

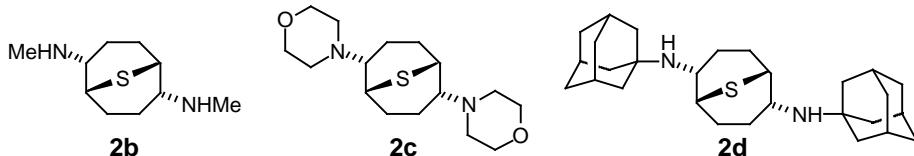
2,6-Dichloro-9-thiabicyclo[3.3.1]nonane: a Privileged, Bivalent Scaffold for Display of Nucleophilic Components

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Supporting Information

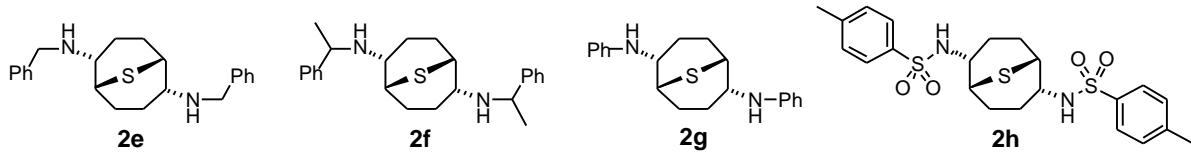
Characterization Data



2,6-Dimethylamino-9-thiabicyclo[3.3.1]nonane (2b). ^1H NMR (400 MHz, CDCl_3) 1.48 (bs, 2H), 1.50 (m, 2H), 1.88 (m, 2H), 2.06 (m, 2H), 2.28 (m, 2H), 2.41 (s, 6H), 2.75 (bs, 2H), 3.08 (m, 2H); ^{13}C NMR (100 MHz, CDCl_3): 26.3, 29.5, 33.4, 34.0, 61.1; HRMS (MALDI) calcd for $\text{C}_{10}\text{H}_{19}\text{N}_2\text{S}[(\text{M}-\text{H})^+]$: 199.1263, found: 199.1264.

2,6-Dimorpholino-9-thiabicyclo[3.3.1]nonane (2c). mp 145-147°C; ^1H NMR (400 MHz, CDCl_3): 1.71 (m, 2H), 1.99 (m, 4H), 2.44 (m, 2H), 2.51 (m, 8H), 2.67 (m, 2H), 2.86 (m, 2H), 3.7 (t, $J = 4.7$ Hz, 8H); ^{13}C NMR (100 MHz, CDCl_3): 26.2, 27.0, 32.1, 50.3, 65.2, 67.2. Elemental analysis calcd. for $\text{C}_{16}\text{H}_{28}\text{N}_2\text{O}_2\text{S}$: C, 61.50; H, 9.03; N, 8.97. Found: C, 61.41; H, 9.06; N, 8.86.

2,6-Diadamantylamino-9-thiabicyclo[3.3.1]nonane (2d). mp 271°C (dec.); ^1H NMR (400 MHz, CDCl_3): 1.53-1.65 (m, 28H), 1.74 (m, 2H), 2.03 (m, 8H), 2.40 (m, 2H), 2.47 (m, 2H), 3.32 (m, 2H); ^{13}C NMR (100 MHz, CDCl_3): 27.4, 29.6, 32.9, 36.6, 38.2, 43.8, 51.1, 52.1. Elemental analysis calcd. for $\text{C}_{28}\text{H}_{44}\text{N}_2\text{S}$: C, 76.31; H, 10.06; N, 6.36. Found C, 75.42; H, 10.04; N, 6.18.

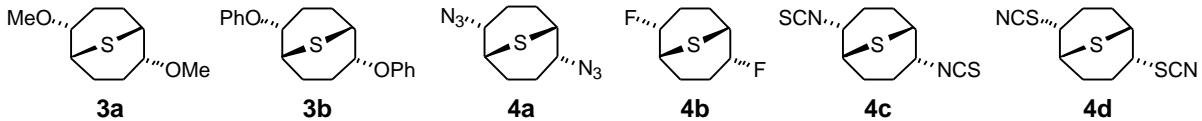


2,6-Dibenzylamino-9-thiabicyclo[3.3.1]nonane (2e). mp 99-100°C; ^1H NMR (400 MHz, CDCl_3): 1.22 (bs, 2H), 1.65 (m, 2H), 1.91 (m, 2H), 2.04 (m, 2H), 2.42 (m, 2H), 2.76 (m, 2H), 3.24 (m, 2H), 3.78 (dd, 4H), 7.30 (m, 10H); ^{13}C NMR (100 MHz, CDCl_3): 26.4, 29.9, 34.4, 50.8, 58.8, 126.9, 128.4, 129.0, 140.5; HRMS (FAB $^+$) calcd for $\text{C}_{22}\text{H}_{28}\text{N}_2\text{SNa} [(\text{M}+\text{Na})^+]$: 375.1871, found: 375.1864.

2,6-Diphenethylamino-9-thiabicyclo[3.3.1]nonane (2f). mp 122-124 °C. NMR shows an equimolar mixture of diastereomers. ^1H NMR (400 MHz, CDCl_3): 1.31 (m, 12H), 1.50-1.61 (m, 2H), 1.78 (m, 2H), 1.87-2.05 (m, 8H), 2.34 (m, 4H), 2.43 (m, 2H), 2.69 (m, 2H), 2.98 (m, 2H), 3.13 (m, 2H), 3.88 (m, 4H), 7.23-7.28 (m, 20H); ^{13}C NMR (100 MHz, CDCl_3): 24.2, 25.4, 26.6, 26.7, 30.1, 30.4, 33.6, 35.1, 53.8, 55.3, 55.7, 57.3, 126.3, 126.5, 126.8, 126.9, 128.4, 128.5, 145.5, 146.2,. Elemental analysis calcd. for $\text{C}_{24}\text{H}_{32}\text{N}_2\text{S}$: C, 75.74; H, 8.47; N, 7.36. Found C, 75.25; H, 8.34; N, 7.15.

2,6-Dianilino-9-thiabicyclo[3.3.1]nonane (2g). mp 222-223°C; ^1H NMR (400 MHz, CDCl_3): 1.72 (m, 2H), 2.13 (m, 4H), 2.35 (m, 2H), 2.96 (m, 2H), 3.7 (bs, 2H), 4.11 (m, 2H), 6.63 (dd, $J= 8.5, 1.2, 4\text{H}$), 6.69 (dt, $J= 7.3, 1.2 \text{ Hz}$, 2H), 7.18 (dd, $J= 8.5, 7.6 \text{ Hz}$, 4H); ^{13}C NMR (100 MHz, CDCl_3): 26.4, 28.6, 32.8, 55.6, 114.3, 118.6, 129.3. HRMS (MALDI) calcd for $\text{C}_{20}\text{H}_{25}\text{N}_2\text{S} [(\text{M}+\text{H})^+]$: 325.1733, found: 325.1724.

2,6-Di-p-toluenesulfonamido-9-thiabicyclo[3.3.1]nonane (2h). mp 230-233°C; ^1H NMR (400 MHz, CDCl_3): 1.58 (m, 4H), 1.90 (m, 2H), 2.23 (m, 2H), 2.41 (s, 6H), 2.62 (bs, 2H), 3.68 (m, 2H), 5.15 (d, $J = 7.3 \text{ Hz}$, 2H), 7.27 (d, $J = 8.1 \text{ Hz}$, 4H), 7.70 (d, $J = 8.0 \text{ Hz}$, 4H); ^{13}C NMR (100 MHz, CDCl_3): 21.5, 26.6, 28.9, 34.8, 55.1, 126.9, 137.2, 143.7; HRMS (FAB $^+$) calcd for $\text{C}_{22}\text{H}_{28}\text{N}_2\text{O}_4\text{S}_3\text{Na} [(\text{M}+\text{Na})^+]$: 503.1109, found: 503.1105.



2,6-Dimethoxy-9-thiabicyclo[3.3.1]nonane (3a). ^1H NMR (400 MHz, CDCl_3): 1.76 (m, 2H), 2.03 (m, 4H), 2.36 (m, 2H), 2.79 (m, 2H), 3.35 (s, 6H), 3.72 (m, 2H); ^{13}C NMR (100 MHz, CDCl_3): 25.9, 27.7, 32.6, 55.3, 80.1. Elemental analysis calcd. for $\text{C}_{10}\text{H}_{18}\text{O}_2\text{S}$: C, 59.37; H, 8.97. Found: C, 59.49; H, 9.01.

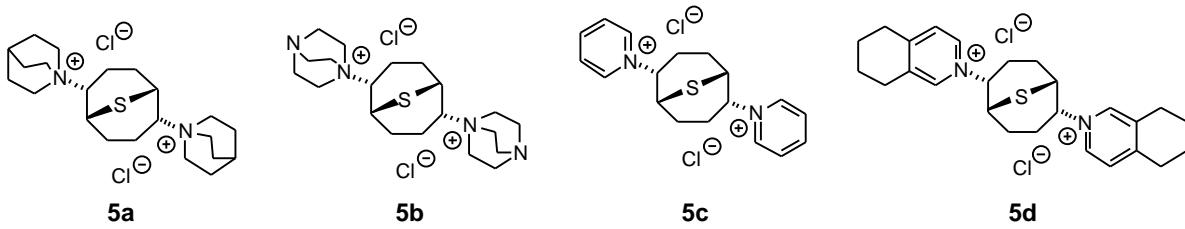
2,6-Diphenoxo-9-thiabicyclo[3.3.1]nonane (3b). mp 146-148°C; ^1H NMR (400 MHz, CDCl_3): 1.56-2.22 (m, 6H), 2.54-2.59 (m, 2H), 2.91-2.93 (m, 2H), 4.85-4.95 (m, 2H), 6.94 (m, 6H), 7.26 (m, 4H); ^{13}C NMR (100 MHz, CDCl_3): 26.6, 28.0, 33.4, 76.7, 116.4, 121.2, 129.6, 157.0. HRMS (MALDI) calcd for $\text{C}_{20}\text{H}_{23}\text{O}_2\text{S} [(\text{M}+\text{H})^+]$: 343.1362, found: 343.1359.

2,6-Diazido-9-thiabicyclo[3.3.1]nonane (4a). ^1H NMR (400 MHz, CDCl_3): 1.85 (m, 2H), 2.02 (m, 2H), 2.13 (m, 2H), 2.40 (m, 2H), 2.73 (bs, 2H), 4.12 (m, 2H); ^{13}C NMR (100 MHz, CDCl_3): 26.7, 27.3, 34.6, 62.7; HRMS (FAB $^+$) calcd for $\text{C}_8\text{H}_{13}\text{N}_6\text{S} [(\text{M}+\text{H})^+]$: 225.0922, found: 225.0920.

2,6-Difluoro-9-thiabicyclo[3.3.1]nonane (4b). ^1H NMR (400 MHz, CDCl_3): 2.03 (m, 2H), 2.18 (m, 4H), 2.5 (m, 2H), 2.8 (m, 2H), 5.04 (dm, $J_{\text{HF}} = 49.3$ Hz, 2H); ^{13}C NMR (100 MHz, CDCl_3): 26.4 ($^3\text{J}_{\text{CF}} = 9.15$), 27.9 ($^2\text{J}_{\text{CF}} = 21.4$ Hz), 34.4 ($^2\text{J}_{\text{CF}} = 21.4$ Hz), 91.6 ($^1\text{J}_{\text{CF}} = 180.1$ Hz). HRMS (MALDI): calcd. for $\text{C}_8\text{H}_{12}\text{FS} [(\text{M}-\text{F})^+]$: 159.0644, found: 159.0640.

2,6-Dithiocyanato-9-thiabicyclo[3.3.1]nonane (4c). mp 106-107 °C; ^1H NMR (400 MHz, CDCl_3): 2.10 (m, 2H), 2.20 (m, 2H), 2.36 (m, 2H), 2.68 (m, 2H), 3.03 (s, 2H), 4.18 (m, 2H); ^{13}C NMR (100 MHz, CDCl_3): 27.9, 28.1, 35.6, 51.4, 110.5; IR (CHCl_3 , cm^{-1}) 2148 cm^{-1} (-S-C-N); HRMS (FAB $^+$) calcd for $\text{C}_{10}\text{H}_{13}\text{N}_2\text{S}_3 [(\text{M}+\text{H})^+]$: 257.0241, found: 257.0245.

2,6-Diisothiocyanato-9-thiabicyclo[3.3.1]nonane (4d). mp 142-143 °C; ^1H NMR (400 MHz, CDCl_3): 2.15 (m, 6H), 2.45 (d, $J = 14.1$ Hz, 2H), 2.85 (s, 2H), 4.32 (m, 2H); ^{13}C NMR (100 MHz, CDCl_3): 26.5, 29.3, 35.2, 58.7, 133.4; IR (CHCl_3 , cm^{-1}): 2074, 2167 (-N=C=S); HRMS (FAB $^+$) calcd for $\text{C}_{10}\text{H}_{13}\text{N}_2\text{S}_3 [(\text{M}+\text{H})^+]$: 257.0241, found: 257.0235.

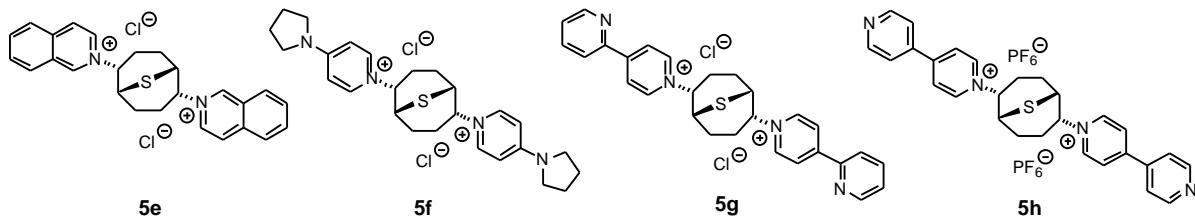


2,6-Diquinuclidinium-9-thiabicyclo[3.3.1]nonane dichloride (5a). White solid, mp 250°C (dec). ^1H NMR (400 MHz, CD₃OD): 1.97-2.11 (m, 12H), 2.12-2.22 (m, 2H), 2.27-2.39 (m, 2H), 2.43-2.65 (m, 4H), 2.78-2.9 (m, 2H), 3.46-3.69 (m, 14H), 4.05-4.16 (m, 2H); ^{13}C NMR (100 MHz, CD₃OD): 20.5, 22.8, 25.0, 31.9, 32.4, 54.2, 77.6.

2,6-Didiazabicyclooctane-9-thiabicyclo[3.3.1]nonane dication dichloride (5b). From 2,6-diazabicyclooctane (1.06 g, 9.5 mmol). White solid, mp 200°C (dec). ^1H NMR (400 MHz, CD₃OD): 2.35-2.38 (m, 2H), 2.48-2.67 (m, 4H), 2.88-2.92 (m, 2H), 3.23 (t, J = 7.34, 12H), 3.51-3.59 (m, 14H), 4.22-4.26 (m, 2H); ^{13}C NMR (100 MHz, CD₃OD): 21.6, 30.6, 31.0, 44.9, 50.7, 77.0.

2,6-Dipyridinium-9-thiabicyclo[3.3.1]nonane dichloride (5c). From pyridine (766 μL , 9.5 mmol). White solid, mp 210-236 °C (subl.). ^1H NMR (400 MHz, CD₃OD): 2.29-2.41 (m, 4H), 2.42-2.56 (m, 2H), 3.38 (m, 2H), 3.44-3.53 (m, 2H), 5.76 (m, 2H), 8.25 (t, J = 6.7, 4H), 8.69 (dt, J = 7.6, 1.2, 2H), 9.40 (dd, J = 6.7, 1.2, 4H); ^{13}C NMR (100 MHz, CD₃OD): 25.8, 28.1, 37.5, 75.3, 129.9, 145.3, 147.8. HRMS (MALDI) calcd for C₁₈H₂₁N₂S [(M-H)⁺]: 297.1425, found: 297.1414.

2,6-Di-5,6,7,8-tetrahydroisoquinolinium-9-thiabicyclo[3.3.1]nonane dichloride (5d). From tetrahydroisoquinoline (1.26 g, 9.5 mmol). Yellow solid, mp 162-164 °C. ^1H NMR (400 MHz, CD₃OD): 1.78-1.98 (m, 8H), 2.16-2.30 (m, 4H), 2.35-2.45 (m, 2H), 2.95-3.03 (m, 8H), 3.22-3.26 (m, 2H), 3.35-3.47 (m, 2H), 5.49-5.54 (m, 2H), 7.81 (d, J = 6.2 Hz, 2H), 8.91 (d, J = 6.2 Hz, 2H), 9.00 (s, 2H); ^{13}C NMR (100 MHz, CD₃OD): 22.1, 22.2, 25.6, 27.5, 28.2, 30.5, 37.5, 74.2, 129.4, 140.5, 140.6, 144.2, 160.8. HRMS (MALDI) calcd for C₂₆H₃₃N₂S [(M-H)⁺]: 405.2359, found: 405.2344.



2,6-Diisoquinolinium-9-thiabicyclo[3.3.1]nonane dichloride (5e). From isoquinoline (1.11 mL, 9.5 mmol). White solid, mp 157-160 °C. ^1H NMR (400 MHz, CD₃OD): 2.24-2.45 (m, 2H), 2.45-2.66 (m, 4H), 3.89-3.99 (m, 2H), 5.78-6.01 (m, 2H), 8.12 (t, J= 7.6 Hz, 2H), 8.03 (dt, J= 7.0, 1.2 Hz, 2H), 8.37 (d, J=8.2 Hz, 2H), 8.62 (d, J=7.0 Hz, 2H), 8.83 (d, J=8.2 Hz, 2H), 9.05 (d, J=7.0 Hz, 2H), 10.59 (s, 2H); ^{13}C NMR (100 MHz, CD₃OD): 25.8, 28.2, 37.6, 74.8, 127.9, 128.4, 129.6, 132.4, 132.6, 135.5, 138.8, 139.5, 149.9. HRMS (MALDI) calcd for C₂₆H₂₅N₂S [(M-H)⁺]: 397.1733, found: 397.1740.

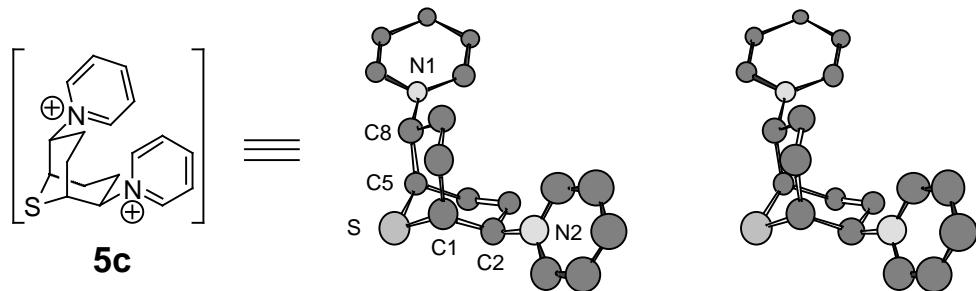
2,6-Dipyrrolidinopyridinium-9-thiabicyclo[3.3.1]nonane dichloride (5f). From pyrrolidino-pyridine (1.40 g, 9.5 mmol). White solid, mp. 209-211°C. ^1H NMR (400 MHz, CD₃OD): 1.97-2.2 (m, 12H), 2.23-2.44 (m, 2H), 2.96-3.19 (m, 4H), 3.40-3.62 (m, 8H), 4.96-5.17 (m, 2H), 6.84 (d, J= 7.9 Hz, 4H), 8.41 (d, J= 7.9 Hz, 4H); ^{13}C NMR (100 MHz, CD₃OD): 25.8, 26.1, 28.4, 37.4, 49.7, 70.7, 109.8, 142.0, 155.2. HRMS (MALDI) calcd for C₂₆H₃₅N₄S [(M-H)⁺]: 435.2577, found: 435.2592.

2,6-Di-2,4'-dipyridyl -9-thiabicyclo[3.3.1]nonane dichloride (5g). From 2,4'-dipyridyl (1.48 g, 9.5 mmol). Slightly yellow solid, mp 229-230 °C. ^1H NMR (400 MHz, CD₃OD): 2.35-2.62 (m, 6H), 3.19-3.27 (m, 2H), 3.28-3.55 (m, 2H), 5.76-5.80 (m, 2H), 7.64 (ddd, J= 7.6, 4.7, 0.88 Hz, 2H), 8.09 (dt, J= 7.9, 1.7 Hz, 2H), 8.40 (ddd, J= 7.9, 1.7, 0.88 Hz, 2H), 8.87 (ddd, J= 4.7, 1.7, 0.88 Hz, 2H), 8.90 (d, J= 7.0 Hz, 4H), 9.46 (d, J= 7.0 Hz, 4H); ^{13}C NMR (100 MHz, CD₃OD): 37.6, 74.7, 124.6, 126.2, 127.9, 139.4, 145.5. HRMS (MALDI) calcd for C₂₈H₂₇N₄S [(M-H)⁺]: 451.1951, found: 451.1942.

2,6-Di-4,4'-dipyridyl -9-thiabicyclo[3.3.1]nonane bis(hexafluorophosphate) (5h). From 4,4'-dipyridyl (1.48 g, 9.5 mmol). Yellow powder, which was purified by dissolution in water and

precipitation by addition of aqueous NaPF₆. mp 211-213°C. ¹H NMR (400 MHz, CD₃OD): 2.10-2.41 (m, 6H), 3.29-3.50 (m, 4H), 5.63-5.76 (m, 2H), 7.66 (dd, J= 4.7, 1.5 Hz. 4H), 8.30 (d, J= 7.0 Hz, 4H), 8.45 (dd, J=4.7, 1.7 Hz, 4H), 8.95 (d, J=7.0 Hz, 4H); ¹³C NMR (100 MHz, CD₃OD): 23.3, 26.8, 35.4, 72.2, 122.2, 125.8, 141.0, 144.4, 150.8, 153.2. HRMS (MALDI) calcd for C₂₈H₂₇N₄S [(M-H)⁺]: 451.1951, found: 451.1962.

Figure S1. Chem3D stereo representation of the x-ray crystal structure of dication **5c**. Significant bond lengths (Å): S–C1, 1.833(3); S–C5, 1.824(3); N1–C8, 1.512(3); N2–C2, 1.520(3).



Crystallographic data (excluding structure factors) for structures **5c** and **8** have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication nos. CCDC 155115 and 155116, respectively. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB21EZ, UK, (fax: +44 1223 336033 or e-mail: deposit@ccdc.cam.ac.uk