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A Microwave-Assisted Heck Reaction in Poly(ethylene glycol) for the Synthesis of Benzazepines

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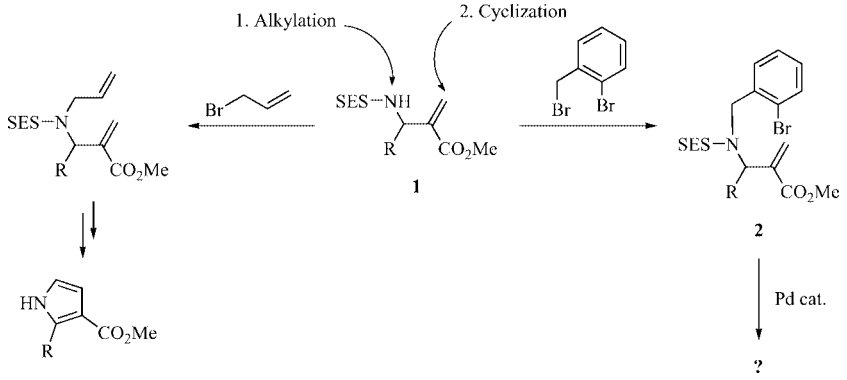
The Heck reaction of alkylated 2-(trimethylsilyl)ethanesulfonyl (SES)-protected β-amino esters provides benzazepines in good yields. Good selectivity towards cyclisation was obtained when the reaction was performed in PEG 3400 as the solvent under microwave activation. Cleavage of the SES group with HF provides the corresponding free benzazepine. (© Wiley-VCH Verlag GmbH & Co. KGaA, 69451 Weinheim, Germany, 2007)

Introduction

Microwave activation has emerged as a powerful technique in organic synthesis to accelerate the preparation of molecules.[1–6] Many examples have demonstrated that this technique can be adapted to most organic transformations. Reactions are generally faster and consequently cleaner and sometimes more selective. Furthermore, the focused heating generated by the microwave enables a high temperature to be reached in a short time. Under microwave irradiation the heating characteristics of a solvent or chemical depend on its dielectric properties.[4] Because of their lack of volatility, ionic liquids have proven to be efficient and less prone to pressure build up compared to low boiling solvents under microwave heating.[7–22] Another family of solvents which can substitute volatile organic solvents are poly(ethylene glycol)s (PEGs). They present some common characteristics with ionic liquids (high polarity, high boiling points) and have been used to a certain extent in substitution, oxidation, reduction and organometallic reactions.[23] Furthermore they present low toxicity. So far, PEGs have not been used extensively in reactions involving microwave activation.[24–35] We now report that novel benzazepines can be obtained by a palladium-catalysed Heck reaction in a PEG solvent under microwave heating.



Scheme 1. Functionalized β-amino ester **1**.

The 2-(trimethylsilyl)ethanesulfonyl (SES)-protected α-methylene β-amino ester **1**, obtained by an aza-Baylis–Hillman reaction, is a useful synthon for the preparation of heterocyclic structures because of the multiple functional groups present on this molecule (Scheme 1). We have previously reported that an alkylation/ring closing metathesis/

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aromatisation sequence leads to the efficient preparation of 2,3-disubstituted pyrroles.[36] We report herein the investigation of microwave-enhanced palladium-catalysed cyclisation of **2**, obtained by alkylation of **1** with 2-bromobenzyl bromide.

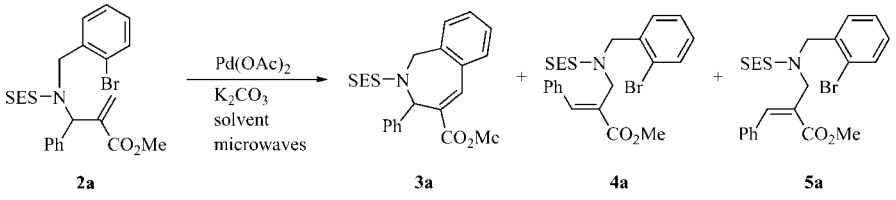
Recently, mixtures of Pd salts and PEG have been studied as catalytic systems for Pd-catalysed transformations.[27,37–46] Consequently, following our experience with PEG-improved Heck reactions,[47,48] we explored the use of PEG 3400 with $Pd(OAc)_2$ under microwave conditions to perform the expected cyclisation.

Results and Discussions

Compound **2a** was heated in the presence of K_2CO_3 and a catalytic amount of $Pd(OAc)_2$ in PEG 3400 in the microwave synthesiser at 100 °C for 10 min (Scheme 2 and Table 1) to yield only the expected cyclized product **3a** (Entry 1). When the experiment was repeated under the same conditions, the reaction did not go to completion (Entry 2). Increasing the reaction time resulted in the formation of by-products **4a** and **5a**, most probably by a Tsuji–Trost rearrangement (Entry 3). These preliminary results demonstrated the importance of the heating mode of the sample. This may be due to the fact that the reaction temperature was entered as the heating instruction in the instrument. The synthesiser therefore adjusted the magnetron power to reach the selected instruction (T = 100 °C). Starting from room temperature, this could take several seconds or minutes. This temperature ramp would include the time needed to melt PEG 3400 (a solid which melts at 45–55 °C). Since the sample mixtures were not homogeneous, this resulted in different heating profiles, which could explain the difficulty in reproducing the experiments. To test this hypothesis, and reduce the starting temperature ramp to a minimum, the starting heating power was set to the maximum level (300 W) for a reaction at 100 °C (Entry 4). Full conversion was obtained with no by-products, and this experiment could be reproduced several times.

According to the same procedure, the reaction could also take place at lower temperature (Entries 5 and 6), and the amount of catalyst could be decreased to 1 mol-% without slowing down the kinetics of the reaction (Entry 7). Switching from an inorganic to an organic base reduced the speed of the reaction (Entry 8). Since low molecular weight PEGs are liquid at room temperature, we tried to substitute PEG 3400 by PEG 300 (Entry 9). This led to a very complicated mixture of products containing **3a**, **4a** and **5a**. Consequently, the use of a higher molecular weight PEG seems necessary. We also used a mixture of PEG 300 and PEG 3400 but the results did not improve (Entry 10), nor did they with a mixture of DMF and PEG. The amount of DMF should be limited to obtain satisfactory results (Entries 11 and 12). In the absence of PEG, the reaction in DMF was slower and not very clean (Entry 13). The reaction carried out in PEG under thermal conditions was slower and only 23% conversion was obtained after 30 min of reaction (Entry 14).

The choice of the solvent is important to direct the transformation of the starting material towards formation of the cyclized product as otherwise the transformations are incomplete or the Tsuji–Trost rearrangement occurs to pro-



2a **3a** **4a** **5a**

Scheme 2. Palladium-catalysed reaction of **2a**.

Table 1. Reaction conditions for microwave-assisted Heck reaction.

Entry	$Pd(OAc)_2$ [equiv.]	Base	PEG (wt. [mg])	Solvent (vol. [mL])	T [°C]	t [min]	Conditions	**2a**	**3a**	**4a**	**5a**
1	0.1	K_2CO_3	3400 (220)	–	100	10	MW	0	100	0	0
2	0.1	K_2CO_3	3400 (220)	–	100	10	MW	22	78	0	0
3	0.1	K_2CO_3	3400 (220)	–	100	30	MW	0	80	14	6
4	0.1	K_2CO_3	3400 (220)	–	100	30	MW 300W	0	100	0	0
5	0.1	K_2CO_3	3400 (220)	–	80	30	MW 300W	0	100	0	0
6	0.1	K_2CO_3	3400 (220)	–	60	30	MW 300W	0	100	0	0
7	0.01	K_2CO_3	3400 (220)	–	100	30	MW 300W	0	100	0	0
8	0.1	Oct_3N	3400 (220)	–	100	30	MW 300W	40	60	0	0
9	0.1	K_2CO_3	–	PEG 300 (0.5)	100	30	MW 300W	complicated mixture			
10	0.1	K_2CO_3	3400 (50)	PEG 300 (0.5)	100	30	MW 300W	complicated mixture			
11	0.01	K_2CO_3	3400 (50)	DMF (1)	100	30	MW 300W	31	62	6	1
12	0.1	K_2CO_3	3400 (50)	DMF (0.5)	100	30	MW 300W	0	100	0	0
13	0.1	K_2CO_3	–	DMF (0.5)	100	30	MW 300W	–	84[a]	–	–
14	0.1	K_2CO_3	3400 (220)	–	100	30	thermal	77	23	0	0
15	precipitate from Entry 4 was used				100	30	MW 300W	14	76	7	3

[a] **3a** was formed along with unidentified products.

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duce a large amount of **4a**. When PEG 300 or a mixture of PEG 3400 and PEG 300 was used, the reaction was slowed down dramatically. Addition of DMF produced the same results. The best conditions were obtained using PEG 3400 as solvent in the presence of K_2CO_3. In addition, the workup conditions are easy to carry out. After dissolving the reaction mixture in CH_2Cl_2, precipitation in diethyl ether followed by filtration to remove the PEG/Pd/base mixture provides the expected product in the filtrate, which was isolated by evaporation of the diethyl ether.

The structure of benzazepine **3a**, especially the position of the trisubstituted olefin, was ascertained by X-ray analysis (Figure 1).

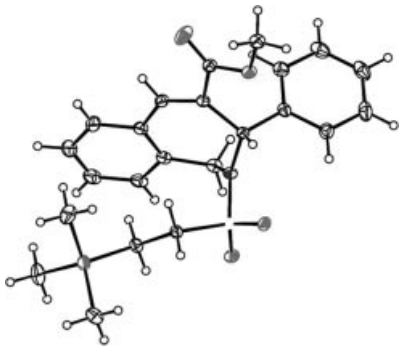


Figure 1. X-ray structures of benzazepine **3a**.

The catalytic system was investigated for the presence of nanoparticles, and we were able to observe nanoparticles of palladium by TEM (Figure 2).

The experimental results described herein can be correlated to the fast formation of nanoparticles of palladium in PEG 3400. Literature results show that larger PEGs (with an average molecular weight equal to, or higher than, 2000) rapidly reduce metallic salts such as $Pd(OAc)_2$ and provide better stabilisation of the particles.[44] When the catalytic system was used again in a second cycle (Entry 15) the reaction was not as efficient. This was also checked in the case of an intermolecular Heck reaction (coupling of phenyl iodide with *tert*-butyl acrylate) under the conditions used for the intramolecular reaction. While the first cycle yielded 100% conversion, the second cycle yielded only 75% conversion. Clearly, the colloidal system does not have the same efficiency after microwave irradiation and this difference may be due to a change in structure, probably a modification of the size of the particles.[49] It is also worth noting that after one cycle, the catalytic system has accumulated 1 equiv. of KBr as a Heck reaction side-product, which may then change the structure of the catalyst and hence the result in the next cycle.

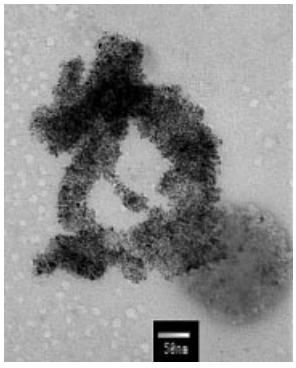
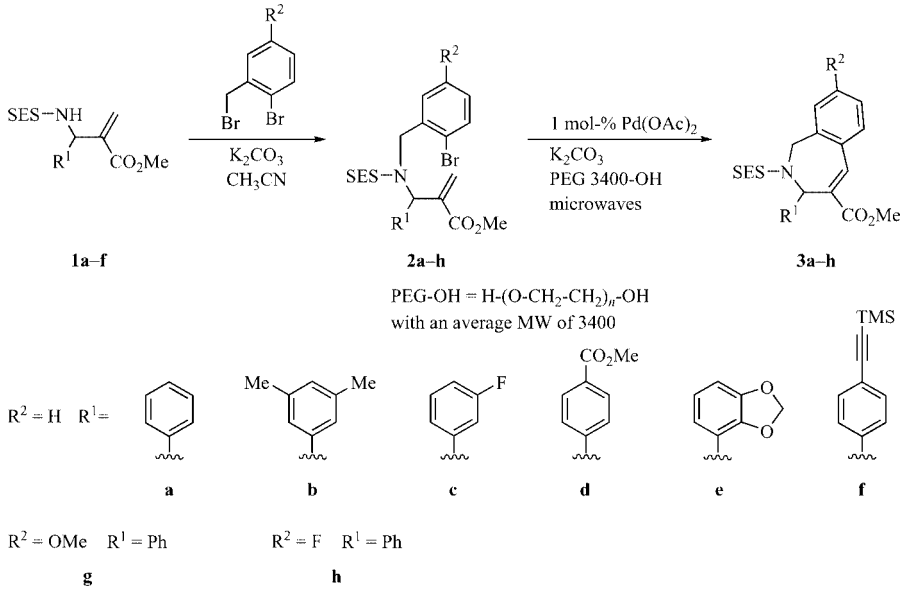


Figure 2. TEM image of a mixture of $Pd(OAc)_2$, PEG 3400 and K_2CO_3 after microwave irradiation at 100 °C for 30 min.

Various benzazepines could be prepared by varying the aldehyde leading to β-amino ester **1** and the alkylating agent (Scheme 3). All of them were obtained in good yield (Table 2), except in the case of **3f**, where deprotection of the TMS group on the alkyne substituent occurred.

The next step was the deprotection of the SES protecting group (Scheme 4 and Table 2). The SES group is usually cleaved in the presence of fluoride ions to yield the free



Scheme 3. Preparation of diverse benzazepines by Heck cyclisation.

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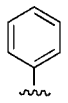
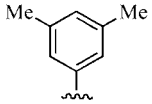
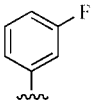
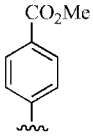
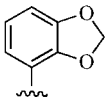
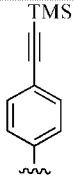
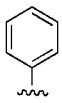
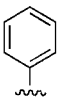
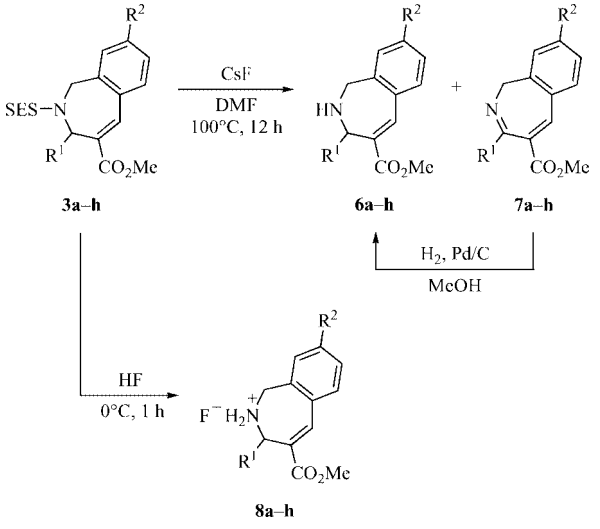
Table 2. Yields of isolated **2a–h**, **3a–h**, **8a–h**.

Product	**a**	**b**	**c**	**d**	**e**	**f**	**g**	**h**
R^1								
R^2	H	H	H	H	H	H	OMe	F
2	81	90	79	89	89	62	76	74
3	95	98	91	82	51	37[a]	83	76
8	98	99	99	–[b]	–[c]	–[d]	100	99

[a] Partial deprotection of the TMS group occurred. [b] Partial deprotection of the ester group on the aryl substituent (R^1) occurred. [c] Deprotection resulted in a complicated mixture. [d] Not performed.

amine by elimination of ethylene and sulfur dioxide.[50,51] When benzazepine **3a** was subjected to classical deprotection reaction conditions (CsF, DMF),[50] the free amine **6a** was obtained along with the imine **7a** resulting from the oxidative elimination of the SES group.[36] Other fluoride sources also gave mixtures of **6a** and **7a**. A deprotection/reduction sequence[52] was performed by treating the **6a/7a** mixture with hydrogen in the presence of palladium on charcoal, which yielded **6a** as the sole product. As an alternative, we used hydrofluoric acid,[53] which gave **8a**, the fluorohydrate of **6a**, as the sole product in quantitative yield. We finally chose to treat **3b–e** and **3g**,**h** with HF. The corresponding benzazepines **8** were obtained as their fluoride salts, except for **3d** (partial deprotection of the side chain methyl ester occurred) and **3e**, which decomposed.



Scheme 4. Deprotection of the SES-protected benzazepines **3**.

Conclusions

We have prepared original benzazepines using Heck chemistry performed in PEG. We have shown that the temperature ramp experienced by the sample could have a strong influence on the selectivity of the reaction. To the best of our knowledge, we have prepared and characterised the first PEG-stabilized palladium nanoparticles obtained under microwave activation. This system promotes the exclusive formation of benzazepines. Deprotection of the nitrogen function provides the heterocycle in good yield. Further studies to improve this catalytic system for recycling are currently underway in our laboratory.

Experimental Section

General Remarks: ^{1}H and ^{13}C NMR analyses were performed with a Bruker AC 300 MHz spectrometer, and calibrated using residual undeuterated solvents as an internal reference. Electrospray ionisation mass spectra were recorded with a Micromass Platform II fitted with an electrospray interface. The mass spectrometer was calibrated in the positive- and negative-ion ESI mode. The samples were dissolved in H_2O/CH_3CN (50:50, v/v). FAB and high-resolution mass spectra were recorded with a JEOL JSM DX300-SX 102 in positive mode using 3-nitrobenzyl alcohol (NBA) as matrix. Infrared spectra were recorded with a Perkin–Elmer Paragon 1000 by diffuse reflectance or by transmittance in KBr salt plates. Melting points were measured with a Büchi melting point B-540 apparatus and are uncorrected. Microwave-assisted reactions were performed with a Biotage Initiator 60 EXP®. The temperature was measured with an IR sensor on the outer surface of the reaction vial.

General Procedure for the Alkylation of β-Amino Esters 1: A mixture of β-amino ester **1** (0.3 mmol, 1 equiv.), 2-benzyl bromide or a related reagent (0.36 mmol, 1.2 equiv.) and K_2CO_3 (414 mg, 3 mmol, 10 equiv.) in 3.5 mL of CH_3CN was refluxed for 6 h. After evaporation of the solvent, the residue was diluted with EtOAc, washed successively with a solution of 5% $KHSO_4$ and brine, dried with $MgSO_4$, and the solvents were evaporated. Silica gel chromatography (Et_2O/cyclohexane) yielded the corresponding *N*-(2-bromobenzyl)-β-amino ester **2**.

Methyl 2-{[*N*-(2-Bromobenzyl)-2′-(trimethylsilyl)ethylsulfonamido]-(phenyl)methyl}acrylate (2a): Alkylation of the β-amino ester **1a** with 2-bromobenzyl bromide yielded 128 mg (81%) of the title compound as a white solid after silica gel chromatography (Et_2O/cyclohexane, 1:9). M.p. 72.7–73.9 °C. IR: $\tilde{\nu}$ = 3054 (m), 2955 (m), 1723 (s), 1264 (s) cm^{-1}. ^{1}H NMR ($CDCl_3$, Me_4Si): δ = –0.07 (s, 9 H), 0.90–1.05 (m, 2 H), 2.50–2.80 (m, 2 H), 3.59 (s, 3 H), 4.76 (s, 2 H), 5.88 (d, J_2 = 1.4 Hz, 1 H), 6.15 (s, 1 H), 6.44 (s, 1 H), 7.02 (dt, J_2 = 1.6, J_3 = 7.7 Hz, 1 H), 7.10–7.45 (m, 8 H) ppm. ^{13}C NMR ($CDCl_3$, Me_4Si): δ = –1.9, 10.3, 50.5, 50.7, 52.2, 62.2, 122.7, 122.2, 128.3, 128.8, 128.9, 129.0, 129.5, 130.4, 132.5, 136.5, 137.5, 139.1, 166.2 ppm. ESIMS: *m*/*z* = 524.0/526.0 $[M + H]^+$. FAB+: *m*/*z* =

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524/526 [M + H]$^+$. HRMS: calcd. for $C_{23}H_{31}BrNO_4SSi$ 524.0926; found 524.0922.

Methyl 2-{[*N*-(2-Bromobenzyl)-2′-(trimethylsilyl)ethylsulfonamido]-(3,5-dimethylphenyl)methyl}acrylate (2b): Alkylation of the β-amino ester **1b** with 2-bromobenzyl bromide yielded 151 mg (91%) of the title compound as a white solid after silica gel chromatography (Et_2O/cyclohexane, 1:9). M.p. 100.1–101.5 °C. IR: $\tilde{\nu}$ = 3054 (m), 2954 (m), 1722 (s), 1265 (s) cm^{-1}. ^{1}H NMR ($CDCl_3$, Me_4Si): δ = –0.05 (s, 9 H), 0.90–1.10 (m, 2 H), 2.28 (s, 6 H), 2.60–2.85 (m, 2 H), 3.59 (s, 3 H), 4.68 (d, J_2 = 16.9 Hz, 1 H), 4.77 (d, J_2 = 16.9 Hz, 1 H), 5.89 (d, J_2 = 1.4 Hz, 1 H), 6.09 (s, 1 H), 6.44 (s, 1 H), 6.78 (s, 1 H), 6.90 (s, 2 H), 7.04 (dt, J_2 = 1.6, J_3 = 7.6 Hz, 1 H), 7.15 (dt, J_2 = 1.1, J_3 = 7.6 Hz, 1 H), 7.30–7.45 (m, 2 H) ppm. ^{13}C NMR ($CDCl_3$, Me_4Si): δ = –2.0, 10.4, 21.4, 50.1, 50.4, 52.2, 61.8, 122.4, 126.6, 126.9, 128.5, 129.9, 130.3, 132.1, 136.5, 136.8, 138.2, 139.3, 166.2 ppm. ESIMS: *m*/*z* = 552.0/553.9 [M + H]$^+$, 574.0/576 [M + Na]$^+$. FAB+: *m*/*z* = 552/554 [M + H]$^+$. HRMS: calcd. for $C_{25}H_{35}BrNO_4SSi$ 552.1239; found 552.1216.

Methyl 2-{[*N*-(2-Bromobenzyl)-2′-(trimethylsilyl)ethylsulfonamido]-(3-fluorophenyl)methyl}acrylate (2c): Alkylation of the β-amino ester **1c** with 2-bromobenzyl bromide yielded 128 mg (79%) of the title compound as a white solid after silica gel chromatography (Et_2O/cyclohexane, 1:9). M.p. 78.6–79.4 °C. IR: $\tilde{\nu}$ = 3064 (m), 2954 (m), 1722 (s), 1251 (s) cm^{-1}. ^{1}H NMR ($CDCl_3$, Me_4Si): δ = –0.03 (s, 9 H), 0.90–1.10 (m, 2 H), 2.60–2.90 (m, 2 H), 3.62 (s, 3 H), 4.72 (d, J_2 = 17.2 Hz, 1 H), 4.78 (d, J_2 = 17.2 Hz, 1 H), 5.89 (d, J_2 = 1.4 Hz, 1 H), 6.14 (s, 1 H), 6.49 (d, J_2 = 0.6 Hz, 1 H), 6.90 (dt, J_2 = 1.8, J_3 = 8.4 Hz, 1 H), 6.95–7.30 (m, 5 H), 7.41 (dd, J_3 = 1.0, J_4 = 8.0 Hz, 2 H) ppm. ^{13}C NMR ($CDCl_3$, Me_4Si): δ = –1.9, 10.4, 50.7, 50.8, 52.3, 61.67 (d, J_4 = 1.9 Hz), 115.2 (d, J_2 = 21.2 Hz), 115.9 (d, J_2 = 22.3 Hz), 122.8, 124.4 (d, J_4 = 2.9 Hz), 127.3, 129.0, 129.9, 130.3 (d, J_3 = 8.2 Hz), 130.4, 132.6, 136.2, 138.6, 140.1 (d, J_3 = 6.8 Hz), 162.8 (d, J_1 = 247.2 Hz), 166.1 ppm. ESIMS: *m*/*z* = 541.9/543.9 [M + H]$^+$. FAB+: *m*/*z* = 542/544 [M + H]$^+$. HRMS: calcd. for $C_{23}H_{30}BrFNO_4SSi$ 542.0832; found 542.0817.

Methyl 2-{[*N*-(2-Bromobenzyl)-2′-(trimethylsilyl)ethylsulfonamido]-[4-(methoxycarbonyl)phenyl]methyl}acrylate (2d): Alkylation of the β-amino ester **1d** with 2-bromobenzyl bromide yielded 125 mg (72%) of the title compound as a white solid after silica gel chromatography (Et_2O/cyclohexane, 2:8). M.p. 44.5–46.1 °C. IR: $\tilde{\nu}$ = 3066 (m), 2954 (m), 1721 (s), 1284 (s), 1251 (s) cm^{-1}. ^{1}H NMR ($CDCl_3$, Me_4Si): δ = –0.06 (s, 9 H), 0.90–1.05 (m, 2 H), 2.55–2.85 (m, 2 H), 3.59 (s, 3 H), 3.86 (s, 3 H), 4.71 (d, J_2 = 16.7 Hz, 1 H), 4.78 (d, J_2 = 16.7 Hz, 1 H), 5.84 (d, J_2 = 1.4 Hz, 1 H), 6.16 (s, 1 H), 6.48 (d, J_2 = 0.6 Hz, 1 H), 7.00 (dt, J_2 = 1.7, J_3 = 7.6 Hz, 1 H), 7.15 (dt, J_2 = 1.2, J_3 = 7.6 Hz, 1 H), 7.35–7.45 (m, 4 H), 7.91 (dd, J_3 = 1.7, J_4 = 6.7 Hz, 2 H) ppm. ^{13}C NMR ($CDCl_3$, Me_4Si): δ = –2.0, 10.3, 50.7, 50.8, 52.21, 52.25, 61.9, 122.8, 127.2, 128.7, 129.0, 129.81, 129.83, 130.1, 130.3, 132.6, 136.0, 138.5, 142.7, 166.0, 166.50 ppm. ESIMS: *m*/*z* = 581.9/583.9 [M + H]$^+$, 603.9/605.9 [M + Na]$^+$. FAB+: *m*/*z* = 582/584 [M + H]$^+$. HRMS: calcd. for $C_{25}H_{33}BrNO_6SSi$ 582.0981; found 582.0936.

Methyl 2-{[*N*-(2-Bromobenzyl)-2′-(trimethylsilyl)ethylsulfonamido]-(benzo[*d*][1,3]dioxol-4-yl)methyl}acrylate (2e): Alkylation of the β-amino ester **1e** with 2-bromobenzyl bromide yielded 152 mg (89%) of the title compound as a white solid after silica gel chromatography (Et_2O/cyclohexane, 2:8). M.p. 79.7–80.9 °C. IR: $\tilde{\nu}$ = 3068 (m), 2953 (m), 1723 (s), 1251 (s) cm^{-1}. ^{1}H NMR ($CDCl_3$, Me_4Si): δ = –0.03 (s, 9 H), 0.95–1.15 (m, 2 H), 2.70–2.85 (m, 2 H), 3.60 (s, 3 H), 4.70 (d, J_2 = 17.1 Hz, 1 H), 4.85 (d, J_2 = 17.1 Hz, 1 H), 5.91 (d, J_2 = 1.3 Hz, 1 H), 5.95 (m, 2 H), 6.24 (s, 1 H), 6.43 (d, J_2 = 1.0 Hz, 1 H), 6.66 (dd, J_4 = 1.5, J_3 = 7.5 Hz, 1 H), 6,74 (dd, J_3 = 7.5, J_3 = 7.9 Hz, 1 H), 6.80 (dd, J_4 = 1.5, J_3 = 7.9 Hz, 1 H), 7.00 (dt, J_4 = 1.6, J_3 = 7.7 Hz, 1 H), 7.15 (dt, J_4 = 1.2, J_3 = 7.6 Hz, 1 H), 7.35–7.45 (m, 2 H) ppm. ^{13}C NMR ($CDCl_3$, Me_4Si): δ = –1.9, 10.3, 50.3, 50.6, 52.2, 57.4, 101.1, 108.8, 119.5, 121.8, 122.1, 122.5, 127.0, 128.7, 129.8, 132.4, 136.5, 138.1, 145.4, 147.5, 166.0 ppm. ESIMS: *m*/*z* = 567.9/569.9 [M + H]$^+$. FAB+: *m*/*z* = 567/569 [M – e$^-$]$^+$, 568/570 [M + H]$^+$. HRMS: calcd. for $C_{24}H_{30}BrNO_6SSi$ 567.0746; found 567.0776.

Methyl 2-([*N*-(2-Bromobenzyl)-2′-(trimethylsilyl)ethylsulfonamido]-{4-[2-(trimethylsilyl)ethynyl]phenyl}methyl)acrylate (2f): Alkylation of the β-amino ester **1f** with 2-bromobenzyl bromide yielded 116 mg (62%) of the title compound as a white solid after silica gel chromatography (Et_2O/cyclohexane, 1:9). M.p. 47.6–49.1 °C. IR: $\tilde{\nu}$ = 3065 (m), 2955 (m), 2158 (m), 1723 (s), 1250 (s) cm^{-1}. ^{1}H NMR ($CDCl_3$, Me_4Si): δ = –0.04 (s, 9 H), 0.23 (s, 9 H), 0.90–1.10 (m, 2 H), 2.55–2.80 (m, 2 H), 3.59 (s, 3 H), 4.73 (s, 2 H), 5.84 (d, J_2 = 1.4 Hz, 1 H), 6.10 (s, 1 H), 6.46 (d, J_2 = 0.7 Hz, 1 H), 7.04 (dt, J_2 = 1.7, J_3 = 7.6 Hz, 1 H), 7.18 (dt, J_2 = 1.2, J_3 = 7.6 Hz, 1 H), 7.26 (d, J_3 = 8.6 Hz, 2 H), 7.37 (d, J_3 = 8.4 Hz, 2 H), 7.35–7.50 (m, 2 H) ppm. ^{13}C NMR ($CDCl_3$, Me_4Si): δ = –1.9, 0.1, 10.4, 50.7, 50.8, 52.3, 62.1, 95.2, 104.5, 122.9, 123.2, 127.3, 128.7, 129.0, 129.8, 130.4, 132.2, 132.7, 136.2, 137.8, 138.8, 166.2 ppm. ESIMS: *m*/*z* = 620.0/622.0 [M + H]$^+$. FAB+: *m*/*z* = 620/622 [M + H]$^+$, 642/644 [M + Na]$^+$.

Methyl 2-{[*N*-(2-Bromo-5-methoxybenzyl)-2′-(trimethylsilyl)ethylsulfonamido](phenyl)methyl}acrylate (2g): Alkylation of the β-amino ester **1a** with 2-bromo-5-methoxybenzyl bromide yielded 127 mg (76%) of the title compound as a white solid after silica gel chromatography (Et_2O/cyclohexane, 2:8). M.p. 119.5–121.7 °C. IR: $\tilde{\nu}$ = 3065 (m), 2953 (m), 1723 (s), 1292 (s), 1251 (s) cm^{-1}. ^{1}H NMR ($CDCl_3$, Me_4Si): δ = –0.07 (s, 9 H), 0.90–1.15 (m, 2 H), 2.50–2.80 (m, 2 H), 3.60 (s, 3 H), 3.74 (s, 3 H), 4.73 (s, 2 H), 5.86 (d, J_2 = 1.4 Hz, 1 H), 6.17 (s, 1 H), 6.43 (s, 1 H), 6.60 (dd, J_2 = 3.1, J_3 = 8.7 Hz, 1 H), 6.96 (d, J_2 = 3.0 Hz, 1 H), 7.20–7.40 (m, 6 H) ppm. ^{13}C NMR ($CDCl_3$, Me_4Si): δ = –2.0, 10.3, 50.4, 50.6, 52.2, 55.5, 62.1, 112.9, 115.2, 115.5, 128.3, 128.7, 128.8, 129.7, 133.0, 137.4, 137.7, 139.2, 158.9, 166.3 ppm. ESIMS: *m*/*z* = 553.9/555.9 [M + H]$^+$, 576.0/557.9 [M + Na]$^+$. FAB+: *m*/*z* = 554/556 [M + H]$^+$. HRMS: calcd. for $C_{24}H_{33}BrNO_5SSi$ 554.1032; found 554.1064.

Methyl 2-{[*N*-(2-Bromo-5-fluorobenzyl)-2′-(trimethylsilyl)ethylsulfonamido](phenyl)methyl}acrylate (2h): Alkylation of the β-amino ester **1a** with 2-bromo-5-fluorobenzyl bromide yielded 121 mg (74%) of the title compound as a white solid after silica gel chromatography (Et_2O/cyclohexane, 2:8). M.p. 86.1–86.9 °C. IR: $\tilde{\nu}$ = 3064 (m), 2954 (m), 1724 (s), 1252 (s) cm^{-1}. ^{1}H NMR ($CDCl_3$, Me_4Si): δ = –0.04 (s, 9 H), 0.90–1.10 (m, 2 H), 2.55–2.90 (m, 2 H), 3.65 (s, 3 H), 4.73 (s, 2 H), 5.82 (d, J_2 = 1.5 Hz, 1 H), 6.21 (s, 1 H), 6.45 (d, 1 = H, J = 0.8 Hz), 6.75 (dt, J_2 = 3.1, J_3 = 8.2 Hz, 1 H), 7.12 (dd, J_2 = 3.0, J_3 = 9.8 Hz, 1 H), 7.15–7.40 (m, 6 H) ppm. ^{13}C NMR ($CDCl_3$, Me_4Si): δ = –1.9, 10.3, 50.4, 52.3, 61.9, 115.9 (d, J_2 = 22.9 Hz), 116.2 (d, J_4 = 3.1 Hz), 117.1 (d, J_2 = 24.7 Hz), 128.5, 128.6, 128.9, 129.5, 133.5 (d, J_3 = 7.9 Hz), 137.3, 139.1 (d, J_3 = 7.2 Hz), 139.2, 162.0 (d, J_1 = 247.0 Hz), 166.1 ppm. ESIMS: *m*/*z* = 541.9/544.0 [M + H]$^+$, 563.9/565.9 [M + Na]$^+$. FAB+: *m*/*z* = 542/544 [M + H]$^+$. HRMS: calcd. for $C_{23}H_{30}BrFNO_4SSi$ 542.0832; found 542.0818.

General Protocol for the Heck Reaction with PEG as Solvent: A mixture (220 mg) of $Pd(OAc)_2$/PEG 3400-OH (1 mg/1 g) [corresponding to 0.001 mmol $Pd(OAc)_2$, 0.01 equiv.] and finely powdered K_2CO_3 (41 mg, 0.3 mmol, 3 equiv.) was added to *N*-(2-bromobenzyl)-β-amino ester **2** (0.1 mmol, 1 equiv.). The reaction mix-

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ture was heated under microwave irradiation at 100 °C (initial power 300 W) for 30 min, cooled, dissolved in CH_2Cl_2, precipitated with diethyl ether, filtered and the solvents were evaporated. Silica gel chromatography (Et_2O/cyclohexane) yielded the corresponding benzazepine **3**.

Methyl 3-Phenyl-2-[2-(trimethylsilyl)ethylsulfonyl]-2,3-dihydro-1*H*-benzo[*c*]azepine-4-carboxylate (3a): Heck reaction of the *N*-(2-bromobenzyl)-β-amino ester **2a** according to the general procedure yielded 42 mg (95%) of the title compound as a white solid after silica gel chromatography (Et_2O/cyclohexane, 1:9). M.p. 83.3–85.1 °C. IR: $\tilde{\nu}$ = 3064 (m), 2953 (m), 1712 (s), 1250 (s) cm^{-1}. ^1H NMR ($CDCl_3$, Me_4Si): δ = –0.22 (s, 9 H), 0.60–0.85 (m, 2 H), 2.25–2.60 (m, 2 H), 3.68 (s, 3 H), 4.12 (d, J_2 = 17.0 Hz, 1 H), 4.43 (dd, J_2 = 17.0, J_4 = 1.5 Hz, 1 H), 6.42 (s, 1 H), 7.20–7.45 (m, 8 H), 7.50–7.60 (m, 1 H), 8.00 (s, 1 H) ppm. ^{13}C NMR ($CDCl_3$, Me_4Si): δ = –2.1, 9.9, 47.5, 50.1, 52.7, 61.7, 128.2, 128.3, 128.78, 128.81, 130.4, 132.21, 132.24, 135.3, 140.6, 140.8, 141.0, 167.4 ppm. ESIMS: *m*/*z* = 444.0 $[M + H]^+$, 466.0 $[M + Na]^+$. FAB+: *m*/*z* = 444 $[M + H]^+$. HRMS: calcd. for $C_{23}H_{30}NO_4SSi$ 444.1665; found 444.1703.

Methyl 3-(3,5-Dimethylphenyl)-2-[2-(trimethylsilyl)ethylsulfonyl]-2,3-dihydro-1*H*-benzo[*c*]azepine-4-carboxylate (3b): Heck reaction of the *N*-(2-bromobenzyl)-β-amino ester **2b** according to the general procedure yielded 45 mg (98%) of the title compound as a white solid after silica gel chromatography (Et_2O/cyclohexane, 1:9). M.p. 81.9–83.6 °C. IR: $\tilde{\nu}$ = 3066 (m), 2953 (m), 1710 (s), 1252 (s) cm^{-1}. ^1H NMR ($CDCl_3$, Me_4Si): δ = –0.21 (s, 9 H), 0.65–0.85 (m, 2 H), 2.29 (s, 6 H), 2.25–2.60 (m, 2 H), 3.70 (s, 3 H), 4.16 (d, J_2 = 17.0 Hz, 1 H), 4.42 (dd, J_2 = 17.1, J_4 = 1.5 Hz, 1 H), 6.35 (s, 1 H), 6.92 (s, 1 H), 6.96 (s, 2 H), 7.20–7.30 (m, 1 H), 7.30–7.45 (m, 2 H), 7.50–7.60 (m, 1 H), 7.98 (s, 1 H) ppm. ^{13}C NMR ($CDCl_3$, Me_4Si): δ = –2.1, 9.9, 21.5, 47.6, 50.1, 52.7, 61.0, 126.6, 128.3, 128.8, 130.0, 130.3, 132.3, 132.5, 135.4, 138.3, 140.6, 140.77, 140.82, 167.6 ppm. ESIMS: *m*/*z* = 472.0 $[M + H]^+$, 494.0 $[M + Na]^+$. FAB+: *m*/*z* = 472 $[M + H]^+$. HRMS: calcd. for $C_{25}H_{34}NO_4SSi$ 472.1978; found 472.2005.

Methyl 3-(3-Fluorophenyl)-2-[2-(trimethylsilyl)ethylsulfonyl]-2,3-dihydro-1*H*-benzo[*c*]azepine-4-carboxylate (3c): Heck reaction of the *N*-(2-bromobenzyl)-β-amino ester **2c** according to the general procedure yielded 42 mg (91%) of the title compound as a white solid after silica gel chromatography (Et_2O/cyclohexane, 1:9). M.p. 81.5–82.8 °C. IR: $\tilde{\nu}$ = 3055 (m), 2954 (m), 1710 (s), 1252 (s) cm^{-1}. ^1H NMR ($CDCl_3$, Me_4Si): δ = –0.22 (s, 9 H), 0.60–0.80 (m, 2 H), 2.25–2.55 (m, 2 H), 3.70 (s, 3 H), 4.11 (d, J_2 = 17.0 Hz, 1 H), 4.46 (dd, J_2 = 17.1, J_4 = 1.6 Hz, 1 H), 6.39 (s, 1 H), 6.95–7.05 (m, 1 H), 7.05–7.45 (m, 6 H), 7.50–7.60 (m, 1 H), 8.01 (s, 1 H) ppm. ^{13}C NMR ($CDCl_3$, Me_4Si): δ = –2.2, 9.9, 47.5, 50.2, 52.7, 60.7 (d, J_4 = 1.7 Hz), 115.2 (d, J_2 = 21.1 Hz), 115.8 (d, J_2 = 22.1 Hz), 124.42 (d, J_4 = 2.9 Hz), 128.48, 128.9, 130.3 (d, J_3 = 8.2 Hz), 130.6, 131.6, 132.1, 135.4, 140.4, 141.2, 143.6 (d, J_3 = 6.7 Hz), 163.0 (d, J_1 = 247.2 Hz), 167.2 ppm. ESIMS: *m*/*z* = 462.0 $[M + H]^+$, 484.0 $[M + Na]^+$. FAB+: *m*/*z* = 462 $[M + H]^+$. HRMS: calcd. for $C_{23}H_{29}FNO_4SSi$ 462.1571; found 462.1544.

Methyl 3-[4-(Methoxycarbonyl)phenyl]-2-[2-(trimethylsilyl)ethylsulfonyl]-2,3-dihydro-1*H*-benzo[*c*]azepine-4-carboxylate (3d): Heck reaction of the *N*-(2-bromobenzyl)-β-amino ester **2d** according to the general procedure yielded 41 mg (82%) of the title compound as a white solid after silica gel chromatography (Et_2O/cyclohexane, 2:8). M.p. 114.6–116.8 °C. IR: $\tilde{\nu}$ = 3065 (m), 2954 (m), 1719 (s), 1285 (s), 1250 (s) cm^{-1}. ^1H NMR ($CDCl_3$, Me_4Si): δ = –0.22 (s, 9 H), 0.60–0.85 (m, 2 H), 2.25–2.55 (m, 2 H), 3.68 (s, 3 H), 3.90 (s, 3 H), 4.06 (d, J_2 = 16.9 Hz, 1 H), 4.43 (dd, J_2 = 17.1, J_4 = 1.3 Hz, 1 H), 6.44 (s, 1 H), 7.20–7.60 (m, 6 H), 8.01 (s, 1 H), 8.03 (s, 2 H) ppm. ^{13}C NMR ($CDCl_3$, Me_4Si): δ = –2.1, 9.9, 47.6, 50.2, 52.3, 52.8, 60.9, 128.5, 128.8, 128.9, 130.0, 130.1, 130.6, 131.5, 132.1, 135.4, 140.3, 141.4, 146.00, 166.8 167.2 ppm. ESIMS: *m*/*z* = 502.0 $[M + H]^+$, 524.0 $[M + Na]^+$. FAB+: *m*/*z* = 502 $[M + H]^+$. HRMS: calcd. for $C_{25}H_{32}NO_6SSi$ 502.1720; found 502.1722.

Methyl 3-(Benzo[*d*][1,3]dioxol-4-yl)-2-[2-(trimethylsilyl)ethylsulfonyl]-2,3-dihydro-1*H*-benzo[*c*]azepine-4-carboxylate (3e): Heck reaction of the *N*-(2-bromobenzyl)-β-amino ester **2e** according to the general procedure yielded 25 mg (51%) of the title compound as a white solid after silica gel chromatography (Et_2O/cyclohexane, 2:8). M.p. 111.8–113.0 °C. IR: $\tilde{\nu}$ = 3055 (m), 2954 (m), 1708 (s), 1271 (s), 1252 (s) cm^{-1}. ^1H NMR ($CDCl_3$, Me_4Si): δ = –0.16 (s, 9 H), 0.70–0.85 (m, 2 H), 2.40–2.70 (m, 2 H), 3.71 (s, 3 H), 4.34 (d, J_2 = 17.1 Hz, 1 H), 4.49 (dd, J_2 = 17.1, J_4 = 1.5 Hz, 1 H), 5.96 (d, J_2 = 1.3 Hz, 1 H), 5.98 (d, J_2 = 1.3 Hz, 1 H), 6.43 (s, 1 H), 6.70–6.85 (m, 3 H), 7.20–7.30 (m, 1 H), 7.30–7.45 (m, 2 H), 7.50–7.60 (m, 1 H), 7.95 (s, 1 H) ppm. ^{13}C NMR ($CDCl_3$, Me_4Si): δ = –2.0, 10.0, 48.5, 50.0, 52.6, 57.0, 101.3, 108.8, 121.8, 122.3, 122.6, 128.2, 128.6, 130.3, 131.9, 132.1, 135.6, 140.6, 141.0, 145.3, 148.1, 167.1 ppm. ESIMS: *m*/*z* = 488.0 $[M + H]^+$, 510.0 $[M + Na]^+$. FAB+: *m*/*z* = 487 $[M - e^-]^+$, 488 $[M + H]^+$. HRMS: calcd. for $C_{24}H_{29}NO_6SSi$ 487.1485; found 487.1480.

Methyl 3-{4-[2-(Trimethylsilyl)ethynyl]phenyl}-2-[2-(trimethylsilyl)-ethylsulfonyl]-2,3-dihydro-1*H*-benzo[*c*]azepine-4-carboxylate (3f): Heck reaction of the *N*-(2-bromobenzyl)-β-amino ester **2f** according to the general procedure yielded 20 mg (37%) of the title compound as a white solid after silica gel chromatography (Et_2O/cyclohexane, 1:9). M.p. 59.3–60.7 °C. IR: $\tilde{\nu}$ = 3056 (m), 2956 (m), 2158 (m), 1711 (s), 1250 (s) cm^{-1}. ^1H NMR ($CDCl_3$, Me_4Si): δ = –0.22 (s, 9 H), 0.24 (s, 9 H), 0.60–0.80 (m, 2 H), 2.25–2.55 (m, 2 H), 3.67 (s, 3 H), 4.06 (d, J_2 = 17.0 Hz, 1 H), 4.42 (dd, J_2 = 17.0, J_4 = 1.4 Hz, 1 H), 6.37 (s, 1 H), 7.20–7.60 (m, 8 H), 8.00 (s, 1 H) ppm. ^{13}C NMR ($CDCl_3$, Me_4Si): δ = –2.1, 0.1, 9.9, 47.5, 50.2, 52.7, 60.9, 95.2, 104.6, 123.0, 128.5, 128.7, 128.9, 130.5, 131.7, 132.2, 132.4, 135.4, 140.4, 141.2, 141.4, 167.3 ppm. ESIMS: *m*/*z* = 540.0 $[M + H]^+$, 562.1 $[M + Na]^+$. FAB+: *m*/*z* = 540 $[M + H]^+$. HRMS: calcd. for $C_{28}H_{38}NO_4SSi_2$ 540.2060; found 540.2076.

Methyl 8-Methoxy-3-phenyl-2-[2-(trimethylsilyl)ethylsulfonyl]-2,3-dihydro-1*H*-benzo[*c*]azepine-4-carboxylate (3g): Heck reaction of the *N*-(2-bromobenzyl)-β-amino ester **2g** according to the general procedure yielded 40 mg (83%) of the title compound as a white solid after silica gel chromatography (Et_2O/cyclohexane, 2:8). M.p. 46.4–47.7 °C. IR: $\tilde{\nu}$ = 3054 (m), 2954 (m), 1706 (s), 1268 (s), 1262 (s) cm^{-1}. ^1H NMR ($CDCl_3$, Me_4Si): δ = –0.19 (s, 9 H), 0.65–1.85 (m, 2 H), 2.35–2.65 (m, 2 H), 3.67 (s, 3 H), 3.82 (s, 3 H), 4.08 (d, J_2 = 16.9 Hz, 1 H), 4.38 (dd, J_2 = 17.2, J_4 = 1.6 Hz, 1 H), 6.40 (s, 1 H), 6.74 (d, J_4 = 2.6 Hz, 1 H), 6.87 (dd, J_3 = 8.5, J_4 = 2.6 Hz, 1 H), 7.25–7.45 (m, 5 H), 7.47 (d, J_3 = 8.6 Hz, 1 H), 7.96 (s, 1 H) ppm. ^{13}C NMR ($CDCl_3$, Me_4Si): δ = –2.1, 10.0, 47.6, 50.1, 52.5, 55.6, 61.0, 113.2, 114.5, 125.0, 128.1, 128.7, 128.8, 137.4, 140.7, 141.0, 142.6, 161.2, 167.7 ppm. ESIMS: *m*/*z* = 474.0 $[M + H]^+$. FAB+: *m*/*z* = 474 $[M + H]^+$. HRMS: calcd. for $C_{24}H_{32}NO_5SSi$ 474.1770; found 474.1767.

Methyl 8-Fluoro-3-phenyl-2-[2-(trimethylsilyl)ethylsulfonyl]-2,3-dihydro-1*H*-benzo[*c*]azepine-4-carboxylate (3h): Heck reaction of the *N*-(2-bromobenzyl)-β-amino ester **2h** according to the general procedure yielded 35 mg (76%) of the title compound as a white solid after silica gel chromatography (Et_2O/cyclohexane, 1:9). M.p. 45.3–46.6 °C. IR: $\tilde{\nu}$ = 3053 (m), 2955 (m), 1710 (s), 1252 (s) cm^{-1}. ^1H NMR ($CDCl_3$, Me_4Si): δ = –0.17 (s, 9 H), 0.65–0.90 (m, 2 H), 2.35–2.65 (m, 2 H), 3.68 (s, 3 H), 4.09 (d, J_2 = 17.2 Hz, 1 H), 4.40 (dd, J_2 = 17.2, J_4 = 1.6 Hz, 1 H), 6.40 (s, 1 H), 6.95 (dd, J_3 = 8.7, J_4 =

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2.6 Hz, 1 H), 7.06 (dt, J_3 = 8.2, J_4 = 2.6 Hz, 1 H), 7.25–7.40 (m, 5 H), 7.51 (dd, J_3 = 8.6, J_4 = 5.6 Hz, 1 H), 7.96 (s, 1 H) ppm. ^{13}C NMR ($CDCl_3$, Me_4Si): δ = –2.1, 10.0, 47.3, 50.2, 52.7, 61.2, 115.2 (d, J_2 = 21.4 Hz), 116.0 (d, J_2 = 22.3 Hz), 128.3, 128.6 (d, J_4 = 3.5 Hz), 128.8, 128.9, 131.4 (d, J_6 = 3.0 Hz), 137.5 (d, J_3 = 8.8 Hz), 139.7, 140.6, 143.6 (d, J_3 = 7.5 Hz), 163.4 (d, J_1 = 254.9 Hz), 167.3 ppm. ESIMS: *m*/*z* = 462.0 $[M + H]^+$, 484.0 $[M + Na]^+$. FAB+: *m*/*z* = 462 $[M + H]^+$. HRMS: calcd. for $C_{23}H_{29}FNO_4SSi$ 462.1571; found 462.1562.

General Protocol for the SES Deprotection with HF: Benzazepine **3** (0.05 mmol) was treated with 1 mL of anhydrous HF in a Teflon vessel at 0 °C for 1 h. Unreacted HF was then removed by distillation. The residue was dissolved in methanol and and the mixture concentrated to give the HF·benzazepine salt **8**.

Methyl 3-Phenyl-2,3-dihydro-1*H*-benzo[*c*]azepine-4-carboxylate Hydrofluoride (8a): Deprotection of the benzazepine **3a** according to the general procedure yielded 14.6 mg (98%) of the title compound as a white solid. M.p. 195.4–197.9 °C (decomposed). ^{1}H NMR (CD_3OD, Me_4Si): δ = 3.67 (s, 3 H), 4.31 (d, J_2 = 15.7 Hz, 1 H), 4.41 (d, J_2 = 15.7 Hz, 1 H), 6.01 (s, 1 H), 7.35–7.60 (m, 8 H), 7.72 (d, J_3 = 7.0 Hz, 1 H), 8.15 (s, 1 H) ppm. ^{13}C NMR (CD_3OD, Me_4Si): δ = 48.0, 53.0, 63.0, 129.1, 130.4, 130.5, 130.9, 131.9, 133.0, 135.6, 136.1, 136.3, 141.6, 167.5 ppm. ESIMS: *m*/*z* = 280.1 $[M – F]^+$. FAB+: *m*/*z* = 280 $[M – F]^+$. HRMS: calcd. for $C_{18}H_{18}NO_2$ 280.1338; found 280.1337.

Methyl 3-(3,5-Dimethylphenyl)-2,3-dihydro-1*H*-benzo[*c*]azepine-4-carboxylate Hydrofluoride (8b): Deprotection of the benzazepine **3b** according to the general procedure yielded 16.2 mg (99%) of the title compound as a white solid. M.p. 192.9–194.6 °C (decomposed). ^{1}H NMR (CD_3OD, Me_4Si): δ = 2.32 (s, 6 H), 3.71 (s, 3 H), 4.32 (d, J_2 = 15.7 Hz, 1 H), 4.39 (d, J_2 = 15.7 Hz, 1 H), 6.02 (s, 1 H), 7.08 (s, 2 H), 7.11 (s, 1 H), 7.40–7.65 (m, 3 H), 7.74 (d, J_3 = 7.3 Hz, 1 H), 8.15 (s, 1 H) ppm. ^{13}C NMR (CD_3OD, Me_4Si): δ = 21.3, 47.9, 53.1, 63.1, 128.0, 128.9, 130.6, 130.9, 131.9, 132.5, 133.0, 135.2, 135.9, 136.1, 140.4, 141.4, 167.5 ppm. ESIMS: *m*/*z* = 308.3 $[M – F]^+$. FAB+: *m*/*z* = 308 $[M – F]^+$. HRMS: calcd. for $C_{20}H_{22}NO_2$ 308.1651; found 308.1654.

Methyl 3-(3-Fluorophenyl)-2,3-dihydro-1*H*-benzo[*c*]azepine-4-carboxylate Hydrofluoride (8c): Deprotection of the benzazepine **3c** according to the general procedure yielded 15.7 mg (99%) of the title compound as a white solid. M.p. 193.6–195.2 °C (decomposed). ^{1}H NMR (CD_3OD, Me_4Si): δ = 3.72 (s, 3 H), 4.36 (d, J_2 = 15.7 Hz, 1 H), 4.45 (d, J_2 = 15.7 Hz, 1 H), 6.12 (s, 1 H), 7.15–7.40 (m, 3 H), 7.40–7.65 (s, 4 H), 7.75 (d, J_3 = 7.3 Hz, 1 H), 8.19 (s, 1 H) ppm. ^{13}C NMR (CD_3OD, Me_4Si): δ = 48.4, 53.1, 62.6, 117.3 (d, J_2 = 22.9 Hz), 117.7 (d, J_2 = 21.3 Hz), 126.4 (d, J_4 = 2.9 Hz), 128.8, 130.6, 130.9, 132.0, 132.3 (d, J_3 = 8.3 Hz), 132.9, 135.7, 136.1, 139.0 (d, J_3 = 7.3 Hz), 142.0, 164.4 (d, J_1 = 246.9 Hz), 167.3 ppm. ESIMS: *m*/*z* = 298.1 $[M – F]^+$. FAB+: *m*/*z* = 298 $[M – F]^+$. HRMS: calcd. for $C_{18}H_{17}FNO_2$ 298.1243; found 298.1237.

Methyl 8-Methoxy-3-phenyl-2,3-dihydro-1*H*-benzo[*c*]azepine-4-carboxylate Hydrofluoride (8g): Deprotection of the benzazepine **3g** according to the general procedure yielded 16.5 mg (100%) of the title compound as a white solid. M.p. 194.8–196.4 °C (decomposed). ^{1}H NMR (CD_3OD, Me_4Si): δ = 3.66 (s, 3 H), 3.86 (s, 3 H), 4.16 (d, J_2 = 15.9 Hz, 1 H), 4.24 (d, J_2 = 15.9 Hz, 1 H), 5.94 (s, 1 H), 6.97 (d, J_4 = 2.5 Hz, 1 H), 7.06 (dd, J_3 = 8.6, J_4 = 2.6 Hz, 1 H), 7.35–7.50 (m, 5 H), 7.64 (d, J_3 = 8.6 Hz, 1 H), 8.08 (s, 1 H) ppm. ^{13}C NMR (CD_3OD, Me_4Si): δ = 47.8, 52.9, 56.2, 63.0, 115.4, 116.4, 125.4, 125.9, 130.37, 130.41, 130.8, 136.8, 137.9, 138.6, 141.6, 163.1, 167.8 ppm. ESIMS: *m*/*z* = 310.2 $[M – F]^+$. FAB+: *m*/*z* = 310 $[M – F]^+$. HRMS: $C_{19}H_{20}NO_3$ 310.1443; found 310.1443.

Methyl 8-Fluoro-3-phenyl-2,3-dihydro-1*H*-benzo[*c*]azepine-4-carboxylate Hydrofluoride (8h): Deprotection of the benzazepine **3h** according to the general procedure yielded 15.7 mg (99%) of the title compound as a white solid. M.p. 194.8–196.5 °C (decomposed). IR: $\tilde{\nu}$ = 3053 (m), 2955 (m), 1710 (s), 1252 (s) cm^{-1}. ^{1}H NMR (CD_3OD, Me_4Si): δ = 3.66 (s, 3 H), 4.26 (d, J_2 = 15.9 Hz, 1 H), 4.35 (d, J_2 = 15.9 Hz, 1 H), 6.04 (s, 1 H), 7.23 (dd, J_4 = 9.1, J_5 = 2.6 Hz, 1 H), 7.28 (dd, J_3 = 8.5, J_4 = 2.7 Hz, 1 H), 7.40–7.50 (m, 5 H), 7.76 (dd, J_4 = 8.5, J_5 = 5.6 Hz, 1 H), 8.11 (s, 1 H) ppm. ^{13}C NMR (CD_3OD, Me_4Si): δ = 47.6, 53.0, 63.2, 117.2 (d, J_2 = 21.7 Hz), 117.9 (d, J_2 = 23.6 Hz), 128.6 (d, J_3 = 2.4 Hz), 129.6 (d, J_3 = 3.3 Hz), 130.39, 130.44, 130.8, 136.4, 138.6 (d, J_4 = 8.8 Hz), 138.8, 140.9, 164.8 (d, J_1 = 252.5 Hz), 167.5 ppm. ESIMS: *m*/*z* = 298.2 $[M – F]^+$. FAB+: *m*/*z* = 298 $[M + H]^+$. HRMS: calcd. for $C_{18}H_{17}FNO_2$ 298.1243; found 298.1242.

X-ray Analysis: Data for compound **3a** were collected with an XCALIBUR-2 4-circle CCD diffractometer with graphite-monochromated Mo-K_α radiation. The structure was solved by direct methods and expanded using Fourier techniques. The non-hydrogen atoms were refined anisotropically. The hydrogen atoms involved in hydrogen bonding were located in electron density maps. The remainder of the hydrogen atoms were placed in idealised positions and allowed to ride on the C atoms to which they are bonded. Crystal data: M_r = 443.62; 0.25 × 0.35 × 0.50 mm; colourless block; T = 170 K, monoclinic; space group $P2_1/n$; Z = 4; a = 11.9397(8), b = 14.6956(8), c = 13.5913(9) Å; β = 106.004(7)°; V = 2292.3(2) Å^3; $\rho_{calcd.}$ = 1.285 g cm^{-3}; θ_{max} = 33.25°; R_1 = 4.74%. CCDC-616640 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

Supporting Information (see footnote on the first page of this article): ^{1}H and ^{13}C NMR spectra for all new compounds.

Acknowledgments

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