Harnessing the Electrophilicity of Keteniminium Ions: A Simple and Straightforward Entry to Tetrahydropyridines and Piperidines from Ynamides

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General Information.

All reactions were carried out in oven-dried glassware under an argon atmosphere employing standard techniques in handling air-sensitive materials.

Tetrahydrofuran and dichloromethane were respectively freshly distilled from sodium/benzophenone and calcium hydride under argon. All solvents were reagent grade.

Copper(I) iodide (99.999% purity) and trifluoromethanesulfonic acid (98+%) were respectively purchased from Aldrich and Alfa Aesar and used as supplied. Finely powdered anhydrous cesium carbonate was used for copper-mediated coupling reactions. All other reagents were used as supplied.

Reactions were magnetically stirred and monitored by thin layer chromatography using Merck-Kiesegel 60F254 plates or Macherey-Nagel Pre Coated TLC-sheets Alugram® Xtra Sil/UV254. Flash chromatography was performed with silica gel 60 (particle size 35-70 µm) supplied by Merck or silica gel 60 (particle size 15 - 40 µm) supplied by Macherey-Nagel. Yields refer to chromatographically and spectroscopically pure compounds unless otherwise stated.

Proton NMR spectra were recorded using an internal deuterium lock at ambient temperature on Bruker 300, 400 and 600 MHz spectrometers. Internal reference of δH 7.26 was used for CDCl3. Data are presented as follows: chemical shift (in ppm on the δ scale relative to δTMS = 0), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, quint. = quintuplet, sext. = sextuplet, m = multiplet, br. = broad, app. = apparent), coupling constant (J/Hz) and integration. Resonances that are either partially or fully obscured are denoted obscured (obs.). Carbon-13 NMR spectra were recorded at 75 or 100 MHz using CDCl3 (δC 77.16) as internal reference.

Melting points were recorded on a Stuart Scientific Analogue SMP11. Infrared spectra were recorded on a Bruker Alpha ATR spectrophotometer. High-resolution mass-spectra were obtained on an Agilent Technologies GC-Q-Tof spectrometer.
Experimental Procedure and Characterization Data:
Synthesis of Starting \(N\)-(4-toluenesulfonyl)- and \(N\)-(methylsulfonyl)- amines

**General procedure I: synthesis of \(N\)-(4-toluenesulfonyl)amines**

To a solution of amine (45.9 mmol) and triethylamine (6.7 mL, 48.1 mmol) in dichloromethane (110 mL) was added dropwise a solution of para-toluenesulfonyl chloride (8.3 g, 43.7 mmol) in dichloromethane (130 mL) at 0 °C over 45 minutes. The resulting mixture was then stirred at 0 °C for 30 minute, warmed to room temperature; stirred overnight and quenched by addition of 1M aqueous solution of hydrochloric acid (250 mL). The organic layer was then successively washed with 1M aqueous solution of hydrochloric acid (250 mL), 1M aqueous solution of sodium hydroxide (250 mL) and brine (250 mL), dried over magnesium sulfate, filtered and concentrated under reduced pressure to give the desired \(N\)-tosyl-amine which could be used in the next step without further purification.

**General procedure II: synthesis of \(N\)-(methylsulfonyl)amines**

To a solution of amine (8.6 mmol) and triethylamine (4.8 mL, 34.4 mmol) in dichloromethane (48 mL) was added dropwise at 0 °C, a solution of methanesulfonyl chloride (1.3 g, 16.8 mmol). The resulting mixture was then warmed to room temperature; stirred overnight and quenched by addition of 1M aqueous solution of sodium hydroxide (50 mL). The organic layer was then successively washed with 1M aqueous solution of hydrochloric acid (50 mL) and distillated water (50 mL), dried over magnesium sulfate, filtered and concentrated under reduced pressure to give the desired \(N\)-mesyl-amine which could be used in the next step, most cases, without further purification.
**A Simple and Straightforward Entry to Tetrahydropyridines and Piperidines from Ynamides**

\[ \text{Ts} \quad \text{HN} \]

*N-*(4-Toluenesulfonyl)-isopentylamine. Prepared according to general procedure I. Yield: 99% (10.4 g, 43.1 mmol). Colorless oil. This compound has been previously reported.\(^{51}\)

\[ \text{Ns} \quad \text{HN} \]

*N-*(4-Nitrobenzenesulfonyl)-isopentylamine. Prepared according to general procedure I starting from 18.1 mmol of 4-nitrobenzenesulfonyl chloride. Yield: 87% (4.3 g, 15.8 mmol). Pale yellow solid; Mp: 85 °C; \(^1\)H NMR (300 MHz, CDCl\(_3\)): \(\delta\) 8.37 (d, \(J = 8.8\) Hz, 2H), 8.06 (d, \(J = 8.8\) Hz, 2H), 4.61 (br. s, 1H), 3.03 (app. q, \(J = 6.8\) Hz, 2H), 1.67-1.51 (m, 1H), 1.37 (app. q, \(J = 7.2\) Hz, 2H), 0.85 (d, \(J = 6.7\) Hz, 6H); \(^13\)C NMR (75 MHz, CDCl\(_3\)): \(\delta\) 150.2, 146.1, 128.4, 124.5, 41.8, 38.6, 25.5, 22.3; IR (ATR): \(\nu_{\text{max}}\) 3262, 2960, 1608, 1535, 1349, 1160, 855, 747, 610 cm\(^{-1}\); ESIHRMS m/z calcd for C\(_{11}\)H\(_{17}\)N\(_2\)O\(_4\)S [M+H]\(^+\) 273.0904, found 273.0912.

\[ \text{Ms} \quad \text{HN} \]

*N-*(Methylsulfonyl)-isopentylamine. Prepared according to general procedure II. Yield: 99% (1.4 g, 8.5 mmol). Brown/orange solid. This compound has been previously reported.\(^{52}\)

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\(^{51}\) N. R. Paz, D. Rodríguez-Sosa, H. Valdés, R. Marticorena, D. Melián, M. B. Copano, C. C. González, A. J. Herrera, *Org. Lett.* **2015**, 17, 2370.
**N-(4-Toluenesulfonyl)-4-methylpentan-2-amine.** Prepared according to general procedure I starting from 13.5 mmol of para-toluenesulfonyl chloride. Yield: 61% (2.1 g, 8.2 mmol). White solid; Mp: 58 °C; $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 7.76 (d, $J = 8.3$ Hz, 2H), 7.29 (d, $J = 8.2$ Hz, 2H), 4.27, (br. s, 1H), 3.42-3.26 (m, 1H), 2.42 (s, 3H), 1.63-1.48 (m, 1H), 1.32-1.20 (m, 1H), 1.19-1.08 (m, 1H), 1.01 (d, $J = 6.5$ Hz, 3H), 0.79 (d, $J = 6.6$ Hz, 3H), 0.72 (d, $J = 6.6$ Hz, 3H); $^{13}$C NMR (75 MHz, CDCl$_3$): $\delta$ 143.3, 138.5, 129.7, 127.2, 48.4, 47.3, 24.7, 22.7, 22.4, 22.3, 21.7; IR (ATR): $\nu_{\text{max}}$ 3274, 2959, 2927, 1598, 1422, 1323, 1158, 1094, 991, 815, 668 cm$^{-1}$; ESIHRMS m/z calcd for C$_{13}$H$_{22}$NO$_2$S [M+H]$^+$ 256.1366, found 256.1369.

**N-(Methylsulfonyl)-4-methylpentan-2-amine.** Prepared according to general procedure II starting from 14.2 mmol of 4-methylpentan-2-amine. Yield: 63% (1.6 g, 8.9 mmol). Brown/orange oil; $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 4.35 (br. s, 1H), 3.52 (m, 1H), 2.96 (s, 3H), 1.78-1.63 (m, 1H), 1.45-1.32 (m, 1H), 1.30-1.19 (obs. m, 1H), 1.22 (d, $J = 6.4$ Hz, 3H), 0.92 (d, $J = 6.5$ Hz, 3H), 0.90 (d, $J = 6.6$ Hz, 3H); $^{13}$C NMR (75 MHz, CDCl$_3$): $\delta$ 48.6, 47.3, 42.1, 24.9, 22.9, 22.7, 22.5; IR (ATR): $\nu_{\text{max}}$ 3298, 2956, 2870, 1419, 1312, 1140, 998, 758 cm$^{-1}$; ESIHRMS m/z calcd for C$_7$H$_{18}$NO$_2$S [M+H]$^+$ 180.1053, found 180.1052.

S2. O'Sullivan, E. Doni, T. Tuttle, J. A. Murphy, *Angew. Chem. Int. Ed.* **2014**, *53*, 474.
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**N-(Methylsulfonyl)-3,5-dimethylhexan-1-amine.** Prepared according to general procedure II starting from 487 μmol of 3,5-dimethylhexan-1-amine. Yield: 98% (99 mg, 477 μmol). Orange oil; \(^1\)H NMR (300 MHz, CDCl\(_3\)): \(\delta\) 4.25 (br. s, 1H), 3.22-3.09 (m, 2H), 2.95 (s, 3H), 1.71-1.49 (m, 3H), 1.46-1.31 (m, 1H), 1.15-1.00 (m, 2H), 0.88 (d, \(J = 6.4\) Hz, 3H), 0.87 (d, \(J = 6.6\) Hz, 3H), 0.84 (d, \(J = 6.6\) Hz, 3H); \(^13\)C NMR (75 MHz, CDCl\(_3\)): \(\delta\) 46.5, 41.5, 40.0, 37.5, 28.0, 25.1, 23.4, 22.2, 19.4; IR (ATR): \(\nu_{\text{max}}\) 3294, 2955, 2870, 1467, 1316, 1152, 1079, 975, 764 cm\(^{-1}\); ESIHRMS \(m/z\) calcd for C\(_9\)H\(_{22}\)NO\(_2\)S [M+H]\(^+\) 208.1366, found 208.1371.

**N-(4-Toluenesulfonyl)-2-cyclohexylethan-1-amine.** Prepared according to general procedure I starting from 7.5 mmol of para-toluenesulfonyl chloride. Yield: 95% (2.0 g, 7.1 mmol). White solid. This compound has been previously reported.\(^{53}\)

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\(^{53}\) T. Nishikata, H. Nagashima, *Angew. Chem. Int. Ed.* **2012**, *51*, 5363.
**N-(Methylsulfonyl)-(2-methylcyclohexyl)methanamine.** Prepared according to general procedure II starting from 2.81 mmol of (2-methylcyclohexyl)methanamine and obtained as a 75:25 mixture of diastereoisomers. Yield: 98% (566 mg, 2.76 mmol). White solid; Mp: 48 °C; $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 4.27 (br. s, 1H), 3.32-3.22 (m, 1H), 3.04-2.97 (obs. m, 1H), 2.95 (s, 3H), 1.85-0.97 (m, 10H), 0.94 (d, J = 5.9 Hz, 2.25H, major diastereoisomer), 0.87 (d, J = 7.0 Hz, 0.75H, minor diastereoisomer); $^{13}$C NMR (75 MHz, CDCl$_3$): $\delta$ 46.8 (major diastereoisomer), 45.8 (minor diastereoisomer), 44.3 (major diastereoisomer), 40.6 (minor diastereoisomer), 40.3 (minor diastereoisomer), 40.2 (major diastereoisomer), 35.5 (major diastereoisomer), 34.6 (major diastereoisomer), 32.5 (minor diastereoisomer), 30.5 (minor diastereoisomer), 30.3 (major diastereoisomer), 26.3 (major diastereoisomer), 26.1 (major diastereoisomer), 25.4 (minor diastereoisomer), 24.9 (minor diastereoisomer), 21.7 (minor diastereoisomer), 20.1 (major diastereoisomer), 13.7 (minor diastereoisomer); IR (ATR): $\nu_{\text{max}}$ 3299, 2917, 2856, 1454, 1307, 1144, 1065, 1053, 981, 859, 764 cm$^{-1}$; ESIHRMS $m/z$ calcd for C$_9$H$_{20}$NO$_2$S [M+H]$^+$ 206.1209, found 206.1211.

**N,N’-Bis(methylsulfonyl)-N-methyl-propane-1,3-diamine.** To a solution of N-methyl-propane-1,3-diamine (5.0 mmol) and triethylamine (3.1 mL, 22.0 mmol) in chloroforme (17 mL) was added dropwise at 0 °C, a solution of methanesulfonyl chloride (1.7 mL, 22.0 mmol). The resulting mixture was then warmed to room temperature; stirred overnight and quenched by addition of distillated water. The layers were separated and the aqueous layer was extracted
with chloroform. Combined organic layers were dried over magnesium sulfate and concentrated. The crude residue was finally purified by flash column chromatography over silica gel (100 % EtOAc). Yield: 38% (465 mg, 1.90 mmol). White solid; Mp: 91 °C; \(^1\)H NMR (300 MHz, CDCl\(_3\)): \(\delta\) 5.02 (br. s, 1H), 3.30-3.19 (m, 4H), 2.95 (s, 3H), 2.85 (s, 3H), 2.82 (s, 3H), 1.83 (app. quint., \(J = 6.1\) Hz, 2H); \(^13\)C NMR (75 MHz, CDCl\(_3\)): \(\delta\) 46.7, 40.3, 39.4, 35.2, 34.9, 28.1; IR (ATR): \(\nu_{\max}\) 3258, 2928, 1464, 1297, 1160, 1137, 980, 790, 759 cm\(^{-1}\); ESIHRMS m/z calcd for \(\text{C}_6\text{H}_{17}\text{N}_2\text{O}_4\text{S}_2\) [M+H]^+ 245.0624, found 245.0629.
Experimental Procedure and Characterization Data:

Synthesis of the Starting Ynamides

General procedure III: synthesis of ynamides from 1,1-dibromo-1-alkenes\textsuperscript{54}

A 15 mL pressure tube was charged with the sulfonamide (1.6 mmol), the 1,1-dibromo-1-alkene (2.4 mmol), cesium carbonate (2.1 g, 6.4 mmol) and copper(I) iodide (38 mg, 0.2 mmol). The tube was fitted with a rubber septum, evacuated under high vacuum and backfilled with argon. Dry 1,4-dioxane or DMF (3 mL) and \(N,N'\)-dimethylethylenediamine (30 µL, 0.3 mmol) were next added, the rubber septum was replaced by Teflon-coated screw cap and the light blue-green suspension was heated at 70 °C for 36 or 48 hours. The blue or brownish suspension was cooled to room temperature. When the reaction was run in 1,4-dioxane, the crude reaction was filtered over a plug of silica gel (washed with EtOAc) and concentrated. When the reaction was run in DMF, the crude mixture was diluted with water, extracted with diethyl ether and the combined organics layers were washed with brine, dried over MgSO\(_4\), filtered and concentrated. The crude residue was in both cases purified by flash column chromatography over silica gel.

General procedure IV: synthesis of ynamides from bromoalkynes\textsuperscript{55}

A 15 mL pressure tube was charged with the sulfonamide (5.0 mmol), potassium carbonate (1.38 g, 10.0 mmol), CuSO\(_4\)·5H\(_2\)O (125 mg, 0.5 mmol) and 1,10-phenanthroline (180 mg, 1.0 mmol). The tube was fitted with a rubber septum, evacuated under high vacuum and backfilled with argon. The bromoalkyne (5.0 mmol) and dry toluene (5 mL) were next added, the rubber septum was replaced by Teflon-coated screw cap and the mixture was heated at 70 °C for 48 hours. The reaction mixture was then cooled to room temperature, filtered over a plug of silica gel (washed with EtOAc) and concentrated. The crude residue was purified by flash column chromatography over silica gel.

\textsuperscript{54} A. Coste, G. Karthikeyan, F. Couty, G. Evano, Angew. Chem. Int. Ed. 2009, 48, 4381.

\textsuperscript{55} Y. Zhang, R. P. Hsung, M. R. Tracey, K. C. M. Kurtz, E. L. Vera, Org. Lett. 2004, 6, 1151.
General procedure V: synthesis of methylated and terminal ynamides from trichloroethylene

To a solution of the sulfonamide (2.5 mmol) in dry DMF (2 mL) was added cesium carbonate (1.2 g, 3.7 mmol). The reaction mixture was heated to 50 °C and trichloroethylene (250 μL, 2.7 mmol) was slowly and carefully added over 10 minutes. The reaction was kept at this temperature until TLC analysis showed the complete disappearance of the starting sulfonamide (typically 1-2 h), cooled to rt before adding water and ethyl acetate. The layers were separated and the aqueous layer was extracted with ethyl acetate. Combined organic layers were washed with water, dried over magnesium sulfate, filtered and concentrated to give the intermediate 1,2-dichloroenamide. The crude residue was dissolved in anhydrous THF (25 mL) and cooled to -78 °C before adding a solution of phenyllithium (2.0 M solution in dibutyl ether, 2.7 mL, 5.5 mmol) dropwise over 10 minutes. The reaction mixture was then stirred at -78 °C until TLC analysis showed a complete conversion to the lithiated ynamide (typically 1-2 h). Iodomethane (190 μL, 3.0 mmol) or a mixture of water (16 mL) and diethylether (16 mL) was added at -78 °C, to obtain the methylated or terminal ynamide, respectively, and the reaction mixture was then warmed to room temperature and stirred at this temperature for 2 hours. Water was then added, the layers were separated and the aqueous layer was extracted with diethylether. Combined organic layers were washed with brine, dried over magnesium sulfate, filtered and concentrated. The crude residue was finally purified by flash column chromatography over silica gel.

General procedure VI: synthesis of chlorinated ynamides from trichloroethylene

To a solution of the sulfonamide (535 μmol) in dry DMF (0.5 mL) was added cesium carbonate (260 mg, 800 μmol). The reaction mixture was heated to 50 °C and trichloroethylene (53 μL, 588 μmol) was slowly and carefully added over 10 minutes. The reaction was kept at this temperature until TLC analysis showed the complete disappearance of the starting sulfonamide (typically 1-2 h), cooled to rt before adding water and ethyl acetate. The layers were separated and the aqueous layer was extracted with ethyl acetate. Combined organic layers were washed with water, dried over magnesium sulfate, filtered and concentrated. Combined organic layers were washed

56 S. J. Mansfield, C. D. Campbell, M. W. Jones, E. A. Anderson, Chem. Commun. 2015, 51, 3316.
with water, dried over magnesium sulfate, filtered and concentrated to give the intermediate 1,2-dichloroenamide. The crude residue was dissolved in anhydrous THF (1 mL) and cooled to 0 °C before adding a solution of Lithium hexamethyldisilazane (LiHMDS, 1.0 M solution in THF, 640 μL, 640 μmol) dropwise. The reaction mixture was then stirred at 0 °C until TLC analysis showed a complete conversion to the lithiated ynamide (30 minutes). The reaction mixture was then warmed to room temperature and quenched with water. The layers were separated and the aqueous layer was extracted with diethylether. Combined organic layers were washed with brine, dried over magnesium sulfate, filtered and concentrated. The crude residue was finally purified by flash column chromatography over silica gel.

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\text{N-Isopentyl-N-(4-toluenesulfonyl)-phenylethynylamine 5a.}\]

Prepared according to general procedure III (in 1,4-dioxane) starting from 5.09 mmol of \(N\)-(4-toluenesulfonyl)-isopentylamine. Yield: 70% (1.21 g, 3.54 mmol). Solvent system for flash column chromatography: cyclohexane/EtOAc: 80/20. White solid; Mp: 42 °C; \(^1\)H NMR (300 MHz, CDCl\(_3\)): \(\delta \) 7.84 (d, \(J = 8.3\) Hz, 2H), 7.41-7.32 (m, 4H), 7.32-7.23 (m, 3H), 3.41 (t, \(J = 7.2\) Hz, 2H), 2.45 (s, 3H), 1.76-1.62 (m, 1H), 1.58 (app. q, \(J = 7.2\) Hz, 2H), 0.92 (d, \(J = 6.6\) Hz, 6H); \(^{13}\)C NMR (75 MHz, CDCl\(_3\)): \(\delta \) 144.7, 134.7, 131.4, 129.9, 128.3, 127.8 (2C), 123.1, 82.6, 70.8, 50.2, 36.8, 25.4, 22.5, 21.8; IR (ATR): \(\nu_{\text{max}}\) 2955, 2237, 1597, 1462, 1358, 1168, 945, 774, 760, 692, 678 cm\(^{-1}\); ESIHRMS \(m/z\) calcd for \(C_{20}H_{24}NO_{2}S\) [M+H]\(^{+}\), 342.1522, found 342.1521.
**N-Isopentyl-N-(4-nitrobenzenesulfonyl)phenylethynylamine 5b.** Prepared according to general procedure III (in 1,4-dioxane) starting from 3.67 mmol of N-(4-nitrobenzenesulfonyl)-isopentylamine. Yield: 80% (1.09 g, 2.93 mmol). Solvent system for flash column chromatography: cyclohexane/EtOAc: 85/15. Pale yellow solid; Mp: 85 °C; \(^1\)H NMR (300 MHz, CDCl\(_3\)): \(\delta\) 8.42 (d, \(J = 8.6\) Hz, 2H), 8.14 (d, \(J = 8.4\) Hz, 2H), 7.42-7.28 (m, 5H), 3.48 (t, \(J = 7.4\) Hz, 2H), 1.76-1.55 (m, 3H), 0.93 (d, \(J = 6.3\) Hz, 6H); \(^{13}\)C NMR (75 MHz, CDCl\(_3\)): \(\delta\) 150.8, 143.1, 131.7, 129.0, 128.6, 128.5, 124.6, 122.2, 81.2, 71.5, 50.7, 36.8, 25.4, 22.4; IR (ATR): \(\nu_{\text{max}}\) 2955, 2237, 1602, 1366, 1353, 1175, 1107, 1086, 1009, 853, 759, 737, 604 cm\(^{-1}\); ESIHRMS \(m/z\) calcd for C\(_{19}\)H\(_{21}\)N\(_2\)O\(_4\)S [M+H]+ 373.1217, found 373.1217.

**N-Isopentyl-N-(methylsulfonyl)phenylethynylamine 5c.** Prepared according to general procedure IV. Yield: 79% (1.04 g, 3.94 mmol). Solvent system for flash column chromatography: cyclohexane/EtOAc: 85/15. Brownish oil; \(^1\)H NMR (300 MHz, CDCl\(_3\)): \(\delta\) 7.46-7.38 (m, 2H), 7.34-7.27 (m, 3H), 3.57 (t, \(J = 7.2\) Hz, 2H), 3.13 (s, 3H), 1.83-1.63 (m, 3H), 0.97 (d, \(J = 6.4\) Hz, 6H); \(^{13}\)C NMR (75 MHz, CDCl\(_3\)): \(\delta\) 131.6, 128.5, 128.1, 122.8, 81.8, 71.2, 50.3, 38.3, 37.2, 25.5, 22.5; IR (ATR): \(\nu_{\text{max}}\) 2958, 2237, 1352, 1166, 963, 791, 760, 692 cm\(^{-1}\); ESIHRMS \(m/z\) calcd for C\(_{14}\)H\(_{20}\)NO\(_2\)S [M+H]+ 266.1209, found 266.1210.
**N-Isopentyl-N-(4-toluenesulfonyl)-(4-fluorophenyl)ethynylamine 5d.** Prepared according to general procedure III (in 1,4-dioxane) starting from 1.24 mmol of *N*(4-toluenesulfonyl)-isopentylamine. Yield: 73% (326 mg, 907 μmol). Solvent system for flash column chromatography: cyclohexane/EtOAc: 90/10. Colorless oil; $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 7.83 (d, $J = 8.2$ Hz, 2H), 7.40-7.30 (m, 4H), 6.99 (app. t, $J = 8.6$ Hz, 2H), 3.40 (t, $J = 7.3$ Hz, 2H), 2.46 (s, 3H), 1.75-1.63 (m, 1H), 1.57 (app. q, $J = 7.3$ Hz, 2H), 0.91 (d, $J = 6.4$ Hz, 6H); $^{13}$C NMR (75 MHz, CDCl$_3$): $\delta$ 162.4 (d, $J_{C-F} = 247$ Hz), 144.7, 134.7, 133.5 (d, $J_{C-F} = 8$ Hz), 129.9, 127.8, 119.1 (d, $J_{C-F} = 4$ Hz), 115.7 (d, $J_{C-F} = 22$ Hz), 82.2, 69.7, 50.1, 36.8, 25.4, 22.5, 21.8; IR (ATR): $\nu_{\text{max}}$ 2958, 2237, 1599, 1509, 1365, 1230, 1171, 1091, 948, 835, 814, 736, 664 cm$^{-1}$; ESIHRMS $m/z$ calcd for C$_{20}$H$_{23}$FNO$_2$S [M+H]$^+$ 360.1428, found 360.1429.

**N-Isopentyl-N-(4-toluenesulfonyl)-(4-chlorophenyl)ethynylamine 5e.** Prepared according to general procedure III (in 1,4-dioxane) starting from 2.80 mmol of *N*(4-toluenesulfonyl)-isopentylamine. Yield: 91% (959 mg, 2.55 mmol). Solvent system for flash column chromatography: cyclohexane/EtOAc: 80/20. Pale yellow solid; M.p: 52 °C; $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 7.81 (d, $J = 8.2$ Hz, 2H), 7.34 (d, $J = 8.1$ Hz, 2H), 7.28-7.22 (m, 4H), 3.40 (t, $J = 7.4$ Hz, 2H), 2.44 (s, 3H), 1.75-162 (m, 1H), 1.56 (app. q, $J = 7.3$ Hz, 2H), 0.90 (d, $J = 6.5$ Hz, 6H); $^{13}$C NMR (75 MHz, CDCl$_3$): $\delta$ 144.8, 134.7, 133.8, 132.6, 129.9, 128.7, 127.8, 121.6, 83.5, 69.8, 50.1, 36.7, 25.4, 22.5, 21.8; IR (ATR): $\nu_{\text{max}}$ 2956, 2237, 1607, 1493, 1359, 1170, 1090, 1003, 829, 714, 653 cm$^{-1}$; ESIHRMS $m/z$ calcd for C$_{20}$H$_{23}$ClNO$_2$S [M+H]$^+$ 376.1133, found 376.1133.
**N-Isopentyl-N-(4-toluenesulfonyl)-4-tolylethynylamine 5f.** Prepared according to general procedure III (in 1,4-dioxane). Yield: 86% (490 mg, 1.38 mmol). Solvent system for flash column chromatography: cyclohexane/EtOAc: 80/20. Pale pink pasty solid; $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 7.84 (d, $J = 8.1$ Hz, 2H), 7.35 (d, $J = 8.2$ Hz, 2H), 7.26 (d, $J = 8.0$ Hz, 2H), 7.10 (d, $J = 8.0$ Hz, 2H), 3.40 (t, $J = 7.3$ Hz, 2H), 2.45 (s, 3H), 2.34 (s, 3H), 1.76-1.63 (m, 1H), 1.58 (app. q, $J = 7.2$ Hz, 2H), 0.91 (d, $J = 6.5$ Hz, 6H); $^{13}$C NMR (75 MHz, CDCl$_3$): $\delta$ 144.6, 138.0, 134.7, 131.5, 129.8, 129.1, 127.8, 119.9, 81.9, 70.7, 50.2, 36.8, 25.4, 22.5, 21.8, 21.5; IR (ATR): $\nu_{max}$ 2956, 2241, 1697, 1357, 1170, 1089, 1002, 816, 730, 666 cm$^{-1}$; ESIHRMS $m/z$ calcd for C$_{21}$H$_{26}$NO$_{3}$S [M+H]$^+$ 356.1679, found 356.1677.

**N-Isopentyl-N-(4-toluenesulfonyl)-(4-methoxyphenyl)ethynylamine 5g.** Prepared according to general procedure III (in 1,4-dioxane) starting from 2.90 mmol of N-(4-toluenesulfonyl)-isopentylamine. Yield: 56% (601 mg, 1.62 mmol). Solvent system for flash column chromatography: cyclohexane/EtOAc: 85/15. Pink pasty solid; $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 7.83 (d, $J = 8.3$ Hz, 2H), 7.35 (d, $J = 8.2$ Hz, 2H), 7.31 (d, $J = 8.8$ Hz, 2H), 6.82 (d, $J = 8.8$ Hz, 2H), 3.81 (d, $J = 8.8$ Hz, 2H), 3.39 (t, $J = 7.2$ Hz, 2H), 2.45 (s, 3H), 1.76-1.63 (m, 1H), 1.57 (app. q, $J = 7.3$ Hz, 2H), 0.91 (d, $J = 6.5$ Hz, 6H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 159.6, 144.6, 134.8, 133.5, 129.8, 127.8, 115.0, 114.0, 81.1, 70.4, 55.5, 50.2, 36.8, 25.5, 22.5, 21.8; IR (ATR): $\nu_{max}$ 2958, 2870, 2233, 1698, 1607, 1513, 1358, 1249, 1170, 1031, 833, 725, 666 cm$^{-1}$; ESIHRMS $m/z$ calcd for C$_{21}$H$_{26}$NO$_{3}$S [M+H]$^+$ 372.1628, found 372.1628.
**N-Isopentyl-N-(methylsulfonyl)-(oct-1-ynyl)amine 5h.** Prepared according to general procedure IV. Yield: 70% (961 mg, 3.51 mmol). Solvent system for flash column chromatography: cyclohexane/EtOAc: 85/15. Pale yellow oil; $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 3.41 (t, $J$ = 7.3 Hz, 2H), 3.03 (s, 3H), 2.29 (t, $J$ = 6.9 Hz, 2H), 1.75-1.45 (m, 5H), 1.44-1.22 (m, 6H), 0.94 (d, $J$ = 6.4 Hz, 6H), 0.89 (obs. t, $J$ = 6.9 Hz, 3H); $^{13}$C NMR (75 MHz, CDCl$_3$): $\delta$ 72.7, 70.9, 50.0, 37.6, 37.0, 31.4, 29.1, 28.7, 25.4, 22.7, 22.5, 18.6, 14.2; IR (ATR): $\nu_{\text{max}}$ 2957, 2931, 2871, 2253, 1467, 1357, 1165, 960, 767 cm$^{-1}$; ESIHRMS m/z calcd for C$_{14}$H$_{28}$NO$_2$S [M+H]$^+$ 274.1835, found 274.1840.

**N-Isopentyl-N-(4-toluenesulfonyl)-(prop-1-ynyl)amine 5i.** Prepared according to general procedure III (in DMF) starting from 2.33 mmol of N-(4-toluenesulfonyl)-isopentylamine. Yield: 38% (246 g, 880 $\mu$mol). Solvent system for flash column chromatography: cyclohexane/EtOAc: 90/10. White solid; Mp: 32 °C; $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 7.77 (d, $J$ = 8.1 Hz, 2H), 7.33 (d, $J$ = 7.9 Hz, 2H), 3.25 (t, $J$ = 7.3 Hz, 2H), 2.44 (s, 3H), 1.89 (s, 3H), 1.70-1.55 (m, 1H), 1.49 (app. q, $J$ = 7.2 Hz, 2H), 0.88 (d, $J$ = 6.6 Hz, 6H); $^{13}$C NMR (75 MHz, CDCl$_3$): $\delta$ 144.4, 134.9, 129.8, 127.7, 72.2, 65.6, 50.0, 36.7, 25.4, 22.5, 21.8, 3.5; IR (ATR): $\nu_{\text{max}}$ 2959, 2250, 1625, 1355, 1164, 1088, 982, 840, 674 cm$^{-1}$; ESIHRMS m/z calcd for C$_{15}$H$_{22}$NO$_2$S [M+H]$^+$ 280.1366, found 280.1365.
**N-Isopentyl-N-(4-toluenesulfonyl)-chloroethynylamine 5j.** Prepared according to general procedure VI. Yield: 81% (130 mg, 434 μmol). Solvent system for flash column chromatography: cyclohexane/EtOAc: 85/15. Yellow oil; $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 7.77 (d, $J = 8.2$ Hz, 2H), 7.36 (d, $J = 8.1$ Hz, 2H), 3.29 (t, $J = 7.4$ Hz, 2H), 2.46 (s, 3H), 1.68-1.56 (m, 1H), 1.49 (app. q, $J = 7.4$ Hz, 2H), 0.89 (d, $J = 6.5$ Hz, 6H); $^{13}$C NMR (75 MHz, CDCl$_3$): $\delta$ 144.9, 134.5, 130.0, 127.6, 63.1, 52.0, 49.8, 36.6, 25.3, 22.4, 21.7; IR (ATR): $\nu_{max}$ 2958, 2237, 1597, 1366, 1171, 1090, 814, 663 cm$^{-1}$; ESIHRMS m/z calcd for C$_{14}$H$_{19}$ClNO$_2$S [M+H]$^+$ 300.0820, found 300.0838.

**N-Isopentyl-N-(4-toluenesulfonyl)-ethynylamine 5k.** Prepared according to general procedure V (with water and diethyl ether). This terminal ynamide was found to be rather unstable and was therefore prepared immediately before use. Yield: 86% (567 mg, 2.14 mmol). Solvent system for flash column chromatography: cyclohexane/EtOAc: 85/15. White solid; Mp: 29 °C; $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 7.80 (d, $J = 8.3$ Hz, 2H), 7.35 (d, $J = 8.1$ Hz, 2H), 3.31 (t, $J = 7.3$Hz, 2H), 2.72 (s, 1H), 2.45 (s, 3H), 1.69-1.58 (m, 1H), 1.52 (app. q, $J = 7.1$ Hz, 2H), 0.89 (d, $J = 6.7$ Hz, 6H); $^{13}$C NMR (75 MHz, CDCl$_3$): $\delta$ 144.8, 134.7, 129.9, 127.8, 76.2, 59.2, 49.7, 36.5, 25.4, 22.4, 21.8; IR (ATR): $\nu_{max}$ 3273, 2954, 2134, 1597, 1355, 1167, 1090, 945, 817, 708, 685, 649 cm$^{-1}$; ESIHRMS m/z calcd for C$_{14}$H$_{22}$NO$_3$S [M+H$_2$O+H]$^+$ 284.1315, found 284.1313.
**N-Isopentyl-N-(4-toluenesulfonyl)-triisopropylsilylethynylamine 5I.** Prepared according to general procedure IV starting from 2.0 mmol of N-(4-toluenesulfonyl)-isopentylamine. Yield: 53% (450 mg, 1.07 mmol). Solvent system for flash column chromatography: cyclohexane/EtOAc: 80/20. White solid; Mp: 42 °C; $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 7.80 (d, $J = 8.3$ Hz, 2H), 7.31 (d, $J = 8.1$ Hz, 2H), 3.33 (t, $J = 7.2$ Hz, 2H), 2.44 (s, 3H), 1.75-1.60 (m, 1H), 1.54 (app. q, $J = 7.1$ Hz, 2H), 1.04 (app. s, 21H); $^{13}$C NMR (75 MHz, CDCl$_3$): $\delta$ 144.6, 134.8, 129.7, 127.9, 96.5, 69.5, 49.7, 36.6, 25.2, 22.4, 21.8, 18.7, 11.5; IR (ATR): $\nu_{max}$ 2942, 2162, 1367, 1170, 883, 817, 737, 665 cm$^{-1}$; ESIHRMS m/z calcd for C$_{23}$H$_{40}$NO$_2$SSi [M+H]$^+$ 422.2544, found 422.2542.

![Diagram of 5I](image)

**N-(4-Methylpentan-2-yl)-N-(4-toluenesulfonyl)phenylethynylamine 5m.** Prepared according to general procedure III (in 1,4-dioxane) starting from 2.70 mmol of N-(4-toluenesulfonyl)-4-methylpentan-2-amine. Yield: 51% (493 g, 1.39 mmol). Solvent system for flash column chromatography: cyclohexane/EtOAc: 80/20. Pale yellow oil; $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 7.85 (d, $J = 8.2$ Hz, 2H), 7.41-7.27 (m, 7H), 4.22-1.09 (m, 1H), 2.45 (s, 3H), 1.67-1.54 (m, 2H), 1.28-1.16 (m, 1H), 1.07 (d, $J = 6.5$ Hz, 3H), 0.89 (d, $J = 6.4$ Hz, 6H); $^{13}$C NMR (75 MHz, CDCl$_3$): $\delta$ 144.5, 136.2, 131.3, 129.8, 128.4, 127.7, 127.6, 123.4, 79.7, 72.8, 55.1, 44.3, 24.8, 23.1, 22.1, 21.8, 19.3; IR (ATR): $\nu_{max}$ 2957, 2232, 1598, 1362, 1172, 1090, 977, 814, 754, 691, 672 cm$^{-1}$; ESIHRMS m/z calcd for C$_{21}$H$_{26}$NO$_2$S [M+H]$^+$ 356.1679, found 356.1676.

![Diagram of 5m](image)
**N-(4-Methylpentan-2-yl)-N-methylsulfonyl-phenylethynylamine 5n.** Prepared according to general procedure III (in 1,4-dioxane) starting from 2.50 mmol of N-(methylsulfonyl)-4-methylpentan-2-amine. Yield: 84% (583 mg, 2.09 mmol). Solvent system for flash column chromatography: cyclohexane/EtOAc: 85/15. Colorless oil. \(^1\)H NMR (300 MHz, CDCl\(_3\)): \(\delta 7.47-7.37 \text{ (m, 2H), 7.36-7.27 \text{ (m, 3H), 4.26-4.14 \text{ (m, 1H), 3.14 \text{ (s, 3H), 1.80-1.65 \text{ (m, 2H), 1.33 \text{ (d, J = 6.5 Hz, 3H), 1.29 \text{ (obs. m, 1H), 0.97 \text{ (d, J = 6.4 Hz, 3H), 0.96 \text{ (d, J = 6.2 Hz, 3H); \(13\)C NMR (75 MHz, CDCl\(_3\)): \(\delta 131.5, 128.4, 128.0, 123.0, 78.8, 73.3, 55.0, 44.1, 39.7, 24.9, 23.1, 22.0, 19.9; IR (ATR): }\nu_{\text{max}} 2958, 2233, 1356, 1169, 982, 959, 776, 754, 692 \text{ cm}^{-1}; \text{ESIHRMS } m/z \text{ calcd for C}_{15}\text{H}_{22}\text{NO}_{2}\text{S } [\text{M+H}]^+ 280.1366, \text{found 280.1366.}

**N-(4-Methylpentan-2-yl)-N-(4-toluenesulfonyl)-(prop-1-ynyl)amine 5o.** Prepared according to general procedure V (with iodomethane). Yield: 92% (686 mg, 2.29 mmol). Solvent system for flash column chromatography: cyclohexane/EtOAc: 90/10. White solid; Mp: 64°C; \(^1\)H NMR (300 MHz, CDCl\(_3\)): \(\delta 7.79 \text{ (d, J = 8.1 Hz, 2H), 7.31 \text{ (d, J = 8.0 Hz, 2H), 4.09-3.94 \text{ (m, 1H), 2.43 \text{ (s, 3H), 1.92 \text{ (s, 3H), 1.62-1.40 \text{ (m, 2H), 1.19-1.06 \text{ (m, 1H), 0.96 \text{ (d, J = 6.6 Hz, 3H), 0.86 \text{ (d, J = 6.0 Hz, 3H), 0.85 \text{ (d, J = 6.3 Hz, 3H); \(13\)C NMR (75 MHz, CDCl\(_3\)): \(\delta 144.1, 136.5, 129.7, 127.6, 68.8, 67.4, 54.3, 44.1, 24.7, 23.1, 22.2, 21.8, 18.9, 3.6; IR (ATR): }\nu_{\text{max}} 2956, 2259, 1586, 1349, 1269, 1166, 1088, 1010, 961, 817, 705, 671 \text{ cm}^{-1}; \text{ESIHRMS } m/z \text{ calcd for C}_{16}\text{H}_{24}\text{NO}_{2}\text{S } [\text{M+H}]^+ 294.1520, \text{found 294.1520.}}
**N-(3,5-Dimethylhexyl)-N-(methylsulfonyl)-phenylethynylamine 5p.** Prepared according to general procedure III (in 1,4-dioxane) starting from 480 μmol of \(N\)-(methylsulfonyl)-3,5-dimethylhexan-1-amine. Yield: 58% (86 mg, 280 μmol). Solvent system for flash column chromatography: cyclohexane/EtOAc: 90/10. Pale yellow oil; \(^1H\) NMR (300 MHz, CDCl\(_3\)): \(\delta\) 7.44-7.37 (m, 2H), 7.34-7.28 (m, 3H), 3.57 (t, \(J = 7.5\) Hz, 2H), 3.13 (s, 3H), 1.91-1.77 (m, 1H), 1.74-1.50 (m, 3H), 1.23-1.02 (m, 2H), 0.93 (d, \(J = 6.4\) Hz, 3H), 0.89 (d, \(J = 6.6\) Hz, 3H), 0.86 (d, \(J = 6.6\) Hz, 3H); \(^{13}\)C NMR (75 MHz, CDCl\(_3\)): \(\delta\) 131.6, 128.5, 128.1, 122.8, 81.8, 71.2, 50.1, 46.6, 38.3, 35.7, 27.9, 25.3, 23.4, 22.4, 19.7; ESIHRMS \(m/z\) calcd for \(C_{17}H_{26}NO_2S\) [M+H]\(^+\) 308.1679, found 308.1690.

**N-(2-Cyclohexylethyl)-N-(4-toluenesulfonyl)-(prop-1-ynyl)amine 5q.** Prepared according to general procedure V (with iodomethane) starting from 1.0 mmol of \(N\)-(4-toluenesulfonyl)-2-cyclohexylethan-1-amine. Yield: 98% (313 mg, 980 μmol). Solvent system for flash column chromatography: cyclohexane/EtOAc: 80/20. Yellow pasty solid; \(^1H\) NMR (300 MHz, CDCl\(_3\)): \(\delta\) 7.77 (d, \(J = 8.3\) Hz, 2H), 7.33 (d, \(J = 8.2\) Hz, 2H), 3.26 (t, \(J = 7.4\) Hz, 2H), 2.44 (s, 3H), 1.89 (s, 3H), 1.73-1.59 (m, 5H), 1.49 (app. q, \(J = 7.2\) Hz, 2H), 1.36-1.08 (m, 4H), 0.94-0.79 (m, 2H); \(^{13}\)C NMR (75 MHz, CDCl\(_3\)): \(\delta\) 144.3, 134.9, 129.7, 127.7, 72.1, 65.6, 49.4, 35.3, 34.8, 33.1, 26.6, 26.2, 21.7, 3.5; IR (ATR): \(\nu_{\text{max}}\) 2922, 2851, 2260, 1597, 1494, 1448, 1168, 813, 675 cm\(^{-1}\); ESIHRMS \(m/z\) calcd for \(C_{18}H_{26}NO_2S\) [M+H]\(^+\) 320.1679, found 320.1693.
**N-Methylsulfonyl-N-[(2-methylcyclohexyl)methyl]phenylethynylamine 5r.** Prepared according to general procedure III (in 1,4-dioxane) starting from 1.56 mmol of N-(methylsulfonyl)-(2-methylcyclohexyl)methanamine and obtained as a 75:25 mixture of diastereoisomers. Yield: 94% (450 mg, 1.47 mmol). Solvent system for flash column chromatography: cyclohexane/EtOAc: 90/10. Pale yellow oil; ¹H NMR (300 MHz, CDCl₃): δ 7.44-7.36 (m, 2H), 7.34-7.27 (m, 3H), 3.71 (A of ABX syst., J = 12.9 and 4.1 Hz, 0.75H, major diastereoisomer), 3.42 (d, J = 7.42 Hz, 0.5 H, minor diastereoisomer), 3.32 (B of ABX syst., J = 13.0 and 9.5 Hz, 0.75H, major diastereoisomer), 3.13 (s, 3H), 2.08-1.97 (m, 1H), 1.83-1.60 (m, 2H), 1.55-1.39 (m, 2H), 1.37-1.15 (m, 3H), 1.16-1.00 (obs. m, 2H), 0.99 and 0.94 (d, J = 6.6 and 6.9 Hz, 3H, diastereoisomer); ¹³C NMR (75 MHz, CDCl₃): δ 131.4, 128.4, 128.0, 122.8, 82.5 (major diastereoisomer), 82.1 (minor diastereoisomer), 70.9 (minor diastereoisomer), 70.8 (major diastereoisomer), 55.9 (major diastereoisomer), 54.1 (minor diastereoisomer), 43.3 (major diastereoisomer), 39.1 (minor diastereoisomer), 38.0 (major diastereoisomer), 37.9 (minor diastereoisomer), 35.6 (major diastereoisomer), 35.1 (major diastereoisomer), 32.5 (minor diastereoisomer), 30.5 (minor diastereoisomer), 30.0 (major diastereoisomer), 26.1 (major diastereoisomer), 25.1 (minor diastereoisomer), 25.9 (major diastereoisomer), 24.8 (minor diastereoisomer), 20.2 (major diastereoisomer) 21.8 (minor diastereoisomer); IR (ATR): νmax 2926, 2854, 2236, 1444, 1359, 1166, 1113, 961, 787, 755, 691 cm⁻¹; ESIHRMS m/z calcd for C₁₇H₂₄NO₂S [M+H]+ 306.1522, found 306.1539.
**N-(N-Methyl-N-methylsulfonyl-3-aminopropyl)-N-(methylsulfonyl)phenylethylnylamine 5s.**

Prepared according to general procedure III (in 1,4-dioxane) starting from 1.80 mmol of \(N,N'\)-bis(methylsulfonyl)-\(N\)-methyl-propane-1,3-diamine. Yield: 76% (472 mg, 1.37 mmol). Solvent system for flash column chromatography: cyclohexane/EtOAc: 30/70. White solid; Mp: 82 °C; \(^1\)H NMR (300 MHz, CDCl\(_3\)): \(\delta\) 7.45-7.37 (m, 2H), 7.35-7.27 (m, 3H), 3.63 (t, \(J = 7.1\) Hz, 2H), 3.27 (t, \(J = 6.8\) Hz, 2H), 3.16 (s, 3H), 2.89 (s, 3H), 2.81 (s, 3H), 2.13 (app. quint., \(J = 6.9\) Hz, 2H); \(^{13}\)C NMR (75 MHz, CDCl\(_3\)): \(\delta\) 131.7, 128.5, 128.3, 122.3, 81.2, 71.5, 49.2, 47.4, 38.2, 35.3, 35.1, 27.1; IR (ATR): \(\nu_{\text{max}}\) 2238, 1351, 1318, 1157, 1151, 972, 788, 761, 694 cm\(^{-1}\); ESIHRMS \(m/z\) calcd for \(C_{14}H_{21}N_{2}O_{4}S_{2} [M+H]^+\) 345.0937, found 345.0948.
Experimental Procedure and Characterization Data:

Synthesis of the Starting Bis- and Tris- Ynamides

General procedure VII: synthesis of bis-ynamides from bis(1,1-dibromo-1-alkenes)

A 50 mL pressure tube was charged with the N-(4-toluenesulfonyl)-isopentylamine (620 mg, 3.75 mmol), the bis(1,1-dibromo-1-alkene) (669 mg, 1.5 mmol), cesium carbonate (2.93 g, 9.0 mmol) and copper(I) iodide (69 mg, 0.36 mmol). The tube was fitted with a rubber septum, evacuated under high vacuum and backfilled with argon. Dry 1,4-dioxane (12 mL) and N,N'-dimethylethylenediamine (58 µL, 0.54 mmol) were next added, the rubber septum was replaced by Teflon-coated screw cap and the light blue-green suspension was heated at 70 °C for 36 hours. The brownish suspension was cooled to room temperature, filtered over a plug of silica gel (washed with AcOEt) and concentrated. Finally, the crude residue was purified by flash column chromatography over silica gel.

General procedure VIII: synthesis of tris-ynamide from tris(1,1-dibromo-1-alkene)

A 15 mL pressure tube was charged with the N-(4-toluenesulfonyl)-isopentylamine (364 mg, 2.20 mmol), the 1,3,5-tris(2,2-dibromovinyl)benzene (370 mg, 588 µmol), cesium carbonate (1.72 g, 5.29 mmol) and copper(I) iodide (42 mg, 220 µmol). The tube was fitted with a rubber septum, evacuated under high vacuum and backfilled with argon. Dry 1,4-dioxane (4.7 mL) and N,N'-dimethylethylenediamine (36 µL, 335 µmol) were next added, the rubber septum was replaced by Teflon-coated screw cap and the light blue-green suspension was heated at 70 °C for 36 hours. The suspension was cooled to room temperature, filtered over a plug of silica gel (washed with AcOEt) and concentrated. Finally, the crude residue was purified by flash column chromatography over silica gel (cyclohexane/EtOAc: 50/50).
N,N'-[1,4-Phenylenebis(ethyne-2,1-diyl)]bis(N-isopentylmethanesulfonamide) 10. Prepared according to general procedure VII. Yield: 66% (449 mg, 992 μmol). Solvent system for flash column chromatography: cyclohexane/EtOAc: 80/20. Pale yellow solid; Mp: 131 °C; ¹H NMR (300 MHz, CDCl₃): δ 7.33 (s, 4H), 3.56 (t, J = 7.3 Hz, 4H), 3.13 (s, 6H), 1.83-1.61 (m, 6H), 0.97 (d, J = 6.3 Hz, 12H); ¹³C NMR (75 MHz, CDCl₃): δ 131.2, 122.3, 83.5, 71.0, 50.3, 38.5, 37.3, 25.5, 22.5; IR (ATR): νmax 2957, 2237, 1349, 1159, 1112, 967, 839, 775 cm⁻¹; ESIHRMS m/z calcd for C₂₂H₃₉N₂O₄S₂ [M+H]⁺ 453.1876, found 453.1876.

N,N'-[1,3-Phenylenebis(ethyne-2,1-diyl)]bis(N-isopentylmethanesulfonamide) 12. Prepared according to general procedure VII. Yield: 77% (525 mg, 1.16 mmol). Solvent system for flash column chromatography: cyclohexane/EtOAc: 80/20. Pale yellow solid; Mp: 49 °C; ¹H NMR (300 MHz, CDCl₃): δ 7.47-7.21 (m, 4H), 3.56 (t, J = 7.2 Hz, 4H), 3.13 (s, 6H), 1.81-1.63 (m, 6H), 0.97 (d, J = 6.3 Hz, 12H); ¹³C NMR (75 MHz, CDCl₃): δ 134.1, 130.8, 128.5, 123.1, 82.4, 70.4, 50.3, 38.4, 37.2, 25.5, 22.5; IR (ATR): νmax 2956, 2238, 1354, 1324, 1163, 962, 772, 684 cm⁻¹; ESIHRMS m/z calcd for C₂₂H₃₉N₂O₄S₂ [M+H]⁺ 453.1876, found 453.1874.
\[N,N',N''-[\text{Benzene-1,3,5-triyltris(ethyne-2,1-diyl)}]\text{tris(N-isopentylmethanesulfonamide)} \] 14.

Prepared according to general procedure VIII. Yield: 49\% (186 mg, 291 \mu mol). Solvent system for flash column chromatography: cyclohexane/EtOAc: 50/50. Yellow pasty solid; \(^1\)H NMR (300 MHz, CDCl\textsubscript{3}): \(\delta\) 7.33 (s, 3H), 3.55 (t, \(J = 7.3\) Hz, 6H), 3.13 (s, 9H), 1.81-1.62 (m, 9H), 0.97 (d, \(J = 6.3\) Hz, 18H); \(^{13}\)C NMR (75 MHz, CDCl\textsubscript{3}): \(\delta\) 133.0, 123.5, 83.0, 69.9, 50.3, 38.6, 37.2, 25.5, 22.5; IR (ATR): \(\nu_{\text{max}}\) 2958, 2236, 1583, 1356, 1325, 1164, 961, 872, 770 cm\(^{-1}\); ESIHRMS \(m/z\) calcd for C\textsubscript{30}H\textsubscript{46}N\textsubscript{3}O\textsubscript{6}S\textsubscript{3} [M+H]\(^+\) 640.2543, found 640.2536.
**Experimental Procedure and Characterization Data:**

**Cyclization to Tetrahydropyridines**

**General procedure:**

To a vigorously stirred solution of the ynamide (350 μmol) in dichloromethane (1.3 mL) under an argon atmosphere was added dropwise trifluoromethanesulfonic acid (155 μL, 1.75 mmol) at -60 °C. The resulting dark brown reaction mixture was then stirred at -60 °C for 15 minutes and poured into a 1M aqueous solution of sodium hydroxide. The layers were separated and the aqueous layer was extracted with dichloromethane. Combined organic layers were dried over magnesium sulfate, filtered and concentrated. The crude residue was finally purified by flash column chromatography over silica gel to give the desired tetrahydropyridine.

![Chemical Structure](image)

**4,4-Dimethyl-5-phenyl-1,2,3,4-tetrahydropyridine 9a.** Prepared according to the general procedure starting from 498 μmol of the corresponding ynamide (at -78°C). Yield: 70% (120 mg, 351 μmol). Solvent system for flash column chromatography: cyclohexane/EtOAc: 90/10. White solid; Mp: 137 °C; ^1H NMR (300 MHz, CDCl₃): δ 7.67 (d, J = 7.9 Hz, 2H), 7.36-7.22 (m, 5H), 7.19-7.09 (m, 2H), 6.51 (s, 1H), 3.45 (t, J = 6.0 Hz, 2H), 2.43 (s, 3H), 1.59 (t, J = 5.9 Hz, 2H), 0.93 (s, 6H); ^13C NMR (75 MHz, CDCl₃): δ 143.8, 139.7, 134.9, 129.9, 129.8, 129.7, 127.8, 127.2, 126.8, 122.3, 40.9, 37.5, 32.0, 28.6, 21.7; IR (ATR): νmax 2959, 1645, 1456, 1354, 1156, 1090, 1060, 971, 778, 705, 667 cm⁻¹; ESIHRMS m/z calcd for C₂₀H₂₄NO₂S [M+H]^+ 342.1522, found 342.1521.
4,4-Dimethyl-1-(4-nitrobenzenesulfonyl)-5-phenyl-1,2,3,4-tetrahydropyridine 9b. Yield: 53% (69 mg, 185 μmol). Solvent system for flash column chromatography: cyclohexane/EtOAc: 90/10. Yellow solid; Mp: 171 °C; ¹H NMR (300 MHz, CDCl₃): δ 8.39 (d, J = 8.6 Hz, 2H), 7.98 (d, J = 8.6 Hz, 2H), 7.35-7.27 (m, 3H), 7.18-7.08 (m, 2H), 6.49 (s, 1H), 3.51 (t, J = 5.8 Hz, 2H), 1.63 (t, J = 5.9 Hz, 2H), 0.95 (s, 6H); ¹³C NMR (75 MHz, CDCl₃): δ 150.3, 143.4, 139.0, 131.8, 129.6, 128.3, 128.0, 127.2, 124.5, 121.1, 41.2, 37.4, 32.1, 28.5; IR (ATR): νmax 2958, 1647, 1531, 1360, 1349, 1159, 1091, 1064, 973, 858, 780, 733, 705, 682, 646 cm⁻¹; ESIHRMS m/z calcd for C₁₉H₂₁N₂O₄S [M+H]+ 373.1217, found 373.1224.

4,4-Dimethyl-1-(methylsulfonyl)-5-phenyl-1,2,3,4-tetrahydropyridine 9c. Yield: 86% (80 mg, 301 μmol). Solvent system for flash column chromatography: cyclohexane/EtOAc: 80/20. Pale yellow solid; Mp: 101 °C; ¹H NMR (300 MHz, CDCl₃): δ 7.39-7.28 (m, 3H), 7.27-7.19 (m, 2H), 6.41 (s, 1H), 3.67 (t, J = 5.8 Hz, 2H), 2.94 (s, 3H), 1.86 (t, J = 5.8 Hz, 2H), 1.16 (s, 6H); ¹³C NMR (75 MHz, CDCl₃): δ 139.5, 129.7, 129.4, 127.9, 126.9, 121.7, 41.0, 38.1, 37.2, 32.2, 28.7; IR (ATR): νmax 2963, 1693, 1643, 1347, 1325, 1263, 1141, 1057, 965, 782, 702 cm⁻¹; ESIHRMS m/z calcd for C₁₄H₂₀NO₂S [M+H]+ 266.1209, found 266.1209.

The procedure for the preparative scale synthesis of 9c can be found on page S37
**5-(4-Fluorophenyl)-4,4-dimethyl-1,4-toluenesulfonyl-1,2,3,4-tetrahydropyridine 9d.** Yield: 63% (79 mg, 220 μmol). Solvent system for flash column chromatography: cyclohexane/EtOAc: 80/20. White solid; Mp: 118 °C; $^1$H NMR (300 MHz, CDCl$_3$): δ 7.67 (d, $J = 8.2$ Hz, 2H), 7.32 (d, $J = 8.1$ Hz, 2H), 7.12-7.04 (m, 2H), 7.02-6.92 (m, 2H), 6.48 (s, 1H), 3.44 (t, $J = 5.9$ Hz, 2H), 2.44 (s, 3H), 1.60 (t, $J = 5.9$ Hz, 2H), 0.92 (s, 6H); $^{13}$C NMR (75 MHz, CDCl$_3$): δ 162.0 (d, $J = 244$ Hz), 143.9, 135.5 (d, $J = 3$ Hz), 134.8, 131.3 (d, $J = 8$ Hz), 129.8, 128.8, 127.2, 122.6, 114.7 (d, $J = 21$ Hz), 40.9, 37.4, 32.0, 28.5, 21.7; IR (ATR): $\nu_{\text{max}}$ 2959, 1641, 1598, 1508, 1355, 1221, 1156, 1091, 1059, 973, 838, 683, 656 cm$^{-1}$; ESIHRMS m/z calcld for C$_{20}$H$_{23}$FNO$_2$S [M+H]$^+$ 360.1428, found 360.1425.

**5-(4-Chlorophenyl)-4,4-dimethyl-1,4-toluenesulfonyl-1,2,3,4-tetrahydropyridine 9e.** Yield: 58% (76 mg, 202 μmol). Solvent system for flash column chromatography: cyclohexane/EtOAc: 80/20. White solid; Mp: 136 °C; $^1$H NMR (300 MHz, CDCl$_3$): δ 7.66 (d, $J = 8.2$ Hz, 2H), 7.32 (d, $J = 8.1$ Hz, 2H), 7.25 (d, $J = 7.8$ Hz, 2H), 7.06 (d, $J = 8.1$ Hz, 2H), 6.50 (s, 1H), 3.44 (t, $J = 5.9$ Hz, 2H), 2.43 (s, 3H), 1.60 (t, $J = 5.9$ Hz, 2H), 0.92 (s, 6H); $^{13}$C NMR (75 MHz, CDCl$_3$): δ 143.9, 138.1, 134.8, 132.8, 131.0, 129.8, 128.5, 128.0, 127.2, 122.7, 40.8, 37.5, 32.0, 28.5, 21.7; IR (ATR): $\nu_{\text{max}}$ 2924, 1641, 1489, 1461, 1353, 1156, 1090, 1055, 968, 834, 711, 681, 667 cm$^{-1}$; ESIHRMS m/z calcld for C$_{20}$H$_{23}$ClNO$_2$S [M+H]$^+$ 376.1133, found 376.1134.
A Simple and Straightforward Entry to Tetrahydropyridines and Piperidines from Ynamides

4,4-Dimethyl-5-(4-tolyl)-1-4-toluenesulfonyl-1,2,3,4-tetrahydropyridine 9f. Yield: 48% (60 mg, 169 μmol). Solvent system for flash column chromatography: cyclohexane/EtOAc: 90/10. White solid; Mp: 128 °C; 1H NMR (300 MHz, CDCl3): δ 7.68 (d, J = 8.1 Hz, 2H), 7.32 (d, J = 8.1 Hz, 2H), 7.11 (d, J = 8.1 Hz, 2H), 7.04 (d, J = 8.1 Hz, 2H), 6.50 (s, 1H), 3.45 (t, J = 5.9 Hz, 2H), 2.44 (s, 3H), 2.35 (s, 3H), 1.60 (t, J = 5.9 Hz, 2H), 0.93 (s, 6H); 13C NMR (75 MHz, CDCl3): δ 143.7, 136.8, 136.5, 134.9, 129.8 (2C), 129.6, 128.6, 127.2, 122.1, 40.9, 37.6, 32.0, 28.6, 21.7, 21.3; IR (ATR): νmax 2962, 1641, 1459, 1353, 1328, 1155, 1089, 1055, 967, 817, 656 cm⁻¹; ESIHRMS m/z calcd for C_{21}H_{26}NO_{2}S [M+H]^+ 356.1679, found 356.1676.

5-(4-Methoxyphenyl)-4,4-dimethyl-1-4-toluenesulfonyl-1,2,3,4-tetrahydropyridine 9g. Yield: 15% (19 mg, 51 μmol). Solvent system for flash column chromatography: cyclohexane/EtOAc: 85/15. White solid; Mp: 124 °C; 1H NMR (300 MHz, CDCl3): δ 7.67 (d, J = 8.0 Hz, 2H), 7.32 (d, J = 8.0 Hz, 2H), 7.05 (d, J = 7.8 Hz, 2H), 6.82 (d, J = 7.8 Hz, 2H), 6.48 (s, 1H), 3.81 (s, 3H), 3.44 (t, J = 5.7 Hz, 2H), 2.44 (s, 3H), 1.59 (obs. t, J = 5.6 Hz, 2H), 0.92 (s, 6H); 13C NMR (75 MHz, CDCl3): δ 158.6, 143.7, 134.9, 132.1, 130.8, 129.8, 129.5, 127.2, 122.1, 113.2, 55.4, 40.9, 37.5, 32.1, 28.6, 21.7; IR (ATR): νmax 2960, 1606, 1513, 1461, 1350, 1245, 1155, 1033, 837, 817, 684, 657 cm⁻¹; ESIHRMS m/z calcd for C_{21}H_{26}NO_{3}S [M+H]^+ 372.1628, found 372.1633.
A Simple and Straightforward Entry to Tetrahydropyridines and Piperidines from Ynamides

5-Hexyl-4,4-dimethyl-1-(methylsulfonyl)-1,2,3,4-tetrahydropyridine 9h. Yield: 74% (71 mg, 260 μmol). Solvent system for flash column chromatography: cyclohexane/EtOAc: 80/20. Colorless oil; \(^1\)H NMR (300 MHz, CDCl\(_3\)): \(\delta 6.12\) (s, 1H), 3.47 (t, \(J = 5.8\) Hz, 2H), 2.82 (s, 3H), 1.97 (t, \(J = 7.5\) Hz, 2H), 1.66 (t, \(J = 5.8\) Hz, 2H), 1.45-1.22 (m, 8H), 1.05 (s, 6H), 0.88 (t, \(J = 6.8\) Hz, 3H); \(^{13}\)C NMR (75 MHz, CDCl\(_3\)): \(\delta 127.9, 117.9, 40.8, 37.8, 36.6, 31.8\) (2C), 29.6, 29.5, 29.1, 28.0, 22.8, 14.2; IR (ATR): \(\nu_{\text{max}}\) 2929, 2858, 1698, 1651, 1465, 1349, 1332, 1153, 1037, 956, 784 cm\(^{-1}\); ESIHRMS \(m/z\) calcd for C\(_{14}\)H\(_{28}\)NO\(_2\)S [M+H]\(^+\) 274.1835, found 274.1836.

4,4,5-Trimethyl-1-4-toluenesulfonyl-1,2,3,4-tetrahydropyridine 9i. Yield: 75% (73 mg, 261 μmol). Solvent system for flash column chromatography: cyclohexane/EtOAc: 90/10. Pale yellow solid; Mp: 68 °C; \(^1\)H NMR (300 MHz, CDCl\(_3\)): \(\delta 7.53\) (d, \(J = 8.3\) Hz, 2H), 7.17 (d, \(J = 8.1\) Hz, 2H), 6.18 (s, 1H), 3.21 (t, \(J = 5.8\) Hz, 2H), 2.30 (s, 3H), 1.48 (s, 3H), 1.30 (t, \(J = 5.8\) Hz, 2H), 0.77 (s, 6H); \(^{13}\)C NMR (75 MHz, CDCl\(_3\)): \(\delta 143.5, 135.2, 129.7, 127.1, 124.2, 118.6, 40.9, 36.7, 31.4, 27.4, 21.6, 16.2\); IR (ATR): \(\nu_{\text{max}}\) 2961, 1700, 1348, 1334, 1160, 1090, 1057, 957, 814, 664 cm\(^{-1}\); ESIHRMS \(m/z\) calcd for C\(_{15}\)H\(_{22}\)NO\(_2\)S [M+H]\(^+\) 280.1366, found 280.1364.
**5-Chloro-4,4-dimethyl-1-4-toluenesulfonyl-1,2,3,4-tetrahydropyridine 9j.** Yield: 62% (65 mg, 217 μmol). Solvent system for flash column chromatography: cyclohexane/EtOAc: 90/10. Pale yellow oil; $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 7.66 (d, $J = 8.0$ Hz, 2H), 7.32 (d, $J = 8.0$ Hz, 2H), 6.74 (s, 1H), 3.35 (t, $J = 5.7$ Hz, 2H), 2.43 (s, 3H), 1.56 (t, $J = 5.6$ Hz, 2H), 1.01 (s, 6H); $^{13}$C NMR (75 MHz, CDCl$_3$): $\delta$ 144.2, 134.7, 130.0, 127.2, 125.8, 121.9, 40.9, 36.8, 34.5, 27.3, 21.7; IR (ATR): $\nu_{\text{max}}$ 2966, 1644, 1596, 1460, 1359, 1178, 1162, 1094, 1071, 966, 760, 682, 655 cm$^{-1}$; ESIHRMS m/z calcd for C$_{14}$H$_{19}$ClNO$_2$S [M+H]$^+$ 300.0820, found 300.0819.

**4,4-Dimethyl-1-4-toluenesulfonyl-1,2,3,4-tetrahydropyridine 9k.** Prepared according to the general procedure starting from 441 μmol of the corresponding ynamic. Yield: 12% (14 mg, 53 μmol). Solvent system for flash column chromatography: cyclohexane/EtOAc: 90/10. Colorless oil; $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 7.66 (d, $J = 7.8$ Hz, 2H), 7.30 (d, $J = 7.9$ Hz, 2H), 6.51 (d, $J = 8.3$ Hz, 1H), 4.77 (d, $J = 8.3$ Hz, 1H), 3.34 (t, $J = 5.8$ Hz, 2H), 2.42 (s, 3H), 1.43 (t, $J = 5.7$ Hz, 2H), 0.89 (s, 6H); $^{13}$C NMR (75 MHz, CDCl$_3$): $\delta$ 143.6, 135.2, 129.8, 127.2, 122.7, 119.1, 41.0, 35.6, 29.9, 29.1, 21.7; IR (ATR): $\nu_{\text{max}}$ 2961, 1652, 1538, 1349, 1331, 1160, 1092, 960, 815, 719, 673, 634 cm$^{-1}$; ESIHRMS m/z calcd for C$_{14}$H$_{20}$NO$_2$S [M+H]$^+$ 266.1209, found 266.1215.
2,4,4-Trimethyl-5-phenyl-1,4-toluenesulfonyl-1,2,3,4-tetrahydropyridine 9m. Yield: 51% (63 mg, 177 μmol). Solvent system for flash column chromatography: cyclohexane/EtOAc: 90/10. White solid; Mp: 88 °C; ¹H NMR (300 MHz, CDCl₃): δ 7.69 (d, J = 8.2 Hz, 2H), 7.36-7.23 (m, 5H), 7.18-7.10 (m, 2H), 6.47 (s, 1H), 3.82 (app. sext., J = 6.2 Hz, 1H), 2.44 (s, 3H), 1.62 (A of ABX syst., J = 13.5 and 6.9 Hz, 1H), 1.48 (d, J = 6.7 Hz, 3H), 1.43 (obs. B of ABX syst., J = 13.7 and 5.3 Hz, 1H), 1.00 (s, 3H), 0.70 (s, 3H); ¹³C NMR (75 MHz, CDCl₃): δ 143.7, 139.7, 135.4, 131.9, 129.7, 129.6, 127.9, 127.3, 126.9, 122.4, 49.2, 45.9, 32.1, 29.5, 28.8, 22.2, 21.7; IR (ATR): νmax 2955, 1636, 1591, 1353, 1333, 1160, 1090, 1004, 867, 758, 706, 672 cm⁻¹; ESIHRMS m/z calcd for C₂₁H₂₅NO₂S [M+H]⁺ 356.1679, found 356.1679.

2,4,4-Trimethyl-1-(methylsulfonyl)-5-phenyl-1,2,3,4-tetrahydropyridine 9n. Yield: 60% (59 mg, 211 μmol). Solvent system for flash column chromatography: cyclohexane/EtOAc: 80/20. White solid; Mp: 52 °C; ¹H NMR (300 MHz, CDCl₃): δ 7.33-7.22 (m, 3H), 7.21-7.13 (m, 2H), 6.29 (s, 1H), 4.11 (app. sext., J = 6.2 Hz, 1H), 2.91 (s, 3H), 1.88 (A of ABX syst., J = 13.8 and 5.3 Hz, 1H), 1.80 (B of ABX syst., J = 13.8 and 6.2 Hz, 1H), 1.50 (d, J = 6.6 Hz, 3H), 1.12 (s, 3H), 1.11 (s, 3H); ¹³C NMR (75 MHz, CDCl₃): δ 139.4, 130.2, 129.6, 127.8, 126.9, 121.4, 49.4, 46.3, 38.9, 32.2, 29.9, 28.9, 21.7; IR (ATR): νmax 2963, 1644, 1348, 1329, 1151, 1007, 961, 871, 767, 703 cm⁻¹; ESIHRMS m/z calcd for C₁₅H₂₂NO₂S [M+H]⁺ 280.1366, found 280.1366.
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2,4,4,5-Tetramethyl-1-4-toluenesulfonyl-1,2,3,4-tetrahydropyridine 9o. This product is contaminated with 4% of an inseparable amide resulting from the hydrolysis of the starting ynamide 5o. Corrected yield: 41% (44 mg, 150 μmol including 4% of the amide). Solvent system for flash column chromatography: cyclohexane/EtOAc: 80/20. Pale yellow oil; $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 7.65 (d, $J = 7.8$ Hz, 2H), 7.27 (d, $J = 7.8$ Hz, 2H), 6.27 (app. s, 1H), 3.81 (app. sext., $J = 6.1$ Hz, 1H), 2.40 (s, 3H), 1.64 (d, $J = 1.4$ Hz, 3H), 1.43 (A of ABX syst., $J = 13.9$ and 5.0 Hz, 1H), 1.31 (d, $J = 6.8$ Hz, 3H), 1.19 (B of ABX syst., $J = 14.0$ and 5.3 Hz, 1H), 1.02 (s, 3H), 0.67 (s, 3H); $^{13}$C NMR (75 MHz, CDCl$_3$): $\delta$ 143.3, 135.9, 129.5, 127.1, 125.7, 117.8, 49.0, 43.9, 31.3, 29.0, 27.6, 21.6, 21.5, 16.0; IR (ATR): $\nu_{\text{max}}$ 2946, 1670, 1598, 1337, 1165, 1090, 981, 813, 670, 613 cm$^{-1}$; ESIHRMS m/z calcd for C$_{16}$H$_{24}$NO$_2$S [M+H]$^+$ 294.1522, found 294.1522.

4-Isobutyl-4-methyl-1-(methylsulfonyl)-5-phenyl-1,2,3,4-tetrahydropyridine 9p. Prepared according to the general procedure starting from 256 μmol of the corresponding ynamide. Yield: 41% (32 mg, 104 μmol). Solvent system for flash column chromatography: cyclohexane/EtOAc: 85/15. Colorless oil; $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 7.31-7.24 (m, 3H), 7.23-7.18 (m, 2H), 6.40 (s, 1H), 3.74 (A of ABXY syst., $J = 10.7$, 6.7 and 3.9 Hz, 1H), 3.70 (B of ABXY syst., $J = 10.7$, 6.7 and 3.8 Hz, 1H), 2.89 (s, 3H), 2.03 (X of ABXY syst., $J = 13.4$, 9.3 and 3.7 Hz, 1H), 1.74 (Y of ABXY syst., $J = 10.1$, 6.7 and 3.3 Hz, 1H), 1.61-1.49 (m, 1H), 1.43 (A’ of A’B’X’ syst., $J = 14.3$ and 9.0 Hz, 1H), 1.31 (B’ of A’B’X’ syst., $J = 14.3$ and 5.9 Hz, 1H), 1.22 (s, 3H), 0.87 (d, $J =$
6.7 Hz, 3H), 0.70 (d, J = 6.7 Hz, 3H); $^{13}$C NMR (75 MHz, CDCl$_3$): $\delta$ 139.7, 129.8, 129.7, 127.9, 126.8, 122.4, 48.4, 40.8, 37.1, 35.8, 34.5, 27.8, 25.7, 25.3, 24.1; IR (ATR): $\nu_{\text{max}}$ 2956, 2869, 1632, 1493, 1350, 1333, 1167, 1151, 1056, 959, 765, 739, 704 cm$^{-1}$; ESIHRMS m/z calcd for C$_{17}$H$_{26}$NO$_2$S [M+H]$^+$ 308.1679, found 308.1686.

$^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 7.63 (d, J = 8.1 Hz, 2H), 7.27 (d, J = 8.1 Hz, 2H), 6.33 (s, 1H), 3.26 (t, J = 5.7 Hz, 2H), 2.39 (s, 3H), 1.65-1.20 (m, 13H), 1.10-0.95 (m, 2H); $^{13}$C NMR (75 MHz, CDCl$_3$): $\delta$ 143.4, 135.0, 129.6, 127.1, 124.6, 119.3, 40.3, 34.5, 33.8, 29.0, 25.7, 21.6, 21.1, 16.3; IR (ATR): $\nu_{\text{max}}$ 2925, 2856, 1655, 1597, 1453, 1350, 1166, 1046, 962, 814, 663 cm$^{-1}$; ESIHRMS m/z calcd for C$_{18}$H$_{26}$NO$_2$S [M+H]$^+$ 320.1679, found 320.1689.

1-Methyl-3-4-toluenesulfonyl-3-azaspiro[5.5]undec-1-ene 9q. Yield: 92% (103 mg, 322 μmol).

Solvent system for flash column chromatography: cyclohexane/EtOAc: 85/15. Colorless oil; $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 7.63 (d, J = 8.1 Hz, 2H), 7.27 (d, J = 8.1 Hz, 2H), 6.33 (s, 1H), 3.26 (t, J = 5.7 Hz, 2H), 2.39 (s, 3H), 1.65-1.20 (m, 13H), 1.10-0.95 (m, 2H); $^{13}$C NMR (75 MHz, CDCl$_3$): $\delta$ 143.4, 135.0, 129.6, 127.1, 124.6, 119.3, 40.3, 34.5, 33.8, 29.0, 25.7, 21.6, 21.1, 16.3; IR (ATR): $\nu_{\text{max}}$ 2925, 2856, 1655, 1597, 1453, 1350, 1166, 1046, 962, 814, 663 cm$^{-1}$; ESIHRMS m/z calcd for C$_{18}$H$_{26}$NO$_2$S [M+H]$^+$ 320.1679, found 320.1689.

$^{cis}$-4a-Methyl-2-(methylsulfonyl)-4-phenyl-1,2,4a,5,6,7,8,8a-octahydroisoquinoline and $^\text{trans}$-4a-Methyl-2-(methylsulfonyl)-4-phenyl-1,2,4a,5,6,7,8,8a-octahydroisoquinoline 9r. Two diastereoisomers are obtained with a dr of 78:22 (measured by $^1$H NMR analysis of the crude reaction mixture). These diastereoisomers are contaminated with 7% of an inseparable amide resulting from the hydrolysis of the starting ynamide 5r. Corrected yield (mixture of...
diastereoisomers): 77% (89 mg, 291 μmol including 7% of the amide). Solvent system for flash
column chromatography (mixture of diastereoisomers): cyclohexane/EtOAc: 80/20. Colorless
oil; \(^1\)H NMR (300 MHz, CDCl\(_3\)): \(\delta\) 7.31-7.23 (m, 5H), 6.45 and 6.35 (s, 0.78H, s, 0.22 H,
diastereoisomers), 3.63 (A of ABX syst., J = 11.8 and 3.2 Hz, 1H), 3.54 (B of ABX syst., J = 11.7
and 2.7 Hz, 1H), 2.91 and 2.89 (s, 2.34 H, s, 0.66 H, diastereoisomers), 1.84-0.95 (m, 9H), 1.35 (s,
3H); \(^13\)C NMR (75 MHz, CDCl\(_3\)): \(\delta\) 139.6 (major diastereoisomer), 138.8 (minor diastereoisomer),
129.4 (minor diastereoisomer), 129.3 (major diastereoisomer), 127.9 (major diastereoisomer),
127.8 (minor diastereoisomer), 126.7 (2C, major diastereoisomer), 125.7 (minor diastereoisomer),
122.4 (major diastereoisomer), 121.0 (minor diastereoisomer), 46.1 (minor diastereoisomer),
46.0 (major diastereoisomer), 41.6 (minor diastereoisomer), 41.0 (major diastereoisomer),
37.6 (major diastereoisomer), 37.0 (minor diastereoisomer), 36.2 (minor diastereoisomer),
36.0 (major diastereoisomer), 35.7 (major diastereoisomer), 35.1 (minor diastereoisomer),
32.2 (major diastereoisomer), 27.6 (major diastereoisomer), 25.9 (minor diastereoisomer),
25.4 (major diastereoisomer), 25.1 (minor diastereoisomer), 22.8 (major diastereoisomer),
21.4 (minor diastereoisomer), 19.7 (minor diastereoisomer); IR (ATR): \(\nu_{\text{max}}\)
2929, 2857, 1632, 1447, 1346, 1335, 1150, 1028, 960, 806, 747, 733, 703 cm\(^{-1}\); ESIHRMS m/z
calcd for C\(_{17}\)H\(_{24}\)NO\(_2\)S [M+H]\(^+\) 306.1522, found 306.1536.

\(\text{N-Methyl-N-}\(\text{1-\text{(methylsulfonyl)}}\)-5-phenyl-1,2,3,6-tetrahydropyridin-4-yl)methanesulfonamide
9s. Prepared according the general procedure. Yield: 48% (58 mg, 168 μmol). Solvent system for
flash column chromatography: cyclohexane/EtOAc: 30/70. Yellow solid; Mp: 143 °C; \(^1\)H NMR
(300 MHz, CDCl\(_3\)): \(\delta\) 7.53 (d, J = 7.8 Hz, 2H), 7.30 (t, J = 7.8 Hz, 2H), 7.25-7.16 (m, 1H), 3.84-3.70
(m, 1H), 3.60-3.46 (m, 1H), 3.36-3.22 (m, 4H), 2.91-2.80 (m, 1H), 2.74 (s, 3H), 2.47-2.17 (m, 5H);
13C NMR (75 MHz, CDCl3): δ151.8, 135.2, 132.1, 128.8, 127.2, 101.0, 47.3, 42.9, 41.7, 40.3, 39.7, 27.4; IR (ATR): νmax 1565, 1435, 1337, 1316, 1154, 1124, 922, 770, 727, 697 cm⁻¹; ESIHRMS m/z calcd for C14H21N2O4S2 [M+H]+ 345.0937, found 345.0945.

1,4-Bis(4,4-dimethyl-1-(methylsulfonyl)-1,4,5,6-tetrahydropyridin-3-yl)benzene 11. Prepared according to the general procedure. Yield: 81% (128 mg, 283 μmol). Solvent system for flash column chromatography: dichloromethane/EtOAc: 50/50. Orange solid; Mp: 250 °C (dec.); 1H NMR (300 MHz, CDCl3): δ7.11 (app. s, 4H), 6.38 (s, 2H), 3.63 (t, J = 5.6 Hz, 4H), 2.90 (s, 6H), 1.82 (t, J = 5.7 Hz, 4H), 1.12 (s, 12H); 13C NMR (75 MHz, CDCl3): δ138.0, 129.1, 129.0, 121.7, 41.0, 38.1, 37.2, 32.2, 28.8; IR (ATR): νmax 2970, 1626, 1359, 1342, 1320, 1157, 1143, 1066, 958, 830, 782 cm⁻¹; ESIHRMS m/z calcd for C22H33N2O4S2 [M+H]+ 453.1876, found 453.1876.

1,3-Bis[4,4-dimethyl-1-(methylsulfonyl)-1,4,5,6-tetrahydropyridin-3-yl]benzene 13. Prepared according to the general procedure. Yield: 61% (97 mg, 214 μmol). Solvent system for flash column chromatography: dichloromethane/EtOAc: 80/20. Yellow solid; Mp: 176 °C; 1H NMR (300 MHz, CDCl3): δ7.27-7.17 (m, 1H), 7.08 (d, J = 7.5 Hz, 2H), 7.00 (s, 1H), 6.36 (s, 2H), 3.62 (t, J = 5.6 Hz, 4H), 2.91 (s, 6H), 1.82 (t, J = 5.7 Hz, 4H), 1.10 (s, 12H); 13C NMR (75 MHz, CDCl3): δ 138.9, 131.0, 129.1, 128.3, 127.3, 121.7, 41.0, 38.0, 37.3, 32.2, 28.7; IR (ATR): νmax 2963, 1638,
1363, 1325, 1153, 1140, 980, 955, 867, 778 cm\(^{-1}\); ESIHRMS \(m/z\) calcd for \(\text{C}_{22}\text{H}_{33}\text{N}_{2}\text{O}_{4}\text{S}_{2}\) \([\text{M+H}]^+\) 453.1876, found 453.1876.

1,3,5-Tris(4,4-dimethyl-1-(methylsulfonyl)-1,4,5,6-tetrahydropyridin-3-yl)benzene \hspace{1cm} 15.
Prepared according to the general procedure starting from 277 \(\mu\)mol of the corresponding ynamide. Yield: 33\% (58 mg, 91 \(\mu\)mol). Solvent system for flash column chromatography: dichloromethane/EtOAc: 50/50. White solid; Mp: 74 °C; \(^1\)H NMR (300 MHz, CDCl\(_3\)): \(\delta\) 6.90 (s, 3H), 6.35 (s, 3H), 3.62 (br. t, \(J = 5.7\) Hz, 6H), 2.92 (s, 9H), 1.81 (br. t, \(J = 5.8\) Hz, 6H), 1.09 (s, 18H); \(^{13}\)C NMR (75 MHz, CDCl\(_3\)): \(\delta\) 138.4, 129.6, 128.8, 121.7, 41.0, 38.0, 37.4, 32.3, 28.8; IR (ATR): \(\nu_{\text{max}}\) 2962, 1644, 1348, 1327, 1259, 1155, 1144, 958, 779 cm\(^{-1}\); ESIHRMS \(m/z\) calcd for \(\text{C}_{30}\text{H}_{46}\text{N}_{3}\text{O}_{6}\text{S}_{3}\) \([\text{M+H}]^+\) 640.2543, found 640.2537.
Experimental Procedure and Characterization Data:
Preparative Scale Cyclization to Tetrahydropyridine 9c

Experimental procedure:

To a vigorously stirred solution of 5c (1.5 g, 5.6 mmol) in dichloromethane (20 mL) under an argon atmosphere was added dropwise trifluoromethanesulfonic acid (2.5 mL, 28.3 mmol) at -60 °C. The resulting dark brown reaction mixture was then stirred at -60 °C for 1 hour and poured into a 1M aqueous solution of sodium hydroxide. The layers were separated and the aqueous layer was extracted with dichloromethane. Combined organic layers were dried over magnesium sulfate, filtered and concentrated. The crude residue was finally purified by flash column chromatography over silica gel (cyclohexane/EtOAc: 80/20) to give the desired tetrahydropyridine 9c (1.28 g, 4.82 mmol, 85%) as a pale yellow solid.

Characterization data for this tetrahydropyridine can be found on page S26.
Experimental Procedure and Characterization Data:

Cyclization to Piperidines

General procedure:

To a vigorous stirred solution of the appropriate ynamide (500 μmol) in freshly distilled dichloromethane (1.9 mL) under an argon atmosphere was added dropwise trifluoromethanesulfonic acid (220 μL, 2.5 mmol) at -60 °C. The resulting dark brown reaction mixture was then stirred at -60 °C for 15 minutes and the nucleophile (2.5 mmol) was added. The reaction mixture was then stirred at the temperature and for a time indicated in Figure 3 and then poured into a 1M aqueous solution of sodium hydroxide. The layers were separated and the aqueous layer was extracted with dichloromethane. Combined organic layers were dried over magnesium sulfate, filtered and concentrated. The crude residue was finally purified by flash column chromatography over silica gel to give the desired piperidine.

\[ \text{trans-2-(2,4-Dimethoxyphenyl)-4,4-dimethyl-1-(methylsulfonyl)-3-phenylpiperidine} \] \hspace{1cm} 16a

Prepared according to the general procedure with 1,3-dimethoxybenzene at -60°C during 3 h; two atropoisomers are obtained in a 86:14 ratio (measured by \(^1\)H NMR analysis of the crude reaction mixture). Yield: 94% (189 mg, 468 μmol). Solvent system for flash column chromatography: cyclohexane/EtOAc: 80/20. For analytical purposes, and in order to assign the relative cis/trans configuration of the two atropoisomers, a sample of each could be obtained by recrystallization from cyclohexane.

- **Major atropoisomer** (obtained as a solid after the recrystallization). White solid; Mp: 128 °C; \(^1\)H NMR (400 MHz, CDCl\(_3\)): \( \delta \) 7.15 (d, \( J = 8.5 \) Hz, 1H), 7.11-7.00 (m, 5H), 6.28 (dd, \( J = \)
8.4 and 2.4 Hz, 1H), 6.22 (d, J = 2.3 Hz, 1H), 5.20 (d, J = 11.1 Hz, 1H), 3.88 (A of ABXY syst., J = 12.9, 5.5 and 5.5 Hz, 1H), 3.72 (s, 3H), 3.68 (s, 3H), 3.50 (B of ABXY syst., J = 13.4, 6.7 and 6.7 Hz, 1H), 3.19 (d, J = 11.1 Hz, 1H), 2.38 (s, 3H), 1.81-1.76 (m, 2H), 1.05 (s, 3H), 0.80 (s, 3H); 13C NMR (75 MHz, CDCl3): δ 160.1, 158.2, 139.1, 131.5 (br.), 130.0 (br.), 127.3, 126.3, 120.4, 104.2, 98.3, 57.0 (br.), 55.4, 55.2, 42.6 (br.), 40.1, 39.8, 33.2, 31.1, 22.3; IR (ATR): νmax 2954, 2910, 1613, 1587, 1508, 1357, 1224, 1153, 1041, 796, 701 cm⁻¹; ESIHRMS m/z calcd for C22H30NO4S [M+H]+ 404.1890, found 404.1883.

The relative configuration of this piperidine was attributed on the basis of coupling constants and NOE experiments.

• Minor atropoisomer (obtained from the mother liquor after the recrystallization). White solid; Mp: 156 °C; 1H NMR (600 MHz, CDCl3): δ 7.36 (d, J = 7.5 Hz, 2H), 7.29 (t, J = 7.8 Hz, 2H), 7.17 (t, J = 7.2 Hz, 1H), 7.03 (d, J = 9.0 Hz, 1H), 6.40 (s, 1H), 6.38 (d, J = 8.4 Hz, 1H), 4.70 (d, J = 10.5 Hz, 1H), 4.63 (d, J = 10.5 Hz, 1H), 3.86 (s, 3H), 3.71 (s, 3H), 3.56 (app. q, J = 9.1 Hz, 1H), 3.08 (app. t, J = 9.2 Hz, 1H), 2.28 (app. q, J = 11.2 Hz, 1H), 1.86 (s, 3H), 1.73 (dd, J = 10.7 and 8.6 Hz, 1H), 1.07 (s, 3H), 0.77 (s, 3H); 13C NMR (75 MHz, CDCl3): δ 159.0, 158.2, 143.5, 131.8, 128.9, 128.5, 126.3, 125.3, 103.9, 98.0, 71.0, 55.6, 55.5, 45.1, 44.4, 42.6, 40.1, 38.6, 27.8, 24.4; IR (ATR): νmax 2961, 2904, 1610, 1585, 1504, 1312, 1209, 1142, 1043, 769, 702 cm⁻¹; ESIHRMS m/z calcd for C22H30NO4S [M+H]+ 404.1890, found 404.1914.

The relative configuration of this piperidine was attributed on the basis of coupling constants and NOE experiments.
A Simple and Straightforward Entry to Tetrahydropyridines and Piperidines from Ynamides

**trans-2-(2,4-Dimethoxyphenyl)-4,4-dimethyl-1-4-toluenesulfonyl-3-phenylpiperidine 16a′.**

Prepared according to the general procedure starting from 1.35 mmol of the corresponding ynamide with 1,3-dimethoxybenzene at -60°C during 3 h; two atropoisomers are obtained in a 61:39 ratio (measured by $^1$H NMR analysis of the crude reaction mixture). Yield: 54% (348 mg, 726 μmol). Solvent system for flash column chromatography: cyclohexane/EtOAc: 85/15.

For analytical purposes, and in order to assign the relative cis/trans configuration of the two atropoisomers, a sample of the major atropoisomer could be obtained by recrystallization from cyclohexane.

- **Major atropoisomer (obtained as a solid after the recrystallization).** White solid; Mp: 180 °C; $^1$H NMR (400 MHz, CDCl$_3$): δ 7.38 (d, $J = 7.1$ Hz, 2H), 7.30 (t, $J = 7.6$ Hz, 2H), 7.18 (t, $J = 7.3$ Hz, 1H), 7.12 (d, $J = 8.3$ Hz, 2H), 7.08 (d, $J = 8.3$ Hz, 2H), 7.02 (d, $J = 8.6$ Hz, 1H), 6.36 (dd, $J = 8.5$ and 2.5 Hz, 1H), 6.20 (d, $J = 2.5$ Hz, 1H), 4.60 (app. s, 2H), 3.75 (s, 3H), 3.64 (s, 3H), 3.38-3.31 (m, 1H), 3.05-3.00 (m, 1H), 2.37 (s, 3H), 2.21-2.14 (m, 1H), 1.62-1.57 (m, 1H), 0.90 (s, 3H), 0.79 (s, 3H); $^1$H NMR (600 MHz, C$_6$D$_6$): δ 7.44 (d, $J = 8.4$ Hz, 2H), 7.34 (d, $J = 9.2$ Hz, 1H), 7.27 (d, $J = 8.2$ Hz, 2H), 7.16-7.14 (obs. m, 2H), 7.03 (t, $J = 7.4$ Hz, 1H), 6.78 (d, $J = 8.0$ Hz, 2H), 6.23-6.21 (m, 2H), 4.99 (d, $J = 9.9$ Hz, 1H), 4.75 (d, $J = 9.9$ Hz, 1H), 3.52-3.47 (m, 1H), 3.30 (s, 3H), 3.16 (s, 3H), 2.97-2.94 (m, 1H), 2.09-2.04 (m, 1H), 1.94 (s, 3H), 1.40-1.35 (m, 1H), 1.06 (s, 3H), 0.78 (s, 3H); $^{13}$C NMR (75 MHz, CDCl$_3$): δ 159.1, 158.0, 143.9, 142.4, 137.0, 132.3, 129.2, 129.0, 128.5, 127.5, 126.2, 124.1, 103.8, 98.2, 71.0, 55.3, 55.2; 45.9, 45.1, 43.2, 38.4, 28.0, 24.8, 21.6; IR (ATR): $\nu_{\text{max}}$ 2973, 2949, 1608, 1503, 1467, 1311, 1211, 1156, 1094, 1036, 812, 701, 674 cm$^{-1}$; ESIHRMS m/z calcd for C$_{28}$H$_{34}$NO$_4$S [M+H]$^+$ 480.2203, found 480.2198.

The relative configuration of this piperidine was attributed on the basis of coupling constants and NOE experiments (in C$_6$D$_6$).
• **Mixture of atropoisomers.** $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 7.43-7.05 (m, 10H), 6.36 and 6.10 (dd, $J = 8.5$ and 2.5 Hz, 0.61H, dd, $J = 8.4$ and 2.3 Hz, 0.39H, atropoisomers), 6.20 and 5.89 (d, $J = 2.5$ Hz, 0.61H, d, $J = 2.3$ Hz, 0.39H atropoisomers), 5.12 (d, $J = 10.6$ Hz, 0.39H, minor atropoisomer), 4.60 (app. s, 1.22H, major atropoisomer), 3.97-3.90 (m, 0.39H, minor atropoisomer), 3.75 (s, 1.83H, major atropoisomer), 3.64 (s, 3H), 3.57-3.50 (m, 0.39H, minor atropoisomer), 3.47 (s, 1.17H, minor atropoisomer), 3.38-3.31 (m, 0.61H, major atropoisomer), 3.11 (d, $J = 10.6$ Hz, 0.39H, minor atropoisomer), 3.05-3.00 (m, 0.61H, major atropoisomer), 2.37 and 2.34 (s, 1.83H, s, 1.17H, atropoisomers), 2.21-2.14 (m, 0.61H, major atropoisomer), 1.82-1.75 (m, 0.78H, minor atropoisomer), 1.62-1.57 (m, 0.61H, major atropoisomer), 0.96 and 0.90 (s, 1.17H, s, 1.83H, atropoisomers), 0.79 and 0.77 (s, 1.83H, s, 1.17H, atropoisomers).

The relative configuration of the minor atropoisomer was attributed on the basis of the coupling constant obtained from the $^1$H NMR spectra of the mixture of atropoisomers.

![Diagram of cis-3-Chloro-2-(2,4-dimethoxyphenyl)-4,4-dimethyl-1-toluenesulfonylpiperidine 16b.](image)

**cis-3-Chloro-2-(2,4-dimethoxyphenyl)-4,4-dimethyl-1-toluenesulfonylpiperidine 16b.** Prepared according to the general procedure starting from 327 μmol of the corresponding ynamide with 1,3-dimethoxybenzene at -60°C during 3 h; a single diastereoisomer is obtained (dr > 95:5 as measured by $^1$H NMR analysis of the crude reaction mixture). Yield: 85% (122 mg, 279 μmol). Solvent system for flash column chromatography: cyclohexane/EtOAc: 80/20. White
pasty solid; $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 7.52 (d, $J = 8.1$ Hz, 2H), 7.19 (d, $J = 8.4$ Hz, 1H), 7.14 (d, $J = 8.3$ Hz, 2H), 6.39 (dd, $J = 8.5$ and 2.5 Hz, 1H), 6.24 (d, $J = 2.4$ Hz, 1H), 5.17 (d, $J = 5.7$ Hz, 1H), 4.51 (d, $J = 5.7$ Hz, 1H), 3.77 (s, 3H), 3.73-3.65 (obs m, 1H), 3.70 (s, 3H), 3.64-3.55 (B of ABXY syst., $J = 13.8$, 5.3 and 5.3 Hz, 1H), 2.38 (s, 3H), 1.78 (X of ABXY syst., $J = 13.9$, 9.5 and 5.1 Hz, 1H), 1.38 (Y of ABXY syst., $J = 13.7$, 6.3 and 5.0 Hz, 1H), 1.03 (s, 3H), 0.87 (s, 3H); $^{13}$C NMR (75 MHz, CDCl$_3$): $\delta$ 160.5, 157.6, 142.6, 137.5, 129.7, 128.9, 127.5, 119.5, 104.0, 98.4, 68.9, 60.1, 55.4, 55.3, 41.1, 34.7, 34.6, 27.3, 26.3, 21.6; IR (ATR): $\nu_{\text{max}}$ 2957, 1613, 1587, 1505, 1465, 1336, 1209, 1154, 1034, 931, 738, 673 cm$^{-1}$; ESIHRMS m/z calcd for C$_{22}$H$_{29}$ClNO$_4$S [M+H]$^+$ 438.1500, found 438.1503.

The relative configuration of this piperidine was attributed on the basis of coupling constants and NOE experiments.

(trans)-4,4-Dimethyl-1-(methylsulfonyl)-3-phenylpiperidine-2-carbonitrile and cis-4,4-Dimethyl-1-(methylsulfonyl)-3-phenylpiperidine-2-carbonitrile 16c. Prepared according to the general procedure with trimethylsilyl cyanide at room temperature during 4h; two unseparable diastereoisomers are obtained with a dr of 88:12 (measured by $^1$H NMR analysis of the crude reaction mixture); their configuration could not be unambiguously assigned on the basis of 1D and 2D NMR experiments. Yield (mixture of diastereoisomers): 79% (116 mg, 397 $\mu$mol). Solvent system for flash column chromatography (mixture of diastereoisomers): cyclohexane/EtOAc: 70/30. White solid; Mp: 128 °C; $^1$H NMR (600 MHz, CDCl$_3$): $\delta$ 7.41-7.26 (m, 5H), 4.99 and 4.87 (br. s, 0.88 H, d, $J = 5.0$ Hz, 0.12 H, diastereoisomers), 3.86 and 3.80 (A of
ABXY syst., \( J = 12.4, 3.8 \) and \( 3.8 \) Hz, 0.88 H, br. app. d, \( J = 12.5 \) Hz, 0.12 H, diastereoisomers), 3.39-3.33 (m, 1H), 3.03 and 3.00 (s, 2.64H, s, 0.36H, diastereoisomers), 2.93 and 2.90 (br. s, 0.88H, d, \( J = 4.9 \) Hz, 0.12H, diastereoisomers), 2.00 and 1.79 (X of ABXY syst., \( J = 14.1, 12.0 \) and 5.0 Hz, 0.88H, X of ABXY syst., \( J = 13.5, 13.5 \) and 4.6 Hz, 0.12H, diastereoisomers), 1.69 and 1.49 (Y of ABXY syst., \( J = 13.4, 2.6 \) and 2.6 Hz, 0.12H, Y of ABXY syst., \( J = 14.6, 2.7 \) and 2.7 Hz, 0.88H, diastereoisomers), 1.40 and 1.34 (s, 2.64H, s, 0.36H, diastereoisomers), 0.81 and 0.67 (s, 2.64H, s, 0.36H).

\(^{13}\text{C NMR} (75 \text{ MHz, CDCl}_3): \delta 140.1 \text{ (major diastereoisomer)}, 135.8 \text{ (minor diastereoisomer)}, 130.0 \text{ (2C, minor diastereoisomer), 128.6 \text{ (2C, major diastereoisomer), 128.3 (minor diastereoisomer), 127.9 (major diastereoisomer), 118.4 (minor diastereoisomer), 118.1 (major diastereoisomer), 54.5 \text{ (minor diastereoisomer), 52.8 \text{ (major diastereoisomer), 48.0 (minor diastereoisomer), 47.4 \text{ (major diastereoisomer), 40.3 (minor diastereoisomer), 39.9 (minor diastereoisomer), 39.6 \text{ (major diastereoisomer), 37.0 \text{ (major diastereoisomer), 36.9 (minor diastereoisomer), 33.8 \text{ (major diastereoisomer), 33.4 (minor diastereoisomer), 32.0 \text{ (major diastereoisomer), 31.1 (minor diastereoisomer), 29.7 (major diastereoisomer), 28.1 (major diastereoisomer), 20.3 (minor diastereoisomer); IR (ATR): } \nu_{\text{max}} 2958, 1454, 1341, 1321, 1156, 1055, 960, 927, 777, 696 \text{ cm}^{-1}; \text{ ESIHRMS } m/z \text{ calcd for } \text{C}_{15}\text{H}_{21}\text{N}_{2}\text{O}_2\text{S } [\text{M+H}]^+ \text{ 293.1318, found 293.1325.}}\

4,4-Dimethyl-1-(methylsulfonyl)-3-phenylpiperidine 16d. Prepared according to the general procedure with triethylsilane at room temperature during 2 h. Yield: 70% (94 mg, 352 \text{ \textmu mol}). Solvent system for flash column chromatography: cyclohexane/EtOAc: 75/25. White solid; Mp: 143 \degree\text{C}; \(^1\text{H NMR} (300 \text{ MHz, CDCl}_3): \delta 7.33-7.20 \text{ (m, 3H), 7.15-7.05 \text{ (m, 2H), 3.75-3.60 \text{ (m, 2H), 3.19 \text{ (B’ of A’B’X’ syst., } J = 11.9 \text{ and 11.9 Hz, 1H), 2.98 \text{ (B of ABXY syst., } J = 15.4, J = 12.4 \text{ and } J = 3.0 \text{ Hz, 1H), 2.83 \text{ (s, 3H), 2.72 \text{ (X’ of A’B’X’ syst., } J = 11.9 \text{ and 3.9 Hz, 1H), 1.73 \text{ (X of ABXY syst., } J =}

\text{s43}
17.6, 13.1 and 4.6 Hz, 1H), 1.57 (Y of ABXY syst., \( J = 13.6, 3.0 \) and 3.0 Hz, 1H), 0.89 (s, 3H), 0.87 (s, 3H); \(^{13}\)C NMR (75 MHz, CDCl\(_3\)): \( \delta \) 139.3, 129.2, 128.0, 127.0, 51.9, 46.3, 42.6, 39.9, 35.1, 32.7, 30.0, 19.3; IR (ATR): \( \nu_{\text{max}} \) 2967, 1474, 1328, 1150, 1049, 969, 936, 785, 768, 698 cm\(^{-1}\); ESIHRMS \( m/z \) calcd for C\(_{14}\)H\(_{22}\)NO\(_2\)S [M+H]\(^+\) 268.1366, found 268.1368.

\[ \text{Ts} \]
\[ \text{Cl} \]
\[ \text{16e} \]

3-Chloro-4,4-dimethyl-1-4-toluenesulfonylpiperidine 16e. Prepared according to the general procedure with triethylsilane at room temperature during 2 h. Yield: 56% (84 mg, 278 \( \mu \)mol). Solvent system for flash column chromatography: cyclohexane/EtOAc: 85/15. Pale brown solid; Mp: 98 °C; \(^1\)H NMR (300 MHz, CDCl\(_3\)): \( \delta \) 7.65 (d, \( J = 8.3 \) Hz, 2H), 7.34 (d, \( J = 8.2 \) Hz, 2H), 3.87-3.76 (m, 2H), 3.58-3.49 (m, 1H), 2.65-2.50 (m, 2H), 2.44 (s, 3H), 1.66-1.58 (m, 2H), 1.04 (s, 3H), 0.84 (s, 3H); \(^{13}\)C NMR (75 MHz, CDCl\(_3\)): \( \delta \) 143.9, 133.6, 130.0, 127.7, 64.9, 48.6, 42.2, 38.3, 34.6, 28.8, 21.7, 18.7; IR (ATR): \( \nu_{\text{max}} \) 2957, 1461, 1341, 1162, 1092, 936, 739, 653 cm\(^{-1}\); ESIHRMS \( m/z \) calcd for C\(_{14}\)H\(_{21}\)ClNO\(_2\)S [M+H]\(^+\) 302.0976, found 302.0979.

\[ \text{Ms} \]
\[ \text{H}_{13}\text{C}_6 \]
\[ \text{16f} \]

3-Hexyl-4,4-dimethyl-1-(methylsulfonyl)piperidine 16f. Prepared according to the general procedure with triethylsilane at room temperature during 2 h. Yield: 70% (97 mg, 352 \( \mu \)mol). Solvent system for flash column chromatography: cyclohexane/EtOAc: 80/20. Colorless oil; \(^1\)H NMR (300 MHz, CDCl\(_3\)): \( \delta \) 3.62-3.46 (m, 2H), 2.87-2.77 (m, 2H), 2.75 (s, 3H), 2.45 (dd, \( J = 11.3 \) and 11.3 Hz, 1H), 1.60-1.17 (m, 12H), 0.95 (s, 3H), 0.86 (t, \( J = 7.0 \) Hz, 3H), 0.80 (s, 3H); \(^{13}\)C NMR
(75 MHz, CDCl$_3$): $\delta$ 46.3, 45.1, 42.4, 39.7, 34.5, 31.8, 31.6, 29.7, 29.3, 28.1, 27.3, 22.7, 19.1, 14.1; IR (ATR): $\nu_{\text{max}}$ 2954, 2928, 2857, 1466, 1323, 1148, 979, 780 cm$^{-1}$; ESIHRMS m/z calcd for C$_{14}$H$_{30}$NO$_2$S [M+H]$^+$ 276.1992, found 276.2001.
Experimental Procedure and Characterization Data:

**In Situ NMR Identification of Iminium Ion 8a**

Experimental procedure for the in situ generation of 4,4-dimethyl-5-phenyl-1-(4-toluencesulfonyl)-2,3,4,5-tetrahydropyridin-1-ium trifluoromethanesulfonate:

To a solution of tetrahydropyridine 9a (30 mg, 88 µmol) in chloroform-d3 (500 µL) was added dropwise trifluoromethanesulfonic acid (14 µL, 154 µmol) at 0 °C under an argon atmosphere. The resulting yellow reaction mixture was stirred at 0 °C for 15 minutes and directly introduced into a NMR tube.

$^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 9.44 (s, 1H), 8.02 (d, $J = 8.2$ Hz, 2H), 7.60 (d, $J = 8.1$ Hz, 2H), 7.48-7.40 (m, 3H), 7.08-6.99 (m, 2H), 4.36 (s, 1H), 4.28-4.16 (m, 1H), 3.99-3.88 (m, 1H), 2.56 (s, 3H), 2.14-2.03 (m, 1H), 2.02-1.93 (m, 1H), 1.07 (s, 3H), 0.78 (s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 184.3, 152.1, 132.2, 131.7, 131.1, 130.2, 129.6 (2C), 125.3, 119.1 (q, $J_{CF} = 316$ Hz), 56.7, 45.6, 33.1, 30.7, 27.4, 23.6, 22.3.

Copies of $^1$H and $^{13}$C NMR spectra can be found on page S106.
Supporting Information

$^1$H and $^{13}$C NMR spectra
A Simple and Straightforward Entry to Tetrahydropyridines and Piperidines from Ynamides
A Simple and Straightforward Entry to Tetrahydropyridines and Piperidines from Ynamides
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A Simple and Straightforward Entry to Tetrahydropyridines and Piperidines from Ynamides

\[ \text{5b} \]
A Simple and Straightforward Entry to Tetrahydropyridines and Piperidines from Ynamides

\[
\text{MeO} \quad \begin{array}{c}
\text{Ts} \\
\text{5g}
\end{array}
\quad \begin{array}{c}
\text{N}
\end{array}
\quad \begin{array}{c}
\text{H}
\end{array}
\]
A Simple and Straightforward Entry to Tetrahydropyridines and Piperidines from Ynamides

\[
\text{C}_6\text{H}_{13} \equiv \equiv \text{N}^\text{Ms}
\]

5h
A Simple and Straightforward Entry to Tetrahydropyridines and Piperidines from Ynamides
A Simple and Straightforward Entry to Tetrahydropyridines and Piperidines from Ynamides
A Simple and Straightforward Entry to Tetrahydropyridines and Piperidines from Ynamides

\[ \text{TIPS-N}^\text{Ts} \]

\[ 51 \]
A Simple and Straightforward Entry to Tetrahydropyridines and Piperidines from Ynamides
A Simple and Straightforward Entry to Tetrahydropyridines and Piperidines from Ynamides

\[
\text{Structure 5p}
\]
A Simple and Straightforward Entry to Tetrahydropyridines and Piperidines from Ynamides

![Chemical Structure](image)

![NMR Spectrogram](image)
A Simple and Straightforward Entry to Tetrahydropyridines and Piperidines from Ynamides

[Diagram of molecular structure]

S71
A Simple and Straightforward Entry to Tetrahydropyridines and Piperidines from Ynamides
A Simple and Straightforward Entry to Tetrahydropyridines and Piperidines from Ynamides

\[ \text{Ms} \equiv \text{N} \equiv \text{N} \equiv \text{Ms} \]

10
A Simple and Straightforward Entry to Tetrahydropyridines and Piperidines from Ynamides

![Chemical Structure](image)

![NMR Spectra](image)

S75
A Simple and Straightforward Entry to Tetrahydropyridines and Piperidines from Ynamides

![Chemical Structure](image)

**9c**

![NMR Spectra](image)

**S78**
A Simple and Straightforward Entry to Tetrahydropyridines and Piperidines from Ynamides
A Simple and Straightforward Entry to Tetrahydropyridines and Piperidines from Ynamides

\[ \text{Structure Image} \]

S80
A Simple and Straightforward Entry to Tetrahydropyridines and Piperidines from Ynamides
A Simple and Straightforward Entry to Tetrahydropyridines and Piperidines from Ynamides
A Simple and Straightforward Entry to Tetrahydropyridines and Piperidines from Ynamides

![Chemical structure and NMR spectra]

S85
A Simple and Straightforward Entry to Tetrahydropyridines and Piperidines from Ynamides
A Simple and Straightforward Entry to Tetrahydropyridines and Piperidines from Ynamides

\[
\text{Ts} \\
\text{N} \\
\text{90}
\]
A Simple and Straightforward Entry to Tetrahydropyridines and Piperidines from Ynamides
A Simple and Straightforward Entry to Tetrahydropyridines and Piperidines from Ynamides
A Simple and Straightforward Entry to Tetrahydropyridines and Piperidines from Ynamides
A Simple and Straightforward Entry to Tetrahydropyridines and Piperidines from Ynamides

![Chemical Structure](image)

![NMR Spectra](image)
A Simple and Straightforward Entry to Tetrahydropyridines and Piperidines from Ynamides

![Chemical Structure](image)

**16a** (major atropoisomer)
A Simple and Straightforward Entry to Tetrahydropyridines and Piperidines from Ynamides

16a (minor atropisomer)
A Simple and Straightforward Entry to Tetrahydropyridines and Piperidines from Ynamides

16a' (major atropoisomer) in CDCl₃

16a' (major atropoisomer) in C₆D₆
A Simple and Straightforward Entry to Tetrahydropyridines and Piperidines from Ynamides

$16a'$ (major atropoisomer) in CDCl$_3$

$16a'$ (mixture of atropoisomers) in CDCl$_3$
A Simple and Straightforward Entry to Tetrahydropyridines and Piperidines from Ynamides

$16b$
A Simple and Straightforward Entry to Tetrahydropyridines and Piperidines from Ynamides

16c
A Simple and Straightforward Entry to Tetrahydropyridines and Piperidines from Ynamides

\[ 16e \]
