One-Pot Synthesis of Polysubstituted Pyrrolidines from Aminonitriles

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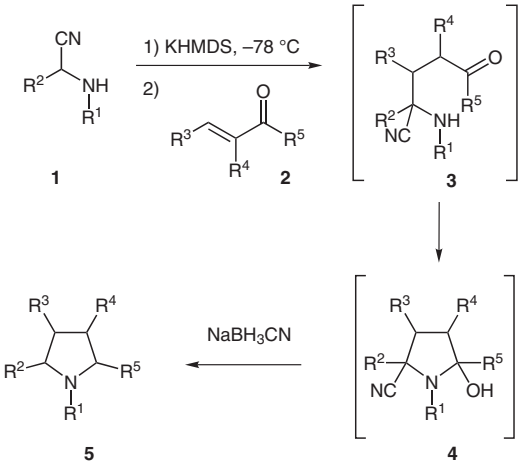
Received 15 October 2004; revised 8 December 2004

Abstract: α-Aminonitriles with a mono- or unsubstituted amino group as well as α-(alkylideneamino)nitriles can be employed as easily accessible α-aminocarbanion equivalents. Their α-deprotonation yields stabilized carbanions, which undergo smooth 1,4-addition to α,β-unsaturated carbonyl compounds. The resulting δ-keto-α-aminonitriles can be reductively cyclized to form polysubstituted pyrrolidines.

Key words: pyrrolidines, aminonitriles, Michael additions, reductions, combinatorial chemistry

Pyrrolidine alkaloids have been isolated from plants like tobacco, the English Bluebells *Hyacinthoides non-scripta*,[1] the shrub *Erythroxylum lucidum*,[2] from mushrooms,[3] microorganisms and various animals.[4–6] Apart from the monocyclic compounds like nicotine or hygrine, the pyrrolidine skeleton is contained in bicyclic alkaloids such as the pyrrolizidines, the indolizidines and the tropanes. These natural products exhibit a variety of biological effects and a considerable number of bioactive synthetic pyrrolidine derivatives are known as well. Consequently, numerous synthetic strategies for the construction of the pyrrolidine ring have been devised. Examples are 1,3-dipolar cycloadditions,[7–10] the Hofmann–Löffler–Freytag reaction,[11,12] the reductive amination of 1,4-diketones,[13] cyclizations of δ,ε-unsaturated amines[14] or aminoallenes,[15] and the aza-Cope–Mannich sequence.[16,17] However, most of these strategies do not allow the facile introduction of substituents into all positions or certain functionalities such as exomethylene or ester groups remain in the products. In addition, the intricate preparation of the respective starting materials is a drawback of many procedures.

The application of α-deprotonated N,N-disubstituted α-aminonitriles as acylanion equivalents is a well documented strategy for the preparation of 1,4-dicarbonyl compounds.[18–24] In contrast, N-monosubstituted and N-unsubstituted α-aminonitriles have only rarely been employed as CH-acidic pronucleophiles because the risk of a base induced elimination of HCN (retro-Strecker reaction) has to be taken into consideration.[25] On the other hand, these building blocks can serve as easily accessible α-aminocarbanion equivalents. To demonstrate the usefulness of this strategy, the preparation of polysubstituted pyrrolidines from aminonitriles was undertaken. N-monosubstituted aminonitriles **1** were deprotonated and reacted with α,β-unsaturated carbonyl compounds to yield the N-substituted δ-oxo-α-aminonitriles **3** which cyclize to 5-cyano-2-hydroxypyrrolidines **4**. These intermediates are unstable if the N-substituent has no electron-withdrawing effect. They can be doubly reduced by $NaBH_3CN$ to yield the corresponding pyrrolidines (Scheme 1).[26] In contrast to the related von Miller–Plöchl pyrrole synthesis,[27] the initial quantitative deprotonation of the aminonitrile **1** with KHMDS permits the free choice of the N-substituent and even α-aminonitriles with an unsubstituted amino group have been successfully employed as aminocarbanion equivalents, which could be illustrated by the synthesis of nornicotine (**5h**) and 3′-methylnornicotine (**5i**) (Table 1).



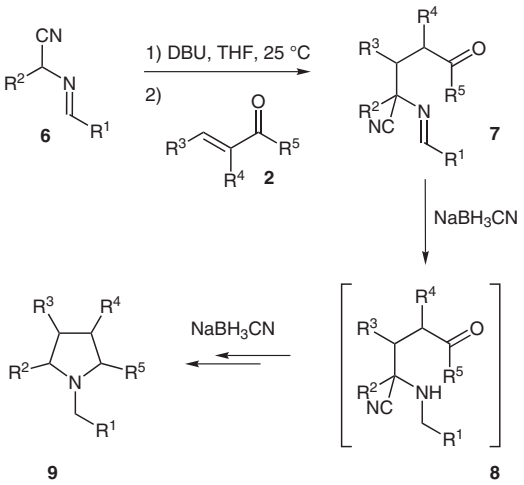
Scheme 1 Synthesis of polysubstituted pyrrolidines from α-aminonitriles

However, the anion-stabilizing effect of an aromatic α-substituent appears to be necessary to prevent the base-induced destruction of the substrate. Another disadvantage of the carbanions derived from compounds **1** is their high basicity, which may lead to the deporotonation of CH-acidic electrophiles like methyl vinyl ketone.

To overcome these drawbacks, a new strategy was developed. As α-(alkylideneamino)nitriles **6** are significantly more acidic than α-aryl aminonitriles, they can already be deprotonated with the amidine base DBU.[28] Their conjugate anions add smoothly to α,β-unsaturated ketones to yield α-(alkylidenamino)-δ-ketonitriles **7** which, unlike the corresponding intermediates **3**, are stable and can be isolated. Upon addition of $NaBH_3CN$ and acetic acid, the

SYNTHESIS 2005, No. 6, pp 0945–0956
Advanced online publication: 21.02.2005
DOI: 10.1055/s-2005-861838; Art ID: T11904SS

imine moiety in **7** is reduced to form the unstable aminoketone **8**. Subsequent reductive ring closure and expulsion of cyanide leads to polysubstituted pyrrolidines **9** (Scheme 2).[29]



Scheme 2 Synthesis of polysubstituted pyrrolidines from α-(alkylidenamino)nitriles

Both methods allow the 1,4-addition and the reduction to be performed in one pot. Although the latter procedure gives slightly lower yields, the presence of an aromatic substituent in position 2 or 5 is no longer required and enones with acidic protons can be used as substrates (Table 1, entries 10–18).

As would be expected from the conformation of the iminium ion formed by expulsion of the cyanide ion from the 2-cyanopyrrolidine in the penultimate reaction step, the *cis*-configured products were predominantly formed.[30] Their relative configuration was assigned via comparative NOE-experiments; the characteristic NMR shifts of 2,5-*cis*- and 2,5-*trans*-substituted pyrrolidines reported by Yamamoto et al. were observed as well.[13,31,32] As an additional proof, the configuration of the major diastereomer of compound **5b** was verified by X-ray crystallography of its picrate salt (See Figure 1).

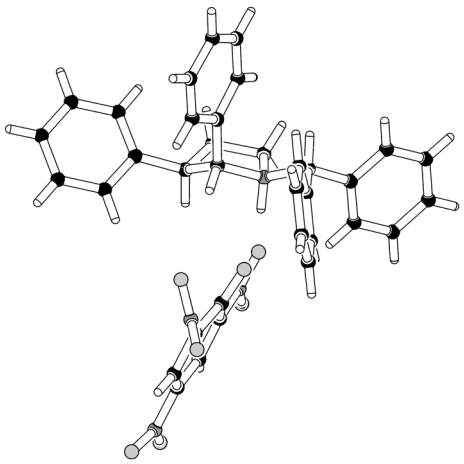
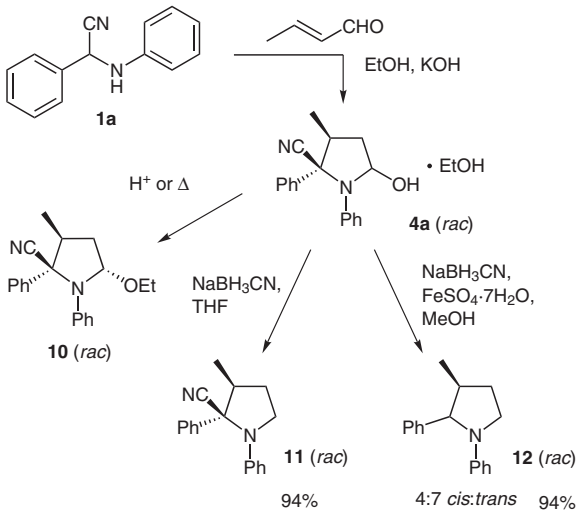


Figure 1 Crystal structure of the picrate salt of *cis*-**5b**

Surprisingly, the 1-substituted 3-alkyl-2-aryl substituted pyrrolidines **5d** and **5g** were obtained predominantly as the *trans*-diastereomers (Table 1, entries 4 and 7), whereas in the absence of a substituent in 1-position, the *cis*-diastereomer was the major product (Table 1, entry 9). Presumably, the conformation of the intermediate iminium ion accounts for this deviant behaviour.

Compounds of type **4** carry two different leaving groups adjacent to the nitrogen atom and represent unsymmetrical double iminium ion equivalents. Apart from their exhaustive reduction to pyrrolidines, a sequential functionalization of both α-positions should therefore be possible. To examine whether the difference in reactivity is sufficiently large, the reduction of compounds **4** was investigated in more detail. If R^1 was an alkyl substituent, the isolation and characterization of the singly reduced product failed. Therefore, the 1-aryl substituted 5-cyano-2-hydroxypyrrolidine **4a** was prepared by addition of aminonitrile **1a** to crotonaldehyde in ethanolic KOH (Scheme 3) according to a protocol by Treibs and Derra.[33]



Scheme 3 Preparation and reactions of hemiaminal **4a**.

The reported direct formation of the 5-cyano-2-ethoxypyrrolidine **10** could not be observed.[33] Instead, a crystalline solid was obtained, which turned out to be a 1:1 cocrystallizate of hemiaminal **4a** with ethanol (The relative configuration at C-2 could not be assigned). Traces of acid, as present in deuterochloroform, or elevated temperatures suffice to convert **4a** to the hemiaminal **10**, the relative configuration of which was elucidated by X-ray crystallography (Figure 2). The lower electron density at the aniline nitrogen decelerates the reduction of **4a** with $NaBH_3CN$. In particular, the elimination of the cyano group was so slow that cyanopyrrolidine **11** could be isolated as the only product in 94% yield. Accordingly, the double reduction of **4a** to the pyrrolidine **12** required the assistance of metal salts. Various authors have employed Hg^{2+} and Ag^+ ions for the activation of aminonitriles,[34–36] whereas we found Fe^{2+} ions to be equally effective. As with compounds **5d** and **5g**, the *trans*-diastereomer of the

Table 1 Synthesis of Pyrrolidines from α-Aminonitriles and α-(Alkylidenamino)nitriles (Schemes 1 and 2)

Entry	Nitrile	R^1	R^2	R^3	R^4	R^5	Product	dr (*cis*/*trans*)[a]	Overall yield (%)
1	**1b**	$CHPh_2$	Ph	H	H	H	**5a**	–	80
2	**1b**	$CHPh_2$	Ph	Ph	H	H	**5b**	4:1	49
3	**1c**	Me	2-naphthyl	H	H	H	**5c**	–	46
4	**1c**	Me	2-naphthyl	Me	H	H	**5d**	1:1.7	77
5	**1c**	Me	2-naphthyl	H	Me	H	**5e**	3:1	82
6	**1c**	Me	2-naphthyl	Ph	H	Ph	**5f**	10:1[b]	83
7	**1d**	4-$MeOC_6H_4CH_2$	Ph	Me	H	H	**5g**	1:2.6	75
8	**1e**	H	3-pyridyl	H	H	H	**5h**	–	12[c]
9	**1e**	H	3-pyridyl	Me	H	H	**5i**	1.5:1	24
10	**6a**	3,4-$(MeO)_2C_6H_3$	H	H	H	Me	**9a**	–	64
11	**6a**	3,4-$(MeO)_2C_6H_3$	H	H	H	Et	**9b**	–	58
12	**6a**	3,4-$(MeO)_2C_6H_3$	H	Ph	H	Ph	**9c**	–[d]	50
13	**6b**	2-naphthyl	H	H	H	Me	**9d**	–	46
14	**6b**	2-naphthyl	H	H	H	Et	**9e**	–	51
15	**6c**	3,4-$(MeO)_2C_6H_3$	$PhCH_2$	H	H	Me	**9f**	1.4:1	77
16	**6c**	3,4-$(MeO)_2C_6H_3$	$PhCH_2$	Ph	H	Ph	**9g**	14:20:1:5[e]	36
17	**6d**	3,4-$(MeO)_2C_6H_3$	Ph	H	H	Me	**9h**	1:1	84
18	**6d**	3,4-$(MeO)_2C_6H_3$	Ph	H	H	Et	**9i**	1.4:1	76

[a] Determined by ^1H NMR spectroscopy.
[b] Only two diastereomers were formed, the major one being the all-*cis*. The configuration of the minor diastereomer was not assigned.
[c] To simplify purification, the compound was converted to the *N*-tosyl derivative.
[d] *trans*-Compound not detected.
[e] All-*cis*:2,3-*trans*-3,5-*cis*:2,3-*cis*-3,5-*trans*:2,3-*trans*-3,5-*trans*.

3-alkyl-2-aryl-substituted pyrrolidine **12** was predominantly formed (vide supra).

In summary, we have demonstrated that polysubstituted pyrrolidines can be synthesized from aminonitriles and α,β-unsaturated carbonyl compounds in a short and efficient manner. *N*-Aryl-substituted 5-cyano-2-hydroxypyrrolidines have been selectively reduced to 2-cyanopyrrolidines, providing the opportunity for further transformations of the nitrile function.

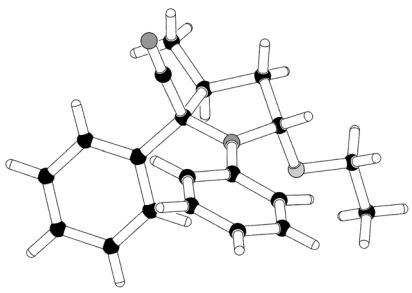


Figure 2 Crystal structure of hemiaminal **10**

THF was dried by distillation from Na/benzophenone. Cinnamaldehyde and benzaldehyde were distilled before use. All other solvents and reagents were purchased from commercial suppliers and were used without further purification. Petroleum ether used had bp 40–70 °C. TLC was performed on aluminum sheets coated with silica gel (60 F_{254}, E. Merck) or alumina (N/UV_{254}, Macherey-Nagel). Preparatvie TLC was performed on PSC glass plates (silica gel 60 F_{254}, 2 mm, 20 × 20 cm, with concentration zone, E. Merck). If not otherwise stated, flash chromatography was carried out on silica gel (32–63 μm, 60 Å, MP Biomedicals GmbH); alternatively, alumina N (50–200 μm, Acros) was used. Analytical RP-HPLC separations were performed with a Merck Hitachi L-6200 pump and a Merck Hitachi L-4200 UV/Vis Detector. For preparative separations, Knauer MiniStar K-500-pumps and a Knauer Variable Wavelength Monitor were used. ^1H NMR and ^{13}C NMR spectra were recorded on a Bruker AC 300 or AMX 400 instrument, chemical shifts were referenced to the signal of the solvent ($CDCl_3$: $\delta_H = 7.26$, $\delta_C = 77.0$). Where indicated, signals were assigned based on DEPT, gs-COSY or gs-HMQC experiments. Some of the coupling constants were determined by Lorentz-Gauss transformation of the FID. The relative configurations of the products were assigned with the aid of transient NOE experiments. ESI mass spectra were recorded on a Finnigan Navigator instrument from a solution of the

sample in MeCN–H_2O (70:30); ESI-HRMS spectra were measured on a Waters Q-TOF-Ultima 3 (HCO_2Na as internal reference), or on the same apparatus equipped with a LockSpray interface (HCO_2Na or NaI/CsI as external reference). IR spectra were recorded on a Perkin-Elmer 1760X FTIR-spectrometer or a Jasco FT/IR-470 plus with ATR unit.

Anilino(phenyl)acetonitrile (1a)[37]

Aniline (22.8 mL, 0.25 mol) and benzaldehyde (25.3 mL, 0.25 mol) were dissolved in HOAc (30 mL). A sat. solution of KCN (16.3 g, 0.25 mol) in H_2O was added and the mixture was stirred for 6 h. The precipitated yellow solid was recrystallized from Et_2O–hexane. The product was collected by filtration and washed with Et_2O–hexane (1:3) to yield **1a** as colorless crystals (43.3 g, 83%); mp 84.5–85 °C (Lit.[37] mp 84–85 °C).

[(Benzhydryl)amino](phenyl)acetonitrile (1b)

This compound was prepared according to Jochims et al.[38] from benzaldehyde (3.18 g, 30 mmol), benzhydrylamine (5.50 g, 30 mmol) and KCN (3.91 g, 60 mmol). Instead of distilling out the solvent, the reaction mixture was partitioned between aq $NaHCO_3$ and CH_2Cl_2. The aqueous phase was extracted with CH_2Cl_2 (2 ×), the combined organic layers were washed with aq $NaHCO_3$ and 0.1 N NaOH, dried (Na_2SO_4) and concentrated in vacuo. Recrystallization from EtOH gave **1b** as colorless crystals (8.07 g, 90%); mp 99 °C (Lit.[38] mp 98–100 °C).

(Methylamino)(2-naphthyl)acetonitrile (1c)

The aminonitrile **1c** was prepared from 2-naphthaldehyde (8.0 g, 51 mmol), methylamine (33% solution in EtOH, 9.6 mL, 77 mmol) and KCN (4.3 g, 66.7 mmol) according to the method of Jochims et al.,[38] but no ultrasonication was used. Work-up was carried out as in the preparation of **1b**. Crystallization from EtOH–cyclohexane gave **1c** as light yellow crystals (8.1 g, 81%); mp 72–73.5 °C; R_f 0.34 (petroleum ether–EtOAc, 1:1).

IR (KBr): 3272, 2227, 1602, 1508, 1450, 1358, 1124, 1096, 823, 779, 761 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 8.03 (s, 1 H, H-1), 7.82–7.91 (m, 3 H, Naph), 7.59 (dd, 1 H, *J* = 8.6, 1.9 Hz, H-3), 7.48–7.55 (m, 2 H, Naph), 4.94 (s, 1 H, $H_α$), 2.62 (s, 3 H, CH_3), 1.61 (br s, 1 H, NH).

^{13}C NMR (75.4 MHz, $CDCl_3$): δ = 133.2, 132.9, 131.8 (C-4a, C-8a, C-2), 128.8, 128.1, 127.6, 126.7, 126.6, 126.4, 124.7 (Naph), 118.5 (CN), 56.0 ($C_α$), 33.6 (CH_3).

ESI-MS: *m*/*z* (%) = 238.2 ([M + H + MeCN]$^+$, 18), 197.2 ([M + H]$^+$, 21), 170.1 ([M – CN]$^+$, 100).

Anal. Calcd for $C_{13}H_{12}N_2$: C, 79.56; H, 6.16; N, 14.27. Found: C, 79.79; H, 6.18; N, 14.07.

(4-Methoxybenzylamino)(phenyl)acetonitrile (1d)

Addition of KCN (4.3 g, 66 mmol) and a solution of benzaldehyde (4.2 g, 40 mmol) in MeOH (25 mL) to a mixture of 4-methoxybenzylamine (8.2 g, 60 mmol), 20% HCl (12 mL) and H_2O (30 mL) gave a light yellow oil, which was purified by column chromatography (cyclohexane–EtOAc, 5:1) to give **1d** (9.1 g, 90%) as a light yellow oil; R_f 0.28 (cyclohexane–EtOAc, 3:1).

IR (film): 3323, 2935, 2227, 1612, 1585, 1513, 1249, 1176, 1033, 831, 698 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.52–7.56 (m, 2 H, C_6H_5), 7.37–7.44 (m, 3 H, C_6H_5), 7.31–7.36 (m, 2 H, H-2′,6′), 6.88–6.92 (m, 2 H, H-3′,5′), 4.73 (s, 1 H, $H_α$), 4.01 (d, 1 H, *J* = 12.7 Hz, ArCH_2-a), 3.90 (d, 1 H, *J* = 12.7 Hz, ArCH_2-b), 3.81 (s, 3 H, OCH_3), 1.85 (s, 1 H, NH).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 159.0 (C-4′), 134.8, 130.0 (2 Ar-C-1), 129.6 (2 C), 128.9 (3 C), 127.2 (2 C), 118.7 (CN), 113.9 (C-3′,5′), 55.2, 53.2 (OCH_3, $ArCH_2$), 50.6 ($C_α$).

ESI-MS: *m*/*z* (%) = 478.2 ([2 M – CN]$^+$, 26), 226.2 ([M – CN]$^+$, 100).

(Amino)(3-pyridyl)acetonitrile (1e)

The compound was prepared according to Sauerberg et al.;[39] brown oil; R_f 0.08 (cyclohexane–EtOAc, 1:1 + 1% $EtNMe_2$, alumina).

IR (film): 3435, 2240, 1642, 1598, 1483, 1431, 1297, 1197, 1090, 1030, 954, 710 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 8.77 (dt, 1 H, J_d = 2.4 Hz, J_t = 0.8 Hz, H-2), 8.61 (br dd, 1 H, *J* = 4.8, 1.7 Hz, H-6), 7.87 (dddd, 1 H, *J* = 7.9, 2.4, 1.7, 0.8 Hz, H-4), 7.34 (ddd, 1 H, *J* = 7.9, 4.8, 0.8 Hz, H-5), 4.95 (br s, 1 H, $H_α$), 2.00 (br s, 2 H, NH_2).

^{13}C NMR (75.4 MHz, $CDCl_3$): δ = 150.3 (C-2), 148.3 (C-6), 134.3 (C-4), 132.0 (C-3), 123.7 (C-5), 120.0 (CN), 45.2 ($C_α$).

ESI-MS: *m*/*z* (%) = 302.2 (50), 134.0 ([M + H]$^+$, 100).

5-Hydroxy-3-methyl-1,2-diphenylpyrrolidine-2-carbonitrile·Ethanol (4a)

To a solution of aminonitrile **1a** (5.0 g, 24.0 mmol) and crotonaldehyde (2.21 mL, 26.8 mmol) in EtOH (25 mL) was added ethanolic KOH until pH 8 was reached. The reaction mixture was stirred overnight under argon. Crystals separated from the mixture and the solution was cooled to 0 °C to complete crystallization. The product was collected by filtration and washed with cold EtOH to yield a colorless crystalline solid (4.81 g, 62%); mp 72 °C (dec.); R_f 0.38 (cyclohexane–EtOAc, 10:1 + 1% $EtNMe_2$).

^1H NMR (300 MHz, $CDCl_3$): δ = 7.52–7.55 (m, 2 H, H-3″,5″), 7.28–7.37 (m, 3 H, H-2″,6″, H-4″), 7.08–7.13 (m, 2 H, H-3′,5′), 6.73–6.79 (m, 3 H, H-2′,6′, H-4′), 5.53–5.55 (m, 1 H, H-5), 3.69 [m, 2 H, CH_2OH (EtOH)], 2.94 (d, 1 H, *J* = 3.9 Hz, 5-OH), 2.65–2.75 (m, 1 H, H-3), 2.13–2.17 (m, 2 H, H-4a, H-4b), 1.54 (t, 1 H, *J* = 3.3 Hz, EtO*H*), 1.21 [t, 3 H, *J* = 6.8 Hz, CH_2CH_3 (EtOH)], 1.20 (d, 3 H, *J* = 6.6 Hz, 3-CH_3).

Pyrrolidines 5 from Aminonitriles 1; General Procedure

To a stirred solution of the α-aminonitrile **1** (2.8 mmol) in THF (27 mL) was added a freshly prepared solution of KHMDS (3.1 mmol, 1.1 equiv) in THF (5 mL) at –78 °C under argon. After 3 min, a solution of the α,β-unsaturated carbonyl compound **2** (3.1 mmol, 1.1 equiv) in THF (5 mL) was added and the mixture was stirred for 30 min. A mixture of EtOH (167 mmol, 60 equiv) and HOAc (17 mmol, 6 equiv) was added and the mixture was warmed to 0 °C. After the addition of solid $NaBH_3CN$ (8.5 mmol, 3 equiv), the mixture was stirred overnight at r.t. The mixture was partitioned between aq 1 N NaOH and EtOAc, the organic layer was separated and washed with a mixture of brine and aq 1 N NaOH (9:1). The organic layer was extracted with 0.2–1 N HCl (3 ×) and the combined aqueous phases were brought to pH 12 by addition of NaOH. Extraction with CH_2Cl_2, drying (Na_2SO_4) and evaporation of the solvent in vacuo gave a crude product, which, if necessary, was further purified by column chromatography or preparative TLC. Those compounds which were too lipophilic for an extraction with aq HCl were directly purified by chromatographic methods.

1-Benzhydryl-2-phenylpyrrolidine (5a)

Compound **5a** was obtained according to the general procedure from **1b** (1 g, 3.4 mmol) and acrolein (246 μL, 3.7 mmol) as a colorless oil without further purification (840 mg, 80%); R_f 0.62 (cyclohexane–EtOAc, 3:1).

IR (film): 3026, 2965, 2830, 1601, 1492, 1453, 1074, 1030, 760, 702 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.27–7.45 (m, 9 H, C_6H_5), 7.10–7.25 (m, 6 H, C_6H_5), 4.86 (s, 1 H, Ph_2CH), 3.59 (dd, 1 H, *J* = 8.2, 6.5 Hz, H-2), 3.15 (ddd, 1 H, *J* = 9.1, 7.4, 2.6 Hz, H-5a), 2.30 (d-pseudo-t, 1 H, J_t = 9.1 Hz, J_d = 7.4 Hz, H-5b), 2.03–2.20, 1.87–2.03, 1.61–1.80 (3 m, 4 H, H-3a, H-3b, H-4a, H-4b).

^{13}C NMR (75.4 MHz, $CDCl_3$): δ = 145.1, 142.8, 138.9 (3 Ph-C-1), 130.0, 128.3, 128.1, 127.8, 127.6, 127.4, 126.9, 126.6, 126.3 (C_6H_5), 66.9, 64.9 (C-2, Ph_2CH), 48.0 (C-5), 34.8 (C-3), 22.8 (C-4).

ESI-MS: *m*/*z* (%) = 370.1 (12), 314.0 ([M + H]$^+$, 100), 167.0 ([Ph_2CH]$^+$, 71).

HRMS: *m*/*z* calcd for [M + H]$^+$: 314.1909; found: 314.1909.

1-Benzhydryl-2,3-diphenylpyrrolidine (5b)

Compound **5b** was obtained according to the general procedure from **1b** (706 mg, 2.37 mmol) and cinnamaldehyde (0.33 mL, 2.65 mmol). The reaction mixture was not extracted with HCl. Purification of the crude product by preparative TLC gave a 4:1 mixture of *cis*- and *trans*-**5b** (457 mg, 49%). A portion of the mixture (104 mg) was separated by preparative HPLC (Phenomenex Luna C18, 250 × 21.2 mm), MeCN + 0.1% formic acid:H_2O + 0.1% formic acid = 50:50 to 90:10 in 45 min, the second product was eluted with pure MeCN.

***cis*-5b**

Yield: 77.4 mg; colorless oil; R_t 70 min; R_f 0.49 (hexane–EtOAc, 10:1 + 1% $EtNMe_2$).

IR (KBr): 3026, 2963, 2817, 1950, 1889, 1808, 1738, 1601, 1493, 1453, 1241, 1074, 1030, 764, 740, 699 cm^{-1}.

^{1}H NMR, COSY (600 MHz, $CDCl_3$): δ = 6.88–7.44 (m, 20 H, C_6H_5), 5.00 (s, 1 H, Ph_2CH), 4.10 (d, 1 H, *J* = 8.2 Hz, H-2), 3.56 (pseudo-q, 1 H, *J* = 8 Hz, H-3), 3.36 (ddd, 1 H, *J* = 9.4, 7.9, 2.3 Hz, H-5a), 2.70 (pseudo-q, 1 H, *J* = 9 Hz, H-5b), 2.35 (mc, 1 H, H-4a), 2.12 (mc, 1 H, H-4b).

Irradiation at 2.12 ppm (H-4b) enhanced the signals at 4.10 ppm (H-2, 0.4%), 3.56 ppm (H-3, 2.6%), 3.36 ppm (H-5a, 0.9%), 2.70 ppm (H-5b, 3.0%), 2.35 ppm (H-4a, 10.6%). Irradiation at 2.35 ppm (H-4a) enhanced the signals at 4.10 ppm (H-2, 0.2%), 3.36 ppm (H-5a, 2.7%), 2.12 ppm (H-4b, 10.6%). Irradiation at 3.56 ppm (H-3) enhanced the signals at 5.00 ppm (Ph_2CH, 0.3%), 4.10 ppm (H-2, 3.4%), 2.70 ppm (H-5b, 1.2%), 2.12 ppm (H-4b, 2.2%). Irradiation at 4.10 ppm (H-2) enhanced the signals at 5.00 ppm (Ph_2CH, 1.3%), 3.56 ppm (H-3, 3.8%), 2.70 ppm (H-5b, 1.0%).

^{13}C NMR, HMQC (150.9 MHz, $CDCl_3$): δ (*cis*/*trans* mixture) = 143.7, 142.4 (2 C), 138.1 (4 Ph-C-1^t) 142.6, 141.3, 140.7, 139.7 (4 Ph-C-1^c), 130.2 (2 C^t), 129.7 (2 C^c), 128.8 (2 C^c), 128.5 (2 C^c), 128.3 (2 C^t), 128.1 (4 C^t), 128.1 (2 C^c), 127.9 (2 C^c), 127.8 (2 C^t), 127.8 (2 C^c), 127.7 (6 C^t) 127.3 (2 C^c), 127.2 (2 C^c), 127.0 (1 C^t), 126.9 (1 C^c), 126.9 (1 C^t), 126.4 (1 C^c) 126.3 (1 C^t) 126.1 (1 C^c, 1 C^t), 125.7 (1 C^c, C_6H_5), 74.1 (C-2^t), 69.8 (C-2^c), 69.1 (Ph_2CH^c), 65.8 (Ph_2CH^t), 54.3 (C-3^t), 49.5 (C-3^c), 48.7 (C-5^c), 46.8 (C-5^t), 31.9 (C-4^t), 29.5 (C-4^c). Note: The indices *c* and *t* denote the *cis*- and *trans*-isomer.

ESI-MS: *m*/*z* (%) = 390.4 ([M + H]$^+$, 100), 167.0 ([Ph_2CH]$^+$, 20).

HRMS: *m*/*z* calcd for [M + H]$^+$: 390.2223; found: 390.2217.

***trans*-5b**

Yield: 10.3 mg (losses due to imperfect HPLC-gradient); yellowish oil; R_f 55 min; R_f 0.49 (hexane–EtOAc, 10:1 + 1% $EtNMe_2$.

IR (film): 3083, 3059, 3026, 2930, 1601, 1492, 1453, 1073, 1029, 769, 733, 700 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.08–7.45 (m, 18 H, C_6H_5), 6.87–6.95 (m, 2 H, C_6H_5), 4.93 (s, 1 H, Ph_2CH), 3.54 (d, 1 H, *J* = 8.0 Hz, H-2), 3.30 (ddd, 1 H, *J* = 9.0, 8.0, 4.1 Hz, H-5a), 3.18 (d-pseudo-t, 1 H, J_d = 9.5 Hz, J_t = 8 Hz, H-3), 2.64 (pseudo-q, 1 H, *J* = 9 Hz, H-5b), 2.41 (mc, 1 H, H-4a), 1.85 (mc, 1 H, H-4b).

Irradiation at 1.85 ppm (H-4b) enhanced the signals at 2.64 ppm (H-5b, 3.9%), 2.41 ppm (H-4a, 20.2%). Irradiation at 3.54 ppm (H-2) enhanced the signals at 4.93 ppm (Ph_2CH, 4.1%), 2.64 ppm (H-5b, 2.7%). Irradiation at 4.93 ppm (Ph_2CH) enhanced the signals at 3.54 ppm (H-2, 2.3%), 2.64 ppm (H-5b, 0.4%).

ESI-MS: *m*/*z* = 390.4 ([M + H]$^+$, 100), 167.0 ([Ph_2CH]$^+$, 29).

HRMS: *m*/*z* calcd for [M + H]$^+$: 390.2223; found: 390.2229.

1-Methyl-2-(2-naphthyl)pyrrolidine (5c)

Compound **5c** was obtained according to the general procedure from **1c** (504 mg, 2.57 mmol) and acrolein (0.19 mL, 2.85 mmol) as a yellow oil (crude yield: 581 mg). Purification of a portion (289 mg) by flash chromatography (hexane–EtOAc, 10:1 +1% $EtNMe_2$) gave pure **5c** (125 mg, 46%) as a colorless oil; R_f 0.20 (hexane–EtOAc, 10:1 + 1% $EtNMe_2$).

IR (film): 2965, 2780, 1601, 1456, 1370, 1323, 1211, 856, 819, 746 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.79–7.87 (m, 3 H, Naph), 7.77 (br s, 1 H, H-1′), 7.52 (dd, 1 H, *J* = 8.5, 1.7 Hz, H-3′), 7.40–7.49 (m, 2 H, Naph), 3.30 (mc, 1 H, H-5a), 3.21 (pseudo-t, 1 H, *J* = 8 Hz, H-2), 2.34 (pseudo-q, 1 H, *J* = 9 Hz, H-5b), 2.22 (s, 3 H, NCH_3), 2.17–2.28, 1.94–2.09, 1.79–1.93 (3 m, 4 H, H-3a, H-3b, H-4a, H-4b).

^{13}C NMR (75.4 MHz, $CDCl_3$): δ = 140.7 (C-2′), 133.4, 132.9 (C-4a′, C-8a′), 128.2, 127.7, 127.6, 126.2, 125.9, 125.6, 125.4 (Naph), 71.8 (C-2), 57.2 (C-5), 40.6 (CH_3N), 35.0 (C-3), 22.6 (C-4).

ESI-MS: *m*/*z* = 212.1 ([M + H]$^+$, 100%).

HRMS: *m*/*z* calcd for [M + H]$^+$: 212.1439; found: 212.1438.

1,3-Dimethyl-2-(2-naphthyl)pyrrolidine (5d)

Compound **5d** was obtained according to the general procedure from **1c** (547 mg, 2.79 mmol) and crotonaldehyde (0.25 mL, 3.00 mmol) as a yellow oil (crude yield: 538 mg, *cis*/*trans* = 1:1.7). Purification of a portion (225 mg) by column chromatography (hexane–EtOAc, 10:1 + 1% $EtNMe_2$) gave pure *cis*-**5d** (77 mg, 29%, colorless oil) and *trans*-**5d** (105 mg, 39%, yellowish oil), as well as 23 mg (9%) of a mixture of both products. For NMR-data of both isomers, see ref.[26]

***cis*-5d**

R_f 0.21 (hexane–EtOAc, 10:1 + 1% $EtNMe_2$).

IR (film): 3056, 2959, 2774, 1509, 1453, 1374, 1208, 1168, 1021, 856, 824, 757 cm^{-1}.

HRMS: *m*/*z* calcd for [M + H]$^+$: 226.1596; found: 226.1592.

***trans*-5d**

R_f 0.14 (hexane–EtOAc, 10:1 + 1% $EtNMe_2$).

IR (film): 3055, 2955, 2774, 1508, 1452, 1375, 1025, 854, 819, 744 cm^{-1}.

HRMS: *m*/*z* calcd for [M + H]$^+$: 226.1596; found: 226.1604.

1,4-Dimethyl-2-(2-naphthyl)pyrrolidine (5e)

Compound **5e** was obtained according to the general procedure from **1c** (500 mg, 2.55 mmol) and methacrolein (231 μL, 2.85 mmol) as a colorless oil (471 mg, 82%, 3:1 mixture of *cis*/*trans*-isomer); R_f 0.44 (cyclohexane–EtOAc, 5:1 + 1% $EtNMe_2$).

IR (film): 2955, 2772, 1601, 1509, 1452, 1372, 1334, 1234, 857, 818, 746 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ (*cis*/*trans* mixture) = 7.80–7.86 (m, 3 H, Naph), 7.77 (br s, 0.75 H, H-1′^{c}), 7.76 (br s, 0.25 H, H-1′^{t}), 7.42–7.56 (m, 3 H, Naph), contained in this multiplet: 7.54 (dd, 0.75

H, J = 8.7, 1.7 Hz, H-3′^{c}), 3.41 (dd, 0.25 H, J = 9.2, 6.9 Hz, H-5a^t), 3.33 (t, 0.25 H, J = 8.5 Hz, H-2^t), 3.28 (dd, 0.75 H, J = 10.0, 6.8 Hz, H-2^c), 2.95 (dd, 0.75 H, J = 9.3, 2.6 Hz, H-5a^c), 2.50–2.63 (m, 1 H, H-5b^c, H-4^t), 2.43 (ddd, 0.75 H, J = 12.5, 8.5, 6.8 Hz, H-3a^c), 2.27–2.37 (m, 0.75 H, H-4^c), 2.21 (s, 0.75 H, $NCH_3{}^t$), 2.18 (s, 2.25 H, $NCH_3{}^c$), 2.09 (ddd, 0.25 H, J = 13.0, 10.0, 8.5 Hz, H-3a^t), 2.01 (t, 0.25 H, J = 9.2 Hz, H-5b^t), 1.83 (ddd, 0.25 H, J = 13.0, 8.5, 5.9 Hz, H-3b^t), 1.47 (ddd, 0.75 H, J = 12.5, 10.0, 6.4 Hz, H-3b^c), 1.22 (d, 2.25 H, J = 6.8 Hz, $CH_3{}^c$), 1.10 (d, 0.75 H, J = 6.8 Hz, $CH_3{}^t$).

Irradiation at 2.95 ppm (H-5a^c) enhanced the signals at 2.57 ppm (H-5b^c, 10.9%), 2.18 ppm ($NCH_3{}^c$, 1.6%), 1.22 ppm ($CH_3{}^c$, 2.0%). Irradiation at 1.47 ppm (H-3b^c) enhanced the signals at 7.77 ppm (H-1′^{c}, 0.8%), 7.54 ppm (H-3′^{c}, 2.2%), 3.28 ppm (H-2^c, 0.9%), 2.43 (H-3a^c, 11.2%), 2.30 (H-4^c, 2.3%), 1.22 ppm ($CH_3{}^c$, 3.2%). Irradiation at 1.22 ppm ($CH_3{}^c$) enhanced the signals at 7.77 ppm (H-1′^{c}, 0.3%), 7.54 ppm (H-3′^{c}, 0.4%), 2.95 ppm (H-5a^c, 1.0%), 2.57 ppm (H-5b^c, 0.2%), 2.43 ppm (H-3a^c, 0.4%), 2.32 ppm (H-4^c, 1.2%), 1.47 ppm (H-3b^c, 1.3%). Irradiation at 1.10 ppm ($CH_3{}^t$) enhanced the signals at 3.41 ppm (H-5a^t, 0.5%), 3.33 ppm (H-2^t, 0.4%), 2.50 ppm (H-4^t, 2.5%), 2.01 ppm (H-5b^t, 0.9%), 1.83 ppm (H-3b^t, 1.1%).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ (*cis*/*trans* mixture) = 141.1 (C-2′^{t}), 140.7 (C-2′^{c}), 133.5, 132.9 (C-4a′^{c}, C-8a′^{c}), 132.9, 133.4 (C-4a″, C-8a″), 128.1 (C^t), 128.1(C^c), 127.7 (C^c), 127.6 (1 C^c, 2 C^t), 126.1 (C^c), 126.0 (C^t), 125.8, 125.6, 125.4 (3 C^c, 3 C^t, Ar), 72.8 (C-2^c), 71.1 (C-2^t), 65.9 (C-5^t), 64.3 (C-5^c), 44.8 (C-3^c), 43.7 (C-3^t), 40.7 ($NCH_3{}^c$), 40.6 ($NCH_3{}^t$), 31.0 (C-4^t), 30.4 (C-4^c), 22.4 ($CH_3{}^c$), 19.8 ($CH_3{}^t$).

ESI-MS: m/z = 226.2 ([M + H]$^+$, 100), 172.1 (17).

HRMS: m/z calcd for [M + H]$^+$: 226.1596; found: 226.1595.

1-Methyl-2-(2-naphthyl)-3,5-diphenylpyrrolidine (5f)
Compound **5f** was obtained according to the general procedure from **1c** (500 mg, 2.55 mmol) and chalcone (557 mg, 2.67 mmol) as a yellow oil (crude yield: 961 mg, 10:1 isomeric mixture). Purification of a portion (167 mg) of the crude product by preparative TLC (petroleum ether–EtOAc, 10:1 + 1% $EtNMe_2$) gave pure 2,3-*cis*-2,5-*cis*-**5f** (121 mg, 75%, colorless oil) and another isomer of **5f** (12 mg, 7.5%, light yellow oil), the configuration of which was not assigned.

2,3-*cis*-2,5-*cis*-5f
R_f 0.42 (petroleum ether–EtOAc, 10:1 + 1% $EtNMe_2$).

IR (film): 3060, 3027, 2782, 1602, 1494, 1454, 1319, 1190, 1058, 909, 817, 747, 700 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.77 (br d, 1 H, J = 7.8 Hz, H-1′), 7.69–7.74 (m, 4 H, Ar), 7.48–7.54 (m, 3 H, Ar), 7.36–7.46 (m, 3 H, Ar), 7.17 (dd, 1 H, J = 8.5, 1.7 Hz, H-3′), 7.04–7.08 (m, 2 H, Ar), 6.95–7.00 (m, 2 H, Ar), 6.88–6.93 (m, 1 H, Ar), 4.10 (d, 1 H, J = 9.1 Hz, H-2), 3.80 (d-pseudo-t, 1 H, J_t = 9 Hz, J_d = 7.8 Hz, H-3), 3.70 (dd, 1 H, J = 9.7, 7.2 Hz, H-5), 2.77 (ddd, 1 H, J = 13.2, 8.8, 7.2 Hz, H-4a), 2.27 (ddd, 1 H, J = 13.2, 9.7, 7.8 Hz, H-4b), 2.21 (s, 3 H, CH_3).

Irradiation at 4.10 ppm (H-2) enhanced the signals at 7.77 ppm (Ar, 6.2%), 7.17 ppm (H-3′, 4.2%), 3.80 ppm (H-3, 6.2%), 3.70 ppm (H-5, 4.6%), 2.21 ppm (CH_3, 4.3%). Irradiation at 3.80 ppm (H-3) enhanced the signals at 7.17 ppm (H-3′, 9.8%), 4.10 ppm (H-2, 5.3%), 2.77 ppm (H-4a, 7.9%). Irradiation at 3.70 ppm (H-5) enhanced the signals at 7.77 ppm (H-1′, 7.8%), 4.10 ppm (H-2, 4.5%), 3.80 ppm (H-3, 0.7%), 2.77 ppm (H-4a, 4.4%), 2.27 ppm (H-4b, 3.9%), 2.21 ppm (CH_3, 3.6%). Irradiation at 2.77 ppm (H-4a) enhanced the signals at 7.77 ppm (H-1′, 0.8%), 3.80 ppm (H-3, 6.3%), 3.70 ppm (H-5, 5.8%), 2.27 ppm (H-4b, 20.8%). Irradiation at 2.27 ppm (H-4b) enhanced the signals at 7.77 ppm (H-1′, 4.5%), 7.17 ppm (H-3′, 8.3%), 2.77 ppm (H-4a, 21.1%).

^{13}C NMR (75.4 MHz, $CDCl_3$): δ = 143.3, 142.4, 138.3, 133.0, 132.4 (3 Ar-C_i, C-4a′, C-8a′), 129.2, 128.6, 127.7, 127.5, 127.4, 127.3, 127.6, 127.0, 126.7, 125.7, 125.4, 125.0 (C_6H_5, Naph), 75.9, 71.2 (C-2, C-5), 49.0 (C-3), 42.5 (C-4), 39.5 (CH_3).

ESI-MS: m/z = 364.2 ([M + H]$^+$, 100%).

HRMS: m/z calcd for [M + H]$^+$: 364.2065; found: 364.2068.

Minor Diastereomer of 5f
R_f 0.25 (petroleum ether–EtOAc, 10:1 + 1% $EtNMe_2$).

IR (film): 3059, 3027, 1790, 1665, 1606, 1494, 1450, 1336, 1215, 748, 701 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ (characteristic signals) = 4.38 (dd, 1 H, J = 8.3, 7.0 Hz, H-5), 4.33 (d, 1 H, J = 7.6 Hz, H-2), 3.56 (ddd, 1 H, J = 10.2, 8.4, 7.6 Hz, H-3), 2.84 (ddd, 1 H, J = 13.2, 8.4, 7.0 Hz, H-4a), 2.24 (ddd, 1 H, J = 13.2, 10.2, 8.3 Hz, H-4b), 1.83 (s, 3 H, CH_3).

ESI-MS: m/z = 364.0 ([M + H]$^+$, 100%).

1-(4-Methoxybenzyl)-3-methyl-2-phenylpyrrolidine (5g)
Compound **5g** was obtained according to the general procedure from **1d** (88 mg, 0.35 mmol) and crotonaldehyde (40 μL, 0.43 mmol) as a mixture of diastereomers (*cis*/*trans* = 1:2.6, yellow oil, 74 mg, 75%). The mixture could be separated by flash chromatography (hexane–EtOAc, 10:1 + 1% $EtNMe_2$).

***cis*-5g**
R_f 0.37 (cyclohexane–EtOAc, 10:1+ 1% $EtNMe_2$).

IR (film): 2957, 1613, 1512, 1454, 1249, 1038, 819, 703 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): d = 7.19–7.42 (m, 7 H, C_6H_5, H-3′,5′), 6.82–6.88 (BB′-part of AA′BB′, 2H, H-2′,6′), 3.85 (d, 1 H, J = 13.1 Hz, ArCH_2-a), 3.80 (s, 3 H, OCH_3), 3.59 (d, 1 H, J = 8.3 Hz, H-2), 3.00–3.12 (m, 2 H, ArCH_2-b, H-5a), 2.38 (mc, 1 H, H-3), 2.21 (dt, 1 H, J_t = 9.2 Hz, J_d = 7.8 Hz, H-5b), 1.96–2.09 (m, 1 H, H-4a), 1.45 (mc, 1 H, H-4b), 0.57 (d, 3 H, J = 7.1 Hz, CH_3).

^{13}C NMR (75.4 MHz, $CDCl_3$): δ = 158.4 (C-4′), 141.4 (C-1″), 131.9 (C-1′), 129.7, 128.3, 127.9, 126.6, 113.5 (Ar), 72.0 (C-2), 57.8, 55.2, 52.4 (C-5, ArCH_2, OCH_3), 37.1, 32.4 (C-3, C-4), 18.4 (CH_3).

ESI-MS: m/z = 282.2 ([M + H]$^+$, 100%).

HRMS: m/z calcd for [M + H]$^+$: 282.1858; found: 282.1848.

***trans*-5g**
R_f 0.32 (cyclohexane–EtOAc, 10:1 + 1% $EtNMe_2$).

IR (film): 2957, 1612, 1514, 1454, 1302, 1255, 1037, 814, 757, 705 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.45–7.49 (m, 2 H, H-2″,6″), 7.34–7.40 (m, 2 H, H-3″,5″), 7.24–7.31 (m, 1 H, H-4″), 7.16–7.21 (AA′ part of AA′BB′, 2 H, H-2′,6′), 6.81–6.85 (BB′ -part of AA′BB′, 2 H, H-3′,5′), 3.79 (s, 3 H, OCH_3), 3.74 (d, 1 H, J = 12.9 Hz, ArCH_2-a), 3.07 (d-pseudo-t, 1 H, J_t = 9 Hz, J_d = 3.2 Hz, H-5a), 2.96 (d, 1 H, J = 12.9 Hz, ArCH_2-b), 2.84 (d, 1 H, J = 8.5 Hz, H-2), 2.27 (d-pseudo-t, 1H, J_t = 9 Hz, J_d = 7.7 Hz, H-5b), 1.94–2.17 (m, 2 H, H-3, H-4a), 1.40 (mc, 1 H, H-4b), 0.97 (d, 3 H, J = 6.5 Hz, CH_3).

^{13}C NMR (75.4 MHz, $CDCl_3$): δ = 158.4 (C-4′), 142.8 (C-1″), 131.7 (C-1′), 129.8, 128.3, 127.9, 127.1, 113.5 (Ar), 77.7 (C-2), 57.6, 55.2, 51.9 (C-5, ArCH_2, OCH_3), 42.7, 31.1 (C-3, C-4), 18.1 (CH_3).

ESI-MS: m/z = 282.2 ([M + H]$^+$, 100%).

HRMS: m/z calcd for [M + H]$^+$: 282.1858; found: 282.1852.

3-[1-(4-Toluenesulfonyl)pyrrolidin-2-yl]pyridine (Tos-5h)
Compound **5h** was prepared according to the general procedure from **1e** (315 mg, 2.36 mmol) and acrolein (166 μL, 2.48 mmol). In

order to destroy borate complexes, the extraction with 1 N HCl was repeated three times. The resulting crude product was then dissolved in THF (10 mL) and stirred for 3 h with a sat. solution of citric acid (0.5 mL). CH_2Cl_2 was added and the aqueous solution was brought to pH 14 by addition of NaOH. The phases were separated and the aqueous phase was reextracted with CH_2Cl_2 (2 ×). Drying of the combined organic layers (Na_2SO_4) and evaporation of the solvent yielded the crude product (141 mg) as a brown oil. As no proper conditions for the purification of the unprotected compound could be found, the product was converted to the *N*-tosyl derivative: The material was dissolved in CH_2Cl_2 (5 mL), and to this solution were added Et_3N (131 μL, 0.94 mmol) and *p*-toluenesulfonyl chloride (180 mg, 0.94 mmol). The mixture was stirred for 1 h, then aq 1 N NaOH (10 mL) was added and the mixture was stirred for 1 h. The phases were separated and the aqueous phase was extracted with CH_2Cl_2 (2 ×). Drying of the combined organic layers (Na_2SO_4) and evaporation of the solvent gave a brown oil (244 mg). Purification by flash chromatography (cyclohexane–EtOAc, 1:2 + 1% Et_2MeN) gave the pure *N*-tosylamide of **5h** (87 mg, 12%) as a brownish oil. The analytical data were in accordance with the values reported in the literature.[9]

3-(3-Methylpyrrolidin-2-yl)pyridine (5i)

Compound **5i** was obtained according to the general procedure from **1e** (180 mg, 1.35 mmol) and crotonaldehyde (122 μL, 1.43 mmol) as an orange oil (crude yield: 191 mg). A portion of the material (144 mg) was separated by flash chromatography (CH_2Cl_2–$EtNMe_2$, 10:1). The collected fractions were partitioned between CH_2Cl_2 and aq 1 N NaOH to remove remaining silicates. Drying of the organic layer (Na_2SO_4) and evaporation of the solvent yielded a mixture of *cis*- and *trans*-**5i** (1.5:1) as a yellow oil (40.0 mg, 24%); R_f 0.25 (CH_2Cl_2–$EtNMe_2$, 10:1).

^{1}H NMR, COSY (400 MHz, $CDCl_3$): δ (*cis*/*trans* mixture) = 8.42–8.56 (m, 2 H, H-2, H-6), 7.69–7.73 (m, 0.4 H, H-4^t), 7.61–7.64 (m, 0.6 H, H-4^c), 7.20–7.25 (m, 1 H, H-5), 4.27 (d, 0.6 H, *J* = 7.2 Hz, H-2′^{c}), 3.57 (d, 0.4 H, *J* = 8.6 Hz, H-2′^{t}), 3.26 (ddd, 0.6 H, *J* = 9.9, 8.1, 4.2 Hz, H-5a′^{c}), 3.16–3.21 (m, 0.4 H, H-5a′^{t}), 3.09–3.14 (m, 0.4 H, H-5b′^{t}), 3.03–3.09 (m, 0.6 H, H-5b′^{c}), 2.43 (mc, 0.6 H, H-3′^{c}), 2.01–2.19 (m, 2 H, H-4a′, NH), 1.92–2.01 (m, 0.4 H, H-3′^{t}), 1.48–1.60 (m, 1 H, H-4b′), 1.01 (d, 1.2 H, *J* = 6.6 Hz, CH_3^c), 0.60 (d, 1.8 H, *J* = 7.0 Hz, CH_3^t). The spectrum showed the presence of minor impurities.

^{13}C NMR, DEPT (75.4 MHz, $CDCl_3$): δ (*cis*/*trans* mixture) = 149.1, 147.9 (C-2,6^t), 149.0, 148.5 (C-2,6^c), 139.1 (C-3^c), 138.1 (C-3^t), 134.9 (C-4^t), 134.4 (C-4^c), 123.4 (C-5^c), 122.9 (C-5^t), 67.9 (C-2′^{c}), 63.1 (C-2′^{t}), 45.6 (C-5′^{c}), 45.3 (C-5′^{t}), 42.6 (C-3′^{c}), 37.3 (C-3′^{t}), 34.2 (C-4′^{c}), 33.3 (C-4′^{t}), 17.2 (CH_3^c), 16.3 (CH_3^t).

ESI-MS: *m*/*z* (%) = 219.2 (18), 217.2 (21), 204.2 ([M + MeCN + H]$^+$, 21), 163.1 ([M + H]$^+$, 100).

HRMS: *m*/*z* calcd for [M + H]$^+$: 163.1235; found: 163.1242.

[(3,4-Dimethoxybenzylidene)amino]acetonitrile (6a)

To a solution of 3,4-dimethoxybenzaldehyde (10 g, 60 mmol) in CH_2Cl_2 (150 mL) was added aminoacetonitrile sulfate (7.0 g, 33 mmol), $EtNMe_2$ (6.5 mL, 60 mmol) and powdered molecular sieves 4 Å (7 g). After stirring for 24 h, the mixture was filtered and the filtrate was concentrated to yield a yellowish oil which crystallized upon cooling. As the ^{1}H NMR spectrum still showed the presence of impurities, the product was dissolved in CH_2Cl_2 and washed with H_2O and brine. After drying (Na_2SO_4), the solvent was removed in vacuo to give yellow crystals (crude yield: 9.1 g). Recrystallization from EtOAc–hexane gave pure **6a** (6.9 g, 56%) as colorless crystals; mp 93–94 °C; R_f 0.21 (cyclohexane–EtOAc, 1:1).

IR (KBr): 3437, 2938, 1648, 1587, 1514, 1470, 1319, 1269, 1147, 1026, 987 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.37 (t, 1 H, *J* = 1.7 Hz, CH=N), 7.39 (d, 1 H, *J* = 1.8 Hz, H-2), 7.20 (dd, 1 H, *J* = 8.2, 1.8 Hz, H-6), 6.88 (d, 1 H, *J* = 8.2 Hz, H-5), 4.58 (d, 2 H, *J* = 1.7 Hz, CH_2), 3.91 (s, 6 H, OCH_3).

^{13}C NMR (75.4 MHz, $CDCl_3$): δ = 164.0 (CH=N), 152.2, 149.4 (C-3, C-4), 127.9 (C-1), 124.0 (C-6), 115.6 (CN), 110.4, 108.7 (C-2, C-5), 55.9, 55.8 (OCH_3), 45.3 (CH_2).

ESI-MS: *m*/*z* (%) = 226.2 (15), 205.2 ([M + H]$^+$, 100), 172.1 (10).

Anal. Calcd for $C_{11}H_{12}N_2O_2$: C, 64.69; H, 5.92; N, 13.72. Found: C, 64.83; H, 6.11; N, 13.61.

{[(2-Naphthyl)methylene]amino}acetonitrile (6b)

To a solution of 2-naphthaldehyde (9.0 g, 58 mmol) in CH_2Cl_2 (50 mL) were added aminoacetonitrile sulfate (7.3 g, 35 mmol), $EtNMe_2$ (8.84 mL, 81 mmol) and $MgSO_4$ (8.3 g, 69 mmol), and the mixture was stirred for 24 h. The $MgSO_4$ was removed by filtration, the filtrate was washed with aq sat. $NaHCO_3$, dried (Na_2SO_4) and the solvent was removed in vacuo. The residue was recrystallized from Et_2O–petroleum ether to give pure **6b** (8.4 g, 75%) as light yellow crystals; mp 86–87 °C; R_f 0.67 (cyclohexane–EtOAc, 1:1 + 1% $EtNMe_2$, alumina).

IR (KBr): 3436, 2877, 2241, 1636, 1412, 1345, 1122, 1000, 917, 833, 757 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.62 (t, 1 H, *J* = 1.8 Hz, CH=N), 8.09 (br s, 1 H, H-1), 7.98 (dd, 1 H, *J* = 8.6, 1.6 Hz, H-3), 7.78–7.94 (m, 3 H, Naph), 7.56 (mc, 2 H, Naph), 4.67 (d, 2 H, *J* = 1.8 Hz, CH_2).

^{13}C NMR (75.4 MHz, $CDCl_3$): δ = 164.6 (CH=N), 135.0, 132.8, 132.4 (C-2, C-4a, C-8a), 131.3, 128.8, 128.7, 127.8, 127.7, 126.7, 123.3 (Naph), 115.4 (CN), 45.6 (CH_2).

ESI-MS: *m*/*z* = 195.2 ([M + H]$^+$, 100%).

Anal. Calcd for $C_{13}H_{10}N_2$: C, 80.39; H, 5.19; N, 14.42. Found: C, 80.27; H, 5.49; N, 14.38.

2-[(3,4-Dimethoxybenzylidene)amino]-3-phenylpropanenitrile (6c)

To a solution of 3,4-dimethoxybenzaldehyde (1.12 g, 6.7 mmol) and 3-phenyl-2-aminopropanenitrile[40] (0.99 g, 6.8 mmol) in CH_2Cl_2 (20 mL) was added $MgSO_4$ (0.8 g, 6.7 mmol) and a few drops of AcOH and the mixture was stirred for 48 h. The mixture was filtered and washed with aq sat. $NaHCO_3$. The organic phase was dried (Na_2SO_4) and concentrated in vacuo. The crude product was recrystallized from Et_2O–cyclohexane, to yield **6c** (1.3 g, 66%) as a colorless crystalline solid; mp 80–81 °C; R_f 0.64 (cyclohexane–EtOAc, 1:1 + 1% $EtNMe_2$, alumina).

IR (KBr): 2247, 1636, 1581, 1511, 1269, 1236, 1157, 1137, 1021, 812, 701 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.21 (d, 1 H, *J* = 1.4 Hz, CH=N), 7.42 (d, 1 H, *J* = 1.8 Hz, H-2′), 7.27–7.36 (m, 5 H, C_6H_5), 7.18 (dd, 1 H, *J* = 8.2, 1.8 Hz, H-6′), 6.89 (d, 1 H, *J* = 8.2 Hz, H-5′), 4.81 (ddd, 1 H, *J* = 7.6, 6.1, 1.4 Hz, H-2), 3.95 (s, 3 H, OCH_3), 3.93 (s, 3 H, OCH_3), 3.31 (dd, 1 H, *J* = 13.6, 6.1 Hz, H-3a), 3.17 (dd, 1 H, *J* = 13.6, 7.6 Hz, H-3b).

^{13}C NMR (75.4 MHz, $CDCl_3$): δ = 162.6 (CH=N), 152.3, 149.4 (C-3′, C-4′), 135.2 (C-1″), 129.8, 128.6 (C-2″,6″, C-3″,5″), 128.0 (C-1′), 127.4 (C-4″), 124.1 (C-2′), 117.7 (CN), 110.5, 109.1 (C-5′, C-6′), 60.0 (C_a), 55.9 (OCH_3), 41.0 (CH_2).

ESI-MS: *m*/*z* = 295.3 ([M + H]$^+$, 100%).

HRMS: *m*/*z* calcd for [M + H]$^+$: 295.1447, found: 295.1439.

[(3,4-Dimethoxybenzylidene)amino](phenyl)acetonitrile (6d)
Amino(phenyl)acetonitrile[40] (3.50 g, 26 mmol) was dissolved in CH_2Cl_2 (50 mL), and to this solution were added $MgSO_4$ (3.50 g) and 3,4-dimethoxybenzaldehyde (4.84 g, 29 mmol). The mixture was refluxed for 8 h and then allowed to stand at 4 °C for 48 h. The $MgSO_4$ was removed by filtration, the filtrate was washed with aq $NaHCO_3$ and dried (Na_2SO_4). Evaporation of the solvent and recrystallization of the residue from Et_2O–petroleum ether gave **6d** (4.62 g, 62%) as yellow crystals; mp 95–96 °C; R_f 0.59 (cyclohexane–EtOAc, 1:1, alumina).

IR (KBr): 2935, 2230, 1649, 1600, 1519, 1269, 1167, 1122, 1011, 701 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 8.52 (d, 1 H, *J* = 1.4 Hz, CH=N), 7.35–7.50 (m, 6 H, C_6H_5, H-2′), 7.28 (dd, 1 H, *J* = 8.2, 1.9 Hz, H-6′), 6.90 (d, 1 H, *J* = 8.2 Hz, H-5′), 5.75 (d, 1 H, *J* = 1.4 Hz, H-2), 3.93, 3.92 (2 s, 6 H, OCH_3).

^{13}C NMR (75.4 MHz, $CDCl_3$): δ = 162.6 (CH=N), 152.3, 149.4 (C-3′, C-4′), 134.9 (C-1″), 129.1, 127.3 (C-2″,6″, C-3″,5″) 128.9 (C-4″), 127.9 (C-1′), 124.4 (C-2′), 117.2 (CN), 110.4, 109.1 (C-5′, C-6′), 61.6 (C_α), 55.9 (OCH_3).

ESI-MS: *m*/*z* = 254.1 ($[M - CN]^+$, 100%).

Anal. Calcd for $C_{17}H_{16}N_2O_2$: C, 72.84; H, 5.75; N, 9.99. Found: C, 73.05; H, 5.87; N, 9.99.

Pyrrolidines 9 from α-Alkylideneaminonitriles 6; General Procedure
To a stirred solution of the α-(alkylideneamino)nitrile **6** (1.45 mmol) in THF (5 mL) was added a solution of DBU (1.59 mmol, 1.1 equiv) in THF (2 mL) under argon at r.t. After the addition of a solution of the electrophile **6** (1.59 mmol, 1.1 equiv) in THF (3 mL), the mixture was stirred until the TLC analysis indicated complete conversion. The reaction was stopped by addition of a mixture of EtOH (87 mmol, 60 equiv) and HOAc (11.6 mmol, 8 equiv). After the addition of $NaBH_3CN$ (5.8 mmol, 4 equiv), the mixture was stirred overnight at r.t. The mixture was washed with aq 1 N NaOH (2 ×) and the combined aqueous phases were extracted with EtOAc. The combined organic layers were extracted with 1 N HCl (3 ×) and the combined aqueous phases were made alkaline by addition of NaOH. Extraction with CH_2Cl_2, drying (Na_2SO_4) and evaporation of the solvent in vacuo gave a crude product, which was further purified by column chromatography, preparative TLC or HPLC if necessary. Those compounds which were too lipophilic for an extraction with aq HCl were directly purified by chromatographic methods.

1-(3,4-Dimethoxybenzyl)-2-methylpyrrolidine (9a)
Compound **9a** was obtained according to the general procedure from **6a** (304 mg, 1.49 mmol) and methyl vinyl ketone (136 μL, 1.64 mmol) as a yellow oil (crude yield: 324 mg). Purification of a portion (53 mg) of the crude product by flash chromatography (10:1 cyclohexane–EtOAc + 1% $EtNMe_2$, alumina) gave pure **9a** (37 mg, 64%) as a colorless oil; R_f 0.24 (cyclohexane–EtOAc, 1:1 + 1% $EtNMe_2$).

IR (film): 2960, 1592, 1515, 1464, 1375, 1263, 1234, 1140, 1030, 765 cm^{-1}.

^1H NMR, COSY (400 MHz, $CDCl_3$): δ = 6.90 (d, 1 H, *J* = 1.5 Hz, H-2′), 6.83 (dd, 1 H, *J* = 8.1, 1.5 Hz, H-6′), 6.78 (d, 1 H, *J* = 8.1 Hz, H-5′), 3.96 (d, 1 H, *J* = 12.7 Hz, ArCH_2-a), 3.88, 3.85 (2 s, 6 H, OCH_3), 3.16 (d, 1 H, *J* = 12.7 Hz, ArCH_2-b), 2.95 (mc, 1 H, H-5a), 2.44 (mc, 1 H, H-2), 2.16 (q, 1 H, *J* = 9.0 Hz, H-5b), 1.87–2.02 (m, 1 H, H-3a), 1.56–1.83 (m, 2 H, H-4a, H-4b), 1.39–1.56 (m, 1 H, H-3b), 1.17 (d, 3 H, *J* = 6.1 Hz, CH_3).

^{13}C NMR (75.4 MHz, $CDCl_3$): δ = 148.7, 147.9 (C-3′, C-4′), 131.8 (C-1′), 121.1, 112.4, 110.8 (C-2′, C-5′, C-6′), 59.6 (C-2), 58.0 (ArCH_2), 55.8 (2 OCH_3), 53.9 (C-5), 32.7 (C-3), 21.4 (C-4), 19.0 (CH_3).

ESI-MS: *m*/*z* (%) = 252.2 (42), 236.3 ($[M + H]^+$, 100), 151.1 ($[(MeO)_2PhCH_2]^+$, 81).

HRMS: *m*/*z* calcd for $[M + H]^+$: 236.1651; found: 236.1652.

1-(3,4-Dimethoxybenzyl)-2-ethylpyrrolidine (9b)
Compound **9b** was obtained according to the general procedure from **6a** (409 mg, 2.0 mmol) and ethyl vinyl ketone (219 μL, 2.2 mmol) as a yellow oil (crude yield: 555 mg). Purification of a portion (154 mg) of the crude product by flash chromatography (cyclohexane–EtOAc, 10:1, alumina) gave pure **9b** (80 mg, 58%) as a colorless oil; R_f 0.18 (cyclohexane–EtOAc, 1:1 + 1% $EtNMe_2$).

IR (film): 2960, 1592, 1515, 1463, 1417, 1262, 1234, 1155, 1031, 765 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 6.76–6.88 (m, 3 H, Ar), 3.96 (d, 1 H, *J* = 12.8 Hz, ArCH_2-a), 3.88, 3.66 (2 s, 6 H, OCH_3), 3.09 (d, 1 H, *J* = 12.8 Hz, ArCH_2-b), 2.90 (ddd, 1 H, *J* = 9.3 7.2, 2.9 Hz, H-5a), 2.24 (d-pseudo-q, 1 H, J_q = 8 Hz, J_d = 3.2 Hz, H-2), 2.09 (pseudo-q, 1 H, *J* = 9 Hz, H-5b), 1.84–1.99 (m, 1 H, H-3a), 1.56–1.83 (m, 3 H, CH_2CH_3, H-4a, H-4b), 1.41–1.55 (m, 1 H, H-3b), 1.21–1.32 (m, 1 H, CH_2CH_3), 0.91 (t, 3 H, *J* = 7.4 Hz, CH_2CH_3).

^{13}C NMR, DEPT (75.4 MHz, $CDCl_3$): δ = 148.7, 147.8 (C-3′, C-4′), 132.4 (C-1′), 121.0, 112.2, 110.8 (C-2′, C-5′, C-6′), 65.7 (C-2), 58.4 (ArCH_2), 55.9, 55.8 (OCH_3), 54.3 (C-5), 29.9 (C-3), 26.6 (CH_2CH_3), 21.8 (C-4), 10.5 (CH_2CH_3).

ESI-MS: *m*/*z* (%) = 250.3 ($[M + H]^+$, 100), 151.1 ($[(MeO)_2PhCH_2]^+$, 92).

HRMS: *m*/*z* calcd for $[M + H]^+$: 250.1808; found: 250.1808.

***cis*-1-(3,4-Dimethoxybenzyl)-2,4-diphenylpyrrolidine (9c)**
Compound **9c** was prepared according to the general procedure from **6a** (406 mg, 1.99 mmol) and chalcone (456 mg, 2.19 mmol). The product could not be extracted with aq HCl. Therefore, the organic layer was dried (Na_2SO_4) and concentrated in vacuo to yield part (634 mg) of the crude product; the aqueous phase was adjusted to pH 12 and extracted with CH_2Cl_2. Drying (Na_2SO_4) and removal of the solvent in vacuo yielded another portion (186 mg) of the crude material. Both fractions were purified separately by flash chromatography (cyclohexane–EtOAc, 14:1 + 1% $EtNMe_2$). A portion (558 mg) of the first fraction afforded *cis*-**9c** (230 mg), a portion (179 mg) of the second crude product gave the same compound (110 mg); total yield: 289 mg (50%); yellowish oil; R_f 0.21 (cyclohexane–EtOAc, 10:1 + 1% $EtNMe_2$).

IR (film): 2931, 1603, 1514, 1454, 1263, 1234, 1155, 1138, 1030, 756, 701 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.54 (m, 2 H, C_6H_5), 7.32–7.42 (m, 4 H, C_6H_5), 7.23–7.31 (m, 3 H, C_6H_5), 7.13–7.20 (m, 1 H, C_6H_5), 6.93 (d, 1 H, *J* = 1.4 Hz, H-2′), 6.84 (dd, 1 H, *J* = 8.2, 1.4 Hz, H-6′), 6.77 (d, 1 H, *J* = 8.2 Hz, H-5′), 3.89 (s, 3 H, OCH_3), 3.88 (d, 1 H, *J* = 13.2 Hz, ArCH_2-a), 3.85 (s, 3 H, OCH_3), 3.56 (dd, 1 H, *J* = 10.1, 6.4 Hz, H-2), 3.25–3.37 (m, 1 H, H-4), 3.16 (dd, 1 H, *J* = 9.8, 3.2 Hz, H-5a), 3.02 (d, 1 H, *J* = 13.2 Hz, ArCH_2-b), 2.60–2.74 (m, 2 H, H-3a, H-5b), 1.87 (ddd, 1 H, *J* = 12.8, 10.1, 7.7 Hz, H-3b).

Irradiation at 3.56 ppm (H-2) enhanced the signals at 3.88 ppm (ArCH_2-a, 2.1%), 3.02 ppm (ArCH_2-b, 4.6%), 2.68 ppm (H-3a, 9.0%). Irradiation at 3.32 ppm (H-4) enhanced the signals at 3.88 ppm (ArCH_2-a, 1.0%), 3.16 ppm (H-5a, 1.0%), 2.68 ppm (H-3a, H-5b, 11.4%).

^{13}C NMR, DEPT (75.4 MHz, $CDCl_3$): δ = 148.8, 147.7, 147.6, 143.0 (C-3′, C-4′, 2 C_6H_5-C-1), 132.4 (C-1′), 128.5, 128.4, 127.6, 127.2, 127.1, 125.9 (Ar), 120.2 (C-6′), 111.5, 110.8 (C-2′, C-5′),

70.4 (C-2), 60.9 (C-5), 57.4 (Ar*C*H$_2$), 55.9, 55.7 (OCH$_3$), 45.8 (C-3), 41.5 (C-4).

ESI-MS: *m*/*z* = 374.4 ([M + H]$^+$, 100%).

HRMS: *m*/*z* calcd for [M + H]$^+$: 374.2121; found: 374.2114.

2-Methyl-1-(2-naphthylmethyl)pyrrolidine (9d)
Compound **9d** was obtained according to the general procedure from **6b** (535 mg, 2.75 mmol) and methyl vinyl ketone (252 μL, 3.03 mmol) as a yellow oil (crude yield: 471 mg). Purification of a portion (192 mg) of the crude product by flash chromatography (cyclohexane–EtOAc, 10:1, alumina) gave pure **9d** (111 mg, 46%) as a yellow oil; R_f 0.74 (cyclohexane–EtOAc, 1:1, alumina).

IR (film): 2961, 2788, 1509, 1459, 1375, 1355, 1310, 1140, 818, 745 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.74–7.85 (m, 4 H, Naph), 7.50 (dd, 1 H, *J* = 8.4, 1.6 Hz, H-3′), 7.42–7.49 (m, 2 H, Naph), 4.20 (d, *J* = 12.8 Hz, ArC*H*$_2$-a), 3.31 (d, *J* = 12.8 Hz, ArC*H*$_2$-b), 2.93 (ddd, 1 H, *J* = 9.4, 8.0, 2.7 Hz, H-5a), 2.46 (mc, 1 H, H-2), 2.17 (q, *J* = 9.0, Hz, H-5b), 1.97 (mc, 1 H, H-3a), 1.60–1.80 (m, 2 H, H-4a, H-4b), 1.43–1.57 (m, 1 H, H-3b), 1.22 (d, 3 H, *J* = 6.1 Hz, CH$_3$).

^{13}C NMR, HMQC (100.6 MHz, $CDCl_3$): δ = 137.2 (C-2′), 133.4, 132.6 (C-4a′, C-8a′), 127.7, 127.7, 127.6 (2 C), 127.3, 125.8, 125.4 (Naph), 59.8 (C-2), 58.5 (Ar*C*H$_2$), 54.1 (C-5), 32.7 (C-3), 21.5 (C-4), 19.2 (CH$_3$).

ESI-MS: *m*/*z* = 226.2 ([M + H]$^+$, 100%).

HRMS: *m*/*z* calcd for [M + H]$^+$: 226.1596; found: 226.1626.

2-Ethyl-1-(2-naphthylmethyl)pyrrolidine (9e)
Compound **9e** was obtained according to the general procedure from **6b** (502.8 mg, 2.59 mmol) and ethyl vinyl ketone (283 μL, 2.85 mmol) as a brown oil (crude yield: 501 mg). Purification of a portion (195 mg) of the crude product by flash chromatography (cyclohexane–EtOAc, 10:1, alumina) gave pure **9e** (124 mg, 51%) as a colorless oil; R_f 0.82 (cyclohexane–EtOAc, 1:1, alumina).

IR (film): 3054, 2961, 2787, 1601, 1509, 1461, 1357, 1125, 854, 818, 747 cm^{-1}.

^{1}H NMR, COSY (400 MHz, $CDCl_3$): δ = 7.78–7.85 (m, 3 H, Naph), 7.75 (br s, 1 H, H-1′), 7.50 (dd, 1 H, *J* = 8.4, 1.6 Hz, H-3′), 7.45 (mc, 2 H, Naph), 4.21 (d, 1 H, *J* = 12.9 Hz, ArC*H*$_2$-a), 3.30 (d, 1 H, *J* = 12.9 Hz, ArC*H*$_2$-b), 2.93 (ddd, 1 H, *J* = 9.3, 7.3, 2.8 Hz, H-5a), 2.33 (d-pseudo-q, J_q = 8 Hz, J_d = 3.3 Hz, H-2), 2.15 (pseudo-q, 1 H, *J* = 9 Hz, H-5b), 1.96 (mc, 1 H, H-3a), 1.83 (mc, 1 H, C*H*$_2$CH$_3$), 1.60–1.76 (m, 2 H, H-4a, H-4b), 1.48–1.59 (m, 1 H, H-3b), 1.38 (mc, 1 H, C*H*$_2$CH$_3$), 0.97 (t, 3 H, *J* = 7.5 Hz, CH$_2$C*H*$_3$).

^{13}C NMR, HMQC (100.6 MHz, $CDCl_3$): δ = 137.5 (C-2′), 133.4, 132.6 (C-4a′, C-8a′), 127.7 (2 C), 127.6, 127.5, 127.1, 125.8, 125.3 (Naph), 65.9 (C-2), 58.9 (Ar*C*H$_2$), 54.5 (C-5), 29.9 (C-3), 26.7 (*C*H$_2$CH$_3$), 21.9 (C-4), 10.5 (CH$_2$*C*H$_3$).

ESI-MS: *m*/*z* = 240.2 ([M + H]$^+$, 100%).

HRMS: *m*/*z* calcd for [M + H]$^+$: 240.1753; found: 240.1743.

2-Benzyl-1-(3,4-dimethoxybenzyl)-5-methylpyrrolidine (9f)
Compound **9f** was obtained according to the general procedure from **6c** (427 mg, 1.45 mmol) and methyl vinyl ketone (133 μL, 1.59 mmol) as a yellow oil (365 mg, 77%, *cis*/*trans* = 1.4:1). The diastereomers were separated by analytical HPLC [Macherey Nagel Nucleosil-NO$_2$ 10μ 250 × 4 mm; *n*-heptane–*i*-PrOH (95:5), 1.0 mL/min]. For NMR data of both compounds, see ref.[29]

***cis*-9f**
IR (film): 2956, 1592, 1514, 1453, 1261, 1139, 1030, 701 cm^{-1}.

ESI-MS: *m*/*z* (%) = 326.5 ([M + H]$^+$, 100), 151.1 {([(MeO)$_2$PhCH$_2$]$^+$, 99)}.

HRMS: *m*/*z* calcd for [M + H]$^+$: 326.2120; found: 326.2135.

***trans*-9f**

IR (film): 2934, 1601, 1514, 1454, 1262, 1157, 1030, 910, 758, 733, 701 cm^{-1}.

ESI-MS: *m*/*z* (%) = 326.3 ([M + H]$^+$, 100), 151.1 ([(MeO)$_2$PhCH$_2$]$^+$, 73).

HRMS: *m*/*z* calcd for [M + H]$^+$: 326.2120; found: 326.2125.

2-Benzyl-1-(3,4-dimethoxybenzyl)-3,5-diphenylpyrrolidine (9g)
Compound **9g** was obtained according to the general procedure from **6c** (328 mg, 1.11 mmol) and chalcone (255 mg, 1.22 mmol). Extraction of the product with 1 N HCl was not possible; therefore, the reaction mixture was washed with aq 1 N NaOH, dried (Na_2SO_4) and concentrated in vacuo to yield a yellow oil (594 mg, 14:20:1:5 mixture of all-*cis*-:2,3-*trans*-3,5-*cis*-:2,3-*cis*-3,5-*trans*-:2,3-*trans*-3,5-*trans*-diastereomer). Purification of a portion (149 mg) of the crude product by flash chromatography (cyclohexane–EtOAc, 20:1 + 1% $EtNMe_2$) gave a mixture of the four diastereomers of **9g** (46.8 mg, 36%) as a colorless oil. A sample (76.1 mg) of the crude product was separated by preparative HPLC [Phenomenex Jupiter C18 250 × 21.2 mm, 5μ, MeCN–H_2O (82:18), 22 mL/min, 4 runs].

2,3-*trans*-3,5-*cis*-9g
Yield: 12.3 mg; colorless oil; R_t 10.1 min; R_f 0.62 (cyclohexane–EtOAc, 1:1 + 1% $EtNMe_2$).

IR (film): 2934, 2253, 1601, 1513, 1454, 1261, 1233, 1138, 1029, 910, 758, 733, 701 cm^{-1}.

^{1}H NMR, COSY (400 MHz, $CDCl_3$): δ = 7.50–7.54 (m, 2 H, C_6H_5), 7.35–7.40 (m, 2 H, C_6H_5), 7.25–7.29 (m, 1 H, C_6H_5), 7.12–7.21 (m, 5 H, C_6H_5), 7.06–7.10 (m, 3 H, C_6H_5), 7.01 (d, 1 H, *J* = 1.8 Hz, H-2′), 6.91–6.95 (m, 2 H, C_6H_5), 6.89 (dd, 1 H, *J* = 8.1, 1.8 Hz, H-6′), 6.79 (d, 1 H, *J* = 8.1 Hz, H-5′), 4.13 (pseudo-t, 1 H, *J* = 8 Hz, H-5), 3.87, 3.81 (2 s, 6 H, OCH$_3$), 3.81 [d, 1 H, *J* = 13.7 Hz, (MeO)$_2$PhC*H*$_2$-a], 3.55 [d, 1 H, *J* = 13.7 Hz, (MeO)$_2$PhC*H*$_2$-b], 3.49 (ddd, 1 H, *J* = 11.1, 3.6, 2.1 Hz, H-2), 3.15 (dd, 1 H, *J* = 12.7, 3.6 Hz, PhC*H*$_2$-a), 3.10 (ddd, 1 H, *J* = 9.6, 5.7, 2.1 Hz, H-3), 2.83 (ddd, 1 H, *J* = 13.4, 9.6, 7.8 Hz, H-4a), 2.53 (dd, 1 H, *J* = 12.7, 11.1 Hz, PhC*H*$_2$-b), 1.97 (ddd, 1 H, *J* = 13.4, 8.6, 5.7 Hz, H-4b).

Irradiation at 3.10 ppm (H-3) enhanced the signals at 4.13 ppm (H-5, 0.8%), 3.49 ppm (H-2, 2.0%), 2.83 ppm (H-4a, 3.8%), 2.53 ppm (PhC*H*$_2$-b, 2.8%), 1.97 ppm (H-4b, 1.7%). Irradiation at 2.83 ppm (H-4a) enhanced the signals at 4.13 ppm (H-5, 5.6%), 3.10 ppm (H-3, 4.9%), 2.53 ppm (PhC*H*$_2$-b, 1.0%), 1.97 ppm (H-4b, 22.9%). Irradiation at 3.15 ppm (PhC*H*$_2$-a) enhanced the signals at 3.55 ppm [(MeO)$_2$PhC*H*$_2$-b, 8.5%], 3.49 ppm (H-2, 6.2%), 2.53 (PhC*H*$_2$-b, 28.0%).

DEPT, HMQC (100.6 MHz, $CDCl_3$): δ = 129.1, 128.4, 128.0, 127.8, 127.4, 127.0, 126.9, 125.3 (Ar), 119.8 (C-6′), 111.0, 110.4 (C-2′, C-5′), 67.9 (C-2), 66.2 (C-5), 55.7, 55.4 (OCH$_3$), 50.2 [(MeO)$_2$PhC*H*$_2$], 45.5 (C-3), 43.5 (C-4), 32.3 (Ph*C*H$_2$).

ESI-MS: *m*/*z* = 464.4 ([M +H]$^+$, 100%).

HRMS: *m*/*z* calcd for [M + H]$^+$: 464.2591; found: 464.2591.

2,3-*trans*-3,5-*trans*-9g
Yield: 5.6 mg; colorless oil; R_f 10.7 min; R_f 0.62 (cyclohexane–EtOAc, 1:1 + 1% $EtNMe_2$).

IR (film): 3468, 2922, 1602, 1513, 1453, 1260, 1140, 1029, 756, 699 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.10–7.39 (m, 13 H, C_6H_5), 6.97–7.01 (m, 2 H, C_6H_5), 6.75 (d, 1 H, *J* = 8.1 Hz, H-5′), 6.70 (dd, 1 H,

J = 8.1, 1.7 Hz, H-6′), 6.64 (d, J = 1.7 Hz, H-2′), 4.00 (pseudo-t, 1 H, J = 8 Hz, H-5), 3.77–3.89 [AB-system, 2 H, $(MeO)_2PhCH_2$], 3.85, 3.73 (2 s, 6 H, OCH_3), 3.35 (mc, 1 H, H-2), 3.08 (dt, 1 H, J_d = 8.7 Hz, J_t = 6.4 Hz, H-3), 2.93 (dd, 1 H, J = 13.9, 6.2 Hz, $PhCH_2$-a), 2.82 (dd, J = 13.9, 4.6 Hz, $PhCH_2$-b), 2.13 (ddd, 1 H, J = 12.8, 7.8, 6.4 Hz, H-4a), 1.99 (ddd, 1 H, J = 12.8, 8.7, 7.5 Hz, H-4b). The sample contains small amounts of the 2,3-*trans*-3,5-*cis* product.

Irradiation at 3.35 ppm (H-2) enhanced the signals at 4.00 ppm (H-5, 2.7%), 3.87 ppm [$(MeO)_2PhCH_2$-a, 1.3%], 3.77 ppm [$(MeO)_2PhCH_2$-b, 2.7%], 2.93 ppm ($PhCH_2$-a, 2.2%), 2.82 ppm ($PhCH_2$-b, 3.0%). Irradiation at 3.08 ppm (H-3) enhanced the signals at 3.35 ppm (H-2, 0.9%), 2.93 ppm ($PhCH_2$-a, 0.6%), 2.82 ppm ($PhCH_2$-b, 1.1%), 2.13 ppm (H-4a, 0.9%), 1.99 ppm (H-4b, 5.0%). Irradiation at 4.00 ppm (H-5) enhanced the signals at 3.87 ppm [$(MeO)_2PhCH_2$-a, 1.3%], 3.77 ppm [$(MeO)_2PhCH_2$-b, 1.1%], 3.35 ppm (H-2, 2.2%), 2.13 ppm (H-4a, 6.8%).

DEPT (100.6 MHz, $CDCl_3$): δ = 130.0, 128.1, 128.1, 127.9, 127.8, 127.4, 126.0, 121.5, 112.9, 110.4 (Ar), 71.1 (C-2), 66.6 (C-5), 55.8, 55.6 (OCH_3), 55.0 [$(MeO)_2PhCH_2$], 47.6 (C-3), 42.9 (C-4), 39.5 ($PhCH_2$). Two aromatic signals are missing due to low S/N-ratio.

HRMS: m/z calcd for $[M + H]^+$: 464.2591; found: 464.2585.

2,3-*cis*-3,5-*cis*-9g

Yield: 11.3 mg; colorless oil; R_t 12.0 min; R_f 0.62 (cyclohexane–EtOAc, 1:1 + 1% $EtNMe_2$).

IR (film): 2932, 2253, 1602, 1513, 1452, 1260, 1140, 1030, 911, 759, 732, 700 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.50–7.54 (m, 2 H, C_6H_5), 7.35 (t, 2 H, J = 7.5 Hz, C_6H_5), 7.16–7.30 (m, 6 H, C_6H_5), 7.05–7.16 (m, 3 H, C_6H_5), 6.85 (mc, 2 H, C_6H_5), 6.73 (d, 1 H, J = 8.1 Hz, H-5′), 6.67 (dd, 1H, J = 8.1, 1.7 Hz, H-6′), 6.59 (d, 1 H, J = 1.7 Hz, H-2′), 3.83–3.90 (m, 1 H, H-5), 3.84, 3.80 (2 s, 6 H, OCH_3), 3.59 [d, 1 H, J = 14.2 Hz, $(MeO)_2PhCH_2$-a], 3.53 (pseudo-q, 1 H, J = 7.0 Hz, H-2), 3.46 [d, 1 H, J = 14.2 Hz, $(MeO)_2PhCH_2$-b], 3.33 (dd, J = 10.0, 7.8 Hz, H-3), 2.67 (dd, 1 H, J = 13.6, 7.0 Hz, $PhCH_2$-a), 2.44 (dt, 1 H, J_d = 12.4 Hz, J_t = 6.8 Hz, H-4a), 2.33 (dd, 1 H, J = 13.6, 7.2 Hz, $PhCH_2$-b), 2.10 (td, J_d = 12.4 Hz, J_t = 10.0 Hz, H-4b).

Irradiation at 3.33 ppm (H-3) enhanced the signals at 3.85 ppm (H-5, 4.7%), 3.53 ppm (H-2, 4.1%), 2.44 ppm (H-4a, 3.4%), 2.33 ppm ($PhCH_2$-b, 0.4%), 2.10 ppm (H-4b, 0.7%). Irradiation at 2.67 ppm ($PhCH_2$-a) enhanced the signals at 3.59 ppm ($(MeO)_2PhCH_2$-a, 1.8%), 3.53 ppm (H-2, 2.9%), 3.46 ppm ($(MeO)_2PhCH_2$-b, 0.9%), 2.33 ppm ($PhCH_2$-b, 28.3%), 2.10 ppm (H-4b, 2.2%). Irradiation at 2.44 ppm (H-4a) enhanced the signals at 3.85 ppm (H-5, 7.0%), 3.80 ppm (OCH_3, 0.4%), 3.53 ppm (H-2, 0.6%), 3.33 ppm (H-3, 6.7%), 2.10 ppm (H-4b, 28.2%).

^{13}C NMR, DEPT (100.6 MHz, $CDCl_3$): δ = 129.1, 128.7, 128.1, 127.7, 127.6, 127.3, 126.7, 125.9, 125.2 (Ar), 121.0 (C-6′), 112.6, 110.3 (C-2′, C-5′), 67.8 (C-2), 67.6 (C-5), 55.6, 55.4 [OCH_3, $(MeO)_2PhCH_2$], 46.1 (C-3), 41.3 (C-4), 38.5 ($PhCH_2$).

ESI-MS: m/z = 464.4 ($[M + H]^+$, 100%).

HRMS: m/z calcd for $[M + H]^+$: 464.2591; found: 464.2610.

The 2,3-*cis*-3,5-*trans*-diastereomer could not be obtained in sufficient quantity.

1-(3′,4′-Dimethoxybenzyl)-5-methyl-2-phenylpyrrolidine (9h)

Compound **9h** was obtained according to the general procedure from **6d** (322 mg, 1.15 mmol) and methyl vinyl ketone (105 µL, 1.26 mmol). Extractive work-up (1 N HCl) gave a 1:1 mixture of *cis*- and *trans*-**9h** (301 mg, 84%) as a light yellow oil; R_f 0.44 (cyclohexane– EtOAc, 3:1 + 1% $EtNMe_2$).

IR (ATR): 2961, 1514, 1465, 1264, 1233, 1029, 908, 733, 702 cm^{-1}.

^1H NMR, COSY (400 MHz, $CDCl_3$): δ (*cis*/*trans* mixture) = 7.28–7.45 (m, 8 H, C_6H_5), 7.19–7.25 (m, 2 H, C_6H_5), 6.82–6.87 (m, 2 H, H-2′^{t}, H-6′^{t}), 6.77 (d, 1 H, J = 7.9 Hz, H-5′^{t}), 6.74 (d, 1 H, J = 8.1 Hz, H-5′^{c}), 6.70 (dd, 1 H, J = 8.1, 1.6 Hz, H-6′^{c}), 6.67 (d, 1 H, J = 1.6 Hz, H-2′^{c}), 3.80–3.91 (m, 13 H, H-2^t, 4 OCH_3), contained in this multiplet: 3.86, 3.86, 3.84, 3.81 (4 s, OCH_3), 3.76 (d, 1 H, J = 14.4 Hz, $PhCH_2$-a^c), 3.53–3.61 (m, 2 H, H-2^c, $PhCH_2$-a^t), contained in this multiplet: 3.58 (d, 1 H, J = 13.5 Hz, $PhCH_2$-a^t), 3.34–3.47 (m, 3 H, H-5^t, $PhCH_2$-b^c, $PhCH_2$-b^t), contained in this multiplet: 3.44 (d, 1 H, J = 14.4 Hz, $PhCH_2$-b^c), 3.37 (d, 1 H, J = 13.5 Hz, $PhCH_2$-b^t), 2.78 (mc, 1 H, H-5^c), 2.32 (mc, 1 H, H-3a^t), 2.17 (mc, 1 H, H-4a^t), 1.96–2.07 (m, 1 H, H-3a^c), 1.86–1.96 (m, 1 H, H-4a^c), 1.59–1.77 (m, 2 H, H-3b^t, H-3b^c), 1.41–1.56 (m, 2 H, H-4b^t, H-4b^c), 1.08 (d, 3 H, J = 6.1 Hz, CH_3^c), 0.98 (d, 3 H, J = 6.4 Hz, CH_3^t).

^{13}C NMR, HMQC (75.5 MHz, $CDCl_3$): δ (*cis*/*trans* mixture) = 148.7, 148.3, 147.6, 147.6 (C-3′, C-4′), 145.3, 145.0 (C-1″), 133.0, 131.4 (C-1′), 128.2, 127.6 (C-2″,6″, C-3″,5″), 126.7 (C-4″), 121.2 (C-6′^{c}), 120.1 (C-6′^{t}), 112.8 (C-2′^{c}), 111.6 (C-2′^{t}), 110.7 (C-5′^{t}), 110.4 (C-5′^{c}), 68.8 (C-2^c), 65.0 (C-2^t), 58.8 (C-5^c), 55.8, 55.7 (OCH_3), 54.7 [$(MeO)_2PhCH_2^c$], 54.0 (C-5^t), 50.8 [$(MeO)_2PhCH_2^t$], 33.9 (C-3^c), 33.4 (C-3^t), 32.2 (C-4^c), 31.3 (C-4^t), 21.1 (CH_3^c), 14.4 (CH_3^t).

ESI-MS: m/z (%) = 312.1 ($[M + H]^+$, 100), 150.9 ($[(MeO)_2PhCH_2]^+$, 42}.

HRMS: m/z calcd for $[M + H]^+$: 312.1964; found: 312.1961.

1-(3′,4′-Dimethoxybenzyl)-5-ethyl-2-phenylpyrrolidine (9i)

Compound **9i** was obtained according to the general procedure from **6d** (310 mg, 1.10 mmol) and ethyl vinyl ketone (120 µL, 1.21 mmol). Extractive work-up (1 N HCl) gave a 1.4:1 mixture of *cis*- and *trans*-**9i** (275 mg, 76%) as a light yellow oil; R_f 0.47 (cyclohexane–EtOAc, 3:1 + 1% $EtNMe_2$).

IR (ATR): 2970, 1514, 1264, 1234, 1140, 1029, 908, 731, 704 cm^{-1}.

^1H NMR, COSY (400 MHz, $CDCl_3$): δ (*cis*/*trans* mixture) = 7.40–7.45 (m, 2.4 H, C_6H_5), 7.27–7.35 (m, 7.2 H, C_6H_5), 7.18–7.24 (m, 2.4 H, C_6H_5), 6.78–6.83 (m, 2 H, H-2′^{t}, H-6′^{t}), 6.76 (d, 1 H, J = 7.9 Hz, H-5′^{t}), 6.73 (d, 1.4 H, J = 8.0 Hz, H-5′^{c}), 6.65–6.70 (m, 2.8 H, H-2′^{c}, H-6′^{c}), 3.84–3.88 (m, 11.2 H, H-2^t, 2 OCH_3^t, OCH_3^c), contained in this multiplet: 3.86, 3.85 (2 s, 6 H, 2 OCH_3^t), 3.84 (s, 4.2 H, OCH_3^c), 3.80 (s, 4.2 H, OCH_3^c), 3.75 (d, 1.4 H, J = 14.1 Hz, $PhCH_2$-a^c), 3.57–3.64 (m, 2.4 H, H-2^c, $PhCH_2$-a^t), contained in this multiplet: 3.61 (d, 1 H, J = 13.8 Hz, $PhCH_2$-a^t), 3.45 (d, 1.4 H, J = 14.1 Hz, $PhCH_2$-b^c), 3.43 (d, 1 H, J = 13.8 Hz, $PhCH_2$-b^t), 3.11 (mc, 1 H, H-5^t), 2.70 (mc, 1.4 H, H-5^c), 2.27 (mc, 1 H, H-4a^t), 2.10 (mc, 1 H, H-3a^t), 1.97–2.05 (m, 1.4 H, H-4a^c), 1.83–1.93 (m, 1.4 H, H-3a^c), 1.51–1.78 (m, 7.2 H, H-3b, H-4b, CH_2Me-a), 1.16–1.35 (m, 2.4 H, CH_2Me-b), 0.87 (t, 4.2 H, J = 7.4 Hz, CH_3^c), 0.82 (t, 1 H, J = 7.4 Hz, CH_3^t).

^{13}C NMR, HMQC (75.5 MHz, $CDCl_3$): δ (*cis*/*trans* mixture) = 148.6, 148.2, 147.6, 147.4 (C-3′, C-4′), 145.2, 145.0 (C-1″), 133.2, 131.5 (C-1′), 128.2, 127.5 (C-2″,6″^{c}, C-3″,5″^{c}), 128.1, 127.7 (C-2″,6″^{t}, C-3″,5″^{t}), 126.7 (C-4″^{c}), 126.6 (C-4″^{t}), 121.1 (C-6′^{c}), 120.0 (C-6′^{t}), 112.7 (C-2′^{c}), 111.5 (C-2′^{t}), 110.7 (C-5′^{t}), 110.4 (C-5′^{c}), 68.8 (C-2^c), 65.5 (C-2^t), 64.6 (C-5^c), 61.0 (C-5^t), 55.8 (OCH_3^t), 55.8 (OCH_3^c), 55.7 (OCH_3^t), 55.6 (OCH_3^c), 55.1 [$(MeO)_2PhCH_2^c$], 50.5 [$(MeO)_2PhCH_2^t$], 34.3 (C-4^c), 33.3 (C-4^t), 29.0 (C-3^c), 28.1 (C-3^t), 27.7 ($MeCH_2^c$), 21.7 ($MeCH_2^t$), 10.6 (CH_3^t), 10.2 (CH_3^c).

ESI-MS: m/z (%) = 326.0 ($[M + H]^+$, 100), 150.9 ($[(MeO)_2PhCH_2]^+$, 20).

HRMS: m/z calcd for $[M + H]^+$: 326.2120; found: 326.2133.

5-Ethoxy-3-methyl-1,2-diphenylpyrrolidine-2-carbonitrile (10)
Compound **4a** (8.2 g, 25.3 mmol) was dissolved in EtOH (70 mL) and stirred with Dowex 50WX8 ion exchange resin (H^+ form) for 1 h at 60 °C. The resin was removed by filtration. The precipitated substance was dissolved in CH_2Cl_2 and added to the filtrate. The solution was concentrated in vacuo and the product was crystallized at –18 °C. The procedure yielded hemiaminal **10** as a colorless crystalline solid (2.8 g, 36%); mp 144 °C (Lit.[33] mp 146 °C); R_f 0.38 (cyclohexane–EtOAc, 10:1 + 1% $EtNMe_2$).

IR (film): 2973, 1598, 1501, 1358, 1212, 1060, 939, 762, 703 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.55–7.63 (m, 2 H, H-2″, 6″), 7.28–7.42 (m, 3 H, H-3″, 5″, H-4″), 7.09–7.16 (m, 2 H, H-3′, 5′), 6.75–6.82 (m, 1 H, H-4′), 6.67–6.72 (m, 2 H, H-2′, 6′), 5.09 (d, 1 H, J = 4.8 Hz, H-5), 3.67 (mc, 2 H, CH_2CH_3), 2.70 (mc, 1 H, H-3), 2.26 (dd, 1 H, J = 13.1, 5.5 Hz, H-4a), 1.98 (dt, 1 H, J_t = 13.1 Hz, J_d = 4.8 Hz, H-4b), 1.36 (t, 3 H, J = 7.0 Hz, CH_2CH_3), 1.23 (d, 3 H, J = 6.8 Hz, 3-CH_3).

^{13}C NMR, DEPT (75.4 MHz, $CDCl_3$): δ = 142.7, 137.7 (C-1′, C-1″), 129.0, 128.7, 128.4, 125.5 (C_6H_5), 119.4 (C-4′), 117.9 (CN), 115.1 (C-2′,6′), 91.4 (C-5), 71.4 (C-2), 61.8 (CH_2CH_3), 47.5 (C-3), 37.5 (C-4), 15.6 (CH_3), 13.1 (CH_2CH_3).

ESI-MS: *m*/*z* (%) = 280.2 ($[M – CN]^+$, 100), 263.4 (52), 234.2 ($[M – CN – EtOH]^+$, 18).

3-Methyl-1,2-diphenylpyrrolidine-2-carbonitrile (11)
Hemiaminal **4a** (400 mg, 1.23 mmol) was dissolved in THF (16 mL). EtOH (4.21 mL) and AcOH (0.42 mL) were added, followed by $NaBH_3CN$ (310 mg, 4.93 mmol). The reaction was stopped after 2 h by addition of aq 1 N NaOH. The organic phase was washed with aq 1 N NaOH (2 ×), dried (Na_2SO_4) and the solvent was evaporated to yield **11** (304 mg, 94%) as a colorless crystalline solid; mp 120–121 °C; R_f 0.29 (cyclohexane–EtOAc, 10:1 + 1% $EtNMe_2$).

IR (film): 2927, 1602, 1503, 1452, 1349, 1326, 1125, 764, 755, 704, 693 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.43–7.49 (m, 2 H, H-3″, 5″), 7.30–7.40 (m, 3 H, H-2″, 6″, H-4″), 7.07–7.15 (m, 2 H, H-3′, 5′), 6.70–6.76 (m, 1 H, H-4′), 6.53–6.56 (m, 2 H, H-2′, 6′), 3.97 (d-pseudo-t, 1 H, J_t = 9 Hz, J_d = 7.0 Hz, H-5a), 3.66 (dt, 1 H, J_t = 9.1 Hz, J_d = 1.5 Hz, H-5b), 2.40 (mc, 1 H, H-3), 2.23–2.33 (m, 1 H, H-4a), 1.95–2.11 (m, 1 H, H-4b), 1.23 (d, 3 H, J = 6.6 Hz, CH_3).

^{13}C NMR (75.4 MHz, $CDCl_3$): δ = 144.4, 138.0 (C-1′, C-1″), 129.0, 128.7, (C-2″,6″, C-3″,5″), 128.3 (C-4″), 125.3 (C-3′,5′), 118.2 (C-4′), 117.9 (CN), 114.8 (C-2′,6′), 71.0 (C-2), 51.1, 50.0 (C-3, C-5), 31.1 (C-4), 13.6 (CH_3).

ESI-MS: *m*/*z* = 236.3 ($[M – CN]^+$, 100%).

HRMS: *m*/*z* calcd for $[M – CN]^+$: 236.1439; found: 236.1430.

3-Methyl-1,2-diphenylpyrrolidine (12)
Compound **4a** (150 mg, 0.46 mmol) was dissolved in MeOH (1 mL). A solution of $FeSO_4·7H_2O$ (128.5 mg, 0.46 mmol) in MeOH (1.5 mL), and $NaBH_3CN$ (58.1 mg, 0.92 mmol) were added. After 3 days, the same amounts of $FeSO_4·7H_2O$ and $NaBH_3CN$ were added. After stirring for 5 more days, an aq solution of $NaHCO_3$ was added. The mixture was extracted with EtOAc, the organic phase was dried (Na_2SO_4) and evaporated to yield a mixture of *cis*-**12** and *trans*-**12** as a colorless oil (103.3 mg, 94%, *cis*/*trans* = 4:7); R_f 0.49 (cyclohexane–EtOAc, 10:1 + 1% $EtNMe_2$).

IR (film): 2960, 1598, 1505, 1485, 1364, 746, 701, 692 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ (*cis*/*trans* mixture) = 7.26–7.38 (m, 4 H, C_6H_5), 7.14–7.24 (m, 3 H, C_6H_5), 6.66 (mc, 1 H, H-4′), 6.50–6.56 (m, 2 H, H-2′, 6′), 4.66 (d, 0.36 H, J = 8.1 Hz, H-2^c), 4.27 (d, 0.64 H, J = 3.9 Hz, H-2^t), 3.72–3.82 (m, 1 H, H-5a), 3.57–3.67 (m, 0.64 H, H-5b^t), 3.46 (ddd, 0.36 H, J = 10.3, 9.1, 6.5 Hz H-5b^c), 2.63 (mc, 0.36 H, H-3^c), 2.06–2.34 (m, 1.64 H, H-3^t, H-4a), 1.86 (mc, 0.36 H, H-4b^c), 1.64–1.76 (m, 0.64 H, H-4b^t), 1.21 (d, 1.90 H, J = 6.8 Hz, CH_3^t), 0.75 (d, 1.10 H, J = 6.8 Hz, CH_3^c).

Irradiation at 4.66 ppm (H-2^c) enhanced the signals at 2.63 ppm (H-3^c, 4.1%), 0.75 ppm (CH_3^c, 1.2%). Irradiation at 4.27 ppm (H-2^t) enhanced the signals at 2.27 ppm (H-3^t, 2.1%), 1.21 ppm (CH_3^t, 3.4%).

^{13}C NMR (75.4 MHz, $CDCl_3$): δ (*cis*/*trans* mixture) = 147.3, 144.1 (C-1″, C-1‴^{t}), 146.9, 141.2 (C-1′^{c}, C-1‴^{c}), 128.8, 128.5 (C-2″, 6‴^{t}, C-3″,5‴^{t}), 128.9, 128.1 (C-2″,6‴^{c}, C-3″,5‴^{c}), 127.3 (C-3′,5′^{c}), 126.8 (C-4‴^{c}), 126.7 (C-4‴^{t}), 125.9 (C-3′,5′^{t}), 115.6 (C-4′^{t}), 115.5 (C-4′^{c}), 112.5 (C-2′,6′^{t}), 111.9 (C-2′,6′^{c}), 70.5 (C-2^t), 66.6 (C-2^c), 48.2 (C-5^t), 48.1 (C-5^c), 44.0 (C-3^t), 38.4 (C-3^c), 31.0 (C-4^c), 30.8 (C-4^t), 18.8 (CH_3^t), 15.7 (CH_3^c).

ESI-MS: *m*/*z* = 238.2 ($[M + H]^+$, 100).

HRMS: *m*/*z* calcd for $[M+H]^+$: 238.1596; found: 238.1590

X-ray Crystallography[41]
Both crystals were measured on a Turbo-CAD4 diffractometer with Cu-K_α radiation (graphite monochromator) at 295 K.

Picrate 5b
Crystal structure solution and refinement were performed using the SIR-97 and SHELXL-97 program, respectively.

$C_{35}H_{30}N_4O_7$, M = 618.63, monoclinic, space group $P2_1/n$, Z = 4, a = 12.591(2) Å, b = 15.683(2) Å, c = 15.523(3) Å, β = 90.214°, $R1$ = 0.0597, $wR2$ = 0.1690.

Hemiaminal 10

Crystal structure solution and refinement were performed using the SIR-92 and SHELXL-97 program, respectively.

$C_{20}H_{24}N_2O$, M = 306.40, orthorhombic, space group $Pca2_1$, Z = 4, a = 7.8372(8) Å, b = 12.6374(11) Å, c = 17.4153(14) Å, $R1$ = 0.0672, $wR2$ = 0.1652.

Acknowledgment

This work was supported by the Deutsche Forschungsgemeinschaft and the Emil und Paul Müller-Gedächtnisstiftung. We thank Prof. Dr. K. Klinkhammer for the helpful discussion, Dr. D. Schollmeyer for the X-ray crystallographic analyses and H. Kolshorn for the 2D NMR spectra and NOE measurements.

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