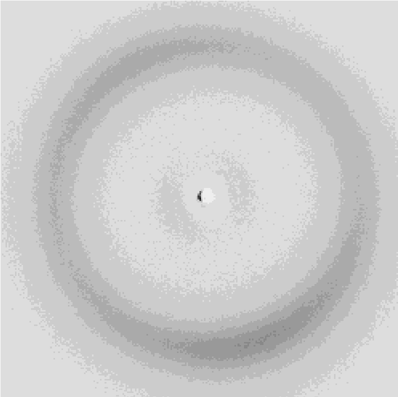

Figure 2. WAXS diagram of **PG1-1**.

time. Interestingly, in pronounced contrast to the structurally related dendrimers with mesogenic end groups[5] broad nematic phases with low viscosities were observed. A complete functionalization of the end groups with mesogens does not seem to be a prerequisite for LC behavior. In comparison with the mesogen-substituted dendrimers, the different behavior may be explained by the spatial distribution of functionalized end groups of the polyglycerols. In contrast to the perfect dendrimer structure the end groups are not located at the same distance from the core. Specific properties of branched molecules, for example, the absence of entanglements and the high concentration of end groups, are promising for the preparation of liquid crystalline materials with low viscosity and possibly short switching times.

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[9] Exemplified description of the synthesis of **PG2-2: PG2**[6] (0.177 g, 0.51 mmol), acid **2** (1.33 g, 3.51 mmol), and *N,N*-dimethylpyridinium *p*-toluenesulfonate (1.06 g, 3.60 mmol) were placed in a 50 mL Schlenk flask and dissolved in anhydrous DMF (13 mL). DIPC (0.6 mL, 3.79 mmol) was added to the clear solution. After the mixture was stirred for five days at room temperature, the solvent was removed and additional acid **2** (0.27 g, 0.71 mmol) suspended in CH_2Cl_2 (15 mL) was added together with DIPC (0.1 mL, 0.63 mmol)(exchange of solvent). After another three days reaction time at room temperature the mixture was twice washed with saturated $NaHCO_3$ solution and water. After removal of the solvent, the organic residue was extracted several times with methanol, dissolved in a little CH_2Cl_2 and precipitated into methanol (crude yield 0.91 g). The crude product was precipitated three times from CH_2Cl_2 into hot ethanol. Yield: 696 mg (61 %) white solid. ^1H NMR (300 MHz, $CDCl_3$, 298 K): $\delta = 7.7-7.3$ (m, 6H; NCC_6H_4), 6.85 (s, 2H; arom. H), 5.05 (d, 1H; COOCH), 4.35–4.0 (d, 1H; $COOCH_2$), 3.85 (s, 2H; $C_6H_4OC\mathit{H}_2$), 3.7–3.2 (m, 4H; $COOCCHC\mathit{H}_2OH$, $COOCHC\mathit{H}_2O$), 2.15 (s, 2H; CH_2COO), 1.65 (s, 2H; $C_6H_4OCH_2C\mathit{H}_2$), 1.6–1.25 (m, 6H; $OCOCH_2C\mathit{H}_2$, $OCO(CH_2)_6(C\mathit{H}_2)_2$), 1.2 (s, 8H; $OCO(CH_2)_2(C\mathit{H}_2)_4$).

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Ultrastable Mesoporous Aluminosilicates by Grafting Routes**

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There is currently great interest in the thermal and hydrothermal stability of surfactant-templated mesoporous silicas, and recent advances indicate that stable pure silica materials are obtainable.[1–3] However, of greater importance is the stabilization of heteroatom-containing mesoporous silicates which are useful as catalysts or ion exchangers. In particular Al-containing mesoporous molecular sieves which combine stability and enhanced acidity are desireable.[1] Despite the need for such aluminosilicates, there have been very few reports on the stabilization of Al-containing mesoporous

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frameworks. A significant step forward is the recent synthesis of Al-MCM-41 of excellent structural integrity and improved stability by postsynthesis grafting routes.[4–6]

Here it is shown that extremely stable mesoporous aluminosilicates with enhanced acidity and catalytic activity can be prepared by a combination of postsynthesis grafting and hydrothermal treatment. The remarkably beneficial effects of hydrothermal treatment on the properties of Al-grafted mesoporous silicas (prepared by aqueous or nonaqueous routes in order to illustrate the versatility of the grafting procedure) are described. The high thermal and hydrothermal stability presented here has not been previously observed for Al-containing mesoporous silicas.[7] Indeed in comparison to previously reported mesoporous aluminosilicates, the present Al-grafted materials can be described as ultrastable. Furthermore the present Al-grafted materials are also unique in that hydrothermal treatment (i.e., prolonged refluxing in distilled water), far from being detrimental, is beneficial with regard to their use as solid acid catalysts; the hydrothermally treated materials show an unusual reduction in Si/Al (the amount of Al per unit mass of material increases) accompanied by a sharp increase in acid content, which is manifested in higher catalytic activity for acid-catalyzed reactions.

The purely siliceous MCM-41 (herein designated Si-MCM) from which the Al-grafted materials were derived was prepared using normal procedures and had a surface area of 887 $m^2 g^{-1}$, a pore volume of 0.85 $cm^3 g^{-1}$, and a pore wall thickness of 16 Å.[8] The Al-grafted materials were prepared by two methods involving the reaction of Si-MCM with either an aqueous solution of aluminum chlorohydrate (ACH, sample CAH5) or with aluminum isopropoxide in nonaqueous media (hexane, sample CAP10). The hydrothermal stability of the Al-grafted materials was tested by subjecting the samples to refluxing in distilled water (with 1 L of water per gram of solid) for 16 to 150 h. This mode of hydrothermal treatment was selected so as to provide the sternest test of hydrothermal stability; MCM-41 materials generally exhibit greater stability to calcination in the presence of water vapor (steaming) than to boiling in water.[9] (For example steaming at 750 °C for 4 h had little effect on the structural integrity of the parent Si-MCM; however, on refluxing in water for 16 h, Si-MCM was virtually rendered amorphous and its surface area reduced by 65 % to 325 $m^2 g^{-1}$; see Figure 1 in the Supporting Information.)

As shown in Figure 1, the X-ray powder diffraction (XRD) patterns of CAH5 and CAP10 are typical of well-ordered MCM-41. Both materials show an intense (100) diffraction peak and some well-resolved higher order (110), (200), and (210) peaks, which are an indication of good long-range hexagonal ordering. There were no significant changes in the basal spacing (d_{100}) or XRD peak intensities and linewidths resulting from refluxing of the sample for up to 48 h, and materials refluxed for 150 h were still remarkably well ordered, indicating that the pore channel system of MCM-41 remains intact during the hydrothermal treatment. The retention of structural integrity in the refluxed Al-grafted samples is confirmed by the fact that their textural properties (Table 1) remain largely unaffected. Interestingly refluxing (for 16 or 48 h) results in an uncommon increase in both the surface area and pore volume. (The stability observed here is brought into sharp focus when one considers that, after 16 h in boiling water, a conventional Al-MCM-41 (Si/Al = 23:1) was rendered amorphous and its surface area reduced from 667 to 285 $m^2 g^{-1}$; see Figure 2 in the Supporting Information.)

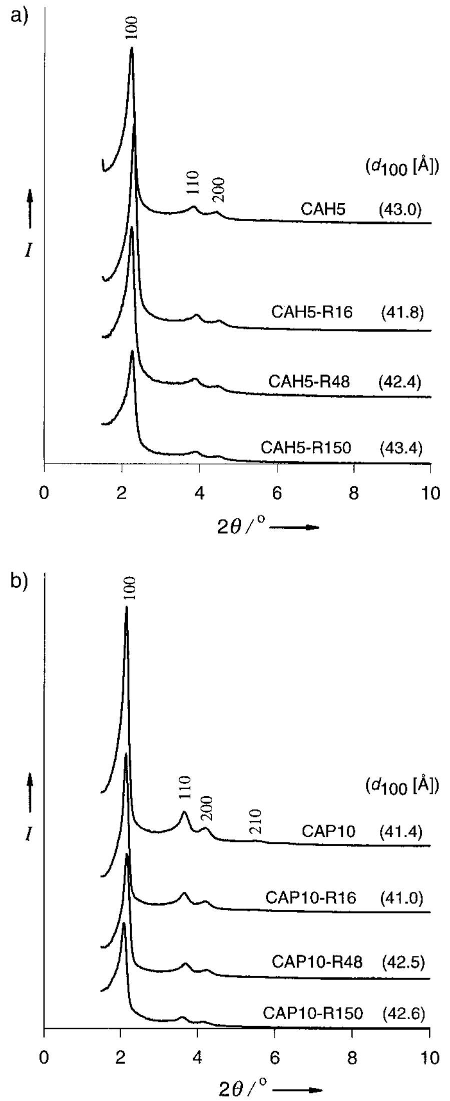

Figure 1. X-ray diffraction patterns of a) the "wet"-grafted CAH5 and b) the "dry"-grafted CAP10 mesoporous aluminosilicates before and after various hydrothermal tretments. The patterns were obtained from a Philips PW1710 diffractometer utilizing $Cu_{K\alpha}$ radiation ($\lambda = 1.5418$ Å) with a Ni filter for $K\beta$ attenuation. I = intensity.

The average pore diameter and pore wall thickness of the Al-grafted materials remained largely unaffected except for materials refluxed for 150 h, which had slightly wider pores and correspondingly thinner pore walls. It is, however, worth noting that the calculation of wall thickness based on XRD and Brunauer-Joyner-Halenda (BJH) data is subject to an element of error, though this will not affect the trends observed. Pore wall thickness is considered an important factor in determining the stability of mesoporous silicas,[2, 3] but despite having thinner pore walls, the "dry"-grafted CAP10 sample exhibits hydrothermal stability similar to that of the thicker walled "wet"-grafted CAH5. The stability of

Table 1. Elemental composition, textural properties, acidity, and catalytic activity of Al-grafted materials before and after various hydrothermal treatments.

Sample	Si/Al	Surface area [m^{2}g^{-1}]	Pore volume [cm^{3}g^{-1}]	APD[a] [Å]	Wall thickness[b] [Å]	Acidity[c]	Cumene conversion[d]
CAH5	6.1:1	753	0.62	25.8	23.9	0.88	0.98
CAH5-R16	5.1:1	834	0.70	24.9	23.4	1.25	1.33
CAH5-R48	4.5:1	902	0.70	26.8	22.2	1.38	1.34
CAH5-R150	4.2:1	724	0.65	31.0	19.1	1.29	1.32
CAP10	9.8:1	850	0.76	30.9	16.9	0.63	0.64
CAP10-R16	8.1:1	894	0.81	31.0	16.3	1.18	1.29
CAP10-R48	7.1:1	864	0.80	32.5	16.6	1.28	1.32
CAP10-R150	6.5:1	810	0.77	33.7	15.5	1.30	1.36

[a] APD = Average pore diameter (determined using BJH analysis of the desorption isotherm). [b] Wall thickness = unit cell parameter (a_o) − APD, where a_o was obtained from the XRD data using the formula $a_o = 2d_{100}/\sqrt{3}$. [c] Given in mmoles of H$^+$ per gram of sample. [d] Cumene cracking rate, in mmol per gram of catalyst per hour, after 20 min on stream. Total conversion equals a rate of 1.52. Under similar conditions the conversion rate over ultrastable Y zeolite (CBV 740, Si/Al = 21:1) and HY zeolite (Si/Al = 3.6:1) was 1.34 and 0.54, respectively.

these materials is therefore not simply due to their thicker (compared to Si-MCM) walls, but may also be related to pore wall stabilization by recrystallization involving the grafted Al.

The nature of the mesoporous structure and pore uniformity of CAH5 and CAP10 along with their refuxed analogues is illustrated by the nitrogen sorption isotherms in Figure 2. The isotherms, which all possess a steep step in the partial pressure range $(P/P_o) = 0.3-0.5$ are representative of materials with uniform sharply distributed pore radii. Only after refluxing for 150 h is there an increase in pore size and a broadening of the pore size distribution. The hydrothermal stability observed here is most likely due to crystallization effects (previously observed in zeolites) involving the grafted Al which act to heal defect sites in the structure of the MCM-41 materials.[10] Such restructuring may reduce the concentration of silanols (which are the weak links in the MCM-41 framework), thus stabilizing the structure. This is likely because the Al is initially grafted onto the pure silica material through silanol groups which are known to occur at defect sites.

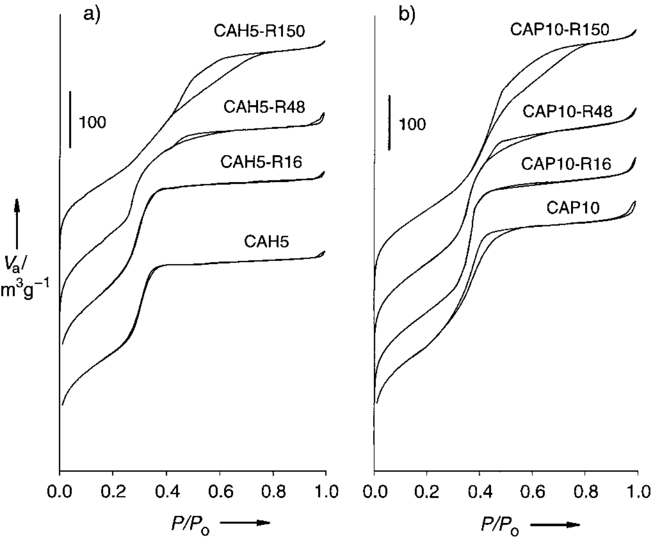

Figure 2. Nitrogen sorption isotherms for a) the "wet"-grafted CAH5 and b) the "dry"-grafted CAP10 mesoporous aluminosilicates before and after various hydrothermal tretments. P/P_o = partial pressure as a fraction of the saturation pressure (P_o), V_a = volume of adsorbed gas.

The effect of refluxing on the chemical composition of the Al-grafted materials (Table 1) is unusual in that the Si/Al ratio is reduced—that is, the amount of Al per gram of material (x_{Al}) is higher for the refluxed samples and increases with the severity of the refluxing. This is in sharp contrast to the extensive dealumination observed for conventional direct mixed-gel synthesized Al-MCM-41. (For example, the Si/Al ratio of a conventional Al-MCM-41 increased from 23:1 to 370:1 when subjected to refluxing in water for 16 h.) For the present Al-grafted materials it is silica and not Al which is preferentially removed by refluxing. Since the refluxing had no significant effect on structural integrity, it is likely that the extracted silica existed as a separate (amorphous) phase which was not part of the ordered aluminosilicate framework. Indeed when analyzed by scanning electron microscopy (SEM), the refluxed samples appeared to have fewer small "fluffy" particles, which were present in larger quantities in the parent Al-grafted samples deposited on larger particle aggregates (see Figure 3a in the Supporting Information). High-resolution transmission electron microscopy (HRTEM) has shown that the small particles are largely amorphous, while the larger particle aggregates are ordered.

Based on these observations it is logical to conclude that the small particles are (nonframework) amorphous silica which is removed during refluxing (by dissolution), leaving the Al-grafted MCM-41 framework (i.e., the large particle aggregates) intact. Further evidence to support the preferential extraction of silica was obtained from X-ray photoelectron spectroscopy (XPS), which indicated that the outer surface of the refluxed samples was enriched in Al—that is, the Al concentration gradient between the surface and bulk was greater for the refluxed samples. Furthermore refluxing (for upto 48 h) did not have any significant effect on the nature and environment of the Al nuclei; the ^{27}Al MAS NMR spectra shown in Figure 3 indicate that the ratio of tetrahedrally coordinated (framework) Al ($\delta = 53$) to octahedrally coordinated (nonframework) Al ($\delta = 0$) changed little. There was, therefore, no significant extraction of Al from tetrahedral (framework) positions except for samples refluxed for 150 h, as shown for CAP10 in Figure 3b.

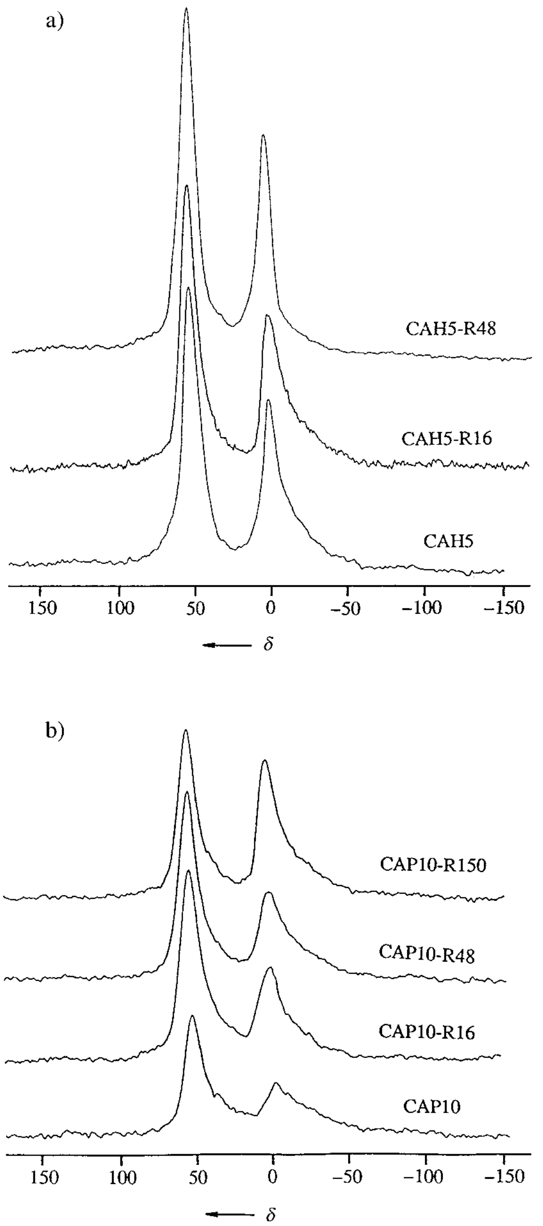

Figure 3. ^{27}Al MAS NMR spectra of a) the "wet"-grafted CAH5 and b) the "dry"-grafted CAP10 mesoporous aluminosilicates before and after various hydrothermal tretments. The spectra were recorded at 9.4 T using a Chemagnetics CMX-400 spectrometer with rotors 4 mm in diameter spun at 10 kHz. Before analysis the samples were fully hydrated.

The acid content of the Al-grafted samples and their refluxed analogues (Table 1) was determined using thermally programmed desorption of cyclohexylamine.[11, 12] Prior to thermogravimetric analysis, the samples containing the base (cyclohexylamine) were heated at 80 °C for 2 h. The weight loss due to amine desorption from acid sites between 300 and 450 °C was used to quantify the acidity in mmol of H$^+$ assuming that each base molecule interacts with one Brønsted acid site. The increase in aluminum per unit mass for the refluxed samples is accompanied by an increase in acid content. However, higher aluminum content alone cannot explain the increase in acidity since the acid content of Al-grafted materials with x_{Al} similar to that of the refluxed samples is much lower; a directly prepared ACH-grafted sample with Si/Al = 4.2:1 had an acid content (in millimoles of H$^+$ per gram of sample) of 0.89:1, compared to an acid content of 1.38 for CAH5-R48 (Si/Al = 4.5). It is therefore likely that refluxing has other beneficial effects. One possibility is that the "cleaning out" of some amorphous silica by desilylation improves access to the Al sites where the acid sites are located. SEM also shows that refluxing breaks up large particle aggregates into smaller ones, which may improve access to acid sites (see Figure 3 b in the Supporting Information).

The conversion of cumene (which requires medium to strong acid sites) was used to illustrate the catalytic potential of the hydrothermally treated Al-grafted materials.[4, 6] Catalytic cracking to benzene and propene was the main reaction with only trace amounts of α-methylstyrene (product of dehydrogenation over Lewis acid sites) being formed, indicating that the active sites are Brønsted acid sites.[13] The catalytic data (Table 1) show that the grafted materials possess considerable catalytic activity which dramatically increases on refluxing (see also Figure 4 in the Supporting Information). The increase in activity is in line with the changes in acid content, which indicates that refluxing results in an increase in Brønsted rather than Lewis acid sites; this was indeed confirmed by monitoring adsorbed pyridine using Fourier transform infrared (FT-IR) spectroscopy, which can distinguish between Brønsted and Lewis acid sites.[14]

The activity of the refluxed samples is comparable to that of USY zeolite (Si/Al = 21:1) and is in any case much higher than that of HY zeolite (Si/Al = 3.6:1) or conventional Al-MCM-41 of comparable aluminum content.[4, 6] This enhanced solid (Brønsted) acid capability combined with a stable, well-ordered structure possessing uniform (meso) pores opens up new opportunities in the use of mesoporous aluminosilicates. Although this report has given prominence to the unusual effects of refluxing in water, it is worth noting that the Al-grafted materials are thermally stable (1000 °C for 4 h) and can also withstand prolonged steaming at 750 °C. Apart from MCM-41, other mesoporous silicas such as MCM48, MSU-*n*, and SBA-*n* have been successfully utilized to prepare ultrastable aluminosilicates.

Experimental Section

The Al-grafted materials were prepared by an aqueous or nonaqueous method; in the aqueous (or wet) method the calcined Si-MCM (1.0 g) was added to a solution (50 mL) of ACH (0.48 mol L^{-1} with respect to Al) at 80 °C and stirred for 2 h at 80 °C. The resulting solid was obtained by filtration and thoroughly washed with distilled water (until it was free of Cl$^-$ ions), dried at room temperature, and calcined in air at 550 °C for 4 h. The resulting Al-grafted material, designated CAH5, had a bulk Si/Al ratio of 6.1:1. In the second nonaqueous (or dry) route Si-MCM (2.0 g) was dispersed in dry hexane (50 mL) and added to 150 mL dry hexane containing the appropriate amount of aluminum isopropoxide to give a grafting gel Si/Al ratio of 10:1. The resulting mixture was stirred for 10 min and allowed to react at room temperature for 24 h. The obtained powder was filtered, washed with dry hexane, dried at room temperature, and calcined at 550 °C for 4 h. The resulting material with a bulk Si/Al ratio of 9.8:1 was designated CAP10. To assess hydrothermal stability CAH5 and CAP10 were subjected to refluxing in distilled water (with 1 L of water per gram of solid) for 16–150 h. After refluxing the samples were dried at

130 °C for 16 h. The refluxed samples were designated CAH5-RX or CAP10-RX, where X is the reflux time in hours.

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Total Synthesis of (±)-Gelsemine[**]

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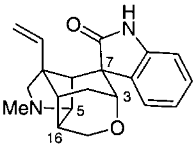
Matthew J. Sharp



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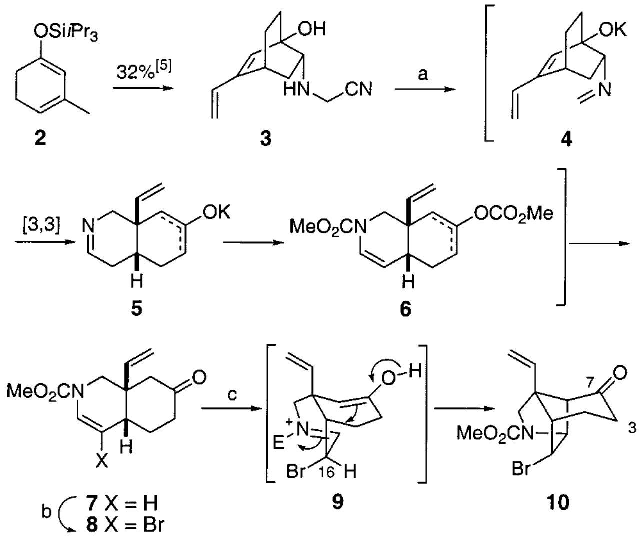
Gelsemine (**1**), the major alkaloid component of *Gelsemium sempervirens* (Carolina or yellow jasmine), was isolated in the 1870s.[1, 2] After eighty years of extensive, and largely inconclusive degradative studies, the structure was solved in 1959 by both NMR and X-ray spectroscopic methods.[3] The densely functionalized hexacyclic skeleton of gelsemine stimulated intensive synthetic efforts throughout the world, which resulted in four total syntheses of (±)-gelsemine.[4] In 1988 we described the preparation of an advanced pentacyclic intermediate,[5] which, although incorporating all the carbon atoms of gelsemine,[5c] did not ultimately prove to be a viable precursor to this hexacyclic alkaloid. Herein we report the total synthesis of (±)-gelsemine by a sequence whose key strategic steps are a sequential anionic aza-Cope rearrangement and Mannich cyclization, an intramolecular Heck reaction, and a complex base-promoted molecular reorganization to generate the hexacyclic ring system.

The azatricyclodecane ring system of gelsemine was assembled using a slight modification of the route we reported earlier (Scheme 1).[5] The sequence began with 1-triisopropylsiloxy-3-methyl-1,3-cyclohexadiene (**2**),[6] which was converted into the bicyclo[2.2.2]octene **3** in eight steps (32 % overall yield).[5] Exposure of **3** to potassium hydride and [18]crown-6 at room temperature promoted the anionic aza-Cope rearrangement of the derived formaldimine alkoxide **4**.[7] Quenching the resulting product **5** with excess methyl chloroformate, followed by selective cleavage of the carbonate functional group of **6** produced *cis*-hexahydroisoquinolinone **7** in 81 % yield. The enecarbamate functional group of **7** was selectively brominated and the resulting product **8** was heated at reflux in trifluoroacetic acid (TFA) to provide the azatricyclodecanone **10** as a single diastereomer in 67 % yield. In this Mannich cyclization, the tetrahydropyridine ring of **8** needs to adopt a high-energy boat conformation **9** in order for the iminium ion and the enol π system to overlap. Preferential cyclization of the thermodynamically favored C16 epimer **9** of the *N*-acyliminium intermediate, delivers tricyclic product, **10** with the bromine substituent on the *exo* face. By using this extensively optimized sequence, **10** could be prepared from commercially available 3-methylanisole in 12 steps and 16 % overall yield.



Scheme 1. Reaction conditions: a) KH, [18]crown-6, THF, rt; ClCO$_2$Me, DTBMP, −78 °C→rt; KOH, MeOH, H$_2$O, rt, 81 %; b) Br$_2$, 1,2,2,6,6-pentamethylpiperidine, CH$_2$Cl$_2$, −78 °C; c) TFA, reflux, 67 % over 2 steps. DTBMP = 2,6-di-*tert*-butyl-4-methylpyridine.

The next stage of the synthesis involved construction of the spirooxindole at C7 of **10** in such a way that C3 was substituted with a group containing an oxygen functionality that could be employed to form the pyran ring of gelsemine. This objective was accomplished by initially oxidizing the

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