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Recalcitrant S_N2 Displacements at Carbon C9 of Quincorine and Quincoridine: 1,2-Amino Halides and Mesylates with Configurationally Rigid Nitrogen

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Dedicated to Professor Rolf Huisgen with respect and admiration

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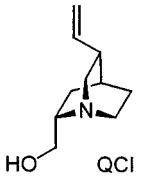
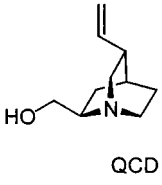
Abstract—S_N2 reactions at carbon C9 of Quincorine (QCI) and Quincoridine (QCD) were investigated and found to be difficult, due to the special structural ('β-amino effect') and conformational factors. Efficient experimental procedures for displacement with a variety of carbon and heteroatom nucleophiles were developed.

QCI and QCD are two pseudo-enantiomeric 1,2-amino alcohols with four stereogenic centres each, including the 1*S*-configurated bridgehead nitrogen.[1] Continuing our work on these building blocks we describe functional group interconversions and carbon–carbon bond forming reactions at carbon C9. The work extends efforts towards the orthogonal elaboration of the two side arms at carbon C2 and C5 of the 1-azabicyclo[2.2.2]octane core.[2]



QCI



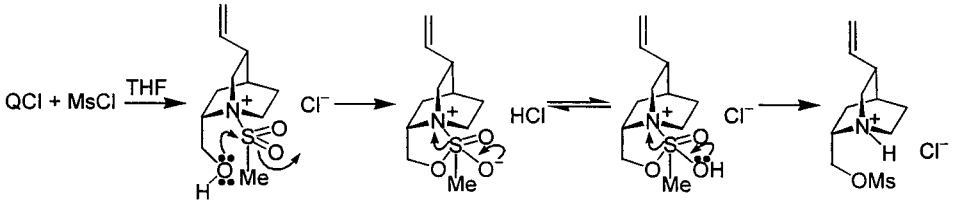
QCD

Results

We have shown previously that O-acylation and O-sulfonylation of the hydroxymethyl group are easy and involve intramolecular catalysis whereby the basic bridgehead nitrogen takes on the role of external pyridine and *p*-dimethylaminopyridine[3] of conventional acylation and sulfonylation (Scheme 1).[2a]

The resulting esters were stable, especially as crystalline hydrochlorides. No evidence for *trans*-acylation of the carboxylic esters was found. The mesylates did not undergo *trans*-alkylation or self-quaternization involving the bridgehead nitrogen and aziridinium intermediates (see Ref. 13).

With the mesylates and tosylates at hand a series of nucleophilic displacements were studied. To our surprise, attempted reactions with cyanide ion (relative nucleophilicity towards CH_3I: $n(CH_3I)=6.70$)[4] were especially disappointing (Scheme 2, Table 1, entries 1–10). Application of phase transfer catalysts made no difference. Both epimeric mesylates **1-OMs** and **2-OMs**, respectively, were equally unreactive. Starting mesylate and tosylate were recovered unchanged. Similarly, azide ion



Scheme 1.

Keywords: S_N2 reactions; cyanide ion; cesium fluoride; Mitsunobu reaction; crown ether.
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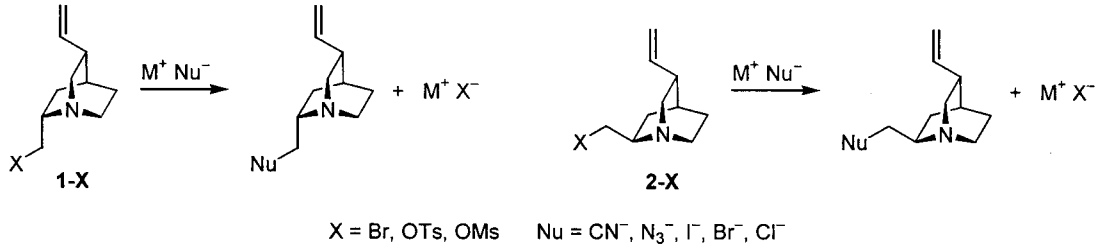


Scheme 2.

Table 1. Attempted nucleophilic displacements

Entry	Reagent M^+ Nu^-	Leaving Group X	Additives	Solvent	Reaction Conditions [°C]	Yield of product [%][a]
1	KCN	Br	KI, 18-C-6	DMF	Reflux	–
2	KCN	OTs	KI, 18-C-6	DMF/H_2O	Reflux	–
3	KCN	OTs	KI	DMF	Reflux	–
4	KCN	OMs	KI, 18-C-6	DMF	Reflux	–
5	KCN	OMs	KI	CH_3CN/MeOH	Ultrasound	–
6	KCN	OMs	nBu_4NHSO_4	Toluene	80°C	–
7	KCN	OMs	nBu_4NHSO_4, KI	$CHCl_3$	Reflux	–
8	NaCN	OMs	Na_2CO_3, NaI	DMSO	120°C	–
9	NaCN	OMs	Na_2CO_3, NaI	CH_3CN	Reflux	–
10	NaCN	OMs	15-C-5	CH_3CN/DMF	Reflux	–
11	$NaSO_2Tol$	OMs		DMF	Reflux	–
12	$NaSO_2Tol$	Br		CH_3CN/DMF	Reflux	–
13	NaN_3	Br		CH_3CN	Ultrasound	–
14	NaN_3	OMs		CH_3CN	Ultrasound	–
15	KI	OMs		CH_3CN	Reflux	4
16	KBr	OMs	18-C-6	Toluene	Reflux	6
17	KBr	OMs		CH_3CN	Reflux	–
18	NaBr	OMs	18-C-6	CH_3CN	Reflux	–
19	NaBr	OMs	18-C-6	DMF	100°C	8
20	NaBr	OMs		CH_3CN	Reflux	–
21	NaCl	OMs	18-C-6	DMF	100°C	–
22	NaCl	OMs		CH_3CN	Reflux	–

[a] Unsuccessful reaction; no conversion within 2 d.

($n(CH_3I)$=5.78)[4] and sterically more demanding arenesulfinate ion $ArSO_2^-$ were ineffective nucleophiles (entries 11–14). Only iodide ion and bromide ion as nucleophiles reacted in low yield (<10%, entries 15, 16, 19).

Second-row and soft nucleophiles derived from sulfur ($n(CH_3I)$=9.92) and phosphorus ($n(CH_3I)$=7.00)[4] were more effective and afforded sulfides and phosphines.[5] Alkyldiphenylphosphines **1-PPh$_2$** and **2-PPh$_2$** were oxygen sensitive and were partially oxidized by air to phosphine oxide. Application of deoxygenated water for the work up led to higher yield of phosphine (Scheme 3).

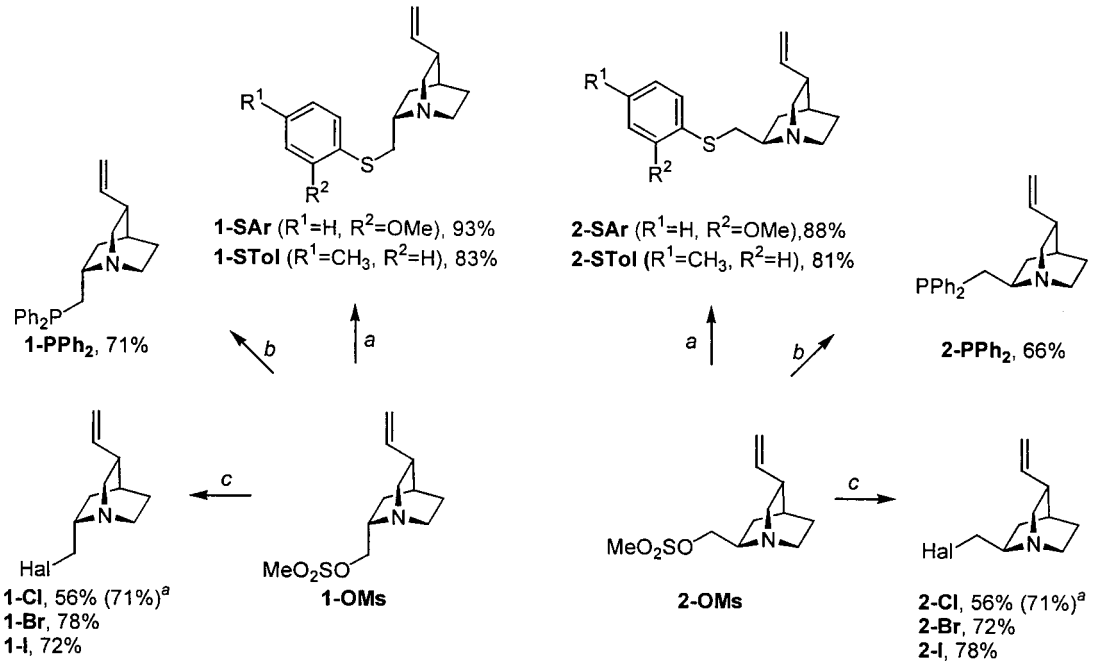
Because of the ready availability of the mesylates **1-OMs** and **2-OMs** we returned to a detailed study. With lithium halides in solvent dioxane the mesylate leaving group was exchanged for halide in good yield (see Discussion).

Introduction of hard oxygen and potentially hard nitrogen nucleophiles by conventional methodology was not successful. In the Mitsunobu reaction[6] a highly reactive ROP^+Ph_3 species is generated in situ and Ph_3PO serves as excellent leaving group. In fact, starting materials QCI and QCD had reacted completely. However, while Mitsunobu reactions usually proceed at room temperature, it was noticeable that refluxing was required for any conversion[7] and the ethyl carbonate was formed as a side product.[8]

Hard phenoxide ion, which is usually difficult to introduce, gave the aryl alkyl ether in respectable 36% yield.[9] Surprisingly, reaction with cyanide ion remained disappointing, although this was the first time that the desired **1-CN** and **2-CN** had been obtained at all. For the introduction of azide the Mitsunobu reaction is the method of choice, giving **1-N$_3$** and **2-N$_3$** in more than 76% yield (Scheme 4).

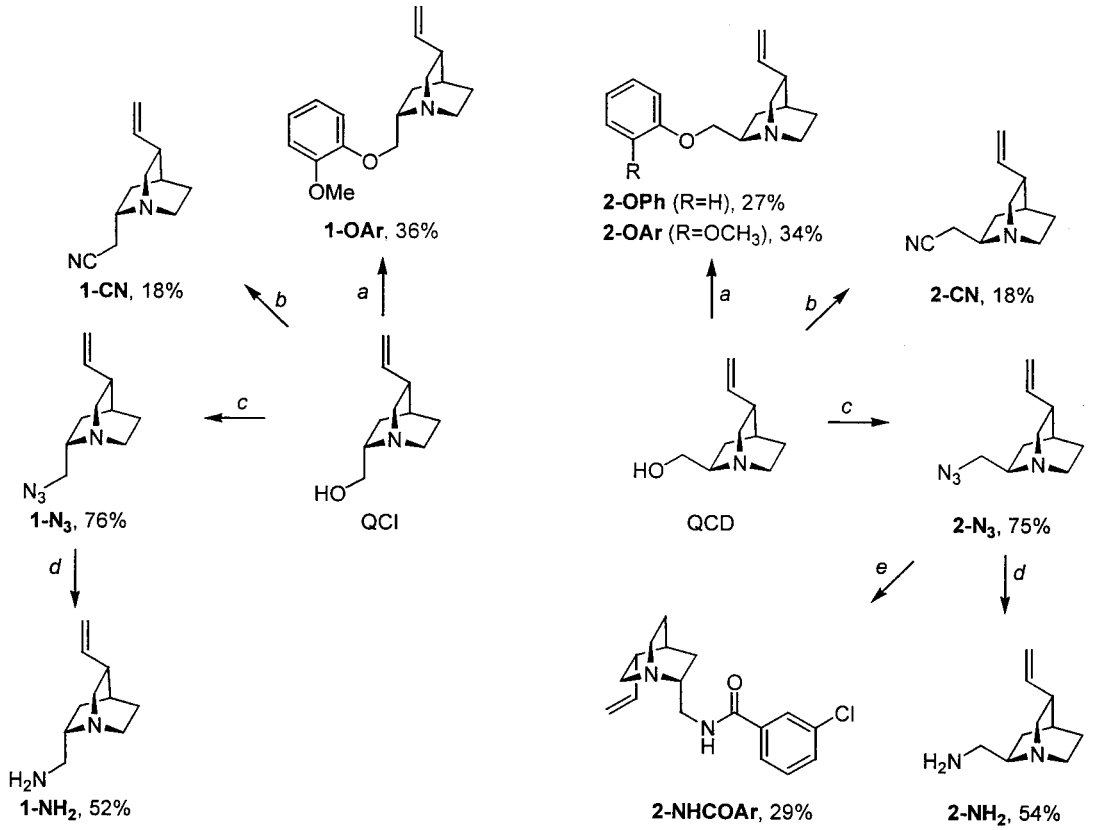
Azides are, of course, latent amines. The Staudinger protocol with triphenylphosphine and trifluoroacetic acid provided 1,2-diamines **1-NH$_2$** and **2-NH$_2$** directly.[10] A variant (PPh_3, 3-$ClC_6H_4CO_2H$) afforded *m*-chlorobenzamide **2-NHCOAr**. Unlike diamine **2-NH$_2$** the derived amide is less water soluble and readily isolable.

In order to promote carbon–carbon bond formation with cyanide ion we varied solvent and additives such as crown ether and cesium salts systematically (Table 2). Optimized conditions using solvent toluene, CsF and crown ether 18-C-6, were highly efficient (entry 4). Furthermore, Table 2 shows failure of the cyanation *when any one of the components was*



Scheme 3. Conditions: (a) thiolate, THF, reflux; (b) phosphide, THF, reflux; (c) LiHal (3 equiv.), reflux. [a]LiHal (6 equiv.).

omitted. In the absence of cesium salts attempted S_N2 reactions were unsuccessful (entry 1), similarly in the presence of Cs_2CO_3 (entry 2). Equally, a change to CsF in solvent DMF gave no nitrile (GC monitoring). Addition of crown ether was essential (entry 4, 5). The conditions of Table 2, entry 4 allowed S_N2 reactions not only with cyanide ion, but even with sterically demanding 4-methylbenzenesulfinate ion Ts^-, giving sulfones **1-Ts** and **2-Ts** (Scheme 5).



Scheme 4. Conditions: (a) PPh_3, DEAD, aryl alcohol, THF, 0°C→reflux, 2.5 h; (b) PPh_3, DEAD, $(CH_3)_2C(OH)CN$, 2,6-di-*tert*-butylphenol, THF, 0°C→reflux, 4 h; (c) PPh_3, DEAD, HN_3, THF, 0°C→reflux, 2.5 h; (d) 1. PPh_3, TFA (catal.), THF, reflux, 1 h; 2. 15% NaOH, rt, 1 d; (e) PPh_3, *m*CBA, THF, reflux, 2.5 h.

Table 2. Influence of additives and reaction conditions on yield of product **1-CN**

Entry	CsF	KCN	18-C-6	Toluene	Yield [%]
1	–	X	X	X	–[a]
2	Cs_2CO_3	X	X	X	–[a]
3	X	X	X	DMF	–[a]
4	X	X	X	X	54–95[b]
5	X	X	–	X	–[a]

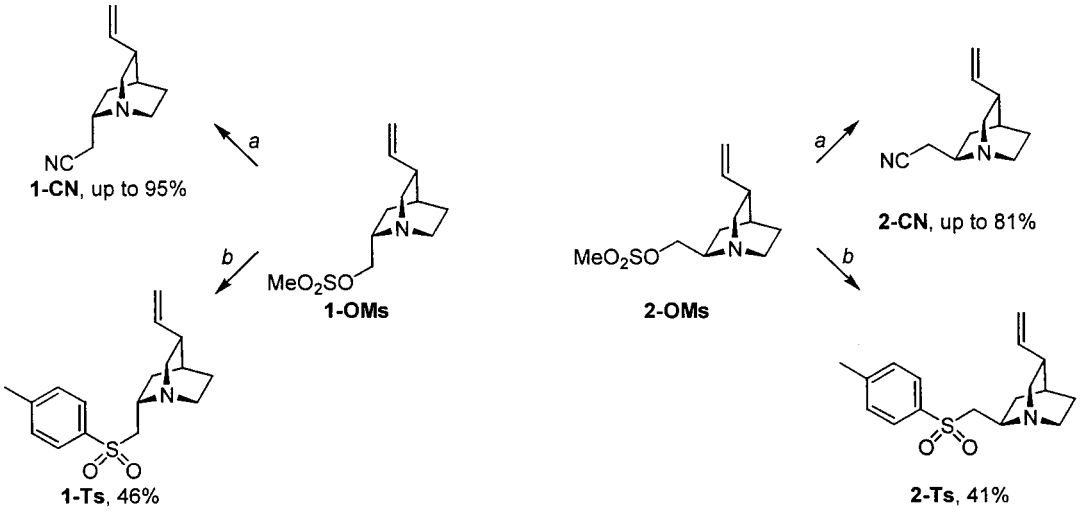
[a] No conversion after 6 d.
[b] 18-C-6 is hygroscopic and has to be anhydrous, like CsF and toluene.

Discussion

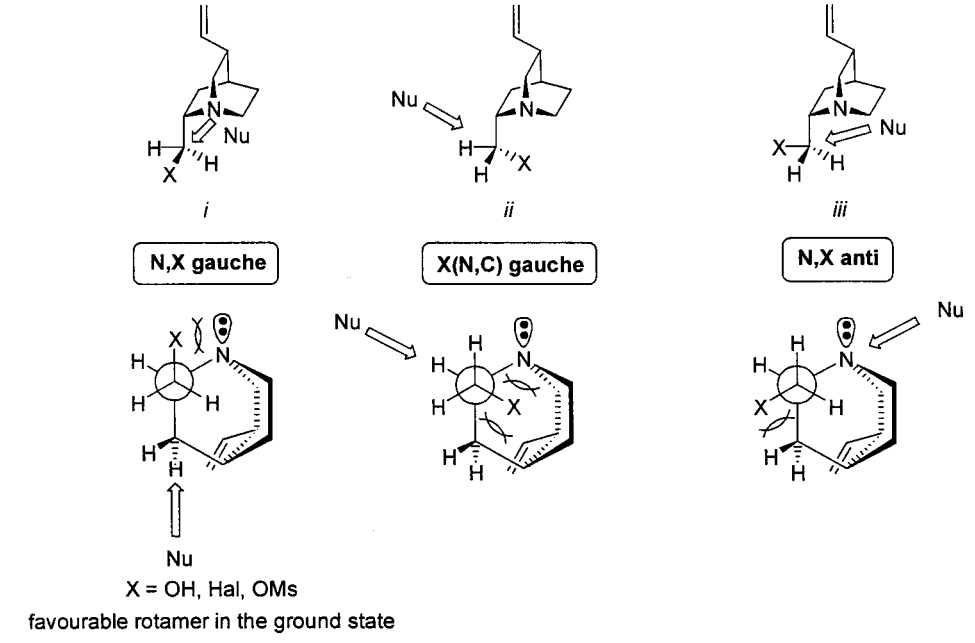
The lone pair of electrons of the basic bridgehead nitrogen is usually considered to hinder approach of the nucleophile and thus S_N2 displacement, because of electron repulsion. Can this be the whole story?

The three conformations *i*, *ii* and *iii* of the C2–C9-bond are considered in Scheme 6. In rotamer *i* the azabicyclic cage interferes with the attacking nucleophile in the preferred S_N2 trajectory. Conformer *iii* does not appear more favourable and also entails electron pair repulsion of the nucleophile and the basic bridgehead nitrogen. Of the three conformers, only rotamer *ii* allows unhindered attack of the nucleophile from the rear. However, rotamer *ii* is also the least populated conformer involving not only an X,N *gauche*, but also an X,C *gauche* interaction.

The X-ray diffraction of protonated mesylate **1-OMs**[11] shows the preferred conformation in the crystal state (N,X



Scheme 5. Conditions: (a) KCN, 18-C-6, CsF, toluene, reflux, 3 d; (b) sodium *p*-methylbenzenesulfinate, 15-C-5, CsF, toluene, reflux, 2 d.



Scheme 6. Trajectory of S_N2 attack on three conformers of C9-functionalized QCI.

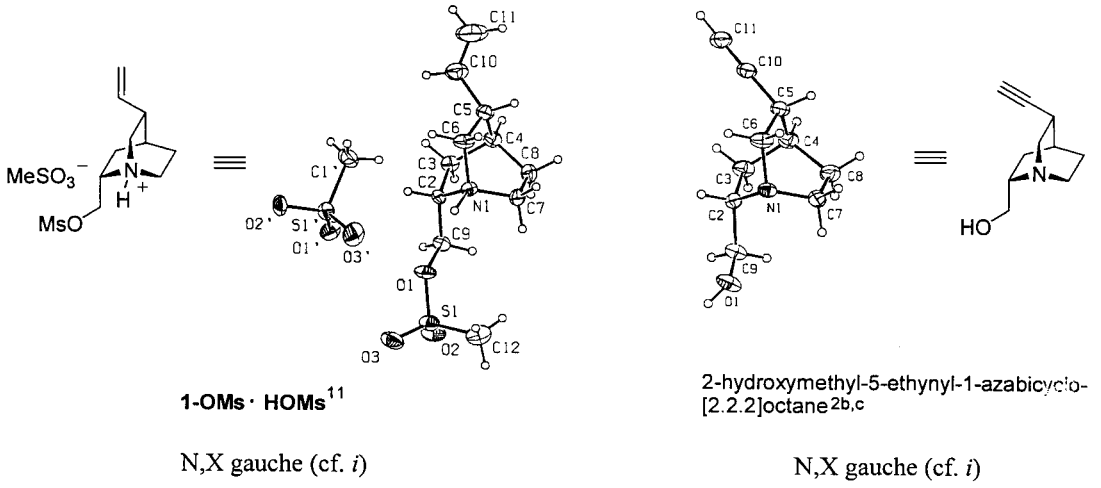


Figure 1. Ground state conformation of Quincorine derivatives.

gauche, cf. Fig. 1). NOESY experiments[12] of unprotonated **1-OMs** show that the same conformation is also preferred in solution ($CDCl_3$ solvent). Further, this conformation shows a minimum of steric energy in MOPAC calculations. Even simple 2-hydroxymethylquinuclidine (with ethynyl substituent at C5)[2b] prefers the conformation with antiperiplanar C3–C2–C9–OH conformation (N,X *gauche*) in the crystal state. Presumably, the N,X *gauche* conformation optimizes through bond interaction of nitrogen lone pair with the C9–X σ^* orbital, via C2–C3.[12,13]

We suggest that the lithium cation is chelated by mesylate **1-OMs** with a change of ground state conformation. Thus, the rear side of CH_2-OMs is now exposed to external nucleophilic attack and conformation *ii* is thought to be populated. Anhydrous cesium fluoride (CsF) represents an ultimate soft–hard combination, which is insoluble in anhydrous toluene. The surface of CsF is more active in toluene than in DMF. Other modes of activating mesylates have been discussed by Mukaiyama[14] and Otera[15] (Fig. 2).

Conclusions

1,2-Amino alcohol reactivity in S_N2 displacements has been studied in the QCI and QCD model systems where inversion at the bridgehead nitrogen is impossible. The title reactions have been developed, including carbon–carbon bond formation with cyanide ion at C9. The Mitsunobu procedure allows introduction of hard phenoxide and nitrogen nucleophiles, including azide ion. The supposedly easy introduction of cyanide was only possible under special and optimized conditions. We hope that these results may be useful when planning other refractory S_N2 reactions, not only of 1,2-amino halides,[16] but also of 1,2-alkoxy halides as encountered in carbohydrate chemistry.[17]

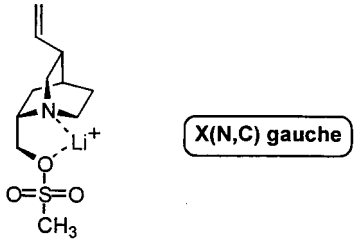


Figure 2. Activation of C9 for S_N2 displacement by changing the ground state conformation with lithium cations.

Experimental

General

Melting points were determined on a Büchi apparatus and are uncorrected. Infrared spectra were recorded on a Perkin–Elmer 1710 infrared spectrometer. ^1H NMR and ^{13}C NMR spectra were recorded on a Bruker AM 400 spectrometer in deuterated chloroform unless otherwise stated, with tetramethylsilane as internal standard. Coupling constants are given in Hz. ^{13}C NMR assignments for each signal were established by dept measurements; multiplicities are indicated by CH_3 (primary), CH_2 (secondary), CH (tertiary) or C_q (quaternary). Mass spectra were recorded on a Finnigan MAT312 (70 eV) or a VG Autospec spectrometer. Preparative column chromatography was performed on J. T. Baker silica gel (particle size 30–60 mm). Analytical TLC was carried out on aluminium-backed 0.2 mm silica gel 60 F_{254} plates (E. Merck). THF was distilled over sodium and benzophenone before use. Ethyl acetate (EA) and methyl *tert*-butyl ether (MTBE) were distilled before use.

General procedure for the preparation of mesylates 1-OMs and 2-Oms

To a solution of amino alcohol in THF (3 ml/mmol) was added mesyl chloride (1.2 equiv.) at 0°C. During addition a white solid precipitated. The mixture was stirred for 10 min and then filtered. The solid was air-dried and then dissolved in $CHCl_3$. K_2CO_3 (2 equiv.) was added and the mixture stirred for 10 min. After filtration and evaporation of the solvent the mesylate was obtained.

(1*S*,2*S*,4*S*,5*R*)-Methanesulfonic acid 5-vinyl-1-azabicyclo-[2.2.2]oct-2-ylmethyl ester (1-OMs). QCI (300 mg,

1.8 mmol) was allowed to react according to the general procedure to afford **1-OMs** (420 mg, 95%), highly viscous oil, $[\alpha]_D^{20}$=19.5° (*c* 0.99, CH_2Cl_2). IR ($CHCl_3$) ν 3072, 2936, 1724, 1636, 1452, 1416, 1396, 1352, 1224, 1172, 1112, 1052, 984, 964, 920, 828, 748, 668 cm^{-1}; ^1H NMR (400 MHz, CD_3OD) δ 5.94–5.83 (m, 1H, H-10), 5.10–5.04 (m, 2H, H-11, H-11), 4.24 (dd, 1H, ^2J=10.8 Hz, ^3J=9.2 Hz, H-9), 4.11 (dd, 1H, ^2J=10.8 Hz, ^3J=5.2 Hz, H-9), 3.19 (dd, 1H, ^2J=14 Hz, ^3J=10.1, H-6_{endo}), 3.20–3.12 (m, 1H, H-2), 3.09 (s, 3H, CH_3), 3.04–2.94 (m, 1H, H-7_{endo}), 2.76–2.68 (m, 2H, H-7_{exo}, H-6_{exo}), 2.37–2.29 (m, 1H, H-5), 1.94–1.85 (m, 1H, H-3_{endo}), 1.82–1.77 (m, 1H, H-4), 1.61–1.47 (m, 2H, H-8, H-8), 0.97–0.89 (m, 1H, H-3_{exo}); ^{13}C NMR (100 MHz, CD_3OD) δ 141.21 (CH, C-10), 114.72 (CH_2, C-11), 69.27 (CH_2, C-9), 55.47 (CH_2, C-6), 54.83 (CH, C-2), 40.86 (CH_2, C-7), 39.40 (CH, C-5), 37.86 (CH_3), 27.58 (CH_2, C-8), 27.15 (CH, C-4), 24.46 (CH_2, C-3); MS *m/z* 245 (M^+, 8), 218 (1), 204 (5), 190 (2), 166 (7), 150 (21), 137 (11), 136 (100), 122 (2), 108 (5), 96 (7), 79 (14); HRMS calcd for $C_{11}H_{19}NO_3S$: 245.3428, found 245.3426.

(1*S*,2*R*,4*S*,5*R*)-Methanesulfonic acid 5-vinyl-1-azabicyclo-[2.2.2]oct-2-ylmethyl ester (2-OMs). QCD (300 mg, 1.8 mmol) was allowed to react according to the general procedure to afford **2-OMs** (420 mg, 95%), highly viscous oil, $[\alpha]_D^{20}$=124.7° (*c* 1.35, CH_2Cl_2). IR ($CHCl_3$) ν 3072, 2964, 2944, 1722, 1636, 1452, 1356, 1231, 1176, 1100, 1036, 968, 920, 832, 740 cm^{-1}; ^1H NMR (400 MHz, CD_3OD) δ 5.92 (ddd, 1H, $^3J_{trans}$=17.5 Hz, $^3J_{cis}$=10.5 Hz, ^2J=7.2 Hz, H-10), 5.08 (ddd, 1H, $^3J_{trans}$=17.3 Hz, ^2J=1.5 Hz, ^4J=1.5 Hz, H-11_{trans}), 5.06 (ddd, 1H, $^3J_{cis}$=10.5 Hz, ^2J=1.5 Hz, ^4J=1.5 Hz, H-11_{cis}), 4.25 (dd, 1H, ^3J=8.8 Hz, ^2J=10.9 Hz, H-9), 4.12 (dd, 1H, ^3J=5.2 Hz, ^2J=10.9 Hz, H-9), 3.21–2.84 (m, 4H, H-7, H-7, H-6_{endo}, H-2), 3.11 (s, 3H, CH_3), 2.76 (ddd, 1H, ^2J=14.2 Hz, *J*=7.7 Hz, *J*=2.2 Hz, H-6_{exo}), 2.39–2.29 (m, 1H, H-5), 1.79–1.75 (m, 1H, H-4), 1.74–1.65 (m, 2H, H-8, H-8), 1.64–1.55 (m, 1H, H-3_{endo}), 1.43–1.35 (m, 1H, H-3_{exo}); ^{13}C NMR (100 MHz, CD_3OD) δ 141.42 (CH, C-10), 116.07 (CH_2, C-11), 70.67 (CH_2, C-9), 56.50 (CH, C-2), 50.12 (CH_2, C-6), 48.48 (CH_2, C-7), 41.20 (CH, C-5), 37.75 (CH_3), 29.25 (CH, C-4), 29.25 (CH_2, C-8), 24.79 (CH_2, C-3); MS *m/z* 245 (M^+, 12) 226 (4), 204 (8), 190 (1), 166 (7), 150 (31), 136 (100), 129 (2), 120 (4), 107 (8), 95 (18), 85 (2), 79 (19); HRMS calcd for $C_{11}H_{19}NO_3S$:, found 245.3431.

General procedure for the preparation of thio ethers 1-STol, 2-STol, 1-SAr, 2-SAr

To a suspension of NaH (1.3 equiv.) in THF (3 ml/mmol substrate) was added a solution of the thiophenol (1.3 equiv.) in THF (2 ml/mmol substrate) slowly via syringe at 0°C. Afterwards the mesylate was added. The mixture was heated to reflux for 2.5 h and then allowed to reach room temperature. The reaction mixture was diluted with CH_2Cl_2 and $CHCl_3$ and treated with sat. aq. $NaHCO_3$ solution. The organic layer was washed with sat. aq. $NaHCO_3$ and and dried (Na_2SO_4). After removal of the solvent the crude product was purified by chromatography (MTBE/MeOH, 10:1).

(1*S*,2*S*,4*S*,5*R*)-2-*p*-Tolylsulfanylmethyl-5-vinyl-1-azabicyclo[2.2.2]octane (1-STol). Mesylate **1-OMs** (300 mg, 1.8 mmol) was allowed to react according to the general procedure to afford **1-STol** (1.97. g, 83%), yellowish oil, $[\alpha]_D^{20}$=27.0° (*c* 1.00, CH_2Cl_2). IR ($CHCl_3$) ν 3070, 3016, 2924, 2860, 1708, 1636, 1600, 1492, 1452, 1420, 1364, 1268, 1212, 1092, 1040, 1016, 992, 912, 804 cm^{-1}; ^1H NMR (400 MHz) δ 7.25 (m, 2H, H-13, H-13), 7.08 (m, 2H, H-14, H-14), 5.83 (ddd, $^3J_{trans}$=17 Hz, $^3J_{cis}$=10.4 Hz, ^2J=7.7 Hz, 1H, H-10), 5.01 (ddd, *J*=17 Hz, *J*=1.4 Hz, *J*=1.4 Hz, 1H, H-11_{trans}), 4.98 (ddd, *J*=10.4 Hz, *J*=1.7 Hz, *J*=1.1 Hz, 1H, H-11_{cis}), 3.19 (dd, *J*=13.7 Hz, *J*=10 Hz, 1H, H-6_{endo}), 3.13 (dd, *J*=11 Hz, *J*=4.6 Hz, 1H, H-9), 3.04–2.95 (m, 1H, H-7_{endo}), 2.95–2.88 (m, 1H, H-2), 2.87 (dd, *J*=11 Hz, *J*=7.5 Hz, 1H, H-9), 2.74–2.65 (m, 1H, H-7_{exo}), 2.65 (ddd, *J*=13.7 Hz, *J*=5 Hz, *J*=2.4 Hz, 1H, H-6_{exo}), 2.30 (s, 3H, CH_3), 2.29–2.21 (m, 1H, H-5), 2.03–1.93 (m, 1H, H-3_{endo}), 1.73 (st, *J*=3.3 Hz, 1H, H-4), 1.54–1.47 (m, 2H, H-8, H-8), 1.07 (dddd, *J*=13.8 Hz, *J*=7.5 Hz, *J*=4 Hz, *J*=2.5 Hz, 1H, H-3_{exo}); ^{13}C NMR (100 MHz) δ 141.80 (CH, C-10), 135.88 (Cq, C-12), 133.02 (Cq, C-15), 129.74 (CH, C-14), 129.62 (CH, C-13), 114.26 (CH_2, C-11), 55.95 (CH_2, C-6), 55.10 (CH, C-2), 40.71 (CH_2, C-7), 39.72 (CH_2, C-9), 39.52 (CH, C-5), 28.62 (CH_2, C-8), 27.88 (CH, C-4), 27.81 (CH_3, C-3), 20.98 (CH_3); MS *m/z* 273 (M^+, 7), 232 (2), 191 (2), 173 (4), 150 (10), 136 (100), 123 (5), 91 (4), 79 (5), 70 (6); HRMS calcd for $C_{17}H_{23}NS$: 273.1551, found 273.1552.

(1*S*,2*R*,4*S*,5*R*)-2-*p*-Tolylsulfanylmethyl-5-vinyl-1-azabicyclo[2.2.2]octane (2-STol). Mesylate **2-OMs** (300 mg, 1.8 mmol) was allowed to react according to the general procedure to afford **2-STol** (1.93. g, 81%), yellowish oil, $[\alpha]_D^{20}$=155.1° (*c* 1.06, CH_2Cl_2). IR ($CHCl_3$) ν 3076, 2940, 2868, 1636, 1600, 1492, 1452, 1428, 1228, 1092, 916 cm^{-1}; ^1H NMR (400 MHz) δ 7.25 (d, *J*,=8 Hz, 2H, H-13), 7.08 (d, *J*=8 Hz, 2H, H-14), 5.86 (ddd, $^3J_{trans}$=17 Hz, $^3J_{cis}$=11 Hz, ^2J=1.7 Hz, 1H, H-10), 5.03 (ddd, *J*=11 Hz, *J*=1.7 Hz, *J*=1.5 Hz, 1H, H-11_{cis}), 5.01 (ddd, *J*=17 Hz, *J*=11 Hz, *J*=1.2 Hz, 1H, H-11_{trans}), 3.14 (m, 1H, H-6_{endo}), 2.98–2.81 (m, H, H-7, H-7, H-2, H-9, H-9), 2.70 (dd, *J*=14 Hz, *J*=1.7 Hz, 1H, H-6_{exo}), 2.31 (s, 3H, CH_3), 2.28–2.19 (m, 1H, H-5), 1.76–1.70 (m, 1H, H-4), 1.69–1.60 (m, 1H, H-3_{endo}), 1.57–1.50 (m, 2H, H-8, H-8), 1.43–1.35 (m, 1H, H-3_{exo}); ^{13}C NMR (100 MHz) δ 140.48 (CH, C-10), 135.86 (Cq, C-12), 132.94 (Cq, C-15), 129.66 (CH, C-14), 129.64 (CH, C-13), 114.55 (CH_2, C-11), 54.91 (CH, C-2), 49.13 (CH_2, C-6), 47.27 (CH_2, C-7), 39.84 (CH, C-5), 38.60 (CH_2, C-9), 28.00 (CH_2, C-8), 27.85 (CH, C-4), 26.46 (CH_2, C-3), 20.99 (CH_3); MS *m/z* 274 (M^++1), 252 (2), 240 (7), 226 (62), 209 (1), 186 (4), 173 (12), 150 (100), 136 (67), 123 (12), 91 (12), 79 (16), 70 (18); HRMS calcd for $C_{17}H_{23}NS$: 273.1551, found 273.1552.

(1*S*,2*S*,4*S*,5*R*)-2-(2-Methoxy-phenylsulfanylmethyl)-5-vinyl-1-azabicyclo[2.2.2]octane (1-SAr). Mesylate **1-OMs** (502 mg, 2.04 mmol) was allowed to react according to the general procedure to afford **1-SAr** (549 mg, 93%), highly viscous oil, $[\alpha]_D^{20}$=24.5° (*c* 1.00, CH_2Cl_2). IR ($CHCl_3$) ν 3068, 3000, 2936, 2864, 2836, 1636, 1576, 1476, 1432, 1292, 1264, 1244, 1132, 1072, 1028, 1024, 916 cm^{-1}; ^1H NMR (400 MHz) δ 7.29 (dd, ^3J=7.5 Hz, ^4J=1.7 Hz, 1H, H-17), 7.17 (ddd, *J*=9 Hz, *J*=7.5 Hz, *J*=1.7 Hz, 1H,

H-15), 6.91 (ddd, J=9 Hz, J=7.5 Hz, ^4J=1.2 Hz, 1H, H-16), 6.83 (dd, J=9 Hz, J=1.2 Hz, 1H, H-14), 5.84 (ddd, $^3J_{trans}$=17.2 Hz, $^3J_{cis}$=10.4 Hz, ^2J=7.7 Hz, 1H, H-10), 5.00 (ddd, J=10.4 Hz, J=1.3 Hz, J=1.2 Hz, 1H, H-11$_{cis}$) 4.99 (ddd, J=17.2 Hz, J=1.3 Hz, J=1.2 Hz, 1H, H-11$_{trans}$), 3.87 (s, 3H, OCH_3), 3.19 (dd, ^2J=14 Hz, ^3J=10.3 Hz, 1H, H-6$_{endo}$), 3.13 (dd, ^2J=11.6 Hz, ^3J=6.8 Hz, 1H, H-9), 3.07–2.98 (m, 1H, H-7$_{endo}$), 2.97–2.90 (m, 1H, H-2), 2.86 (dd, ^2J=11.6 Hz, ^2J=8 Hz, 1H, H-9), 2.75–2.68 (m, 1H, H-7$_{exo}$), 2.67 (ddd, ^2J=14 Hz, J=5 Hz, J=2.4 Hz, 1H, H-6$_{exo}$), 2.30–2.21 (m, 1H, H-5), 2.06–1.97 (dddd, J=13.6 Hz, J=9.4 Hz, J=3.6 Hz, J=2 Hz, 1H, H-3$_{endo}$), 1.77–1.71 (st, J=3 Hz, 1H, H-4), 1.58–1.46 (m, 2H, H-8, H-8), 1.16–1.08 (dddd, J=13.6 Hz, J=6.5 Hz, J=2.4 Hz, J=1.5 Hz, 1H, H-3$_{exo}$); ^{13}C NMR (100 MHz) δ 157.44 (Cq, C-13), 141.83 (CH, C-10), 129.42 (CH-17), 127.03 (CH, C-15), 124.91 (Cq, C-12), 120.97 (CH, C-16), 114.24 (CH_2, C-11), 110.40 (CH, C-14), 55.96 (CH_2, C-6), 55.73 (CH, C-2), 55.10 (OCH_3), 40.78 (CH_2, C-7), 39.55 (CH, C-5), 37.62 (CH_2, C-9), 28.72 (CH_2, C-8), 27.88 (CH, C-4), 27.83 (CH_2, C-3); MS m/z 289 (M^+, 14), 183 (14), 150 (51), 136 (100), 110 (31), 97 (35), 69 (33); FAB-MS m/z 290 (M^++1), 189 (M^+), 175, 165, 159, 150, 136,121; HRMS calcd for $C_{17}H_{23}NOS$ 289.1500:, found 289.1503.

(1*S*,2*R*,4*S*,5*R*)-2-(2-Methoxy-phenylsulfanylmethyl)-5-vinyl-1-azabicyclo[2.2.2]octane (2-SAr). Mesylate **2-OMs** (500 mg, 2.04 mmol) was allowed to react according to the general procedure to afford **2-SAr** (520 mg, 88%), highly viscous oil, $[\alpha]_D^{20}$=125.7° (c 1.535, CH_2Cl_2). IR ($CHCl_3$) ν 3069, 2999, 2938, 2873, 1636, 1579, 1477, 1433, 1273, 1245, 1182, 1132, 1072, 1043, 1026, 917 cm^{-1}; ^{1}H NMR (400 MHz) δ (H 7.29 (dd, J=8 Hz, J=1.5 Hz, 1H, H-17), 7.17 (ddd, J=9.2 Hz, J=8 Hz, J=1.5 Hz, 1H, H-15), 6.92 (ddd, J=8.5 Hz, J=7.5 Hz, J=1.2 Hz, 1H, H-16), 6.84 (dd, J=8 Hz, J=1 Hz, 1H, H-14), 5.87 (dddd, $^3J_{trans}$=17 Hz, $^3J_{cis}$=10 Hz, J=4.6 Hz, J=2 Hz, 1H, H-10), 5.03 (ddd, J=10 Hz, J=1.4 Hz, J=1 Hz, 1H, H-11$_{cis}$), 5.02 (ddd, J=17 Hz, J=1.5 Hz, J=1 Hz, 1H, H-11$_{trans}$), 3.87 (s, 3H, OCH_3), 3.13 (), 2.98–2.82 (m, 5H, H-9, H-9, H-7, H-7, H-), 2.73 (ddd, J=14 Hz, J=7.4 Hz, J=1.8 Hz, 1H, H-6$_{exo}$), 2.30–2.20 (m, 1H, H-5), 1.76–1.72 (m, 1H, H-4), 1.72–1.64 (m, 1H, H-3$_{endo}$), 1.58–1.50 (m, 2H, H-8, H-8), 1.47–1.39 (m, 1H, H-3$_{exo}$); ^{13}C NMR (100 MHz) δ 157.47 (Cq, C-13), 140.58 (CH, C-10), 129.47 (CH, C-16), 127.03 (CH, C-15), 124.86 (Cq, C-12), 120.99 (CH, C-16), 114.49 (CH_2, C-11), 110.45 (CH, C-14), 55.75 (OCH_3), 54.96 (CH, C-2), 49.18 (CH_2, C-6), 47.37 (CH_2, C-7), 39.91 (CH, C-5), 36.61 (CH_2, C-9), 28.12 (CH_2, C-8), 27.87 (CH, C-4), 26.52 (CH_2, C-3); MS m/z 289 (M^+, 29), 269 (6), 248 (16), 223 (3), 189 (9), 168 (3), 150 (100), 136 (59), 121 (10), 91 (9), 70 (18); HRMS calcd for $C_{17}H_{23}NOS$: 289.1500, found 289.1501.

General procedure for the preparation of 1-PPh$_2$, 2-PPh$_2$

A round-bottomed flask was dried with a heat gun, charged with mesylate and flushed with argon. A $KPPh_2$ solution (1.2 equiv., 0.5. M in THF) was added slowly at room temperature. The mixture was stirred for 1 h and then heated for a short time to complete the reaction (TLC control). After being cooled to room temperature the mixture was diluted with DCM. Degassed water (20 min under argon) was added. The following work up should be fast. The layers were separated and the aqueous layer was extracted with DCM. The combined organic layer was dried (Na_2SO_4), the solvent evaporated and the crude product purified by chromatography (MTBE→MTBE/MeOH, 10:1).

(1*S*,2*S*,4*S*,5*R*)-2-Diphenylphosphanylmethyl-5-vinyl-1-azabicyclo[2.2.2]octane (1-PPh2). Mesylate **1-OMs** (1.55 g, 6.33 mmol) was allowed to react according to the general procedure to afford **1-PPh$_2$** (1.51. g, 71%), highly viscous, brownish oil. IR ($CHCl_3$) ν 3080, 2992, 2948, 2868, 1664, 1636, 1592, 1500, 1436, 1420, 1380, 1320, 1180, 1132, 1112, 1068, 1020, 996, 944, 908, 844, 808, 648, 608, 560, 532 cm^{-1}; ^{1}H NMR (400 MHz) δ 7.88–7.79 (m, 4H, H-13, H-13′), 7.54–7.42 (m, 6H, H-14, H-14′, H-15, H-15′), 5.87 (ddd, $^3J_{trans}$=16.4 Hz, $^3J_{cis}$=9.6 Hz, ^2J=7.5 Hz, 1H, H-10), 5.05 (ddd, J=16.4 Hz, J=1.3 Hz, J=1.3 Hz, 1H, H-11$_{trans}$), 5.03 (ddd, J=9.6 Hz, J=1.3 Hz, J=1.2 Hz, 1H, H-11$_{cis}$), 4.04–1.93 (m, 2H, H-9, H-9), (3.18 (dd, J=13.6 Hz, J=10 Hz, 1H, H-6$_{endo}$), 3.18–3.12 (m, 1H, H-7$_{endo}$), 2.98 (m, 1H, H-7$_{exo}$), 2.75–2.64 (m, 2H, H-6$_{exo}$, H-2), 2.35–2.27 (m, 1H, H-5), 1.94–1.84 (m, 1H, H-3$_{endo}$), 1.77 (st, J=3.1 Hz, 1H, H-4), 1.54–1.46 (m, 2H, H-8, H-8), 1.09 (dddd, J=13.8 Hz, J=7 Hz, J=2.4 Hz, J=1.9 Hz, 1H, H-3$_{exo}$); ^{13}C NMR (100 MHz) δ 141.40 (CH, C-10), 132.25 (Cq, C-12), 132.22 (Cq, C-12′), 131.20, 132.17 (CH, C-15, C-15′), 131.91, 131.81, 131.69, 131.59 (CH, C-13, C-13′), 128.63, 128.58, 128.50, 128.45 (CH, C-14, C-14′), 114.65 (CH_2, C-11), 65.72, 65.67 (CH_2, C-9), 55.84 (CH, C-2), 55.77 (CH_2, C-6), 41.26 (CH_2, C-7), 39.46 (CH, C-5), 27.41 (CH, C-4), 27.34 (CH_2, C-8), 24.81 (CH_2, C-3); MS m/z 335 (M^+, 3), 310 (3), 272 (2), 259 (5), 243 (3), 219 (23), 201 (43), 183 (8), 149 (91), 136 (100), 120 (15), 108 (36), 95 (14), 77 (32), 67 (10); HRMS calcd for $C_{22}H_{26}NOP$: 335.1803, found 335.1805.

(1*S*,2*R*,4*S*,5*R*)-2-Diphenylphosphanylmethyl-5-vinyl-1-azabicyclo[2.2.2]octane (2-PPh2). Mesylate **2-OMs** (2.40. g, 9.80 mmol) was allowed to react according to the general procedure to afford **2-PPh$_2$** (2.17. g, 66%), yellowish wax, $[\alpha]_D^{20}$=81.0° (c 1.00, CH_2Cl_2). IR ($CHCl_3$) ν 3080, 2994, 2944, 2866, 1664, 1636, 1592, 1436, 1320, 1180, 1133, 1112, 1066, 1020, 997, 908, 844, 808, 562, 532 cm^{-1}; ^{1}H NMR (500 MHz) δ 7.52–7.29 (m, 10H, Haromat.), 5.85 (ddd, $^3J_{trans}$=17.3 Hz, $^3J_{cis}$=10.5 Hz, ^2J=6.9 Hz, 1H, H-10), 5.06 (ddd, J=10.5 Hz, J=1.4 Hz, J=1.4 Hz, 1H, H-11$_{cis}$), 5.04 (ddd, J=17.3 Hz, J=1.6 Hz, J=1.6 Hz, 1H, H-11$_{trans}$), 3.03 (ddd, J=13.7 Hz, J=10.7 Hz, J=1 Hz, 1H, H-6), 2.95–2.83 (m, 3H, H-2, H-7, H-7), 2.82–2.69 (m, 1H, H-6), 2.61 (dd, J=13 Hz, J=5.3 Hz, 1H, H-9), 2.36–2.26 (m, 1H, H-5), 2.17 (dd, J=13 Hz, J=10 Hz, 1H, H-9), 1.78–1.73 (m, 1H, H-4), 1.70–1.64 (m, 1H, H-3$_{endo}$), 1.59–1.46 (m, 3H, H-8, H-8, H-3); ^{13}C NMR (125 MHz) δ 139.70 (CH, C-10), 138.53 (Cq, C-12), 137.69 (Cq, C-12′), 132.86, 132.81, 132.67, 132.58 (CH, C-13, C-13′), 130.85, 130.62 (Cq, C-15, C-15′), 128.66, 128.61, 128.57, 128.54 (CH, C-14, C-14′), 115.02 (CH_2, C-11), 54.95 (CH, C-2), 48.59 (CH_2, C-6), 46.93 (CH_2, C-7), 39.39 (CH, C-5), 34.98 (CH_2, C-9), 29.34 (CH_2, C-8), 27.79 (CH, C-4), 25.66 (CH_2, C-3); MS m/z 335 (M^+, 3), 310 (2), 272 (2), 259 (4), 243 (2), 219 (31),

201 (47), 183 (4), 149 (77), 136 (100), 120 (14), 108 (26), 95 (13), 77 (21), 67 (18); HRMS calcd for $C_{22}H_{26}NOP$: 335.1803, found 335.1804.

General procedure for the preparation of halides 1-I, 2-I, 1-Br, 2-Br, 1-Cl, 2-Cl

A round-bottomed flask was charged with mesylate, evacuated and flushed with N_2. Dioxane (4 ml/mmol) was added under a stream of N_2 followed by lithium halide (3 equiv.). The mixture was heated to reflux for several hours (LiI, 1 h; LiBr, 6 h; LiCl, 18 h). Then sat. aq. $NaHCO_3$ solution was added (and for the iodination reaction solid $Na_2S_2O_3$). The aqueous layer was extracted with DCM, the combined organic layer washed with sat. aq. $NaHCO_3$ solution (3×) and brine (3×). The combined organic layer was dried ($MgSO_4$), the solvent removed and the crude product purified by chromatography (MTBE/MeOH, 10:1).

(1*S*,2*S*,4*S*,5*R*)-2-Iodomethyl-5-vinyl-1-azabicyclo[2.2.2]-octane (1-I). Mesylate **1-OMs** (250 mg, 1.02 mmol) was allowed to react according to the general procedure to afford **1-I** (202 mg, 72%), highly viscous oil, $[\alpha]_D^{20}=-23.5°$ (*c* 1.00, MeOH). IR ($CHCl_3$) ν 3079, 3998, 2942, 2870, 1636, 1452, 1420, 1262, 1172, 1096, 996, 916, 862, 828, 624, 624, 596 cm^{-1}; ^1H NMR (400 MHz) δ 5.86 (ddd, ^3J=17.0, 10.5, 7.5 Hz, H-10) 5.08–5.02 (m, 2H-11) 3.23 (dd, ^3J=8.4, ^2J=9.9 Hz, H-9) 3.22 (dd, ^3J=10.1, ^2J=13.7 Hz, H-6) 3.18 (dd, ^3J=7.3, ^2J=9.9 Hz, H-9) 3.03–2.95 (m, H-2) 2.95–2.85 (m, H-7) 2.73–2.61 (m, H-7,-6) 2.29–2.21 (m, H-5) 2.06–1.98 (m, H-3) 1.80 (m, H-4) 1.62–1.48 (m, H-8,8) 1.01 (dddd, ^3J=6.8, ^2J=13.6, *J*=2.5, *J*=1.6 Hz, H-3); ^{13}C NMR (100 MHz) δ 141.58 (CH, C-10), 114.49 (CH_2, C-11), 57.73 (CH, C-2), 55.94 (CH_2, C-6), 40.24 (CH_2, C-7), 39.04 (CH, C-5), 29.18 (CH_2, C-3), 28.73 (CH, C-4), 27.59 (CH_2, C-8), 10.16 (CH_2, C-9); MS *m*/*z* 278 (M^++1), 5), 277 (M^+, 38), 237 (2) 236 (19) 183 (2) 182 (32) 151 (11 150 (100) 137 (9) 136 (82) 134 (2) 128 (2) 127 (2) 122 (2) 109 (7) 108 (9) 96 (7) 95 (7) 82 (12) 79 (14); HRMS calcd for $C_{10}H_{16}NI$: 277.0328, found 277.0326.

(1*S*,2*R*,4*S*,5*R*)-2-Iodomethyl-5-vinyl-1-azabicyclo[2.2.2]-octane (2-I). Mesylate **2-OMs** (250 mg, 1.02 mmol) was allowed to react according to the general procedure to afford **2-I** (206 mg, 78%), white crystalline solid, mp 178°C (decomposition), $[\alpha]_D^{20}=106.0°$ (*c* 1.18, CH_2Cl_2). IR ($CHCl_3$) ν 3080, 3000, 2940, 2868, 1636, 1452, 1420, 1320, 1264, 1176, 1096, 1044, 992, 916, 864, 828, 624, 624, 596 cm^{-1}; ^1H NMR (400 MHz) δ 5.84 (ddd, $^3J_{trans}$=17 Hz, $^3J_{cis}$=10.4 Hz, ^2J=7 Hz, 1H, H-10), 5.04 ddd, *J*=10.4 Hz, *J*=1.5 Hz, *J*=1.5 Hz, 1H, H-11), 5.02 (ddd, *J*=17 Hz, *J*=1.5 Hz, *J*=1.5 Hz, 1H, H-11), 3.22 (dd, *J*=10 Hz, *J*=7.8 Hz, 1H, H-9), 3.16 (ddd, *J*=10 Hz, *J*=7.8 Hz, 1H, H-9), 3.00–2.85 (m, 4H, H-7, H-7, H-6, H-2), 2.60 (ddd, *J*=14.2 Hz, *J*=7.7 Hz, *J*=2 Hz, 1H, H-6), 2.30–2.23 (m, 1H, H-5), 1.81–1.73 (m, 1H, H-4), 1.72–1.66 (m, 1H, H-3), 1.62–1.48 (m, 2H, H-8, H-8), 1.36–1.28 (m, 1H, H-3); ^{13}C NMR (100 MHz) δ 140.24 (CH, C-10), 114.71 (CH_2, C-11), 57.77 (CH, C-2), 49.28 (CH_2, C-6), 47.00 (CH_2, C-7), 39.68 (CH, C-5), 28.70 (CH, C-4), 28.52 (CH_2, C-8), 26.23 (CH_2, C-3), 9.48 (CH_2, C-9); MS *m*/*z* 277 (M^+, 28), 277 (28.46), 236 (10), 182 (20), 150 (100), 136 (18), 122 (2), 108 (6), 96 (6), 81 (10), 79 (14), 70 (14), 67 (10); HRMS calcd for $C_{10}H_{16}NI$: 277.0328, found 277.0326.

(1*S*,2*S*,4*S*,5*R*)-2-Bromomethyl-5-vinyl-1-azabicyclo[2.2.2]-octane (1-Br). Mesylate **1-OMs** (250 mg, 1.02 mmol) was allowed to react according to the general procedure to afford **1-Br** (183 mg, 78%), colourless oil, $[\alpha]_D^{20}=26.0°$ (*c* 1.40, MeOH). IR ($CHCl_3$) ν 3080, 2944, 2868, 1720, 1636, 1458, 1342, 1324, 1300, 1268 (m, 1228, 1080, 992, 916, 832 cm^{-1}; ^1H NMR (400 MHz) δ 5.88 (ddd, ^3J=17.1 Hz, ^3J=10.4 Hz, ^3J=7.4 Hz, H-10)) 5.05 (ddd, ^3J=17.1 Hz, ^2J=1.5 Hz, ^4J=1.5 Hz, H-11$_{trans}$) 5.04 (ddd, ^3J=10.4 Hz, ^2J=1.5 Hz, ^4J=1.5 Hz, H-11$_{cis}$) 3.43 (dd, ^3J=8.4 Hz, ^2J=10.2 Hz, H-9) 3.33 (dd, ^3J=7 Hz, ^2J=10.3 Hz, H-9) 3.23 (dd, ^3J=10, ^2J=13.8 Hz, H-6) 3.07–2.97 (m, H-2) 2.97–2.87 (m, H-6) 2.77–2.67 (m, H-7,7) 2.32–2.24 (m, H-5) 2.05–1.96 (m, H-3)1.79 (m, H-4) 1.56–1.48 (m, H-8,8) 1,02 (dddd, ^3J=6.7 Hz, ^2J=13.7 Hz, *J*=2.3 Hz, *J*=1.6 Hz, H-3); ^{13}C NMR (100 MHz) δ 141.53 (CH, C-10), 114.53 (CH_2, C-11), 57.35 (CH, C-2), 55.85 (CH_2, C-6), 40.58 (CH_2, C-7), 39.23 (CH, C-5), 35.26 (CH_2, C-9), 28.01 (CH_2, C-3), 27.99 (CH, C-4), 27.62 (CH_2, C-8); MS *m*/*z* 231(M^++2, 14), 230 (M^++1, 2), 229(M^+, 17), 191 (1) 190 (10) 189 (1) 188 (9) 151 (12) 150 (100) 137 (9) 136 (96) 134 (23) 123 (2) 108 (8) 96 (5) 82 (11) 79 (11); HRMS calcd for $C_{10}H_{16}NBr$: 229.0466, found 229.0467.

(1*S*,2*R*,4*S*,5*R*)-2-Bromomethyl-5-vinyl-1-azabicyclo[2.2.2]-octane (2-Br). Mesylate **2-OMs** (250 mg, 1.02 mmol) was allowed to react according to the general procedure to afford **2-Br** (169 mg, 72%), yellowish oil, IR ($CHCl_3$) ν 3078, 2942, 2868, 1720, 1640, 1452, 1324, 1300, 1266, 1228, 1100, 1072, 992, 918, 832 cm^{-1}; ^1H NMR (400 MHz) δ 5.87 (ddd, $^3J_{trans}$=17 Hz, $^3J_{cis}$=10.4 Hz, ^2J=7.5 Hz, 1H, H-10), 5.05 (ddd, *J*=17 Hz, *J*=1.5 Hz, *J*=1.5 Hz, 1H, H-11), 5.04 (ddd, *J*=10.4 Hz, *J*=1.5 Hz, *J*=1.2 Hz), 3.43 (dd, *J*=10.3, *J*=8.5 Hz, 1H, H-9), 3.34 (dd, *J*=10.3 Hz, *J*=7 Hz, 1H, H-10), 3.23 (dd, *J*=13 Hz, *J*=10 Hz, 1H, H-6), 3.05 (m, 1H, H-2), 2.92 (m, 1H, H-7), 2.75–2.66 (m, 2H, H-7, H-6), 2.28 (m, 1H, H-5), 2.01 (m, 1H, H-3), 1.79 (st, *J*=3 Hz, 1H, H-4), 1.58–1.48 (m, 2H, H-8, H-8), 1.02 (m, 1H, H-3); ^{13}C NMR (100 MHz) δ 141.56 (CH, C-10), 114.54 (CH_2, C-11), 57.26 (CH, C-2), 55.87 (CH_2, C-6), 40.60 (CH_2, C-7), 39.26 (CH, C-5), 35.237 (CH_2, C-9), 28.03 (CH_2, C-8), 28.02 (CH, C-4), 27.66 (CH_2, C-3); MS *m*/*z* 231(M^++2, 13), 229(M^+, 17); HRMS calcd for $C_{10}H_{16}NBr$: 229.0466, found 229.0467.

(1*S*,2*S*,4*S*,5*R*)-2-Chloromethyl-5-vinyl-1-azabicyclo[2.2.2]-octane (1-Cl). Mesylate **1-OMs** (312 mg, 1.27 mmol) was allowed to react according to the general procedure to afford **1-Cl** (132 mg, 56%), yellowish oil, $[\alpha]_D^{20}=57.0°$ (*c* 1.00, CH_2Cl_2). IR ($CHCl_3$) ν 3080, 2928, 2868, 1720, 1636, 1452, 1376, 1344, 1324, 1304, 1272, 1152, 1100, 1020, 992, 916, 864, 820 cm^{-1}; ^1H NMR (400 MHz) δ 5.88 (ddd, $^3J_{trans}$=17.5 Hz, $^3J_{cis}$=10.4 Hz, ^2J=7.5 Hz, 1H, H-10), 5.05 (ddd, *J*=17.5 Hz, *J*=1.5 Hz, *J*=1.5 Hz, 1H, H-11), 5.04 (ddd, *J*=10.5 Hz, *J*=1.5 Hz, *J*=1.5 Hz, 1H, H-11), 3.56 (dd, *J*=11 Hz, *J*=9 Hz, 1H, H-9), 3.45 (dd, *J*=11 Hz, *J*=7 Hz, 1H, H-9), 3.22 (dd, *J*=13.8 Hz, *J*=10 Hz, 1H, H-6), 3.07–2.98 (m, 1H, H-2), 2.97–2.87 (m, 1H, H-7), 2.76–2.67 (m, 2H, H-7), H-6), 2.34–2.25

(m, 1H, H-5), 2.02–1.93 (m, 1H, H-3), 1.78 (st, J=3 Hz, 1H, H-4), 1.58–1.46 (m, 2H, H-8, H-8), 1.03–0.96 (m, 1H, H-3); ^{13}C NMR (100 MHz) δ 141.56 (CH, C-10), 114.52 (CH_2, C-11), 57.46 (CH, C-2), 55.81 (CH_2, C-6), 46 (CH_2, C-9), 40.76 (CH_2, C-7), 39.43 (CH, C-5), 27.70 (CH_2, C-8), 27.65 (CH, C-4), 27.06 (CH_2, C-3); MS m/z 185 (M^+, 14), 151 (9) 150 (77) 146 (4) 145 (1) 144 (11) 137 (10) 136 (100) 122 (2) 108 (6) 95 (11) 93 (5) 92 (10) 90 (33), 81(9) 79 (10) 67 (6); HRMS calcd for $C_{10}H_{16}NCl$: 185.0971, found 185.0973.

(1*S*,2*R*,4*S*,5*R*)-2-Chloromethyl-5-vinyl-1-azabicyclo[2.2.2]-octane (2-Cl). Mesylate **2-OMs** (304 mg, 1.24 mmol) was allowed to react according to the general procedure to afford **2-Cl** (128 mg, 56%), yellowish oil. IR ($CHCl_3$) ν 3080, 2940, 2868, 1720, 1636, 1456, 1344, 1324, 1300, 1268 (m, 1228, 1100, 1080, 992, 916, 832 cm^{-1}; ^{1}H NMR (400 MHz) δ 5.85 (ddd, $^3J_{trans}$=17 Hz, $^3J_{cis}$=10.5 Hz, ^2J=7 Hz, 1H, H-10), 5.05 (ddd, J=10.5 Hz, J=1.5 Hz, J=1.4 Hz, 1H, H-11), 5.03 (ddd, J=17 Hz, J=1.5 Hz, J=1.4 Hz, 1H, H-11), 3.57 (dd, J=10 Hz, J=8 Hz, H-9), 3.43 (dd, J=10 Hz, J=5 Hz, 1H, H-9), 3.04–2.86 (m, 4H, H-7, H-7, H-6, H-2), 2.62 (ddd J=14.5 Hz, J=7.6 Hz, J=2 Hz, 1H, H-6), 2.31–2.22 (m, 1H, H-5), 1.81–1.76 (m, 1H, H-4), 1.72–1.55 (m, H-8, H-8, H-3), 1.37–1.27 (m, 1H, H-3); ^{13}C NMR (100 MHz) 140.20 (CH, C-10), 114.73 (CH_2, C-11), 57.45 (CH, C-2), 49.19 (CH_2, C-9), 47.37 (CH_2, C-6), 45.76 (CH_2, C-7), 39.62 (CH, C-5), 34.72 (CH, C-4), 27.68 (CH_2, C-8), 26.49 (CH_2, C-3) δ; MS m/z 185 (M^+, 21), 150 (100), 144 (13), 136 (68), 92 (13), 90 (34); HRMS calcd for $C_{10}H_{16}NCl$: 185.0971, found 185.0972.

General procedure for the preparation of azides 1-N$_3$, 2-N$_3$

To a suspension of NaN_3 (5 equiv.) in H_2O (1 ml/g NaN_3) was added DCM (6 ml/ml H_2O). The mixture was cooled to 0°C and conc. H_2SO_4 (1.1 mmol/mmol NaN_3) was added slowly. The mixture was stirred for 10 min, then the organic layer was transferred (syringe) into a flask charged with $MgSO_4$. This solution was used for the the following reaction. To a solution of PPh_3 (1.2 equiv.) in THF (2 ml/mmol PPh_3) was added DEAD (1.1 equiv.) dropwise at 0°C (the mixture became inhomogeneous and the colour changed to orange). The mixture was stirred for 20 min. A solution of 1,2-amino alcohol in THF (2 ml/mmol) was added and stirring was continued for a further 20 min. Then the HN_3 solution was added slowly and dropwise. The mixture was stirred for 10 min and then heated to reflux for 2.5 h. After being cooled to room temperature the mixture was diluted with DCM or $CHCl_3$ and treated with sat. aq. $NaHCO_3$ solution. The aqueous layer was extracted with DCM or $CHCl_3$ and the combined organic layer dried (Na_2SO_4). After removal of the solvent the crude product was purified by chromatography (MTBE).

(1*S*,2*S*,4*S*,5*R*)-2-Azidomethyl-5-vinyl-1-azabicyclo[2.2.2]-octane (1-N$_3$). QCI (1.5. g, 9 mmol) was allowed to react according to the general procedure to afford **1-N$_3$** (2.19. g, 76%), yellowish solid, $[\alpha]_D^{20}$=46.8° (c 0.985, CH_2Cl_2). IR ($CHCl_3$) ν 2932, 2868, 2796, 2104, 1708, 1636, 1560, 1480, 1464, 1444, 1416, 1380, 1236, 1176, 1132, 1092, 1060, 1024, 992, 916, 540 cm^{-1}; ^{1}H NMR (400 MHz) δ 5.88 (ddd, $^3J_{trans}$=17.5 Hz, $^3J_{cis}$=10.5 Hz, ^2J=7.7 Hz, 1H, H-10), 5.05 (ddd, J=17.5 Hz, J=1.6 Hz, J=1.5 Hz, 1H H-11), 5.04 (ddd, J=9 Hz, J=1.6 Hz, J=1.5 Hz, 1H, H-11), 3.38 (dd, J=11.7 Hz, J=9.6 Hz, 1H, H-9), 3.24–3.15 (m, 2H, H-9, H-6), 3.02–2.88 (m, 2H, H-2, H-7), 2.76–2.66 (m, 2H, H-7, H-6), 2.34–2.25 (m, 1H, H-5), 1.95–1.86 (m, 1H, H-3), 1.75 (st, J=3 Hz, 1H, H-4), 1.57–1.44 (m, 2H, H-8, H-8), 0.94-.086 (m, 1H, H-3); ^{13}C NMR (100 MHz) δ 141.68 (CH, C-10), 114.49 (CH_2, C-11), 55.80 (CH_2, C-6), 55.46 (CH, C-2), 53.68 (CH_2, C-9), 40.73 (CH_2, C-7), 39.58 (CH, C-5), 27.87 (CH_2, C-8), 27.31 (CH, C-4), 26.37 (CH_2, C-3); MS m/z 192 (M^+, 2), 163 (6), 150 (6), 136 (100), 122 (3), 108 (4), 95 (6), 91 (5), 81 (13), 77 (4), 69 (12); HRMS calcd for $C_{10}H_{16}N_4$: 192.1375, found 192.1374.

(1*S*,2*R*,4*S*,5*R*)-2-Azidomethyl-5-vinyl-1-azabicyclo[2.2.2]-octane (2-N$_3$). QCD (1.5. g, 9 mmol) was allowed to react according to the general procedure to afford **2-N$_3$** (1.31. g, 75%), yellowish solid, $[\alpha]_D^{20}$=201.4° (c 1.06, CH_2Cl_2). IR ($CHCl_3$) ν 3079, 2941, 2875, 2101, 1636, 1457, 1438, 164, 1120, 1058, 993, 916, 822, 542 cm^{-1}; ^{1}H NMR (400 MHz) δ 5.84 (ddd, $^3J_{trans}$=17 Hz, $^3J_{cis}$=10.5 Hz, ^2J=7 Hz, 1H, H-10), 5.05 (ddd, J=10.5 Hz, J=1.5 Hz, J=1.5 Hz, 1H, H-11), 5.03 (ddd, J=17 Hz, J=1.5 Hz, J=1.5 Hz, 1H, H-11), 3.38 (dd, J=12.7 Hz, J=9 Hz, 1H, H-9), 3.16 (dd, J=12.7 Hz, J=6 Hz, 1H, H-9), 3.00–2.82 (m, 4H, H-7, H-7, H-6, H-2), 2.64 (ddd, J=12 Hz, J=8 Hz, J=2 Hz, 1H, H-6), 2.30–2.21 (m, 1H, H-5), 1.78–1.73 (m, 1H, H-4), 1.63–1.56 (m, 2H, H-8, H-8), 1.55 (dddd, J=13.8 Hz, J=9.3 Hz, J=4.6 Hz, J=1.8 Hz, 1H, H-3), 1.30–1.21 (m, 1H, H-3); ^{13}C NMR (100 MHz) δ 140.26 (CH, C-10), 114.48 (CH_2, C-11), 55.35 (CH, C-2), 52.89 (CH_2, C-6), 49.06 (CH_2, C-9), 47.15 (CH, C-2), 39.72 (CH, C-5), 27.40 (CH, C-4), 26.62 (CH_2, C-8), 25.56 (CH_2, C-3; MS m/z 192 (M^+, 96), 163 (27), 150 (75), 136 (100), 122 (19), 108 (28), 99 (12), 94 (31), 85 (11), 81 (52), 77 (24), 69 (38); HRMS calcd for $C_{10}H_{16}N_4$192.1375:, found 192.1375.

General procedure for the preparation of diamines 1-NH$_2$, 2-NH$_2$

The crude azides **1-N$_3$** and **2-N$_3$** (contaminated with Ph_3PO) could be used for the preparation of diamines. To a solution of azide in THF (4 ml/mmol substrate) was added PPh_3 (2 equiv.). Gas evolution could be observed which became stronger after addition of catalytic amounts of TFA. The mixture was stirred for 2 h at room temperature. Occasionally it was necessary to heat the mixture at reflux for an additional 1 h (TLC control). Then 2 N NaOH was added and the mixture was stirred overnight. The aqueous phase was extracted with DCM or $CHCl_3$ and the combined organic layer was dried (Na_2SO_4). The solvent was evaporated and the residue purified by chromatography (MTBE→MTBE/MeOH, 5:1).

(1*S*,2*S*,4*S*,5*R*)-2-(Aminomethyl)-5-vinyl-1-azabicyclo-[2.2.2]octane (1-NH$_2$). Azide **1-N$_3$** (3.00. g, 15.6 mmol) was allowed to react according to the general procedure to afford **1-NH$_2$** (1.34. g, 52%), yellowish oil, $[\alpha]_D^{20}$=38.4° (c 0.945, CH_2Cl_2). IR ($CHCl_3$) ν 3392, 3080, 2996, 2940, 2868, 1660, 1600, 1560, 1528, 1480, 1452, 1380, 1324,

1260, 1236, 1176, 1100, 1056, 992, 868 cm^{-1}; ^1H NMR (400 MHz) δ 5.86 (ddd, $^3J_{trans}$=17 Hz, $^3J_{cis}$=10.8 Hz, ^2J=4 Hz, 1H, H-10), 5.04 (ddd, J=17 Hz, J=1.3 Hz, J=1.1 Hz, 1H, H-11), 5.03 (ddd, J=10.8 Hz, J=1.2 Hz, J=1.1 Hz, 1H, H-11), 3.85 (bs, 2H, NH2), 3.38–3.29 (m, 1H, H-9), 3.16 (dd, J=14.7 Hz, J=10.2 Hz, 1H, H-6_{endo}) 3.09–2.83 (m, 3H, H-7_{endo}, H-9, H-2), 2.65–2.56 (m, 2H, H-6_{exo}, H-7_{exo}), 2.36–2.27 (m, 1H, H-5), 1.94–1.84 (m, 1H, H-3_{endo}), 1.77–1.71 (m, 1H, H-4), 1.58–1.49 (m, 2H, H-8, H-8), 0.90 (dddd, J=13.5 Hz, J=9 Hz, J=5 Hz, J=2.5 Hz, 1H, H-3_{exo}); ^{13}C NMR (100 MHz) δ 141.23 (CH, C-10), 114.31 (CH_2, C-11), 55.91 (CH, C-2), 55.81 (CH_2, C-6), 42.79 (CH_2, C-9), 40.33 (CH_2, C-7), 39.45 (CH, C-5), 27.55 (CH_2, C-8), 27.33 (CH, C-4), 26.69 (CH_2, C-3); MS m/z 166 (M^+, 36), 165 (2), 150 (10), 137 (14), 136 (100), 125 (8), 134 (10), 125 (27), 123 (12), 122 (10), 110 (11), 108 (21), 95 (19), 83 (47), 71 (14); HRMS calcd for $C_{10}H_{18}N_2$: 166.1470, found 166.1468.

(1*S*,2*R*,4*S*,5*R*)-2-(Aminomethyl)-5-vinyl-1-azabicyclo-[2.2.2]octane (2-NH$_2$). Azide **2-N$_3$** (2.50. g, 13.0 mmol) was allowed to react according to the general procedure to afford **2-NH$_2$** (1.16. g, 54%), yellowish solid, mp 60–63°C, $[\alpha]_D^{20}$=169.0° (c 1.20, CH_2Cl_2). IR ($CHCl_3$) ν 3389, 3079, 2941, 2872, 1657, 1526, 1456, 1324, 1230, 1099, 1061, 993, 822 cm^{-1}; ^1H NMR (400 MHz) δ 5.84 (ddd, $^3J_{trans}$=17.4 Hz, $^3J_{cis}$=11.3 Hz, ^2J=4 Hz, 1H, H-10), 5.02 (ddd, J=11.3 Hz, J=1.4 Hz, J=1.1 Hz, 1H, H-11), 5.01 (ddd, J=17.4 Hz, J=1.6 Hz, J=1.1 Hz, 1H, H-11), 3.38–3.29 (m, 1H, H-9), 3.02–2.73 (m, 5H, H-6_{endo}, H-9, H-7_{endo}, H-2, H-7_{exo}), 2.67 (ddd, J=14.7 Hz, J =7.8 Hz, J=1.4 Hz, 1H, H-6_{exo}), 2.29–2.19 (m, 1H, H-5), 1.75–1.69 (m, 1H, H-4), 1.64–1.55 (m, 2H, H-8, H-8), 1.52 (dddd, J=13.7 Hz, J=9.3 Hz, J=4.4 Hz, J=2.5 Hz, 1H, H-3_{endo}), 1.28–1.19 (m, 1H, H-3_{exo}); ^{13}C NMR (100 MHz) δ 140.20 (CH, C-10), 114.42 (CH_2, C-11), 55.75 (CH, C-2), 48.78 (CH_2, C-6), 46.38 (CH_2, C-9), 41.92 (CH_2, C-7), 39.81 (CH, C-5), 27.54 (CH, C-4), 26.67 (CH_2, C-8), 25.47 (CH_2, C-3); MS m/z 166 (M^+, 57), 165 (8), 150 (12), 137 (21), 136 (100), 125 (9), 134 (10), 125 (27), 123 (13), 122 (11), 110 (13), 108 (24), 95 (20), 83 (52), 71 (13); HRMS calcd for $C_{10}H_{18}N_2$: 166.1470, found 166.1469.

3-Chloro-(1*S*,2*R*,4*S*,5*R*)-*N*-(5-vinyl-1-azabicyclo[2.2.2]-oct-2-ylmethyl)-benzamide (2-NHCOAr). To a solution of PPh_3 (2 equiv.) in THF (5 ml/mmol substrate) was added azide **2-N$_3$** (200 mg, 1.04 mmol) and *m*-CBA (2.08 mmol, 325 mg) and the mixture was heated to reflux for 2.5 h. Then sat. aq. $NaHCO_3$ solution was added and the aqueous phase was extracted with DCM or $CHCl_3$. The combined organic layer was dried (Na_2SO_4), evaporated and purified by chromatography (MTBE→MTBE/MeOH, 5:1) to afford **2-NHCOAr** (89 mg, 29%), highly viscous oil. IR ($CHCl_3$) ν 3398, 2999, 2931, 2867, 1719, 1654, 1600, 1571, 1512, 1469, 1382, 1291, 1230, 1132, 1075, 991, 912 cm^{-1}; ^1H NMR (400 MHz) δ 7.84–7.30 (m, 4H, Ar-H), 5.88 (ddd), $^3J_{trans}$=17.5 Hz, $^3J_{cis}$=10 Hz, ^2J=7.5 Hz, 1H, H-10), 5.07 (ddd, J=17.5 Hz, J=10.5 Hz, J=1.4H, 1H, H-11), 5.06 (ddd, J=10.5 Hz, J=1.4H, J=1.4 Hz, 1H, H-11), 3.76 (ddd, J=11.8 Hz, J=7.5 Hz, J=5.5 Hz, 1H, H-), 3.21 (dd, J=13.7 Hz, J=10 Hz, 1H, H-), 3.16 (ddd, J=13.7 Hz, J=11.3 Hz, J=2.5 Hz, 1H, H-), 3.06–2.96 (m, 2H, H-, H-), 2.76–2.65(m, 2H, H-, H-), 2.41–2.32 (m, 1H, H-5), 2.05–1.95 (m, 1H, H-3), 1.81 (st, J=3 Hz, 1H, H-4), 1.65–1.55 (m, 2H, H-8, H-8), 1.05–0.98 (m, 1H, H-3); ^{13}C NMR (100 MHz) δ 166.10 (C=O), 141.19 (CH, C-10), 136.28, 134.58 (Cq, C-13, C-15) 131.34, 129.73, 127.53, 125.28 (CH, C-Ar.), 114.91 (CH_2, C-11), 68.16 (CH_2, C-9), 55.30 (CH, C-2), 55.29 (CH_2, C-6), 42.19 (CH_2, C-7), 39.43 (CH, C-5), 27.46 (CH, C-4), 26.22 (CH_2, C-8), 23.74 (CH_2, C-3); MS m/z 304 (M^+, 1), 280 (10), 238 (3), 193 (4), 167 (12), 149 (31), 136 (100), 116 (4), 95 (4), 71 (8); HRMS calcd for $C_{17}H_{21}N_2OCl$: 304.1342, found 304.1342.

General procedure for the preparation of aryl ethers 2-OPh, 1-OAr, 2-Oar

To a solution of PPh_3 (1.2 equiv.) in THF (2 ml/mmol PPh_3) was added DEAD (1.1 equiv.) at 0°C (the mixture became inhomogeneous and the colour changed to orange). The mixture was stirred for 20 min, then the 1,2-amino alcohol in THF (2 ml/mmol) was added dropwise. Stirring was continued for 20 min at 0°C. A solution of phenol (1.6 equiv.) in THF (3 ml/mmol) was added. The mixture was stirred for 10 min and then heated to reflux for 4 h. After being cooled to room temperature the mixture was diluted with DCM or $CHCl_3$ and treated with sat. aq. $NaHCO_3$ solution. The aqueous layer was extracted with DCM or $CHCl_3$, the combined organic layer was washed with sat. aq. NaHCO3 solution and dried (Na_2SO_4). After removal of the solvent the crude product was purified by chromatography (MTBE→MTBE/MeOH, 10:1).

(1*S*,2*R*,4*S*,5*R*)-2-Phenoxymethyl-5-vinyl-1-azabicyclo-[2.2.2]octane (2-OPh). QCD (240 mg, 1.44 mmol) was allowed to react according to the general procedure to afford **2-OPh** (95 mg, 27%), highly viscous, light-yellowish oil. IR ($CHCl_3$) ν 2945, 2874, 1717, 1598, 1515, 1377, 1334, 1265, 1231, 1163, 1059, 918, 836 cm^{-1}; ^1H NMR (400 MHz) δ 7.15–6.85 (m, 2H, H-14), 6.77–6.48 (m, 3H, H-13, H-15), 5.82 (ddd, J=16.5 Hz, J=10.4 Hz, J=5 Hz, 1H, H-10), 5.04 (ddd, J=10.4 Hz, J=1.4 Hz, J=0.8 Hz, 1H, H-11_{cis}), 5.02 (ddd, J=16.5 Hz, J=1.5 Hz, J=0.8 Hz, 1H, H-11_{trans}), 4.16 (dd, J=11 Hz, J=2.6 Hz, 1H, H-9), 3.99 (dd, J=11 Hz, J=5.4 Hz, 1H, H-9), 3.18–2.82 (m, 4H, H-6_{endo}, H-2, H-7, H-7), 2.72 (ddd, J=14 Hz, J=7.7 Hz, J=2 Hz, 1H, H-6_{exo}), 2.36–2.17 (m, 1H, H-5), 1.82–1.73 (m, 1H, H-4), 1.63–1.53 (m, 2H, H-8, H-8), 1.52 (dddd, J=14 Hz, J=10 Hz, J=4.5 Hz, J=1.5 Hz, 1H, H-3_{endo} 1.39–1.22 (m, 1H, H-3_{exo}); ^{13}C NMR (100 MHz) δ 156.58 (Cq, C-12), 140.04 (CH, C-10), 133.48 (CH, C-14), 115.73 (CH, C-15), 115.41 (CH, C-13), 114.85 (CH_2, C-11), 64.37 (CH_2, C-9), 54.49 (CH, C-2), 48.80 (CH_2, C-6), 47.04 (CH_2, C-7), 39.57 (CH, C-5), 26.98 (CH, C-4), 6.54 (CH_2, C-8), 24.05 (CH_2, C-3); MS m/z 243 (M^+, 3),; HRMS calcd for $C_{16}H_{21}NO_2$: 243.1623, found 243.1625. MS m/z: 209 (22), 198 (2), 192 (8), 181 (2), 169 (15), 162 (3), 150 (46), 136 (82), 126 (4), 114 (8), 108 (10), 99 (3), 94 (22), 81 (7), 73 (100).

(1*S*,2*S*,4*S*,5*R*)-2-(2-Methoxy-phenoxymethyl)-5-vinyl-1-azabicyclo[2.2.2]octane (1-OAr). QCI (612 mg, 3.67 mmol) was allowed to react according to the general procedure to afford **1-OAr** (360 mg, 36%), highly viscous oil,

$[\alpha]_D^{20}$=15.6° (*c* 1.13, CH_2Cl_2). IR ($CHCl_3$) ν 3060, 2980, 2960, 2868, 1740, 1664, 1636, 1592, 1564, 1452, 1436, 1396, 1376, 1328, 1252, 1176, 1120, 1048, 1028, 996, 940 cm^{-1}; ^1H NMR (400 MHz) δ 6.96–6.86 (m, 4H, H-Ar), 5.92 (ddd, $^3J_{trans}$=17 Hz, $^3J_{cis}$=10.3 Hz, ^2J=7 Hz, 1H, H-10), 5.07 (ddd, *J*=17 Hz, *J*=1.5 Hz, *J*=1.5 Hz, 1H, H-11), 5.05 (ddd, *J*=10.3 Hz, *J*=1.5 Hz, *J*=1.5 Hz, 1H, H-11), 4.09 (dd, *J*=10 Hz, *J*=7.7 Hz, 1H, H-9), 3.90 (dd, *J*=10 Hz, *J*=6 Hz, 1H, H-9), 3.36–3.27 (m, 1H, H-2), 3.22 (dd, *J*=13.8 Hz, *J*=9.8 Hz, 1H, H-6), 3.15–3.06 (m, 1H, H-7), 2.84–2.70 (m, 2H, H-7, H-6), 2.39–2.30 (m, 1H, H-5), 2.03–1.93 (m, 1H, H-3), 1.80 (st, *J*=3 Hz, 1H, H-4), 1.64–1.50 (m, 2H, H-8, H-8), 1.41 (dddd, *J*=13.3 Hz, *J*=6.8 Hz, *J*=2 Hz, *J*=2 Hz, 1H, H-3); ^{13}C NMR (100 MHz) δ 141.59 (CH, C-10), 132.14, 132.04, 121.96, 131.93, 128.56, 128.44 (C-Ar), 114.02 (CH_2, C-11), 70.97 (OCH_3), 55.82 (CH_2, C-9), 55.65 (CH_2, C-6), 55.07 (CH, C-2), 41.46 (CH_2, C-7), 39.66 (CH, C-5), 27.61 (CH_2, C-8), 27.52 (CH, C-4), 25.16 (CH_2, C-3); MS *m*/*z* 273 (M^+, 11), 242 (3), 232 (2), 199 (3), 188 (3), 166 (2), 150 (22), 136 (100), 124 (5), 95 (5), 81 (7); HRMS calcd for $C_{17}H_{23}NO_2$: 273.1729, found 273.1726.

(1*S*,2*R*,4*S*,5*R*)-2-(2-Methoxy-phenoxymethyl)-5-vinyl-1-azabicyclo[2.2.2]octane (2-OAr). QCD (742 mg, 4.44 mmol) was allowed to react according to the general procedure to afford **2-OAr** (413 mg, 34%), highly viscous oil, $[\alpha]_D^{20}$=113.4° (*c* 1.005, CH_2Cl_2). IR ($CHCl_3$) ν 3068, 3000, 2940, 2876, 1716, 1636, 1592, 1504, 1456, 1420, 1400, 1376, 1324, 1252, 1180, 1142, 1052, 1028, 940, 916 cm^{-1}; ^1H NMR (400 MHz) δ 6.95–6.86 (m, 4H, Ar-H), 5.92 (ddd, $^3J_{trans}$=16 Hz, $^3J_{cis}$=11 Hz, ^2J=7 Hz, 1H, H-10), 5.05 (ddd, *J*=16 Hz, *J*=11 Hz, *J*, 1.6 Hz, 1H, H-11), 5.04 (ddd, *J*=11 Hz, *J*=1.6 Hz, *J*=1.4 Hz, 1H, H-11), 4.10 (dd, *J*=9.8 Hz, *J*=7.4 Hz, 1H, H-9), 3.87 (dd, *J*=9.8 Hz, *J*=6 Hz, 1H, H-9), 3.84 (s, 3H, OCH_3), 3.29–3.19 (m, 1H, H-2), 3.07–2.82 (m, 4H, H-7, H-7, H-6, H-6), 2.32–2.23 (m, 1H H-5), 1.81–1.76 (st, *J*=2 Hz, 1H, H-4), 1.70–1.58 (m, 3H, H-8, H-8, H-3), 1.54–1.46 (m, 1H, H-3); ^{13}C NMR (100 MHz) δ 149.67 (Cq, C-13), 148.51 (Cq, C-12), 140.59 (CH, C-10), 121.34 (CH, C-17), 120.84 (CH, C-15), 113.83 (CH, C-16), 111.90 (CH, C-14), 114.52 (CH_2, C-11), 70.40 (CH_2, C-9), 55.78 (OCH_3), 54.83 (CH, C-2), 49.05 (CH_2, C-6), 47.97 (CH_2, C-7), 39.95 (CH, C-5), 27.64 (CH, C-4), 26.72 (CH_2, C-8), 24.70 (CH_2, C-3); MS *m*/*z* 273 (M^+, 44), 242 (23), 218 (9), 190 (9), 162 (10), 150 (100), 136 (75), 121 (16), 108 (14), 82 (16); HRMS calcd for $C_{17}H_{23}NO_2$: 273.1729, found 273.1728.

General procedure for the preparation of cyanides 1-CN, 2-CN

A round bottomed flask was charged with KCN (5 equiv.) and CsF (4 equiv.), heated (heat gun) under vacuum and then flushed with N_2. Toluene (1.3 ml/mmol substrate) was added followed by the 1,2-amino alcohol. Under a stream of N_2 anhydrous 18-crown-6 (catal.) was added and then toluene (0.7 ml/mmol substrate). The resulting mixture was heated to reflux for 2–4 d (TLC control). The warm reaction mixture was treated with sat. aq. $NaHCO_3$ solution and stirred for 10 min. The aqueous phase was extracted with DCM (5×), the combined organic layer washed with sat. aq. $NaHCO_3$ solution (3×), brine (3×) and dried ($MgSO_4$). After removal of the solvent the crude product was purified by chromatography (MTBE).

((1*S*,2*S*,4*S*,5*R*)-5-Vinyl-1-azabicyclo[2.2.2]oct-2-yl)-acetonitrile (1-CN). Mesylate **1-OMs** (4.00 g, 16.3 mmol) was allowed to react according to the general procedure to afford **1-CN** (2.73. g, 95%), oil, $[\alpha]_D^{20}$=64.1° (*c* 1.285, CH_2Cl_2). IR ($CHCl_3$) ν 3080, 2952, 2868, 2252, 1636, 1452, 1420, 1344, 1324, 1228, 1044, 992, 944, 916, 812 cm^{-1}; ^1H NMR (400 MHz) δ 5.87 (ddd, $^3J_{trans}$=17.5 Hz, $^3J_{cis}$=10 Hz, ^2J=7.1 Hz, 1H, H-10), 5.07 (ddd, *J*=17.5 Hz, *J*=10 Hz, *J*=1.5 Hz, 1H, H-11$_{trans}$), 5.06 (ddd, *J*=10 Hz, *J*=1.5 Hz, *J*=1.5 Hz, 1H, H-11$_{cis}$), 3.19 (dd, *J*=13.8 Hz, *J*=10 Hz, 1H, H-6$_{endo}$), 3.15–3.06 (m, 1H, H-2), 2.95–2.85 (m, 1H, H-7$_{endo}$), 2.89–2.69 (m, 2H, H-7$_{exo}$, H-6$_{exo}$), 2.55 (dd, *J*=16.7 Hz, *J*=7.5 Hz, 1H, H-9), 2.47 (dd, *J*=16.7 Hz, *J*=7.5 Hz, 1H, H-9), 2.34–2.25 (m, 1H, H-5), 2.11–2.02 (m, 1H, H-3$_{endo}$), 1.83–1.77 (st, *J*=3 Hz, 1H, H-4), 1.57–1.51 (m, 2H, H-8, H-8), 1.09–1.01 (m, 1H, H-3$_{exo}$); ^{13}C NMR (100 MHz) δ 141.28 (CH, C-10), 118.37 (Cq, CN), 114.78 (CH_2, C-11), 55.80 (CH_2, C-6), 52.98 (CH, C-2), 40.62 (CH_2, C-7), 38.95 (CH, C-5), 28.08 (CH_2, C-9), 27.57 (CH_2, C-8), 27.53 (CH, C-4), 23.28 (CH_2, C-3); MS *m*/*z* 176 (M^+, 21), 161 (5), 150 (5), 136 (100), 122 (5), 109 (9), 95 (10), 91 (6), 81 (22), 77 (11), 67 (8); HRMS calcd for $C_{11}H_{16}N_2$: 176.1314, found 176.1383.

((1*S*,2*R*,4*S*,5*R*)-5-Vinyl-1-azabicyclo[2.2.2]oct-2-yl)-acetonitrile (2-CN). Mesylate **2-OMs** (4.00. g, 16.3 mmol) was allowed to react according to the general procedure to afford **2-CN** (2.33. g, 81%), oil, $[\alpha]_D^{20}$=183.0° (*c* 1.00, CH_2Cl_2). IR (film) ν 3075, 2938, 2871, 2248, 1636, 1455, 1420, 1323, 1088, 1057, 993, 913, 752, 664 cm^{-1}; ^1H NMR (400 MHz) δ 5.84 (ddd, ^3J=17.3 Hz, ^3J=10.5 Hz, ^3J=6.8 Hz, 1H, H-10) 5.07 (ddd, ^3J=10.3 Hz, ^2J=1.5 Hz, ^4J=1.5 Hz, 1H, H-11$_{cis}$) 5.04 (ddd, ^3J=17.1 Hz, ^2J=1.5 Hz, ^4J=1.5 Hz, 1H, H-11$_{trans}$) 3.08 (m, 1H, H-2) 3.02–2.84 (m, 3H, H-7, H-7, H-6$_{endo}$) 2.59 (ddd, ^3J=7.6 Hz, ^2J=14.3 Hz, *J*=2.3 Hz, 1H, H-6$_{exo}$) 2.53 (dd, ^3J=7.9 Hz, ^2J=16.7 Hz, 1H, H-9) 2.44 (dd, ^3J=7.7 Hz, ^2J=16.7 Hz, 1H, H-9) 2.27 (m, 1H, H-5) 1.79 (m, 1H, H-4) 1,73 (dddd, ^3J=9.2 Hz, ^3J=4.6 Hz, ^2J=13.6 Hz, *J*=1.7 Hz, 1H, H-8) 1.63–1.56 (m, 2H, H-8, H-3$_{endo}$) 1.39 (H-3$_{exo}$); ^{13}C NMR (100 MHz) δ 139.9 (CH, C-10), 118.4 (Cq, CN), 114.9 (C2, C-11), 53.0 (CH, C-2), 49.2 (C2, C-6), 47.0 (CH_2, C-7), 39.5 (CH, C-5), 27.6 (CH, C-4), 27.4 (CH_2, C-9), 26.1 (CH_2, C-8), 22.4 (CH_2, C-3); MS *m*/*z* 177 (M^++1, 9), 176 (M^+, 53), 175 (11) 162 (2) 161 (7) 150 (2) 149 (3) 148 (4) 147 (6) 137 (12) 136 (100) 135 (23) 134 (7) 133 (6) 122 (9) 121 (9) 109 (12) 108 (17) 107 (5) 96 (7) 95 (12) 94 (12) 83 (15) 81 (37) 80 (12) 79 (16) 67 (12); HRMS calcd for $C_{11}H_{16}N_2$: 176.1314, found 176.1315.

General procedure for the preparation of sulfones 1-Ts, 2-Ts

Sodium *p*-methylbenzenesulfinate (3 equiv.), CsF (3 equiv.) and anhydrous 15-crown-5 (catal.) were allowed to react as described for the cyanides **1-CN** and **2-CN**.

(1*S*,2*S*,4*S*,5*R*)-2-(Toluene-4-sulfonylmethyl)-5-vinyl-1-azabicyclo[2.2.2]octane (1-Ts). Mesylate **1-OMs** (250 mg,

1.02 mmol) was allowed to react according to the general procedure to afford **1-Ts** (143 mg, 46%), highly viscous oil, $[\alpha]_D^{20}$=17.4° (*c* 1.065, CH_2Cl_2). IR ($CHCl_3$) ν 3029, 2948, 2868, 1637, 1598, 1453, 1402, 1315, 1302, 1231, 1150, 1088, 918, 577, 541 cm^{-1}; ^1H NMR (400 MHz) δ 7.82–7.78 (m, 2H, H-14), 7.37–7.31 (m, 2H, H-13), 5.85 (ddd, $^3J_{trans}$=16.6 Hz, $^3J_{cis}$=11 Hz, ^2J=7.5 Hz, 1H, H-10), 5.03 (ddd, *J*=11 Hz, *J*=1.3 Hz, *J*=1.1 Hz, 1H, H-11), 5.01 (ddd, *J*=16.6 Hz, *J*=1.5 Hz, *J*=1.1 Hz, 1H, H-11), 3.37–3.30 (m, 1H, H-9), 3.27–3.17 (m, 2H, H-2, H-9), 3.08 (dd, *J*=13.8 Hz, *J*=10.2 Hz, 1H, H-6_{endo}), 2.77–2.56 (m, 3H, H-6_{exo}, H-7, H-7), 2.45 (s, 3H, CH_3), 2.27–2.19 (m, 1H, H-3_{endo}), 2.09–2.00(m, 1H, H-5), 1.74–1.69 (m, 1H, H-4), 1.53–1.45 (m, 2H, H-8, H-8), 1.16 (dddd, *J*=13.5 Hz, *J*=6.2 Hz, *J*=2.2 Hz, *J*=1.6 Hz, 1H, H-3); ^{13}C NMR (100 MHz) δ 144.55 (Cq, C-12), 140.42 (CH, C-10), 137.08 (Cq, C-15), 129.73 (CH, C-14), 128.12 (CH, C-13), 114.58 (CH_2, C-11), 62.11 (CH_2, C-9), 55.60 (CH_2, C-6), 51.23 (CH, C-2), 41.20 (CH_2, C-7), 39.21 (CH, C-5), 28.77 (CH_2, C-8), 27.60 (CH_2, C-3), 27.31 (CH, C-4), 21.64 (CH_3); MS *m/z* 305 (M^+, 8), 264 (14), 241 (20), 226 (1), 210 (3), 182 (3), 150 (82), 136 (100), 124 (3), 123 (3), 109 (4), 108 (6), 91 (25), 81 (12), 70 (11); HRMS calcd for $C_{17}H_{23}NO_2S$:, found 305.1448.

(1*S*,2*R*,4*S*,5*R*)-2-(Toluene-4-sulfonylmethyl)-5-vinyl-1-azabicyclo[2.2.2]octane (2-Ts). Mesylate **2-OMs** (320 mg, 1.31 mmol) was allowed to react according to the general procedure to afford **2-Ts** (164 mg, 41%), highly viscous oil, $[\alpha]_D^{20}$=63.5° (*c* 1.15, CH_2Cl_2). IR ($CHCl_3$) ν 3080, 2928, 2868, 1720, 1636, 1596, 1456, 1400, 1380, 1316, 1264, 1228, 1148, 1084, 1044, 1016, 992, 916, 880, 816, 584, 536 cm^{-1}; ^1H NMR (400 MHz) δ 7.80 (d, *J*=8.3 Hz, 2H, H-14), 7.34 (d, *J*=8 Hz, 2H, H-15), 5.81 (ddd, $^3J_{trans}$=17 Hz, $^3J_{cis}$=10.4 Hz, ^2J=6.8 Hz, 1H, H-10), 5.03 (ddd, *J*=10.3 Hz, *J*=1.3 Hz, *J*=1.3 Hz, 1H, H-11), 4.99 (ddd, *J*=17 Hz, *J*=1.5 Hz, *J*=1.3 Hz, 1H, H-11), 3.35 (dd, *J*=12 Hz, *J*=3.8 Hz, 1H, H-9), 3.27–3.16 (m, 2H, H-2, H-9), 2.96–2.89 (m, 1H, H-7), 2.88–2.72 (m, 2H, H-6, H-7), 2.45 (s, 3H, CH_3), 2.43 (ddd, *J*=14.2 Hz, *J*=7.6 Hz, *J*=2.2 Hz, 2.26–2.17 (m, 1H, H-3), 1.75–1.69 (m, 2H, H-5, H-4), 1.60–1.41 (m, 2H, H-8, H-8), 0.91–0.81 (m, 1H, H-3); ^{13}C NMR (100 MHz) δ 144.49 (Cq, C-12), 140.11 (CH, C-10), 137.23 (Cq, C-15), 129.73 (CH, C-14), 128.10 (CH, C-13), 114.78 (CH_2, C-11), 61.47 (CH_2, C-9), 50.97 (CH, C-2), 48.82 (CH_2, C-6), 47.75 (CH_2, C-7), 39.47 (CH, C-5), 28.30 (CH_2, C-8), 27.34 (CH, C-4), 26.20 (CH_2, C-3), 21.64 (CH_3); MS *m/z* 305 (M^+, 7), 280 (3), 264 (2), 241 (31), 226 (2), 210 (5), 198 (3), 150 (100), 136 (30), 123 (4), 109 (8), 91 (27), 81 (12), 70 (17); HRMS calcd for $C_{17}H_{23}NO_2S$: 305.1450, found 305.1451.

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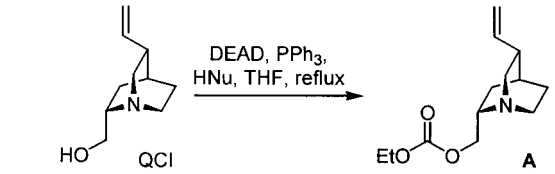

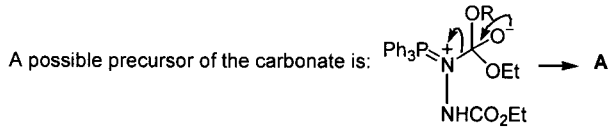

We have found that even sterically hindered di *t*-butyl azodicarboxylate provided the *t*-butyl carbonate of QCI.
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