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Silicon- and sulfur-mediated synthesis of benzoannulated cyclooctanols

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ABSTRACT

The reaction of a silyl-substituted thioacetal with *ortho*-difunctionalized benzenes as biselectrophiles allows access to multifunctional cyclooctanols.

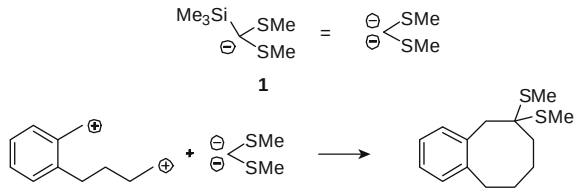
1. Introduction

Recently, our group has developed a flexible domino process for the synthesis of carbocycles.[1] This is based on the one-pot reaction of silyl-substituted thioacetal carbanions as dianion equivalents with epoxy-tosylates. Following epoxide ring opening by the carbanion, a reversible C→O silyl migration (Brook rearrangement)[2] is the key step. The method has been expanded using bis-epoxides,[3] vinyl-epoxides,[4] epoxy-aziridines[5] or multifunctional esters[6–8] as biselectrophilic reaction partners of the carbanion. Best results are usually obtained for cyclopentane synthesis, while the seven-membered rings are only obtained in modest yields. So the method does not seem attractive for the synthesis of eight-membered rings.[9] Still, the synthesis of cyclooctanols would be quite interesting, taking into account the limited accessibility to this ring system. Now we reasoned that the formation of the larger ring might be favoured by a benzene unit as backbone in the carbon chain connecting an oxirane moiety and a leaving group as electrophilic centres (Scheme 1). Here we report our encouraging results which nicely complement the existing methods[10] for benzocyclooctane synthesis.

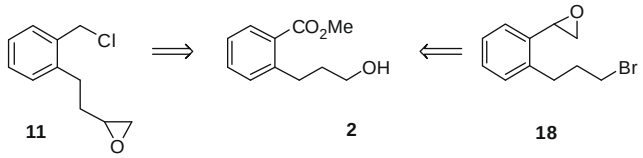
2. Results and discussion

For the two promising biselectrophiles **11** and **18** retro synthesis leads to hydroxyester **2** as a common precursor (Scheme 2), which is easily available from 2-carboxy-cinnamic acid.[6,11] After protection[12] of the alcohol as TBS-ether, ester **3**[13] is reduced[14] to benzyl alcohol **4**[15] by DIBAL in high yield (Scheme 3).

The hydroxy group of compound **4** is converted[16] into THP-ether **5**[17] by acid-catalyzed addition to 3,4-dihydro-2*H*-pyran. Desilylation with TBAF provides alcohol **6**[18] which is oxidized to the corresponding aldehyde **7**[19] using IBX[20] in DMSO. Aldehyde **7** can alternatively be synthesized in two steps from 2-iodo-benzyl alcohol **12**.[21]



Scheme 1. A silyl-substituted thioacetal as 1,1-dianion equivalent and 1,7-biselectrophiles as synthons for the Si-induced domino synthesis of eight-membered carbocycles.



Scheme 2. Retro synthesis of two biselectrophiles.

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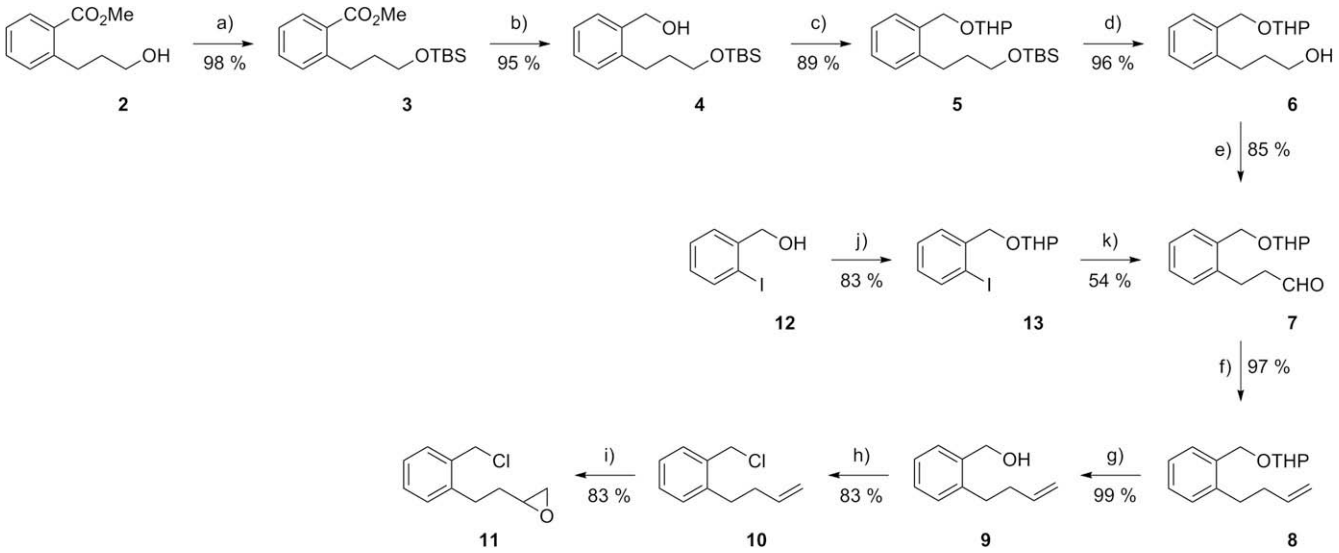


Scheme 3. Synthesis of biselectrophile **11**. Reagents and conditions: (a) TBSCl (1.2 equiv), imidazole (1.5 equiv), CH_2Cl_2, room temperature, 24 h; (b) DIBAL (2.2 equiv), toluene, −78 °C, 35 min; (c) DHP (1.5 equiv), *p*-TsOH·H_2O (5 mol %), CH_2Cl_2, room temperature, 20 h; (d) TBAF·$3H_2O$ (1.5 equiv), THF, room temperature, 60 min; (e) IBX (1.1 equiv), DMSO, room temperature, 20 h; (f) $MePPh_3Br$ (1.5 equiv), NaHMDS (2 equiv), THF, 0 °C→room temperature, 18 h; (g) *p*-TsOH·H_2O (5 mol %), MeOH, room temperature, overnight; (h) CCl_4 (1.7 equiv), PPh_3 (1.5 equiv), CH_2Cl_2, 0 °C→room temperature, 2.5 d; (i) *m*-CPBA (1.4 equiv), CH_2Cl_2, room temperature, 6.5 h; (j) DHP (1.5 equiv), *p*-TsOH·H_2O (5 mol %), CH_2Cl_2, room temperature, 70 h; (k) allyl alcohol (1.5 equiv), TBAB (1 equiv), $Pd(OAc)_2$ (2 mol %), $KHCO_3$ (2 equiv), DMF, 90 °C, 2 h.

The aldehyde is then transformed into olefin **8**[22] by a Wittig reaction using methyl-triphenylphosphonium bromide. Acid-catalyzed deprotection of the THP-ether to benzyl alcohol **9**,[23] followed by an Appel reaction, yields chloride **10**,[24] which is oxidized to epoxide **11**[25] using *m*-CPBA.

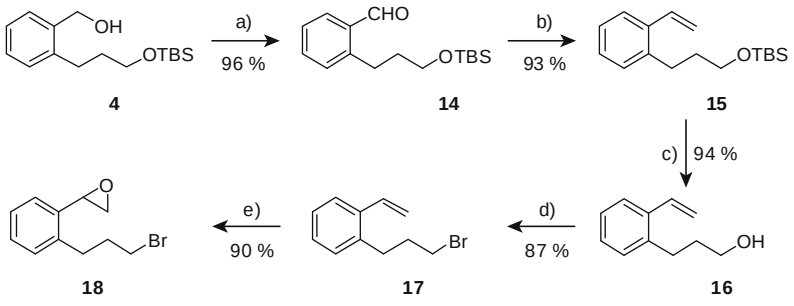
For the synthesis of the second C_7-building block **18** (Scheme 4), benzyl alcohol **4** is first oxidized to benzaldehyde **14**[26] by IBX[20] in DMSO. The reduction of ester **3** by DIBAL cannot be stopped at the stage of the aldehyde, so that it is necessary to prepare compound **14** in two steps.

The Wittig reaction of aldehyde **14** with methyl-triphenylphosphonium bromide yields styrene **15**[27], which is then deprotected to alcohol **16**[28] by TBAF. An Appel reaction[29] with carbon tetrabromide and triphenylphosphine leads to compound **17**,[30] which is finally transformed into the biselectrophilic bromo-epoxide **18**[31] by *m*-CPBA in high yield.

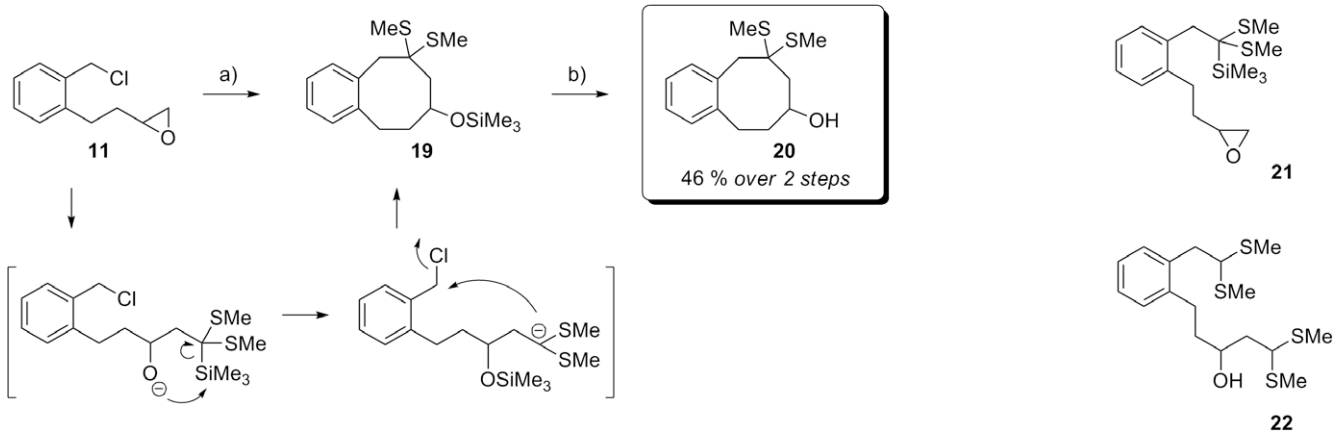
The reaction of benzyl chloride **11** with dianion equivalent **1**[6,32] yields in fact the eight-membered carbocycle **19** in a one-pot domino process (Scheme 5).[33] After work-up carbocycle **19** is separated from side product **21** by flash chromatography. Compound **21** is found in 14% yield and obviously results from substitution of the chloride. Another contamination of silyl ether **19** by a trace of the silylated derivative of alcohol **22** can be removed after desilylation with an excess of TBAF (yield 4%) finally providing pure **20** in 46% yield.

Compound **20** could not be characterized by standard 200 MHz NMR measurements in $CDCl_3$. The multiple possible conformations of the eight-membered ring made some methylene groups undetectable in the ^{13}C NMR spectrum. Also signals in the ^1H NMR spectrum were indistinct broad multiplets. Finally a 400 MHz NMR analysis in deuterated DMSO at 55 °C gave sharp signals as ring inversion becomes sufficiently fast on the NMR time scale. So cyclooctanol **20** could be fully characterized by ^1H–^{13}C-HSQC, ^1H–^1H-COSY and ^1H–^{13}C-HMBC correlation spectroscopy.

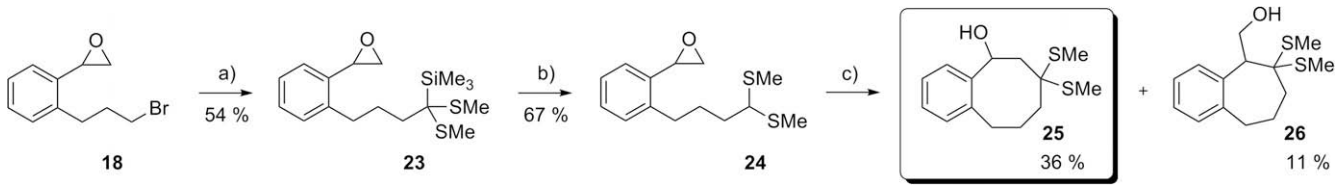
The epoxide function of the second biselectrophile, styrene oxide **18**, turned out to be less reactive (Scheme 6). Employing the corresponding chloride or tosylate in the domino process gave no carbocycle. Nevertheless a second cyclooctanol is prepared in three steps. From the reaction of bromide **18** with carbanion **1** silylated compound **23** is isolated in 54% yield.[34] After desilylating with TBAF, thioacetal **24**[35] can finally be cyclized by *n*-BuLi in the presence of DMPU.[36] DMPU as lithium complexing agent allows deprotonation of the thioacetal CH-functionality at low temperatures such as −78 °C so that the ring can selectively be formed by intramolecular attack at the terminal carbon of the epoxide ring. Cyclooctanol **25** is isolated in 36% yield along with 11% of



Scheme 4. Reagents and conditions: (a) IBX (1.1 equiv), DMSO, room temperature, 21 h; (b) $MePPh_3Br$ (1.5 equiv), NaHMDS (2.0 equiv), THF, 0 °C→room temperature, 21 h; (c) TBAF·$3H_2O$ (1.5 equiv), THF, room temperature, 60 min; (d) CBr_4 (1.1 equiv), PPh_3 (1.1 equiv), CH_2Cl_2, 0 °C→room temperature, 20 h; (e) *m*-CPBA (1.5 equiv), CH_2Cl_2, room temperature, 18 h.



Scheme 5. Silicon-induced domino synthesis of cyclooctanol **20**. Reagents and conditions: (a) **1** (1.3 equiv), THF, −78→−50 °C, 18 h; (b) TBAF·3H_2O (3 equiv), THF, room temperature, 30 min.



Scheme 6. Silicon–sulfur-mediated preparation of cyclooctanol **25**. Reagents and conditions: (a) **1** (1.3 equiv), THF, −78→−30 °C, 21 h; (b) TBAF, THF; (c) *n*-BuLi (1.3 equiv), DMPU (1.0 equiv), THF, 20 h at −78→0 °C + 7 h at room temperature.

cycloheptane **26** and 36% of recovered starting material **24**. For carbocycle **25** standard NMR analysis is possible in $CDCl_3$ solution and signals could be assigned by ^1H–^{13}C-HSQC, ^1H–^1H-COSY and ^1H–^{13}C-HMBC correlation techniques.

3. Conclusion

Applying the silicon-induced domino reaction of dianion equivalent **1** to biselectrophile **11** containing an epoxide moiety and a leaving group provides the eight-membered carbocycle **19** in a one-pot reaction involving a [1,4]-silyl shift followed by ring closure. Cyclooctanol **25** is obtained exploiting the CH-acidity of the thioacetal function in **24** by *n*-BuLi/DMPU for intramolecular cyclization. Two isomeric cyclooctanols **20** and **25** are therefore available from hydroxyester **2**.

Acknowledgements

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13. *Selected data of compounds*: Ester **3**: Colourless liquid. ^1H NMR (200 MHz, $CDCl_3$ = 7.26): δ = 7.87–7.83 (m, 1H), 7.46–7.37 (m, 1H), 7.29–7.17 (m, 2H), 3.88 (s, 3H), 3.66 (t, *J* = 6.4 Hz, 2H), 3.00 (t, *J* = 7.8 Hz, 2H), 1.89–1.75 (m, 2H), 0.91 (s, 9H), 0.06 (s, 6H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$ = 77.4): δ = 168.5, 144.4, 132.2, 131.4, 131.0, 130.0, 126.2, 63.1, 52.3, 35.0, 31.2, 26.4, 18.7, -4.9 ppm. IR (film): ν = 1726 (C=O), 1090 (OSi) cm^{-1}.
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15. Benzyl alcohol **4**: Colourless oil. ^1H NMR (200 MHz, $CDCl_3$ = 7.26): δ = 7.38–7.34 (m, 1H), 7.25–7.15 (m, 3H), 4.70 (s, 2H), 3.63 (t, *J* = 5.9 Hz, 2H), 2.79 (t, *J* = 7.5 Hz, 2H), 2.43 (s, 1H), 1.91–1.82 (m, 2H), 0.91 (s, 9H), 0.07 (s, 6H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$ = 77.4): δ = 140.6, 139.2, 129.8 129.3, 128.4, 126.6, 63.6, 62.5, 34.5, 28.2, 26.3, 18.7, −4.9 ppm. **IR** (film): ν = 3346 (OH), 1100 (OSi) cm^{-1}.
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17. THP-ether **5**: Colourless oil. ^1H NMR (200 MHz, $CDCl_3$ = 7.26): δ = 7.42–7.34 (m, 1H), 7.24–7.14 (m, 3H), 4.82 (d, *J* = 11.9 Hz, 1H), 4.76–4.70 (m, 1H), 4.52 (d, *J* = 11.9 Hz, 1H), 3.98–3.87 (m, 1H), 3.67 (t, *J* = 6.3 Hz, 2H), 3.61–3.50 (m, 1H), 2.77–2.69 (m, 2H), 1.89–1.50 (m, 8H), 0.91 (s, 9H), 0.06 (s, 6H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$ = 77.4): δ = 141.2, 136.3, 129.6, 129.4, 128.1, 126.3, 98.3, 67.2, 63.0, 62.5, 34.6, 31.0, 29.1, 26.4, 25.9, 19.8, 18.7, −4.9 ppm.
18. *Alcohol* **6**: Colourless oil. ^1H NMR (200 MHz, $CDCl_3$ = 7.26): δ = 7.38–7.15 (m, 4H), 4.88 (d, *J* = 11.5 Hz, 1H), 4.73–4.69 (m, 1H), 4.52 (d, *J* = 11.5 Hz, 1H), 4.00–3.89 (m, 1H), 3.63 (t, *J* = 6.0 Hz, 2H), 3.64–3.51 (m, 1H), 7.92–7.70 (m, 2H), 2.10 (s, 1H), 1.97–1.50, 8H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$ = 77.4): δ = 141.2, 135.9, 130.2, 129.8, 128.6, 126.4, 98.6, 67.6, 63.1, 62.0, 34.3, 31.0, 28.3, 25.8, 20.0 ppm. **IR** (film): ν = 3417 (OH) cm^{-1}.
19. *Aldehyde* **7**: Colourless oil. ^1H NMR (200 MHz, $CDCl_3$ = 7.26): δ = 9.84 (t, *J* = 1.3 Hz, 1H), 7.39–7.14 (m, 4H), 4.83 (d, *J* = 11.8 Hz, 1H), 4.72–4.69 (m, 1H), 4.50 (d, *J* = 11.8 Hz, 1H), 3.96–3.85 (m, 1H), 3.61–3.51 (m, 1H), 3.07–2.97 (m, 2H), 2.87–2.76 (m, 2H), 1.93–1.50 (m, 6H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$ = 77.4): δ = 202.0, 139.8, 136.2, 130.1, 129.6, 128.6, 126.9, 98.4, 67.6, 62.7, 45.6, 31.0, 25.8, 25.2, 19.8 ppm. **IR** (film): ν = 1723 (CHO) cm^{-1}.
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22. *Olefin* **8**: Colourless oil. ^{1}H NMR (200 MHz, $CDCl_3$ = 7.26): δ = 7.42–7.37 (m, 1H), 7.30–7.15 (m, 3H), 6.00–5.80 (m, 1H), 5.12–4.96 (m, 2H), 4.83 (d, J = 11.9 Hz, 1H), 4.73 (t, J = 3.2 Hz, 1H), 4.51 (d, J = 11.9 Hz, 1H), 3.99–3.88 (m, 1H), 3.62–3.52 (m, 1H), 2.81–2.74 (m, 2H), 2.42–2.31 (m, 2H), 1.95–1.51 (m, 6H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$ = 77.4): δ = 140.9, 138.6, 136.2, 129.6, 129.5, 128.2, 126.4, 115.2, 98.3, 67.4, 62.5, 35.6, 32.2, 31.0, 25.9, 19.7 ppm.
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25. *Biselectrophile* **11**: Colourless liquid. ^{1}H NMR (200 MHz, $CDCl_3$ = 7.26): δ = 7.38–7.17 (m, 4H), 4.65 (s, 2H), 3.04–2.83 (m, 3H), 2.79 (dd, J = 5.0, 4.0 Hz, 1H), 2.52 (dd, J = 5.0, 2.7 Hz, 1H), 2.06–1.74 (m, 2H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$ = 77.4): δ = 140.5, 135.6, 130.9, 130.1, 129.5, 127.1, 52.1, 47.6, 44.6, 34.2, 28.9 ppm. **IR** (film): ν_{max} = 2982, 2922, 1492, 1455, 1265, 916, 837, 767, 739, 671 cm^{-1}. **MS** (ESI+): m/z = 219 [M+Na]$^+$. **HRMS** (ESI+): [M+Na]$^+$ found 219.0553, calcd 219.0553.
26. *Benzaldehyde* **14**: Colourless oil. ^{1}H NMR (200 MHz, $CDCl_3$ = 7.26): δ = 10.31 (s, 1H), 7.84 (dd, J = 7.5, 1.5 Hz, 1H), 7.50 (ddd, J = 7.5, 1.6 Hz, 1H), 7.40–7.27 (m, 2H), 3.66 (t, J = 6.2 Hz, 2H), 3.14–3.06 (m, 2H), 1.90–1.76 (m, 2H), 0.91 (s, 9H), 0.06 (s, 6H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$ = 77.4): δ = 192.8, 145.6, 134.2, 131.8, 131.5, 126.9, 62.5, 35.5, 29.1, 26.3, 18.7, −4.9 ppm. **IR** (film): ν = 1699 (C=O), 1100 (OSi) cm^{-1}.
27. *Styrene* **15**: Colourless oil. ^{1}H NMR (200 MHz, $CDCl_3$ = 7.26): δ = 7.53–7.45 (m, 1H), 7.24–7.12 (m, 3H), 7.02 (dd, J = 17.4, 10.9 Hz, 1H), 5.65 (dd, J = 17.4, 1.5 Hz, 1H), 5.28 (dd, J = 10.9, 1.5 Hz, 1H), 3.64 (t, J = 6.2 Hz, 2H), 2.79–2.71 (m, 2 H), 1.85–1.71 (m, 2H), 0.92 (s, 9H), 0.06 (s, 6H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$ = 77.4): δ = 140.1, 136.8, 135.0, 130.0, 128.1, 126.6, 126.0, 115.6, 62.8, 34.5, 29.9, 26.3, 18.7, −4.9 ppm.
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30. *Bromide* **17**: Colourless liquid. ^{1}H NMR (200 MHz, $CDCl_3$ = 7.26): δ = 7.61–7.53 (m, 1H), 7.32–7.20 (m, 3H), 7.06 (dd, J = 17.3, 10.9 Hz, 1H), 5.72 (dd, J = 17.3, 1.4 Hz, 1H), 5.38 (dd, J = 10.9, 1.4 Hz, 1H), 3.48 (t, J = 6.5 Hz, 2H), 2.95–2.88 (m, 2H), 2.25–2.11 (m, 2H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$ = 77.4): δ = 138.3, 136.9, 134.7, 130.1, 128.2, 127.1, 126.3, 116.2, 34.0, 33.7, 31.9 ppm.
31. *Biselectrophile* **18**: Colourless oil. ^{1}H NMR (200 MHz, TMS = 0.00): δ = 7.30–7.16 (m, 4H), 4.06 (dd, J = 4.1, 2.7 Hz, 1H), 3.45 (t, J = 6.4 Hz, 2H), 3.18 (dd, J = 5.7, 4.1 Hz, 1H), 3.05–2.82 (m, 2H), 2.71 (dd, J = 5.7, 2.7 Hz, 1H), 2.26–2.12 (m, 2H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$ = 77.4): δ = 139.3, 135.9, 129.6, 128.3, 127.1, 125.0, 50.8, 50.5, 34.1, 33.5, 31.2 ppm. **IR** (film): ν_{max} = 2961, 1492, 1452, 1385, 1241, 1211, 986, 882, 760 cm^{-1}. **MS** (EI, DCP, 70 eV): m/z = 242 [8%, M$^+$], 240 [5%, M$^+$], 129 [41%], 117 [34%], 91 [85%], 77 [100%]. **HRMS** (EI): [M$^+$] found 240.0151, calcd 240.0150.
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33. *9,9-Bis(methylthio)benzocyclooctan-7-ol* (**20**): Carbanion **1** [obtained using bis(methylthio)trimethylsilylmethane (298 mg, 1.65 mmol, 1.3 equiv), abs THF (4 mL), *n*-BuLi (*2.4 M in hexane,* 0.74 mL, 1.78 mmol, 1.4 equiv)] is added to a solution of biselectrophile **11** (250 mg, 1.27 mmol, 1.0 equiv) in abs THF (5 mL) at −78 °C. The mixture is stirred overnight at −78 °C to −50 °C. After 18 h water is added in the cold, the mixture is extracted with Et_2O, the extracts are dried (Na_2SO_4), the solvents are removed and the residue is purified by flash chromatography (SiO_2, petroleum ether / EtOAc = 100:0, 500:1, 100:1). To the resulting mixture containing carbocycle **19** (260 mg, <0.76 mmol, 1 equiv) in THF (15 mL) TBAF·3H$_2$O (723 mg, 2.29 mmol, 3 equiv) is added. After 30 min at room temperature silica gel is added and the solvents are evaporated. Purification by flash chromatography (SiO_2, petroleum ether/EtOAc = 15:1, 6:1) yields cyclooctanol **20** (156 mg, 46%). Colourless solid. Mp 101–103 °C; ^{1}H NMR (400 MHz, 55 °C, DMSO-d_6 = 2.54): δ = 7.25–7.12 (m, 4H), 4.45 (s, 1H), 3.92 (s, 1H), 2.99 (s, 2H), 2.83–2.71 (m, 2H), 2.16 (s, 3H), 2.13–2.06 (m, 1H), 2.11 (s, 3H), 1.81 (d, J = 14.6 Hz, 1H), 1.58–1.49 (m, 2H) ppm. ^{13}C NMR (100 MHz, 55 °C, DMSO-d_6 = 40.4): δ = 141.9, 134.8, 132.3, 129.8, 127.9, 126.0, 67.9, 63.5, 46.0, 41.2, 40.8, 30.5, 12.0, 11.5 ppm. **IR** (KBr): ν = 3362 (OH) cm^{-1}. **MS** (ESI+): m/z = 307 [M+K]$^+$, 291 [M+Na]$^+$. **HRMS** (ESI+): [M+Na]$^+$ found 291.0857, calcd 291.0853.
34. Silyl thioacetal **23**: Carbanion **1** [obtained using bis(methylthio)trimethylsilylmethane (290 mg, 1.61 mmol, 1.3 equiv), abs THF (3.5 mL), *n*-BuLi (2.4 M in hexane, 0.73 mL, 1.74 mmol, 1.4 equiv)] is added to a solution of bromide **18** (300 mg, 1.24 mmol, 1.0 equiv) in abs THF (5 mL) at −78 °C. The mixture is stirred overnight at −78 °C to −30 °C, quenched with water after 21 h and extracted with CH_2Cl_2. The combined organic layers are dried (Na_2SO_4) and the solvents are evaporated. Purification of the residue by flash chromatography (SiO_2, petroleum ether/EtOAc = 300:1, 200:1, 100:1) yields 230 mg (54%) of a colourless oil. ^{1}H NMR (400 MHz, $CDCl_3$ = 7.26): δ = 7.25–7.15 (m, 4H), 4.03 (dd, J = 4.1, 2.7 Hz, 1H), 3.17 (dd, J = 5.7, 4.1 Hz, 1H), 2.83–2.66 (m, 2H), 2.69 (dd, J = 5.7, 2.7 Hz, 1H), 1.99 (s, 3H), 1.97 (s, 3H), 1.89–1.79 (m, 4H), 0.15 (s, 9H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$ = 77.4): δ = 140.5, 135.7, 129.5, 128.2, 126.9, 124.6, 50.9, 50.6, 47.6, 37.8, 33.5, 28.2, 11.5, 11.4, −0.6 ppm.
35. *Thioacetal* **24**: ^{1}H NMR (200 MHz, $CDCl_3$ = 7.26): δ = 7.28–7.14 (m, 4H), 4.05 (dd, J = 4.0, 2.7 Hz, 1H), 3.70–3.64 (m, 1H), 3.17 (dd, J = 5.8, 4.0 Hz, 1H), 2.85–2.65 (m, 2H), 2.70 (dd, J = 5.8, 2.7 Hz, 1H), 2.08 (s, 3H), 2.07 (s, 3H), 1.93–1.79 (m, 4H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$ = 77.4): δ = 140.5, 135.8, 129.4, 128.2, 126.8, 124.6, 54.5, 50.9, 50.5, 34.6, 32.5, 29.1, 12.9, 12.8 ppm.
36. *7,7-Bis(methylthio)benzocyclooctan-5-ol* (***25***) *and 6,6-bis(methylthio)-5-hydroxymethyl-6,7,8,9-tetrahydro-5H-benzo[7]annulene* (**26**): To a solution of thioacetal **24** (110 mg, 0.41 mmol, 1.0 equiv) in abs THF at −78 °C are added *n*-BuLi (2.4 M in hexane, 0.22 mL, 0.53 mmol, 1.3 equiv) and DMPU (0.05 mL, 0.41 mmol, 1.0 equiv). The orange mixture is slowly warmed to 0 °C in 20 h and is stirred for 7 h at room temperature Water is added and the mixture is extracted with CH_2Cl_2. The combined organic layers are dried (Na_2SO_4) and the solvents are removed. The residue is purified by flash chromatography (SiO_2, petroleum ether/EtOAc = 15:1). Cyclooctanol **25**: 40 mg (36%) yellowish oil. ^{1}H NMR (400 MHz, $CDCl_3$, TMS = 0.00): δ = 7.55 (dd, J = 7.6, 1.4 Hz, 1H), 7.27 (ddd, J = 7.5, 1.5 Hz, 1H), 7.22 (ddd, J = 7.3, 1.5 Hz), 7.05 (dd, J = 7.3, 1.4 Hz, 1H), 5.24 (dd, J = 10.4, 2.8 Hz, 1H), 3.05 (ddd, J = 13.7, 10.6, 6.3 Hz, 1H), 2.76 (ddd, J = 13.7, 6.4, 3.0 Hz, 1H), 2.50 (dd, J = 14.0, 2.7 Hz, 1H), 2.11 (dd, J = 14.0, 10.5 Hz, 1H), 2.09 (s, 3H), 1.99 (s, 3H), 2.01–1.91 (m, 2H), 1.72–1.61 (m, 2H), 1.44–1.37 (m, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$ = 77.4): δ = 144.1, 138.0, 129.5, 128.0, 127.2, 125.3, 69.0, 61.5, 50.4, 34.2, 31.2, 28.3, 12.3, 11.9 ppm. **IR** (film): ν = 3406 (OH) cm^{-1}. **MS** (ESI+): m/z = 291 [M+Na]$^+$. **HRMS** (ESI+): [M+Na]$^+$ found 291.0847, calcd 291.0853. Cycloheptane **26**: 12 mg (11%) colourless solid. Mp 132–134 °C. ^{1}H NMR (400 MHz, $CDCl_3$,TMS = 0.00): δ = 7.22–7.08 (m, 4H), 4.53 (dd, J = 11.2, 5.7 Hz, 1H), 4.02 (dd, J = 10.3, 8.0 Hz, 1H), 3.16 (t, J = 6.3 Hz, 1H), 3.00–2.94 (m, 1H), 2.73 (dd, J = 14.9, 5.7 Hz, 1H), 2.19 (s, 3H), 2.17–1.98 (m, 4H), 1.87 (s, 3H), 1.87–1.79 (m, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$ = 77.4): δ = 141.2, 138.3, 132.4, 131.1, 128.2, 126.5, 64.8, 62.7, 57.8, 36.2, 35.8, 24.3, 12.4, 11.1 ppm. **IR** (film): ν = 3299 (OH) cm^{-1}. **MS** (EI, DCP, 70 eV): m/z = 268 [7%, M$^+$], 221 [100%, M$^+$−SCH$_3$], 203 [11%], 191 [28%], 173 [20%], 155 [33%], 145 [20%], 143 [69%], 128 [63%], 115 [46%], 91 [22%], 77 [15%]. **HRMS** (EI): [M$^+$] found 268.0958, calcd 268.0956.