Synthesis of Nitrogen-Containing Spiro Compounds from Lactams by Allylboration and Subsequent Ring-Closing Metathesis

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A series of nitrogen-containing spiro[4.*n*]alkenes was prepared with excellent yields starting from lactams in two steps: allylboration on the carbonyl carbon and subsequent ring-closing metathesis of the 2,2-diallyl N-heterocycles.

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Introduction

Many natural and biologically active compounds contain ring systems connected with each other by a spiro carbon atom. For example, the alkaloids depicted in Figure 1 all share an azaspirocyclic framework. Pinnaic acid, isolated from the Okinawan bivalic *Pinna muricata*, exhibits inhibitory activity against phospholipase A_2.[1] Halichlorine, produced by the marine sponge *Halichondria okadai*, was found to inhibit the vascular cell adhesion molecule-1 (VCAM-1).[1,2] Cephalotaxine, the major alkaloid of *Cephalotaxus harringtonia* var. *drupacea*, and its esters (harringtonines) show high antileukaemic activity.[3]

The selective construction of the spiro fragment presents the main synthetic challenge for these unique alkaloids and various related products. Several methods have been devised to tackle this problem.[4]

With the advent of well-defined, practically air-stable, and functional-group-tolerant metathesis catalysts, e.g. the first, [$RuCl_2$(=CHPh)(PCy_3)$_2$] (**1a**), and second, [$RuCl_2$(=CHPh)(IMesH_2)(PCy_3)] (**1b**), generation of Grubbs' ruthenium-based catalysts, a new route to spiro compounds has been opened. In the last decade, ring-closing metathesis (RCM)[5] has been employed in the synthesis of several types of nitrogen-containing spiro systems. The azaspiro systems were built by ring closing of either the carbocycle[6] or the azacycle,[7] or by formation of two rings through a tandem RCM reaction of tetraenes.[8] The first approach was extensively employed in the metathesis of various geminal dialkenyl, alkenyl−alkynyl, and dialkynyl derivatives of a chiral bislactim (2*R*)-2-isopropyl-3,6-dimethoxy-2,5-dihydropyrazine as an entry towards rigidified chiral amino acids.[9]

Recently, a method for the preparation of various pyrrolidine spiro compounds **C** employing RCM in the presence of **1a** has been developed (Scheme 1).[10] The 2,2-dialkenylpyrrolidines **B** were synthesized by electrochemical oxidation of N-protected 2,2-bis(trimethylsilyl)pyrrolidines **A**, followed by alkenylation with e.g. allyltrimethylsilane and/or 3-butenylmagnesium bromide.

In this publication, we present a straightforward route to 6-azaspiro[4.*n*]alkenes starting from commercially available lactams by allylboration of the carbonyl carbon atoms followed by ring-closing metathesis of the obtained diallyl derivatives.[11]

Results and Discussion

2,2-Diallyl-substituted nitrogen heterocycles **2**, of any size, are readily obtained in 50−95% yield by reductive allylation of lactams containing an N−H bond with triallyl- or tris(2-methylallyl)borane.[12] These compounds with a quaternary carbon atom in an α position with respect to the nitrogen atom can then be subjected to a metathesis catalyst (after protection of the amino moiety), producing azaspiro compounds, and more specifically 6-azaspiro[4.*n*]-alk-2-enes (Scheme 2).

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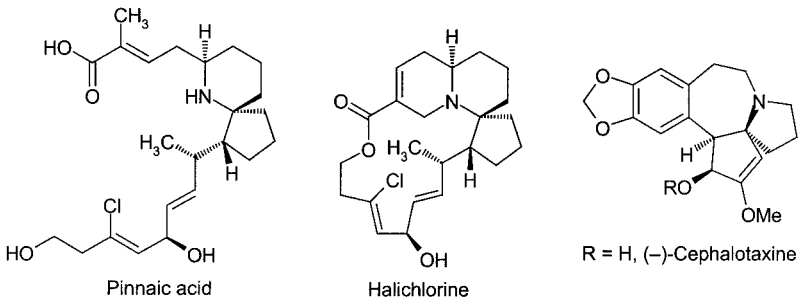
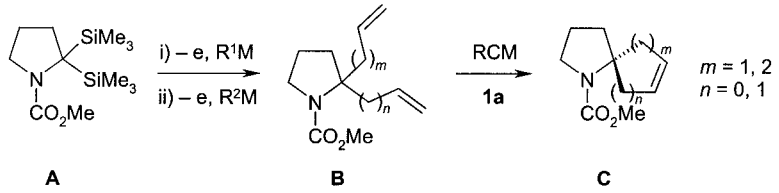
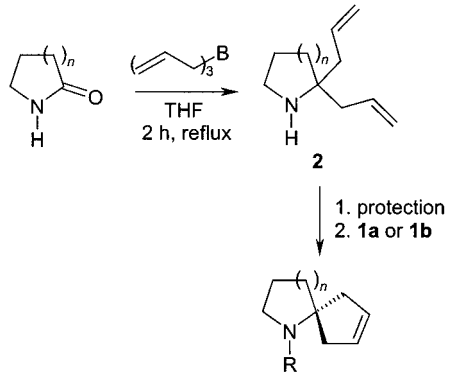


Figure 1. Alkaloids containing an azaspirocyclic ring system



Scheme 1. The synthesis of pyrrolidine spiro compounds **C** by the electrochemical alkenylation of **A** and ring-closing metathesis of **B**



2	n	%
a	1	90
b	2	79
c	3	50
d	9	83

Scheme 2. Synthesis of 6-azaspiro[4.*n*]alk-2-enes from lactams by an allylboration-RCM sequence

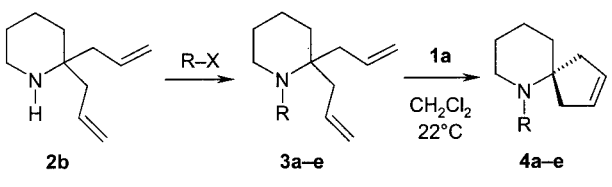
Despite the fact that the ruthenium carbene complexes **1a** and **1b** show remarkable functional-group tolerance, they are not compatible with a free amino group. Although some examples of the metathesis of substrates containing unprotected amino functionalities are known,[7b] these require large, substoichiometric rather than catalytic, amounts of the catalyst and long reaction times for complete conversion of the substrates. Since the purification of the reaction product in the presence of large amounts of ruthenium-containing products (from the decomposition of the catalyst) can also be troublesome, we decided to protect the nitrogen atoms of the diallyl compounds. To elucidate the efficiency of various protecting groups in RCM using catalyst **1a**, 2,2-diallylpiperidine (**2b**) was selected as a model system and functionalized at the nitrogen atom by conversion into the corresponding benzyl **3a**, benzoyl **3b**, acetyl **3c**, trifluoroacetyl **3d**, and *tert*-butoxycarbonyl **3e** derivatives (Scheme 3, Table 1).

Table 1. Metathesis of protected 2,2-diallylpiperidine derivatives

Substrate	Catalyst **1a**[a] [mol %]	Time [h]	Conversion[b] [%]	Yield[c] [%]	Product
3a	1	4	29	–	**4a**
	5	2	94	79	
3b	1	1 (4)	86 (99)	90	**4b**
	5	1	99	–	
3c	1	1 (4)	85 (99)	99	**4c**
	5	1	100	–	
3d	1	2	97	95	**4d**
	5	2	97	–	
3e	1	4	97	98	**4e**
	5	1	98	–	

[a] Conditions: indicated amount of **1a**, 22 °C, solvent CH_2Cl_2. [b] Conversions determined by GC analysis of samples from the reaction mixture. [c] Yields of isolated products after silica gel chromatography.

In a first attempt, the benzyl group was used as a protecting group, because it is relatively easy to remove by hydro-



3, 4	R
a	$PhCH_2$
b	PhCO
c	CH_3CO
d	CF_3CO
e	$tBuO_2C$

Scheme 3. Ring-closing metathesis of *N*-protected 2,2-diallylpiperidines

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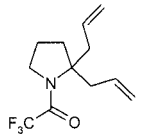
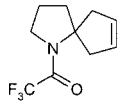
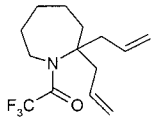
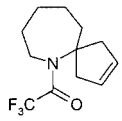
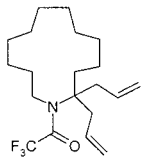
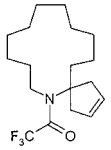
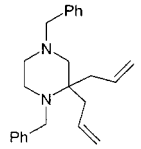
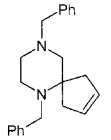
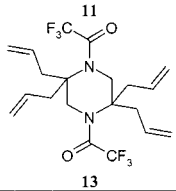
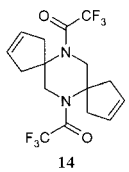
genation over Pd/C, a process that also saturates the double bond of the metathesis product to give the azaspiroalkane product. It turned out that metathesis of benzyl protected compounds was feasible, but as much as 5 mol % of catalyst **1a** was needed to achieve a good conversion (94% after 2 h) to the spiro compound **4a**. When 1 mol % of **1a** was used, only 29% conversion (after 4 h) to **4a** was achieved, presumably due to the deactivation of the catalyst by the basic tertiary amine. Although 5 mol % of catalyst is a standard amount used in metathesis transformations,[5] we consider this a relatively large quantity as the catalyst can be used more efficiently.[13]

Much better results in terms of catalyst efficiency and activity were achieved when the acylated derivatives **3b**−**e** were used as substrates. Thus, 1 mol % of **1a** was sufficient for full conversion of **3b**−**e** to the metathesis products 6-azaspiro[4.5]dec-2-enes **4b**−**e** within 4 h (Table 1). Use of 5 mol % of **1a** resulted in the quantitative conversion within 1 h of all four acyl derivatives **3b**−**e**. In our further studies we chose the trifluoroacetyl group as the protecting group, mainly because of the higher volatility of derivative **3d** with respect to the other three, facilitating the GC analysis of the reaction mixtures.

Table 2. Metathesis of 2,2-diallyl-N-heterocycles.[a]

Substrate	Catalyst **1a** (mol%)	Time (h)	Conversion[b] (%)	Yield[c] (%)	Product
 **5**	1	1 (4)	91 (100)	91	 **8**
 **6**	1	1	100	95	 **9**
 **7**	1	1	100	99	 **10**
 **11**	1	4	30	–	 **12**
	4	1	95	58	
 **13**	2	2	100	89	 **14**

[a] Conditions: indicated amount of **1a**, 22 °C, solvent CH_2Cl_2. [b] Conversions determined by GC analysis of samples from the reaction mixture. [c] Yields of isolated products after silica gel chromatography.

To extend the scope of the procedure, we prepared diallyl derivatives of pyrrolidine (**5**), azepane (**6**), and azacyclotridecane (**7**) by allylboration of the corresponding lactams,[12] followed by treatment with trifluoroacetic anhydride. In the presence of 1 mol % of **1a**, these compounds were smoothly converted by RCM to the corresponding 6-azaspiro[4.*n*]alkenes **8**−**10**, which could be isolated in nearly quantitative yields (Table 2). The size of the nitrogen-containing ring seemed to have no effect on the formation of the pentene ring by RCM. It should be mentioned that a close isomer of **5** has recently been used in the formal total synthesis of racemic cephalotaxine.[10]

We also prepared two piperazine derivatives. 2-Piperazinone and glycine anhydride were subjected to the allylboration and protection procedure, producing 2,2-diallyl-1,4-dibenzylpiperazine (**11**) and 1,4-bis(trifluoroacetyl)-2,2,5,5-tetraallylpiperazine (**13**), respectively. Metathesis of these compounds proceeded in the same manner as observed for the benzyl and trifluoroacetyl derivatives with 4 mol % and 2 mol % of **1a**, respectively, leading to quantitative conversions. Product **12** underwent partial decomposition during the reaction and purification, apparently due to its intrinsic instability. The acylated dispiro compound **14** was isolated in a very good yield as a colourless solid.

We were able to grow good quality crystals by concentration of a dichloromethane/hexanes solution of **14** and confirmed its structure crystallographically (Figure 2). A search of the Cambridge Structural Database revealed that this is the first crystal structure of a non-keto dispiropiperazine.

Contrary to the majority of substituted piperazine derivatives that adopt the more favourable chair conformation, compound **14** exists in a shallow twist-boat conformation. The piperazine ring is bent to release the strain of the dispiro system, so the cyclopentene rings are in a very shallow envelope-like orientation. Furthermore, the cyclo-

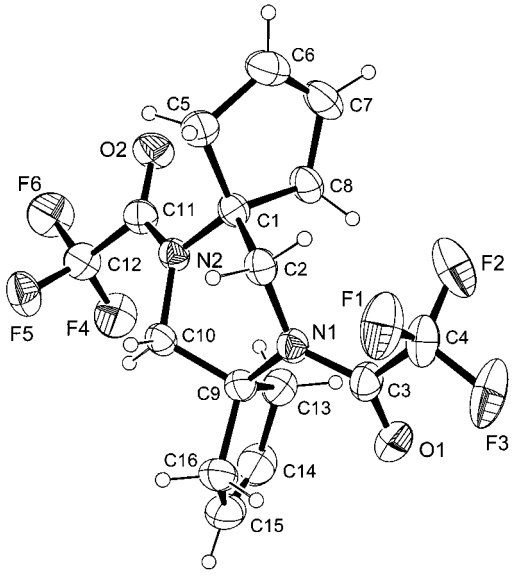


Figure 2. An ORTEP presentation of the crystal structure of compound **14**. Ellipsoids are drawn at the 30% probability level

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pentene rings do not lie parallel to each other and form a dihedral angle of 35.7°. A pair of weak hydrogen bonds between adjacent molecules was found for atoms C2 and C10 with oxygen O2 of one of the carbonyl groups. Distances for C2···O2 of 3.380 Å (C2−H···O2 = 2.51 Å) and for C10···O2 of 3.320 Å (C10−H···O2 = 2.41 Å) were measured. This interaction is facilitated by the fact that those two carbon atoms are folded towards the trifluoroacetyl group of an adjacent molecule. The compound showed ring-flipping behaviour in solution at room temperature (22°C), which was evident from the NMR spectra where the signals of protons and carbon atoms of the methylene groups were very broad.

There are several studies on the solid state behaviour of dispiropiperazine-2,5-diones.[14,15] In general, derivatives bearing exclusively aliphatic rings, including the closest analogue of **14**, 6,13-diazadispiro[4.2.4.2]tetradeca-7,14-dione,[14] the heterocyclic ring is planar, while when an indane moiety is present,[15] the central ring adopts a twist-boat conformation in most of the cases. On this point, the crystal structure of **14** mostly resembles the latter system.

Conclusion

We have demonstrated that the combination of diallylboration of lactams and the subsequent ring-closing metathesis of the resulting α,α-diallyl N-heterocyclic compounds is an efficient route towards 6-azaspiro[4.*n*]alk-2-enes. Protection of the free amine with an appropriate group that neutralizes the catalyst-deteriorating basicity of the nitrogen atom greatly facilitated the ring-closing metathesis. Amine derivatives containing a cyclopentene ring on the α-carbon might also be obtained following the same protocol with acyclic amides; this is currently under investigation.

Experimental Section

General Remarks: All operations with organoboron compounds were carried out in a strictly dry nitrogen atmosphere using standard Schlenk techniques. Triallylboron was prepared according to the literature procedure.[16] Solvents (hexanes, tetrahydrofuran, and dichloromethane) were dried according to standard procedures.[17] Acylation of amines and metathesis were performed under N_2 using dry solvents. Catalyst **1a** was purchased from Fluka; all organic substrates were used as received from commercial sources. The following instruments were used: Varian Mercury 300 spectrometer for ^{1}H NMR (300 MHz), ^{13}C NMR (75.47 MHz), and ^{19}F NMR (282.41 MHz) with external standards; Carlo Erba 8000^{Top} chromatograph (DB-5 column from J&W Scientific) for GC analyses; Jeol JMS SX/SX102A spectrometer for (high resolution) mass spectra (3-nitrobenzyl alcohol was used as matrix for some samples). Elemental analyses were performed with a Carlo Erba EA1108 CHNS-O Elemental Analyser at the Department of Organic Chemistry, University of Nijmegen.

General Allylboration Procedure: Allylboration of lactams was carried out as described in an earlier paper.[12] As an example, the synthesis of a new tetraallyl derivative of piperazine is described below.

Synthesis of 2,2,5,5-Tetraallylpiperazine (13NH): Triallylborane (0.535 g, 4.00 mmol) was added dropwise by syringe to a stirred suspension of glycine anhydride (0.172 g, 1.50 mmol) in THF (10 mL). The mixture was gently refluxed for 15 h. Methanol (2 mL) was then added at room temperature (22 °C) and the mixture was refluxed for 1 h. NaOH (5 mL of a 5 M solution) was added and the mixture was vigourously stirred until complete deboronation (no longer green colouration of flame) of the organic layer had taken place (ca. 2 h). The organic layer was then separated and the aqueous layer extracted with diethyl ether. The combined organic layers were washed with brine, dried with K_2CO_3, and concentrated. The crude product (a light-brown oil) was then purified by silica-gel chromatography [hexanes/ethyl acetate, 2:1 to 0:1, and additional methanol (1 vol%) as eluent]. A yellow oil (0.236 g, 64% yield) was obtained, which was used for the preparation of compound **13**. ^{1}H NMR ($CDCl_3$, ppm): δ = 1.70 (br. s, 2 H, NH), 2.13 (q, *J* = 13.8, 7.2 Hz, 4 H, H_2C=CHC*H*H), 2.33 (dd, *J* = 14.1, 7.2 Hz, 4 H, H_2C=CHCH*H*), 2.64 (s, 4 H, NCH_2), 5.06−5.14 (m, 8 H, CH=CH_2), 5.63 (ddt, *J* = 16.2, 10.5, 7.5 Hz, 4 H, C*H*=CH_2).

Acylation and Benzylation: The protection of the free amino group was performed using standard procedures to give the protected amines in near to quantitative yields. The concise descriptions for the preparation of piperidine derivatives **3a**−**e** follows.

2,2-Diallyl-1-benzylpiperidine (3a): Prepared according to the literature procedure.[11] ^{1}H NMR ($CDCl_3$, ppm): δ = 1.47−1.62 (m, 6 H, CH_2 cyclic), 2.16 (dd, *J* = 14.4, 7.8 Hz, 2 H, H_2C=CHC*H*H), 2.48 (pseudo t, J_{app} = 5.4 Hz, 2 H, CH_2N), 2.66 (dd, *J* = 14.4, 7.2 Hz, 2 H, H_2C=CHCH*H*), 3.66 (s, 2 H, CH_2Ph), 5.06−5.15 (m, 4 H, CH=CH_2), 6.00 (ddt, *J* = 15.9, 11.1, 7.5 Hz, 2 H, C*H*=CH_2), 7.21−7.42 (m, 5 H, C_6H_5). ^{13}C NMR ($CDCl_3$, ppm): δ = 20.8, 26.5, 32.5 (3 *C*H_2 cyclic), 38.3 (*C*H_2CH), 46.3 (*C*H_2N), 53.2 (C_{quat}), 58.4 (*C*H_2Ph), 117.1 (CH=*C*H_2), 126.7 (Ph), 128.4 (Ph), 128.5 (Ph), 135.6 (*C*H=CH_2), 141.2 (Ph, C_{ipso}). FAB-MS (rel. intensity, %): *m*/*z* = 256 [M + H]$^+$ (61), 255 [M]$^+$ (39), 254 [M − H]$^+$ (95), 215 [M − All + H]$^+$ (80), 214 [M − All]$^+$ (100), 178 [M − Ph]$^+$ (24), 124 [M − All − $PhCH_2$ + H]$^+$ (24), 92 [$PhCH_2$ + H]$^+$ (83). HRMS (FAB): calcd. for $C_{18}H_{26}N$ ([M + H]$^+$) 256.2065, observed 256.2067.

2,2-Diallyl-1-benzoylpiperidine (3b): 2,2-Diallylpiperidine (**2**) (0.607 g, 3.00 mmol) was placed in a round bottom flask together with potassium carbonate (1.24 g, 9.0 mmol) and dichloromethane (20 mL). Benzoyl chloride (0.42 mL, 0.516 g, 3.60 mmol) was added dropwise and the reaction mixture was stirred for 5 h at room temperature (22°C). Water (20 mL) was then carefully added and the mixture was extracted with dichloromethane. After drying over anhydrous K_2CO_3, the solvent was evaporated and the crude product was purified on a silica gel column (hexanes/ethyl acetate, 6:1) to give the product **3b** (0.800 g, 99%) as a slightly yellow oil. ^{1}H NMR ($CDCl_3$, ppm): δ = 1.52−1.74 (m, 6 H, CH_2 cyclic), 2.62 (dd, *J* = 13.4, 7.5 Hz, 2 H, H_2C=CHC*H*H), 3.13 (dd, *J* = 13.5, 7.2, 2 H, H_2C=CHCH*H*), 3.26 (pseudo t, J_{app} = 5.6 Hz, 2 H, CH_2N), 5.06−5.18 (m, 4 H, CH=CH_2), 5.85 (ddt, *J* = 17.1, 9.9, 7.5 Hz, 2 H, C*H*=CH_2), 7.30−7.45 (m, 5 H, C_6H_5). ^{13}C NMR ($CDCl_3$, ppm): δ = 17.7, 23.6, 30.3 (3 *C*H_2 cyclic), 40.5 (*C*H_2CH), 45.9 (*C*H_2N), 60.9 (C_{quat}), 118.4 (CH=*C*H_2), 127.1 (Ph), 128.6 (Ph), 129.6 (Ph), 134.6 (*C*H=CH_2), 139.0 (Ph, C_{ipso}), 173.3 (*C*=O). FAB-MS (rel. intensity, %): *m*/*z* = 270 [M + H]$^+$ (62), 268 [M − H]$^+$ (14), 228 [M − All]$^+$ (52), 105 [PhCO]$^+$ (100), 77 [Ph]$^+$ (16). HRMS (FAB): calcd. for $C_{18}H_{24}NO$ ([M + H]$^+$) 270.1858, observed 270.1870.

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1-Acetyl-2,2-diallylpiperidine (3c): The compound was obtained by a similar procedure as for **3d**, but using acetyl anhydride in place of trifluoroacetic anhydride. After silica gel chromatography (hexanes/ethyl acetate, 15:1) **3c** (90%) was obtained as a colourless oil. ^{1}H NMR ($CDCl_3$, ppm): δ = 1.54−1.69 (m, 6 H, CH_2 cyclic), 2.03 (s, 3 H, CH_3CO), 2.48 (dd, J = 13.5, 7.8 Hz, 2 H, H_2C=CHCHH), 2.97 (ddt, J_d = 13.5, 7.2, J_t = 1.2 Hz, 2 H, H_2C=CHCHH), 3.29 (pseudo t, J = 6.0 Hz, 2 H, CH_2N), 4.98−5.09 (m, 4 H, CH=CH_2), 5.72 (ddt, J = 17.1, 9.6, 7.2 Hz, 2 H, CH=CH_2). ^{13}C NMR ($CDCl_3$, ppm): δ = 16.7, 23.0 (2 CH_2 ring), 25.3 (CH_3CO), 29.8 (CH_2 ring), 41.0 (CH_2CH), 44.0 (CH_2N), 61.1 (C_{quat}), 118.0 (CH=CH_2), 134.9 (CH=CH_2), 171.2 (CO). EI-MS (rel. intensity, %): m/z = 208 [M + H]$^+$ (24), 207 [M]$^+$ (27), 192 [M − CH_3]$^+$ (16), 167 [M − All + H]$^+$ (83), 166 [M − All]$^+$ (100), 164 [M − $COCH_3$]$^+$ (19), 148 (46), 125 [M − 2All]$^+$ (100), 124 [M − All − $COCH_3$ + H]$^+$ (100), 91 (44), 82 [M − 2All − $COCH_3$]$^+$ (100), 55 (77), 42 [All + H]$^+$ (88). HRMS (EI): calcd. for $C_{13}H_{21}NO$ ([M]$^+$) 207.1623, observed 207.1625.

2,2-Diallyl-1-(trifluoroacetyl)piperidine (3d): 2,2-Diallylpiperidine hydrochloride (0.609 g, 3.02 mmol) was placed in a round bottom flask with dry dichloromethane (20 mL). Triethylamine (2.5 mL, 6 equiv.) and a small amount of 4-DMAP were added, followed by addition of trifluoroacetic anhydride (1.28 mL, 1.998 g, 9.37 mmol). After stirring for 5 h at room temperature the reaction mixture was quenched with an aqueous $NaHCO_3$ solution. After extraction with diethyl ether, drying over magnesium sulfate and solvent evaporation, the crude product was purified on a silica gel column (hexanes/ethyl acetate, 15:1), obtaining **3d** (0.783 g, 100%) as a colourless oil. ^{1}H NMR ($CDCl_3$, ppm): δ = 1.62−1.80 (m, 6 H, 3 CH_2 cyclic), 2.55 (dd, J = 13.8, 7.2 Hz, 2 H, CHH-CH=CH_2), 2.93 (dd, J = 13.8, 7.2 Hz, 2 H, CHH-CH=CH_2), 3.41 (pseudo t, 2 H, J_{app} = 5.7 Hz, NCH_2), 5.05−5.14 (m, 4 H, CH=CH_2), 5.71 (distorted ddt, J_d ≈ 17.7, 9.3, J_t = 7.5 Hz, 2 H, CH=CH_2). ^{13}C NMR ($CDCl_3$, ppm): δ = 15.6, 21.8, 28.7 (3 CH_2), 39.9 (2 C, CH_2CH=CH_2), 42.1 (q, $^4J_{C,F}$ = 3.6 Hz, NCH_2), 63.2 (C), 116.7 (q, $^2J_{C,F}$ = 289.3 Hz, CF_3), 119.2 (2 C, =CH_2), 133.3 (2 C, CH), 156.7 (q, $^3J_{C,F}$ = 34.2 Hz, CO). ^{19}F NMR ($CDCl_3$, ppm): δ = −69.5. EI-MS (rel. intensity, %): m/z = 261 [M]$^+$ (3), 244 (24), 220 [M − All]$^+$ (100), 212 (63), 182 (65), 162 [M − $COCF_3$ − 2H]$^+$ (99), 150 [M − All − CF_3 − H]$^+$ (71), 132 (46), 112 [M − 2All − CF_3 + 2H]$^+$ (49). HRMS (EI): calcd. for $C_{13}H_{18}F_3NO$ ([M]$^+$) 261.1340, observed 261.1339.

2,2-Diallyl-1-*tert*-butoxycarbonylpiperidine (3e): The compound was obtained with a similar procedure as for **3d** using di-*tert*-butyl dicarbonate in place of trifuoroacetic anhydride. After silica gel chromatography (hexanes/ethyl acetate, 15:1) **3e** (67%, loss on evaporation) was obtained as a colourless oil. ^{1}H NMR ($CDCl_3$, ppm): δ = 1.46 [s, 9 H, C(CH_3)$_3$], 1.58 (br. s, 6 H, CH_2 ring), 2.35 (dd, J = 13.5, 7.8 Hz, 2 H, CHH-CH=CH_2), 2.86 (dd, J = 13.8, 6.9 Hz, 2 H, CHH-CH=CH_2), 3.41 (pseudo t, J = 5.7 Hz, 2 H, NCH_2), 5.03−5.10 (m, 4 H, =CH_2), 5.77 (ddt, J = 16.5, 10.2, 7.2 Hz, 2 H, CH=). ^{13}C NMR ($CDCl_3$, ppm): δ = 17.8, 23.4 (2 CH_2 ring), 28.8 (CH_3), 31.0 (CH_2 ring), 42.1 (CH_2N), 59.3 (C_{quat}), 79.6 (Me_3C-O), 117.9 (CH=), 135.0 (=CH_2), 156.0 (C=O). FAB-MS (rel. intensity, %): m/z = 266 [M + H]$^+$ (44), 264 [M − H]$^+$ (10), 224 [M − All]$^+$ (75), 210 [M − C(CH_3)$_3$ + 2H]$^+$ (100), 208 [M − C(CH_3)$_3$]$^+$ (28), 192 [M − OC(CH_3)$_3$]$^+$ (18), 168 [M − All − C(CH_3)$_3$ + H]$^+$ (89), 164 [M − Boc]$^+$ (23), 124 [M − All − Boc + H]$^+$ (62), 57 (47). HRMS (FAB): calcd. for $C_{16}H_{28}NO_2$ [M + H]$^+$ 266.2120, observed 266.2117.

2,2-Diallyl-1-(trifluoroacetyl)pyrrolidine (5): Prepared as for **3d** in a 96% yield after silica gel chromatography (hexanes/ethyl acetate, 15:1) as a colourless oil. ^{1}H NMR ($CDCl_3$, ppm): δ = 1.70−1.88 (m, 4 H, CH_2CH_2C), 2.29 (dd, J = 13.5, 7.5 Hz, 2 H, CHH-CH=CH_2), 2.84 (dd, J = 13.5, 7.2 Hz, 2 H, CHH-CH=CH_2), 3.49 (pseudo t, 2 H, J_{app} = 6.6 Hz, NCH_2), 4.95−5.04 (m, 4 H, CH=CH_2), 5.57 (distorted ddt, J ≈ 17.7, 9.6, 7.2 Hz, 2 H, CH=CH_2). ^{13}C NMR ($CDCl_3$, ppm): δ = 23.4 ($CH_2$$CH_2$N), 33.6 ($CH_2$CN), 40.6 (2 C, CH_2CH=CH_2), 49.2 (q, $^4J_{C,F}$ = 3.6 Hz, NCH_2), 69.9 (C_{quat}), 116.3 (q, $^2J_{C,F}$ = 288.7 Hz, CF_3), 119.1 (2 C, CH=CH_2), 133.1 (2 C, CH=CH_2), 154.9 (q, $^3J_{C,F}$ = 35.8 Hz, C=O). ^{19}F NMR ($CDCl_3$, ppm): δ = −73.2. FAB-MS (rel. intensity, %): m/z = 248 [M + H]$^+$ (32), 246 [M − H]$^+$ (12), 206 [M − All]$^+$ (100). HRMS (FAB): calcd. for $C_{12}H_{17}F_3NO$ ([M + H]$^+$) 248.1262, observed 248.1261.

2,2-Diallyl-1-(trifluoroacetyl)azepane (6): Prepared as for **3d** in a 91% yield after silica gel chromatography (hexanes/ethyl acetate, 20:1) as a colourless oil. ^{1}H NMR ($CDCl_3$, ppm): δ = 1.50 (q, J = 6.1 Hz, 2 H, CH_2 ring), 1.61−1.78 (m, 4 H, 2 CH_2 ring), 1.80−1.88 (m, 2 H, CH_2 ring), 2.77 (dd, J = 13.8, 7.2 Hz, 2 H, CHH-CH=CH_2), 2.87 (dd, J = 14.1, 7.5 Hz, 2 H, CHH-CH=CH_2), 3.40 (pseudo t, J = 4.2 Hz, 2 H, CH_2N), 5.07 (pseudo d, J_{app} = 12.6 Hz, 4 H, CH=CH_2), 5.72 (ddt, J = 17.4, 9.9, 7.5 Hz, 2 H, CH=CH_2). ^{13}C NMR ($CDCl_3$, ppm): δ = 23.4, 28.2, 31.1, 35.1 (4 CH_2 ring), 40.2 (2 C, CH_2CH=CH_2), 46.5 (q, $^4J_{C,F}$ = 3.6 Hz, NCH_2), 67.5 (C_{quat}), 117.0 (q, $^2J_{C,F}$ = 289.3 Hz, CF_3), 119.2 (2 C, CH=CH_2), 133.6 (2 C, CH=CH_2), 157.8 (q, $^3J_{C,F}$ = 34.2 Hz, C=O). ^{19}F NMR ($CDCl_3$, ppm): δ = −68.8. FAB-MS (rel. intensity, %): m/z = 276 [M + H]$^+$ (76), 274 [M − H]$^+$ (18), 234 [M − All]$^+$ (100), 109 (18), 95 [C_6H_9N]$^+$ (35), 81 (36), 69 [CF_3]$^+$ (37), 55 (52), 41 (29). HRMS (FAB): calcd. for $C_{14}H_{21}F_3NO$ [M + H]$^+$ 276.1575, observed 276.1587.

2,2-Diallyl-1-(trifluoroacetyl)azacyclotridecane (7): Prepared in a similar manner as for **3d** in an 87% yield after silica gel chromatography (hexanes/ethyl acetate, 20:1) as a colourless oil. ^{1}H NMR ($CDCl_3$, ppm): δ = 1.25−1.52 (m, 16 H, 8 CH_2 cycle), 1.57−1.68 (m, 2 H, CH_2 cycle), 1.75−1.80 (m, 2 H, CH_2 cycle), 2.23 (dd, J = 14.4, 7.5 Hz, 2 H, CH_2N), 3.25 (dd, J = 14.4, 7.5 Hz, 4 H, CH_2CH=), 5.04−5.14 (m, 4 H, CH=CH_2), 5.67 (ddt, J = 16.9, 10.5, 7.2 Hz, 2 H, CH=CH_2). ^{13}C NMR ($CDCl_3$, ppm): δ = 23.4, 24.14, 24.39, 24.74, 24.77, 25.7, 26.9, 27.1, 28.8, 31.9 (10 CH_2 ring), 37.7 (2 C, CH_2CH=CH_2), 44.2 (q, $^4J_{C,F}$ = 2.5 Hz, CH_2N), 68.5 (C_{quat}), 116.9 (q, $^2J_{C,F}$ = 289.7 Hz, CF_3), 118.9 (2 C, CH=CH_2), 133.5 (2 C, CH=CH_2), 157.5 (q, $^3J_{C,F}$ = 33.8 Hz, C=O). ^{19}F NMR ($CDCl_3$, ppm): δ = −68.6. FAB-MS (rel. intensity, %): m/z = 360 [M + H]$^+$ (75), 318 [M − All]$^+$ (100), 109 (10), 95 (20), 81 (22), 67 (18), 55 (27), 41 (18). HRMS (FAB): calcd. for $C_{20}H_{33}F_3NO$ [M + H]$^+$ 360.2514, observed 360.2495. Anal.: calcd. C 66.83, H 8.97, N 3.90; found C 66.49, H 9.18, N 3.91.

2,2-Diallyl-1,4-dibenzylpiperazine (11): 2,2-Diallylpiperazine (0.600 g, 3.60 mmol) was placed in a round bottom flask equipped with a reflux condenser and methanol (20 mL) was added. Potassium carbonate (2.0 g, 4 equiv.) was then introduced, followed by benzyl chloride (1.30 g, 7.56 mmol, 2.1 equiv.), and the reaction mixture was subsequently refluxed for 5 h and stirred for an additional 15 h (overnight) at room temperature. The reaction mixture was filtered and concentrated. Water and diethyl ether were added to the residue, the layers were separated, and the aqueous layer was extracted twice with diethyl ether. The combined organic fractions were washed twice with water, once with brine, dried with $MgSO_4$, filtered, and concentrated. After column chromatography [petroleum ether (40−60 °C)/ethyl acetate, 10:1] **11** (1.13 g, 91%) was obtained as a colourless liquid. Upon storing in air, the compound turned yellow and was therefore passed through a plug of alumina and

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stored under an atmosphere of nitrogen at −20 °C. ^{1}H NMR ($CDCl_3$, ppm): δ = 2.07 (dd, *J* = 14.1, 7.8 Hz, 2 H, C*H*HCH=), 2.31 (br. dd, 2 H, CH*H*CH=), 2.35 (br. s, 2 H, CH_2CH_2), 2.52 (t, *J* = 5.1 Hz, 2 H, NCH_2C), 2.72 (br. dd, 2 H, CH_2CH_2), 3.41 (s, 2 H, C*H*HPh), 3.63 (br. s, 2 H, CH*H*Ph), 4.98−5.05 (m, 4 H, CH=CH_2), 5.88 (br. ddt, 2 H, C*H*=CH_2), 7.18−7.37 (m, 10 H, C_6H_5). ^{13}C NMR ($CDCl_3$, ppm): δ = 46.3 (2 C, CH_2CH=), 52.8, 54.3 (both CH_2CH_2), 58.8 (2 C, CH_2Ph), 59.4 (NCH_2C), 63.4 (C_{quat}), 117.3 (2 C, CH=CH_2), 126.9, 127.2, 128.43, 128.48, 128.7, 129.3 (all Ph), 135.5 (2 C, CH=CH_2), 139.2, 140.5 (both C_{ipso}). FAB-MS (rel. intensity, %): *m*/*z* = 347 $[M + H]^+$ (45), 346 $[M]^+$ (14), 345 $[M - H]^+$ (46), 305 $[M - All]^+$ (100), 304 $[M - All - H]^+$ (49), 264 $[M - 2All]^+$ (77), 213 $[M - All - PhCH_2 - H]^+$ (25), 173 $[M - 2All - PhCH_2]^+$ (28), 91 $[PhCO]^+$ (85). HRMS (FAB): calcd. for $C_{24}H_{31}N_2$ ($[M + H]^+$) 347.2487, observed 347.2490. Anal.: calcd. C 83.19, H 8.73, N 8.08; found C 83.15, H 8.69, N 8.05.

2,2,5,5-Tetraallyl-1,4-bis(trifluoroacetyl)piperazine (13): Prepared as for **3d** from **13NH** in a 90% yield after silica gel chromatography (hexanes/ethyl acetate, 20:1) as a colourless oil. ^{1}H NMR ($CDCl_3$, ppm): δ = 2.48 (br. dd, 4 H, *J* = 12.3, 6.8 Hz, CH_2CH=), 3.03 (dd, *J* = 14.1, 7.2 Hz, 4 H, CH_2CH=), 3.57 (s, 4 H, NCH_2), 5.17 (d, *J* = 7.5 Hz, 4 H, CH=CH*H*), 5.22 (s, 4 H, CH=C*H*H), 5.63 (ddt, *J* = 16.2, 10.8, 7.5 Hz, 4 H, C*H*=CH_2). ^{13}C NMR ($CDCl_3$, ppm): δ = 37.5 (4 C, CH_2CH=), 48.2 (q, $^4J_{C,F}$ = 3.6 Hz, 2 C, CH_2N), 63.6 (2 C, C_{quat}), 116.1 (q, $^2J_{C,F}$ = 288.9 Hz, 2 C, CF_3), 121.4 (4 C, CH=CH_2), 131.0 (4 C, CH=CH_2), 157.2 (q, $^3J_{C,F}$ = 35.4 Hz, 2 C, C=O). ^{19}F NMR ($CDCl_3$, ppm): δ = −68.8. FAB-MS (rel. intensity, %): *m*/*z* = 439 $[M + H]^+$ (100), 437 $[M - H]^+$ (18), 397 $[M - All]^+$ (44), 301 $[M - All - COCF_3 + H]^+$ (7), 259 $[M - 2All - COCF_3]^+$ (9), 204 (9), 136 (13), 107 (43), 91 (30), 79 (55), 41 (37). HRMS (FAB): calcd. for $C_{20}H_{25}F_6N_2O_2$ $[M + H]^+$ 439.1820, observed 439.1807. Anal.: calcd. C 54.79, H 5.52, N 6.39; found C 55.00, H 5.63, N 6.15.

General RCM Procedure: Catalyst **1a** (4.1 mg, 5.00 μmol) was dissolved in CH_2Cl_2 (1 mL) in a small Schlenk tube at 22 °C. The diene under investigation (500 μmol, 100 equiv.) was added to the solution by syringe. The progress of the reaction was checked by GC analysis of small aliquots of the reaction mixture. Once the reaction was completed (4−6 h), DMSO (0.10 mL) was added to the reaction mixture[18] and stirring continued for 18 h in order to facilitate the removal of the catalyst decomposition products. Purification by silica gel chromatography gave the desired product. In experiments performed with 5 mol % of the catalyst, 100.0 μmol of diene was used while keeping the amount of catalyst and solvent at the same level; the progress of the reaction was monitored by GC, but the products were not isolated.

6-Benzyl-6-azaspiro[4.5]dec-2-ene (4a): Isolated as a yellow oil, in a 79% yield after silica gel chromatography [petroleum ether (40−60 °C)/ethyl acetate, 15:1]. ^{1}H NMR ($CDCl_3$, ppm): δ = 1.45−1.55 (m, 4 H, 2 CH_2 azacycle), 1.71 (pseudo t, 2 H, CH_2C), 2.21 (d, *J* = 15.3 Hz, 2 H, CH_2CH=), 2.37 (pseudo t, 2 H, CH_2N), 2.62 (d, *J* = 15 Hz, 2 H, CH_2CH=), 3.33 (s, 2 H, CH_2Ph), 5.69 (s, 2 H, C*H*=C*H*), 7.18−7.39 (m, 5 H, Ph). ^{13}C NMR ($CDCl_3$, ppm): δ = 22.2, 26.5 (both CH_2 azacycle), 40.8 (2 C, CH_2CH=), 48.5 (CH_2N), 54.8 (CH_2Ph), 65.4 (C_{spiro}), 126.6 (Ph), 128.3 (2 C, CH=CH), 128.6 (Ph), 129.6 (Ph), 141.4 (C_{ipso}). FAB-MS (rel. intensity, %): *m*/*z* = 228 $[M + H]^+$ (64), 227 $[M]^+$ (60), 226 $[M - H]^+$ (100), 198 (20), 186 (11), 150 $[M - Ph]^+$ (12), 122 (15), 91 $[PhCH_2]^+$ (78), 55 (15). HRMS (FAB): calcd. for $C_{16}H_{22}N$ $[M + H]^+$ 228.1752, observed 228.1734.

6-Benzoyl-6-azaspiro[4.5]dec-2-ene (4b): Isolated in a 90% yield after chromatography (hexanes/ethyl acetate, 12:1) as a colourless oil. ^{1}H NMR ($CDCl_3$, ppm): δ = 1.44−1.54 (m, 2 H, CH_2 azacycle), 1.65−1.80 (m, 4 H, 2 CH_2 azacycle), 2.54 (d, *J* = 14.4 Hz, 2 H, CH_2CH=), 2.93 (d, *J* = 14.7 Hz, 2 H, CH_2CH=), 3.37 (pseudo t, *J* = 5.6 Hz, 2 H, CH_2N), 5.68 (s, 2 H, C*H*=C*H*), 7.32−7.39 (m, 3 H, Ph), 7.46−7.50 (m, 2 H, Ph). ^{13}C NMR ($CDCl_3$, ppm): δ = 19.3, 25.1 (both CH_2 azacycle), 34.7 (CH_2C), 44.1 (2 C, CH_2CH=), 47.7 (CH_2N), 65.6 (C_{spiro}), 128.0 (Ph), 128.6 (CH=CH), 130.2 (Ph), 138.2 (C_{ipso}), 173.9 (C=O). FAB-MS (rel. intensity, %): *m*/*z* = 242 $[M + H]^+$ (100), 241 $[M]^+$ (28), 240 $[M - H]^+$ (23), 136 $[M - PhCO]^+$ (5), 105 $[PhCO]^+$ (74). HRMS (FAB): calcd. for $C_{16}H_{20}NO$ $[M + H]^+$ 242.1545, observed 242.1550. Anal.: calcd. C 79.63, H 7.94, N 5.80; found C 79.57, H 7.87, N 5.80.

6-Acetyl-6-azaspiro[4.5]dec-2-ene (4c): Isolated in a 99% yield after chromatography (hexanes/ethyl acetate, 4:1 to 3:1) as a colourless oil. ^{1}H NMR ($CDCl_3$, ppm): δ = 1.56−1.70 (m, 6 H, 3 CH_2 azacycle), 2.03 (s, 3 H, CH_3CO), 2.35 (d, *J* = 14.7 Hz, 2 H, CH_2CH=), 2.85 (d, *J* = 14.7 Hz, 2 H, CH_2CH=), 3.40 (pseudo t, J_{app} = 5.4 Hz, 2 H, CH_2N), 5.59 (s, 2 H, C*H*=C*H*). ^{13}C NMR ($CDCl_3$, ppm): δ = 17.8, 24.0 (both CH_2 azacycle), 24.5 (CH_3), 34.6 (CH_2C), 44.4 (3 C, CH_2N & 2 CH_2CH=), 65.1 (C_{spiro}), 128.6 (CH=CH), 171.4 (C=O). FAB-MS (rel. intensity, %): *m*/*z* = 180 $[M]^+$ (100), 179 $[M - H]^+$ (24), 178 $[M - 2H]^+$ (25), 136 $[M - COCH_3]^+$ (20), 120 (12). HRMS (FAB): calcd. for $C_{11}H_{18}NO$ $[M + H]^+$ 180.1388, observed 180.1383.

6-(Trifluoroacetyl)-6-azaspiro[4.5]dec-2-ene (4d): Obtained as a colourless oil, in a 95% yield after chromatography (hexanes/ethyl acetate, 12:1). ^{1}H NMR ($CDCl_3$, ppm): δ = 1.65−1.80 (m, 6 H, 3 CH_2 azacycle), 2.43 (d, *J* = 14.4 Hz, 2 H, CH_2CH=), 2.85 (d, *J* = 14.7 Hz, 2 H, CH_2CH=), 3.54 (pseudo t, J_{app} = 5.4 Hz, 2 H, CH_2N), 5.63 (s, 2 H, C*H*=C*H*). ^{13}C NMR ($CDCl_3$, ppm): δ = 17.1, 23.8 (both CH_2 azacycle), 33.9 (CH_2C), 43.0 (q, $^4J_{C,F}$ = 3.6 Hz, CH_2N), 43.5 (CH_2CH=), 66.9 (C_{spiro}), 116.8 (q, $^2J_{C,F}$ = 289.3 Hz, CF_3), 128.3 (CH=CH), 156.8 (q, $^3J_{C,F}$ = 34.6 Hz, C=O). ^{19}F NMR ($CDCl_3$, ppm): δ = −69.8. FAB-MS (rel. intensity, %): *m*/*z* = 234 $[M + H]^+$ (100), 232 $[M - H]^+$ (63), 95 (43), 83 (30), 81 (52), 69 $[CF_3]^+$ (62), 57 (75), 55 (84), 43 (49), 41 (48). HRMS (FAB): calcd. for $C_{11}H_{15}F_3NO$ $[M + H]^+$ 234.1106, observed 234.1104.

6-*tert*-Butoxycarbonyl-6-azaspiro[4.5]dec-2-ene (4e): Isolated after silica gel column chromatography (eluent hexanes/ethyl acetate, 10:1) in a 98% yield as a colourless oil. ^{1}H NMR ($CDCl_3$, ppm): δ = 1.43 [s, 9 H, $C(CH_3)_3$], 1.45−1.65 (m, 6 H, 3 CH_2 azacycle), 2.37 (d, *J* = 14.1 Hz, 2 H, CH_2CH=), 2.82 (d, *J* = 14.7 Hz, 2 H, CH_2CH=), 3.45 (pseudo t, *J* = 5.7 Hz, 2 H, CH_2N), 5.61 (s, 2 H, C*H*=C*H*). ^{13}C NMR ($CDCl_3$, ppm): δ = 18.4, 23.7 (both CH_2 azacycle), 28.7 (3 C, CH_3), 35.4 (CH_2C), 43.1 (CH_2N), 45.2 (2 C, CH_2CH=), 64.2 (C_{spiro}), 79.5 (C-O), 128.6 (CH=CH), 156.3 (C=O). FAB-MS (rel. intensity, %): *m*/*z* = 238 $[M + H]^+$ (26), 237 $[M]^+$ (10), 182 $[M - C(CH_3)_3 + 2H]^+$ (100), 181 $[M - C(CH_3)_3 + H]^+$ (31), 180 $[M - C(CH_3)_3]^+$ (19), 136 $[M - Boc]^+$ (13), 120 (10), 57 $[C(CH_3)_3]^+$ (26). HRMS (FAB): calcd. for $C_{14}H_{24}NO_2$ $[M + H]^+$ 238.1807, observed 238.1806.

1-(Trifluoroacetyl)-1-azaspiro[4.4]non-7-ene (8): Obtained as a colourless oil in a 91% yield after chromatography (hexanes/ethyl acetate, 12:1). ^{1}H NMR ($CDCl_3$, ppm): δ = 1.89−2.00 (m, 4 H, 2 CH_2 azacycle), 2.16 (d, *J* = 14.4 Hz, 2 H, CH_2CH=), 3.12 (d, *J* = 14.4 Hz, 2 H, CH_2CH=), 3.68 (tt, *J* = 6.2, 1.2 Hz, 2 H, CH_2N), 5.66 (s, 2 H, C*H*=C*H*). ^{13}C NMR ($CDCl_3$, ppm): δ = 24.0 ($CH_2CH_2CH_2$), 42.5 (CH_2C), 43.7 (2 C, CH_2CH=), 48.4 (q, $^4J_{C,F}$ = 4.1 Hz, CH_2N), 72.0 (C_{spiro}), 116.5 (q, $^2J_{C,F}$ = 288.5 Hz,

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CF_3), 128.9 (*C*H=*C*H), 155.0 (q, $^3J_{C,F}$ = 36.2 Hz, *C*=O). ^{19}F NMR ($CDCl_3$, ppm): δ = −73.3. FAB-MS (rel. intensity, %): *m/z* = 220 [M + H]$^+$ (36), 218 [M − H]$^+$ (18), 206 (21), 149 [M − CF_3-H]$^+$ (22), 97 [$COCF_3$]$^+$ (43), 95 (65), 81 (62), 69 [CF_3]$^+$ (86), 57 (100), 55 (96), 43 (58), 41 (50). EI-MS (rel. intensity, %): *m/z* = 220 [M + H]$^+$ (28), 219 [M]$^+$ (60), 178 [M − All]$^+$ (10), 150 [M − CF_3]$^+$ (66), 122 [M − $COCF_3$]$^+$ (12), 106 (100), 91 (67), 80 (58). HRMS (FAB): calcd. for $C_{10}H_{13}F_3NO$ ([M + H]$^+$) 220.0949, observed 220.0952.

6-(Trifluoroacetyl)-6-azaspiro[4.6]undec-2-ene (9): Isolated as a colourless oil in a 95% yield after chromatography (hexanes/ethyl acetate, 15:1). ^{1}H NMR ($CDCl_3$, ppm): δ = 1.54−1.62 (m, 2 H, CH_2 azacycle), 1.67−1.80 (m, 4 H, 2 CH_2 azacycle), 1.81−1.88 (m, 2 H, CH_2C), 2.33 (d, *J* = 14.1 Hz, 2 H, CH_2CH=), 2.84 (d, *J* = 13.5 Hz, 2 H, CH_2CH=), 3.57 (pseudo t, *J* = 8.3 Hz, 2 H, CH_2N), 5.64 (s, 2 H, C*H*=C*H*). ^{13}C NMR ($CDCl_3$, ppm): δ = 24.2, 27.6, 30.8 (3 *C*H_2 azacycle), 39.6 (*C*H_2C), 44.4 (2 C, *C*H_2CH=), 44.8 (q, $^4J_{C,F}$ = 3.7 Hz, *C*H_2N), 70.3 (C_{spiro}), 117.0 (q, $^2J_{C,F}$ = 288.9 Hz, *C*F_3), 128.3 (*C*H=*C*H), 157.5 (q, $^3J_{C,F}$ = 34.2 Hz, *C*=O). ^{19}F NMR ($CDCl_3$, ppm): δ = −69.0. FAB-MS (rel. intensity, %): *m/z* = 248 [M + H]$^+$ (100), 247 [M]$^+$ (55), 246 [M − H]$^+$ (82), 178 [M − CF_3]$^+$ (24), 135 (30), 133 (15), 93 (28), 91 (27), 79 (30), 67 (34), 55 (34), 41 (25). HRMS (FAB): calcd. for $C_{12}H_{17}F_3NO$ [M + H]$^+$ 248.1262, observed 248.1247.

6-(Trifluoroacetyl)-6-azaspiro[4.12]heptadec-2-ene (10): Isolated in a 99% yield after chromatography (hexanes/ethyl acetate, 15:1) as a colourless oil. ^{1}H NMR ($CDCl_3$, ppm): δ = 1.23−1.50 (m, 16 H, 8 CH_2 azacycle), 1.65 (t, *J* = 6.9 Hz, 2 H, CH_2C), 1.80 (m, 2 H, CH_2 azacycle), 2.52 (d, *J* = 14.7 Hz, 2 H, CH_2CH=), 2.78 (d, *J* = 15.3 Hz, 2 H, CH_2CH=), 3.53 (t, *J* = 14.7 Hz, 2 H, CH_2N), 5.61 (s, 2 H, C*H*=C*H*). ^{13}C NMR ($CDCl_3$, ppm): δ = 23.43, 23.47, 23.7, 25.0, 25.3, 25.8, 26.1, 26.9, 28.3 (9 *C*H_2 azacycle), 38.1 (*C*H_2C), 43.9 (2 C, *C*H_2CH=), 44.8 (q, *J* = 3.6 Hz, *C*H_2N), 70.5 (C_{spiro}), 117.0 (q, $^2J_{C,F}$ = 289.3 Hz, *C*F_3), 128.5 (*C*H=*C*H), 157.8 (q, $^3J_{C,F}$ = 34.6 Hz, *C*=O). ^{19}F NMR ($CDCl_3$, ppm): δ = −68.4. FAB-MS (rel. intensity, %): *m/z* = 332 [M + H]$^+$ (100), 331 [M]$^+$ (50), 330 [M − H]$^+$ (70), 262 [M − CF_3]$^+$ (14), 147 (15), 95 (19), 93 (19), 81 (22), 80 (21), 79 (23), 67 (27), 55 (17). HRMS (FAB): calcd. for $C_{18}H_{29}F_3NO$ [M + H]$^+$ 332.2201, observed 332.2200. Anal.: calcd. C 65.23, H 8.52, N 4.23; found C 65.37, H 8.81, N 4.13.

6,9-Dibenzyl-6,9-diazaspiro[4.5]dec-2-ene (12): Isolated as a pale yellow oil in a 58% yield after chromatography [petroleum ether (40−60 °C)/ethyl acetate, 12:1 to 4:1, with 1% ethanol]. ^{1}H NMR ($CDCl_3$, ppm): δ = 2.20−2.68 (m, 10 H, all CH_2 azacycle and carbocycle), 3.50 (s, 4 H, CH_2Ph), 5.65 (s, 2 H, C*H*=C*H*), 7.19−7.37 (m, 10 H, Ph). ^{13}C NMR ($CDCl_3$, ppm): δ = 47.9 (2 C, *C*H_2CH=), 54.2 (2 C, *C*H_2CH_2), 63.1 (NCH_2C), 65.3 (2 C, *C*H_2Ph), 65.5 (C_{spiro}), 126.8 (Ph), 127.2 (Ph), 128.37 (Ph), 128.43 (*C*H=*C*H), 128.8 (Ph), 129.1 (Ph), 129.5 (br., Ph), 138.8, 140.6 (both C_{ipso}). FAB-MS (rel. intensity, %): *m/z* = 319 [M + H]$^+$ (32), 318 [M]$^+$ (33), 317 [M − H]$^+$ (47), 227 [M − $PhCH_2$]$^+$ (11), 134 [M − 2$PhCH_2$ − 2H]$^+$ (34), 91 [$PhCH_2$]$^+$ (100). HRMS (FAB): calcd. for $C_{22}H_{27}N_2$ [M + H]$^+$ 319.2174, observed 319.2173.

6,13-Bis(trifluoroacetyl)-6,13-diazadispiro[4.2.4.2]tetradeca-2,10-diene (14): Isolated as a colourless solid (mp. 212−213°C) in a 89% yield after chromatography (hexanes/ethyl acetate, 20:1). ^{1}H NMR ($CDCl_3$, ppm): δ = 2.27 (very br. d, J_{app} = 74.1 Hz, 4 H, CH_2-CH=), 3.05 (very br. d, J_{app} = 50.7 Hz, 4 H, CH_2CH=), 3.72 (br. s, 4 H, CH_2N), 5.69 (s, 4 H, C*H*=C*H*). ^{13}C NMR ($CDCl_3$, ppm): δ = 39.5 (br. s, 2 C, *C*H_2CH=), 41.1 (br. s, 2 C, *C*H_2CH=), 50.2 (2 C, *C*H_2N), 67.1 (2 C, C_{spiro}), 116.1 (q, $^2J_{C,F}$ = 288.9 Hz, 2 C, *C*F_3), 128.3 (4 C, *C*H=*C*H), 156.1 (q, $^3J_{C,F}$ = 35.4 Hz, 2 C, *C*=O). ^{19}F NMR ($CDCl_3$, ppm): δ = −69.3. FAB-MS (rel. intensity, %): *m/z* = 383 [M + H]$^+$ (100), 381 [M − H]$^+$ (40), 307 (16), 289 (11), 285 [M − $COCF_3$]$^+$ (7), 190 [M − 2$COCF_3$ + 2H]$^+$ (38), 79 [$C_4H_4N_2$ − H]$^+$ (99). HRMS (FAB): calcd. for $C_{16}H_{17}F_6N_2O_2$ [M + H]$^+$ 383.1194, observed 383.1204. Anal.: calcd. C 50.27, H 4.22, N 7.33; found C 50.41, H 4.17, N 7.21.

X-ray Crystallographic Study: Intensity data were collected on an Enraf−Nonius CAD-4 diffractometer, using a crystal of dimensions 0.50 × 0.35 × 0.25 mm, with graphite-monochromated Mo-K_α X-rays (λ = 0.71069) and ω-2θ scan. A total of 1849 reflections (of which 1841 were unique) in the range 2.4° < 2θ < 26.4° were collected at room temperature (ca. 20°C), and these were subsequently corrected for Lorentz effects, polarisation effects, and for linear absorption by a Ψ-scan method ($T_{max.,min.}$ = 0.98, 0.79). Crystal data: $C_{16}H_{16}F_6N_2O_2$ (382.31), crystal class monoclinic, space group $P2_1$, *a* = 8.254(2), *b* = 11.977(2), *c* = 8.972(2) Å, β = 105.63(3)°, V_c = 854.1(3) Å^3, D_c = 1.487 g cm^{-3}, *Z* = 2, *F*(000) = 392, μ(Mo-K_α) = 0.142 mm^{-1}.

The structure was solved using the direct methods option of SHELXS-97[19] and subsequently refined using SHELXL-97.[20] All non-hydrogen atoms were assigned anisotropic temperature factors and all hydrogen atom positions were determined by calculations. The refinement converged with R_1 = 0.0788 for 1642 data with $I \geq 2\sigma(I)$, 0.0819 for all data; wR_2 = 0.1699 {$w = 1/[\sigma^2(F_o^2) + (0.1322P)^2 + 0.0101P]$ where $P = (F_o^2 + 2F_c^2)/3$}, and GoF = 1.149. No parameter shifted in the final cycle. The Flack *x* parameter refined to 0.0(13) indicating that the correct absolute structure was chosen. The final difference map showed no peaks or troughs of electron density greater than +0.60 and −0.35 e·Å^{-3}, respectively.

CCDC-219722 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge at www.ccdc.cam.ac.uk/conts/retrieving.html [or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; Fax: (internat.) + 44-1223-336-033; E-mail: deposit@ccdc.cam.ac.uk].

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