); yield: 2.03 g (74%). The product was additionally purified by crystallization from MeOH; yield: 1.64 g (60%); yellow solid; mp 101.1–102.3 °C (dec.).

HRMS (ESI +ve): m/z calcd for C_{16}H_{14}N_{2}O_{5}SNa [M + Na]^+: 297.0302; found: 297.0302.

1-(Methylsulfonyl)propan-2-one (1m)

The title compound was synthesized according to GP1 from commercially available mesyl chloride and chloroacetone; yield: 1.17 g (72%). The product was additionally purified by crystallization from MeOH; yield: 0.83 g (51%); pale yellow solid; mp 43.2–44.8 °C.

1H NMR (400 MHz, CDCl₃): δ = 3.31 (s, 3 H), 2.41 (s, 3 H). 13C NMR (101 MHz, CDCl₃): δ = 185.3 (C=O), 84.1 (C=N₂), 45.6, 26.9.

1-Diazo-1-[(isopropylsulfonyl)propan-2-one (1n)

The title compound was synthesized according to GP1 from commercially available propane-2-sulfonyl chloride and chloroacetone and purified by flash column chromatography on silica gel (hexane/EtOAc 6:1 to 3:1), yield: 0.99 g (52%); light yellow solid; mp 49.0–52.2 °C.

1H NMR (400 MHz, CDCl₃): δ = 7.96 (d, J = 8.0 Hz, 1 H), 7.92 (dd, J = 8.7, 1.8 Hz, 1 H), 7.74–7.66 (m, 2 H), 2.33 (s, 3 H).

HRMS (ESI +ve): m/z calcd for C_{15}H_{14}N_{2}O_{5}SNa [M + Na]^+: 271.0193; found: 271.0200.

1-(Cyclohexylsulfonyl)-1-diazopropan-2-one (1o)

The title compound was synthesized according to GP1 from commercially available cyclohexanesulfonyl chloride and chloroacetone and purified by flash column chromatography on silica gel (hexane/EtOAc 5:1 to 4:1); yield: 0.83 g (51%); pale yellow solid; mp 43.2–44.8 °C.

HRMS (ESI +ve): m/z calcd for C_{15}H_{14}N_{2}O_{5}SNa [M + Na]^+: 265.0054; found: 265.0057.
The title compound was synthesized according to GP1 from commercially available thiophene-2-sulfonyl chloride and chloroacetone and purified by flash column chromatography on silica gel (DCM); yield: 1.32 g (47%); yellow solid; mp 121.1–121.9 °C (dec.).

HRMS (ESI +ve): m/z calcd for C_{12}H_{17}N_{2}O_{3}SNa [M + Na]^+: 345.0879; found: 345.0881.

2-Diazo-1-(3-chloro-4-methoxyphenyl)sulfonyl)-1-(4-chlorophenyl)-2-diazoethanone (1v)
The title compound was synthesized according to GP1 from commercially available 3-chloro-4-methoxybenzenesulfonyl chloride and α-bromo-p-chloroacetophenone. The isolated product was purified by flash column chromatography on silica gel (n-hexane/EtOAc 8:1 to 3:1); yield: 1.74 g (54%); light yellow solid; mp 64.2–65.6 °C.

1H NMR (400 MHz, CDCl₃): δ = 8.31 (d, J = 8.6 Hz, 2 H), 7.54 (d, J = 8.6 Hz, 2 H), 7.06 (d, J = 8.6 Hz, 2 H), 3.44 (s, 3 H).

13C NMR (101 MHz, CDCl₃): δ = 127.4, 116.1 (d, J = 255.3 Hz), 130.0, 129.3, 129.2, 128.9, 123.4, 111.5, 83.8 (C=N=S), 56.7.

HRMS (ESI +ve): m/z calcd for C_{16}H_{16}Cl_{2}N_{2}O_{2}SNa [M + Na]^+: 406.9631; found: 406.9631.

2-Diazo-1-(4-fluorophenyl)-2-tosylethanone (1w)
The title compound was synthesized according to GP1 from commercially available 3-chloro-4-methoxybenzenesulfonyl chloride and α-bromo-p-chloroacetophenone. The isolated product was purified by flash column chromatography on silica gel (n-hexane/ EtOAc 8:1 to 3:1); yield: 1.32 g (47%); yellow solid; mp 121.1–121.9 °C (dec.).

1H NMR (400 MHz, CDCl₃): δ = 7.74–7.66 (m, 2 H), 7.66–7.60 (m, 1 H), 7.53 (t, J = 7.6 Hz, 2 H), 3.44 (s, 3 H).

13C NMR (101 MHz, CDCl₃): δ = 183.3 (C=O), 135.6, 133.4, 129.1, 127.4, 82.0 (C=N=S), 45.0.

HRMS (ESI +ve): m/z calcd for C_{16}H_{16}Cl_{2}N_{2}O_{2}SNa [M + Na]^+: 345.0879; found: 345.0881.

2-Cyclohexanesulfonyl)-2-diazo-1-(4-methoxyphenylethenone (1u)
The title compound was synthesized according to GP1 from commercially available cyclohexanesulfonfyl chloride and α-chloro-p-methoxyacetophenone. The isolated product was purified by flash column chromatography on silica gel (n-hexane/ EtOAc 8:1 to 3:1); yield: 1.74 g (54%); light yellow solid; mp 64.2–65.6 °C.

1H NMR (400 MHz, CDCl₃): δ = 7.71 (d, J = 8.9 Hz, 1 H), 6.99 (d, J = 8.9 Hz, 1 H), 3.90 (s, 3 H), 3.68 (t, J = 12.2, 3.5 Hz, 1 H), 2.22–2.15 (m, 2 H), 1.99–1.91 (m, 2 H), 1.79–1.72 (m, 1 H), 1.65 (qd, J = 12.4, 3.5 Hz, 2 H), 1.42–1.18 (m, 3 H).

13C NMR (101 MHz, CDCl₃): δ = 182.1 (C=O), 161.7, 129.9, 128.3, 114.3, 77.6 (C=N=S), 64.7, 55.5, 25.13, 25.07, 25.02.

HRMS (ESI +ve): m/z calcd for C_{12}H_{10}N_{2}O_{2}SNa [M + Na]^+: 230.0519; found: 230.0527.

1-Diazo-1-(4-(methoxybenzenesulfonyl))propan-2-one (1r)
The title compound was synthesized according to GP1 from commercially available p-TsCl and chloroacetone and purified by flash column chromatography on silica gel (n-hexane/EtOAc 8:1 to 4:1); yield: 2.39 g (62%); yellow solid; mp 94.7–96.2 °C.

HRMS (ESI +ve): m/z calcd for C_{16}H_{18}N_{2}O_{4}SNa [M + Na]^+: 330.0519; found: 330.0527.

13C NMR (101 MHz, CDCl₃): δ = 128.3, 124.3, 81.8 (C=N₂), 63.3, 26.5, 21.2.

1-Diazo-3,3-dimethyl-1-tert-butyl-2-one (1s)
The title compound was synthesized according to GP1 from commercially available p-TsCl and α-bromopinacolone. In diazo transfer step, the mixture was stirred for 15 h; yield: 3.12 g (81%). The product was additionally purified by crystallization from MeOH; yield: 2.39 g (62%); yellow solid; mp 117.3–118.2 °C (dec.).

1H NMR (400 MHz, CDCl₃): δ = 8.03–7.93 (m, 2 H), 7.54 (d, J = 8.6 Hz, 2 H), 7.45 (d, J = 8.6 Hz, 2 H), 7.06 (d, J = 9.4 Hz, 1 H), 4.01 (s, 3 H).

13C NMR (101 MHz, CDCl₃): δ = 181.5 (C=O), 159.7, 139.6, 134.0, 133.4, 130.0, 129.3, 129.2, 128.9, 123.4, 111.5, 83.8 (C=N=S), 56.7.

HRMS (ESI +ve): m/z calcd for C_{10}H_{12}Cl_{2}N_{2}O_{2}SNa [M + Na]^+: 406.9631; found: 406.9631.

1-Diazo-1-(4-fluorophenyl)ethanone (1t)
The title compound was synthesized according to GP1 from commercially available 3-chloro-4-methoxybenzenesulfonyl chloride and α-bromo-p-chloroacetophenone. The isolated product was purified by flash column chromatography on silica gel (n-hexane/ EtOAc 8:1 to 4:1); yield: 1.94 g (61%); pale yellow solid; mp 92.8–94.0 °C.

1H NMR (400 MHz, CDCl₃): δ = 7.81 (dd, J = 3.8, 1.3 Hz, 1 H), 7.76 (dd, J = 5.0, 1.4 Hz, 1 H), 7.18 (dd, J = 5.0, 3.8 Hz, 1 H), 2.39 (s, 3 H).

13C NMR (101 MHz, CDCl₃): δ = 185.7 (C=O), 143.1, 143.3, 133.9, 127.9, 87.1 (C=N₂), 27.1.

HRMS (ESI +ve): m/z calcd for C_{12}H_{17}N_{2}O_{3}S [M + H]^+: 231.0794; found: 231.0794.
2-Diazo-1-(4-nitrophenyl)-2-tosylethan-1-one (1x)\(^6\)

The title compound was synthesized according to GP1 from commercially available p-TsCl and α-bromo-α-nitroacetophenone; yield: 2.69 g (78%); pale yellow solid; mp 147.1–147.9 °C (dec.).

\(^1\)H NMR (400 MHz, CDCl\(_3\)): δ = 8.30 (d, J = 8.8 Hz, 2 H), 7.85 (d, J = 8.4 Hz, 2 H), 7.72 (d, J = 8.8 Hz, 2 H), 7.37 (d, J = 8.1 Hz, 2 H), 2.48 (s, 3 H).

\(^13\)C NMR (101 MHz, CDCl\(_3\)): δ = 181.5 (C=O), 150.0, 145.9, 140.9, 138.4, 130.0, 128.7, 124.0, 124.0, 85.3 (C=Ns), 217.7.

HRMS (ESI +ve): m/z calcd for C\(_{13}\)H\(_{11}\)N\(_2\)O\(_5\)SNa [M + Na]+: 368.0312; found: 368.0321.

2-Diazo-1-(3,4-dimethoxyphenyl)-2-tosylethan-1-one (1y)

The title compound was synthesized according to GP1 from commercially available p-TsCl and 2-bromo-3,4′-dimethoxyacetophenone and purified by crystallization from MeOH/MeCN (2:1); yield: 2.74 g (78%); yellow solid; mp 133.0–133.9 °C (dec.).

\(^1\)H NMR (400 MHz, CDCl\(_3\)): δ = 7.96 (d, J = 8.4 Hz, 2 H), 7.36 (d, J = 8.0 Hz, 2 H), 7.26 (dd, J = 8.4, 2.1 Hz, 1 H), 7.15 (d, J = 2.1 Hz, 1 H), 6.87 (d, J = 8.4 Hz, 1 H), 3.94 (s, 3 H), 3.88 (s, 3 H), 2.46 (s, 3 H).

\(^13\)C NMR (101 MHz, CDCl\(_3\)): δ = 181.3 (C=O), 153.3, 149.3, 145.3, 138.8, 129.7, 128.5, 128.2, 121.5, 110.6, 110.2 (C=N), 56.1, 56.0, 21.7.


2-Diazo-1-(4-nitrophenyl)-2-[(3-phenylpropyl)sulfonyl]ethanone (1z)

The title compound was synthesized according to GP1 from commercially available 3-phenylpropane-1-sulfonyl chloride and α-bromo-α-nitroacetophenone. The isolated product was purified by flash column chromatography on silica gel (n-hexane/EtOAc 8:1 to 3:1); yield: 2.20 g (59%); tan solid; mp 116.3–117.5 °C (dec.).

\(^1\)H NMR (400 MHz, CDCl\(_3\)): δ = 8.35 (d, J = 8.9 Hz, 2 H), 7.81 (d, J = 8.9 Hz, 2 H), 7.39–7.30 (m, 2 H), 7.28–7.23 (m, 1 H), 7.21–7.18 (m, 2 H), 3.51–3.45 (m, 2 H, 2.82 (t, J = 7.4 Hz, 2 H), 2.27–2.16 (m, 2 H).

\(^13\)C NMR (101 MHz, CDCl\(_3\)): δ = 181.7 (C=O), 150.2, 140.5, 139.7, 128.8, 128.6, 128.4, 127.4, 81.9 (C=Ns), 56.4, 33.8, 24.3.

HRMS (ESI +ve): m/z calcd for C\(_{17}\)H\(_{16}\)NO\(_5\)S [M + H]+: 346.0744; found: 346.0748.

Pyrazoles 4; General Procedure 3 (GP3)

To a solution of diazo ketosulfone 1f or 1z (0.5 mmol) in anhyd DCM (15 mL) was added Al\(_2\)O\(_3\) (10 g) and the suspension was stirred at r.t. in the dark for 12–15 h (controlled by TLC). Al\(_2\)O\(_3\) was filtered off and washed with DCM (2 × 8 mL). The filtrate was evaporated in vacuo at 30 °C to reduce the volume by three quarters. To the resulting yellow solution was added methyl propiolate (267 μL, 3.0 mmol) or dimethyl acetylenedicarboxylate (245 μL, 2.0 mmol) and the mixture was kept in the dark at r.t. for 18–20 h. The discolored reaction mixture was concentrated under reduced pressure, the residual solid was washed with hexane, and dried in vacuo to afford the desired pyrazole.

Methyl 3-(5-Tosyl-1H-pyrazole-5(3)-carboxylate (4a)

The title compound was synthesized according to GP3 from diazoketosulfone 1b and methyl propiolate. The product was additionally purified by flash column chromatography (DCM/acetone 95:5 to 85:15); yield: 165 mg (59%); white solid; mp 167.7–169.8 °C.

\(^1\)H NMR (400 MHz, CDCl\(_3\)): δ = 11.64 (br s, 1 H), 7.95 (d, J = 8.3 Hz, 2 H), 7.35 (d, J = 8.4 Hz, 2 H), 7.32 (s, 1 H), 3.96 (s, 3 H), 2.44 (s, 3 H).

\(^13\)C NMR (101 MHz, CDCl\(_3\)): δ = 158.9, 145.0, 137.2, 130.0, 128.2, 109.7, 52.9, 21.6.*
Diethyl 3-([3,4-Dimethoxyphenyl]sulfonyl)-1H-pyrazole-4,5-dicarboxylate (4b)

The title compound was synthesized according to GP3 from diazo ketosulfone 1j and dimethyl acetylenedicarboxylate; yield: 269 mg (61%); white solid; mp 246.5–247.3 °C (MeOH).


* Signals of 3-C and 5-C carbon atoms of pyrazole ring (and carbonyl atom of 5-CO_2Me for 4a and 4c) do not appear in ^13C NMR spectra, due to low intensity because of NH-tautomerism.

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References


