A New Access to 2-(Alkylamino)- and 2-(Arylamino)pyrroles by Addition of Isocyanides to Protonated 1-Azabutadienes

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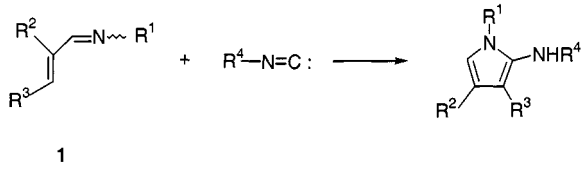
A number of 5-(alkylamino)- or 5-(arylamino)-2*H*-pyrrolium salts **3** or **5** have been obtained by treating the 1-aza-1,3-diene hydrochlorides **2** with isocyanides R^4NC in refluxing acetonitrile or chloroform for a few hours. Depending on the experimental conditions, deprotonation of these species can occur in the reaction medium to furnish the corresponding 2-aminopyrroles **4** and **6**. Insertion of isocyanide into a carbon–hydrogen bond of the pyrrolium salts can also lead to the generation of the (pyrrol-2-yl)methyleneiminium chlorides **7**–**9**. Under similar conditions, treatment with an excess of *tert*-butyl isocyanide converts the protonated α-chlorocinnamaldimines **2j**,**k** into the 5-(*tert*-butylamino)-pyrrole-2-carbonitriles **13**. Structural assignments of all the cycloadducts have been made on the basis of their NMR-spectroscopic properties, particularly the effects observed in NOEDIFF experiments. Mechanisms are suggested to account for the ring-closure reactions and autoxidation of pyrroles **4** and **6** under atmospheric oxygen to give the 5-imino-2-pyrrolinones **17** and **18**.

Substituted pyrroles are a class of heterocycles of considerable interest owing to their wide distribution in nature and the remarkable diversity of their biological activities. They form part of the molecular structure of many alkaloids and natural macrocycles (hemes, bile pigments, chlorophylls, etc.) and are used in constructing attractive materials such as porphyrins,[1] expanded porphyrins and their heterologs,[2] porphyrazines,[3] and open-chain polypyrroles.[4]

Consequently, it is not surprising that a vast amount of work has and is still being devoted to the development of practical methods for the synthesis of pyrroles bearing appropriate substitution patterns.[5][6] In connection with our ongoing interest in the chemistry of isocyanides and especially in their formal [1+4] cycloadditions to conjugated diaza and azathiadienes[7] or related iminium salts,[8−10] we wondered whether it might be possible, under suitable conditions, to utilize the 1-azabutadiene system **1** in a similar procedure. If successful, this reaction with subsequent aromatization could provide a useful and straightforward route to *N*-substituted 2-aminopyrroles (Scheme 1). The main characteristic of this method is clearly the construction of the ring by formation of both the N(1)−C(2) and the C(2)−C(3) bonds. This is a rather new and scarcely applied approach in pyrrole synthesis. It can be classified as C_3+C_1 in terms of the number of carbon atoms supplied to the heterocycle by the starting reagents.[5] In this way, the base-catalyzed reactions of acidic isocyanides with Michael acceptors, that have been known for many years to give pyrroles or related compounds,[5,11,12] can be classified as C_2+C_2 methods.



Scheme 1. Straightforward route to 2-aminopyrroles

Despite the large number of published methods for the elaboration of various pyrroles, relatively few examples have been reported for the preparation of simple 2-amino derivatives. Most compounds of this type have been obtained by reaction of a nitrogen-two-carbon compound with an appropriate two-carbon unit (C_2+C_2), e.g. base-promoted condensation of an α-amino ketone[13] or a conjugated azoalkene[14] with a nitrile containing an active methylene group; 1,3-dipolar cycloaddition of conjugated azoalkenes with 1-propynyldiethylamine;[15] or base-induced 1,3-dipolar cycloaddition of 4,5-diaminothiazolium salts with electrophilic alkynes.[16] Other miscellaneous and limited methods were also described in the review by Trofimov et al.[5b] In particular, nickel- and palladium-catalyzed reactions of alkynes with a large excess of either *tert*-butyl isocyanide[17] or trimethylsilyl cyanide[18] led to the generation of the corresponding 5-aminopyrrole-2-carbonitriles according to unexplained processes.

Our assumption that α,β-unsaturated aldimines might be involved in the route depicted in Scheme 1 was supported by the known nucleophilic behaviour of isocyanides[19] as well as numerous precedents in analogous reactions with electron-deficient heterodienes.[11] Notably, there have been several literature studies dealing with the addition of isocyanides to 2-azabutadiene and 1,3-diazabutadiene systems. For instance, it has been shown that a protic acid induces

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the reaction of *tert*-butyl isocyanide with arylideneanilines to afford 2-aryl-3-(*tert*-butylamino)indoles.[20] The uncatalyzed [1+4] cycloadditions of *N*-arylketene imines,[21] vinyl carbodiimides,[22] and vinyl isocyanates[23] are also known to produce highly functionalized dihydroindoles and dihydropyrroles. About ten years ago, we found that the protonation of 1,3-diazabutadienes markedly increases their reactivity towards isocyanides.[8] By similar reasoning, we have explored the treatment of chloro imino sulfides or phenyl chlorodithioformate with aldimines, azines, or dimethylthioformamide in the presence of isocyanides as new routes to 4-aminoimidazolium[9] or 5-aminothiazolium[10] salts. Such useful synthetic methodologies involve imidoyl- or (thiocarbonyl)iminium chlorides as transient intermediates, which readily undergo cycloaddition reactions.

In contrast, only isolated efforts have been made to carry out similar transformations of 1-azabutadiene. To the best of our knowledge, [1+4] cycloadditions of this type have been limited to the preparation of diiminopyrroles from imidoylketene imines[22] and the preparation of 1-aminoisoindole derivatives from 1,4-benzoquinone or naphthoquinone[24] and 5,8-quinoxalinediones.[25] In the latter reactions, the authors assumed the first step of the sequence to be a formal insertion of isocyanide into a carbon−hydrogen bond. The 1-azadiene species was formed as an intermediate and addition of a second isocyanide molecule led to the observed 1:2 adduct.[24][25]

The purpose of the present study is to develop the scope of the novel one-step procedure outlined in Scheme 1 and to report our observations on the stability of α-aminopyrroles and pyrrolium salts.

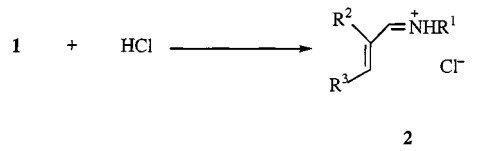
Results and Discussion

Preparation of 2-Aminopyrrole Derivatives

The starting α-methylenaldimines **1** were readily accessible from the corresponding aldehydes by condensation with appropriate primary amines.[26] Most of our examples were based on *trans*-cinnamaldimines and α-methyl- or α-chloro-*trans*-cinnamaldimines. Attempts to prepare 2-aminopyrroles by treatment of heterodienes **1** with isocyanides were generally unsuccessful, the starting dienes **1** being completely recovered even after prolonged heating at reflux in acetonitrile containing a large excess of *tert*-butyl isocyanide.

Consequently, and according to the procedure mentioned above, we decided to examine the HCl-catalyzed modification of this cycloaddition reaction. The hydrochloride salts **2** were quantitatively obtained from the Schiff bases **1** by treatment with gaseous HCl in anhydrous Et_2O, and were easily isolated as crystalline materials (Scheme 2).

Studies of the reactions of the iminium chlorides **2** with isocyanides were undertaken in MeCN and $CHCl_3$ solutions. Extended reflux times were frequently required. Thus, when a twofold excess of *tert*-butyl isocyanide was added to **2a** in dry acetonitrile and the resulting mixture was refluxed



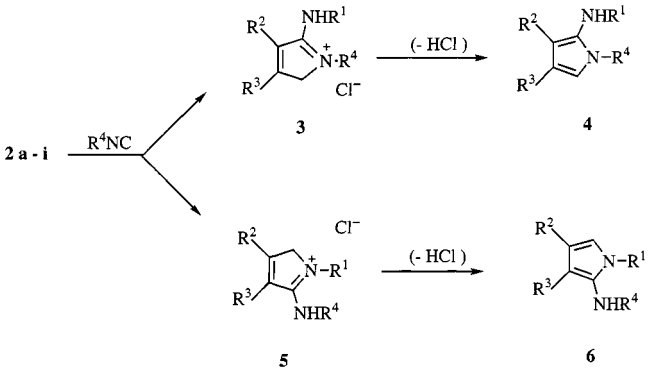
2

1, 2	R^1	R^2	R^3
a	*t*Bu	H	Ph
b	*i*Pr	H	Ph
c	$CHPh_2$	H	Ph
d	Tos	H	Ph
e	*t*Bu	H	Me
f	*t*Bu	Me	H

1, 2	R^1	R^2	R^3
g	*t*Bu	Me	Ph
h	*i*Pr	Me	Ph
i	Tos	Me	Ph
j	*t*Bu	Cl	Ph
k	*i*Pr	Cl	Ph

Scheme 2. Protonation of α-methylenaldimines

overnight, the 2*H*-pyrrolium salt **3a** was isolated in 47% yield after purification. Conversion of **3a** to unprotonated pyrrole **4a** was readily carried out in $CHCl_3$ solution by treatment with triethylamine or aluminium oxide. Structural assignments of products **3a**, **4a** will be rationalized below. It is interesting to note at this point that they are at variance with the related stuctures **5**, **6**, which may be expected considering the common cycloaddition process (Scheme 3).



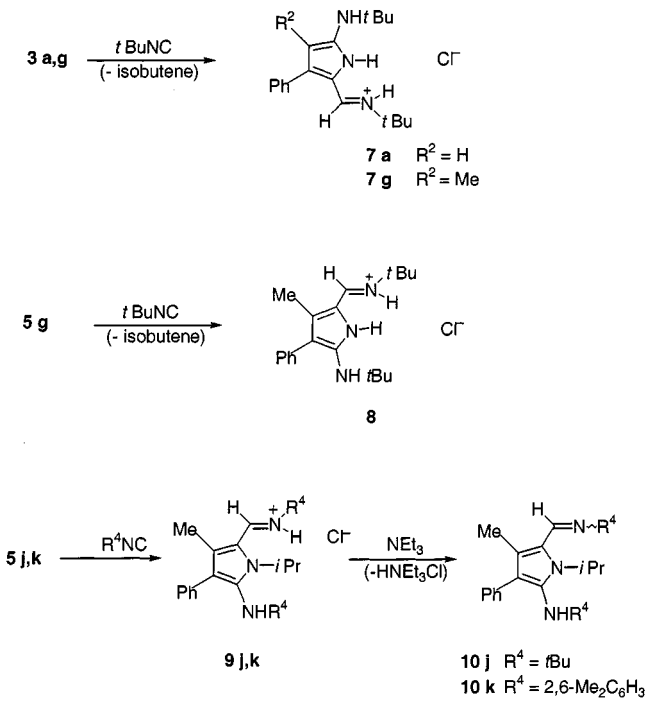
3-6	R^1	R^2	R^3	R^4
a	*t*Bu	H	Ph	*t*Bu
b	*t*Bu	H	Ph	2,6-$Me_2C_6H_3$
c	*i*Pr	H	Ph	*t*Bu
d	$CHPh_2$	H	Ph	*t*Bu
e	Tos	H	Ph	*t*Bu
f	*t*Bu	H	Me	*t*Bu

3-6	R^1	R^2	R^3	R^4
g	*t*Bu	Me	Ph	*t*Bu
h	*t*Bu	Me	Ph	Et
i	*t*Bu	Me	Ph	2,6-$Me_2C_6H_3$
j	*i*Pr	Me	Ph	*t*Bu
k	*i*Pr	Me	Ph	2,6-$Me_2C_6H_3$
l	Tos	Me	Ph	*t*Bu

Scheme 3. Reactions of 1-azabutadiene hydrochlorides with isocyanides

Various 1-azabutadiene hydrochlorides **2** and isocyanides have been tested in this reaction, under a range of experimental conditions; the results are collected in Table 1. They are consistent with the following interpretations:

1. Depending on the nature of starting compounds, either the anticipated cycloadducts **5**, **6** or the rearranged counterparts **3**, **4** are obtained. A significant example is the formation of the same isomeric 3-methyl-2*H*-pyrrolium salt **3f**, using the *N*-protonated azadienes **2e** and **2f** derived from



Scheme 4. Insertion reaction of isocyanides into pyrrolium salts

trans-crotonaldehyde and methacrolein (entries 7, 8, 9). Some reactions also provided small quantities of the (pyrrol-2-yl)methyleniminium chlorides **7**, **8**, **9**, which requires a formal insertion of isocyanide into a carbon−hydrogen bond of the pyrrolium salts **3**, **5** (Scheme 4). Insertion reactions of isocyanides into pyrroles in acidic media have been reported previously.[27] We have verified that the salt **3a** readily adds *tert*-butyl isocyanide in dry refluxing MeCN solution, giving the corresponding hydrochloride **7a** in good yield. The compounds **9j**,**k** were characterized as their unprotonated species **10** after treatment with Al_2O_3 (entries 14−16).

2. As expected, the cycloaddition was clearly faster and higher yields of the unprotonated pyrrole were obtained when the concentration of the isocyanide was increased. However, these conditions also promoted the insertion reaction (entries 1, 2).

3. CH_3CN proved to be more effective as the solvent than $CHCl_3$ (see, for instance, entries 7, 8), but also increased the proportion of insertion products (compare entry 10 with entry 11 and entry 14 with entry 15).

4. *N*-Tosyl α,β-unsaturated aldimines show higher reactivity in such cyclizations, owing to the enhancement of their electrophilic properties. Thus, satisfactory efficiencies were observed even upon reaction of unprotonated derivatives **1d**,**i** with *tert*-butyl isocyanide (entries 6, 17).

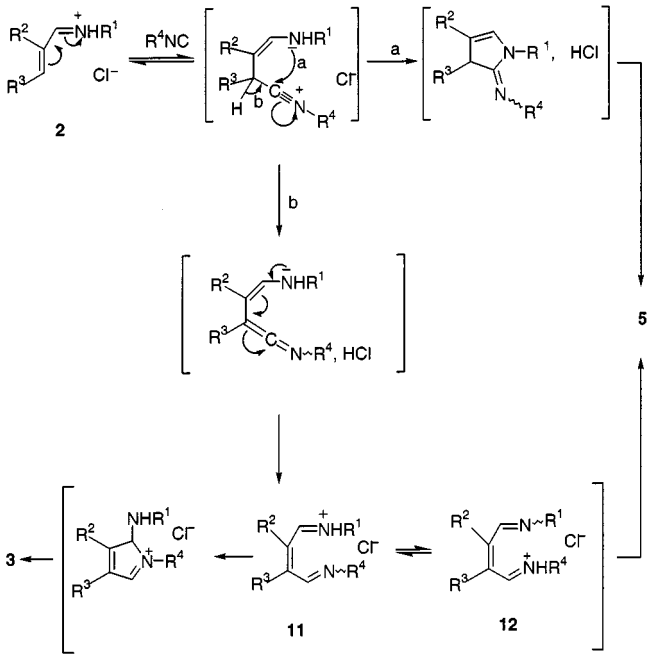
The formation of pyrrolium salts **3**, **5** from *N*-protonated 1-azabutadienes **2** can be rationalized in terms of the addition of isocyanide to the electrophilic terminal C-4, thereby giving a transient nitrilium chloride in the initial step (Scheme 5). Straightforward ring-closure reaction takes place by nucleophilic attack of the amino nitrogen atom on the nitrilium carbon atom (path a). Subsequent tautomerism yields the anticipated salt **5**. Protonation of pyrroles,[28] especially of 2-aminopyrroles[13], is known to occur at the 5-position rather than at the heteroatom, thereby producing a cyclic amidinium species.

Table 1. Reactions of 1-azabutadiene systems with isocyanides

Entry	Reactants Diene	Isocyanide (R^4)	R^4NC/**2**	Reaction conditions[a] Solvent	Time[b] (h)	Products [yield (%)][c]
1	**2a**	*t*Bu	2	MeCN	15	**3a** (47); **7a** (13)
2	**2a**	*t*Bu	3	MeCN	24[d]	**4a** (25); **7a** (37)
3	**2a**	2,6-$Me_2C_6H_3$	2	$CHCl_3$	120	**6b** (45)
4	**2b**	*t*Bu	2.5	$CHCl_3$	20	**6c** (44)
5	**2c**	*t*Bu	2	$CHCl_3$	15	**6d** (40)
6	**1d**	*t*Bu	2	MeCN	90	**6e** (71)
7	**2e**	*t*Bu	2	MeCN	0.5	**3f** (55)
8	**2e**	*t*Bu	2	$CHCl_3$	6	**3f** (40)
9	**2f**	*t*Bu	2	MeCN	0.5	**3f** (50)
10	**2g**	*t*Bu	3	MeCN	2	**4g** + **6g**[e] (30); **7g** (17); **8** (17)
11	**2g**	*t*Bu	3	$CHCl_3$	5	**4g** + **6g**[e] (35); **7g** (14); **8** (14)
12	**2g**	Et	2.5	$CHCl_3$	17	**5h** (45)
13	**2g**	2,6-$Me_2C_6H_3$	2	$CHCl_3$	36	**5i** (65)
14	**2h**	*t*Bu	3	MeCN	3	**6j** (30); **10j** (37)
15	**2h**	*t*Bu	3	$CHCl_3$	7	**6j** (37); **10j** (31)
16	**2h**	2,6-$Me_2C_6H_3$	2	MeCN	70	**5k** (35); **10k** (10)
17	**1i**	*t*Bu	2	MeCN	96	**6l** (63)
18	**2j**	*t*Bu	3	$CHCl_3$	2	**13a** (55)
19	**2k**	*t*Bu	3	MeCN	0.5	**13b** (45)
20	**2k**	*t*Bu	3	$CHCl_3$	2	**13b** (40)
21	**15**	*t*Bu	3	$CHCl_3$	120	**16** (35)

[a] The reactions were performed in refluxing solvents, starting from a 0.4 M solution of salt **2**. − [b] Times required for complete conversion of the azabutadiene system. − [c] Yields of purified products after flash chromatography on silica gel and/or crystallization. − [d] ^{1}H-NMR analysis of the mixture obtained after a shorter reaction time (5 h) revealed complete cyclization of **2a** and the formation of the salts **3a** and **7a** (60:40). − [e] **4g**/**6g** ≈ 75:25 (by ^{1}H-NMR estimated composition of the crude mixture).

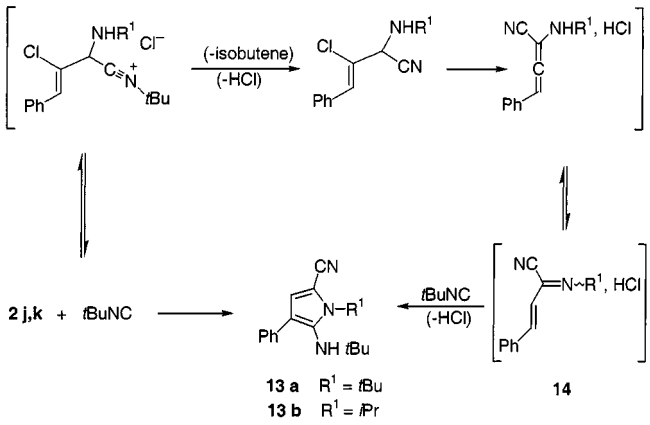
Another possibility (path b) is rearrangement of the initially generated nitrilium salt by a 1,2-proton transfer, as reported in analogous examples.[24][25] The resulting insertion product **11** or **12** furnishes the 2-aminopyrrolium salt **3** or **5** through an intramolecular attack of the imino nitrogen atom on the iminium moiety.



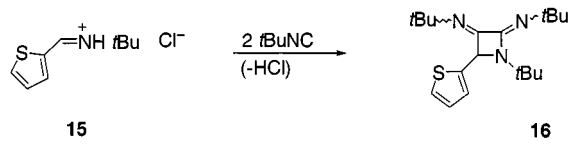
Scheme 5. Postulated mechanisms for the formation of pyrrolium salts

In order to extend the scope of this method, the protonated α-chlorocinnamaldimines **2j**,**k** were treated under similar conditions with excess *tert*-butyl isocyanide. The 5-aminopyrroles **13**, bearing a cyano group at the 2-position, were the somewhat surprising products of this reaction (Table 1, entries 18−20). Their formation certainly involves the 2-cyano-1-azabutadiene hydrochlorides **14** as reactive intermediates, which cyclize according to the aforementioned route a. The formation of azadienes **14** presumably proceeds by the addition of isocyanide at the 2-position of the 3-chloro-1-azabutadiene systems **2j**,**k**, followed by elimination of isobutene and HCl as seen in the overall mechanism outlined in Scheme 6.

Imines derived from 2-thiophenecarboxaldehyde are interesting substrates in similar reactions as they can lead to the formation of fused pyrrole derivatives. However, the addition of *t*BuNC to the iminium salt **15** required prolonged reflux under standard conditions and provided mainly the 2,3-bis(*tert*-butylimino)azetidine **16** (Table 1, entry 21). This reaction involves a [1+1+2] cycloaddition of two isocyanide molecules across the C−N double bond (Scheme 7). Similar 2:1 addition patterns giving rise to four-membered heterocyclic compounds have been reported previously in the literature.[11,20,29]



Scheme 6. Reaction of protonated α-chlorocinnamaldimines with *tert*-butyl isocyanide



Scheme 7. Reaction of protonated 2-(formimidoyl)thiophene with *tert*-butyl isocyanide

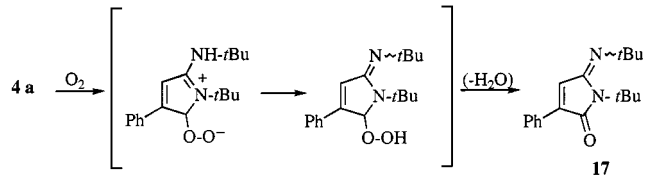
Air-Induced Oxidation of 2-Aminopyrroles

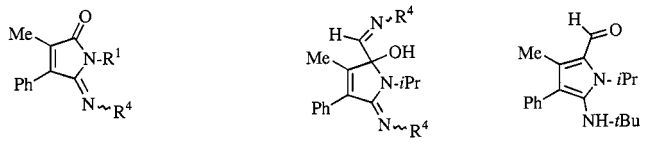
Autoxidation of monocyclic pyrroles to form various carbonyl compounds and peroxidic polymers has some precedence in the literature.[30][31] The pyrroles **4**, **6** proved to be less stable than the corresponding pyrrolium salts **3**, **5**, being oxidized to complex mixtures on leaving them to stand exposed to atmospheric oxygen at room temperature. The major product of the reactions starting from **4a** or **6i−k** was identified as the 5-imino-2-pyrrolinone **17** or **18**, generated by addition of O_2 and loss of H_2O. This conversion may be rationalized in terms of the addition of triplet oxygen to the electron-rich 2-aminopyrrole and spontaneous dehydration of the transient peroxide (see Scheme 8 for the representative formation of pyrrolinone **17**). Similar air-induced oxidations have recently been mentioned in related studies.[9a,10b,32]

The 2-cyanopyrroles **13** exhibit good stability upon exposure to air. Likewise, the pyrrole hydrochlorides **7**, **8**, **9** do not show any sensitivity to oxygen. On the contrary, the unprotonated 2-(formimidoyl)pyrrole **10k** was readily converted into the 5-imino-2-pyrrolinol **19**. The related compound **10j** was hydrolyzed in the course of silica gel chromatography to afford the 2-pyrrolecarboxaldehyde **20**.

Structural Assignments

All structures were supported by NMR-spectroscopic evidence, high-resolution mass-spectral data, and satisfactory elemental analyses (see Experimental Section). Where necessary, unambiguous ^{1}H- and ^{13}C-NMR assignments were derived from decoupling experiments, either by selec-





18	R^1	R^4	19, R^4 = 2,6-$Me_2C_6H_3$	20
i	*t*Bu	2,6-$Me_2C_6H_3$		
j	*i*Pr	*t*Bu		
k	*i*Pr	2,6-$Me_2C_6H_3$		

Scheme 8. Air-induced oxidation of 2-aminopyrroles

tive irradiations or by addition of D_2O in the case of compounds **7**, **8**.

In particular, accurate determination of the coupling constants between the protons on endocyclic carbon atoms allows the isomers **4a−f** and **6a−f** to be distinguished. Thus, the protons 4-H and 5-H in cycloadducts **6b−e** couple with values between 3.1−3.8 Hz, consistent with literature data on similar 4- and 5-unsubstituted 1*H*-pyrroles (^3J = 2.4−3.1 Hz).[33][34] The protons 3-H and 5-H in cycloadducts **4a** and **4f** couple only with 2.1−2.4 Hz, in agreement with the lower values of long-range coupling constants found for structurally related pyrroles (^4J = 1.4−2.5 Hz).[33][34] The isomeric assignment of compounds **6g−l** (R^2 = CH_3) was also deduced from a very low coupling constant between the methyl protons on C-4 and the proton on C-5 (^4J = 0.7−1 Hz).[34]

Selected ^{13}C-NMR data are given in Tables 2 and 3. Spectra of 2-aminopyrroles **4**, **6** feature a large doublet for carbon atom C-5 (δ ≈ 115, ^1J = 180−194 Hz) and another doublet at about δ = 106 for carbon atom C-3 or C-4 when R^2 = H (^1J = 166−173 Hz). These values compare favourably with chemical shifts and typical $^1J_{CH}$ values for a pyrrole nucleus.[35] The multiplicity of the signal attributed to C-5 conclusively establishes the structure **4** or **6**. For example, this carbon atom gives rise to a doublet in the case of **4g** and a doublet of quadruplets in the case of **6g** as a result of an additional long-range coupling with the three protons of R^2 ($^3J_{CCCH}$ = 4.5 Hz). The multiplicity of the methyl carbon atom on C-3 or C-4 (R^2) confirms these assignments.

The 2-cyanopyrroles **13a**,**b** have been fully characterized by their IR- and ^{13}C-NMR-spectroscopic properties and by comparing the ^{1}H-NMR-spectral data of the known com-

Table 2. NMR chemical shifts and multiplicities for the main carbon atoms of 2-aminopyrroles[a,b]

No.	C-2	C-3	C-4	C-5	CH_3 (R^2 or R^3) (^1J = 126 Hz)	CH=NR^4, C≡N or CH=O
4a	137.1 (t, ^2J = ^3J = 7)	100.1 (dd, ^1J = 167, ^3J = 6)	120.2 (m)	110.1 (dd, ^1J = 182, ^3J = 6)		
4f[c]	135.9 (t, ^2J = ^3J = 7)	103.1 (dm, ^1J = 166)	114.3 (m)	110.7 (dm, ^1J = 181)	12.4 (qt, ^3J = 2.1)	
4g[d]	133.7 (m)	112.9 (qd, ^2J = ^3J = 6)	121.2 (m)	112.9 (d, ^1J = 181)	13.3 (q)	
6b	128.0 (t, ^3J = 7.2)	120.5 (m)	104.8 (dd, ^1J = 170, ^2J = 6.5)	115.4 (dd, ^1J = 184, ^2J = 7.5)		
6c	130.0 (td, ^3J = 7 and 2)	118.5 (m)	107.2 (dd, ^1J = 169, ^2J = 6)	112.5 (ddd, ^1J = 182, ^2J = 7.5, ^3J = 4.5)		
6d	131.6 (br. t, ^3J = 7.5)	120.0 (m)	107.1 (dd, ^1J = 170, ^2J = 6)	117.0 (ddd, ^1J = 186, ^2J = 7.5, ^3J = 4.5)		
6e	134.2 (dd, ^3J = 7.3 and 4.6)	124.4 (m)	113.6 (dd, ^1J = 173, ^2J = 7.7)	119.5 (dd, ^1J = 194, ^2J = 6.6)		
6g[d]	132.3 (d, ^3J = 6.8)	122.2 (m)	113.7 (qd, ^2J = 6)	112.8 (dq, ^1J = 181, ^3J = 4.5)	11.5 (qd, ^3J = 2.8)	
6i[c]	128.7 (d, ^3J = 7.4)	119.0 (m)	113.5 (qd, ^2J = 6.2)	112.7 (dq, ^1J = 182, ^3J = 5.6)	11.6 (qd, ^3J = 1.9)	
6j	130.6 (dd, ^3J = 6.9 and 1)	118.2 (m)	115.4 (qd, ^2J = 6.2)	110.2 (dm, ^1J = 180)	11.6 (qd, ^3J = 2)	
6k[c]	128.3 (dd, ^3J = 8 and 4.8)	117.0 (m)	115.6 (qd, ^2J = 6)	110.0 (dm, ^1J = 181)	11.9 (qd, ^3J = 1.9)	
6l	134.9 (d, ^3J = 4.9)	123.1 (m)	122.2 (qd, ^2J = 6.5)	116.0 (dq, ^1J = 192, ^3J = 6.4)	11.7 (qd, ^3J = 3)	
10j	123.3 (m)	121.7 (qd, ^2J = 6.3, ^3J = 3.7)	120.3 (m)	134.3 (d, ^3J = 3.6)	11.7 (q)	147.4 (d, ^1J = 152)
13a	99.3 (d, ^2J = 7.5)	122.8 (d, ^1J = 175)	122.6 (m)	138.4 (d, ^3J = 7.9)		117.4 (d, ^3J = 2.5)
13b	96.5 (t, ^2J = ^3J = 6)	120.9 (d, ^1J = 175)	120.3 (m)	135.6 (dd, ^3J = 8 and 3)		115.7 (d, ^3J = 2.3)
20	124.6 (dm, ^2J = 27.6)	134.4 (q, ^2J = 6.2)	121.2 (m)	141.5 (d, ^3J = 3.4)	10.5 (q)	175.8 (d, ^1J = 170)

[a] δ (ppm) and *J* (Hz) in $CDCl_3$ solutions at 75.5 MHz. − [b] The endocyclic carbon atoms are numbered in such a way that the amino group is at C-2 in pyrroles **4**, **6** and at C-5 in pyrroles **10**, **13**, **20**. The multiplicities of signals attributed to ring-connected exocyclic carbon atoms can unequivocally establish the isomeric structure. − [c] From a $CDCl_3$ solution of pyrrolium salt in the presence of Al_2O_3. − [d] In a 75:25 mixture of the isomers **4g**, **6g**.

Table 3. Selected ^{13}C-NMR data for 2*H*-pyrrolium salts **3**, **5** and other pyrrole derivatives[a,b]

No.	C-2	C-3	C-4	C-5	CH_3 (R^2 or R^3) (^1J = 128 Hz)	CH=NR^4 (^1J = 164−171 Hz)
3a	58.0 (td, ^1J = 145, ^3J = 7.1)	161.2 (m)	113.3 (dm, ^1J = 178)	162.9 (d, ^2J = 7.9)		
3f	60.3 (tm, ^1J = 144)	163.3 (m)	116.7 (dm, ^1J = 179)	162.6 (d, ^2J = 9)	15.1 (qd, ^3J = 2.9)	
5h	59.4 (tq, ^1J = 144, ^3J = 4.3)	157.9 (m)	131.0 (m)	161.4 (s)	13.2 (q)	
5i	59.9 (tq, ^1J = 144, ^3J = 4)	159.4 (m)	131.7 (m)	161.2 (s)	13.3 (q)	
5k	55.6 (tm, ^1J = 143)	159.3 (m)	131.2 (m)	161.4 (s)	13.7 (q)	
7a	114.4 (m)	148.2 (m)	101.2 (dt, ^1J = 176, ^3J = 5.3)	151.7 (dd, ^2J = 6.7 and 1.2)		135.9 (d)
7g	115.5 (m)	144.6 (m)	109.6 (m)	150.3 (br)	9.0 (q)	135.0 (d)
8	115.8 (m)	139.6 (m)	116.3 (m)	149.5 (br)	10.1 (q)	132.6 (d)
17	169.7 (d, ^3J = 10)	140.2 (t, ^3J = 4)	119.0 (d, ^1J = 175)	152.8 (d, ^2J = 8)		
18i	171.5 (q, ^3J = 4)	139.0 (q, ^2J = 7.2)	137.1 (m)	152.6 (s)	9.0 (q)	
18j	170.2 (m)	141.3 (q, ^2J = 7.3)	136.1 (m)	146.0 (d, ^3J = 2.5)	9.5 (q)	
19	92.3 (dq, ^2J = 14.3, ^3J = 3)	147.4 (q, ^2J = 7.4)	137.0 (m)	152.6 (d, ^3J = 5.4)	10.8 (q)	164.3 (dd, ^3J = 2)

[a] δ (ppm) and multiplicities [*J* (Hz)] in $CDCl_3$ solutions at 75.5 MHz. − [b] The ring carbon atoms are numbered in such a way that the amino group or imino nitrogen atom is at C-5.

Table 4. NOEDIFF experiments for some 2-aminopyrroles **4**, **6** and 5-amino-2-(formimidoyl)pyrrole hydrochlorides **7**, **8**[a]

Compound	Selective irradiation δ	Protons	Enhancement δ	Protons	NOE (%)
4a	1.31	2-(N*t*Bu)	6.17	3-H	11
	1.66	1-*t*Bu	6.88	5-H	7
	6.17	3-H	7.50	4-Ph[b]	9
	6.88	5-H	7.50	4-Ph[b]	10
6e	0.94	2-(N*t*Bu)	7.54	3-Ph[b]	4
			7.65	1-Tos[b]	3
	6.34	4-H	7.03	5-H	11
			7.54	3-Ph[b]	5
	7.03	5-H	7.65	1-Tos[b]	3
7a	1.40	2-(C=N^+*t*Bu)	7.00	2-(CH=N^+)	16
	1.46	5-(N*t*Bu)	5.97	4-H	23
			6.11	5-(NH)	14
	5.97	4-H	7.35	3-Ph[b]	5
	7.00	2-(CH=N^+)	7.35	3-Ph[b]	6
7g	1.85	4-Me	4.78	5-(NH)	7
			7.24	3-Ph[b]	4
	7.24	3-Ph[b]	6.74	2-(CH=N^+)	10
8	1.48	2-(C=N^+*t*Bu)	7.07	2-(CH=N^+)	15
			11.06	2-(C=N^+H)	5
	1.57	5-(N*t*Bu)	4.95	5-(NH)	20
			11.81	1-H	11
	2.13	3-Me	7.07	2-(CH=N^+)	19
			7.22	4-Ph[b]	6
	7.22	4-Ph[b]	4.95	5-(NH)	5

[a] δ (ppm) in $CDCl_3$ solutions at 300 MHz. − [b] Aromatic *ortho* protons.

pound **13a** with those reported in the literature.[17] The multiplicity of the cyano carbon atom signal is significant as it shows coupling to the proton on C-3 ($^3J_{CCCH} \approx 2.4$ Hz).

The structures of the 2-aminopyrroles **10**, **20**, the 2*H*-pyrrolium salts **3**, **5**, and other pyrrole derivatives were determined by similar carbon resonance observations, as indicated in Tables 2 and 3. Additionally, the substitution patterns of the pyrrole hydrochlorides **7**, **8** and representative 2-aminopyrroles **4a**, **6e** were unequivocally established by NOEDIFF experiments. Significant enhancements were observed, which revealed the relative positions of various substituents (Table 4). These explicit NOE perturbations also corroborate the chemical shift assignments collected in the Experimental Section.

Conclusion

We have shown that nucleophilic attack by isocyanides on acyclic 1-aza-1,3-dienes and subsequent ring-closure reaction require initial protonation at the nitrogen atom. The novelty of our methodology lies in the generation and for-

mal [1+4] cycloaddition of *C*-vinyliminium ions. This approach opens an unprecedented and useful route to 2-(alkyl- or arylamino)pyrroles that are not easily accessible by other methods. A mechanism is suggested to account for the unexpected rearrangement that was observed in the course of some sequences. Although synthetic application might appear to be limited by modest yields, owing principally to the insertion reaction of isocyanide into the pyrrolium salts, this is offset by the ready availability of the starting materials and the simplicity of process.

Experimental Section

General: NMR: Bruker ARX 200 spectrometer (200 MHz for ^1H) or Bruker AM 300 WB spectrometer (300 MHz for ^1H, 75.5 MHz for ^{13}C, and 30.4 MHz for ^{15}N) in $CDCl_3$ (internal standard: Me_4Si for ^1H and ^{13}C; external reference: $MeNO_2$ for ^{15}N). – HRMS: Centre Régional de Mesures Physiques de l'Ouest; Varian MAT 311 spectrometer, EI mode using a potential of 70 eV; with the exception of molecular-ion peaks, only mass-spectral fragments with relative intensities of 10% or more are reported. – IR: Perkin–Elmer 1420 spectrophotometer; suspensions in Nujol. – Elemental analyses: Analytical laboratory CNRS.

Starting Materials: *tert*-Butyl isocyanide and ethyl isocyanide were prepared as described previously[36] employing the customary Hofmann carbylamine method. 2,6-Dimethylphenyl isocyanide was purchased from Fluka. *N*-Tosylaldimines **1d**,**i** were readily accessible from the condensation of *p*-toluenesulfonamide (4.3 g, 25 mmol) with commercially available *trans*-cinnamaldehyde and α-methyl-*trans*-cinnamaldehyde (25 mmol). The reactions were carried out at room temp. in CH_2Cl_2 solution using $TiCl_4/NEt_3$ as catalyst, according to a known procedure.[37] Other α,β-unsaturated aldimines **1** and 2-(*N*-*tert*-butylformimidoyl)thiophene were conveniently generated by condensing the corresponding aldehydes with appropriate primary amines on alumina over a period of a few hours. Such conditions have been reported several times in the literature.[9a,10,38] Crude 1-aza-1,3-dienes were converted directly to the hydrochlorides **2** and **15** without prior purification. Thus, a solution of the imine (10 mmol) in anhydrous diethyl ether (50 mL) was saturated with dry HCl, resulting in the immediate separation of a white solid. This was collected by filtration, washed with Et_2O, and recrystallized from Et_2O/CH_2Cl_2 (1:1), except where otherwise indicated. The salts **2** and **15** belong to a rather stable class of compounds, which can be stored for several years under dry conditions without any decomposition. They were found to melt with decomposition (Kofler apparatus; instantaneous melting points). Overall yields are based on starting aldehydes.

4-Phenyl-1-tosyl-1-aza-1,3-butadiene (1d): M.p. 123°C (Et_2O/CH_2Cl_2) (5.6 g, 78% yield). – ^1H NMR (200 MHz): δ = 2.37 (s, 3 H), 6.90 (dd, *J* = 16 and 9 Hz, 1 H, 3-H), 7.25–7.55 (m, 8 H), 7.85 (d, *J* = 8 Hz, 2 H), 8.75 (d, *J* = 9 Hz, 1 H, 2-H).

3-Methyl-4-phenyl-1-tosyl-1-aza-1,3-butadiene (1i): M.p. 116°C (Et_2O/CH_2Cl_2) (5.95 g, 79% yield). – ^1H NMR (200 MHz): δ = 2.16 (s, 3 H), 2.43 (s, 3 H), 7.24–7.50 (m, 8 H), 7.87 (d, *J* = 8.3 Hz, 2 H), 8.71 (s, 1 H, 2-H).

1-*tert*-Butyl-4-phenyl-1-aza-1,3-butadiene Hydrochloride (2a): M.p. 185°C (2.0 g, 93% yield). – ^1H NMR (200 MHz): δ = 1.62 (s, 9 H), 7.30–7.70 (m, 5 H), 7.95 (dd, *J* = 15.6 and 9.5 Hz, 1 H, 3-H), 8.20 (d, *J* = 15.6 Hz, 1 H, 4-H), 9.03 (dd, *J* = 15.4 and 9.5 Hz, 1 H, 2-H).

1-Isopropyl-4-phenyl-1-aza-1,3-butadiene Hydrochloride (2b): M.p. 125°C (1.9 g, 60% yield). – ^1H NMR (200 MHz): δ = 1.54 (d, *J* = 6.7 Hz, 6 H), 4.30 (m, 1 H), 7.30–8.20 (m, 7 H), 9.20 (d, *J* = 9 Hz, 1 H, 2-H), 14.20 (br., NH).

1-(Diphenylmethyl)-4-phenyl-1-aza-1,3-butadiene Hydrochloride (2c): M.p. 189°C ($MeCN/CHCl_3$) (3.0 g, 70% yield). – ^1H NMR (200 MHz): δ = 6.40 (s, 1 H), 7.25–7.60 (m, 15 H), 7.65 (d, *J* = 15.5 Hz, 1 H, 4-H), 8.18 (dd, *J* = 15.5 and 10.2 Hz, 1 H, 3-H), 8.82 (d, *J* = 10.2 Hz, 1 H, 2-H), 14.95 (br., NH). – $C_{22}H_{20}ClN$ (333.86): calcd. C 79.15, H 6.04, Cl 10.62, N 4.20; found C 79.27, H 6.01, Cl 10.98, N 4.06.

1-*tert*-Butyl-1-aza-1,3-pentadiene Hydrochloride (2e): M.p. 128°C (1.45 g, 65% yield). – ^1H NMR (200 MHz): δ = 1.58 (s, 9 H), 2.11 (d, *J* = 6.8 Hz, 3 H), 7.22 (dd, *J* = 15.3 and 9.8 Hz, 1 H, 3-H), 7.61 (dq, *J* = 15.3 and 6.8 Hz, 1 H, 4-H), 8.88 (dd, *J* = 16.3 and 9.8 Hz, 1 H, 2-H).

1-*tert*-Butyl-3-methyl-1-aza-1,3-butadiene Hydrochloride (2f): Amorphous semi-solid (1.45 g, 65% yield). – ^1H NMR (200 MHz): δ = 1.67 (s, 9 H), 2.35 (s, 3 H), 6.35 (br., 1 H), 6.87 (br., 1 H), 8.95 (d, *J* = 17 Hz, 1 H, 2-H).

1-*tert*-Butyl-3-methyl-4-phenyl-1-aza-1,3-butadiene Hydrochloride (2g): M.p. 188°C (2.15 g, 85% yield). – ^1H NMR (200 MHz): δ = 1.71 (s, 9 H), 2.59 (s, 3 H), 7.40–7.60 (m, 5 H), 8.25 (s, 1 H, 4-H), 8.85 (br. d, *J* = 12.8 Hz, 1 H, 2-H).

1-Isopropyl-3-methyl-4-phenyl-1-aza-1,3-butadiene Hydrochloride (2h): M.p. 142°C (2.0 g, 80% yield). – ^1H NMR (200 MHz): δ = 1.62 (d, *J* = 6.6 Hz, 6 H), 2.49 (s, 3 H), 4.46 (m, 1 H), 7.40–7.60 (m, 5 H), 8.12 (s, 1 H, 4-H), 9.25 (d, *J* = 16.7 Hz, 1 H, 2-H).

1-*tert*-Butyl-3-chloro-4-phenyl-1-aza-1,3-butadiene Hydrochloride (2j): Undetermined melting point (2.3 g, 55% yield). – ^1H NMR (200 MHz): δ = 1.77 (s, 9 H), 7.40–7.50 (m, 3 H), 8.03 (d, *J* = 7 Hz, 2 H), 9.30 (br., 1 H, 4-H), 9.88 (br., 1 H, 2-H), 13.00 (br., NH).

3-Chloro-1-isopropyl-4-phenyl-1-aza-1,3-butadiene Hydrochloride (2k): Undetermined melting point (2.2 g, 55% yield). – ^1H NMR (200 MHz): δ = 1.65 (d, *J* = 6.7 Hz, 6 H), 4.57 (m, 1 H), 7.40–8.05 (m, 5 H), 8.85 (s, 1 H, 4-H), 10.10 (s, 1 H, 2-H), 12.50 (br., NH).

2-(*N*-*tert*-Butylformimidoyl)thiophene Hydrochloride (15): M.p. 175°C (55% yield). – ^1H NMR (200 MHz): δ = 1.69 (s, 9 H), 7.29 (t, *J* = 4.5 Hz, 1 H), 8.08 (d, *J* = 4.5 Hz, 1 H), 9.02 (br., 1 H), 9.05 (d, *J* = 4.5 Hz, 1 H), 14.60 (br., NH).

Cycloaddition Reactions of *N*-Tosyl Cinnamaldimines: A solution of 1-azabutadiene **1d**,**i** (10 mmol) and *tert*-butyl isocyanide (1.7 g, 20 mmol) in anhydrous MeCN (25 mL) was refluxed for about 4 d. Removal of the solvent under reduced pressure left a brownish residue, which was purified by column chromatography on Merck silica gel 60 using petroleum ether/diethyl ether (3:2) as eluent. The cycloadducts **6e**,**l** were recrystallized from MeOH (selected ^{13}C-NMR data: see Table 2).

2-(*tert*-Butylamino)-3-phenyl-1-tosyl-1*H*-pyrrole (6e): M.p. 94°C (2.61 g, 71% yield). – ^1H NMR (300 MHz): δ = 0.94 (s, 9 H), 2.37 (s, 3 H), 3.45 (br., NH), 6.34 (d, *J* = 3.8 Hz, 1 H, 4-H), 7.03 (d, *J* = 3.8 Hz, 1 H, 5-H), 7.15–7.36 (m, 5 H), 7.54 (m, 2 H), 7.65 (d, *J* = 8.4 Hz, 2 H). – $C_{21}H_{24}N_2O_2S$ (368.49): calcd. C 68.45, H 6.56, N 7.60, S 8.70; found C 68.36, H 6.59, N 7.53, S 8.65.

2-(*tert*-Butylamino)-4-methyl-3-phenyl-1-tosyl-1*H*-pyrrole (6l): M.p. 99°C (2.41 g, 63% yield). – IR: $\tilde{\nu}$ = 3360 cm^{-1} (NH), 1590 (C=C). – ^1H NMR (200 MHz): δ = 0.84 (s, 9 H), 1.90 (d, *J* = 1 Hz, 3 H), 2.37 (s, 3 H), 3.37 (br., NH), 6.85 (q, *J* = 1 Hz, 1 H, 5-H),

7.19−7.35 (m, 7 H), 7.69 (d, J = 8.4 Hz, 2 H). − $C_{22}H_{26}N_2O_2S$ (382.52): calcd. C 69.08, H 6.85, N 7.32, S 8.38; found C 69.35, H 6.86, N 7.14, S 8.47.

Reactions of *N*-Protonated 1-Azabutadienes with Isocyanides. − General Procedure: A solution of salt **2** or **15** (10 mmol) and the appropriate isocyanide was prepared in dry MeCN or $CHCl_3$ (25 mL). The excess of isocyanide used and the requisite reflux time are indicated in Table 1. The progress of the reaction was monitored by ^{1}H NMR. The solvent was subsequently evaporated in vacuo, the residual syrup was triturated with anhydrous Et_2O, and then slowly decanted. Concentration of the ethereal solution afforded the pyrroles **4a**, **6b**,**c**,**d**,**j** and **13a**,**b**, which were purified by flash chromatography on silica gel using petroleum ether/diethyl ether (3:1) as eluent. In some cases, the products were recrystallized. The material insoluble in Et_2O was worked-up with dry THF to give the pyrrolium salts **3a**,**f**, **5h**,**i**,**k** or the 2-(formimidoyl)pyrrole hydrochlorides **7a**, **9j**,**k**. The crude products obtained in entry 1 (**3a**, **7a**) and entry 16 (**5k**, **9k**) were separated by repeated crystallizations from THF. − In the case of entries 10, 11 and 21, the reaction mixture was concentrated to a viscous material, which was treated with diethyl ether and washed with H_2O. After decantation, the organic phase was dried with Na_2SO_4 and the solvent was evaporated to furnish a mixture of isomeric adducts **4g** and **6g** (75:25) or the crystalline azetidine **16**. The aqueous solution was extracted with CH_2Cl_2 to provide the salts **7g** and **8**, which were isolated by fractional crystallization from Et_2O. − Conversion of pyrrolium salts **3a**,**f**, **5h**,**i**,**k** and 2-(imidoyl)pyrrole hydrochlorides **9j**,**k** to the corresponding pyrroles **4**, **6** and **10** was quantitatively achieved by treatment with $Al_2O_3/CHCl_3$ or $NEt_3/CHCl_3$ at room temperature for 30 min. according to standard procedures.[8,9a] The pyrrole hydrochlorides **7a**,**g**, **8** remained unaltered under the same conditions. The pyrroles **10** were purified by flash chromatography on alumina using petroleum ether/Et_2O (3:1) as eluent. The pyrroles **4f**, **6h**,**i**,**k** were very susceptible to oxidation and were only characterized by NMR spectroscopy of $CDCl_3$ solutions of the corresponding salts in the presence of Al_2O_3. − Selected ^{13}C-NMR data: see Tables 2 and 3.

1-*tert*-Butyl-5-(*tert*-butylamino)-3-phenyl-2*H*-pyrrolium Chloride (3a): M.p. 200°C (dec.) (CH_2Cl_2/Et_2O); yield 1.44 g (47%). − IR: $\tilde{\nu}$ = 3500 cm^{-1} (NH), 1608 (C=N$^+$), 1568 (C=C). − ^{1}H NMR (200 MHz): δ = 1.64 (s, 9 H), 1.77 (s, 9 H), 5.40 (s, 2 H, 2-H), 6.72 (s, NH), 6.95 (s, 1 H, 4-H), 7.47 (m, 3 H), 7.80 (m, 2 H). − MS: calcd. for $C_{18}H_{26}N_2$ m/z = 270.2096 [M − HCl]$^{+\cdot}$; found 270.2092.

1-*tert*-Butyl-5-(*tert*-butylamino)-3-methyl-2*H*-pyrrolium Chloride (3f): M.p. 200°C (dec.) (CH_2Cl_2/Et_2O); yield 1.34 g (55%). − IR: $\tilde{\nu}$ = 3235, 3080 cm^{-1} (NH), 1623 (C=N$^+$), 1572 (C=C). − ^{1}H NMR (300 MHz): δ = 1.58 (s, 9 H), 1.69 (s, 9 H), 2.34 (d, J = 1.4 Hz, 3 H), 4.89 (s, 2 H, 2-H), 6.55 (q, J = 1.4 Hz, 1 H, 4-H), 6.59 (br., NH). − MS: calcd. for $C_{13}H_{24}N_2$ m/z = 208.1939 [M − HCl]$^{+\cdot}$; found 208.1948; m/z (%): 208 (50), 151 (10), 96 (100), 95 (75).

1-*tert*-Butyl-5-(ethylamino)-3-methyl-4-phenyl-2*H*-pyrrolium Chloride (5h): M.p. 200°C (dec.) (CH_2Cl_2/Et_2O); yield 1.32 g (45%). − IR: $\tilde{\nu}$ = 3100 cm^{-1} (NH), 1630 (C=N$^+$), 1595 (C=C). − ^{1}H NMR (300 MHz): δ = 0.83 (t, J = 6.9 Hz, 3 H), 1.64 (s, 9 H), 1.82 (s, 3 H), 3.14 (m, 2 H), 4.60 (s, 2 H, 2-H), 7.12 (m, 2 H), 7.33 (m, 3 H), 8.77 (br. t, J = 6.1 Hz, NH). − MS: calcd. for $C_{17}H_{25}N_2$ m/z = 257.2018 [M − Cl]$^+$; found 257.2025; m/z (%): 257 (65), 200 (100), 171 (50), 154 (15), 144 (10). − $C_{17}H_{25}ClN_2$ (292.85): calcd. C 69.72, H 8.60, Cl 12.11, N 9.57; found C 69.10, H 8.81, Cl 12.40, N 9.62.

1-*tert*-Butyl-5-[(2,6-dimethylphenyl)amino]-3-methyl-4-phenyl-2*H*-pyrrolium Chloride (5i): M.p. 210°C (dec.) ($CHCl_3/Et_2O$); yield 2.4 g (65%). − IR: $\tilde{\nu}$ = 3050 cm^{-1} (NH), 1625 (C=N$^+$), 1585, 1567 (C=C). − ^{1}H NMR (200 MHz): δ = 1.78 (s, 3 H), 1.83 (s, 9 H), 2.11 (s, 6 H), 4.62 (s, 2 H, 2-H), 6.56 (m, 3 H), 6.90 (m, 2 H), 10.74 (br., NH). − MS: calcd. for $C_{23}H_{28}N_2$ m/z = 332.2252 [M − HCl]$^{+\cdot}$; found 332.2251; m/z (%): 332 (70), 276 (100).

5-[(2,6-Dimethylphenyl)amino]-1-isopropyl-3-methyl-4-phenyl-2*H*-pyrrolium Chloride (5k): M.p. 240°C (dec.) ($CHCl_3/Et_2O$); yield 1.24 g (35%). − ^{1}H NMR (200 MHz): δ = 1.45 (d, J = 6.5 Hz, 6 H), 1.90 (s, 3 H), 2.15 (s, 6 H), 4.50 (s, 2 H, 2-H), 5.63 (m, 1 H), 6.62 (m, 3 H), 6.96 (m, 2 H). − $C_{22}H_{27}ClN_2$ (354.92): calcd. C 74.45, H 7.67, N 7.89; found C 74.26, H 7.88, N 7.86.

1-*tert*-Butyl-2-(*tert*-butylamino)-4-phenyl-1*H*-pyrrole (4a): M.p. 112°C (MeOH); yield 0.68 g (25%). − IR: $\tilde{\nu}$ = 3280 cm^{-1} (NH), 1610 (C=C). − ^{1}H NMR (300 MHz): δ = 1.31 (s, 9 H), 1.66 (s, 9 H), 6.17 (d, J = 2 Hz, 1 H, 3-H), 6.88 (d, J = 2 Hz, 1 H, 5-H), 7.11 (t, J = 7 Hz, 1 H), 7.30 (t, J = 7 Hz, 2 H), 7.50 (d, J = 7 Hz, 2 H). − MS: calcd. for $C_{18}H_{26}N_2$ m/z = 270.2096 [M$^{+\cdot}$]; found 270.2092; m/z (%): 270 (44), 214 (12), 213 (13), 158 (95), 157 (100), 130 (18).

1-*tert*-Butyl-2-(*tert*-butylamino)-4-methyl-1*H*-pyrrole (4f): ^{1}H NMR (300 MHz): δ = 1.24 (s, 9 H), 1.57 (s, 9 H), 2.04 (dd, J = 0.9 and 0.4 Hz, 3 H), 5.65 (br. d, J = 2.1 Hz, 1 H, 3-H; sharp doublet by selective irradiation of the methyl group on C-4), 6.29 (dq, J = 2.1 and 0.9 Hz, 1 H, 5-H).

1-*tert*-Butyl-2-(*tert*-butylamino)-3-methyl-4-phenyl-1*H*-pyrrole (4g): ^{1}H NMR (300 MHz) of an oily mixture of the isomers **4g** and **6g** (0.99 g, 35% yield): δ = 1.26 (s, 9 H), 1.64 (s, 9 H), 2.16 (s, 3 H), 6.74 (s, 1 H, 5-H), 7.10−7.40 (m, 5 H). − MS: calcd. for $C_{19}H_{28}N_2$ m/z = 284.2252 [M$^{+\cdot}$]; found 284.2254; m/z (%): 284 (40), 227 (60), 171 (100), 116 (20).

1-*tert*-Butyl-2-[(2,6-dimethylphenyl)amino]-3-phenyl-1*H*-pyrrole (6b): M.p. 110°C (pentane); yield 1.43 g (45%). − IR: $\tilde{\nu}$ = 3380 cm^{-1} (NH), 1620 (C=C). − ^{1}H NMR (300 MHz): δ = 1.62 (s, 9 H), 1.96 (s, 6 H), 5.08 (br., NH), 6.24 (d, J = 3.5 Hz, 1 H, 4-H), 6.52 (t, J = 7.5 Hz, 1 H), 6.75 (d, J = 3.5 Hz, 1 H, 5-H), 6.77 (d, J = 7.5 Hz, 2 H), 6.93−7.28 (m, 5 H). − MS: calcd. for $C_{22}H_{26}N_2$ m/z = 318.2096 [M$^{+\cdot}$]; found 318.2095.

2-(*tert*-Butylamino)-1-isopropyl-3-phenyl-1*H*-pyrrole (6c): Oily crude product; yield 1.13 g (44%). − ^{1}H NMR (200 MHz): δ = 0.91 (s, 9 H), 1.37 (d, J = 7 Hz, 6 H), 2.78 (br., NH), 4.76 (m, 1 H), 6.24 (d, J = 3.4 Hz, 1 H, 4-H), 6.61 (d, J = 3.4 Hz, 1 H, 5-H), 7.10−7.40 (m, 5 H).

2-(*tert*-Butylamino)-1-(diphenylmethyl)-3-phenyl-1*H*-pyrrole (6d): M.p. 93°C (MeOH); yield 1.52 g (40%). − ^{1}H NMR (200 MHz): δ = 0.97 (s, 9 H), 2.42 (br., NH), 6.21 (d, J = 3.1 Hz, 1 H, 4-H), 6.32 (d, J = 3.1 Hz, 1 H, 5-H), 6.92 (s, 1 H), 7.00−7.50 (m, 15 H).

1-*tert*-Butyl-2-(*tert*-butylamino)-4-methyl-3-phenyl-1*H*-pyrrole (6g): ^{1}H NMR (300 MHz) of an oily mixture of the isomers **4g** and **6g**: δ = 0.78 (s, 9 H), 1.65 (s, 9 H), 1.96 (d, J = 0.9 Hz, 3 H), 6.48 (q, J = 0.9 Hz, 1 H, 5-H), 7.10−7.40 (m, 5-H).

1-*tert*-Butyl-2-(ethylamino)-4-methyl-3-phenyl-1*H*-pyrrole (6h): ^{1}H NMR (300 MHz): δ = 0.92 (t, J = 7.1 Hz, 3 H), 1.64 (s, 9 H), 2.02 (d, J = 0.7 Hz, 3 H), 2.58 (q, J = 7.1 Hz, 2 H), 6.32 (q, J = 0.7 Hz, 1 H, 5-H), 7.28 (m, 5 H).

1-*tert*-Butyl-2-[(2,6-dimethylphenyl)amino]-4-methyl-3-phenyl-1*H*-pyrrole (6i): ^{1}H NMR (300 MHz): δ = 1.67 (s, 9 H), 1.96 (s, 6 H), 2.04 (d, J = 0.7 Hz, 3 H), 6.41 (t, J = 7.2 Hz, 1 H), 6.56 (br., 1 H, 5-H), 6.62 (d, J = 7.2 Hz, 2 H), 7.03 (m, 5 H).

2-(*tert*-Butylamino)-1-isopropyl-4-methyl-3-phenyl-1*H*-pyrrole (6j): Oily crude product; yield 1.0 g (37%). − IR: $\tilde{\nu}$ = 3350 cm^{-1} (NH),

1630, 1585 (C=C). − ^{1}H NMR (200 MHz): δ = 0.81 (s, 9 H), 1.35 (d, *J* = 6.8 Hz, 6 H), 2.06 (d, *J* = 0.7 Hz, 3 H), 2.94 (br., NH), 4.73 (m, 1 H), 6.42 (q, *J* = 0.7 Hz, 1 H, 5-H), 7.13−7.37 (m, 5 H). − MS: calcd. for $C_{18}H_{26}N_2$ *m*/*z* = 270.2096 [$M^{+\cdot}$]; found 270.2092; *m*/*z* (%): 270 (100), 213 (90), 171 (30).

2-[(2,6-Dimethylphenyl)amino]-1-isopropyl-4-methyl-3-phenyl-1*H*-pyrrole (6k): ^{1}H NMR (300 MHz): δ = 1.32 (d, *J* = 6.7 Hz, 6 H), 1.97 (s, 6 H), 2.10 (br., 3 H), 4.32 (m, 1 H), 6.44 (br., 1 H, 5-H), 6.56 (t, *J* = 7.2 Hz, 1 H), 6.77 (d, *J* = 7.2 Hz, 2 H), 7.16 (m, 5 H).

1-*tert*-Butyl-5-(*tert*-butylamino)-2-cyano-4-phenyl-1*H*-pyrrole (13a): M.p. 85°C (Et_2O/petroleum ether); yield 1.62 g (55%). − IR: $\tilde{\nu}$ = 3380 cm^{-1} (NH), 2186 (C≡N), 1595 (C=C). − ^{1}H NMR (300 MHz): δ = 0.82 (s, 9 H), 1.86 (s, 9 H), 2.85 (br., NH), 6.92 (s, 1 H, 3-H), 7.18−7.33 (m, 5 H). − $C_{19}H_{25}N_3$ (295.43): calcd. C 77.25, H 8.53, N 14.22; found C 77.26, H 8.40, N 14.38.

5-(*tert*-Butylamino)-2-cyano-1-isopropyl-4-phenyl-1*H*-pyrrole (13b): M.p. 119°C (Et_2O/petroleum ether); yield 1.26 g (45%). − IR: $\tilde{\nu}$ = 3323 cm^{-1} (NH), 2189 (C≡N), 1590 (C=C). − ^{1}H NMR (300 MHz): δ = 0.90 (s, 9 H), 1.59 (d, *J* = 7 Hz, 6 H), 3.08 (br., NH), 5.00 (m, 1 H), 6.87 (s, 1 H, 3-H), 7.19−7.36 (m, 5 H). − $C_{18}H_{23}N_3$ (281.40): calcd. C 76.83, H 8.24, N 14.93; found C 76.56, H 8.23, N 15.07.

***tert*-Butyl-{[5-(*tert*-butylamino)-3-phenylpyrrol-2-yl]methylene}ammonium Chloride (7a):** M.p. 260°C (CH_2Cl_2/Et_2O); yield 1.23 g (37%). − IR: $\tilde{\nu}$ = 3178, 3040 cm^{-1} (NH), 1652 (C=N$^+$), 1583 (C=C). − ^{1}H NMR (300 MHz): δ = 1.40 (s, 9 H), 1.46 (s, 9 H), 5.97 (d, *J* = 1.4 Hz, 1 H, 4-H), 6.11 (s, 5-NH), 7.00 (d, *J* = 14.9 Hz, 1 H), 7.35 (m, 2 H), 7.48 (m, 3 H), 10.2 (br. d, *J* = 14.9 Hz, =NH$^+$), 12.36 (br., NH). − ^{15}N NMR: δ = −230.52, −243.56, −282.30 (NH). − MS: calcd. for $C_{19}H_{27}N_3$ *m*/*z* = 297.2205 [M − HCl]$^{+\cdot}$; found 297.2220; *m*/*z* (%): 297 (85), 282 (50), 241 (15), 226 (50), 184 (100). − $C_{19}H_{28}ClN_3$ (333.90): calcd. C 68.35, H 8.45, Cl 10.62, N 12.58; found C 68.26, H 8.33, Cl 10.85, N 12.60.

***tert*-Butyl-{[5-(*tert*-butylamino)-4-methyl-3-phenylpyrrol-2-yl]methylene}ammonium Chloride (7g):** M.p. 160°C then 220°C (CH_2Cl_2/petroleum ether); yield 0.59 g (17%). − IR: $\tilde{\nu}$ = 3240 (br), 3115, 3060 cm^{-1} (NH), 1660 (C=N$^+$), 1575 (C=C). − ^{1}H NMR (300 MHz): δ = 1.35 (s, 9 H), 1.65 (s, 9 H), 1.85 (s, 3 H), 4.78 (s, 5-NH), 6.74 (d, *J* = 14.7 Hz, 1 H), 7.24 (m, 2 H), 7.48 (m, 3 H), 10.89 (br. d, *J* = 14.7 Hz, =NH$^+$), 11.84 (br., NH). − $C_{20}H_{30}ClN_3$ (347.93): calcd. C 69.04, H 8.69, N 12.08; found C 68.87, H 8.82, N 12.02.

***tert*-Butyl-{[5-(*tert*-butylamino)-3-methyl-4-phenylpyrrol-2-yl]methylene}ammonium Chloride (8):** M.p. 262°C (CH_2Cl_2/petroleum ether); yield 0.59 g (17%). − IR: $\tilde{\nu}$ = 3377, 3040 cm^{-1} (NH), 1650 (C=N$^+$), 1568 (C=C). − ^{1}H NMR (300 MHz): δ = 1.48 (s, 9 H), 1.57 (s, 9 H), 2.13 (s, 3 H), 4.95 (br., 5-NH), 7.07 (d, *J* = 14.6 Hz, 1 H), 7.22 (d, *J* = 7 Hz, 2 H), 7.30−7.55 (m, 3 H), 11.06 (br. d, *J* = 14.6 Hz, =NH$^+$), 11.81 (br., NH). − $C_{20}H_{30}ClN_3$ (347.93): calcd. C 69.04, H 8.69, Cl 10.19, N 12.08; found C 68.94, H 8.88, Cl 10.13, N 12.14.

5-(*tert*-Butylamino)-2-(*N*-*tert*-butylformimidoyl)-1-isopropyl-3-methyl-4-phenyl-1*H*-pyrrole (10j): Oily crude product; yield 1.31 g (37%). − IR: $\tilde{\nu}$ = 3340 cm^{-1} (NH), 1620 (C=N), 1585 (C=C). − ^{1}H NMR (300 MHz): δ = 0.82 (s, 9 H), 1.30 (s, 9 H), 1.52 (d, *J* = 7.1 Hz, 6 H), 2.24 (s, 3 H), 5.18 (m, 1 H), 7.20−7.50 (m, 6 H), 8.52 (s, 1 H). − MS: calcd. for $C_{23}H_{35}N_3$ *m*/*z* = 353.2831 [$M^{+\cdot}$]; found 353.2822; *m*/*z* (%): 353 (85), 338 (50), 296 (100), 282 (65).

5-[(2,6-Dimethylphenyl)amino]-2-[*N*-(2,6-dimethylphenyl)formimidoyl]-1-isopropyl-3-methyl-4-phenyl-1*H*-pyrrole (10k): Oily crude product; yield 0.45 g (10%). − ^{1}H NMR (200 MHz): δ = 1.66 (d, *J* = 7 Hz, 6 H), 2.34 (s, 6 H), 2.13 (s, 3 H), 2.23 (s, 6 H), 5.17 (br., 1 H), 6.55−7.10 (m, 12 H), 8.17 (s, 1 H).

1-*tert*-Butyl-2,3-bis(*tert*-butylimino)-4-(2-thienyl)azetidine (16): M.p. 97°C (MeOH); yield 1.17 g (35%). − IR: $\tilde{\nu}$ = 1696, 1661 cm^{-1} (C=N). − ^{1}H NMR (300 MHz): δ = 1.07 (s, 9 H), 1.27 (s, 9 H), 1.34 (s, 9 H), 5.27 (s, 1 H), 6.92 (dd, *J* = 5 and 3.5 Hz, 1 H), 6.99 (dd, *J* = 3.5 and 1 Hz, 1 H), 7.23 (dd, *J* = 5 and 1 Hz, 1 H). − ^{13}C NMR (75.5 MHz): δ = 27.3, 29.9, 30.8 (3 qm, ^1J = 126 Hz), 53.0, 54.0, 57.5 (3 m), 63.9 (dd, ^1J = 148 Hz, ^3J = 2.6 Hz), 125.3 (dd, ^1J = 184 Hz, ^3J = 10 Hz), 125.5 (dm, ^1J = 171 Hz), 126.4 (dt, ^1J = 167 Hz, ^2J = 4.9 Hz), 146.8 (m), 153.4 (d, ^3J = 2.6 Hz), 155.5 (d, ^2J = 4.2 Hz). − $C_{19}H_{31}N_3S$ (333.54): calcd. C 68.42, H 9.37, N 12.60, S 9.61; found C 68.58, H 9.60, N 12.48, S 9.71.

Insertion Reaction of *tert*-Butyl Isocyanide into Pyrrolium Chloride 3a: A solution of salt **3a** (1.5 g, 5 mmol) and the isocyanide (1.25 g, 15 mmol) in dry MeCN (25 mL) was refluxed for 45 h. The solvent was subsequently removed in vacuo and the hydrochloride **7a** was precipitated by the addition of THF as described above (1.15 g, 69% yield).

Autoxidation of Pyrroles: The reaction was studied with a few selected 2-aminopyrroles as examples. A sample of **4a** or **6j** was maintained at room temp. under atmospheric O_2 for 3 or 12 d. The pyrrolinone **17** thus produced was suspended in MeOH and filtered, while pyrrolinone **18j** was purified by flash chromatography on silica gel using diethyl ether/petroleum ether (1:3) as eluent. A CH_2Cl_2 solution of in situ generated **6i** or **6k** was concentrated to give the corresponding pyrrolinone **18i**,**k**, which was worked up by column chromatography using CH_2Cl_2/hexane (2:1) as eluent. − The 2-(formimidoyl)pyrroles **10k**,**j** were quantitatively converted into their derivatives **19**, **20** in the course of chromatography on SiO_2 using Et_2O as eluent. − Selected ^{13}C-NMR data: see Tables 2 and 3.

1-*tert*-Butyl-5-(*tert*-butylimino)-3-phenyl-3-pyrrolin-2-one (17): M.p. 86°C (MeOH). − IR: $\tilde{\nu}$ = 1690 cm^{-1} (C=O), 1626 (C=N). − ^{1}H NMR (200 MHz): δ = 1.42 (s, 9 H), 1.69 (s, 9 H), 6.95 (s, 1 H, 4-H), 7.40 (m, 3 H), 7.84 (m, 2 H). − MS: calcd. for $C_{18}H_{24}N_2O$ *m*/*z* = 284.1888 [$M^{+\cdot}$]; found 284.1884; *m*/*z* (%): 284 (70), 227 (100), 213 (55), 173 (50), 171 (50). − $C_{18}H_{24}N_2O$ (284.40): calcd. C 76.02, H 8.51, N 9.85; found C 75.86, H 8.50, N 9.80.

1-*tert*-Butyl-5-[(2,6-dimethylphenyl)imino]-3-methyl-4-phenyl-3-pyrrolin-2-one (18i): M.p. 148°C (MeOH). − IR: $\tilde{\nu}$ = 1701 cm^{-1} (C=O), 1631 (C=N), 1580 (C=C). − ^{1}H NMR (300 MHz): δ = 1.77 (s, 3 H), 1.82 (s, 9 H), 1.99 (s, 6 H), 6.43−7.00 (m, 8 H). − $C_{23}H_{26}N_2O$ (346.47): calcd. C 79.73, H 7.56, N 8.09; found C 79.56, H 7.54, N 8.37.

5-(*tert*-Butylimino)-1-isopropyl-3-methyl-4-phenyl-3-pyrrolin-2-one (18j): M.p. 98°C (pentane). − IR: $\tilde{\nu}$ = 1693 cm^{-1} (C=O), 1640 (C=N). − ^{1}H NMR (300 MHz): δ = 1.02 (s, 9 H), 1.41 (d, *J* = 6.9 Hz, 6 H), 1.70 (s, 3 H), 4.61 (m, 1 H), 7.12 (m, 2 H), 7.39 (m, 3 H). − MS: calcd. for $C_{18}H_{24}N_2O$ *m*/*z* = 284.1889 [$M^{+\cdot}$]; found 284.1896. − $C_{18}H_{24}N_2O$ (284.40): calcd. C 76.02, H 8.51; found C 75.79, H 8.44.

5-[(2,6-Dimethylphenyl)imino]-1-isopropyl-3-methyl-4-phenyl-3-pyrrolin-2-one (18k): M.p. 120°C (Et_2O/petroleum ether). − IR: $\tilde{\nu}$ = 1700 cm^{-1} (C=O), 1640 (C=N), 1580 (C=C). − ^{1}H NMR (300 MHz): δ = 1.54 (d, *J* = 6.2 Hz, 6 H), 1.86 (s, 3 H), 1.98 (s, 6 H), 4.73 (br., 1 H), 6.53−7.00 (m, 8 H). − $C_{22}H_{24}N_2O$ (332.45): calcd. C 79.47, H 7.28, N 8.43; found C 79.58, H 7.19, N 8.53.

2-[*N*-(2,6-Dimethylphenyl)formimidoyl]-5-[(2,6-dimethylphenyl)-imino]-2,5-dihydro-2-hydroxy-1-isopropyl-3-methyl-4-phenyl-1*H*-

pyrrole (19): M.p. 125°C (petroleum ether). − IR: $\tilde{\nu}$ = 3384 cm^{-1} (OH), 1637 (C=N), 1580 (C=C). − ^1H NMR (200 MHz): δ = 1.60 (d, *J* = 6.8 Hz, 3 H), 1.67 (d, *J* = 6.8 Hz, 3 H), 1.73 (s, 3 H), 1.95 (s, 3 H), 2.08 (s, 3 H), 2.17 (s, 6 H), 3.84 (m, 1 H), 5.63 (s, OH), 6.35−6.60 (m, 3 H), 6.80−7.15 (m, 8 H), 7.55 (s, 1 H). − $C_{31}H_{35}N_3O$ (465.64): calcd. C 79.96, H 7.58, N 9.02; found C 80.13, H 8.01, N 8.71.

5-(*tert*-Butylamino)-1-isopropyl-3-methyl-4-phenyl-1*H*-pyrrole-2-carboxaldehyde (20): M.p. 78°C (petroleum ether). − IR: $\tilde{\nu}$ = 3340 cm^{-1} (NH), 1635 (C=O). − ^1H NMR (300 MHz): δ = 0.88 (s, 9 H), 1.57 (d, *J* = 7 Hz, 6 H), 2.29 (s, 3 H), 3.15 (br., NH), 5.05 (m, 1 H), 7.18−7.42 (m, 5 H), 9.72 (s, 1 H). − MS: calcd. for $C_{19}H_{26}N_2O$ *m/z* = 298.2045 [M^+]; found 298.2042; *m/z* (%): 298 (40), 242 (65), 213 (10), 200 (100), 171 (15). − $C_{19}H_{26}N_2O$ (298.43): calcd. C 76.47, H 8.78, N 9.39; found C 76.34, H 8.85, N 9.31.

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