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The aza-xylylene Diels–Alder approach for the synthesis of naturally occurring 2-alkyl tetrahydroquinolines

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Dedicated to Professor K. C. Nicolaou for his achievements in the total synthesis of complex natural products

Abstract—The recently discovered intramolecular aza-xylylene Diels–Alder reaction, based on a 1,4-dehydrohalogenation reaction, was extended in terms of substrates and leaving groups allowing the assembly of tetrahydroquinolines in two synthetic steps. Intramolecular cleavage of a thiocarbamate using triphenylphosphine and tetrachloromethane (Appel conditions) to give chloromethyl phenylisocyanate has been presented for the first time. The synthetic feasibility of this process was demonstrated in the first total syntheses of the alkaloids *rac*-Angustureine and 1-methyl-2-propyltetrahydroquinoline.

1. Introduction

Tetrahydroquinolines play an important role in material sciences and as key elements in many natural products. Numerous ring-annulated or 3- and 4-substituted tetrahydroquinolines can be found in nature and can be prepared efficiently via a Grieco type reaction.[1] Much simpler 2-alkyl tetrahydroquinolines which are not directly accessible by this route are present in a recently discovered relatively small class of natural products **2b**,[2] **3b**,[3] **4b**,[4] **5b**[5] and **6b**[3] (Fig. 1). Some members of this family have interesting pharmacological properties.[3,6]

Owing to our interest in heterocyclic chemistry, in particular using solid-phase chemistry[7] and searching for new lead structures in combinatorial drug discovery based on natural products, we envisaged a general synthesis of this class of compounds.[8] We were intrigued by the smooth generation of substituted tetrahydroquinolines using the base-induced 1,4-elimination aza-xylylene[9] Diels–Alder[10] approach lately explored by Nishiyama et al.[11] and Corey and Steinhagen.[12] Nicolaou et al. very recently used a novel access to *o*-imidoquinones and their Diels–Alder reaction to generate benzomorpholines[13] (Y=O, Scheme 1).

An elegant approach to tetrahydroquinoline systems is based on the 1,4-dehydrohalogenation of 2-chloromethylphenyl carbamates having an internal or external dienophile. The scope of this reaction was demonstrated in the total synthesis of the anti-viral Virantmycin.[14]

In order to expand the scope of this useful reaction, we explored the access to building blocks suitable for the intramolecular cyclization. The carbamate structure can be assembled by the reaction of isocyanates with alcohols or via the reaction of anilines with chloroformates. Since only few unsaturated chloroformates are commercially available and, moreover, only (*Z*)-configured double bonds are suitable dienophiles,[12] the synthesis of carbamates using isocyanates as starting material was more promising with regards to the anticipated solid-phase reaction. Therefore, an alternative route to chloromethyl phenylisocyanates was investigated. Some thirty years ago, Appel described the cleavage of arylthiocarbamates by means of triphenylphosphine/tetrachloromethane to yield alkyl chlorides and arylisocyanates.[15] This transformation and in particular the subsequent reaction with external nucleophiles has, to our knowledge, never been described since. However, an intramolecular Appel reaction on arylthiocarbamates would enable an access to chloromethyl arylisocyanates. The required known 1,4-dihydro-benzo[*d*][1,3]oxazine-2-thione **8** was synthesized using carbon disulfide under standard conditions.[16] Other entries to this class of compounds such as the conversion of the corresponding carbamate using Lawesson reagent have not met with success. The reaction of the thiocarbamate **8** with triphenylphosphine in the presence of tetrachloromethane yielded the desired 2-chloromethylphenylisocyanate (**9**)[17] in quantitative yield

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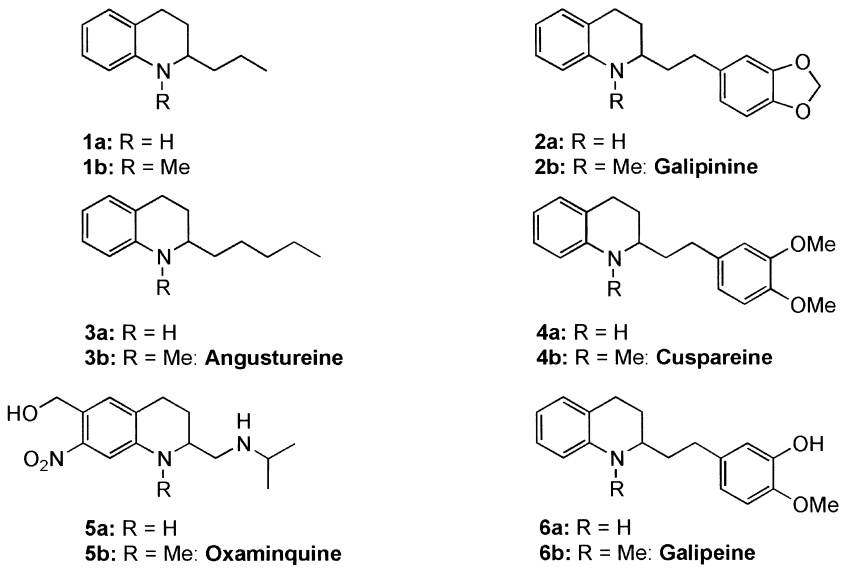
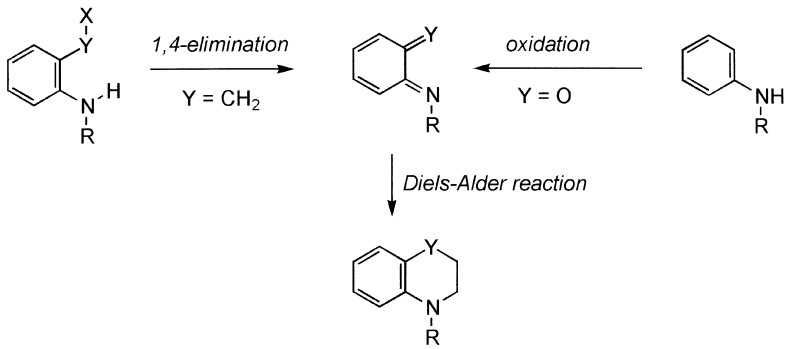


Figure 1. Naturally occurring 2-alkyltetrahydroquinolines.

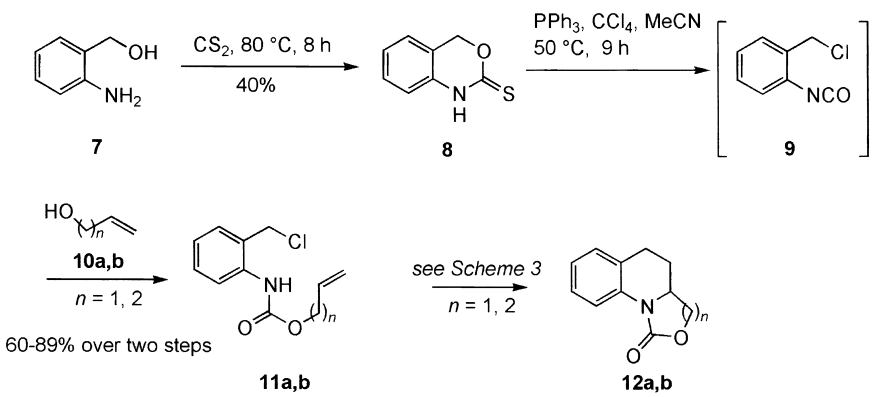


Scheme 1. Aza-xylylene and imidoqinone synthesis and subsequent Diels–Alder reactions towards tetrahydroquinolines and benzomorpholines, respectively.

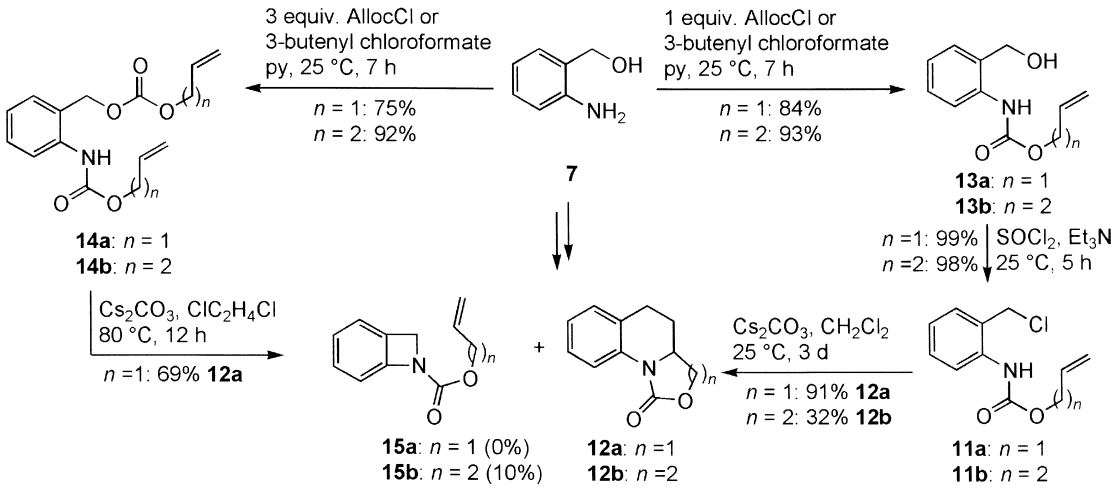
according to gas chromatographic analysis. Crucial for the complete conversion was the employment of elevated temperature (50°C). At lower temperature, e.g. at 0°C triphenylphosphine oxide was isolated next to the expected by-product triphenylphosphine sulfide. Presumably, a phosphine-promoted rearrangement serves as source for triphenyl phosphine oxide.

This bis-electrophile **9**, which also is a useful building block for 2-amino-4*H*-benzo[*d*][1,3]oxazines,[18] can be converted into the desired carbamates **11** with different allyl alcohols in good to excellent yields. This transformation turns into a viable method for combinatorial synthesis as in principle any dienophile possessing a suitable nucleophilic group reacting with isocyanates might be used. This reaction is promising and was demonstrated in the present work for allyl alcohol and homoallyl alcohol[19] (Scheme 2).

For the envisaged solid-phase synthesis of tetrahydroquinolines having a triazene linkage[20] a different leaving group for this reaction was also explored. Since carbonates act as potential leaving groups displaying a leaving tendency



Scheme 2. Synthesis of 2-chloromethyl isocyanate (**9**) via an intramolecular Appel reaction and its conversion to carbamates **11a**,**b**.



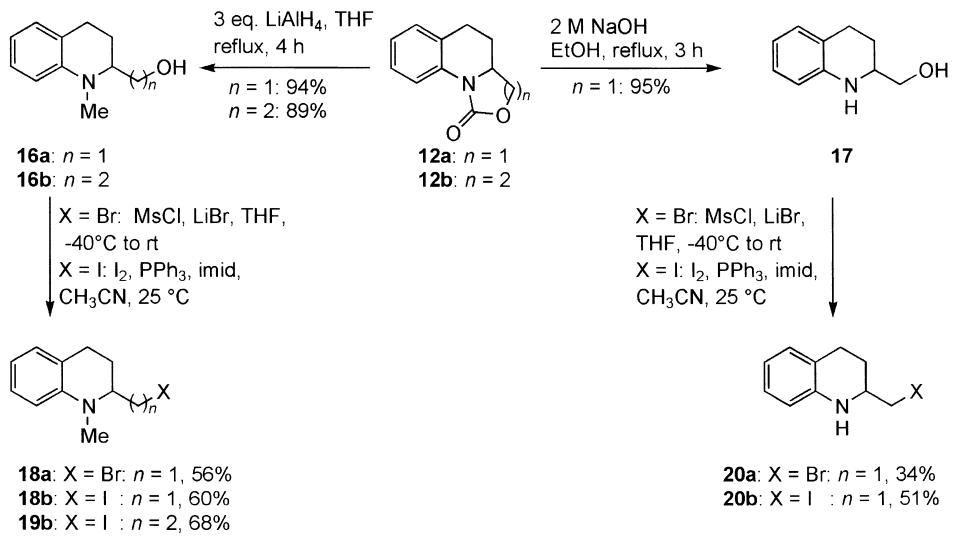
Scheme 3. Synthesis of cyclic carbamates **12**. Alloc=allyloxycarbonyl.

similar to chlorides,[21] 2-amino benzylalcohol (**7**) was converted into the corresponding mixed carbamates/carbonates **14** with unsaturated chloroformates. The utilization of carbonates as leaving groups in an intramolecular aza-xylylene Diels–Alder reaction either by base-induced elimination[11] as well as by pyrolysis[22] has been described earlier. Gratifyingly, the cyclization of the carbonate **14a** using cesium carbonate as a base at elevated temperature proceeded smoothly to generate the tetrahydroquinoline **12a** in 69% yield. Although the overall yield of this route is somewhat lower compared to the previously described route using the benzylic chloride **11a** this access allows the assembly of the tetrahydroquinoline **12a** in just two steps. Furthermore, acid sensitive material might be used in this case.

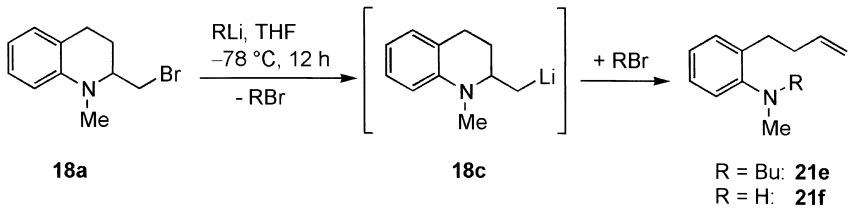
The cyclization of the chlorides **11**, either prepared from the alcohols **13**[23] or by the above-mentioned route, delivers the tetrahydroquinolines **12a**,**b**. However, this cyclization furnished the homologous butenyl substituted material in lesser yields due to the formation of the benzazetine **15b** as a by-product.[24] Apparently, a longer spacer within the internal dienophile inhibits the Diels–Alder reaction to a considerable extent (Scheme 3).

With the cyclic carbamates **12** at hand, model reactions for the synthesis of the targeted natural products have been performed. The nearly quantitative conversion of the carbamate **12a** into the amino alcohol **17**[25] was carried out with sodium hydroxide in ethanol,[26] while reduction of the carbamates **12a**,**b** with lithium aluminium hydride furnished the N-methylated alcohols **16a**,[27] **16b** in very good yields. Standard transformations to the corresponding bromides **18a**, **20a** and iodides **18b**,[25] **19b**, **20b**, respectively, were also met with success (Scheme 4).

The bromide **18a** was converted to its lithio derivative **18c** by treatment with *n*-butyl lithium in THF at −78°C and warming this mixture to room temperature within 12 hours. After aqueous work-up, *N*-(2-but-3-enylphenyl)-*N*-butyl-*N*-methylamine (**21e**) was isolated as the major product (55%) (Scheme 5, Table 1, entry 2). The alkylated product 1-methyl-2-pentyl tetrahydroquinoline (**18e**) could not be detected. The butenyl derivative **21e** derives from a



Scheme 4. Ring opening and subsequent transformations of cyclic carbamates.



Scheme 5. Synthesis and ring opening of 2-lithiomethyl tetrahydroquinoline **18c**.

Table 1. Addition of nucleophilic reagents at tetrahydroquinolyl derivatives **18** and **19**

Entry	Starting material	Conditions	Product	Yield (%)[a]
1	**18a**	MeLi, THF, −78°C to rt, 12 h	**18d**	14
			21f	26
2	**18a**	BuLi, THF, −78°C to rt, 12 h	**21e**	85 (55)[b]
3	**18a**	PhLi, THF, −78°C to rt, 12 h	**18g**	67
4	**18a**	CuBr·SMe_2, BuLi, Et_2O, −78°C to rt, 12 h	**18e** (**3b**)	15
			21e	28
			21f	49
5	**18a**	CuI, BuLi, Et_2O, −78°C to rt, 12 h	**18e** (**3b**)	18
			21e	12
			21f	47
6	**18a**	Li_2CuCl_4, EtMgBr, THF, −5°C to rt, 5 h	**18f** (**1b**)	4
			18g	76 (40)[b]
			21f	14 (5)[b]
7	**18b**	CuI, BuLi, Et_2O, −78°C to rt, 12 h	**21e**	34
			21f	58
8	**18b**	Li_2CuCl_4, C_2H_3MgBr, THF, −5°C to rt, 24 h	**18i**	61 (27)[b]
9	**18b**	PPh_3, MeCN, reflux, 4 days	–	–
10	**19b**	Li_2CuCl_4, PhMgBr, THF, −5°C to rt, 24 h	**18h**	52 (47)[b]
11	**19b**	Li_2CuCl_4, MeMgBr, THF, −5°C to rt, 24 h	**18f** (**1b**)	96 (67)[b]

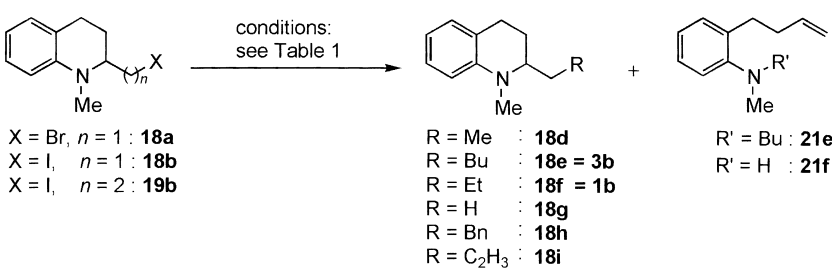
[a] Product ratio according to GC–MS.
[b] Isolated yield.

metal–halogen exchange and a subsequent unexpected[28] elimination of the 2-lithiotetrahydroquinoline **18c**. Finally, alkylation with the formed bromobutane gave the amine **21e**. According to gas chromatic analysis, the rearrangement to any benzo[*b*]azepine did not occur. To our knowledge, the 2-piperidinylmethyl-3-azepinyl rearrangement, which is quite common,[29] has not been observed for the 2-benzannelated series.[25] The reaction of **18a** with methyl lithium at −78°C yielded predominantly *N*-(2-but-3-enylphenyl)-*N*-methylamine **21f** after warming to room temperature. As a side product (approx. 14%), 2-ethyl-1-methyltetrahydroquinoline **18d** was detected (Scheme 5, Table 1, entry 1).[30]

The cuprate generated from copper-(I)-bromide dimethyl sulfide complex and butyl lithium (1:2)[31] introduces a butyl moiety to furnish racemic Angustureine (**3b**=**18e**) in 15% yield (Scheme 6, Table 1, entry 4). Major product is the ring-opened **21f** (R=H). Copper-(I)-iodide in the presence of butyl lithium gave similar results with the bromide **18a**, while the iodide **18b** gives rise only to ring-opened material (Table 1, entries 5, 7). Lithium chloro cuprate Li_2CuCl_4[32] facilitates the transfer of a vinyl group to iodide **18b** effectively using vinyl magnesium bromide to furnish allyl tetrahydroquinoline **18i** in good selectivity (Scheme 6, Table 1, entry 8). However, ethyl magnesium bromide leads to reduction of the bromide group, presumably via a β-hydride transfer (Table 1, entry 6).

The reaction with other nucleophiles such as triphenyl phosphine with bromide **18a** failed even at elevated temperatures due to the neopentyl type structure of **18a** and diminished nucleophilicity of the phosphine (Table 1, entry 9).

Gratifyingly, the reaction of the iodide **19b** with carbon nucleophiles such as methyl magnesium bromide or phenyl magnesium bromide smoothly proceeds in the presence of



Scheme 6. Synthesis of substituted tetrahydroquinolines **18**.

copper salts to give rise to substituted tetrahydroquinolines **18f** and **18h**, respectively (Table 1, entries 10, 11). Hence, the homologous haloethyl tetrahydroquinolines **19** are apparently more suitable substrates for nucleophilic displacement since the ring-opening reaction to yield aniline derivatives was not observed.

Although 2-alkyl tetrahydroquinolines can in principle be prepared by the classical Reissert type addition of nucleophiles to quinolines,[33] the preparation via aminobenzyl alcohol is advantageous in terms of substitution pattern at the arene core as well as possible (cyclic) dienophiles leading to tri- and tetrasubstituted carbamates.

In summary, a rapid access to tetrahydroquinoline derivatives starting from aminobenzylalcohol has been presented. The first intermolecular cleavage of thiocarbamates using triphenylphosphine and tetrachloromethane to give chloromethyl phenylisocyanate has been presented. Finally, total syntheses of some natural occurring 2-alkyl-1-methyltetrahydroquinolines have been reported.

2. Experimental

2.1. General

All reactions were conducted in dried glassware under an atmosphere of dry argon. THF (Na, benzophenone), dichloromethane (CaH_2), acetonitrile (CaH_2), methanol (Mg) and tetrachloromethane (K_2CO_3, molecular sieves) were distilled from the drying agent indicated in argon atmosphere. Pentane, hexane, diethyl ether, dichloromethane, ethanol and 1,2-dichloroethane were distilled and used without further purification. Cesium carbonate was dried before use (40°C, 2 h in high vacuum). All chemicals and solvents were purchased from Aldrich, Acros, Fluka and Merck (Darmstadt) and used as received unless otherwise stated. TLC analyses were performed on silica gel precoated aluminium plates Kieselgel 60 (Merck) UV. Column chromatography was performed on Kieselgel 60 (Merck). NMR: Bruker AMX-400 or DP 400 (400.13 MHz for ^1H), $CDCl_3$ and CD_3OD as solvents, δ_H ($CHCl_3$)=7.27 and δ_H (CD_3OD)=3.31. Abbreviations for ^1H NMR: s=singlet, d=doublet, t=triplet and DEPT multiplicities for ^{13}C NMR. Infrared spectra were recorded on a Perkin–Elmer FTIR 1750. Mass spectra were recorded on a KRATOS MS 50 (70 eV) or KRATOS MS 890A (70 eV) respectively. HPLC: Lichrospher 100 (Merck) RP-18, 1 ml/min. GC: column HP-1 (cross-linked Methyl Siloxane) 12 m×0.25 mm×0.33 μm film thickness. Init. temp: 60°C, init. time: 0.5 min, rate: 50°C/min. Elemental analysis: elementar vario EL at the Mikroanalytisches Labor des Instituts für Organische Chemie der Universität Bonn. Melting points are corrected.

2.1.1. 1,4-Dihydrobenzo[*d*][1,3]oxazine-2-thione (8).[16] A stirred solution of 500 mg (4.06 mmol) of 2-aminobenzylalcohol (**7**) and 5.00 ml (6.33 g, 83.4 mmol, 20.5 equiv.) of carbon disulfide in a sealed tube was heated at 80°C for 8 h, cooled to room temperature and concentrated to dryness in vacuum. Compound **8** was isolated as beige solid after column chromatography on silica (60 g, 4×15 cm, pentane/ether 1:1). Yield 270 mg (40%). TLC: R_f=0.72 (pentane/ether, 1:1). GC: R_t=4.42 min. HPLC [MeOH/H_2O 70:30, 1.0 ml/min]: R_t=1.55 min. IR (neat): ν=3249 (w), 3181 (m), 3132 (m), 3060 (w), 3014 (m), 2967 (m), 1623 (m), 1530 (m), 1492 (m), 1449 (m), 1412 (m), 1315 (m), 1222 (m), 1150 (s, C=S), 1104 (m), 969 (m), 890 (m), 856 (m), 750 (s) cm^{-1}. ^1H NMR (400 MHz, CD_3OD): δ=4.86 (s, 1H, NH), 5.29 (s, 2H, CH_2), 6.92 (bd, ^3J=7.52 Hz, 1H, Ar-H), 7.12 (ddd, ^3J=7.52, 7.52 Hz, ^4J=1.00 Hz, 1H, Ar-H), 7.18 (bd, ^3J=7.52 Hz, 1H, Ar-H), 7.29 (dd, ^3J=7.52, 7.52 Hz, 1H, Ar-H). ^{13}C NMR (100 MHz, CD_3OD): δ=71.0 (+, CH_2), 115.5 (−, C-Ar), 120.9 (quart, C_{quart}-Ar), 126.4 (−, C-Ar), 126.7 (−, C-Ar), 131.8 (−, C-Ar), 135.8 (quart, C_{quart}-Ar), 188.4 (quart, C=S). MS (70 eV, EI), *m*/*z* (%): 165 (100) [M^+], 132 (11), 104 (41), 78 (28), 63 (3), 51 (8). C_8H_7NOS (165.02): calcd C 58.16, H 4.27, N 8.48, S 19.41; found C 58.11, H 4.17, N 8.51, S 19.16.

2.1.2. (2-Chloromethylphenyl)carbamic acid allyl ester (11a). (a) *From* **13a**. To a solution of 3.80 g (18.4 mmol) of (2-hydroxymethylphenyl)carbamic acid allyl ester (**13a**) in 150 ml of dichloromethane and 2.50 ml (1.85 g, 18.3 mmol) of triethylamine was added 1.50 ml (2.38 g, 20.2 mmol, 1.1 equiv.) of thionylchloride dropwise at 0°C. The reaction mixture was stirred for 5 h, while warming to room temperature. It was concentrated to dryness in vacuum and subsequently dissolved in 50 ml of diethyl ether, washed with 30 ml of water, dried over sodium sulfate, filtered and again concentrated to dryness in vacuum. Compound **11a** was furnished as white solid. Yield 4.09 g (99%).

(b) *From* **8**. To a stirred solution of 504 mg (3.05 mmol) of 1,4-dihydro-benzo[*d*][1,3]oxazine-2-thione (**8**) in 10 ml of dry acetonitrile was added 962 mg (3.67 mmol, 1.20 equiv.) of triphenylphosphine and 0.40 ml (636 mg, 4.19 mmol, 1.37 equiv.) of tetrachloromethane at room temperature. The reaction mixture was stirred at 50°C for 3 h. During that time, the colour of the solution changed from colourless to deep red. The reaction mixture was cooled to 0°C, 0.35 ml (298 mg, 5.13 mmol, 1.67 equiv.) of allyl alcohol (**10a**) were added and stirred again at 50°C for 6 h. The reaction mixture was concentrated to dryness in vacuum and compound **11a** was isolated as white solid after column chromatography on silica (30 g, 2.5×18 cm, hexane/ether 2:1). Yield 611 mg (89%). Mp: 63°C. TLC: R_f=0.30 (pentane/ether, 3:1). GC: R_t=4.08 min. HPLC [MeOH/H_2O 70:30, 1.0 ml/min]: R_t=2.56 min. IR (KBr): ν=2993 (m), 2978 (m), 2938 (m), 2870 (m), 2769 (w), 2369 (w), 2345 (w), 2285 (w), 2196 (w), 1972 (w), 1845 (w), 1698 (vs), 1647 (s), 1609 (s), 1593 (s), 1531 (vs), 1487 (s), 1458 (s), 1450 (s), 1410 (s), 1300 (vs), 1250 (vs), 1110 (s), 1090 (s), 1060 (s), 1010 (s) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ=4.59 (s, 2H, CH_2Cl), 4.68 (dt, ^3J=5.72 Hz, ^4J=1.35 Hz, 2H, CH_2OCO), 5.27 (dd, ^2J=2.87 Hz, ^3J=10.45 Hz, 1H, CH=CH_2), 5.37 (ddd, ^2J=2.87 Hz, ^3J=17.19 Hz, ^4J=1.35 Hz, 1H, CH=CH_2), 5.98 (ddd, ^3J=5.72, 10.45, 17.19 Hz, 1H, CH), 6.96 (bs, 1H, NH), 7.09 (dd, ^3J=7.64 Hz, ^4J=1.12 Hz, 1H, Ar-H_4), 7.27 (dd, ^3J=7.64 Hz, ^4J=1.45 Hz, 1H, Ar-H_3), 7.35 (dd, ^3J=8.02 Hz, ^4J=1.45 Hz, 1H, Ar-H_5), 7.84 (bd, ^3J=8.02 Hz, 1H, Ar-H_6). ^{13}C NMR (100 MHz, $CDCl_3$): δ=44.0 (+, Ar-CH_2Cl), 66.3 (+, CH_2OCO), 118.5 (+,

CH=*C*H$_2$), 123.1 (−, C$_6$-Ar), 124.6 (−, C$_4$-Ar), 127.5 (quart, CC$_{quart}$-Ar), 130.1 (−, C-Ar*), 130.2 (−, C-Ar*), 132.5 (−, *C*H=CH$_2$), 136.7 (quart, NC$_{quart}$-Ar), 153.6 (quart, C=O). MS (70 eV, EI), *m*/*z* (%): 225/227 (96/30) [M$^+$], 184 (83), 166 (86), 148 (50), 132 (100), 118 (27), 104 (68), 91 (14), 77 (50), 58 (15). HRMS $C_{11}H_{12}ClNO_2$: calcd 225.0557; found 225.0552. $C_{11}H_{12}ClNO_2$ (225.06): calcd C 58.54, H 5.36, N 6.21; found C 58.66, H 5.46, N 6.25.

2.1.3. (2-Chloromethylphenyl)carbamic acid but-3-enyl ester (11b). (a) *From* **13b**. To a solution of 4.90 g (22.2 mmol) of (2-hydroxymethylphenyl)carbamic acid but-3-enyl ester (**13b**) in 50 ml of dichloromethane and 3.00 ml (2.22 g, 22.0 mmol, 1.0 equiv.) of triethylamine was added 1.80 ml (2.87 g, 24.4 mmol, 1.1 equiv.) of thionylchloride dropwise at 0°C. The reaction mixture was stirred for 5 h, while warming to room temperature. It was concentrated to dryness in vacuum and subsequently dissolved in 50 ml of diethyl ether, washed with 30 ml of water, dried over sodium sulfate, filtered and again concentrated to dryness in vacuum. Compound **13b** was furnished as white solid. Yield 5.21 g (98%).

(b) *From* **8**. To a stirred solution of 504 mg (3.05 mmol) of 1,4-dihydro-benzo[*d*][1,3]oxazine-2-thione (**8**) in 10 ml of dry acetonitrile was added 962 mg (3.67 mmol, 1.20 equiv.) of triphenylphosphine and 0.40 ml (636 mg, 4.19 mmol, 1.37 equiv.) of tetrachloromethane at room temperature. The reaction mixture was stirred at 50°C for 3 h. During that time, the colour of the solution changed from colourless to deep red. The reaction mixture was cooled to 0°C, 0.45 ml (0.38 g, 5.26 mmol, 1.72 equiv.) of homoallyl alcohol (**10b**) were added and stirred again at 50°C for 6 h. The reaction mixture was concentrated to dryness in vacuum and compound **11b** was isolated as white solid after column chromatography on silica (30 g, 2.5×18 cm, hexane/ether 2:1). Yield 434 mg (60%). Mp: 69°C. TLC: R_f=0.52 (pentane/ether, 1:1). GC: R_t=4.28 min. HPLC [MeOH/H$_2$O 70:30, 1.0 ml/min]: R_t=3.24 min. IR (KBr): ν=3293 (s), 3076 (w), 2975 (w), 1694 (s), 1592 (m), 1541 (s), 1459 (m), 1255 (s), 1076 (m), 921 (m), 770 (m), 670 (s) cm^{-1}. ^{1}H NMR (400 MHz, CDCl$_3$): δ=2.47 (dq, ^3J=1.44, 6.76 Hz, 2H, CHC*H*$_2$), 4.25 (t, ^3J=6.76 Hz, 2H, CH$_2$O), 4.60 (s, 2H, CH$_2$Cl), 5.11 (ddd, ^2J=3.03 Hz, ^3J=1.23, 10.28 Hz, 1H, CH=C*H*$_2$), 5.16 (ddd, ^2J=3.03 Hz, ^3J=1.44, 17.16 Hz, 1H, CH=C*H*$_2$), 5.84 (ddd, ^3J=6.77, 10.28, 17.16 Hz, 1H, C*H*=CH$_2$), 6.91 (bs, 1H, NH), 7.10 (ddd, ^3J=7.61 Hz, ^3J=7.61 Hz, ^4J=1.14 Hz, 1H, Ar-H$_4$), 7.28 (dd, ^3J=7.61 Hz, ^4J=1.39 Hz, 1H, Ar-H$_3$), 7.36 (ddd, ^3J=7.81 Hz, ^3J=7.61 Hz, ^4J=1.39 Hz, 1H, Ar-H$_5$), 7.82 (bd, ^3J=7.81 Hz, 1H, Ar-H$_6$). ^{13}C NMR (100 MHz, CDCl$_3$): δ=33.5 (+, CH*C*H$_2$), 44.0 (+, CH$_2$Cl), 64.7 (+, OCH$_2$), 117.5 (+, CH=*C*H$_2$), 123.1 (−, C$_6$-Ar), 124.6 (−, C$_4$-Ar), 127.5 (quart, CC$_{quart}$-Ar), 130.1 (−, C-Ar*), 130.2 (−, C-Ar*), 133.9 (−, *C*H=CH$_2$), 136.7 (quart, NC$_{quart}$-Ar), 153.9 (quart, C=O). MS (70 eV, EI), *m*/*z* (%): 239/241 (48/16) [M$^+$], 204 (12), 185 (40), 166 (15), 150 (25), 132 (85), 105 (32), 97 (17), 55 (100). HRMS $C_{12}H_{14}ClNO_2$: calcd 239.0713; found 239.0720. $C_{12}H_{14}ClNO_2$ (239.06): calcd C 60.13, H 5.89, N 5.84; found C 60.08, H 5.91, N 5.78.

2.1.4. 3,3a,4,5-Tetrahydrooxazol[3,4,-*a*]quinolin-1-one (12a). (a) *From* **11a**. A suspension of 5.00 g (22.2 mmol) of (2-chloromethylphenyl)carbamic acid allyl ester (**11a**) and 24.6 g (75.5 mmol, 3.4 equiv.) of cesium carbonate was stirred in 170 ml of dry dichloromethane at room temperature for 3 days. Subsequently, the mixture was filtered over Celite® and thoroughly washed with dichloromethane. The filtrate was concentrated to dryness in vacuum. Heterocycle **12a** was furnished as beige solid. Yield 3.84 g (91%).

(b) *From* **14a**. A solution of 4.50 g (15.4 mmol) of carbonic acid allyl ester 2-allyloxycarbonylamino-benzyl ester (**14a**) and 15.1 g (46.3 mmol, 3 equiv.) of cesium carbonate was stirred in 200 ml of dry dichloroethane at 80°C for 12 h. After being cooled to room temperature, the mixture was filtered over Celite® and thoroughly washed with dichloromethane. The filtrate was concentrated to dryness in vacuum. After column chromatography on silica (100 g, 4×25 cm, pentane/ether 3:1), heterocycle **12a** was isolated as beige solid. Yield 2.02 g (69%). Mp: 84°C. TLC: R_f=0.11 (pentane/ether, 1:1). GC: R_t=4.62 min. HPLC [MeOH/H$_2$O 70:30, 1.0 ml/min]: R_t=2.04 min. IR (KBr): ν=2931 (m), 2903 (m), 2847 (m), 1742 (vs), 1700 (s), 1602 (s), 1548 (m), 1495 (vs), 1456 (s), 1400 (vs), 1327 (s), 1298 (s), 1290 (s), 1219 (s), 1186 (m), 1139 (s), 1113 (s), 1087 (m), 1035 (s), 974 (m), 944 (m), 789 (m), 754 (vs), 718 (m) cm^{-1}. ^{1}H NMR (400 MHz, CDCl$_3$): δ=1.79–1.90 (m, 1H, CH$_2$), 2.15–2.21 (m, 1H, CH$_2$), 2.89–3.03 (m, 2H, CH$_2$), 4.04 (t, ^3J=8.33 Hz, 1H, CH$_2$), 4.14–4.21 (m, 1H, CH), 4.58 (m, ^3J=8.33 Hz, 1H, CH$_2$), 7.03 (dd, ^3J=7.57 Hz, ^3J=7.57 Hz, 1H, Ar-H), 7.13 (bd, ^3J=7.57 Hz, 1H, Ar-H), 7.23 (dd, ^3J=8.28 Hz, ^3J=7.57 Hz, 1H, Ar-H), 8.23 (bd, ^3J=8.28 Hz, 1H, Ar-H). ^{13}C NMR (100 MHz, CDCl$_3$): δ=26.7 (+, CH$_2$), 26.8 (+, CH$_2$), 54.6 (−, CH), 67.5 (+, CH$_2$O), 118.5 (−, C-Ar), 123.6 (−, C-Ar), 124.9 (quart, CC$_{quart}$-Ar), 127.3 (−, C-Ar), 129.2 (−, C-Ar), 135.0 (quart, NC$_{quart}$-Ar), 154.5 (quart, C=O). MS (70 eV, CI), *m*/*z* (%): 189 (100) [M$^+$], 144 (53), 130 (30), 117 (40), 103 (6), 90 (10), 77 (11), 65 (3), 51 (6). HRMS $C_{11}H_{11}NO_2$: calcd 189.0790; found 189.0795. $C_{11}H_{11}NO_2$ (189.21) calcd C 69.83, H 5.86, N 7.40; found C 69.54, H 5.94, N 7.33.

2.1.5. 4,4a,5,6-Tetrahydro-3*H*-[1,3]oxazin[3,4-*a*]quinolin-1-one (12b) and butenyloxy carbonylbenzoazetedine (15b). A suspension of 4.60 g (19.2 mmol) of (2-chloromethylphenyl)carbamic acid but-3-enyl ester (**11b**) and 15.6 g (47.9 mmol, 2.5 equiv.) of cesium carbonate was stirred in 350 ml of dry dichloromethane at room temperature for 3 days. Subsequently, the reaction mixture was filtered over Celite® and thoroughly washed with dichloromethane. The filtrate was concentrated to dryness in vacuum. After column chromatography on silica, heterocycle **12b** was isolated as white solid. Yield 1.18 g (32%). Mp: 101°C. TLC: R_f=0.03 (pentane/ether, 1:1). GC: R_t=5.46 min. HPLC [MeOH/H$_2$O 70:30, 1.0 ml/min]: R_t=3.64 min. IR (KBr): ν=2922 (s), 2903 (m), 1692 (s), 1604 (w), 1491 (m), 1469 (m), 1410 (m), 1282 (m), 1224 (m), 1205 (w), 1124 (m), 1087 (m), 1020 (w), 960 (m), 946 (w), 782 (w), 756 (s), 714 (m) cm^{-1}. ^{1}H NMR (400 MHz, CDCl$_3$): δ=1.81–1.91 (m, 1H, CH$_2$), 1.93–2.02 (m, 1H, CH$_2$), 2.10–2.17 (m, 1H, CH$_2$), 2.28–2.35 (m, 1H, CH$_2$), 2.87–2.91 (m, 2H, CH$_2$), 3.67–3.75 (m, 1H, CH), 4.28–4.33 (m, 2H, CH$_2$), 7.02 (ddd, ^3J=7.38 Hz, ^3J=7.38 Hz, ^4J=0.76 Hz, 1H, Ar-H), 7.09 (dd, ^3J=7.38 Hz, ^4J=0.88 Hz, 1H, Ar-H), 7.16 (ddd, ^3J=8.28 Hz,

^3J=8.28 Hz, ^4J=0.88 Hz, 1H, Ar-H), 7.76 (dd, ^3J=8.28 Hz, ^4J=0.76 Hz, 1H, Ar-H). ^{13}C NMR (100 MHz, $CDCl_3$): δ=26.2 (+, CH_2), 30.0 (+, CH_2), 30.7 (+, CH_2), 54.1 (−, CH), 64.3 (+, CH_2O), 124.3 (−, C-Ar), 124.4 (−, C-Ar), 126.2 (−, C-Ar), 128.3 (quart, CC_{quart}-Ar), 129.2 (−, C-Ar), 138.1 (NC_{quart}-Ar), 152.8 (quart, C=O). MS (70 eV, CI), *m/z* (%): 203 (100) [M^+], 158 (65), 144 (27), 130 (100), 117 (28). HRMS $C_{12}H_{13}NO_2$: calcd 203.0946; found 203.0947. $C_{12}H_{13}NO_2$ (203.24) calcd C 70.92, H 6.45, N 6.89; found C 70.95, H 6.53, N 6.83. As a side-product, benzazetidine **15b** was isolated. Yield 368 mg (10%). ^{1}H NMR (300 MHz, C_6D_6): δ=2.26 (dddd, ^3J=6.76, 6.76, 1.44, 1.44 Hz, 2H, CHC*H*$_2$), 4.25 (t, ^3J=6.76 Hz, 2H, CH_2O), 4.70 (s, 2H, CH_2), 4.90 (ddd, ^2J=3.03 Hz, ^3J=1.23, 10.28 Hz, 1H, CH=C*H*$_2$), 4.95 (ddd, ^2J=3.03 Hz, ^3J=1.44, 17.16 Hz, 1H, CH=C*H*$_2$), 5.84 (ddd, ^3J=6.77, 10.28, 17.16 Hz, 1H, C*H*=CH_2), 7.10 (ddd, ^3J=7.61 Hz, ^3J=7.61 Hz, ^4J=1.14 Hz, 1H, Ar-H), 7.28 (dd, ^3J=7.61 Hz, ^4J=1.39 Hz, 1H, Ar-H), 7.36 (ddd, ^3J=7.81 Hz, ^3J=7.61 Hz, ^4J=1.39 Hz, 1H, Ar-H), 7.82 (bd, ^3J=7.81 Hz, 1H, Ar-H). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ=33.3 (+, CH*C*H$_2$), 67.6 (+, OCH_2), 68.7 (+, CH_2), 117.1 (+, CH=*C*H$_2$), 123.1 (−, C-Ar), 124.6 (−, C-Ar), 127.5 (quart, CC_{quart}-Ar), 130.1 (−, C-Ar*), 130.2 (−, C-Ar*), 133.9 (−, *C*H=CH_2), 136.7 (quart, NC_{quart}-Ar), 157.0 (quart, C=O). MS (70 eV, CI), *m/z* (%): 203 (50) [M^+], 149 (53), 132 (21), 118 (23), 105 (100), 77 (33), 55 (27).

2.1.6. (2-Hydroxymethylphenyl)carbamic acid allyl ester (13a).[23] To a solution of 6.00 g (48.8 mmol) of 2-aminobenzylalcohol (**7**) in 80 ml of dichloromethane and 4.00 ml (3.88 g, 49.1 mmol, 1.0 equiv.) of pyridine was added 5.20 ml (5.92 g, 49.3 mmol, 1.0 equiv.) of allyl chloroformate dropwise at −5°C. The reaction mixture was stirred for 7 h, while warming to room temperature. Subsequently, the mixture was washed with each 20 ml of aq. sodium hydrogen carbonate solution, brine and water. The organic layer was dried over sodium sulfate, filtered and concentrated to dryness in vacuum. After column chromatography on silica (70 g, 4×14 cm, pentane/ether 1:1) compound **13** was furnished as white solid. Yield 8.50 g (84%). Mp: 54°C. TLC: R_f=0.29 (pentane/ether, 1:1). GC: R_t=4.20 min. HPLC [MeOH/H_2O 70:30, 1.0 ml/min]: R_t=1.76 min. IR (KBr): ν=2953 (m), 2895 (m), 2283 (w), 1691 (vs), 1590 (s), 1535 (vs), 1481 (s), 1456 (s), 1421 (s), 1376 (m), 1346 (m), 1295 (s), 1238 (vs), 1163 (m), 1111 (s), 1070 (s), 1036 (s) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ=3.46 (bs, 1H, OH), 4.55 (bs, 2H, C*H*$_2$OH), 4.58 (ddd, ^3J=1.47, 5.73 Hz, 2H, OCC*H*$_2$), 5.23 (ddd, ^2J=2.77 Hz, ^3J=1.23, 10.41 Hz, 1H, C*H*$_2$=CH), 5.33 (ddd, ^2J=2.77 Hz, ^3J=1.47, 17.23 Hz, 1H, C*H*$_2$=CH), 5.93 (ddd, ^3J=5.73, 10.41, 17.23 Hz, 1H, CH_2=C*H*), 7.00 (ddd, ^3J=7.65 Hz, ^3J=7.46 Hz, ^4J=1.05 Hz, 1H, Ar-H_4), 7.09 (dd, ^3J=7.46 Hz, ^4J=1.54 Hz, 1H, Ar-H_3), 7.25 (ddd, ^3J=7.87 Hz, ^3J=7.65 Hz, ^4J=1.54 Hz, 1H, Ar-H_5), 7.80 (bd, ^3J=7.87 Hz, 1H, Ar-H_6), 8.05 (bs, 1H, NH). ^{13}C NMR (100 MHz, $CDCl_3$): δ=63.6 (+, *C*H$_2$OH), 65.8 (+, CO*C*H$_2$), 118.1 (+, *C*H$_2$=CH), 121.1 (−, C_6-Ar), 123.6 (−, C_4-Ar), 128.7 (−, C-Ar*), 128.8 (−, C-Ar*), 129.4 (quart, CC_{quart}-Ar), 132.4 (−, *C*H=CH_2), 137.2 (quart, NC_{quart}-Ar), 154.0 (quart, C=O). MS (70 eV, EI), *m/z* (%): 207 (48) [M^+], 148 (6), 132 (22) [$C_8H_6NO^+$], 122 (100) [$C_7H_8NO^+$], 104 (10) [$C_7H_6N^+$], 94 (17), 77 (18), 65 (4), 52 (2). HRMS $C_{11}H_{13}NO_3$: calcd 207.0895; found 207.0900. $C_{11}H_{13}NO_3$ (207.9): calcd C 63.76, H 6.32, N 6.76; found C 63.75, H 6.29, N 6.72.

2.1.7. (2-Hydroxymethylphenyl)carbamic acid but-3-enyl ester (13b). To a solution of 4.58 g (37.2 mmol) of 2-aminobenzylalcohol (**7**) in 80 ml of dichloromethane and 3.00 ml (2.94 g, 37.2 mmol, 1.0 equiv.) of pyridine was added 4.60 ml (5.00 g, 37.3 mmol, 1.0 equiv.) of 3-butenyl chloroformate dropwise at −5°C. The reaction mixture was stirred for 24 h, while warming to room temperature. Subsequently, the mixture was washed with each 20 ml of sodium hydrogen carbonate solution, brine and water. The organic layer was dried over sodium sulfate, filtered and concentrated to dryness in vacuum. After column chromatography on silica (220 g, 6×22 cm, pentane/ether 1:1), carbamate **13b** was isolated as yellowish oil. Yield 7.65 g (93%). TLC: R_f=0.42 (pentane/ether, 1:1). GC: R_t=4.83 min. HPLC [MeOH/H_2O 70:30, 1.0 ml/min]: R_t=2.05 min. IR (KBr): ν=3285 (s), 2955 (m), 2895 (w), 2287 (w), 1692 (s), 1588 (w), 1535 (m), 1481 (w), 1456 (w), 1421 (w), 1376 (m), 1352 (w), 1294 (w), 1253 (m), 1163 (m), 1112 (w), 1070 (w), 1037 (m) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ=2.40 (dq, ^3J=6.76 Hz, ^4J=1.43 Hz, 2H, OCH_2CH_2), 3.70 (bs, 1H, OH), 4.13 (t, ^3J=6.82 Hz, 2H, OC*H*$_2$CH$_2$), 4.54 (t, ^2J=5.30 Hz, 2H, C*H*$_2$OH), 5.09 (ddd, ^2J=3.07 Hz, ^3J=1.16, 10.28 Hz, 1H, CH=C*H*$_2$), 5.13 (ddd, ^2J=3.07 Hz, ^3J=17.18 Hz, ^4J=1.43 Hz, 1H, CH=C*H*$_2$), 5.80 (ddd, ^3J=6.76, 10.28, 17.18 Hz, 1H, C*H*=CH_2), 7.00 (d, ^3J=7.46 Hz, 1H, Ar-H_4), 7.08 (dd, ^3J=7.46 Hz, ^4J=1.44 Hz, 1H, Ar-H_3) 7.25 (dd, ^3J=7.78 Hz, ^4J=1.44 Hz, 1H, Ar-H_5), 7.79 (bd, ^3J=7.78 Hz, 1H, Ar-H_6), 8.02 (bs, 1H, NH). ^{13}C NMR (100 MHz, $CDCl_3$): δ=33.1 (+, OCH_2CH_2), 63.5 (+, CH_2OH), 64.2 (+, O*C*H$_2$CH$_2$), 117.2 (+, CH=*C*H$_2$), 121.1 (−, C_6-Ar), 123.4 (−, C_4-Ar), 128.6 (−, C-Ar*), 128.7 (−, C-Ar*), 129.5 (quart, CC_{quart}-Ar), 133.8 (−, *C*H=CH_2), 137.2 (quart, NC_{quart}-Ar), 154.3 (quart, C=O). MS (70 eV, EI), *m/z* (%): 221 (41) [M^+], 149 (19), 132 (36), 122 (100), 105 (37), 94 (11), 78 (16), 55 (49). HRMS $C_{12}H_{15}NO_3$: calcd 211.1052; found 211.1050. $C_{12}H_{15}NO_3$ (221.11): calcd C 65.14, H 6.83, N 6.33; found C 65.02, H 6.86, N 6.38.

2.1.8. Carbonic acid allyl ester 2-allyloxycarbonylaminobenzyl ester (14a). To a solution of 2.00 g (16.2 mmol) of 2-aminobenzylalcohol (**7**) in 20 ml of dichloromethane and 3.9 ml (3.84 g, 48.6 mmol, 3.0 equiv.) of pyridine was added 5.2 ml (5.86 g, 48.6 mmol, 3 equiv.) of allyl chloroformate dropwise at room temperature. The reaction mixture was stirred for 7 h. Subsequently, the mixture was washed with each 20 ml of sodium hydrogen carbonate solution, brine and water. The organic layer was dried over sodium sulfate, filtered and concentrated to dryness in vacuum. After column chromatography on silica (50 g, 4×14 cm, pentane/ether 4:1), carbamate **14a** was isolated as yellowish oil. Yield 3.55 g (75%). TLC: R_f=0.22 (pentane/ether, 4:1). GC: R_t=5.33 min. HPLC [MeOH/H_2O 70:30, 1.0 ml/min]: R_t=3.06 min. IR (capillary): ν=2984 (w), 2951 (w), 2893 (w), 1739 (vs), 1649 (m), 1609 (m), 1594 (s), 1528 (s), 1483 (m), 1456 (s), 1425 (m), 1388 (s), 1360 (m), 1300 (s), 1255 (vs), 1222 (vs), 1163 (w), 1123 (w), 1102 (w), 1056 (s) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ=4.63 (ddd, ^3J=5.63 Hz, ^3J=5.63 Hz, ^4J=1.23 Hz, 2H,

CH_2OCO), 4.68 (ddd, ^3J=5.63 Hz, ^3J=5.63 Hz, ^4J=1.23 Hz, 2H, CH_2OCO), 5.17 (s, 2H, Ar-CH_2), 5.27 (ddd, ^2J=1.37 Hz, ^3J=10.44 Hz, ^4J=1.23 Hz, 2H, CH=CH_2), 5.34 (ddd, ^2J=1.37 Hz, ^3J=17.20 Hz, ^4J=1.65 Hz, 1H, CH=CH_2), 5.38 (ddd, ^2J=1.37 Hz, ^3J=17.20 Hz, ^4J=1.65 Hz, 1H, CH=CH_2), 5.86–6.04 (m, 2H, CH), 7.12 (ddd, ^3J=7.42 Hz, ^3J=7.42 Hz, ^4J=1.23 Hz, 1H, Ar-H_4), 7.36 (dd, ^3J=7.42 Hz, ^4J=1.23 Hz, 1H, Ar-H_3), 7.38 (ddd, ^3J=7.42 Hz, ^4J=1.23 Hz, 1H, Ar-H_5), 7.67 (bs, 1H, NH), 7.84 (bd, ^3J=7.42 Hz, 1H, Ar-H_6). ^{13}C NMR (100 MHz, $CDCl_3$): δ=66.3 (+, CH_2OCO), 67.2 (+, Ar-CH_2), 69.2 (+, CH_2OCO), 118.4 (+, CH_2CH), 119.5 (+, CH_2CH), 123.0 (−, C-Ar), 124.6 (−, C-Ar), 125.6 (quart, C_q-Ar), 130.4 (−, $CHCH_2$), 131.4 (−, $CHCH_2$), 131.5 (−, C-Ar), 132.7 (−, C-Ar), 137.2 (quart, C_q-Ar), 154.0 (+, OC=O), 155.5 (quart, C=O). MS (70 eV, EI), *m/z* (%): 291 (51) [M^+], 190 (34) [$C_{11}H_{12}NO_2^+$], 148 (100) [$C_8H_6NO_2^+$], 144 (64), 132 (71) [$C_8H_6NO^+$], 118 (34), 104 (38), 93 (19), 77 (15), 57 (4), 52 (3). HRMS $C_{15}H_{17}NO_5$: calcd 291.1107; found 291.1120. $C_{15}H_{17}NO_5$ (291.10): calcd C 61.85, H 5.88, N 4.81; found C 61.70, H 5.90, N 4.77.

2.1.9. Carbonic acid 3-butenyl ester 3-butenyloxycarbonylamino-benzyl ester (14b). To a solution of 1.53 g (1.24 mmol) of 2-aminobenzylalcohol (**7**) in 30 ml of dichloromethane and 3.0 ml (2.94 g, 37.2 mmol, 3.0 equiv.) of pyridine was added 5.00 g (37.2 mmol, 3 equiv.) of 3-butenyl chloroformate dropwise at room temperature. The reaction mixture was stirred for 12 h. Subsequently, the mixture was washed with each 20 ml of sodium hydrogen carbonate solution, brine and water. The organic layer was dried over sodium sulfate, filtered and concentrated to dryness in vacuum. After column chromatography on silica (120 g, 4×20 cm, pentane/ether 4:1), carbamate **14b** was isolated as yellowish oil. Yield 3.66 g. (92%). TLC: R_f=0.42 (pentane/ether, 1:1). GC: R_t=5.79 min. IR (KBr): ν=3078 (w), 2981 (w), 2962 (w), 2906 (w), 1739 (s), 1527 (m), 1456 (m), 1397 (m), 1300 (m), 1252 (s), 1219 (s), 1065 (m), 921 (m), 790 (w), 768 (m) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ=2.38–2.48 (m, 4H, CH_2), 4.17–4.24 (m, 4H, CH_2), 5.06–5.17 (m, 6H, CH_2), 5.70–5.88 (m, 2H, C*H*=CH_2), 7.10 (dd, J=1.01, 7.57 Hz, 1H, Ar-H), 7.33–7.38 (m, 2H, Ar-H), 7.61 (bs, 1H, NH), 7.82 (bd, ^3J=6.13 Hz, 1H, Ar-H). ^{13}C NMR (100 MHz, $CDCl_3$): δ=33.0 (+, CH_2), 33.5 (+, CH_2), 64.5 (+, Ar-CH_2), 66.8 (+, CH_2), 67.5 (+, CH_2), 117.4 (+, CH_2CH), 117.8 (+, CH_2CH), 122.8 (−, C-Ar) 124.3 (−, C-Ar), 125.4 (quart, C_{quart}-Ar), 130.2 (−, C-Ar), 131.3 (−, $CHCH_2$), 133.3 (−, $CHCH_2$), 134.1 (−, C-Ar), 137.1 (quart, C_{quart}-Ar), 154.2 (quart, C=O), 155.6 (quart, C=O). MS (70 eV, EI), *m/z* (%): 319 (83) [M^+], 204 (20), 149 (43), 132 (100), 122 (18), 105 (59), 91 (6), 77 (11), 55 (67). HRMS $C_{17}H_{21}NO_5$: calcd 319.1420; found 319.1425. $C_{17}H_{21}NO_5$ (319.35) calcd C 63.94, H 6.63, N 4.39; found C 64.03, H 6.70, N 4.45.

2.1.10. (1-Methyl-1,2,3,4-tetrahydroquinolin-2-yl)-methanol (16a).[27] To a solution of 2.00 g (10.6 mmol) of 3,3a,4,5-tetrahydrooxazol[3,4,-a]quinolin-1-one (**12a**) in 70 ml of dry tetrahydrofuran was added 1.2 g (31.8 mmol, 3 equiv.) of lithium aluminum hydride and refluxed for 4.5 h. After being cooled to room temperature, the mixture was treated with water in small portions to furnish a white precipitate and filtered. The remaining white solid was suspended in 50 ml of dichloromethane and refluxed for 30 min. After filtration, the organic layers were combined and washed with each 40 ml of brine and water. The organic layer was dried over sodium sulfate, filtered and concentrated to dryness in vacuum. After column chromatography on silica (20 g, 1.5×12 cm, hexane/ether 1:1), alcohol **16a** was isolated as yellowish oil. Yield 1.76 g (94%). TLC: R_f=0.08 (pentane/ether, 2:1). GC: R_t=3.79 min. IR (KBr): ν=3369 (w), 2928 (w), 2877 (w), 1601 (m), 1498 (m), 1479 (m), 1455 (w), 1433 (w), 1328 (w), 1307 (m), 1212 (m), 1036 (m), 1010 (m) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ=1.84–1.93 (m, 1H, CHCH_2), 2.04–2.10 (m, 1H, CHCH_2), 2.67–2.83 (m, 2H, Ar-CH_2), 2.95 (s, 3H, CH_3), 3.33–3.39 (m, 1H, CH), 3.61–3.70 (m, 2H, CH_2OH), 6.63 (bd, ^3J=7.77 Hz, 1H, Ar-H_5), 6.67 (dd, ^3J=7.27 Hz, ^4J=1.01 Hz, 1H, Ar-H_7), 7.00 (bd, ^3J=7.27 Hz, 1H, Ar-H_8), 7.13 (dd, ^3J=7.77 Hz, ^4J=1.52 Hz, 1H, Ar-H_6). ^{13}C NMR (100 MHz, $CDCl_3$, coupled): δ=22.9 (+, t, J=129.8 Hz, Ar-CH_2), 24.2 (+, t, J=126.6 Hz, CH*C*H_2), 38.5 (−, q, J=135.3 Hz, CH_3), 60.0 (−, d, J=136.6 Hz, CH), 63.2 (+, t, J=126.6 Hz, CH_2OH), 111.2 (−, d, J=155.9 Hz, C_5-Ar), 116.1 (−, d, J=160.5 Hz, C_7-Ar), 122.4 (quart, s, C_{quart}-Ar), 127.2 (−, d, J=157.1 Hz, C_6-Ar), 128.6 (−, d, J=154.4 Hz, C_8-Ar), 145.5 (s, NC_{quart}-Ar). MS (70 eV, EI), *m/z* (%): 177 (16) [M^+], 146 (100), 131 (15), 118 (6), 91 (3), 77 (3). HRMS $C_{11}H_{15}NO$: calcd 177.1154; found 177.1153. $C_{11}H_{15}NO$ (177.24) calcd C 74.54, H 8.53, N 7.90; found C 74.52, H 8.59, N 7.93.

2.1.11. (1-Methyl-1,2,3,4-tetrahydroquinolin-2-yl)ethanol (16b). To a solution of 97 mg (0.48 mmol) of 4,4a,5,6-tetrahydro-3*H*-[1,3]oxazin[3,4-a]quinolin-1-one (**12b**) in 30 ml of dry tetrahydrofuran was added 127 mg (3.3 mmol, 7 equiv.) of lithium aluminum hydride and refluxed for 4 h. After being cooled to room temperature, the mixture was treated with water in small portions and filtered. The white solid was suspended in 50 ml of dichloromethane and refluxed for 30 min. After filtration, both fractions were combined and washed with each 40 ml of brine and water. The organic layer was dried over sodium sulfate, filtered and concentrated to dryness in vacuum. After column chromatography on silica (8 g, 1×16 cm, pentane/ether 1:1), alcohol **16b** was isolated as yellowish oil. Yield 81 mg (89%). TLC: R_f=0.10 (pentane/ether, 1:1). GC: R_t=4.57 min. ^{1}H NMR (400 MHz, $CDCl_3$): δ=1.55–1.65 (m, 2H, CH_2), 1.80–1.55 (m, 3H, CH_2), 2.50–2.60 (m, 1H, Ar-CH_2), 2.70–2.80 (m, 1H, Ar-CH_2), 3.40 (s, 3H, CH_3), 3.61–3.70 (m, 2H, CH_2OH), 6.63 (bd, ^3J=7.77 Hz, 1H, Ar-H_5), 6.67 (ddd, ^3J=7.27 Hz, ^3J=7.27 Hz, ^4J=1.01 Hz, 1H, Ar-H_7), 7.00 (bd, ^3J=7.27 Hz, 1H, Ar-H_8), 7.13 (ddd, ^3J=7.77 Hz, ^3J=7.27 Hz, ^4J=1.52 Hz, 1H, Ar-H_6). ^{13}C NMR (100 MHz, $CDCl_3$): δ=23.6 (+, Ar-CH_2), 24.7 (+, CH*C*H_2), 34.5 (+, CH*C*H_2), 38.9 (−, CH_3), 56.1 (−, CH), 60.4 (+, CH_2OH), 111.8 (−, C_5-Ar), 116.1 (−, C_7-Ar), 122.1 (quart, C_{quart}-Ar), 127.4 (−, C_6-Ar), 128.8 (−, C_8-Ar), 145.3 (quart, NC_{quart}-Ar). MS (70 eV, EI), *m/z* (%): 191 (20) [M^+], 146 (100) [$C_{10}H_{12}N$], 131 (10), 118 (6), 91 (3), 77 (3). HRMS $C_{12}H_{17}NO$: calcd 191.1310; found 191.1309. $C_{12}H_{17}NO$ (191.27) calcd C 75.35, H 8.96, N 7.32; found C 75.02, H 8.89, N 7.62.

2.1.12. (1,2,3,4-Tetrahydroquinolin-2-yl)methanol (17).[25] 500 mg (2.64 mmol) of 3,3a,4,5-tetrahydro-

oxazol[3,4,-*a*]quinolin-1-one (**12a**) in 20 ml of a 10% solution of sodium hydroxide in ethanol were refluxed for 3 h. After being cooled, the mixture was added to 50 ml of dichloromethane and washed with each 40 ml of brine and water. The organic layer was dried over sodium sulfate, filtered and concentrated to dryness in vacuum. Heterocycle **17** was furnished as yellow oil without further purification. Yield 410 mg (95%). TLC: R_f=0.08 (pentane/ether, 1:1). GC: R_t=3.74 min. IR (KBr): ν=3373 (s), 2927 (m), 2844 (w), 1601 (m), 1496 (s), 1435 (w), 1310 (m), 1209 (w), 1029 (w) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ=1.64–1.77 (m, 1H, CHCH_2), 1.86–1.95 (m, 1H, CHCH_2), 2.70–2.91 (m, 2H, Ar-CH_2), 3.39–3.47 (m, 1H, CH), 3.54 (dd, ^2J=10.36 Hz, ^3J=7.65 Hz, 1H, CH_2OH), 3.72 (dd, ^2J=10.36 Hz, ^3J=3.74 Hz, 1H, CH_2OH), 6.54 (bd, ^3J=7.91 Hz, 1H, Ar-H_5), 6.66 (d, ^3J=7.34 Hz, 1H, Ar-H_7), 6.96–7.04 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ=24.4 (+, Ar-CH_2), 25.9 (+, CH*C*H_2), 52.8 (−, CH), 66.7 (+, CH_2OH), 114.6 (−, C_5-Ar), 117.5 (−, C_7-Ar), 121.5 (quart, C_{quart}-Ar), 126.9 (−, C_6-Ar), 129.3 (−, C_8-Ar), 141.2 (quart, NC_{quart}-Ar). MS (70 eV, EI), *m/z* (%): 163 (20) [M^+], 132 (100) [$C_9H_9N^+$], 119 (18). HRMS $C_{10}H_{13}NO$: calcd 163.0997; found 163.1001. $C_{10}H_{13}NO$ (163.10) calcd C 73.59, H 8.03, N 8.58; found C 73.11, H 8.22, N 8.50.

2.1.13. 2-Brommethyl-1-methyl-1,2,3,4-tetrahydroquinoline (18a). To a solution of 500 mg (2.8 mmol) of (1-methyl-1,2,3,4-tetrahydroquinolin-2-yl)-methanol (**12a**) in 15 ml of dry tetrahydrofuran and 0.78 ml (570 mg, 5.64 mmol, 2.0 equiv.) of triethylamine was added 420 mg (3.67 mmol, 1.3 equiv.) of mesylchloride dropwise at −40°C. The reaction mixture was stirred at −40°C for 1.5 h and subsequently treated with 980 mg (11.3 mmol, 4.0 equiv.) of lithium bromide, dissolved in 10 ml of dry tetrahydrofuran. After stirring additional 30 min at −40°C, the mixture was warmed to room temperature within 4 h. The mixture was dissolved in 70 ml of dichloromethane and washed with each 50 ml of aq. sodium hydrogen carbonate solution and brine. After back extraction of the aqueous layer with dichloromethane, the combined organic layers were dried over sodium sulfate, filtered and concentrated to dryness in vacuum. After column chromatography on silica (70 g, 3×30 cm, pentane/ether 1:1), compound **18a** was furnished as yellowish oil. Yield 573 mg (86%). TLC: R_f=0.59 (pentane/ether, 9:1). ^1H NMR (400 MHz, $CDCl_3$): δ=1.90–2.00 (m, 1H, CHCH_2), 2.20–2.30 (m, 1H, CHCH_2), 2.55–2.80 (m, 2H, CH_2), 3.00 (s, 3H, CH_3), 3.35–3.45 (m, 1H, CH), 3.55–3.80 (m, 2H), 6.40 (bd, ^3J=7.80 Hz, 1H, Ar-H), 6.67 (dd, ^3J=7.30 Hz, ^3J=7.30 Hz, 1H, Ar-H), 7.00 (d, ^3J=7.30 Hz, 1H, Ar-H), 7.13 (dd, ^3J=7.30 Hz, ^3J=7.80, 1H, Ar-H). ^{13}C NMR (100 MHz, $CDCl_3$): δ=22.8 (+, Ar-CH_2), 31.1 (+, CH*C*H_2), 38.1 (−, CH_3), 43.1 (+, CH_2Br), 60.0 (−, CH), 110.5 (−,C_5-Ar), 116.3 (−, C_7-Ar), 121.7 (quart, C_{quart}-Ar), 127.3 (−, C_6-Ar), 128.8 (−,C_8-Ar), 144.2 (quart, NC_{quart}-Ar). HRMS $C_{11}H_{14}NBr$: calcd 239.0310; found 239.0309. $C_{11}H_{14}NBr$ (240.14) calcd C 55.02, H 5.88, N 5.83; found C 55.54, H 5.95, N 5.96.

2.1.14. 2-Iodmethyl-1-methyl-1,2,3,4-tetrahydroquinoline (18b). To a stirred solution of 500 mg (2.82 mmol) of 1-methyl-1,2,3,4-tetrahydroquinolin-2-yl)-methanol (**16a**) in 15 ml of a mixture of ether and acetonitrile (3:2) was added 360 mg (5.29 mmol, 1.88 equiv.) of imidazole, 1.33 g (5.07 mmol, 1.79 equiv.) of triphenylphosphine and 1.30 g (5.12 mmol, 1.82 equiv.) of iodine at room temperature. The reaction mixture was stirred at room temperature for 24 h and then treated in small portions with sat. aq. $Na_2S_2O_3$ solution until the reaction mixture got colourless. It was added 50 ml of ether, the organic layer was separated and washed with each 30 ml of aq. sodium hydrogen carbonate solution, brine and water. The organic layer was dried over sodium sulfate, filtered and concentrated to dryness in vacuum. After column chromatography on silica (30 g, 2.5×18 cm, hexane/ether 2:1) compound **18b** was furnished as yellowish oil. Yield 487 mg (60%). TLC: R_f=0.78 (hexane/ether, 1:1). GC: R_t=4.38 min. ^1H NMR (400 MHz, $CDCl_3$): δ=1.91–2.02 (m, 1H, CHCH_2), 2.38–2.46 (m, 1H, C*H*CH_2), 2.73–2.80 (m, 2H, Ar-CH_2), 3.05 (s, 3H, CH_3), 3.10–3.15 (m, 1H, CH_2I), 3.39–3.43 (m, 1H, CH_2I), 3.58–3.65 (m, 1H, CH), 6.62 (bd, ^3J=8.04 Hz, 1H, Ar-H), 6.71 (dd, ^3J=7.04, 7.52 Hz, 1H, Ar-H), 7.06 (bd, ^3J=7.04 Hz, 1H, Ar-H), 7.16 (dd, ^3J=7.52, 8.04 Hz, 1H, Ar-H). ^{13}C NMR (100 MHz, $CDCl_3$): δ=7.7 (+, CH_2I), 22.6 (+, Ar-CH_2), 23.9 (+, CH*C*H_2), 37.9 (−, CH_3), 59.9 (−, CH), 110.6 (−, C-Ar), 116.3 (−, C-Ar), 121.8 (quart, CC_{quart}-Ar), 127.4 (−, C-Ar), 128.9 (−, C-Ar), 144.1 (quart, NC_{quart}-Ar). MS (70 eV, EI), *m/z* (%): 287 (41) [M^+], 159 (52), 146 (100), 131 (55), 117 (44), 91 (57), 77 (54), 65 (37). HRMS $C_{11}H_{14}IN$: calcd 287.0171; found 287.0175.

2.1.15. 2-(2-Iodo-ethyl)-1-methyl-1,2,3,4-tetrahydroquinoline (19b). To a stirred solution of 202 mg (1.06 mmol) of 2-(1-methyl-1,2,3,4-tetrahydroquinolin-2-yl)-ethanol (**16b**) in 15 ml of a mixture of ether and acetonitrile (3:2) was added 136 mg (1.99 mmol, 1.87 equiv.) of imidazole, 498 mg (1.89 mmol, 1.78 equiv.) of triphenylphosphine and 489 mg (1.92 mmol, 1.81 equiv.) of iodine at room temperature. The reaction mixture was stirred at room temperature for 24 h and then treated in small portions with sat. aq. $Na_2S_2O_3$ solution until the reaction mixture got colourless. It was added 50 ml of ether and the organic layer was separated and washed with each 30 ml of aq. sodium hydrogen carbonate solution, brine and water. The organic layer was dried over sodium sulfate, filtered and concentrated to dryness in vacuum. After column chromatography on silica (74.0 g, 3×19 cm, pentane/ether 50:1) compound **19b** was furnished as yellowish oil. Yield 215 mg (68%). TLC: R_f=0.23 (pentane/ether, 50:1). GC: R_t=5.09 min. ^1H NMR (400 MHz, $CDCl_3$): δ=1.82–1.98 (m, 3H), 2.12–2.20 (m, 1H, CH_2), 2.70–2.78 (m, 2H, CH_2), 3.00 (s, 3H, CH_3), 3.13–3.19 (m, 1H, CH_2), 3.25–3.31 (m, 1H, CH_2), 3.41–3.47 (m, 1H, CH), 6.56 (bd, ^3J=8.14 Hz, 1H, Ar-H), 6.63 (dd, ^3J=7.19, 7.70 Hz, 1H, Ar-H), 6.98 (bd, ^3J=7.19 Hz, 1H, Ar-H), 7.10 (dd, ^3J=7.70, 8.14 Hz, 1H, Ar-H). ^{13}C NMR (100 MHz, $CDCl_3$): δ=2.9 (+, CH_2I), 23.5 (+, CH_2), 24.0 (+, CH_2), 35.4 (+, CH_2), 38.4 (−, CH_3), 59.0 (−, CH), 111.1 (−, C-Ar), 115.9 (−, C-Ar), 121.4 (quart, CC_{quart}-Ar), 127.2 (−, C-Ar), 128.8 (−, C-Ar), 145.0 (quart, NC_{quart}-Ar). GC–MS (70 eV, EI), *m/z* (%): 301 (35) [M^+], 173 (4), 146 (100), 130 (30), 118 (14), 103 (6), 91 (10), 77 (9), 65 (6), 51 (5).

2.1.16. Reaction of 18a with BuLi. A solution of 48.0 mg (0.20 mmol, 1.0 equiv.) of bromide **18a** in 2 ml of THF was treated with 128 μl (0.20 mmol, 1.0 equiv.) 1.6 M BuLi in

hexanes at −78°C. After warming to room temperature within 12 h, the mixture was quenched with aq. sodium hydroxide solution. Aqueous workup and chromatography on silica (8.0 g, 1×17 cm, pentane/ether 20:1), provided (2-but-3-enylphenyl)butylmethylamine (**21e**) as colourless liquid. Yield 24.0 mg (55%). TLC: R_f=0.59 (pentane/ether, 9:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ=0.91 (t, J=7.32 Hz, 3H), 1.29–1.38 (m, 2H, CH_2), 1.45–1.54 (m, 2H, CH_2), 2.36–2.42 (m, 2H, CH_2), 2.63 (s, 3H, NCH_3), 2.77–2.86 (m, 4H, CH_2), 4.97 (dd, J=3.39, 10.27 Hz, 1H, CH=CH_2), 5.05 (dd, J=3.39, 17.02 Hz, 1H, CH=CH_2), 5.91 (ddd, J=6.60, 10.27, 17.02 Hz, 1H, CH=CH_2), 7.01 (dd, J=1.51, 7.26 Hz, 1H, Ar-H), 7.11 (dd, J=1.51, 7.95 Hz, 1H, Ar-H), 7.14–7.21 (m, 2H, Ar-H). ^{13}C NMR (100 MHz, $CDCl_3$): δ=14.1 (−, CH_3), 20.5 (+, CH_2), 30.2 (+, CH_2), 30.3 (+, CH_2), 34.7 (+, CH_2), 43.0 (−, CH_3), 57.1 (+, CH_2), 114.5 (+, CH=CH_2), 121.1 (−, C-Ar), 123.6 (−, C-Ar), 126.6 (−, C-Ar), 129.7 (−, C-Ar), 137.9 (quart, CC_{quart}-Ar), 139.0 (−, CH=CH_2), 152.7 (quart, NC_{quart}-Ar). GC–MS (70 eV, EI), m/z (%): 217 (10) [M^+], 174 (100) [$M^+-C_3H_7$], 159 (12) [$M^+-C_4H_{10}$], 146 (20) [$M^+-C_5H_{11}$], 144 (22) [$M^+-C_5H_{13}$], 132 (75) [$M^+-C_5H_{13}$], 117 (30), 91 (33).

2.1.17. Reaction of 18a with the cuprate generated from BuLi and CuBr·Me$_2$S. A suspension of 205 mg (1.00 mmol) of CuBr·Me_2S in 2 ml of ether was treated with 1.3 ml (2.08 mmol, 10.5 equiv.) of BuLi (1.6 M, hexanes) at −78 and stirred at −30°C for 30 min. After being cooled again to −78°C, 48.0 mg (0.20 mmol) of bromide **18a** in 2 ml of ether were added. After warming slowly to room temperature, the mixture was quenched with a sat. solution of ammonium chloride in aqueous ammonia. Aqueous workup provided 1-methyl-2-pentyl-1,2,3,4-tetrahydroquinoline (**18e**, 15%) together with **21f** (49%) and **21e** (28%) as colourless liquid. **18e**: MS (70 eV, EI), m/z (%): 217 (5) [M^+], 146 (100) [$M^+-C_5H_{11}$], 130 (10). The spectroscopic data of **18e** are in accordance with the literature values [3].

2.1.18. 2-Allyl-1-methyl-1,2,3,4-tetrahydroquinoline (18i). To a stirred solution of 97.4 mg (2.29 mmol, 2.2 equiv.) of lithium chloride and 155 mg (1.15 mmol, 1.1 equiv.) of copper-(II)-chloride in 5 ml of THF was added 300 mg (1.05 mmol) of 2-iodomethyl-1-methyl-1,2,3,4-tetrahydroquinoline (**18b**) dissolved in 5 ml of THF at −5°C. Subsequently, 1.57 ml (1.57 mmol, 1.5 equiv.) of vinyl magnesium bromide solution (1 M, THF) were slowly added and stirred for 24 h. After warming slowly to room temperature, the mixture was quenched with sat. ammonia solution (25%, water). It was added 40 ml of ether and the organic layer was separated and washed with each 20 ml of sat. ammonium chloride solution, brine and water. The organic layer was dried over sodium sulfate, filtered and concentrated to dryness in vacuum. Compound **18i** was furnished as yellowish oil. Yield 52.7 mg (27%). GC: R_t=3.97 min. ^{1}H NMR (400 MHz, $CDCl_3$): δ=2.12–2.20 (m, 1H, CH_2), 2.40–2.46 (m, 1H, CH_2), 2.64–2.69 (m, 2H, CH_2), 2.78–2.85 (m, 2H, CH_2), 2.94 (s, 3H, CH_3), 3.31–3.36 (m, 1H, C$H$$NCH_3$), 5.06–5.11 (m, 2H, CH_2), 5.81 (dddd, J=6.49, 8.04, 10.34, 16.88 Hz 1H, CH=CH_2), 6.54 (bd, ^3J=8.09 Hz, 1H, Ar-H), 6.60 (dd, ^3J=7.26, 7.39 Hz, 1H, Ar-H), 6.97 (bd, ^3J=7.26 Hz, 1H, Ar-H), 7.07 (dd, ^3J=7.39, 8.09 Hz, 1H, Ar-H). ^{13}C NMR (100 MHz, $CDCl_3$): δ=24.3 (+, CH_2), 29.7 (+, CH_2), 35.9 (+, CH_2), 37.8 (−, NCH_3), 58.7 (−, CHNCH_3), 110.5 (−, C-Ar), 115.5 (−, C-Ar), 117.0 (+, CH=CH_2), 121.8 (quart, CC_{quart}-Ar), 127.1 (−, C-Ar), 128.6 (−, C-Ar), 135.4 (−, CH=CH_2), 145.2 (quart, NC_{quart}-Ar). GC–MS (70 eV, EI), m/z (%): 187 (16) [M^+], 146 (100), 131 (20), 118 (8), 91 (6), 77 (5), 65 (2).

2.1.19. 1,2-Dimethyl-1,2,3,4-tetrahydroquinoline (18g) and (2-but-3-enylphenyl)-methyl-amine (21f). To a stirred solution of 55.0 mg (1.29 mmol, 1.1 equiv.) of lithium chloride and 81.0 mg (0.60 mmol, 0.5 equiv.) of copper-(II)-chloride in 6 ml of THF was added 297 mg (1.24 mmol) of 2-bromomethyl-1-methyl-1,2,3,4-tetrahydroquinoline (**18a**) dissolved in 6 ml of THF at −5°C. Subsequently, 0.67 ml (2.01 mmol, 1.5 equiv.) of ethyl magnesium bromide solution (3 M in ether) were slowly added and stirred for 5 h. After warming slowly to room temperature, the mixture was quenched with 1 M hydrochloric acid. It was added 30 ml of ether and the organic layer was separated and washed with each 20 ml of aq. sodium hydrogen carbonate solution, brine and water. The organic layer was dried over sodium sulfate, filtered and concentrated to dryness in vacuum. After column chromatography on silica (40 g, 2.5×16 cm, pentane/ether 40:1) compound **18g** was furnished as yellowish oil. Yield 80.0 mg (40%). ^{1}H NMR (400 MHz, $CDCl_3$): δ=1.17 (d, ^3J=6.45 Hz, CH_3), 1.76–1.82 (m, 1H, CH_2), 1.98–2.07 (m, 1H, CH_2), 2.69–2.76 (m, 1H, CH_2), 2.84–2.89 (m, 1H, CH_2), 2.94 (s, 3H, NCH_3), 3.44–3.51 (m, 1H, C$H$$CH_3$), 6.59 (bd, ^3J=8.21 Hz, 1H, Ar-H), 6.63 (dd, ^3J=7.32, 7.83 Hz, 1H, Ar-H), 7.01 (bd, ^3J=7.32 Hz, 1H, Ar-H), 7.12 (dd, ^3J=7.83, 8.21 Hz, 1H, Ar-H). ^{13}C NMR (100 MHz, $CDCl_3$): δ=16.5 (−, CHCH_3), 22.8 (+, CH_2), 27.1 (+, CH_2), 35.9 (−, NCH_3), 52.8 (−, CHCH_3), 109.6 (−, C-Ar), 114.4 (−, C-Ar), 121.0 (quart, CC_{quart}-Ar), 126.0 (−, C-Ar), 127.5 (−, C-Ar), 144.4 (quart, NC_{quart}-Ar). GC–MS (70 eV, EI), m/z (%): 161 (98) [M^+], 146 (100), 131 (90), 118 (48), 91 (33), 77 (28), 65 (17), 51 (16).

As a second fraction compound **21f** was isolated. Yield 10.0 mg (5%). ^{1}H NMR (400 MHz, $CDCl_3$): δ=2.35–2.41 (m, 2H, CH_2), 2.55 (d, J=8.59 Hz, 1H, CH_2), 2.57 (d, J=10.11 Hz, 1H, CH_2), 2.89 (s, 3H, CH_3), 3.68 (bs, 1H, NH), 5.02 (dd, J=3.17, 10.26 Hz, 1H, CHCH_2), 5.09 (dd, J=3.17, 17.08 Hz, 1H, CHCH_2), 5.91 (ddd, ^3J=6.58, 10.26, 17.08 Hz, 1H, C$H$$CH_2$), 6.64 (bd, ^3J=7.66 Hz, 1H, Ar-H), 6.70 (dd, ^3J=7.52, 7.66 Hz, 1H, Ar-H), 7.06 (bd, ^3J=7.51 Hz, 1H, Ar-H), 7.17 (dd, ^3J=7.51, 7.52 Hz, 1H, Ar-H). ^{13}C NMR (100 MHz, $CDCl_3$): δ=30.6 (+, CH_2), 31.0 (−, CH_3), 32.7 (+, CH_2), 109.8 (−, C-Ar), 115.1 (+, CHCH_2), 117.1 (−, C-Ar), 125.6 (quart, CC_{quart}-Ar), 127.4 (−, C-Ar), 128.9 (−, C-Ar), 138.3 (−, CHCH_2), 146.9 (quart, NC_{quart}-Ar). GC–MS (70 eV, EI), m/z (%): 161 (40) [M^+], 120 (100), 91 (26), 77 (7), 65 (9), 51 (5).

2.1.20. 1-Methyl-2-phenethyl-1,2,3,4-tetrahydroquinoline (18h). To a stirred solution of 32.8 mg (0.77 mmol, 2.2 equiv.) of lithium chloride and 51.9 mg (0.38 mmol, 1.1 equiv.) of copper-(II)-chloride in 15 ml of THF was added 105 mg (0.35 mmol) of 2-(2-iodoethyl)-1-methyl-1,2,3,4-tetrahydroquinoline (**19b**) dissolved in 10 ml of THF at −5°C. Subsequently, 1.00 ml (2.00 mmol, 5.7 equiv.) of phenyl magnesium chloride solution (2 M,

THF) were slowly added and the mixture was stirred for 24 h. After warming slowly to room temperature, the mixture was quenched with sat. ammonia solution (25% in water). It was added 40 ml of ether and the organic layer was separated and washed with each 20 ml of sat. ammonium chloride solution, brine and water. The organic layer was dried over sodium sulfate, filtered and concentrated to dryness in vacuum. After column chromatography on silica (29 g, 2.5×20 cm, pentane/ether 50:1) compound **18h** was furnished as white solid. Yield 41.0 mg (47%). ^{1}H NMR (400 MHz, $CDCl_3$): δ=1.72–1.83 (m, 1H, CH_2), 1.90–2.01 (m, 3H, CH_2), 2.56–2.63 (m, 1H, CH_2), 2.67–2.76 (m, 2H, CH_2), 2.82–2.89 (m, 1H, CH_2), 2.92 (s, 3H, CH_3), 3.27–3.32 (m, 1H, C*H*NCH$_3$), 6.54 (bd, ^3J=8.14 Hz, 1H, Ar-H), 6.60 (dd, ^3J=7.14, 7.33 Hz, 1H, Ar-H), 6.98 (bd, ^3J=7.14 Hz, 1H, Ar-H), 7.08 (dd, ^3J=7.32, 8.14 Hz, 1H, Ar-H), 7.18–7.21 (m, 3H, Ar′-H), 7.27–7.30 (m, 2H, Ar′-H). ^{13}C NMR (100 MHz, $CDCl_3$): δ=23.6 (+, CH_2), 24.4 (+, CH_2), 32.3 (+, CH_2), 32.9 (+, CH_2), 38.0 (−, NCH_3), 58.4 (−, *C*HNCH$_3$), 110.6 (−, C-Ar), 115.4 (−, C-Ar), 121.8 (quart, CC_{quart}-Ar), 125.8 (−, C-Ar), 127.1 (−, C-Ar), 128.2 (−, C-Ar′), 128.4 (−, C-Ar′), 128.6 (−, C-Ar′), 142.0 (quart, CH_2C_{quart}-Ar′), 145.2 (quart, NC_{quart}-Ar). GC–MS (70 eV, EI), *m*/*z* (%): 251 (34) [M$^+$], 146 (100), 130 (15), 118 (7), 91 (6), 77 (5), 65 (5).

2.1.21. 1-Methyl-2-propyl-1,2,3,4-tetrahydroquinoline (18f). To a stirred solution of 30.8 mg (0.73 mmol, 2.1 equiv.) of lithium chloride and 51.1 mg (0.38 mmol, 1.1 equiv.) of copper-(II)-chloride in 15 ml of THF was added 105 mg (0.35 mmol) of 2-(2-iodoethyl)-1-methyl-1,2,3,4-tetrahydroquinoline (**19b**) dissolved in 10 ml of THF at −5°C. Subsequently, 1.00 ml (3.00 mmol, 8.6 equiv.) of methyl magnesium bromide solution (3 M, ether) were slowly added and the mixture was stirred for 24 h. After warming slowly to room temperature, the mixture was quenched with sat. ammonia solution (25%, water). It was added 40 ml of ether and the organic layer was separated and washed with each 20 ml of sat. ammonium chloride solution, brine and water. The organic layer was dried over sodium sulfate, filtered and concentrated to dryness in vacuum. Compound **18f** was furnished as yellowish oil. Yield 44.0 mg (67%). GC: R_t=3.99 min. ^{1}H NMR (400 MHz, $CDCl_3$): δ=0.96 (t, J=7.12 Hz, 3H, CH_3), 1.28–1.35 (m, 1H, CH_2), 1.37–1.47 (m, 2H, CH_2), 1.57–1.61 (m, 1H, CH_2), 1.88–1.93 (m, 2H, CH_2), 2.64–2.70 (m, 1H, CH_2), 2.78–2.84 (m, 1H, CH_2), 2.95 (s, 3H, NCH_3), 3.24–3.29 (m, 1H, C*H*NCH$_3$), 6.54 (bd, ^3J=8.08 Hz, 1H, Ar-H), 6.60 (dd, ^3J=7.32, 7.32 Hz, 1H, Ar-H), 6.98 (bd, ^3J=7.32 Hz, 1H, Ar-H), 7.09 (dd, ^3J=7.32, 8.08 Hz, 1H, Ar-H). ^{13}C NMR (100 MHz, $CDCl_3$): δ=14.4 (−, CH_3), 19.4 (+, CH_2), 23.7 (+, CH_2), 24.6 (+, CH_2), 33.7 (+, CH_2), 38.1 (−, NCH_3), 58.8 (−, *C*HNCH$_3$), 110.5 (−, C-Ar), 115.3 (−, C-Ar), 121.9 (quart, CC_{quart}-Ar), 127.1 (−, C-Ar), 128.7 (−, C-Ar), 145.56 (quart, NC_{quart}-Ar). GC–MS (70 eV, EI), *m*/*z* (%): 189 (23) [M$^+$], 146 (100), 130 (13), 118 (7), 91 (5), 77 (5), 65 (3).

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