Pergamon

Tetrahedron 57 (2001) 1939–1950

TETRAHEDRON

Reaction of the lithio-derivative of methoxyallene with hydrazones. Part 1: Synthesis and transformation of α-allenyl hydrazines☆

Valérie Breuil-Desvergnes and Jacques Goré*

Laboratoire de Chimie Organique I, associé au CNRS, Université Claude Bernard 5622, Bât 308, CPE-Lyon, 43 Bd du 11 novembre 1918, 69622 Villeurbanne, France

Received 2 August 2000; revised 7 December 2000; accepted 4 January 2001

Abstract—The lithio-derivative of methoxyallene reacts with aldehyde hydrazones leading to expected α-allenyl hydrazines when ether is the solvent of the reaction. The yields are good as well as the diastereoselectivity observed in the case of SAMP-hydrazones. These hydrazines are cleanly transformed to *N*-dialkylamino-3-methoxy-3-pyrrolines when they are reacted with *n*-BuLi in THF. These compounds are sometimes accompanied by the isomeric 4-methyl azetidines. The *N*-dialkylamino-3-methoxy-3-pyrrolines are transformed to 3-methoxy-3-pyrrolines by hydrogenolysis of the nitrogen–nitrogen bond, to 3-alkoxy-pyrroles by treatment with a peracid and to 3-amino-pyrroles by acidic migration of the dialkylamino group. In the case of SAMP-hydrazines, the obtained 3-methoxy-3-pyrrolines have a high enantiomeric purity. Lastly, attempts to prepare α-hydrazino-esters (and subsequently α-amino-esters) by ozonolysis of the allenyl moiety failed due to the formation of a methyl glyoxylate.

Since the pioneering work of Brandsma et al.,[1] who demonstrated that methoxyallene **1** can be regioselectively metallated at C_1 by reaction with *n*-butyllithium, a lot of work has been devoted to the use of the so formed α-lithio methoxyallene **2** and to its reaction with various electrophiles. Mainly, the addition of **2** to aldehydes and ketones has been studied; it gives exclusively the α-allenic alcohol,[2] which can be hydrolysed to conjugated ketones or involved in cyclization processes (Fig. 1).[3]

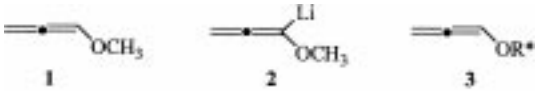


Figure 1.

In our group, we were particularly interested in the stereochemical behaviour of the lithio-derivative of chiral alkoxyallene **3** (R=enantiopure substituent such as ephedrine derivatives or diacetoneglucose). They react with aromatic aldehydes giving α-allenic alcohols in good yield with a correct stereo differentiation (d.e. up to 85%);[4] this reaction has been used in the multi-step synthesis of the styrryl lactone (+)-gonodiol.[5]

Comparatively, only a few studies dealt with the addition of **2** (or the lithio derivative of **3**) on a carbon–nitrogen double bond in order to prepare α-allenic amines or derivatives thereof. Very recently this addition was studied with achiral[6] or chiral[7] nitrones and with various imines.[8] In our case, we tried to add the lithio-derivative of enantiopure alkoxyallene **3** to aromatic silylimines but the reaction, sometimes successful, was not reproducible and gave tars more often than tractable products. Consequently, we turned our attention to hydrazones, which have been used extensively as reagents for electrophilic amination. In this context, Enders et al.[9] described the use of hydrazones bearing an α-methoxymethyl pyrrolidinyl group (SAMP- or RAMP-hydrazones) in various reactions, and particularly in the asymmetric addition of organometallics; this was the motivation for this study.

1. Results and discussion

1.1. Preparation of the hydrazones

The hydrazones required for this study were prepared as shown in Scheme 1 by reaction of the aldehydes with the commercially available hydrazines as previously reported.[10]

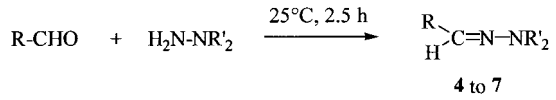
The yields of this reaction are nearly quantitative and the hydrazones are pure enough to be used without any

☆ For preliminary results, see Refs. 19 and 20.

Keywords: organolithium; allenes; asymmetric synthesis; pyrrolines; pyrroles.

* Corresponding author. Tel.: +33-04-72-44-81-35; fax: +33-04-72-43-12-14; e-mail: gore@univ-lyon1.fr

0040–4020/01/$ - see front matter
PII: S0040-4020(01)00030-8



Scheme 1.

purification. In any case, they are easily purified by FC on alumina gel. As anticipated, only one isomer is detected by ^{1}H and ^{13}C NMR, the configuration being *E* on the basis of literature data. In Table 1 are listed the prepared hydrazones which differ from each other by the aromatic or aliphatic nature of R and by the structure of the hydrazine moiety.

1.2. Reaction of lithio methoxyallene with hydrazones; obtention of α-allenyl hydrazines

We will describe here some results of our study of this reaction and will present in the following paper[11] that the nature of the product can be dramatically modified by the type of solvent and by the experimental conditions (temperature and reaction time). The results listed in Table 2 are those, in ether, of the reaction of hydrazones with α-lithio methoxyallene **2** prepared by the reaction at −30°C of 1 equiv. of *n*-BuLi with **1**. The addition of the organometallic is made at −78°C, the temperature being raised to −20°C after 2 h, the reaction time then being 16 h. A preliminary study showed that 6 M equiv. of **2** are

Table 1. Hydrazones prepared for this study

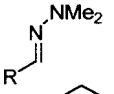
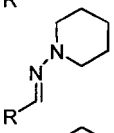
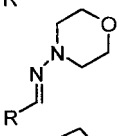
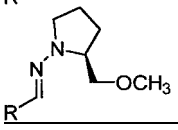
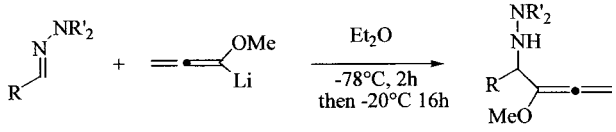
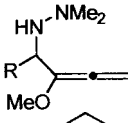
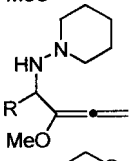
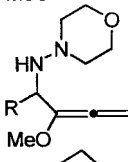
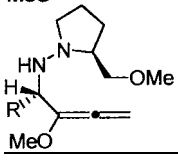
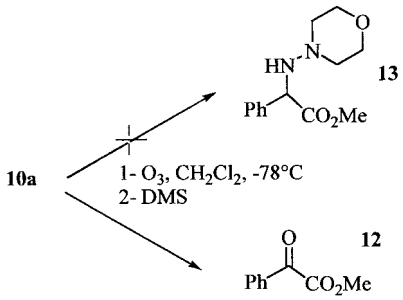
	Ph	β-naphthyl	*p*-MePh	*p*-MeOPh	Et	*iso*Pr	*t*Bu
	**4a**	**4b**	**4c**	**4d**	**4e**	**4f**	**4g**
	**5a**	**5b**	**5c**	**5d**	**5e**	**5f**	**5g**
	**6a**	**6b**	**6c**	**6d**	**6e**	**6f**	**6g**
	**7a**	**7b**	**7c**	**7d**	**7e**	**7f**	**7g**

Table 2. Reaction of **2** with various hydrazones in ether



4-7 **8-11**

	Ph	β-naphthyl	*p*-MePh	*p*-MeOPh	Et	*iso*Pr	*t*Bu
	**8a**	**8b**	**8c**		**8e**	**8f**	
	**9a**	**9b**	**9c**	**9d**	**9e**	**9f**	**9g**
	**10a**	**10b**	**10c**	**10d**	**10e**	**10f**	**10g**
	**11a** d.e. >99%	**11b** d.e. >99%	**11c** d.e. >99%	**11d** d.e. >99%	**11e** d.e. 93%	**11f** d.e. 95%	**11g** d.e. 98%



Scheme 2.

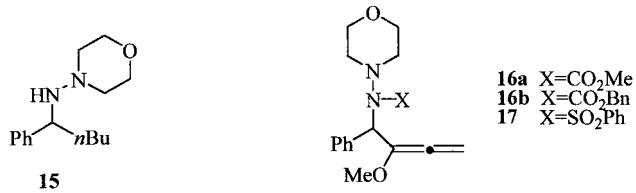


Figure 2.

necessary to engage completely the hydrazones; surprisingly, no reaction is observed when the reaction is run with 2 equiv. and a variable amount of hydrazone is recovered when intermediate quantities of **2** are used.[12]

Uniformly, this reaction led to α-allenyl hydrazines **8**–**11**. These compounds are fairly unstable under chromatographic conditions, either on silica gel or on neutral alumina, but ^{1}H and ^{13}C NMR spectra showed that the crude product resulting from the usual work-up has a purity ≥95%, this crude product being obtained in almost quantitative yield (Table 2).

In the case of SAMP-hydrazones, the reaction is highly diastereoselective and the α-allenyl hydrazines **11** are obtained with a diastereomeric excess, ranging from 93 to ≥99% determined by GC and ^{1}H NMR. The *S* configuration of the stereogenic carbon was assigned by reference to the model proposed by Enders et al. for the diastereoselection of the addition of organometallics to such hydrazones.[13] It was confirmed later by X-ray diffraction study of a derived compound (see below).

1.3. Reaction in ether of 2 with various hydrazones. Attempts to prepare α-amino acids from α-allenyl hydrazines

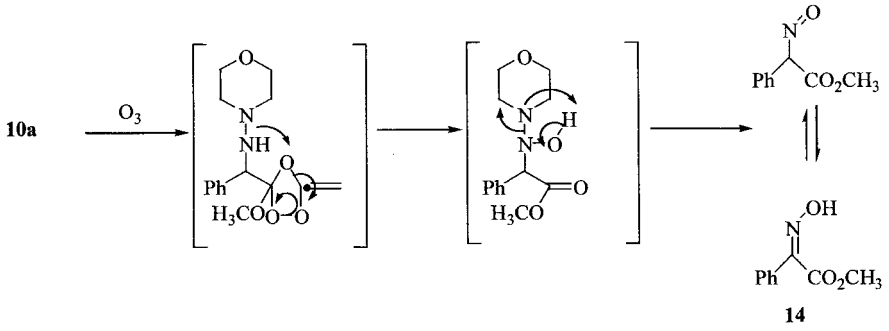
In every case studied so far, α-allenyl hydrazines were the only products formed in the reaction of α-lithio methoxyallene **2** with hydrazones **4**–**7** and the diastereoselection was high in the case of SAMP-hydrazones **7**. These hydrazines could be the precursors of α-amino acids by a two-step sequence involving the ozonolysis of the allenic moiety followed by hydrogenolysis of the N–N bond; both reactions are known to give good yields: ozonolysis of the methoxyallene group has been reported previously[8] and the reduction of the hydrazine to an amine will be discussed further in this paper. Of course, this two-step sequence was particularly attractive in the case of SAMP-hydrazines **11**, as it could provide a potential access to enantiopure α-amino acids by a formal asymmetric formation of the C–CO_2H bond.[14]

The first attempts at ozonolysis were carried out with the hydrazine **10a** in the classical way by using dichloromethane as solvent, the ozonolysis being followed by a supposed reduction of the ozonide by dimethylsulfide. Surprisingly, this reaction led only to methyl phenylglyoxylate **12** with no trace of the expected α-hydrazino ester **13** (Scheme 2).

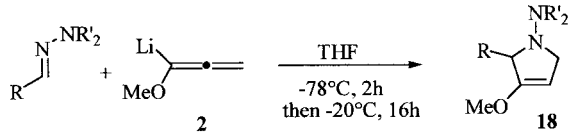
It is noteworthy that the crude product contains, besides **12**, the corresponding oxime **14** identified mainly by GC–MS coupling and that morpholine is also formed in the ozonolysis reaction. Since the saturated hydrazine **15** does not react with ozone and α-aminoalkoxyallenes give α-amino esters in the same conditions,[7] it appeared that the transformation of **10a** to **12** via **14** could involve the intramolecular reduction of the ozonide by the hydrazine group as depicted in Scheme 3.

In order to avoid this intramolecular reduction by decreasing the nucleophilicity of nitrogen, attempts to prepare carbamates **16a**,**b** or sulfamide **17** were made under different conditions; they were all unsuccessful (Fig. 2). Also, the ozonolysis was run in dichloromethane in the presence of 1–5 equiv. of pyridine[15] as we expected a different mechanistic pathway. The hydrazino ester **13** was effectively obtained with a maximum yield of about 10% mixed with the oxime **14** and morpholine in the crude product and it was impossible to isolate it in pure form from this mixture.

In a last experiment, we ran the same reaction with the diastereopure SAMP-hydrazine **11a** but the result was the



Scheme 3.



Scheme 4.

same, discounting the possibility of preparing enantiopure α-amino acids by this sequence.

1.4. Formation of *N*-dialkylamino-3-pyrrolines

As will be shown in the following paper,[11] the reaction of α-lithio-methoxyallene **2** with hydrazones in THF led in many cases and in good yield to *N*-dialkylamino-3-pyrrolines **18** (Scheme 4); these compounds are also obtained diastereoselectively in the case of SAMP-hydrazones **7**.

As it was probable that compounds **18** came from the cyclization of the α-allenyl lithium hydrazides, we treated some of the α-allenyl hydrazines **8**–**11** with *n*-BuLi in THF to try to obtain the same cyclization.

First of all, **11a** was treated with 1 equiv. of *n*-BuLi under the same conditions (time, temperature) as those used in the direct cyclization depicted in Scheme 4. Effectively, **18a** was then obtained in a 60% yield mixed with the non-engaged starting material. When 2 equiv. of *n*-BuLi were used, **18a** was obtained with almost quantitative yield after purification by flash chromatography over alumina.

Consequently, the reaction with other hydrazines was run by using 2 equiv. of base. The results are given in Table 3. They show marked differences in the behaviour of the cyclization, which is fairly dependent on the nature of the substituent R and on those of the terminal nitrogen of the hydrazine. With SAMP-hydrazines the cyclization to the corresponding pyrrolines is observed regardless of the nature of R, either aromatic or aliphatic. The yields are high and the diastereomeric excess is retained.

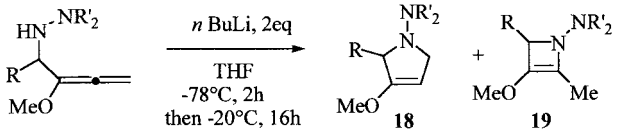
In the case of morpholine hydrazines, the cyclization to pyrrolines is observed only when R is an aromatic group. On the contrary, the aliphatic compounds remained unchanged under the same experimental conditions. Lastly, in the dimethyl and piperidinyl series, the hydrazines when R is aliphatic are again inert under these reaction conditions, while when R is aromatic, cyclization occurs giving a mixture of the corresponding pyrroline with an azetidine **19**; both compounds are difficult to separate by flash chromatography but, in the two series, it was possible to isolate the azetidine in pure form and to propose its structure on the basis of MS and NMR spectra. These azetidines are also obtained, but with better yield, in the reaction of hydrazones **4**, **5**, **6** with α-lithio methoxyallene **2** in THF, where the cyclized products are obtained directly without stopping at the α-allenyl hydrazine step.[11]

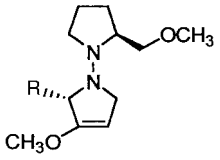
Evidently, the most interesting results are those concerning the SAMP-hydrazines **11** since the cyclization gives exclusively the *N*-dialkylaminopyrrolines **18** in high yield and diastereomeric excess. The exact structure of **18a** has been demonstrated by X-ray diffraction at −50°C (Fig. 3). The asymmetric carbon of the pyrroline has the *S* configuration as expected by the model proposed by Enders et al. for the addition of organometallics to SAMP-hydrazones.[13]

1.5. Transformation of *N*-dialkylamino-3-pyrrolines to 3-pyrrolines and to 3-alkoxy and 3-amino pyrroles

Having in hand *N*-dialkylamino-3-pyrrolidines in racemic or in diastereomeric pure form, it was interesting to try to obtain the parent 3-pyrrolines by reduction of the N–N bond; although numerous reports have described the synthesis of diversely substituted 3-pyrrolines,[16] compounds such as **20** bearing an enol ether functionality, a potential precursor of polyfunctionalized pyrrolidines, were never described. The interest is increased by the diastereomeric

Table 3. Cyclization of α-allenyl lithium hydrazides



Starting hydrazone	Product	Yield (%)	D.e. (%)
11a	 **18a** R=Ph	97	>99
11b	**18b** R=β-naphthyl	95	>99
11c	**18c** R=*p*-CH_3Ph	96	>99
11e	**18e** R=Et	94	98
11f	**18f** R=*iso*Pr	93	>99
R, R′=–$(CH_2)_5$–			
9a	R=Ph **18g**+**19a**	20 (7/1)	
9e	R=Et no cyclization		
R,R′=–$(CH_2)_2$–O–$(CH_2)_2$–			
10a	R=Ph **18h**+**19b**	97 (8/1)	
10b	R=β-naphthyl **18i**	96	
10e	R=Et no cyclization		
R, R′=CH_3			
8a	R=Ph **18j**+**19c**	20 (7/1)	
8e	R=Et no cyclization		

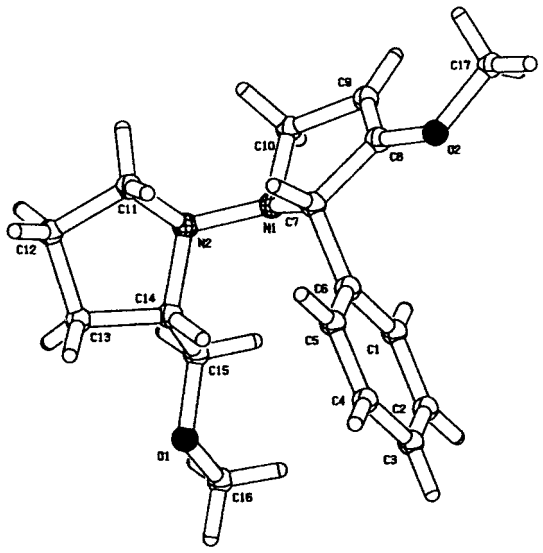


Figure 3.

purity of the starting material and by an expected high enantiomeric excess for the parent 3-pyrroline coming from the SAMP series.

Many conditions have been described for the reduction of the N–N bond of hydrazines but they concern mainly compounds having a free N–H[17] or an *N*-acyl bond.[18] They involve hydrogenolysis catalysed by Raney nickel, hydroboration or reduction by electron transfer (Li or Na/NH_3, SmI_2 with a proton source, Zn/AcOH etc). Most of these methods were tested using **18a** as model compound but they all proved to be unsuccessful. These repeated failures were then attributed to the structure of **18a** and analogues where both nitrogens are trisubstituted but without the presence of an acyl group. Considering that such an acyl group has a beneficial effect on the reduction by polarizing the N–N bond, we treated **18a** with methyl- and benzylchloroformate to form the ammonium salts **22a** or **22b** (not isolated). The hypothesis was good since the hydrogenation of these compounds in the presence of Raney nickel led to a mixture of the two possible reaction products **20a** and **21a**, their ratio being closely dependent on the experimental conditions (Scheme 5). 2-Methoxymethyl pyrrolidine is also present in the crude product and its purification is quite difficult due to the similarity of the physical properties of the three products. Surprisingly, this crude product is free of the corresponding carbamates but we have no explanation for the obvious hydrogenolysis of the N–CO_2R bond.

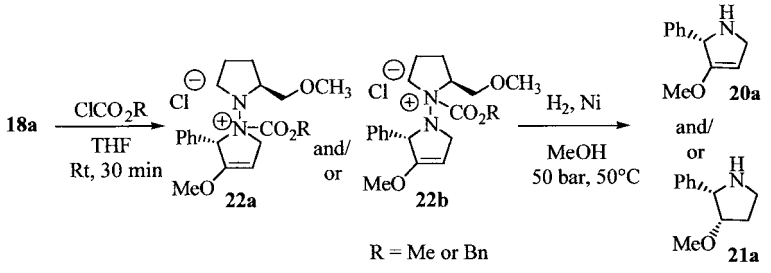
Fortunately, it was possible to turn the reaction selectively towards each product by changing the reaction time. In the case of 2×10^{-4} mol of **18a**, the reaction run at 50°C in a stainless steel bomb led preferentially to **20a** (75%) when the reaction time is 24 h and to **21a** (82%) when the reaction time is 48 h. The purity of the obtained compounds is around 95% since it is almost impossible to separate **20a** and **21a** by flash chromatography and the reaction is never totally selective. At 30°C, the reaction gives a mixture of both compounds, a reaction time of 48 h being necessary to engage all the starting material.

Having in hand satisfactory results for the hydrogenolysis of the N–N bond, we extended the method to some homologues of **18a**. It was done primarily with compounds **18** of the SAMP series in order to obtain the pyrrolines **20** in enantioenriched form. For analytical purposes, it was also necessary to obtain racemic pyrrolines (±)-**20**. They were obtained starting with morpholinyl pyrrolines **18h**,**k**. The results are all listed in Table 4.

The enantiomeric excess of **20a** was difficult to determine due to the instability of this compound. All the attempts made in GC and HPLC on chiral columns were unsuccessful. Fortunately, it was possible to determine this excess by ^{1}H NMR using Eu(hfc)$_3$ as chiral shift reagent.[19] While racemic **20a** exhibited two signals for the vinylic proton, only one remained for the enantioenriched **20a**; consequently its e.e. was estimated ≥95% showing that no epimerization occurred in the hydrogenolysis step. The same observation was also made in the case of **20c**, showing that the entire sequence starting from SAMP-hydrazones constitutes a good method for the preparation of enantiopure pyrrolines of type **20**. In this sequence, the most difficult step was the breaking of the N–N bond of hydrazines **18**.

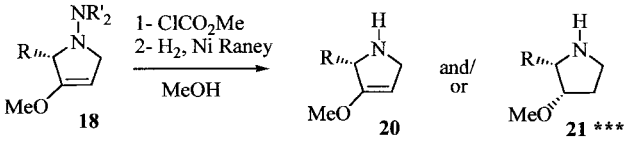
Surprisingly, this operation proved to be very easy in two other transformations of aromatic *N*-dialkyl aminopyrrolines **18**, transformations found in a serendipitous manner and which convert **18** to valuable pyrroles substituted in position 3 by an electron donating group.

When compounds **18**[20] were treated with *m*-chloroperbenzoic acid in dichloromethane at 20°C, they were cleanly transformed to 3-alkoxy-2-aryl pyrroles **23**. A proposed mechanism for this transformation is depicted in Scheme 6, the key step being a Cope elimination of the *N*-oxide **24**. Some examples of the alkoxy pyrroles prepared in this way are given in the same scheme. These compounds, which can be valuable for the preparation of polypyrroles,[21] have been rarely reported in the literature.[22]



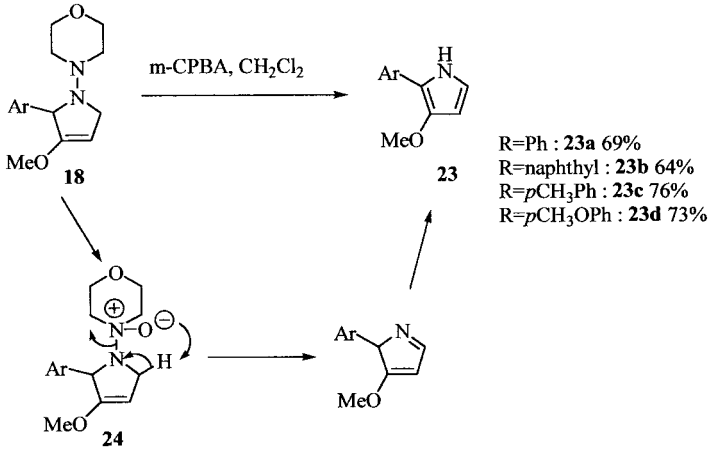
Scheme 5.

Table 4. Hydrogenolysis of the N–N bond of *N*-dialkylamino pyrrolines **18** (in each series, only one diastereomer of **21** was observed to which the *cis* structure was attributed, assuming that hydrogenation occurred by the less hindered half space of the double bond)

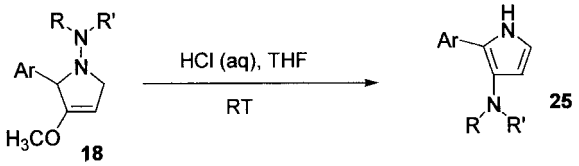


Starting material	Experimental conditions for hydrogenation	20		21	
18a					
R=Ph; R′, R′=SMP[a]	50°C, 24 h, 50 bar	(+)-**20a**	75%	(+)-**21a**	<5%
2×10^{-4} mol	50°C, 48 h, 50 bar		<5%		82%
18b					
R=β-naphthyl	50°C, 48 h, 50 bar	(+)-**20b**	79%	(+)-**21b**	–
R′, R′=SMP[a]	50°C, 72 h, 50 bar		–		63%
4×10^{-4} mol					
18d[b]					
R=*p*-MeOPh	50°C, 48 h, 50 bar	(+)-**20c**	68%	(+)-**21c**	–
R′, R′=SMP[a]	50°C, 72 h, 50 bar		–		57%
$4\times10^{\times4}$ mol					
18h					
R=Ph	50°C, 36 h, 30 bar	(±)-**20a**	57%	(±)-**21a**	<5%
R′, R′=$-(CH_2)_2O(CH_2)_2-$					
$2\times10^{\times4}$ mol					
18k[b]					
R=*p*-MeOPh	50°C, 36 h, 40 bar	(±)-**20c**	69%	–	
R′, R′=$-(CH_2)_2O(CH_2)_2-$					
3×10^{-4} mol					

[a] (*S*)-Methoxymethylpyrrolidine.
[b] For preparation, see Ref. 11.



Scheme 6.



Scheme 7. 18h: Ar=Ph, R, R′=dimethyl→**25a** (95%); **18g**: Ar=Ph, R, R′=morpholinyl→**25b** (95%); **18f**: Ar=Ph, R, R′=piperidinyl→**25c** (90%) (not pure enough to be totally characterized but characteristic signals of pyrrole skeleton are present on NMR spectra); **18a**: Ar=Ph, R, R′=(*S*)-2-methoxymethylpyrrolidinyl → **25d** (97%); **18c**: Ar=*p*-CH_3Ph, R, R′=(*S*)-2-methoxymethylpyrrolidinyl→**25e** (97%).

It is noteworthy that the same reaction gives lower yield with other amino groups: with Ar being a *p*-methoxyphenyl group, the yields are, respectively, 42 and 38% in the piperidinyl and in the dimethylamino series. Lastly, only traces of pyrrole were observed when the aromatic substituent is replaced by an ethyl group in the morpholinyl series.

Still more surprising was the result of the treatment of compounds **18** with 0.2N HCl in a mixture THF/H_2O 4:1; 3-amino-2-aryl pyrroles **25** were obtained in almost quantitative yields. They arise from a 1,3-migration of the amino group, the mechanism of which being undetermined for the moment (Scheme 7).

Again, this reaction does not work when Ar is replaced by an aliphatic group. In this case, the corresponding 3-aza-cyclopentanone is obtained in low yield.

2. Experimental

2.1. General remarks

All procedures were conducted in oven-dried glassware under positive nitrogen pressure and using syringe–needle transfer techniques. THF was distilled from sodium–benzophenone and diethyl ether from CaH_2. ^1H NMR (200 or 300 MHz) and ^{13}C NMR (50 or 75 MHz) spectra were recorded on a Bruker AC 200 or AM 300. Chemical shifts are reported as δ value relative to the solvent peak of $CHCl_3$ set to 7.26 for ^1H and 77.16 for ^{13}C. IR spectra were carried out on a Perkin–Elmer 298 spectrophotometer. Melting points were determined in open capillaries and are uncorrected. Optical rotation values were determined using a Perkin–Elmer 241 polarimeter. Flash chromatography (FC) was performed using alumina N/UV 254. Mass spectrometry was performed on a NERMAG R 10-10 H coupled with a GC DELSI DI 700 (EI=70 eV, column type DB5 30 m, CI gas:ammonia). HRMS spectra were carried out on a Thermoquest Finnigan (MAT 95 XL) spectrometer (CI gas:isobutane).

2.2. Preparation of α-allenic hydrazines

2.2.1. General procedure. α-Lithio methoxyallene was synthesized in situ by addition of an equivalent of *n*-butyllithium (2.5 MHz hexane solution) to a solution of 5 mmol methoxyallene in ether (5 ml) at −40°C. The solution was chilled to −78°C, then after 20 min, a solution of hydrazones **4**–**7** (0.833 mmol in 2 ml of ether) was added dropwise. The mixture was warmed to −20°C. After 16 h at this temperature, the mixture was quenched with 5 ml of water and extracted with ether (2×5 ml). The combined organic phases were dried (Na_2SO_4) and concentrated. The crude product obtained in quantitative yield was not purified because of its instability on silica or alumina gel. Its ^1H and ^{13}C NMR spectra indicate a purity ≥95% as well as TLC on neutral alumina (petroleum ether EP/ethyl acetate AcOEt) using phosphomolybdic acid as chemical tracer.

As shown in Table 2, 25 homologous α-allenyl hydrazines have been prepared which differ by the nature of the substituents of the terminal nitrogen and by that of the starting aldehydes. We describe below 13 of them which are representative of the different substitutions. The spectra of the others can be deduced from those described.

2.2.2. 1-*N*-Dimethylaminyl-amino-1-phenyl-2-methoxy-buta-2,3-diene (8a). R_f=0.33 (EP/AcOEt 97:3). IR (film): ν=3300, 2920–2840, 1950, 1450. ^1H NMR ($CDCl_3$, 300 MHz): δ=1.93 (s, 1H), 2.53 (s, 6H), 3.44 (s, 3H), 4.59 (s, 1H), 5.56 (m, 2H), 7.0–7.5 (m, 5H). ^{13}C NMR ($CDCl_3$, 50 MHz): δ=48.1 (CH_3), 56.2 (CH_3), 64.1 (CH), 92.0 (CH_2), 136.0 (C), 136.0 (C), 140.6 (C), 128.3 (CH), 128.4 (CH), 128.6 (CH), 198.7 (C). EI MS *m/z* (%): 203 (6), 174 (12), 144 (8), 128 (5), 115 (7), 91 (5), 77 (6), 59 (100). HRMS: theoretical: 218.14191; measured: 218.14193.

2.2.3. 1-*N*-Piperidinyl-amino-1-phenyl-2-methoxy-buta-2,3-diene (9a). R_f=0.63 (EP/AcOEt 90:10). IR (film): ν=3300, 3060–3020, 2960–2880, 1960, 1610, 1455. ^1H NMR ($CDCl_3$, 300 MHz): δ=1.28–1.36 (m, 2H), 1.51–1.58 (m, 4H), 2.57–2.69 (m, 5H), 3.35 (s, 3H), 4.57 (m, 1H), 5.48 (m, 2H), 7.25–7.41 (m, 5H). ^{13}C NMR (50 MHz): δ=23.9 (CH_2), 26.0 (CH_2), 56.2 (CH_3), 57.8 (CH_2), 63.8 (CH), 91.9 (CH_2), 127.2 (CH), 127.9 (CH), 128.3 (CH), 134.6 (C), 141.1 (C), 199 (C). EI MS *m/z* (%): 258 (10), 159 (12), 145 (5), 129 (9), 115 (12), 91 (12), 70 (15), 55 (32), 42 (100). HRMS CI: theoretical: 259.18103; measured: 259.18132.

2.2.4. 1-*N*-Morpholinyl-amino-1-phenyl-2-methoxy-buta-2,3-diene (10a). R_f=0.5 (EP/AcOEt 90:10). IR (film): ν=3300, 2970–2820, 1950, 1610, 1450. ^1H NMR ($CDCl_3$, 300 MHz): δ=2.63–2.75 (m, 5H), 3.39 (s, 3H), 3.66 (t, 4H), 4.58 (m, 1H), 5.45 (m, 2H), 7.24–7.40 (m, 5H). ^{13}C NMR (50 MHz): δ=49.9 (CH_2), 56.3 (CH_3), 63.3 (CH), 67.0 (CH_2), 92.0 (CH_2), 127.27 (CH), 127.6 (CH), 128.1 (CH), 157.2 (C), 198.8 (C). EI MS *m/z* (%): 245 (22), 174 (47), 159 (10), 144 (13), 115 (15), 101 (100), 77 (9), 57 (23), 29 (13). HRMS EI: theoretical: 260.15247; measured: 260.15167.

2.2.5. (1*S*,2*S*′)-1-*N*-[(2′-Methoxymethyl)pyrrolidin-1′-yl]-amino-1-phenyl-2-methoxy-buta-2,3-diene (11a). R_f=0.38 (EP/AcOEt 97:3). $[\alpha]_D^{20}$=−26 (*c*=0.53, $CHCl_3$). IR (film): ν=3300, 3080–2820, 1920, 1610, 1450. ^1H NMR ($CDCl_3$, 300 MHz): δ=1.53 (m,1H), 1.67 (m, 2H), 1.89 (m, 1H), 2.33 (m, 1H), 2.99 (s, 1H), 3.15 (m, 1H), 3.37 (s, 3H), 3.39 (s, 3H), 3.35–3.66 (m, 2H), 4.53 (m, 1H), 5.52 (m, 2H), 7.27–7.42 (m, 5H). ^{13}C NMR (50 MHz): δ=21.2 (CH_2), 36.4 (CH_2), 56.2 (CH_3), 57.3 (CH_2), 59.1 (CH_3), 65.5 (CH), 65.9 (CH), 75.7 (CH_2), 91.8 (CH_2), 127.4 (CH), 127.7 (CH), 128.4 (CH), 135.9 (C), 141.3 (C), 199.2 (C). EI MS *m/z* (%): 243 (7), 211 (17), 174 (19), 129 (100), 97 (45), 71 (27), 70 (15), 45 (36). HRMS EI: theoretical: 288.18377; measured: 288.18294.

2.2.6. 1-*N*-Dimethylaminyl-amino-1-β-naphthyl-2-methoxy-buta-2,3-diene (8b). R_f=0.42 (EP/AcOEt 97:3). IR (film): ν=3300, 3060–3020, 2970–2800, 1960, 1660, 1460. ^1H NMR ($CDCl_3$, 300 MHz): δ=1.82 (s, 1H), 2.52 (s, 6H), 3.40 (s, 3H), 4.74 (s, 1H), 5.54 (m, 2H), 7.44 (s, 3H), 7.79–7.89 (m, 4H). ^{13}C NMR ($CDCl_3$, 50 MHz): δ=48.1 (CH_3), 56.3 (CH_3), 64 (CH), 92.3 (CH_2), 125.6 (CH), 126.1 (CH), 126.8 (CH), 127.6 (CH), 127.7 (CH), 127.8 (CH), 128.0 (CH), 133.2 (C), 133.4 (C), 135.9 (C), 157.3 (C), 198.7 (C). EI MS *m/z* (%): 268 (60), 253 (40), 224 (56), 209 (87), 194 (53), 179 (71), 165 (100), 127 (30). HRMS: theoretical: 268.15756; measured: 268.15734.

2.2.7. 1-*N*-Piperidinyl-amino-1-β-naphthyl-2-methoxy-buta-2,3-diene (9b). R_f=0.70 (EP/AcOEt 90:10). IR (film): ν=3350, 3030–3010, 2980–2680, 1955, 1650, 1440. ^1H NMR ($CDCl_3$, 300 MHz): δ=1.27–1.39 (m, 2H), 1.47–1.60 (m, 4H), 2.24 (s, 1H), 2.58–2.82 (m, 4H), 3.39 (s, 3H), 4.75 (m, 1H), 5.49 (m, 2H), 7.42 (m, 2H), 7.54 (s, 1H), 7.75–7.83 (m, 4H). ^{13}C NMR (50 MHz): δ=23.9 (CH_2), 25.9 (CH_2), 56.3 (CH_3), 57.8 (CH_2), 63.9 (CH), 92.0 (CH_2), 125.5 (CH), 125.6 (CH), 126.0 (CH), 126.1 (CH), 126.7 (CH), 127.8 (CH), 128.1 (CH), 133.0 (C), 133.3 (C),

136.1 (C), 138.7 (C), 198.9 (C). CI MS *m/z* (%): 309 (100), 239 (88), 209 (15), 99 (34), 81 (28), 71 (38). HRMS CI: theoretical: 309.196688; measured: 309.19679.

2.2.8. 1-*N*-Piperidinyl-amino-1-(*p*-methylphenyl)-2-methoxy-buta-2,3-diene (9c). R_f=0.58 (EP/AcOEt 90:10). IR (film): ν=3300, 3030, 2980–2780, 1960, 1610, 1450. ^{1}H NMR ($CDCl_3$, 300 MHz): δ=0.83 (m, 2H), 1.45 (m, 4H), 1.76 (s, 3H), 3.10 (m, 4H), 3.36 (s, 3H), 4.75 (m, 1H), 5.44 (m, 2H), 7.34 (m, 2H), 7.69 (m, 2H). ^{13}C NMR (50 MHz): δ=21.2 (CH_2), 24.2 (CH_2), 25.9 (CH_2), 52.0 (CH_2), 56.8 (CH_3), 67.9 (CH), 92.8 (CH_2), 128.4 (CH), 130.2 (CH), 136.4 (C), 137.3 (C), 157.5 (C), 199.0 (C). EI MS; *m/z* (%): 272 (4), 257 (17), 202 (25), 188 (68), 105 (20), 99 (100), 84 (34), 55 (48), 42 (33). HRMS EI: theoretical: 272.18886; measured: 272.18719.

2.2.9. 1-*N*-Piperidinyl-amino-1-ethyl-2-methoxy-buta-2,3-diene (9e). R_f=0.65 (EP/AcOEt 90:10). IR (film): ν=3310, 2980–2790, 1960, 1450. ^{1}H NMR ($CDCl_3$, 300 MHz): δ=0.85 (m, 5H), 125 (m, 4H), 1.56 (t, *J*=4.5 Hz, 4H), 2.58 (m, 2H), 3.22 (t, *J*=5.8 Hz, 1H), 4.58 (s, 3H), 5.44 (m, 2H). ^{13}C NMR (50 MHz): δ=10.6 (CH_3), 24.0 (CH_2), 26.1 (CH_2), 32.5 (CH_2), 56.0 (CH_3), 57.9 (CH_2), 61.6 (CH), 90.7 (CH_2), 135.1 (C), 198.9 (C). EI MS *m/z* (%): 195 (32), 181 (11), 99 (100), 84 (20), 69 (13), 55 (88), 41 (49). HRMS CI: theoretical: 211.18104; measured: 211.18107.

2.2.10. 1-*N*-Morpholinyl-amino-1-(*p*-methoxyphenyl)-2-methoxy-buta-2,3-diene (10d). R_f=0.57 (EP/AcOEt 80:20). IR (film): ν=3300, 3020, 2970–2770, 1960, 1610, 1460. ^{1}H NMR ($CDCl_3$, 300 MHz): δ=1.61 (s, 1H), 2.70 (m, 4H), 3.39 (s, 3H), 3.67 (t, *J*=4.8 Hz, 4H), 3.79 (s, 3H), 4.53 (m, 1H), 5.51 (m, 2H), 6.83–6.85 (m, 2H), 7.30–7.33 (m, 2H). ^{13}C NMR (50 MHz): δ=55.2 (CH_3), 56.3 (CH_3), 57.0 (CH_2), 63.0 (CH), 67.0 (CH_2), 91.9 (CH_2), 113.5 (CH), 129.0 (CH), 132.8 (C), 135.9 (C), 158.9 (C), 198.9 (C). EI MS; *m/z* (%): 275 (8), 204 (23), 189 (100), 174 (40), 158 (18), 115 (25), 101 (43), 77 (13), 57 (19), 29 (15). $C_{16}H_{22}N_2O_3$ (290.3): calcd C 66.18, H 7.63, N 9.64; found C 65.59, H 7.62, N 9.30.

2.2.11. 1-*N*-Morpholinyl-amino-1-isopropyl-2-methoxy-buta-2,3-diene (10f). R_f=0.68 (EP/AcOEt 90:10). IR (film): ν=3300, 2980–2840, 1905, 1450. ^{1}H NMR ($CDCl_3$, 300 MHz): δ=0.84 (d, *J*=6.6 Hz,, 3H), 0.91 (d, 3H), 1.72 (m, 1H), 2.58 (m, 4H), 3.06 (d, *J*=7.35 Hz, 1H), 3.35 (s, 3H), 3.64 (t, 4H), 5.39 (m, 2H). ^{13}C NMR (50 MHz): δ=19.5 (CH_3), 19.6 (CH_3), 30.5 (CH), 55.9 (CH_3), 57.1 (CH_2), 66.6 (CH), 67.1 (CH_2), 90.4 (CH_2), 134.8 (C), 199.2 (C). EI MS *m/z* (%): 226 (8), 211 (100), 183 (26), 139 (6), 112 (21), 101 (34), 86 (4). HRMS EI: theoretical: 226.16812; measured: 226.16810.

2.2.12. (1*S*,2*S*′)-1-*N*-[(2′-Methoxymethyl)pyrrolidin-1′-yl]-amino-1-(*p*-methylphenyl)-2-methoxy-buta-2,3-diene (11c). R_f=0.42 (EP/AcOEt 95:5). IR (film): ν=3300, 3030–2810, 1960, 1610, 1460. ^{1}H NMR ($CDCl_3$, 300 MHz): δ=1.26–1.86 (m, 2H), 1.64 (m, 2H), 2.23; 3.18 (m, 2H), 2.93 (m, 1H), 3.32 (s, 3H), 3.38 (s, 3H), 3.45–3.64 (m, 2H), 4.48 (s, 1H), 5.52 (m, 2H), 7.07 (m, 2H), 7.28 (m, 2H). ^{13}C NMR (50 MHz): δ=21.12 (CH_3), 21.22 (CH_2), 26.4 (CH_2), 56.2 (CH_3), 57.3 (CH_2), 59.0 (CH_3), 65.3 (CH), 65.9 (CH), 75.7 (CH_2), 91.6 (CH_2), 127.9 (CH), 128.8 (CH), 136.1 (C), 136.8 (C), 138.4 (C), 199.2 (C). EI MS *m/z* (%): 302 (4), 287 (5), 257 (8), 233 (6), 225 (9), 211 (5), 188 (17), 173 (8), 129 (100), 115 (10), 97 (24), 85 (13), 70 (20), 55 (7), 45 (15). HRMS EI: theoretical: 302.19942; measured: 302.19788.

2.2.13. (1*S*,2*S*′)-1-*N*-[(2′-Methoxymethyl)pyrrolidin-1′-yl]-amino-1-isopropyl-2-methoxy-buta-2,3-diene (11f). R_f=0.34 (EP/AcOEt 95:5). IR (film): ν=3300, 2980–2810, 1960, 1470. ^{1}H NMR ($CDCl_3$, 300 MHz): δ=0.99 (d, *J*=7.3 Hz, 6H), 1.27 (m, 1H), 1.64 (m, 3H), 2.52; 3.24 (m, 2H), 2.91 (m, 1H), 3.06 (m, 1H), 3.31 (s, 3H), 3.31–3.49 (m, 2H), 3.55 (s, 3H), 3.64 (m, 1H), 5.44 (m, 2H). ^{13}C NMR (50 MHz): δ=19.5 (CH_3), 19.7 (CH_3), 21.3 (CH_2), 26.6 (CH_2), 30.2 (CH), 55.7 (CH_3), 56.5 (CH_2), 58.9 (CH), 65.2 (CH_3), 67.5 (CH), 75.5 (CH_2), 90.1 (CH_2), 135.0 (C), 200.0 (C). EI MS *m/z* (%): HRMS EI: theoretical: 254.19942; measured: 254.19936.

2.2.14. (1*S*,2*S*′)-1-*N*-[(2′-Methoxymethyl)pyrrolidin-1′-yl]-amino-1-*tert*-butyl-2-methoxy-buta-2,3-diene (11g). R_f=0.56 (EP/AcOEt 97:3). IR (film): ν=3400, 2970–2820, 1950, 1450. ^{1}H NMR ($CDCl_3$, 300 MHz): δ=0.92 (s, 6H), 1.05 (s, 3H), 1.29 (m, 3H), 1.67 (m, 1H), 1.88; 2.42 (m, 2H), 2.96 (s, 1H), 3.33(s, 3H), 3.39 (s, 3H), 3.29–3.55 (m, 2H), 5.43 (m, 2H). ^{13}C NMR (50 MHz): δ=21.4 (CH_2), 26.6 (CH_2), 27.3 (2CH_3), 28.3 (CH_3), 50.0 (CH_2), 55.8 (CH_3), 59.0 (CH_3), 64.7 (CH), 69.2 (CH), 75.5 (CH_2), 92.1 (CH_2), 147.3 (C), 200.5 (C). EI MS *m/z* (%): 223 (9), 211 (90), 179 (12), 135 (10), 98 (35), 70 (50), 55 (80), 41 (100).

2.3. Preparation of *N*-dialkyl-amino-3-pyrrolines 18

2.3.1. General procedure. 0.83 mmol of compound **8**–**11** were put in solution with 5 ml of THF, the mixture was chilled to −78°C, and 2 equiv. of *n*-BuLi (2.5 M hexane solution) were added dropwise. Then, the mixture was warmed to −20°C. After 16 h at this temperature, the mixture was quenched with 5 ml of water and extracted with ether (2×5 ml). The combined organic phases were dried (Na_2SO_4) and concentrated. The crude product was purified by FC on neutral alumina (Merck 90 type II–III: 0.063–0.20 mm) using a petroleum ether EP/ethyl acetate mixture as a solvent to give **18** as an oil. The purity of **18** was verified by TLC on neutral alumina using phosphomolybdic acid as chemical tracer.

2.3.2. *N*-(−)-(*S*)-2-Methoxymethylpyrrolidinyl-(*S*)-2-phenyl-3-methoxy-2,5-dihydropyrrole (18a). Yield: 97%. R_f=0.22 (95:5 EP/AcOEt). $[\alpha]_D^{20}$=+113 (*c*=1.55, $CHCl_3$). IR (film): ν=3080–3020, 2980–2820, 1660, 1450. ^{1}H NMR ($CDCl_3$, 300 MHz): δ=1.27 (m, 1H), 1.67–1.73 (m, 3H), 2.62 (m, 1H), 2.92 (m, 2H), 3.18 (s, 3H), 3.32 (m, 2H), 3.53 (s, 3H), 3.77–3.93 (m, 2H), 4.61 (m, 1H), 4.98 (m, 1H), 7.26–7.31 (m, 5H). ^{13}C NMR (50 MHz): δ=21.0 (CH_2), 26.08 (CH_2), 43.8 (CH_2), 55.2 (CH_3), 59.0 (CH_3), 64.2 (CH), 64.3 (CH), 74.3 (CH_2), 90.2 (CH), 127.3 (CH), 128.1 (CH), 128.2 (CH), 142.9 (C), 157.3 (C). EI MS *m/z* (%): 288 (48), 243 (88), 174 (11), 159 (62), 129 (31), 115 (28), 91 (31), 71 (100), 45 (72), 27 (20). $C_{17}H_{24}N_2O_2$ (288.4): calcd C 70.8, H 8.38, N 9.71; found C 70.62, H 8.41, N 9.56.

2.3.3. *N*-(−)-(*S*)-2-Methoxymethylpyrrolidinyl-(*S*)-2-β-naphthyl-3-methoxy-2,5-dihydropyrrole (18b). Yield: 95%. R_f=0.26 (97:3 EP/AcOEt). $[\alpha]_D^{20}$=+64.3 (*c*=1.15, $CHCl_3$). IR (film): ν=3030, 2990–2920, 1660, 1640, 1450. ^{1}H NMR ($CDCl_3$, 300 MHz): δ=1.24 (m, 1H), 1.54–1.58 (m, 1H), 1.61–1.71 (m, 2H), 2.64 (m, 1H), 2.92–3.03 (m, 2H), 3.16 (s, 3H), 3.32 (m, 2H), 3.52 (s, 3H), 3.82–4.02 (m, 2H), 4.66 (m, 1H), 5.20 (m, 1H), 7.42–7.47 (m, 3H), 7.81–7.86 (m, 4H). ^{13}C NMR (50 MHz): δ=20.9 (CH_2), 25.8 (CH_2), 43.8 (CH_2), 55.4 (CH_2), 56.4 (CH_3), 58.8 (CH_3), 59.6 (CH), 64.2 (CH), 74.1 (CH_2), 90.2 (CH), 125.4 (CH), 125.7 (CH), 126.1 (CH), 126.8 (CH), 126.9 (CH), 127.6 (CH), 128.0 (CH), 133.1 (C), 133.2 (C), 140.4 (C), 157.1 (C). EI MS *m*/*z* (%): 338 (75), 293 (100), 209 (35), 179 (38), 152 (16), 127 (13), 71 (65). $C_{21}H_{26}N_2O_2$ (338.4): calcd C 74.52, H 7.74, N 8.27; found C 74.75, H 7.95, N 7.97.

2.3.4. *N*-(−)-(*S*)-2-Methoxymethylpyrrolidinyl-(*S*)-2-(*p*-methylphenyl)-3-methoxy-2,5-dihydropyrrole (18c). Yield: 96%. R_f=0.25 (97:3 EP/AcOEt). $[\alpha]_D^{20}$=+137.5 (*c*=0.52, $CHCl_3$). IR (film): ν=3050, 2980–2820, 1660, 1510, 1450. ^{1}H NMR ($CDCl_3$, 300 MHz): δ=1.27–1.70 (m, 2H), 1.66 (m, 2H), 2.64 (m, 1H), 2.35 (s, 3H), 2.67 (m, 1H), 2.92 (m, 2H), 3.23 (s, 3H), 3.36 (m, 2H), 3.53 (s, 3H), 3.72–4.02 (m, 2H), 4.61 (m, 1H), 4.97 (m, 1H), 7.11–7.15 (m, 2H), 7.31–7.35 (m, 2H). ^{13}C NMR (50 MHz): δ=21.1 (CH_2), 21.3 (CH_3), 26.0 (CH_2), 43.8 (CH_2), 55.2 (CH_2), 56.6 (CH_3), 59.0 (CH_3), 59.6 (CH), 64.0 (CH), 74.4 (CH_2), 90.4 (CH), 128.1 (CH), 128.9 (CH), 136.9 (C), 139.8 (C), 157.5 (C). EI MS *m*/*z* (%): 302 (19), 257 (84), 173 (31), 159 (60), 143 (18), 91 (4), 71 (16). $C_{18}H_{26}N_2O_2$ (302.4): calcd C 71.39, H 8.77, N 9.18; found C 71.44, H 8.65, N 9.25.

2.3.5. *N*-(−)-(*S*)-2-Methoxymethylpyrrolidinyl-(*S*)-2-(ethyl)-3-methoxy-2,5-dihydropyrrole (18e). Yield: 94%. $[\alpha]_D^{20}$=−27 (*c*=0.45, $CHCl_3$). IR (film): ν=3020, 2980–2840, 1660, 1450. ^{1}H NMR ($CDCl_3$, 300 MHz): δ=0.86 (t, *J*=7.7 Hz, 3H), 1.33–1.40, 1.62–1.81 (m, 2H), 1.51–1.60 (m, 2H), 2.65–2.73, 2.88–2.95 (m, 2H), 3.08 (m, 1H), 3.26–3.29 (m, 2H), 3.33 (s, 3H), 3.54, 3.69–3.86 (m, 2H), 3.61 (s, 3H), 3.84 (m, 1H), 4.49 (m, 1H). ^{13}C NMR (50 MHz): δ=8.8 (CH_3), 21.4 (CH_2), 27.0 (CH_2), 29.7 (CH_2), 46.2 (CH_2), 53.4 (CH_2), 56.4 (CH_3), 59.2 (CH_3), 59.8 (CH), 62.8 (CH), 75.6 (CH_2), 90.0 (CH), 158.0 (C). EI MS *m*/*z* (%): 240 (61), 211 (28), 195 (82), 126 (10), 111 (16), 97 (42), 71 (100), 45 (94). $C_{13}H_{24}N_2O_2$ (240.3): calcd C 64.9, H 10.0, N 11.6; found C 64.6, H 9.84, N 11.43.

2.3.6. *N*-(−)-(*S*)-2-Methoxymethylpyrrolidinyl-(*S*)-2-(isopropyl)-3-methoxy-2,5-dihydropyrrole (18f). Yield: 93%. R_f=0.60 (95:5 EP/AcOEt). $[\alpha]_D^{20}$=−41.6 (*c*=0.48, $CHCl_3$). IR (film): ν=3040, 2980–2810, 1655, 1460. ^{1}H NMR ($CDCl_3$, 300 MHz): δ=0.89 (t, *J*=7.3 Hz, 6H), 1.61–1.78 (m, 2H), 1.66 (m, 2H), 1.83 (m, 1H), 2.63–2.91 (m, 2H), 3.03 (m, 1H), 3.24–3.52 (m, 2H), 3.33 (s, 3H), 3.48–3.58, 3.68–3.78 (m, 1H), 3.65 (m, 1H), 4.51 (m, 1H). ^{13}C NMR (50 MHz): δ=18.0 (CH_3), 18.1 (CH_3), 21.3 (CH_2), 27.2 (CH_2), 31.3 (CH), 46.8 (CH_2), 53.8 (CH), 56.4 (CH_3), 58.5 (CH), 59.1 (CH_3), 68.3 (CH), 75.7 (CH_2), 91.0 (CH), 158.2 (C). EI MS *m*/*z* (%): 254 (18), 211 (100), 209 (18), 179 (22), 138 (18), 129 (19), 114 (40), 98 (60), 82 (18), 70 (41), 55 (24), 45 (53), 41 (54). HRMS EI: theoretical: 254.199428; measured: 254.20021.

2.3.7. *N*-Piperidino-2-phenyl-3-methoxy-2,5-dihydropyrrole (18g). Yield: 17%. R_f=0.29 (90:10 EP/AcOEt). IR (film): ν=3020, 2970–2790, 1650, 1450. ^{1}H NMR ($CDCl_3$, 300 MHz): δ=1.53 (m, 2H), 2.59 (m, 4H), 2.81 (t, *J*=5.5 Hz, 4H), 3.51 (s, 3H), 3.77–3.94 (m, 2H), 4.57 (m, 1H), 4.98 (m, 1H), 7.27–7.34 (m, 4H), 7.44 (m, 1H). ^{13}C NMR (50 MHz): δ=24.4 (CH_2), 26.4 (CH_2), 51.3 (CH_2), 56.2 (CH_2), 56.6 (CH_3), 58.4 (CH), 89.9 (CH), 127.0 (CH), 128.0 (CH), 128.1 (CH), 143.2 (C), 157.4 (C). EI MS *m*/*z* (%): 258 (100), 243 (14), 189 (5), 174 (56), 159 (31), 144 (9), 129 (23), 115 (18), 98 (15), 91 (22), 84 (12), 70 (21), 55 (34). HRMS EI: theoretical: 258.173213; measured: 258.173207.

2.3.8. *N*-Morpholino-2-phenyl-3-methoxy-2,5-dihydropyrrole (18h). Yield: 86%. R_f=0.22 (97:3 EP/AcOEt). IR (film): ν=3020, 2980–2820, 1660, 1450. ^{1}H NMR ($CDCl_3$, 300 MHz): δ=2.64–2.77 (m, 4H), 3.53 (s, 3H), 3.63–3.70 (m, 4H), 4.59 (m, 1H), 4.93 (m, 1H), 7.25–7.32 (m, 5H). ^{13}C NMR (50 MHz): δ=49.9 (CH_2), 56.6 (CH_3), 57.0 (CH_2), 65.2 (CH), 67.3 (CH_2), 89.8 (CH), 127.9 (CH), 128.0 (CH), 128.1 (CH), 135.7 (C), 142.4 (C). EI MS; *m*/*z* (%): 260 (10), 159 (30), 129 (18), 115 (16), 91 (13), 77 (10), 45 (30), 43 (100). $C_{15}H_{20}N_2O_2$ (260.3): calcd C 69.2, H 7.74, N 10.76; found C 68.8, H 7.65, N 10.74.

2.3.9. *N*-Morpholino-2-naphthyl-3-methoxy-2,5-dihydropyrrole (18i). Yield: 96%. R_f=0.25 (90:10 EP/AcOEt). IR (film): ν=3025, 2980–2810, 1660, 1450. ^{1}H NMR ($CDCl_3$, 300 MHz): δ=2.66 (m, 4H), 3.54 (s, 3H), 3.61 (m, 4H), 3.88 (m, 2H), 4.64 (m, 1H), 5.13 (m, 1H), 7.45 (m, 2H), 7.63 (s, 1H), 7.83 (m, 4H). ^{13}C NMR (50 MHz): δ=50.09 (CH_2), 50.6 (CH_2), 56.7 (CH_3), 65.3 (CH), 67.3 (CH_2), 90.0 (CH), 125.5 (CH), 125.8 (CH), 126.3 (CH), 127.3 (CH), 127.7 (CH), 127.8 (CH), 128.0 (CH), 133.2 (C), 133.4 (C), 140.1 (C), 157.2 (C). EI MS *m*/*z* (%): 310 (100), 295 (7), 241 (6), 240 (15), 224 (6), 211 (13), 210 (99), 180 (13), 179 (50), 165 (18), 152 (12), 127 (12), 107 (11), 86 (15), 84 (24), 56 (8), 43 (14). HRMS EI: theoretical: 310.16813; measured: 310.16827.

2.3.10. *N*-Dimethylamino-2-phenyl-3-methoxy-2,5-dihydropyrrole (18j). Yield: 17%. R_f=0.27 (96:4 EP/AcOEt). IR (film): ν=3040–3010, 2990–2780, 1660, 1450. ^{1}H NMR ($CDCl_3$, 300 MHz): δ=2.39 (s, 6H), 3.52 (s, 3H), 3.77 (m, 2H), 4.54 (m, 1H), 4.81 (m, 1H), 7.23 (m, 1H), 7.31 (M, 2H), 7.43 (m, 2H). ^{13}C NMR (50 MHz): δ=40.8 (CH_3), 48.1 (CH_2), 56.6 (CH_3), 65.9 (CH), 89.5 (CH), 127.2 (CH), 128.0 (CH), 128.1 (CH), 142.5 (CH), 157.4 (C). EI MS; *m*/*z* (%): 218 (100), 203 (6), 160 (34), 145 (8), 129 (19), 115 (9), 91 (10), 77 (6), 58 (14), 43 (44). HRMS EI: theoretical: 218.141913; measured: 218.141907.

2.3.11. *N*-Piperidino-2-phenyl-3-methoxy-4-methyl-azacyclobut-3-ene (19a). That compound was always obtained with **18g** in a mixture. It was identified and characterized by use of 2D NMR: COSY, HSQC and HMBC. Yield: 3%. R_f=0.31 (90:10 EP/AcOEt). ^{1}H NMR ($CDCl_3$, 300 MHz): δ=1.30 (m, 2H), 1.73 (m, 4H), 2.16 (s, 1H), 2.66 (m, 4H), 3.70 (s, 3H), 6.20 (s, 1H), 7.27–7.34 (m,

4H), 7.70 (d, J=7 Hz, 1H). ^{13}C NMR (50 MHz): δ=15.0 (CH_3), 24.0 (CH_2), 25.6 (CH_2), 50.8 (CH_2), 64.8 (CH_3), 116.7 (CH), 127.3 (CH), 128.8 (CH), 129.4 (CH), 135.2 (C), 154.9 (C), 159.4 (C). EI MS *m/z* (%): 258 (4), 243 (3), 174 (100), 118 (10), 91 (18), 42 (22). HRMS EI: theoretical: 258.173213; measured: 258.173207.

2.3.12. *N*-Morpholino-2-(*p*-methoxyphenyl)-3-methoxy-4-methyl-azacyclobut-3-ene (19b). Same remark as for **19a**. Yield: 11%. R_f=0.24 (97:3 EP/AcOEt). IR (film): ν=3020, 2960–2810, 1610, 1510, 1440. ^{1}H NMR ($CDCl_3$, 300 MHz): δ=2.18 (s, 3H), 2.88 (t, J=4.4 Hz, 4H), 3.69 (s, 3H), 3.85 (t, J=4.4 Hz, 4H), 6.24 (s, 1H), 7.30 (m, 3H), 7.68 (m, 2H). ^{13}C NMR (50 MHz): δ=15 (CH_3), 55.2 (CH_2), 58.5 (CH_3), 66.4 (CH_2), 117.4 (CH), 127.5 (CH), 128.4 (CH), 134.9 (C), 154.5 (C), 160.6 (C). EI MS *m/z* (%): 260 (12), 145 (6), 201 (4), 188 (5), 176 (100), 118 (25), 90 (23), 77 (3), 56 (17), 28 (13). HRMS CI: theoretical: 261.160303; measured: 261.161252.

2.3.13. *N*-Dimethylamino-2-phenyl-3-methoxy-4-methyl-azacyclobut-3-ene (19c). Same remark as for **19a**. Yield: 3%. R_f=0.35 (94:6 EP/AcOEt). IR (film): ν=3030, 2990–2780, 1620, 1450. ^{1}H NMR ($CDCl_3$, 300 MHz): δ=2.15 (s, 3H), 2.61 (s, 6H), 3.68 (s, 3H), 6.18 (s, 1H), 7.24 (m, 1H), 7.31 (m, 2H), 7.70 (m, 2H). ^{13}C NMR (50 MHz): δ=14.9 (CH_3), 47.3 (CH_3), 58.4 (CH_3), 116.6 (CH), 127.3 (CH), 128.3 (CH), 129.3 (CH), 135.1 (C), 154.7 (C), 159.0 (C). EI MS; *m/z* (%): 218 (9), 203 (18), 134 (100), 118 (14), 90 (22), 44 (15), 42 (19). HRMS EI: theoretical: 218.141913; measured: 218.14151.

2.4. Formation of ^{1}H-3-pyrrolines 20 and pyrrolidines 21

The ammonium derivative salt of **18** was formed in situ by addition of 1.2 equiv. of chloroformate to a solution of *N*-dialkylamino-3-pyrrolines in 500 μl of THF. After 30 min, the mixture was placed into an autoclave with 5 ml of MeOH and 10% of Raney Ni under a 50 bar pressure of hydrogen. The mixture was then warmed at 50°C during 12 h by 0.1 mmol of starting product. After cooling, the mixture was filtered on celite and purified by FC on silica gel (Kieselgel Si 60, 40–63 μm): 100% CH_2Cl_2 then 90% CH_2Cl_2/10% MeOH; the purity was then controlled by TLC using iodine as chemical tracer. Compounds **20** are unstable compounds which degrade rapidly at room temperature and under SM spectra conditions.

2.4.1. H-2-(*S*)-Phenyl-3-methoxy-2.5-dihydropyrrole ((+) 20a). Yield: 75%. R_f=0.26 (80:20 CH_2Cl_2/MeOH). $[\alpha]_D^{20}$=+1.8 (c=0.7, $CHCl_3$). IR (film): ν=3400, 3020, 2970–2830, 1610, 1450. ^{1}H NMR ($CDCl_3$, 300 MHz): δ=2.82 (s, 1H), 3.19–3.58 (m, 2H), 3.34 (s, 3H), 3.99 (s, 1H), 4.48 (m, 1H), 7.34 (m, 3H), 7.56 (m, 2H). ^{13}C NMR (50 MHz): δ=47.7 (CH_2), 57.5 (CH_3), 66.7 (CH), 81.2 (CH), 128.2 (CH), 128.9 (CH), 129.6 (CH), 130.9 (C), 152.4 (C).

2.4.2. H-2-(*S*)-β-Naphthyl-3-methoxy-2.5-dihydropyrrole ((+) 20b). Yield: 79%. R_f=0.22 (90:10 CH_2Cl_2/MeOH). $[\alpha]_D^{20}$=+1.95 (c=0.25, $CHCl_3$). IR (film): ν=3400, 3050–3020, 2960–2750, 1610, 1450. ^{1}H NMR ($CDCl_3$, 300 MHz): δ=2.74 (s, 1H), 3.12 (s, 3H), 3.27–3.43 (m, 2H), 3.91 (m, 1H), 4.15 (m, 1H), 7.08–7.53 (m, 7H). ^{13}C NMR (75 MHz): δ=44.0 (CH_2), 57.6 (CH_3), 66.9 (CH), 82.5 (CH), 125.4 ((CH), 126.4 (CH), 126.7 (CH), 127.4 (CH), 128.0 (CH), 128.4 (CH), 129.5 (CH), 133.2 (C), 133.6 (C), 137.2 (C), 152.3 (C).

2.4.3. H-2-(*S*)-*p*-Methoxyphenyl-3-methoxy-2.5-dihydropyrrole ((+)-20c). Yield: 68%. R_f=0.31 (80:20 CH_2Cl_2/MeOH). $[\alpha]_D^{20}$=+2.4 (c=0.85, $CHCl_3$). IR (film): ν=3400, 3030, 2970–2800, 1600, 1450. ^{1}H NMR ($CDCl_3$, 300 MHz): δ=2.68 (s, 1H), 3.10 (s, 3H), 3.15–3.51 (m, 2H), 3.77 (s, 3H), 3.90 (m, 1H), 4.36 (m, 1H), 6.84 (m, 2H), 7.46 (m, 2H). ^{13}C NMR (50 MHz): δ=55.2 (CH_3), 57.5 (CH_3), 60.4 (CH_2), 66.0 (CH), 81.3 (CH), 113.9 (CH), 123.0 (C), 130.7 (CH), 160.0 (C), 171.1 (C).

2.4.4. H-2-(*S*)-Phenyl-3-methoxy-pyrrolidine ((+)-21a). Yield: 82%. R_f=0.21 (90:10 CH_2Cl_2/MeOH). $[\alpha]_D^{20}$=+1.86 (c=0.8, $CHCl_3$). IR (film): ν=3300, 3020, 2970–2830, 1450. ^{1}H NMR ($CDCl_3$, 300 MHz): δ=2.04 (m, 2H), 2.84 (s, 1H), 3.02 (s, 3H), 3.03–3.30 (m, 2H), 3.92 (m, 1H), 4.05 (m, 1H), 7.26 (m, 1H), 7.33 (m, 2H), 7.40 (m, 2H). ^{13}C NMR (50 MHz): δ=32.1 (CH_2), 44.7 (CH_2), 57.5 (CH_3), 67.5 (CH), 83.4 (CH), 127.5 (CH), 128.3 (CH), 128.4 (CH), 138.6 (C). EI MS *m/z* (%): 177 (4), 162 (4), 118 (100), 104 (6), 91 (25), 77 (12), 57 (7), 41 (11), 28 (13).

2.4.5. H-2-(*S*)-β-Naphthyl-3-methoxy-pyrrolidine ((+)-21b). Yield: 63%. R_f=0.18 (90:10 CH_2Cl_2/MeOH). $[\alpha]_D^{20}$=−1.6 (c=0.15, $CHCl_3$). IR (film): ν=3300, 3050–3020, 2970–2830, 1450. ^{1}H NMR ($CDCl_3$, 300 MHz): δ=2.08 (m, 2H), 2.74 (s, 1H), 3.01 (s, 3H), 3.39–3.85 (m, 2H), 4.02 (m, 1H), 4.22 (m, 1H), 7.45 (m, 3H), 7.81 (m, 2H). ^{13}C NMR (50 MHz): δ=32.2 (CH_2), 44.8 (CH_2), 57.5 (CH_3), 67.6 (CH), 83.5 (CH), 125.9 (CH), 126.2 (CH), 126.7 (CH), 126.8 (CH), 127.8 (CH), 127.9 (CH), 128.3 (CH), 133.0 (C), 133.6 (C), 136.3 (C). EI MS *m/z* (%): 227 (9), 212 (4), 183 (4), 169 (59), 168 (100), 155 (8), 141 (19), 123 (16), 115 (5), 99 (41), 83 (6), 69 (5), 57 (13), 41 (7). HRMS EI: theoretical: 227.13101; measured: 227.13100.

2.5. Preparation of 3-methoxypyrroles (23)

2.5.1. General procedure. 1.5 equiv. of *meta*-perbenzoic acid chloride (*m*-CPBA) was added dropwise to a solution of **18** in 5 ml of methylene chloride (CH_2Cl_2). The mixture was stirred under room atmosphere during 4 h, controlling the reaction advance by TLC. Then, 200 mg of Na_2CO_3 were added and the mixture was stirred during 15 min. 10 ml of water were added and the mixture was extracted with CH_2Cl_2 (2×5 ml) and then washed with brine (3×10 ml). The combined organic phases were dried (Na_2SO_4) and concentrated. The crude product was purified by FC on alumina gel (Merck 90 type II–III: 0.063–0.20 mm), using a petroleum/AcOEt mixture as solvent, to give pure **23** as a coloured oil. The purity was controlled by TLC on alumina using phosphomolybdic acid as chemical tracer.

2.5.2. 1*H*-2-Phenyl-3-methoxy pyrrole (23a). Yield: 69%. R_f=0.21 (85:15 EP/AcOAEt). λ_{max}=577 nm (ϵ 541), 612 nm (ϵ 527). IR (film): ν=3450, 3030, 2980, 1540,

1450. ^{1}H NMR ($CDCl_3$, 300 MHz): δ=2.9 (m, 1H), 3.86 (s, 3H), 6.09 (t, J=2.9 Hz, 1H), 6.64 (t, J=2.9 Hz, 1H), 7.14 (m, 1H), 7.36 (m, 2H), 7.62 (m, 2H). ^{13}C NMR (50 MHz): δ=58.4 (CH_3), 97.9 (CH), 114.8 (C), 115.8 (CH), 123.6 (CH), 124.9 (CH), 128.7 (CH), 132.2 (C), 145.9 (C). EI MS m/z (%): 173 (100), 159 (10), 158 (88), 130 (45), 104 (10), 77 (13), 43 (7). HRMS EI: theoretical: 173.0840; measured: 173.0849.

2.5.3. 1*H*-2-β-Naphthyl-3-methoxy pyrrole (23b). Yield: 64%. R_f=0.40 (90:10 EP/AcOAEt). λ_{max}=638 nm (ϵ 1308), 595 nm (ϵ 1208). IR (film): ν=3550, 3030, 2990, 1560, 1420. ^{1}H NMR ($CDCl_3$, 300 MHz): δ=2.85 (m, 1H), 3.91 (s, 3H), 6.12 (t, J=2.9 Hz, 1H), 6 (t, J=2.9 Hz, 1H), 7.41 (m, 2H), 7.82 (m, 4H), 7.95 (s, 1H). ^{13}C NMR (50 MHz): δ=58.8 (CH_3), 98.3 (CH), 115.1 (C), 116.6 (CH), 120.8 (CH), 123.0 (CH), 124.9 (CH), 126.1 (CH), 127.00 (CH), 127.6 (CH), 128.2 (CH), 130.1 (C), 131.3 (C), 135.7 (C), 146.2 (C). EI MS m/z (%): 223 (60), 208 (79), 180 (58), 153 (31), 127 (35), 87 (14), 57 (53), 43 (89), 29 (100). HRMS CI: theoretical: 224.107539; measured: 224.107450.

2.5.4. 1*H*-2-(*p*-Methyl)-phenyl-3-methoxy pyrrole (23c). Yield: 76%. R_f=0.27 (90:10 EP/AcOAEt). λ_{max}=553 nm (ϵ 438). IR (film): ν=3450, 3030, 2980, 1540, 1450. ^{1}H NMR ($CDCl_3$, 300 MHz): δ=2.17 (m, 1H), 2.34 (s, 3H), 3.84 (s, 3H), 6.09 (t, J=2.9 Hz, 1H), 6.61 (t, J=2.9 Hz, 1H), 7.10 (m, 2H), 7.48 (m, 2H). ^{13}C NMR (50 MHz): δ=21.5 (CH_3), 58.8 (CH_3), 98.3 (CH), 115.4 (C), 115.6 (CH), 124.0 (CH), 129.5 (C), 129.7 (CH), 134.9 (C), 145.7 (C). EI MS m/z (%): 187 (56), 172 (100), 144 (34), 131 (12), 118 (45), 104 (9), 91 (34), 89 (11), 69 (38), 51 (14), 43 (6). HRMS EI: theoretical: 187.0997; measured: 187.10014.

2.5.5. 1*H*-2-(*p*-Methoxy)-phenyl-3-methoxy pyrrole (23d). Yield: 73%. R_f=0.15 (80:20 EP/AcOAEt). λ_{max}= 587 nm (ϵ 705). IR (film): ν=3480, 3025, 2990, 1520, 1420. ^{1}H NMR ($CDCl_3$, 300 MHz): δ=2.57 (m, 1H), 3.81 (s, 3H), 3.84 (s, 3H), 6.07 (t, J=2.9 Hz, 1H), 6.60 (t, J=2.9 Hz, 1H), 6.08 (m, 2H), 7.53 (m, 2H). ^{13}C NMR (50 MHz): δ=55.3 (CH_3), 58.8 (CH_3), 98.0 (CH), 113.6 (C), 114.2 (CH), 114.9 (CH), 125.1 (CH), 129.1 (C), 132.3 (C), 144.7 (C). EI MS m/z (%): 203 (15), 169 (5), 155 (7), 147 (15), 135 (52), 111 (18), 97 (29), 85 (36), 71 (45), 57 (100), 43 (76). HRMS EI: theoretical: 203.0946; measured: 203.0960.

2.6. Preparation of 3-amino-2-aryl pyrroles (25)

2.6.1. General procedure. *N*-Amino-3-pyrroline was stirred during several hours in a mixture of THF and HCl (4 ml/1 ml). The progress of the reaction was followed by TLC. The mixture was quenched with a saturated solution of $NaHCO_3$ until neutrality and extracted with Et_2O (3×5 ml). The combined organic phases were dried (Na_2SO_4) and concentrated. The crude product was obtained as a highly coloured oil and did not require any purification; its purity was shown by TLC (EP/AcOEt as solvent and phosphomolybdic acid as chemical tracer) as well as by NMR spectra.

2.6.2. 1*H*-3-Dimethylamino-2-phenyl-pyrrole (25a). Yield: 95%. R_f=0.36 (90:10 EP/AcOAEt). IR (film): ν= 3300, 3050–3020, 2980–2830, 1650, 1610. ^{1}H NMR ($CDCl_3$, 300 MHz): δ=2.45 (s, 6H), 2.78 (s, 1H), 5.86 (t, J=2.9 Hz, 1H), 6.52 (t, J=2.9 Hz, 1H), 7.33 (m, 5H). ^{13}C NMR (50 MHz): δ=37.8 (CH_3), 101.3 (CH), 114.6 (C), 115.9 (CH), 123.6 (CH), 124.5 (CH), 128.7 (CH), 132.8 (C), 141.7 (C). EI MS m/z (%): 186 (8), 159 (100), 130 (37), 118 (9), 104 (24), 77 (14), 43 (7). HRMS EI: theoretical: 186.115698; measured: 186.116553.

2.6.3. 1*H*-3-Morpholino-2-phenyl-pyrrole (25b). Yield: 95%. R_f=0.26 (90:10 EP/AcOAEt). IR (film): ν=3400, 3040–3010, 2970–2820, 1650, 1610. ^{1}H NMR ($CDCl_3$, 300 MHz): δ=3.15 (m, 4H), 3.66 (m, 4H), 5.90 (t, J= 2.9 Hz, 1H), 6.57 (t, J=2.9 Hz, 1H), 7.56–7.64 (m, 5H). ^{13}C NMR (50 MHz): δ=15.3 (CH_2), 65.9 (CH_2), 101.2 (CH), 115.8 (CH), 127.3 (C), 128.7 (CH), 128.8 (CH), 132.3 (C), 140.7 (C), 153.2 (C). EI MS m/z (%): 228 (5), 176 (58), 145 (20), 133 (26), 131 (30), 129 (20), 105 (65), 89 (27), 77 (39), 63 (13), 51 (22), 43 (100). HRMS EI: theoretical: 228.12626; measured: 228.12591.

2.6.4. 1*H*-3-((*S*)-2-Methoxymethylpyrrolidinyl)-2-phenyl-pyrrole (25d). Yield: 97%. R_f=0.33 (95:5 EP/AcOAEt). IR (film): ν=3300, 3050–3010, 2980–2800, 1660, 1610, 1450. ^{1}H NMR ($CDCl_3$, 300 MHz): δ=1.38–1.76 (m, 2H), 1.70 (m, 2H), 2.67–3.03 (m, 2H), 3.23–3.35 (m, 2H), 3.34 (s, 3H), 5.89 (s, 1H), 6.55 (s, 1H), 7.31–7.38 (m, 3H), 7.63–7.66 (m, 2H). ^{13}C NMR (50 MHz): δ=25.0 (CH_2), 27.6 (CH_2), 46.0 (CH_2), 57.7 (CH), 58.8 (CH_3), 74.7 (CH_2), 101.4 (CH), 114.6 (C), 115.8 (CH), 123.5 (CH), 124.4 (CH), 125.1 (CH), 132.7 (C), 141.6 (C).

2.6.5. 1*H*-3-((*S*)-2-Methoxymethylpyrrolidinyl)-2-*p*-methyl-phenyl-pyrrole (25e). Yield: 97%. R_f=0.22 (97:3 EP/AcOAEt). IR (film): ν=3300, 3050, 2980–2760, 1660, 1610, 1450. ^{1}H NMR ($CDCl_3$, 300 MHz): δ=1.42 (m, 1H),1.67–1.73 (m, 2H), 1.75–1.86 (m, 1H), 2.31 (s, 3H), 2.77–2.98 (m, 3H), 3.24 (m, 1H), 3.27–3.38 (m, 2H), 3.30 (s, 3H), 5.85 (s, 1H), 6.47 (s, 1H), 7.12 (m, 2H), 7.53 (m, 2H). ^{13}C NMR (50 MHz): δ=21.1 (CH_3), 24.6 (CH_2), 27.7 (CH_2), 46.0 (CH_2), 57.7 (CH_3), 58.9 (CH), 75.0 (CH_2), 101.4 (CH), 114.8 (C), 115.4 (CH), 123.6 (CH), 129.3 (CH), 130.1 (C), 133.9 (C), 141.2 (C). EI MS m/z (%): 270 (6), 225 (25), 186 (11), 173 (100), 168 (11), 158 (13), 144 (18), 119 (27), 91 (16), 70 (34), 43 (10). HRMS EI: theoretical: 270.1732; measured: 270.1704.

Acknowledgements

The efficient help of Dr Philippe Compain at the beginning of this study was greatly appreciated. V. B. D. thanks MENSR for a scholarship.

References

1. Hoff, Th.; Brandsma, L.; Arens, J. F. *Rec. Trav. Chim. Pays Bas* **1968**, *87*, 917–924.
2. Rochet, P.; Vatèle, J. M.; Goré, J. *Synthesis* **1994**, 795–799. Hormuth, S.; Reissig, H-U.; Dorsch, D. *Liebigs Ann.* **1994**, 121–127.
3. Goldstein, S.; Overman, L. E.; Rabinowitz, H. *J. Org. Chem.* **1992**, *57*, 1179–1190. Gange, D.; Magnus, P. *J. Am. Chem. Soc.* **1978**, *100*, 7746–7747. Magnus, P.; Albaugh-Robertson,

P. *J. Chem. Soc., Chem. Commun.* **1984**, 804–806. Hormuth, S.; Schade, W.; Reissig, H.-U. *Liebigs Ann.* **1996**, 2001–2006. Derguini, F.; Linstrumelle, G. *Tetrahedron Lett.* **1984**, *25*, 5763–5766. Tackle, A.; Kocienski, P. *Tetrahedron* **1990**, *46*, 4503–4516. Tackle, A.; Kocienski, P. *Tetrahedron Lett.* **1989**, *30*, 1675–1678.

4. Rochet, P.; Vatèle, J. M.; Goré, J. *Synthesis* **1994**, 795–799.
5. Surivet, J. P.; Goré, J.; Vatèle, J. M. *Tetrahedron Lett.* **1996**, *37*, 371–374. Surivet, J. P.; Goré, J.; Vatèle, J. M. *Tetrahedron* **1996**, *52*, 14877–14890.
6. Dumez, E.; Dulcère, J. P. *J. Chem. Soc., Chem. Commun.* **1998**, 479–480.
7. Schade, W.; Reissig, H.-U. *Synlett* **1999**, 632–634.
8. Okala Amombo, M.; Hausherr, A.; Reissig, H.-U. *Synlett* **1999**, 1871–1874.
9. Enders, D.; Bartzen, D. *Liebigs Ann., Recueil* **1997**, 1115–1123. Enders, D.; Schubert, H.; Nübling, C. *Angew. Chem., Int. Ed. Engl.* **1986**, *25*, 1109–1110. Enders, D.; Müller, P.; Klein, D. *Synlett* **1998**, 43–44. Enders, D.; Meiers, M. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 2261–2263. Enders, D.; Reinhold, U. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 1219–1222. Enders, D.; Funk, R.; Klatt, M.; Raabe, G.; Hovestreydt, E. R. *Angew. Chem., Int. Ed. Engl.* **1993**, *32*, 418–421. Enders, D.; Bartzen, D. *Liebigs Ann., Recueil* **1991**, 569–574. Enders, D.; Brauer-Scheib, S.; Fey, P. *Synthesis* **1985**, 393–396. Enders, D.; Vasquez, J. *Synlett* **1999**, 629–632.
10. Enders, D.; Eichenauer, H. *Chem. Ber.* **1979**, *112*, 2933–2960. Schubert, H. Dissertation, University of Bonn, 1985.
11. Breuil-Desvergnes, V.; Goré, J. *Tetrahedron* **2001**, *57*, 1951–1960.
12. Lochtman, R.; Enders, D. *Synlett* **1997**, 355–356.
13. Enders, D.; Nübling, C.; Schubert, H. *Liebigs Ann., Recueil* **1997**, 1089–1100.
14. For previous work, see: Jeanjean, F.; Fournet, G.; Goré, J. *Eur. J. Org. Chem.* **2000**, 1297–1305.
15. Conia, J. M.; Leriverend, P.; Ripoll, J. L. *Bull. Soc. Chim. Fr.* **1961**, 1803.
16. Claesson, A.; Sahlerg, C.; Luthman, K. *Acta Chem. Scand.* **1979**, 309–310. Jayaprakash, K.; Venkatachalam, C.; Balasubramanian, K. *Tetrahedron Lett.* **1999**, *40*, 6493–6496. Padwa, A.; Nimmersgern, H.; Wong, G. S. K. *J. Org. Chem.* **1985**, *50*, 5620–5627. Padwa, A.; Norman, B. H. *Tetrahedron Lett.* **1998**, *25*, 3041–3044. Jones, A. D.; Knight, D. W.; Redfern, A. L.; Gilmore, J. *Tetrahedron Lett.* **1999**, *40*, 3267–3270. Ishii, K.; Ohno, H.; Takemoto, Y.; Ibuka, T. *Synlett* **1999**, 228–230. Hassner, T.; Balasubramanian, T. *Tetrahedron Lett.* **1996**, *37*, 5755–5758. Xu, Z.; Lu, X. *Tetrahedron Lett.* **1997**, *38*, 3461–3464. Xu, Z.; Lu, X. *Tetrahedron Lett.* **1999**, *40*, 549–552. Xu, Z.; Lu, X. *J. Org. Chem.* **1998**, *63*, 5031–5041. Oliveira, D. F.; Severino, E. A.; Correia, C. R. D. *Tetrahedron Lett.* **1999**, *40*, 2083–2086. Fugami, K.; Oshima, K.; Murizawa, Y.; Nozaki, H. *Tetrahedron Lett.* **1985**, *26*, 857–860. Miura, K.; Fugami, K.; Oshima, K.; Utimoto, K. *Tetrahedron Lett.* **1988**, *29*, 1543–1546.
17. Enders, D.; Bartzen, D. *Liebigs Ann., Recueil* **1997**, 1115–1123. Alexakis, A.; Lensen, N.; Mangeney, P. *Synlett* **1991**, 625–626. Alexakis, A.; Lensen, N.; Mangeney, P.; Tranchier, J. P.; Feneau-Dupont, J.; Declercq, J. P. *Synthesis* **1995**, 1038–1050. Feuer, H.; Brown Jr., F. *J. Org. Chem.* **1970**, *35*, 1468–1471. Enders, D.; Lochtman, R.; Meiers, M.; Müller, S.; Lazny, R. *Synlett* **1998**, 1182–1184. Enders, D.; Demir, A. S. *Tetrahedron Lett.* **1987**, *28*, 3795–3798.
18. Burk, M. J.; Feaster, J. E. *J. Am. Chem. Soc.* **1992**, *114*, 6266–6267. Enders, D.; Demir, A. S. *Tetrahedron Lett.* **1987**, *28*, 3795–3798. Suzuki, T.; Anoyagi, S.; Kibayashi, C. *Tetrahedron Lett.* **1995**, *36*, 935–936. Denmark, S.; Nicaise, O.; Edwards, J. *J. Org. Chem.* **1990**, *55*, 6219–6223.
19. Breuil-Desvergnes, V.; Compain, P.; Vatèle, J. M.; Goré, J. *Tetrahedron Lett.* **1999**, *40*, 5009–5012.
20. Breuil-Desvergnes, V.; Compain, P.; Vatèle, J. M.; Goré, J. *Tetrahedron Lett.* **1999**, *40*, 8789–8792.
21. Merz, A.; Meyer, T. *Synthesis* **1999**, 94–99. Merz, A.; Kronberger, J.; Dunsch, A.; Neudeck, A.; Petr, A.; Parkanyi, L. *Angew. Chem., Int. Ed. Engl.* **1999**, *38*, 1442–1444. Wasserman, H.; Xia, M.; Wang, J.; Petersen, A. K.; Jorgensen, M. *Tetrahedron Lett.* **1999**, *40*, 6145–6148 (and references cited therein).
22. Nedolya, N.; Brandsma, L.; Tarasova, O.; Verkruijsse, H. D.; Trofinov, B. *Tetrahedron Lett.* **1998**, *39*, 2409–2410. Chadwick, D.; Hodgson, S. *J. Chem. Soc., Perkin Trans. 1* **1983**, 93–100. Komatsu, M.; Takamatsu, S.; Uesaka, M.; Yamamoto, S.; Oshiro, Y.; Agawa, T. *J. Org. Chem.* **1984**, *49*, 2691–2699. Dieck, H. T.; Verfürth, U.; Diblitz, K.; Ehlers, J.; Fendesak, G. *Chem. Ber.* **1989**, 129–131.