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Substituted 3-Hydroxypyrroles from 1-Azapenta-1,4-dien-3-ones: The Aza-Nazarov Reaction – Synthesis and Quantum Chemical Calculations

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Dedicated to Professor Gerhard Erker on the occasion of his 60th birthday

Keywords: Aza-Nazarov reaction / Ring-closure reactions / 3-Hydroxypyrroles / Quantum chemistry / Cations / Ring contraction

On the basis of quantum chemical calculations, 1-azapenta-1,4-dien-3-ones were chosen as candidates for a thorough theoretical and experimental investigation of their electrocyclization reactivity upon protonation. According to G3 theory, the *O*-protonated 1-azapenta-1,4-dien-3-one cyclizes with high exothermicity and modest activation barrier to give the corresponding 3-hydroxydihydropyrrolium ion ("aza-Nazarov reaction"), whereas the corresponding *O*-protonated 2-azapenta-1,4-dien-3-one shows endothermicity and a huge barrier to the electrocyclization reaction. The stereochemistry of the cyclization reaction (torquoselectivity) was studied in detail theoretically as well as the cyclization properties of vinylogous system **4**, which may give either five- or seven-membered heterocyclic cations (**5** versus **6**). 1-Amino- and 1-alkoxy-1-azapenta-1,4-dien-3-ones **9** and **10** were easily prepared from corresponding α-imino-carbonyl compounds **7** and **8** by aldol condensation. Experimentally, as evidenced by in situ NMR experiments, 1-azapenta-1,4-dien-3-ones gave dihydropyrrole cations upon protonation at a low temperature. For preparative purposes, trapping of the 3-hydroxypyrrole intermediates with the use of anhydrides proved to be advantageous. Thus, a large variety of new, fully substituted 3-hydroxypyrrole derivatives **13**–**17** have become accessible in moderate-to-good yields, including two bis-pyrrole compounds **17a**,**b**. All new compounds were thoroughly characterized, including a number of X-ray diffraction studies.

Introduction

The Nazarov cyclization reaction [Figure 1, Equation (1)] is a very valuable method for the synthesis of five-membered carbocycles.[1–3] The key step of this pericyclic reaction is a conrotatory 4π electrocyclization of a pentadienyl cation, which is controlled by the principle of preservation of orbital symmetry, thus resulting in predictable stereochemistry of the products. The intermediate pentadienyl cations are usually prepared from penta-1,4-dien-3-ones with the use of strong Brønsted acids, but Lewis acids might also be used.

As part of an ongoing project investigating the influence of heteroatoms on the reactivity of charged polyenyl compounds[4–6] we were interested in finding out if a Nazarov-type reaction may also be applied as a general method for the synthesis of heterocycles, for example, pyrroles.

With this in mind, we performed quantum chemical calculations in order to identify cationic species suitable for exothermic ring-closure reactions to yield pyrrole derivatives. Furthermore, we studied the mechanism and the stereochemistry of the cyclization reaction in detail, including the cyclization of a vinylogous system able to form five- and/or seven-membered heterocyclic products. In the next step of the study we synthesized suitable precursors of these cationic intermediates, which turned out to be promising candidates for the ring-closure reaction ("aza-Nazarov reaction"). Finally, in a low-temperature NMR study and on a preparative scale, we investigated the suitability of these precursors for the preparation of derivatives of various 3-hydroxypyrroles by the cyclization reaction, including those that may give either a five- and/or a seven-membered heterocyclic system upon cyclization.

In the literature, only sparse information concerning such cyclization reactions is available. Ciufolini and Roschangar coined, to the best of our knowledge, the term "aza-Nazarov".[7] They observed that a special quinoline derivative containing a 1-azadienone subunit reacted upon treatment with Lewis acids like $Yb(fod)_3$ to give an indolizine derivative. In the authors opinion, "this interesting reaction…has

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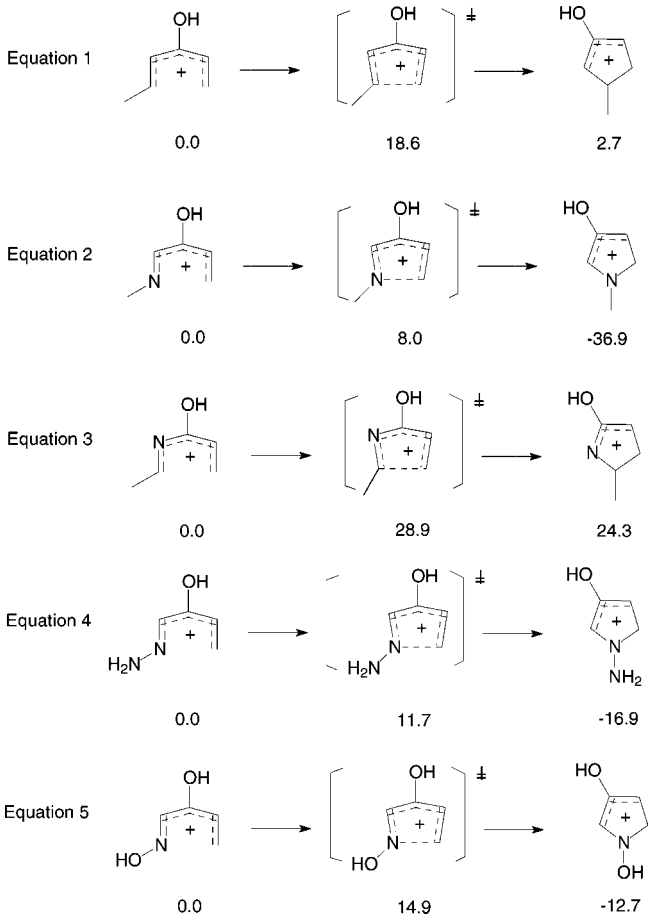


Figure 1. Cyclization reactions of 3-hydroxypentadienylium and various aza-3-hydroxypentadienylium systems. Relative energies [kcal/mol] with respect to the starting material are given for the transition states and the cyclic products (G3 level of theory).

yet to be fully explored, but it already appears to have limited scope". In a study by Matoba and coworkers, a number of heterocyclic chalcones derived from aza-heterocycles underwent cyclization to the corresponding pyrrole systems on treatment with strong acids (HCl, $HClO_4$).[8–10] They also included a vinylogous chalcone in their study. This reacted to give a five-membered heterocyclic system, not a seven-membered one. Hill et al. reported the photocyclization of heterocyclic enones giving indolo[1,2-*a*]quinoxalines.[11] In all these examples, at least one double bond of the 1-azadienones was part of an aromatic system.

In this work we were interested in studying the scope and limitations of the aza-Nazarov reaction carried out as closely as possible to the parent Nazarov system. Instead of cyclopentenones, hydroxypyrroles were the expected products from such cyclization reactions, which have, to the best of our knowledge, been described in the literature only once. In 1927, Diels et al. reported in a contribution concerning the Beckmann rearrangement "new transformations and rearrangements of oximes and hydrazones".[12] They treated oximes, oxime ethers and hydrazones of diacetylbenzal with perchloric acid in acetic anhydride to obtain five-membered ring systems, which they identified as 2-amino- or 2-alkoxy-2,3-dihydropyrrol-3-ones resulting from a Beckmann rearrangement and cyclization reaction. The structures of the products of these cyclization reactions as formulated by Diels et al. are close, but not identical, to the correct ones, as we will show in this contribution.

The cationic cyclization reaction presented herein is a preparatively useful alternative to the anionic cyclization of 2-azapentadienyl metal systems in the synthesis of pyrroles.[13–15]

Results and Discussion

Quantum Chemical Calculations

Starting with the parent Nazarov reaction, that is, the electrocyclization of the 3-hydroxypentadienylium ion to give the 2-hydroxycyclopentenylium ion, we examined the thermodynamics of the cyclization reactions of the U-shaped 3-hydroxy-1- and -2-azapentadienylium ions to give the corresponding positively charged azaheterocycles (Figure 1) in order to learn more about the electronic influence of nitrogen atoms in such conversions. According to the calculations, all of the reactions proceed starting from the U-shaped conformation/configuration in a concerted, pericyclic, conrotatory mode, in which one single transition state interconnects the starting materials and products.

Whereas the cyclization of the methyl-substituted Nazarov system [Figure 1, Equation (1)][16–18] is indicated to be slightly endothermic (3 kcal/mol) with a substantial activation barrier (19 kcal/mol) (G3[19] level of theory, Gaussian 98[20] and 03[21]), a nitrogen atom in the 1-position [3-hydroxy-1-methyl-1-azapentadienylium ion, Equation (2)] results in a very exothermic ring-closure reaction (ca. –37 kcal/mol) with a reduced activation barrier (8 kcal/mol). In contrast, the corresponding cation with a nitrogen atom in the 2-position [3-hydroxy-2-azapentadienylium system, Equation (3)] is not expected to form cyclic products because of the positive heat of reaction (ca. 24 kcal/mol) and the huge activation barrier (29 kcal/mol). In general terms, this very strong influence of the position of the nitrogen atom within the unsaturated chain may be attributed to the nature of the electronic structure of the open chain cation: a nitrogen atom in an odd position of a positively charged unsaturated chain (1-azaallyl cation substructure with some nitrenium character) leads to highly destabilized, very reactive systems, whereas a nitrogen atom in an even position (2-azapropenylium moiety) significantly stabilizes such cations, thus decreasing its reactivity. On the other hand, the heterocyclic product ion in Equation (2) is well stabilized (iminium ion structure), whereas the heterocyclic product ion from Equation (3) is highly reactive (again a 1-azaallyl cation substructure). The electronic properties of 1-azapentadienylium ions have been discussed previously.[22]

From these calculations it is evident that a Nazarov-type cyclization reaction might only be expected if the more electronegative nitrogen atom is located in the 1-position of the

pentadienylium moiety. Therefore, we concentrated our study on 3-hydroxy-1-azapentadienylium systems. For preparative reasons, however, we have not investigated the imine-derived 3-hydroxy-1-azapentadienylium systems experimentally, but we have instead examined the less reactive 1-amino- and 1,3-dihydroxy-1-azapentadienylium ions [Equations (4) and (5)], which were generated by protonation of the corresponding hydrazones and oximes. Figure 1 clearly shows the strong influence of these donor groups[18] on the general reactivity of the intermediate cationic species, especially with respect to the reaction enthalpies, but the influence of the nitrogen atom in the 1-position of the 1-azapentadienylium moiety still dominates and leads to substantial exothermicity for the reactions of the oxime and hydrazone with modest activation barriers.

In order to perform quantum chemical calculations of systems larger than the ones discussed above, we repeated these calculations at two additional lower levels of theory, with the use of the recently developed SCS-MP2/6-31G(d)//RHF/6-31G(d)[23] method and the B3LYP/6-311+G(d,p) DFT method. Owing to the excellent performance of SCS-MP2/6-31G(d)//RHF/6-31G(d) observed here and elsewhere,[24] we used this method to evaluate details of the reaction mechanism and its stereochemistry. In comparison to SCS-MP2 (and G3), the reaction enthalpy calculated by the DFT method for the cyclization reaction was too low by about 6–9 kcal/mol. By using the classical uncorrected MP2 method, the heat of the cyclization reaction was calculated to be about 2–10 kcal/mol more exothermic than that calculated with the SCS-MP2 method.

For a more detailed look at the reaction mechanism of the conrotatory, thermally allowed ring-closure reaction and its stereochemical features, model system **1** leading to heterocyclic cation **2**, which is similar to some of the experimentally studied compounds, was investigated computationally in detail [SCS-MP2/6-31G(d)//RHF/6-31G(d)]. The special emphasis of these calculations was the evaluation of effects produced by the phenomenon known as torquoselectivity[25,26] on pentadienylium systems with electron-donating or -withdrawing substituents attached to the 1- and/or 5-positions (Figure 2).[27] We were interested to see whether 3-hydroxy-1-methoxy-1-azapentadienylium ion **1** (with a lone pair of electrons on the N1 atom and the C=N π electron system) also shows substantial differences in the activation barriers for inward and outward rotation, as known for the Nazarov reaction.[18] Thus, the four conceivable transition states with the stereochemical combinations *out*,*out*, *in*,*out*, *out*,*in* and *in*,*in*, where the first descriptor refers to the substituent at the nitrogen atom in the 1-position, the second to the methyl group attached to the C5 atom, were calculated for complete analysis of the cyclization of molecule **1**. In general, the aza-Nazarov cyclization of **1** is calculated to be a strongly exothermic reaction with a low energy barrier provided that the methoxy group adopts an outward position during the cyclization process. In contrast, the corresponding alternative inward position of the electron-donating substituent during the rotation is kinetically extremely disfavoured by 30–35 kcal/mol.

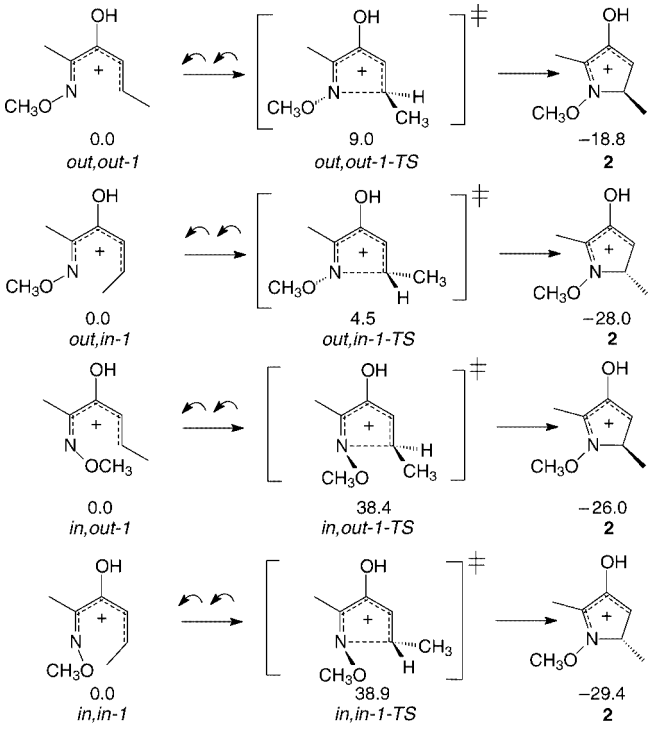


Figure 2. Four different modes for the cyclization reaction of 3-hydroxy-1-methoxy-1-azapentadienylium ion **1** to give **2**. Relative energies were calculated at the SCS-MP2/6-31G(d)//RHF/6-31G(d) level of theory and are given in kcal/mol.

From a comparison of the *out*,*out* to the *out*,*in* transition states on the one hand and of the *in*,*out* to the *in*,*in* transition states on the other hand, it can be clearly seen that the orientation of the methyl substituent in the 5-position has only a small effect on the activation barrier. On the other hand, the *outward* or *inward* position of the methoxy group attached to the nitrogen atom in the 1-position of the 1-azapentadienylium moiety (*out*,*out* versus *in*,*out* and *out*,*in* versus *in*,*in*) leads to considerable differences in the activation energy, as described in the literature.[18]

The conrotatory transition states *out*,*out*-**1**-TS and *out*,*in*-**1**-TS deviate by 30–35° from planarity and resemble each other closely. The torsional angle of the atoms C3–C2–N1–O(Me) amounts to –166° in both structures, indicating that a simultaneous interaction of the C=N π system and the lone pair of electrons on the nitrogen atom with the carbon atom in the 5-position is important for ring formation. The partially formed C–N bonds have a length of 2.14 or 2.24 Å, indicating an early transition state. Houk et al. reported typical transition state C–C distances for the forming bond of 1.95–2.28 Å for pericyclic reactions.[28]

The binding interaction in these transition states is dominated by the second highest occupied molecular orbital (HOMO-1, see Supporting Information). The electronegative nitrogen atom causes a shift of the nodal plane of the pentadienylium HOMO from the C3 atom into the vicinity of the C4 atom in 1-azapentadienylium system **1** (HOMO-1).

In contrast, the *in*,*out*-**1**-TS and *in*,*in*-**1**-TS transition states are helix-shaped late transition states (1.95 and

2.04 Å) with very substantial deviations from planarity (up to 86°). Here, owing to the steric requirements of the inward substituents, the cation cannot easily take advantage of orbital stabilization by delocalization, thus explaining the high activation barrier. In addition to this effect, the *in*,*out*-**1**-TS and *in*,*in*-**1**-TS transition states show a strong antibonding interaction between the free electron pair on the oxygen atom of the methoxy function and the partially formed new σ bond (see Supporting Information for a graphical representation of the relevant orbitals).

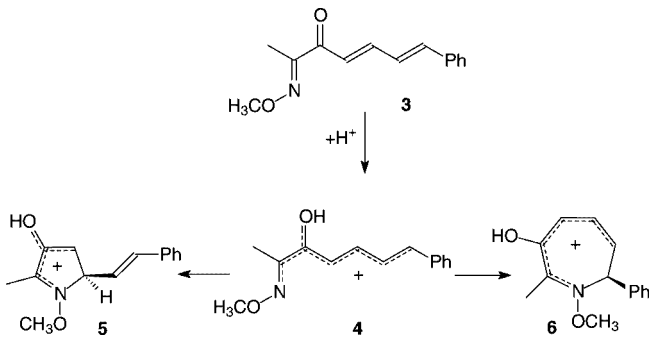
The ionic character of these pericyclic reactions is small: the NBO charge separation between the N1 atom (–0.05*e*) and the C5 atom (0.09*e*) amounts to only 0.14*e* for *out*,*out*-**1**-TS, 0.18*e* for *in*,*out*-**1**-TS (N1: –0.06; C5: 0.12), 0.19*e* for *in*,*out*-**1**-TS (N1: –0.17; C5: 0.02) and 0.18*e* for *in*,*in*-**1**-TS (N1: –0.16; C5: 0.02).

The NICS[29,30] values for the four discussed transition states have also been determined with respect to an axis perpendicular to the centre of the forming heterocycle [B3LYP/6-311+G(d,p)]. The following maximal NICS values were found: *in*,*out*-**1**-TS –8.6; *out*,*out*-**1**-TS –8.6; *out*,*in*-**1**-TS –8.2 and *in*,*in*-**1**-TS –6.1. The value for the Nazarov reaction itself is 10.4, which is well in line with these values, clearly indicating aromatic character and underlining the pericyclic nature of these cyclization reactions. Probably because of strong steric crowding, the NICS value for the *in*,*in*-transition state is somewhat smaller.

Calculations on Experimentally Studied System 3

Five- versus Seven-Membered Ring Formation

Acid-induced cyclization reactions of vinylogous compound **3** allow the possibility of forming either five- (**5**) or seven-membered (**6**) ring systems (Scheme 1). Experimentally (vide infra), only the formation of the five-membered ring is observed upon protonation with the use of trifluoromethanesulfonic acid. In order to understand this selectivity, the energy hyperfaces of both cyclization modes were studied computationally, concentrating on the lowest energy *out*,*out* isomers.



Scheme 1.

The kinetically favoured route to the five-membered ring involves rotation about the C3–C4 bond of protonated intermediate **4** and leads to the corresponding U-shaped isomer U-**4**. This local minimum structure has the ability to cyclize in a conrotatory mode via an *out*,*out* transition-state structure to form pentacyclic cation **5**. The calculated energies for this reaction path are shown in Figure 3. As expected, the thermodynamic and kinetic data for the 1,5-electrocyclization reaction are comparable to those of the model systems (compare Figures 1 and 2).

The alternative, thermally allowed, disrotatory 6π 1,7-electrocyclization to give seven-membered ring system **6** is slightly more exothermic than the 1,5-electrocyclization reaction (Figure 1), but requires more C–C bond rotations. Furthermore, the activation barriers necessary to achieve a conformation that allows the transition to a seven-membered ring are significantly higher and are much larger than that required for the 1,5-electrocyclization.

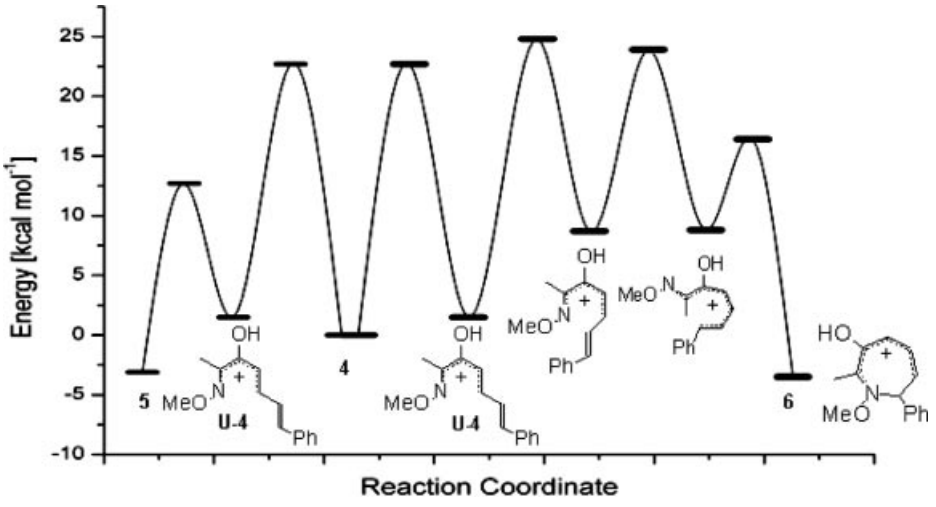
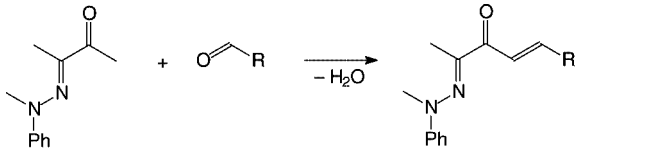


Figure 3. Energy profiles for the cyclization of cation **4** to form either five-membered heterocyclic system **5** or seven-membered ring system **6** [SCS-MP2/6-31G(d)//RHF/6-31G(d)].

Experimental Studies

Synthesis of 1-Azapenta-1,4-dien-3-ones 3, 9–11

To synthesize 1-azapenta-1,4-dien-3-ones **3**, **9**–**11**, we took advantage of a procedure published by Diels et al. in 1927.[12,31] This synthetic route starts from the highly reactive dicarbonyl compound diacetyl. Donor-substituted nitrogen functionalities in the 1-position were introduced easily through condensation reactions with hydrazines and hydroxylamines (acetic acid catalysis) following literature procedures to give corresponding *N*-methyl-*N*-phenylhydrazone **7**[32] and oxime, respectively. In all the cases studied, condensation took place only once. The oxime was converted into corresponding oxime ether **8a** by benzylation and to **8b** by methylation of the oxime anion.[33]

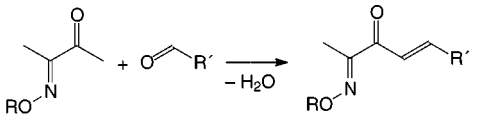


7

9a (R = Ph, 66%)
9b (R = 4-NO_2-Ph, 76%)
9c (R = -HC=CH-Ph, 57 %)

Scheme 2.

In the case of diacetylhydrazone derivative **7**, vinyl moieties were introduced by an aldol condensation giving compounds **9** in 57–76% yields; this approach is, however, applicable only to nonenolizable aldehydes (Scheme 2). It proved best to deprotonate α-imino-carbonyl compound **7** first and to then treat it with the aldehyde. The structural properties of **9a**,**c** were determined by X-ray crystallography



8a (R = CH_2Ph)
8b (R = CH_3)

3 (R = CH_3, R´ = -CH=CH-Ph, 44%)
10a (R = CH_2Ph, R´ = Ph, 70%)
10b (R = CH_2Ph, R´ = 4-Me-Ph, 84%)
10c (R = CH_2Ph, R´ = 2-Br-Ph, 84%)
10d (R = CH_2Ph, R´ = 4-NO_2-Ph, 69%)
10e (R = CH_2Ph, R´ = -CH=CH-Ph, 54%)
10f (R = CH_3, R´= Ph, 84%)
10g (R = CH_3, R´= 4-Me-Ph, 73%)
10h (R = CH_3, R´ = 2-Br-Ph, 78%)
10i (R = CH_3, R´ = 4-Cl-Ph, 95%)
10j (R = CH_3, R´ = 4-NO_2-Ph, 85%)
10k (R = CH_3, R´= -CH=CH-C_6H_4-(4-OCH_3), 60%)
10l (R =CH_3, R´ = 2-pyridyl, 40%)
10m (R = CH_3, R´ = 3-thienyl, 86%)
10n (R = CH_3, R´= 2-(3-bromothienyl), 82%)
10o (R = CH3, R´= 2-pyrrolyl, 47%)

Scheme 3.

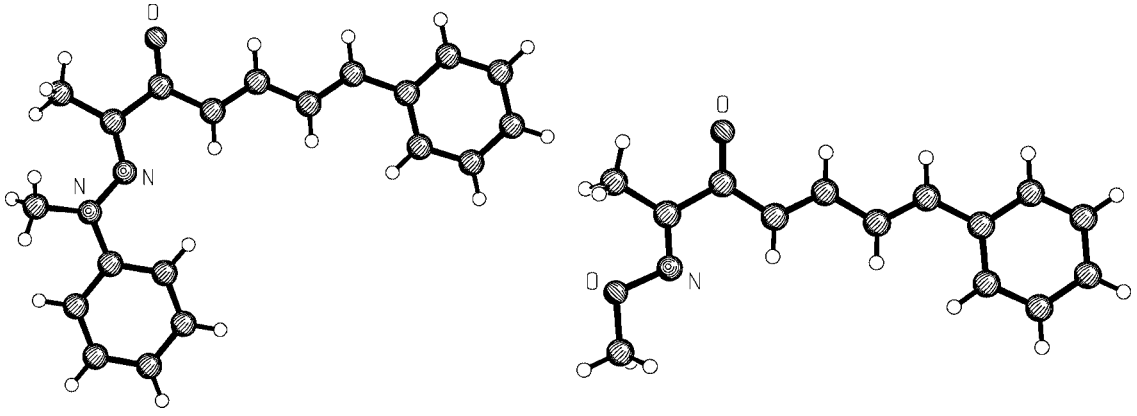
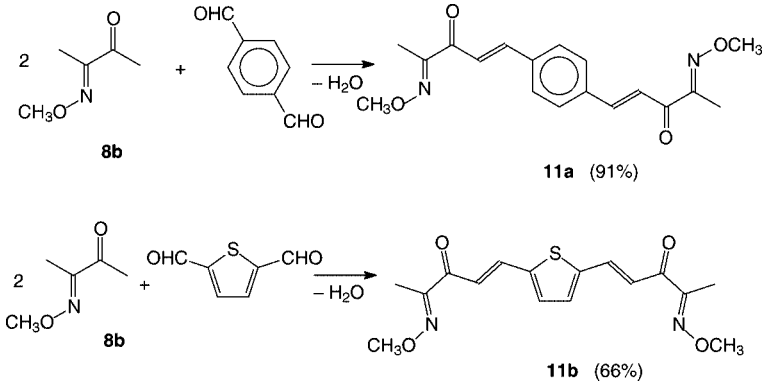


Figure 4. Molecular structures of **9c** (left) and **3** (right), as obtained by X-ray diffraction, showing the (*E*,*E*) configuration of both compounds.



8b **11a** (91%)

8b **11b** (66%)

Scheme 4.

(Figure 4, **9c**). In all cases (*E*)-configured C=C and C=N double bonds were found with adjacent C=O and C=N moieties in the *anti* positions.

In a similar manner, oximes **8a**,**b** gave a great variety of 1-azapenta-1,4-dien-3-one derivatives **3** and **10** in 44–95% yields by aldol condensation (Scheme 3), including vinylogous systems and those with heterocyclic substituents in the 5-position of the azadienone. X-ray structures were obtained for **3** (Figure 4) and **10a**,**o**, again showing (*E*)-configured C=C and C=N double bonds with C=O and C=N in the *anti* positions.

Bis-aldehydes like terephthalaldehyde or thiophene-2,5-dicarbaldehyde reacted twice in the aldol condensation of **8b** to give products **11a**,**b** in 91 and 66% yields, respectively (Scheme 4).

Protonation of Compound 3: In situ NMR Characterization of the Cation in Acidic Solution

In order to study the course of the protonation reaction of compounds **3** and **9**–**11**, experiments in a NMR tube were first undertaken. For this purpose, compound **3** was treated at –60 °C with an excess of trifluoromethanesulfonic acid. Oxime **3** is particularly interesting since it may cyclize to form either a five- or a seven-membered heterocyclic system (Scheme 1, vide supra). Figure 5 shows two ^{13}C NMR spectra; the upper spectrum is that of compound **3**, the lower spectrum was obtained after the addition of trifluoromethanesulfonic acid to **3**, dissolved in CD_2Cl_2, at –60 °C. All of the signals could be assigned by using 2D experiments (COSY, HMQC and HMBC correlation techniques). During the addition of the acid, the colour of the solution changed from colourless to intense pink, which indicated the successful protonation of **3** and the formation of a positively charged, conjugated π system.

Each signal that is present in the spectrum of **3** corresponds exactly to one new signal in the spectrum of protonated compound **5**, that is, 1-azadienone **3** reacts completely to give only one new compound. The signal due to the carbonyl group disappeared as a result of proton attack at the oxygen atom. The large shift of the signal arising from C10 to a high field indicates its rehybridization from sp^2 to sp^3. Thus, cyclization to form dihydropyrrolium ion **5** takes place at a low temperature (–60 °C). This is in contrast to the observations of Howell et al.[34] who only observed the cyclization of the (nitrogen-free) Nazarov system 4-hydroxyhepta-2,4-dien-5-ylium at 20 °C.

In order to determine whether a five- or a seven-membered heterocycle was formed, quantum chemical NMR shift calculations for compounds **5** and **6** were performed

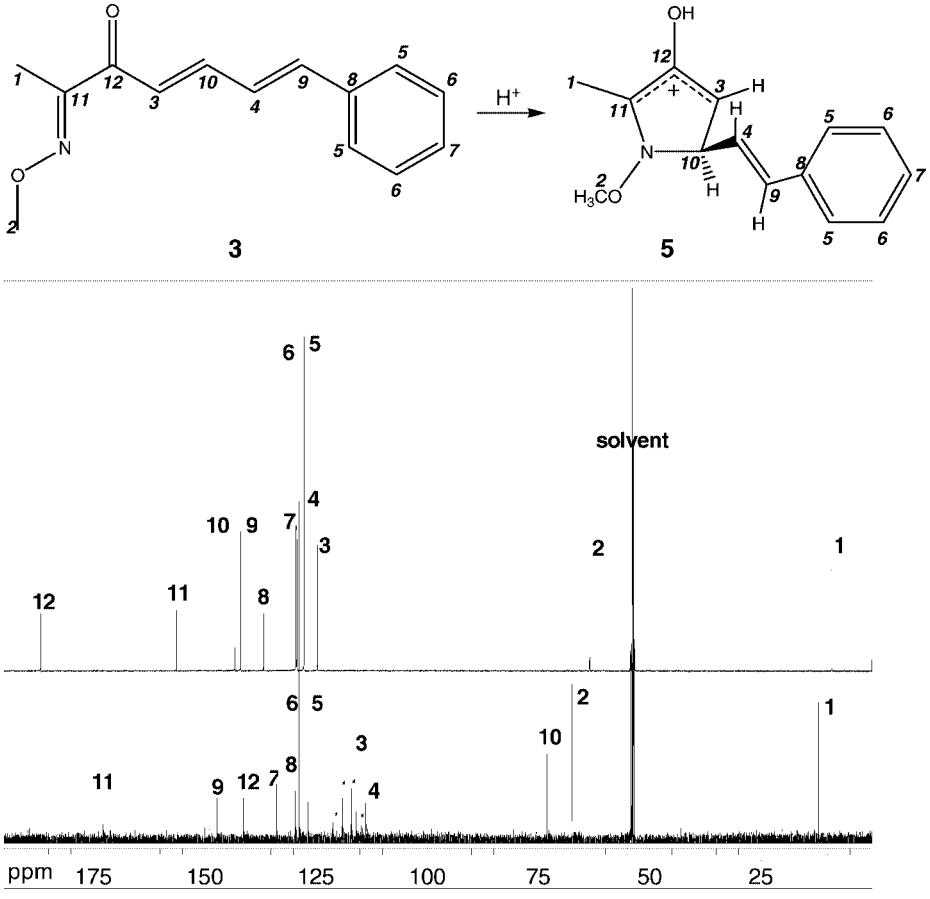


Figure 5. ^{13}C NMR spectra for the protonation of **3** with numbering scheme for the carbon atoms. Upper spectrum: compound **3** before addition of trifluoromethanesulfonic acid (room temperature); lower specrum: after addition of the acid to form **5** (CD_2Cl_2, –60 °C, 100 MHz). The signals from CF_3 are marked with asterisks.

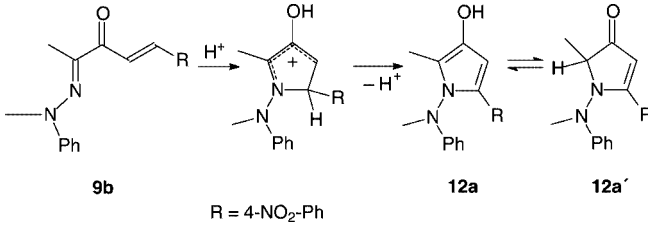
at the DFT B3LYP/6-311+G(d,p) level of theory with the use of the GIAO method as implemented in the Gaussian 03 package. According to the calculations for the five-membered ring, two groups of signals are expected between δ = 5 and 6 ppm (for 4-H and 10-H), one between 6 and 6.5 ppm (3-H) and one signal between 7 and 7.5 ppm (9-H) besides the aromatic signals. These predicted data for the five-membered ring fit nicely with the experimental spectrum, whereas the calculated set of signals for a possible seven-membered ring system with one group between 4 and 4.5 ppm and three groups between 6.5 and 7.5 ppm disagrees with the experimental spectrum. The ^{13}C NMR spectroscopic data also fit much better for a five-membered ring system than for a seven-membered ring (certainty value R^2 = 0.9902 versus 0.9792 for a correlation of all signals). Besides the chemical shifts, experimental and calculated coupling constants also confirm the preferred formation of the five-membered ring system, as predicted by the quantum chemical calculations (vide supra).

These NMR studies together with the X-ray structure determinations (see below) clearly show the nature of the reaction products (1-amino- or 1-alkoxy-3-hydroxypyrrole derivatives) first isolated by Diels et al.[12] They further prove unambiguously that the aza-Nazarov mechanism postulated in the introduction takes place, instead of a Beckmann rearrangement, as proposed by Diels et al. Quite clearly, under the reaction conditions employed (strong acid at low temperature), protonation of starting materials **3**, **9** and **10** takes place mainly at the carbonyl oxygen atom, thus opening the aza-Nazarov channel, whereas we observed no sign of an oxime oxygen protonation, which would give rise to Beckmann-type rearrangement products.

Preparation of Pyrroles

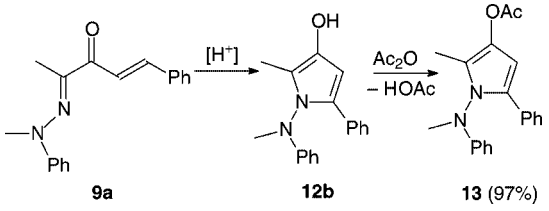
The NMR experiments clearly showed that 1-azapenta-1,4-dien-3-one **3** cyclizes to give the five-membered ring systems upon protonation by using strong organic acid. Bearing in mind the well-known generally poor thermal stability of this class of compound, we were interested in developing a preparative route to 3-hydroxypyrrole derivatives[35,36] based on these mechanistic findings.

Thus, at –78 °C a solution of azadienone **9b** in anhydrous dichloromethane was treated with 1.2 equiv. of trifluoromethanesulfonic acid. This solution was treated at –78 °C with a large excess of an aqueous sodium hydrogen carbonate solution in order to quickly neutralize the crude acidic reaction mixture under mild conditions. Then the reaction mixture was slowly warmed to room temperature. The layers were separated, followed by very quick work up (drying, evaporation of the solvent) in order to avoid thermal decomposition. NMR spectroscopic data ($CDCl_3$) suggest the formation of very sensitive 3-hydroxypyrrole **12a** (Scheme 5), which exists in the less polar solvent dichloromethane at room temperature exclusively as two diastereomers (resulting from rotation around the N–N bond) of the keto form **12a′**, equilibrating via **12a**. The preference for this tautomer is in accord with the observations by McNab and Monahan.[35,36] They found that unsubstituted 3-hydroxypyrroles in nonpolar solvents exclusively form the keto tautomer, whereas in polar solvents like dimethyl sulfoxide the enol form (like **12a**) predominates (up to 85–95%).



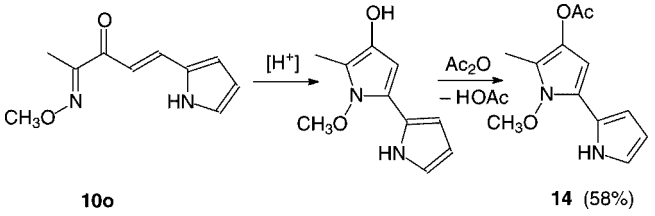
Scheme 5.

In order to isolate more stable products in subsequent experiments, 2.5–3 equiv. of anhydrides were added to the acidic reaction mixture of **9a** at –10 °C without isolation of presumed intermediate **12b**, following a suggestion by Diels et al.[12] Then work up with aqueous $NaHCO_3$ was carried out. Indeed, after column filtration spectroscopically pure pyrrole **13** was obtained in 97% yield (Scheme 6). This compound is more stable than **12a**, but also decomposes within a couple of days with darkening.



Scheme 6.

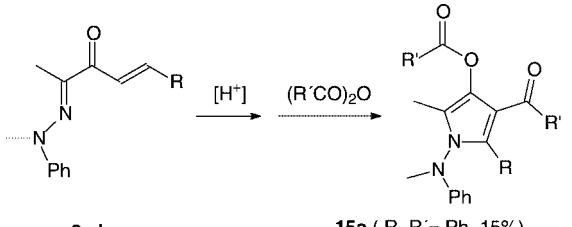
In a similar way, oxime derivative **10o** was converted into corresponding *N*-methoxypyrrolylpyrrole **14** on treatment with trifluoromethanesulfonic acid and subsequent addition of acetic anhydride, followed by aqueous work up (58%, Scheme 7).



Scheme 7.

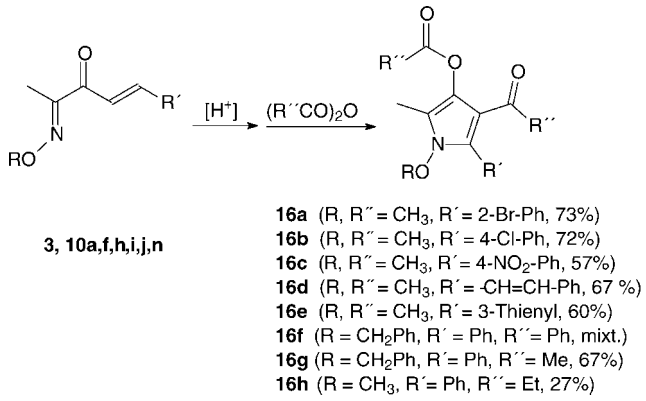
Additional experiments showed that the formation of compounds **13** and **14** is an exception. All other in situ prepared 3-hydroxypyrroles **12**, being very electron-rich aromatic compounds, reacted twice with the anhydrides, first at the hydroxy group and secondly in the 4-position by electrophilic substitution leading to fully substituted compounds **15** (from hydrazones **9**, Scheme 8) and **16** (from oximes **3** and **10**, Scheme 9). Generally, acetic anhydride gave the most stable products. Treatment of the reaction mixture

with benzoic or propionic anhydride led to pyrroles **15a**,**c** and **16f**,**h**. Compound **15c** is a reddish gum which decomposes quickly. Compounds **15a** and **16f** form mixtures with another product that lacks the acetyl group in the 4-position and could not be separated completely.



Scheme 8.

In general, many different types of azadienones **3**, **9** and **10** were successfully converted into the corresponding 3-hydroxypyrrole derivatives **15** and **16** without any indication of major side-reactions (e.g., Beckmann-type rearrangements).



Scheme 9.

X-ray structure determinations were performed on **16d**,**e** (Figure 6). Vinylogous compound 1-azahepta-1,4,6-trien-3-one **3** (see above for quantum chemical calculations and NMR experiments), which has the (hypothetical) possibility of forming either a five- or a seven-membered ring system, exclusively yields pyrrole derivative **16d**.

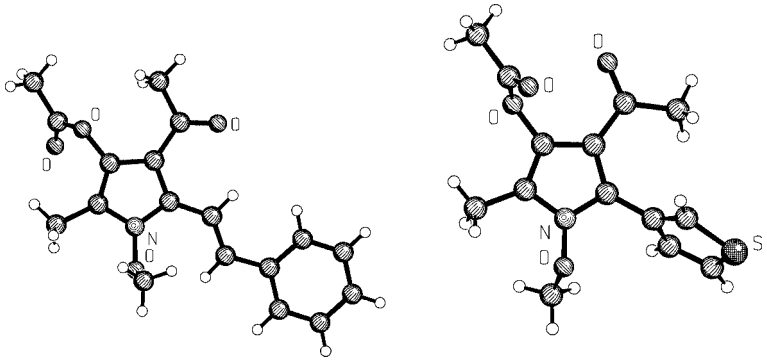
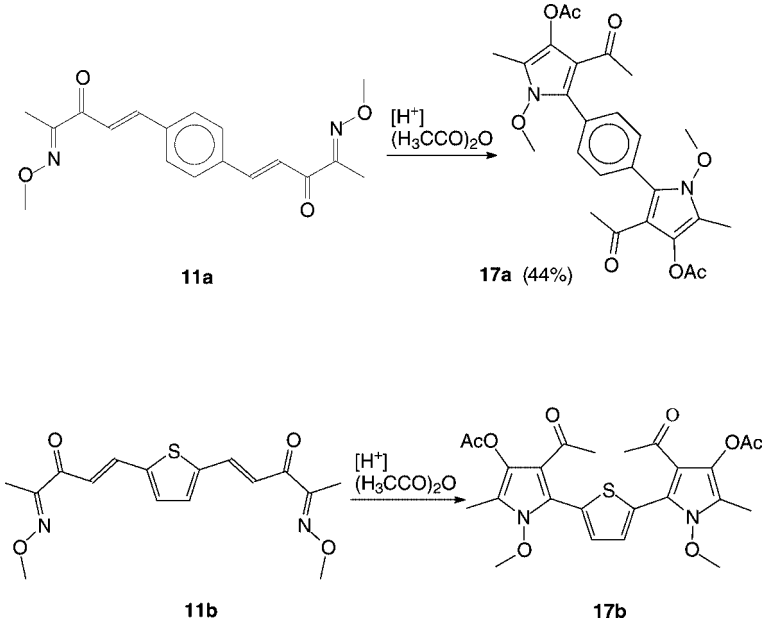


Figure 6. Molecular structures of **16d** (left) and **16e** (right), as obtained by X-ray crystallography.



Scheme 10.

Successful cyclization of bis(azadienone)s **11a**,**b** was also achieved under aza-Nazarov conditions. For these experiments, an excess of 4 equiv. (or more) of the acid was used before the reaction was quenched with 6 equiv. of acetic acid anhydride. Both azadienone subunits cyclized simultaneously (Scheme 10). Spectroscopically pure compound **17a** was obtained in 95% yield after column filtration (44% after recrystallization). The structure of this compound was elucidated by X-ray diffraction (Figure 7). Thiophene derivative **17b** was also obtained, but complete purification was not possible. Compounds of this type are of interest with regard to electric conductivity.[37]

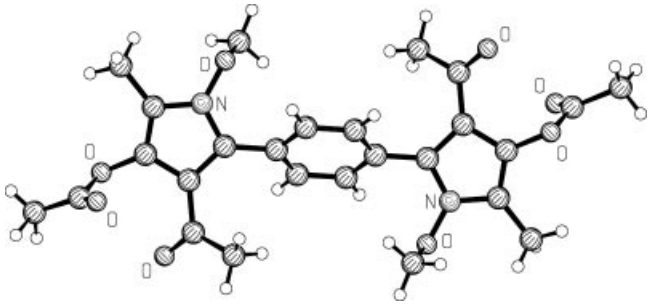


Figure 7. Molecular structure of compound **17a**, as obtained by X-ray diffraction.

Conclusions

In this report we have shown that the long-known Nazarov reaction of 1,4-pentadien-3-ones may successfully be applied to the corresponding nitrogen derivatives, 1-aza-1,4-pentadien-3-ones. These precursors give access to highly substituted 3-hydroxypyrrole derivatives by the aza-Nazarov route. By carrying out quantum chemical calculations we have demonstrated the importance of the position of the nitrogen atom within the conjugated chain in pericyclic cyclization reactions. The stereochemical course and the conrotatory mode of the cyclization reaction have also been studied in detail by quantum chemical methods, including the cyclization of a system that may give either a five- or seven-membered heterocyclic system. On the basis of the experiments of Diels et al.,[12] a number of new precursors suitable for ring formation were prepared. An in situ NMR study provided information on the temperature range necessary for the cyclization reaction and strongly indicated the aza-Nazarov reaction mode rather than a Beckmann-type rearrangement mechanism as originally proposed by Diels et al. On a preparative scale, various 1-amino- and 1-alkoxy-3-hydroxypyrrole derivatives have been prepared and fully characterized, including a number of X-ray structure determinations. Thus, starting with a mechanistic proposal, we have finally been able to develop a new general procedure for the synthesis of fully substituted 3-hydroxypyrrole derivatives.

Experimental Section

Materials and Methods: IR: Nicolet 5DXC spectrometer. ^{1}H- and ^{13}C NMR: Bruker WM 300 and Varian Unity 600 spectrometers, tetramethylsilane or solvent as internal reference. CHN elemental analysis: Elementar Vario El III. Melting points are uncorrected. All solvents were rigorously dried by standard methods. When necessary, the experiments were carried out with complete exclusion of moisture (argon atmosphere, septum-syringe technique) in glassware that had been thoroughly dried by repeated heating under an atmosphere of argon and subsequent evacuation.

2-Methoxyimino-7-phenylhepta-4,6-dien-3-one (3): 3-Methoxyiminobutan-2-one (**8b**)[29] (3.0 g, 26.1 mmol) and cinnamaldehyde (5.6 mL, 5.9 g, 44.6 mmol) were treated with an aqueous solution of potassium hydroxide (30%, 3 mL) at 0 °C. A yellow precipitate was formed immediately after addition of the first drop of base. The reaction mixture was stirred for 1 h at 0 °C and treated with methanolic potassium hydroxide solution (7 mL) at room temperature for complete reaction. The resulting solid was filtered off and recrystallized from methanol. Pale yellow solid, 2.6 g (11.3 mmol, 43.6%), m.p. 94.8 °C, b.p. 145 °C (0.007 mbar, Kugelrohr oven). R_f (TLC) = 0.35 (silica gel, petroleum ether/TBME, 3:1), R_t (GC) = 17.48 min [40–10/min–280(5)]. ^{1}H NMR (600 MHz, CD_2Cl_2): δ = 2.01 [s, 3 H, $H_3CC(N)$], 4.11 (s, 3 H, OCH_3), 6.98–7.06 (m, 2 H, $H_{olef.}$), 7.29 (d, ^3J = 15.2 Hz, 1 H, $H_{olef.}$), 7.34–7.41 (m, 3 H, $H_{arom./olef.}$), 7.51–7.57 (m, 3 H, $H_{arom./olef.}$) ppm. ^{13}C NMR (150 MHz, CD_2Cl_2): δ = 9.04 [$H_3CC(N)$], 63.17 (OCH_3), 123.35 [H*C*C(O)], 126.75 (PhCH*C*H), 127.10 (*o*-$C_{arom.}$), 128.71 (*m*-$C_{arom.}$), 129.09 (*p*-$C_{arom.}$), 135.65 (*ipso*-$C_{arom.}$), 141.69 (Ph-CH), 143.27 [*C*H=CHC(O)], 155.69 (C=N), 186.70 (C=O) ppm. IR (film): $\tilde{\nu}$ = 3080 (w, $CH_{arom.}$), 3026 (w, $CH_{arom.}$), 2978 (w, $CH_{aliph.}$), 2936 (s, $CH_{aliph.}$), 2820 (m, $CH_{aliph.}$), 2650 (w), 1975 (w), 1956 (w), 1659 (vs, $C{=}O_{ketone}$), 1608 (sh., $C{=}C_{olef.}$), 1587 (vs, br., C=C), 1578 (m, C=C), 1447 (m, $CH_{aliph.}$), 1356 (m, CH), 1317 (s), 1213 (s), 1177 (m), 1051 (vs), 934 (s), 853 (s), 756 (s, $CH_{arom.}$), 708 (m), 689 (m, $CH_{arom.}$), 615 (w), 529 (m), 507 (m) cm^{-1}. GC–MS (70 eV): *m*/*z* (%) = 229 (10) $[M]^+$, 198 (16), 170 (14), 157 (45), 129 (80) $[Ph(CHCH)_2]^+$, 128 (100), 115 (12), 102 (14), 77 (9) $[C_6H_5]^+$. $C_{14}H_{15}NO_2$ (229.27): calcd. C 73.34, H 6.59, N 6.11; found C 73.20, H 6.36, N 6.01.

X-ray Crystal Structure Analysis of 3:[38] Formula $C_{14}H_{15}NO_2$, M = 229.27, colourless crystal, 0.50 × 0.30 × 0.05 mm, a = 6.860(1), b = 7.945(1), c = 23.943(2) Å, β = 96.49(1)°, V = 1296.6(3) Å^3, $\rho_{calcd.}$ = 1.174 g cm^{-3}, μ = 0.632 mm^{-1}, empirical absorption correction ($0.743 \leq T \leq 0.969$), Z = 4, monoclinic, space group $P2_1/c$ (No. 14), λ = 1.54178 Å, T = 223 K, $\omega/2\theta$ scans, 2861 reflections collected ($-h$, $-k$, $\pm l$), [$(\sin\theta)/\lambda$] = 0.62 Å^{-1}, 2636 independent (R_{int} = 0.021) and 2104 observed reflections [$I \geq 2\sigma(I)$], 157 refined parameters, R = 0.041, wR_2 = 0.130, max. residual electron density 0.17 (–0.14) e Å^{-3}, hydrogen atoms calculated and refined as riding atoms.

Low-Temperature NMR Investigation of the Protonation of 3 to 5: Under complete exclusion of moisture in an NMR tube that had been thoroughly dried by repeated heating under an atmosphere of argon and subsequent evacuation, **3** (55 mg, 0.24 mmol) was dissolved in deuteriated dichloromethane (0.2 mL, freshly distilled from P_2O_5). In a pear-shaped flask under an atmosphere of argon, trifluoromethanesulfonic acid (0.04 mL, 0.07 g, 0.5 mmol) was dissolved in deuteriated dichloromethane (0.6 mL). Both solutions were vigorously shaken (Vortex) and cooled to –78 °C. The acid solution was added to the NMR tube with the use of Schlenk techniques. The colour of the reaction mixture changed immediately from slightly yellow to intense pink. The solution was shaken again (Vortex) and ^{1}H- and ^{13}C NMR spectra were measured at –60 °C (Figure 5). ^{1}H NMR (600 MHz, –60 °C, CD_2Cl_2): δ = 2.67 (s, 3 H, H_3C-1), 4.20 (s, 3 H, H_3C-2), 5.71–5.80 (m, 2 H, HC-4, HC-10),

6.28 (s, 1 H, HC-3), 7.09 (d, ^3J = 15.3 Hz, 1 H, HC-9), 7.41–7.49 (m, 5 H, $H_{arom.}$), 11.87 (br., OH) ppm. ^{13}C NMR (150 MHz, –60 °C, CD_2Cl_2): δ = 11.96 (C-1), 67.45 (C-2), 73.07 (C-10), 113.69 (C-4), 115.90 (C-3), 126.76 (2 C, C-5), 128.69 (2 C, C-6), 129.52 (C-8), 133.69 (C-7), 141.26 (C-12), 147.15 (C-9), 172.78 (C-11) ppm.

4-(2-Methyl-2-phenylhydrazono)-1-phenylpent-1-en-3-one (9a): 3-(2-Methyl-2-phenylhydrazono)butan-2-one (**7**)[39] (5.0 g, 26.3 mmol) and benzaldehyde (2.9 mL, 3.0 g, 28.3 mmol) were dissolved in methanol (20 mL). The solution was treated with aqueous NaOH (40%, 0.5 g) according to a procedure described by Diels et al.[12,40] After about 4 h a yellow precipitate was formed. Stirring of the reaction mixture was continued for 48 h for complete reaction. The precipitate was filtered off and washed with water until a neutral reaction was obtained. The product was purified by recrystallization from ethyl acetate. Yellow solid, 4.8 g (17.2 mmol, 65.6%), m.p. 139.5 °C (decomp.), 138–139 °C.[35] R_f (TLC) = 0.35 (silica gel, petroleum ether/TBME, 3:1), R_t (GC) = 19.43 min [40–10/min–280(5)]. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.11 [s, 3 H, $H_3CC(N)$], 3.54 (s, 3 H, NCH_3), 7.03–7.09 (m, 1 H, $H_{arom.}$), 7.21–7.24 (m, 2 H, $H_{arom.}$), 7.33–7.42 (m, 5 H, $H_{arom.}$), 7.61–7.65 (m, 2 H, $H_{arom.}$), 7.71 [d, ^3J = 16.0 Hz, 1 H, C(O)CH], 8.01 (d, ^3J = 16.0 Hz, 1 H, PhCH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.8 [$CH_3C(N)$], 43.8 (NCH_3), 117.7 (*o*/*m*-$C_{arom.}$), 121.5 (*p*-$C_{arom.}$), 122.8 (*o*/*m*-$C_{arom.}$), 128.3 (*o*/*m*-$C_{arom.}$), 128.8 (*o*/*m*-$C_{arom.}$), 129.1 (*p*-$C_{arom.}$), 129.9 ($C_{olef.}$), 135.7 (*ipso*-$C_{arom.}$), 141.5 ($C_{olef.}$), 149.2, 149.5 (*ipso*-$C_{N–Ph.}$, C=N), 188.5 (C=O) ppm. IR (KBr): $\tilde{\nu}$ = 3049 (w, $CH_{arom.}$), 3005 (w, sh., $CH_{arom.}$), 2968 (w, $CH_{aliph.}$), 1647 (vs, C=O), 1607 (s, C=C), 1550 (vs, br., C=C), 1489 (s), 1369 (w, $CH_{aliph.}$), 1352 (w), 1303 (s), 1281 (m), 1215 (vs), 1176 (w), 1117 (m), 1067 (s), 993 (m), 899 (w), 866 (w), 795(w), 762 (m), 752 (s, $CH_{arom.}$), 692 (s, $CH_{arom.}$) cm^{-1}. MS (70 eV): *m*/*z* (%) = 278 (96) $[M]^+$, 209 (36), 172 (33), 131 (87) $[C_9H_7O]^+$, 106 (100) $[C_7H_8N]^+$, 77 (38) $[C_6H_5]^+$. $C_{18}H_{18}N_2O$ (278.35): calcd. C 77.67, H 6.52, N 10.06; found C 77.53, H 6.54, N 10.01.

X-ray Crystal Structure Analysis of 9a:[38] Formula $C_{18}H_{18}N_2O$, *M* = 278.34, yellow crystal, 0.60 × 0.10 × 0.03 mm, *a* = 31.410(3), *b* = 13.160(2), *c* = 7.287(1) Å, β = 92.34(1)°, *V* = 3009.6(7) Å^3, $\rho_{calcd.}$ = 1.229 g cm^{-3}, μ = 0.606 mm^{-1}, empirical absorption correction (0.713 ≤ *T* ≤ 0.982), *Z* = 8, monoclinic, space group *C*2/*c* (No. 15), λ = 1.54178 Å, *T* = 293 K, $\omega/2\theta$ scans, 3335 reflections collected (±*h*, +*k*, –*l*), [(sin θ)/λ] = 0.62 Å^{-1}, 3075 independent (R_{int} = 0.037) and 1768 observed reflections [$I \geq 2\sigma(I)$], 193 refined parameters, *R* = 0.047, wR_2 = 0.122, max. residual electron density 0.17 (–0.17) e Å^{-3}, hydrogen atoms calculated and refined as riding atoms.

4-(2-Methyl-2-phenylhydrazono)-1-(4-nitrophenyl)pent-1-ene-3-one (9b): *p*-Nitrobenzaldehyde (300 mg, 2.0 mmol) and 3-(2-methyl-2-phenylhydrazono)butan-2-one (**7**)[39] (380 mg, 2.0 mmol) were dissolved in methanol (4 mL) and cooled to 0 °C. After treatment with potassium *tert*-butoxide (224 mg, 2.0 mmol) the colour of the solution changed from intense yellow to deep red. A precipitate was formed after about 2 h. Stirring was continued for 8 h for complete reaction before the precipitate was filtered off and washed with cold methanol. Red solid, 0.49 g (1.5 mmol, 75.8%), m.p. 123–124 °C (decomp.). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.12 [s, 3 H, $H_3CC(N)$], 3.61 (s, 3 H, NCH_3), 7.09–7.14 (m, 1 H, $H_{N–Ph.}$), 7.23–7.26 (m, 2 H, $HN_{N–Ph.}$), 7.36–7.41 (m, 2 H, $H_{N–Ph.}$), 7.65–7.76 (m, 3 H, $H_{arom./olef.}$), 8.11 (d, ^3J = 16.0 Hz, 1 H, $H_{olef.}$), 8.22–8.25 (m, 2 H, $H_{arom.}$) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.7 [$CH_3C(N)$], 43.9 (NCH_3), 118.1 (*o*/*m*-$C_{arom.}$), 123.4 (*p*-$C_{arom.}$), 124.1 (*o*/*m*-$C_{arom.}$), 125.6 ($C_{olef.}$), 128.7 (*o*/*m*-$C_{arom.}$), 129.2 (*o*/*m*-$C_{arom.}$), 138.0 ($C_{olef.}$), 142.0, 147.3 (*ipso*-C), 148.2, 149.2 (*ipso*-$C_{aminearom.}$, C=N), 187.7 (C=O) ppm. IR (KBr): $\tilde{\nu}$ = 3063 (w, $CH_{arom.}$), 3032 (sh., $CH_{arom.}$), 2974 (s, $CH_{aliph.}$), 2940 (m, $CH_{aliph.}$), 2882 (sh., $CH_{aliph.}$), 1641 (vs, C=O), 1599 (s, C=C), 1579 (s, C=C), 1556 (s), 1494 (m), 1357 (s, $CH_{aliph.}$), 1305 (w), 1294 (m), 1255 (m), 1228 (s), 1110 (w), 1056 (w), 1002 (w), 881 (w), 840 (w), 831 (w), 784 (w), 744 (vs, $CH_{arom.}$), 705, 684 (vs, $CH_{arom.}$) cm^{-1}. MS (70 eV): *m*/*z* (%) = 323 (87) $[M]^+$, 254 (20), 217 (9), 176 (41), 130 (17), 113 (28), 106 (100) $[NPhCH_3]^+$, 102 (18), 77 (25), 57 (9). $C_{18}H_{17}N_3O_3$ (323.13): calcd. C 66.86, H 5.30, N 13.00; found C 66.65, H 5.20, N 12.94.

6-(2-Methyl-2-phenylhydrazono)-1-phenylhepta-1,3-dien-5-one (9c): 3-(2-Methyl-2-phenylhydrazono)butan-2-one (**7**) (3.6 g, 18.9 mmol) and cinnamaldehyde (2.4 mL, 2.5 g, 28.0 mmol) were dissolved in methanol (15 mL) at 0 °C. The solution was treated with a methanolic solution of potassium hydroxide (30%, 5 mL, 27.0 mmol) at room temperature and stirred for 4 h. The crude product was filtered off by using a glass filter funnel (D3) and washed several times with cold water. The crude product was recrystallized from cold ethyl acetate. Orange solid, 3.3 g (10.8 mmol, 57.1%), m.p. 95.5 °C (decomp.). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.10 [s, 3 H, $H_3CC(N)$], 3.51 (s, 3 H, NCH_3), 6.92–7.08 (m, 3 H, $H_{arom./olef.}$), 7.20–7.38 (m, 7 H, $H_{arom./olef.}$), 7.45–7.57 (m, 4 H, $H_{arom./olef.}$) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.8 [$H_3CC(N)$], 43.7 (NCH_3), 117.6 (*o*/*m*-$C_{arom.}$), 122.7 (*p*-$C_{arom.}$), 125.1 ($C_{olef.}$), 127.1 (*o*/*m*-$C_{arom.}$), 127.7 (*p*-$C_{arom.}$), 128.8 (3 C, *o*/*m*-$C_{arom.}$/$C_{olef.}$), 129.1 (*o*/*m*-$C_{arom.}$), 136.5 (*ipso*-$C_{arom.}$), 140.5 ($C_{olef.}$), 141.8 ($C_{olef.}$), 149.7 [2 C, *ipso*-$C_{arom.}$/(C=N)], 188.6 (C=O) ppm. IR (KBr): $\tilde{\nu}$ = 3061 (w, $CH_{arom.}$), 3030 (w, $CH_{arom.}$), 3011 (sh., $CH_{arom.}$), 2910 (s, $CH_{aliph.}$), 1641 (vs, C=O), 1599 (s, C=C), 1580 (s, C=C), 1557 (s), 1495 (m), 1358 (s, $CH_{aliph.}$), 1306 (w), 1296 (m), 1256 (m), 1222 (s), 1177 (w), 1111 (w), 1056 (w), 1005 (w), 883 (w), 841 (w), 831 (w), 785 (w), 745 (m, $CH_{arom.}$), 708 (m), 685 (m, $CH_{arom.}$) cm^{-1}. MS (70 eV): *m*/*z* (%) = 304 (68) $[M]^+$, 235 (100), 198 (9) $[M – NCH_3Ph]^+$, 157 (53) $[Ph(CH)_4CO]^+$, 128 (77), 113 (18), 106 (85) $[NPhCH_3]^+$, 77 (30), 57 (29). $C_{20}H_{20}N_2O$ (304.39): calcd. C 78.92, H 6.62, N 9.20; found C 78.79, H 6.50, N 9.17.

X-ray Crystal Structure Analysis of 9c:[38] Formula $C_{20}H_{20}N_2O$, *M* = 304.38, yellow crystal, 0.60 × 0.20 × 0.15 mm, *a* = 6.236(1), *b* = 8.618(1), *c* = 15.923(1) Å, α = 83.95(1), β = 84.48(1), γ = 82.09(1)°, *V* = 840.0(2) Å^3, $\rho_{calcd.}$ = 1.203 g cm^{-3}, μ = 0.586 mm^{-1}, empirical absorption correction (0.720 ≤ *T* ≤ 0.917), *Z* = 2, triclinic, space group $P\bar{1}$ (No. 2), λ = 1.54178 Å, *T* = 223 K, $\omega/2\theta$ scans, 3748 reflections collected (+*h*, ±*k*, ±*l*), [(sin θ)/λ] = 0.62 Å^{-1}, 3418 independent (R_{int} = 0.015) and 3018 observed reflections [$I \geq 2\sigma(I)$], 211 refined parameters, *R* = 0.044, wR_2 = 0.138, max. residual electron density 0.23 (–0.15) *e* Å^{-3}, hydrogen atoms calculated and refined as riding atoms.

4-(Benzyloxyimino)-1-phenylpent-1-en-3-one (10a): 3-(Benzyloxyimino)butan-2-one (**8a**)[41] (7.5 g, 39.2 mmol) and benzaldehyde (7.4 mL, 7.8 g, 73.5 mmol) were treated with a methanolic sodium hydroxide solution (10%, 15 mL, 38.0 mmol) at 0 °C. A colourless precipitate was formed. The solution was stirred for 2 h for complete reaction before the precipitate was filtered off by using a glass filter funnel. This crude product was recrystallized from methanol twice. Colourless solid, 7.6 g (27.2 mmol, 69.7%), m.p. 80.0 °C (80 °C[12]). R_t (GC): 20.47 min [40–10/min–280(5)]. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.06 [s, 3 H, $H_3CC(N)$], 5.34 (s, 2 H, OCH_2), 7.33–7.43 (m, 8 H, $H_{arom./olef.}$), 7.56–7.75 (m, 4 H, $H_{arom./olef.}$) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 9.3 [$CH_3C(N)$], 77.6 (OCH_2), 120.8 ($C_{olef.}$), 128.2 ($C_{arom.}$), 128.3 ($C_{arom.}$), 128.5 ($C_{arom.}$), 128.8 ($C_{arom.}$), 130.3 ($C_{arom.}$), 135.1 (*ipso*-C), 137.0 (*ipso*-C), 143.1 (Ph-$CH_{olef.}$), 156.4 (C=N), 186.7 (C=O) ppm. IR (KBr):

$\tilde{\nu}$ = 3082 (w), 3065 (w), 3026 (m, $CH_{arom.}$), 2974 (w), 2945 (m, $CH_{aliph.}$), 2887, 1666 (vs, C=O), 1608 (br.), 1574 (sh.), 1495 (m), 1450 (m), 1344 (s, $CH_{aliph.}$), 1204 (w), 1069 (s), 1016 (vs), 984 (s), 953 (m), 893 (m), 867 (w), 759 (s, $CH_{arom.}$), 709 (s, $CH_{arom.}$), 678 (m) cm^{-1}. MS (70 eV): *m*/*z* (%) = 279 (48) $[M]^+$, 131 (30) $[Ph(CH)_2CO]^+$, 103 (33) $[Ph(CH_2)]^+$, 91 (100), 77 (32), 51 (8) cm^{-1}. MS (ESI, $CHCl_3/CH_3OH$ with $LiClO_4$ present): *m*/*z* (%) = 286.2 (100) $[M + Li]^+$, 302.2 (55) $[M + Na]^+$, 318.2 (8) $[M + K]^+$, 565.4 (42) $[M_2 + Li]^+$, 581.4 (17) $[M_2 + Na]^+$, 844.6 (9) $[M_3 + Li]^+$. $C_{18}H_{17}NO_2$ (279.33): calcd. C 77.40, H 6.13, N 5.01; found C 77.33, H 6.13, N 4.90.

X-ray Crystal Structure Analysis of 10a:[38] Formula $C_{18}H_{17}NO_2$, M = 279.33, light yellow crystal, 0.60 × 0.50 × 0.15 mm, a = 23.681(2), b = 7.754(1), c = 17.056(2) Å, β = 106.31(1)°, V = 3005.8(6) $Å^3$, $\rho_{calcd.}$ = 1.234 $g\,cm^{-3}$, μ = 0.642 mm^{-1}, empirical absorption correction ($0.700 \leq T \leq 0.910$), Z = 8, monoclinic, space group *C*2/*c* (No. 15), λ = 1.54178 Å, T = 223 K, $\omega/2\theta$ scans, 6120 reflections collected ($\pm h$, $\pm k$, $+l$), $[(\sin\theta)/\lambda]$ = 0.62 $Å^{-1}$, 3074 independent (R_{int} = 0.032) and 2784 observed reflections [$I \geq 2\sigma(I)$], 192 refined parameters, R = 0.041, wR_2 = 0.125, max. residual electron density 0.23 (–0.16) $e\,Å^{-3}$, hydrogen atoms calculated and refined as riding atoms.

4-(Benzyloxyimino)-1-(*p*-tolyl)pent-1-en-3-one (10b): 3-(Benzyloxyimino)butan-2-one (**8a**)[41] (5.3 g, 27.7 mmol) and *p*-tolualdehyde (3.3 mL, 3.4 g, 28.3 mmol) were treated with a methanolic solution of potassium hydroxide (6 mL, 30%, 32 mmol) at 0 °C. A solid was formed after about 5 min. The mixture was stirred for 1 h at room temperature for complete reaction. The solid was then filtered off and washed with water until neutral. The crude product was recrystallized from methanol. Colourless solid, 6.9 g (23.5 mmol, 83.9%), m.p. 62.4 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.06 [s, 3 H, $H_3CC(N)$], 2.36 (s, 3 H, *p*-CH_3), 5.33 (s, 2 H, OCH_2), 7.17–7.20 (m, 2 H, $H_{arom./olef.}$), 7.32–7.42 (m, 5 H, $H_{arom.}$), 7.43–7.47 (m, 2 H, $H_{arom./olef.}$), 7.55–7.72 (m, ^3J = 16.2 Hz, 2 H, $H_{arom./olef.}$) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 9.34 [*C*H_3C(N)], 21.47 (*p*-Ph-CH_3), 77.54 (OCH_2), 119.79 ($C_{olef.}$), 128.17 (*p*-$C_{arom.}$), 128.28 (*o*/*m*-$C_{arom.}$), 128.49–128.50 (4 C, *o*/*m*-$C_{arom.}$), 129.56 (*o*/*m*-$C_{arom.}$), 132.36 (*ipso*-C), 137.00 (*ipso*-C), 140.75 (*ipso*-C), 143.17 ($C_{olef.}$), 156.38 (C=N), 186.70 (C=O) ppm. IR (KBr): $\tilde{\nu}$ = 3063 (w, $CH_{arom.}$), 3026 (w, $CH_{arom.}$), 2957 (m, $CH_{aliph.}$), 2920 (m, $CH_{aliph.}$), 2887 (m), 1659 (s, C=O), 1595 (vs), 1568 (sh.), 1510 (m), 1454 (w), 1410 (w), 1362 (m), 1340 (s, $CH_{aliph.}$), 1177 (w), 1070 (s), 1020 (vs), 984 (s), 962 (s), 897 (m), 810 (s), 750 (s), 698 (s, $CH_{arom.}$), 613 (m) cm^{-1}. MS (70 eV): *m*/*z* (%) = 293 (34) $[M]^+$, 145 (27) $[C_{10}H_9O]^+$, 117 (16) $[C_9H_9]^+$, 91 (100) $[C_7H_7]^+$. $C_{19}H_{19}NO_2$ (293.14): calcd. C 77.79, H 6.53, N 4.77; found C 77.75, H 6.50, N 4.63.

2-(Benzyloxyimino)-5-(2-bromophenyl)pent-4-en-3-one (10c): 3-(Benzyloxyimino)butan-2-one (**8a**)[41] (3.8 g, 19.9 mmol) and 2-bromobenzaldehyde (4.0 g, 21.6 mmol) were treated with a methanolic solution of potassium hydroxide (20 mmol, 4.0 mL, 30%) at 0 °C. The product was immediately formed after addition of the base. The solid was filtered off and washed with water until neutral. The crude product was recrystallized twice from methanol. Colourless solid, 6.0 g (16.7 mmol, 83.7%), m.p. 114.4 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.1 [s, 3 H, $H_3CC(N)$], 5.3 (s, 2 H, OCH_2), 7.2–7.4 (m, 7 H, $H_{arom./olef.}$), 7.5–7.7 (m, 3 H, $H_{arom./olef.}$), 8.1 (d, ^3J = 16 Hz, 1 H, $H_{olef.}$) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 9.3 [*C*H_3C(N)], 77.7 (OCH_2), 123.4 ($C_{olef.}$), 125.9 (*ipso*-C-Br), 127.5 ($C_{arom.}$), 127.9 ($C_{arom.}$), 128.2 (3 C, *o*/*m*-$C_{arom.}$, $C_{arom.}$), 128.5 (*o*/*m*-$C_{arom.}$), 131.1 ($C_{arom.}$), 133.4 ($C_{arom.}$), 135.1 (*ipso*-C), 136.8 (*ipso*-C), 141.3 ($C_{olef.}$), 156.3 (C=N), 186.3 (C=O) ppm. IR (KBr): $\tilde{\nu}$ = 3063 (w, $CH_{arom.}$), 3036 (w, $CH_{arom.}$), 2964 (m, $CH_{aliph.}$), 2947 (m, $CH_{aliph.}$), 2887 (m), 1665 (s, C=O), 1603 (vs), 1468 (m), 1439 (w), 1362 (w), 1337 (s, $CH_{aliph.}$), 1283 (w), 1072 (s), 1009 (vs), 982 (s), 959 (m), 895 (m), 752 (s), 712 (s, $CH_{arom.}$), 700 (m, $CH_{arom.}$) cm^{-1}. MS (70 eV): *m*/*z* (%) = 357 (9) $[M]^+$, 102 (9), 91 (100) $[C_8H_7]^+$. $C_{18}H_{16}BrNO_2$ (357.04): calcd. C 60.35, H 4.50, N 3.91; found C 60.28, H 4.41, N 3.75.

2-(Benzyloxyimino)-5-(4-nitrophenyl)pent-4-en-3-one (10d): 3-(Benzyloxyimino)butan-2-one (**8a**)[41] (3.0 g, 15.7 mmol) and 4-nitrobenzaldehyde (2.4 g, 15.9 mmol) were treated with a methanolic solution of potassium hydroxide (3.6 mL, 30%, 19.2 mmol) at 0 °C. After addition of the base the aldehyde completely dissolved. A yellow precipitate was formed from the dark solution after about 12 h. The solid was filtered off and washed with water until neutral. The crude product was refluxed with boiling methanol to remove impurities. Filtration gave a yellow solid, 3.5 g (10.8 mmol, 68.7%), m.p. 131 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.1 [s, 3 H, $H_3CC(N)$], 5.4 (s, 2 H, OCH_2), 7.2–7.8 (m, 9 H, $H_{arom./olef.}$), 8.21–8.22 (m, 2 H, $H_{nitroarom.}$) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 9.3 [*C*H_3C(N)], 77.8 (OCH_2), 124.1 (*o*/*m*-$C_{arom.}$), 124.6 ($C_{olef.}$), 128.3 (*o*/*m*-$C_{arom.}$), 128.3 (*p*-$C_{arom.}$), 128.5 (*o*/*m*-$C_{arom.}$), 128.9 (*o*/*m*-$C_{arom.}$), 136.8 (*ipso*-C), 139.7 ($C_{olef.}$), 141.2 (*ipso*-C), 148.5 (*ipso*-C), 156.3 (C=N), 186.1 (C=O) ppm. IR (KBr): $\tilde{\nu}$ = 3458 (br.), 3111 (m), 3076 (m), 3034 (w, $CH_{arom.}$), 2972 (w), 2937 (m, $CH_{aliph.}$), 1668 (s, C=O), 1614 (s), 1597 (sh.), 1512 (vs), 1340 (vs, $CH_{aliph.}$), 1109 (w), 1069 (s), 997 (br.), 885 (w), 841 (m), 799 (w), 756 (m), 721 (m), 700 (m, $CH_{arom.}$) cm^{-1}. MS (70 eV): *m*/*z* (%) = 324 (11) $[M]^+$, 176 (7) $[C_9H_6NO_3]^+$, 102 (9), 91 (100) $[C_7H_7]^+$. $C_{18}H_{16}N_2O_4$ (324.11): calcd. C 66.66, H 4.97, N 8.64; found C 66.38, H 4.90, N 8.58.

2-(Benzyloxyimino)-7-phenylhepta-4,6-dien-3-one (10e): 3-(Benzyloxyimino)butan-2-one (**8a**)[41] (5.3 g, 27.7 mmol) and cinnamaldehyde (5.6 mL, 5.9 g, 44.5 mmol) were treated with a methanolic solution of potassium hydroxide (53.5 mmol, 10 mL, 30%) at 0 °C. A yellow precipitate was formed after about 5 min. For complete reaction the mixture was stirred for 1 h at room temperature. The solid was filtered off and washed with water until neutral. The crude product was recrystallized from methanol. Yellow solid, 4.6 g (15.1 mmol, 53.8%), m.p. 90.8 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.04 [s, 3 H, $H_3CC(N)$], 5.31 (s, 2 H, OCH_2), 6.92–7.52 (m, 14 H, $H_{arom./olef.}$) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 9.27 [*C*H_3C(N)], 77.45 (OCH_2), 124.26 ($C_{olef.}$), 127.19 (4 C, *o*/*m*-$C_{arom.}$), 128.15 (*o*/*m*-$C_{arom.}$), 128.47 (2 C, *p*-$C_{arom.}$), 128.74 (*o*/*m*-$C_{arom.}$), 129.01 ($C_{olef.}$) ppm. IR (KBr): $\tilde{\nu}$ = 3022 (w, $CH_{arom.}$), 2931 (m, $CH_{aliph.}$), 1663 (vs, C=O), 1587 (s), 1495 (m), 1448 (w), 1439 (w), 1354 (s, $CH_{aliph.}$), 1306 (w), 1207 (m), 1067 (s), 1015 (vs), 986 (s), 883 (w), 849 (m), 745 (m, $CH_{arom.}$) 696 (m, $CH_{arom.}$) cm^{-1}. MS (70 eV): *m*/*z* (%) = 305 (9) $[M]^+$, 214 (9), 157 (19), 128 (31) $[C_{10}H_8]^+$, 91 (100) $[C_7H_7]^+$, 57 (10). MS (ESI, $CHCl_3/CH_3OH$): *m*/*z* (%) = 328.3 (100) $[M + Na]^+$. $C_{20}H_{19}NO_2$ (305.37): calcd. C 78.66, H 6.27, N 4.59; found C 78.64, H 6.09, N 4.53.

General Procedure for the Preparation of Compounds 10f–10o: 3-Methoxyiminobutan-2-one (**8b**)[33] (2.4 g, 20.8 mmol) was dissolved in ethanol (5 mL), treated dropwise with an aqueous solution of potassium hydroxide (10%, 15 mL, 25 mmol) and stirred vigorously at about –10 °C. The aldehyde (20.8 mmol) was dissolved in methanol (5 to max. 20 mL, depending on its solubility) and added dropwise to the enolate at –10 °C. The ice bath was removed and after about 2–4 h a precipitate started to form. If not, the usual ways to initiate a crystallization were used (addition of a piece of potassium hydroxide as a seed crystal; rubbing against the wall of the flask, ultrasonification). For complete reaction the mixture was stirred for 12 h until the reaction mixture became solid. The solid

was filtered off (glass filter funnel D3 or D4) and washed with a small amount of methanol. The product was recrystallized from ethyl acetate or methanol. In other cases the product was dried in vacuo and purified by Kugelrohr distillation.

4-Methoxyimino-1-phenylpent-1-en-3-one (10f): From 3-methoxyiminobutan-2-one (**8b**)[33] (2.4 g, 20.8 mmol) and benzaldehyde (2.1 mL, 2.2 g, 20.7 mmol). Colourless solid, 3.6 g (17.7 mmol, 84.3%), m.p. 83.5 °C (82 °C[29]). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.03 [s, 3 H, $H_3CC(N)$], 4.11 (s, 3 H, OCH_3), 7.35–7.41 (m, 3 H, $H_{arom./olef.}$), 7.60–7.75 (m, 4 H, $H_{arom./olef.}$) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 8.95 [$CH_3C(N)$], 63.17 (OCH_3), 120.64 ($C_{olef.}$), 128.51 (*o*/*m*-$C_{arom.}$), 128.80 (*o*/*m*-$C_{arom.}$), 130.27 (*p*-$C_{arom.}$), 135.10 (*ipso*-C), 143.01 ($C_{olef.}$), 156.02 (C=N), 186.62 (C=O) ppm. IR (KBr): $\tilde{\nu}$ = 3442 (br.), 3321 (w), 3082 (w, $CH_{arom.}$), 3061 (w), 3001 (m, $CH_{arom.}$), 2945 (m, $CH_{aliph.}$), 2824 (m), 1665 (s, C=O), 1607 (vs), 1574 (m), 1495 (w), 1448 (m), 1339 (s, $CH_{aliph.}$), 1200 (m), 1070 (s), 1043 (vs), 984 (s), 932 (m), 887 (m), 862 (m), 764 (s), 706 (s, $CH_{arom.}$), 681 (m, $CH_{arom.}$) cm^{-1}. MS (ESI, MicroTOF): calcd. 226.0838 [M + Na]$^+$; found 226.0843 [M + Na]$^+$. $C_{12}H_{13}NO_2$ (203.09): calcd. C 70.92, H 6.45, N 6.89; found C 70.68, H 6.40, N 6.80.

4-Methoxyimino-1-(*p*-tolyl)pent-1-en-3-one (10g): From 3-methoxyiminobutan-2-one (**8b**)[33] (2.4 g, 20.8 mmol) and *p*-tolualdehyde (2.5 mL, 2.5 g, 20.8 mmol). Colourless solid, 3.1 g (15.3 mmol, 72.6%), m.p. 71 °C, b.p. 120 °C (0.001 mbar). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.02 [s, 3 H, $H_3CC(N)$], 2.37 (s, 3 H, H_3C-Ph), 4.11 (s, 3 H, OCH_3), 7.18–7.20 (m, 2 H, $H_{arom.}$), 7.51–7.53 (m, 2 H, $H_{arom.}$), 7.71 (d, ^3J = 16 Hz, 1 H, $H_{olef.}$), 7.62 (d, ^3J = 16 Hz, 1 H, $H_{olef.}$) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 9.00 [$CH_3C(N)$], 21.47 (H_3C-Ph), 63.15 (OCH_3), 119.63 ($C_{olef.}$), 128.55 (*o*/*m*-$C_{arom.}$), 129.55 (*o*/*m*-$C_{arom.}$), 132.38 (*ipso*-C), 140.76 (*ipso*-C), 143.12 ($C_{olef.}$), 156.04 (C=N), 186.68 (C=O) ppm. IR (KBr): $\tilde{\nu}$ = 3017 (w, $CH_{arom.}$), 2986 (m, $CH_{aliph.}$), 2945 (s, $CH_{aliph.}$), 2905 (sh., $CH_{aliph.}$), 1665 (vs, C=O), 1603 (s), 1568 (s, C=C), 1510 (m), 1463 (m), 1410 (w), 1337 (s, $CH_{aliph.}$), 1178 (m), 1057 (s), 1036 (vs), 986 (s), 935 (m), 889 (m), 816 (s), 762 (m, $CH_{arom.}$), 698 (m, $CH_{arom.}$), 676 (w, sh.) cm^{-1}. MS (70 eV): *m*/*z* (%) = 217 (64) [M]$^+$, 186 (17) [M – OCH_3]$^+$, 158 (51), 145 (100) [$C_{10}H_9O$]$^+$, 117 (52) [C_9H_9]$^+$, 115 (20), 91 (20) [C_7H_7]$^+$. $C_{13}H_{15}NO_2$ (217.26): calcd. C 71.87, H 6.96, N 6.45; found C 71.77, H 6.84, N 6.40.

1-(2-Bromophenyl)-4-methoxyiminopent-1-en-3-one (10h): From 3-methoxyiminobutan-2-one (**8b**)[33] (2.3 g, 20.0 mmol) and 2-bromobenzaldehyde (2.3 mL, 3.7 g, 20.0 mmol). Colourless solid, 4.4 g (15.6 mmol, 78.0%), m.p. 70–72 °C, b.p. 138–140 °C (0.004 mbar). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.03 [s, 3 H, $H_3CC(N)$], 4.11 (s, 3 H, OCH_3), 7.18–7.35 (m, 2 H, $H_{arom.}$), 7.55–7.62 (m, 2 H, $H_{arom./olef.}$), 7.69–7.73 (m, 1 H, $H_{arom./olef.}$), 8.08 (d, ^3J = 16 Hz, 1 H, $H_{olef.}$) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 9.0 [$CH_3C(N)$], 63.3 (OCH_3), 123.4 ($C_{olef.}$), 126.0 (C-Br), 127.5 ($C_{arom.}$), 127.9 ($C_{arom.}$), 131.1 ($C_{arom.}$), 133.4 ($C_{arom.}$), 135.2 (*ipso*-C-C), 141.4 ($C_{olef.}$), 156.0 (C=N), 186.2 (C=O) ppm. IR (KBr): $\tilde{\nu}$ = 3096 (w, $CH_{arom.}$), 3071 (w, $CH_{arom.}$), 2984 (m, $CH_{aliph.}$), 2937 (s, $CH_{aliph.}$), 2818 (w, $CH_{aliph.}$), 1967 (w), 1935 (w), 1668 (vs, C=O), 1601 (s), 1585 (s, sh.), 1560 (m, C=C), 1510 (m), 1462 (m), 1410 (w), 1366 (s, $CH_{aliph.}$), 1335 (s), 1279 (w), 1200 (m), 1153 (m), 1070 (s), 1042 (vs), 980 (s), 928 (m), 881 (m), 858 (w, sh.), 762 (m, $CH_{arom.}$), 717 (m, $CH_{arom.}$), 657 (w) cm^{-1}. MS (70 eV): *m*/*z* (%) = 281 (37) [M]$^+$, 222 (18), 202 (71), 181 (37), 143 (12), 127 (17), 102 (100) [C_8H_6]$^+$, 75 (13), 57 (11). $C_{12}H_{12}BrNO_2$ (282.13): calcd. C 51.09, H 4.29, N 4.96; found C 51.12, H 4.08, N 4.81.

1-(4-Chlorophenyl)-4-methoxyiminopent-1-en-3-one (10i): From 3-methoxyiminobutan-2-one (**8b**)[33] (2.3 g, 20.0 mmol) and *p*-chlorobenzaldehyde (2.8 g, 19.9 mmol). Colourless solid, 4.5 g (18.9 mmol, 94.7%), m.p. 109.4 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.02 [s, 3 H, $H_3CC(N)$], 4.12 (s, 3 H, OCH_3), 7.35–7.37 (m, 2 H, $H_{arom./olef.}$), 7.53–7.55 (m, 2 H, $H_{arom./olef.}$), 7.64–7.65 (m, 2 H, $H_{arom./olef.}$) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 8.95 [$CH_3C(N)$], 63.24 (OCH_3), 121.06 ($C_{olef.}$), 129.07 (*o*/*m*-$C_{arom.}$), 129.63 (*o*/*m*-$C_{arom.}$), 133.57 (*ipso*-C), 136.15 (*ipso*-C), 141.43 ($C_{olef.}$), 155.97 (C=N), 186.36 (C=O) ppm. IR (KBr): $\tilde{\nu}$ = 3443 (br.), 3323 (w), 3260 (w), 3032 (w, $CH_{arom.}$), 2978 (w, $CH_{aliph.}$), 2938 (m, $CH_{aliph.}$), 2822 (m), 1666 (s, C=O), 1605 (vs), 1562 (w), 1489 (w), 1404 (w), 1335 (s, $CH_{aliph.}$), 1050 (vs, br.), 1005 (s), 939 (w), 889 (m), 808 (m), 725 (m, $CH_{arom.}$) cm^{-1}. MS (70 eV): *m*/*z* (%) = 237 (58) [M]$^+$, 206 (11) [M – OCH_3]$^+$, 178 (65), 165 (100) [C_9H_6ClO]$^+$, 137 (61) [C_8H_6Cl]$^+$, 127 (17), 102 (46) [C_8H_6]$^+$, 75 (11). $C_{12}H_{12}ClNO_2$ (237.68): calcd. C 60.64, H 5.09, N 5.89; found C 60.61, H 4.91, N 5.82.

1-(4-Nitrophenyl)-4-methoxyiminopent-1-en-3-one (10j): From 3-methoxyiminobutan-2-one (**8b**)[33] (2.3 g, 20.0 mmol) and 4-nitrobenzaldehyde (3.0 g, 19.9 mmol). Yellow solid, 4.2 g (16.9 mmol, 84.5%), m.p. 174.5 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.95 [s, 3 H, $H_3CC(N)$], 4.06 (s, 3 H, OCH_3), 7.58–7.73 (m, 4 H, $H_{arom./olef.}$), 8.15–8.18 (m, 2 H, $H_{arom./olef.}$) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 8.9 [$CH_3C(N)$], 63.4 (OCH_3), 124.0 (*o*/*m*-$C_{arom.}$), 124.4 ($C_{olef.}$), 129.0 (*o*/*m*-$C_{arom.}$), 139.6 ($C_{olef.}$), 141.2 (*ipso*-C), 148.4 (*ipso*-C), 156.0 (C=N), 186.0 (C=O) ppm. IR (KBr): $\tilde{\nu}$ = 3113 (w), 3069 (w, $CH_{arom.}$), 2990 (w, $CH_{aliph.}$), 2945 (m, $CH_{aliph.}$), 2899 (w), 2843 (w), 2816 (w), 1670 (vs, $C{=}O_{ketone}$), 1616 (s, $C{=}C_{olef.}$), 1597 (s, C=C), 1520 (vs, C=C), 1493 (sh.), 1412 (m, $CH_{aliph.}$), 1342 (vs, br., CH), 1070 (m), 1042 (s), 986 (m), 893 (m), 843 (w), 843 (m), 802 (w), 756 (w, $CH_{arom.}$), 712 (w) cm^{-1}. MS (70 eV): *m*/*z* (%) = 248 (73) [M]$^+$, 189 (69), 176 (100) [$C_9H_6NO_3$]$^+$, 143 (18), 130 (56), 102 (64), 90 (26), 76 (20). $C_{12}H_{12}N_2O_4$ (248.23): calcd. C 58.06, H 4.87, N 11.29; found C 58.11, H 4.81, N 11.29.

2-Methoxyimino-7-(4-methoxyphenyl)hepta-4,6-dien-3-one (10k): From 3-methoxyiminobutan-2-one (**8b**)[33] (2.3 g, 20.0 mmol) and 4-methoxycinnamaldehyde (3.2 g, 19.7 mmol). After about 20 min a solid precipitated from the yellow solution. The solid was recrystallized from methanol twice. Intensely yellow solid, 3.1 g (12.0 mmol; 60.2%), m.p. 139–141 °C, b.p. 185 °C (0.036 mbar). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.0 [s, 3 H, $H_3CC(N)$], 3.8 (s, 3 H, Ph-OCH_3), 4.1 (s, 3 H, $NOCH_3$), 6.8–7.0 (m, 4 H, $H_{arom./olef.}$), 7.1–7.3 (m, 1 H, $H_{arom./olef.}$), 7.4–7.5 (m, 3 H, $H_{arom./olef.}$) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 8.9 [$CH_3C(N)$], 55.3 (Ph-OCH_3), 63.0 ($NOCH_3$), 114.3 (2 C, $HC_{arom.}$-$COCH_3$), 123.0 ($C_{olef.}$), 125.1 ($C_{olef.}$), 128.7 (2 C, $C_{arom.}$), 129.1 ($C_{q,arom.}$), 141.4 ($C_{olef.}$), 143.6 ($C_{olef.}$), 156.0 (C=N), 160.5 ($C_{q,C\text{-}OMe}$), 186.7 (C=O) ppm. IR (KBr): $\tilde{\nu}$ = 2999 (w, $CH_{arom.}$), 2963 (w, $CH_{aliph.}$), 2936 (m, $CH_{aliph.}$), 2837 (w), 2814 (w), 1657 (m, C=O), 1580 (vs), 1510 (m), 1358 (m), 1250 (s, $CH_{aliph.}$), 1171 (m), 1065 (sh.), 1047 (vs), 1028 (m), 1013 (m), 932 (w), 847 (s), 721 (w) cm^{-1}. MS (70 eV): *m*/*z* (%) = 259 (100) [M]$^+$, 228 (50) [M – OMe]$^+$, 200 (48), 187 (64) [$C_{12}H_{11}O_2$]$^+$, 159 (33) [$C_{11}H_{11}O$]$^+$, 144 (37), 127 (33), 105 (26). $C_{15}H_{17}NO_3$ (259.27): calcd. C 69.48, H 6.61, N 5.40; found C 69.34, H 6.38, N 5.16.

4-Methoxy-1-(2-pyridyl)iminopent-1-en-3-one (10l): From 3-methoxyiminobutan-2-one (**8b**)[33] (2.0 g, 17.4 mmol) and pyridine-2-carbaldehyde (1.7 mL, 1.9 g, 17.0 mmol) by using ethanol as solvent. Yellow solid, 1.4 g (6.9 mmol, 40.3%), m.p. 102–104 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.03 [s, 3 H, $H_3CC(N)$], 4.12 (s, 3 H, H_3CO), 7.22–7.29 (m, 1 H, $H_{arom.}$), 7.47–7.50 (m, 1 H, $H_{arom.}$), 7.68–7.74 (m, 1 H, $H_{arom.}$), 7.70 (d, ^3J = 15.7 Hz, 1 H, $H_{olef.}$), 8.10 (d, ^3J = 15.7 Hz, 1 H, $H_{olef.}$), 8.66–8.69 (m, 1 H, $H_{arom.}$) ppm. ^{13}C

NMR (75 MHz, $CDCl_3$): δ = 8.9 [$H_3CC(N)$], 63.3 (OCH_3), 124.1 ($C_{arom.}$), 124.4 ($C_{arom.}$), 124.8 ($C_{olef.}$), 136.6 ($C_{arom.}$), 141.4 ($C_{arom.}$), 150.1 ($C_{olef.}$), 153.5 (C=N), 155.8 (C=N), 186.9 (C=O) ppm. IR (KBr): $\tilde{\nu}$ = 3059 (w), 3003 (w, CH), 2941 (m, $CH_{aliph.}$), 2905 (w, sh.), 1693 (vs, $C{=}O_{ketone}$), 1678 (sh.), 1591 (m, $C{=}C_{olef.}$), 1566 (w), 1475 (m), 1435 (m, $CH_{aliph.}$), 1362 (w), 1340 (w, CH), 1315 (w), 1070 (sh.), 1045 (vs), 899 (m), 849 (w), 789 (w), 748 (w) cm^{-1}. MS (ESI, $CH_3OH/CHCl_3$): *m*/*z* (%) = 205 (100) $[M + H]^+$. $C_{11}H_{12}N_2O_2$ (204.09): calcd. C 64.69, H 5.92, N 13.72; found C 64.52, H 5.91, N 13.65.

4-Methoxyimino-1-(3-thienyl)pent-1-en-3-one (10m): From 3-methoxyiminobutan-2-one (**8b**)[33] (2.3 g, 20.0 mmol) and thiophene-3-carbaldehyde (1.8 mL, 2.2 g, 19.6 mmol). The solid was recrystallized from methanol. Pale yellow solid, 3.6 g (17.2 mmol; 86.0%), m.p. 139.5 °C, b.p. 122 °C (0.024 mbar). ^1H NMR (300 MHz, $CDCl_3$): δ = 2.02 [s, 3 H, $H_3CC(N)$], 4.10 (s, 3 H, OCH_3), 7.33 (dd, J = 2.9 Hz, J = 5.1 Hz, 1 H, $H_{thiophene}$), 7.39 (dd, J = 1.2 Hz, J = 5.1 Hz, 1 H, $H_{thiophene}$), 7.56–7.57 (m, 1 H, $H_{thiophene}$), 7.47 (d, ^3J = 15.9 Hz, 1 H, $H_{olef.}$), 7.71 (d, ^3J = 15.9 Hz, 1 H, $H_{olef.}$) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 9.0 [$H_3CC(N)$], 63.1 (OCH_3), 120.4 ($C_{thiophene}$), 125.6 ($C_{thiophene}$), 126.7 ($C_{olef.}$), 128.7 ($C_{thiophene}$), 136.4 ($C_{olef.}$), 138.4 (*ipso*-$C_{thiophene}$), 156.0 (C=N), 186.8 (C=O) ppm. IR (KBr): $\tilde{\nu}$ = 3094 (m, CH), 3015 (w, CH), 2980 (w, $CH_{aliph.}$), 2936 (m, $CH_{aliph.}$), 2816 (w, $CH_{aliph.}$), 1665 (vs, $C{=}O_{ketone}$), 1593 (s, $C{=}C_{olef.}$), 1514 (m, C=C), 1437 (w, $CH_{aliph.}$), 1329 (m, CH), 1292 (w), 1246 (m), 1067 (s), 1051 (vs), 1003 (m), 934 (m), 872 (m), 822 (m), 802 (s), 777 (w), 662 (m, C–H), 606 (m), 588 (m), 530 (w) cm^{-1}. MS (70 eV): *m*/*z* (%) = 209 (100) $[M]^+$, 178 (20) $[M - OCH_3]^+$, 150 (48), 137 (96) $[C_7H_5OS]^+$, 109 (69) $[C_6H_5S]^+$, 65 (38). $C_{10}H_{11}NO_2S$ (209.26): calcd. C 57.39, H 5.30, N 6.69; found C 57.31, H 5.16, N 6.63.

1-(3-Bromo-2-thienyl)-4-methoxyiminopent-1-en-3-one (10n): From 3-methoxyiminobutan-2-one (**8b**)[33] (1.6 g, 13.9 mmol) and 3-bromothiophene-2-carbaldehyde[42] (3.2 g, 16.6 mmol). Yellow solid, 3.3 g (11.5 mmol, 82.4%), m.p. 123.5 °C, b.p. 165 °C (0.006 mbar). ^1H NMR (400 MHz, $CDCl_3$): δ = 2.02 [s, 3 H, $H_3CC(N)$], 4.12 (s, 3 H, OCH_3), 7.04 (d, ^3J = 5.3 Hz, 1 H, $H_{thiophene}$), 7.34 (dd, J = 0.7 Hz, J = 5.3 Hz, 1 H, $H_{thiophene}$), 7.48 (d, ^3J = 15.8 Hz, 1 H, $H_{olef.}$), 7.89 (dd, ^3J = 15.8, J = 0.9 Hz, 1 H, $H_{olef.}$) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 8.98 [$H_3CC(N)$], 63.27 (OCH_3), 116.93 (C-Br), 121.31 ($C_{thiophene}$), 127.71 ($C_{olef.}$), 131.59 ($C_{thiophene}$), 133.40 ($C_{olef.}$), 135.26 (*ipso*-$C_{thiophene}$), 155.83 (C=N), 185.98 (C=O) ppm. IR (KBr): $\tilde{\nu}$ = 3445 (br.), 3101 (w), 3084 (m, $CH_{arom.}$), 2982 (w), 2939 (w, $CH_{aliph.}$), 2828 (w), 1659 (m, C=O), 1585 (br., vs), 1423 (m), 1362 (w), 1325 (s, $CH_{aliph.}$), 1240 (w), 1159 (w), 1068 (sh.), 1040 (vs), 968 (m), 932 (m), 883 (w), 851 (m), 739 (m), 710 (m), 692 (m) cm^{-1}. MS (70 eV): *m*/*z* (%) = 287 (16) $[M]^+$, 256 (12) $[M - OMe]^+$, 215 (62) $[C_7H_4BrOS]^+$, 208 (100) $[M - Br]^+$, 187 (28), 159 (33) $[C_{11}H_{11}O]^+$, 136 (27) $[C_7H_4OS]^+$, 108 (87) $[C_6H_4S]^+$, 63 (19). $C_{10}H_{10}BrNO_2S$ (288.16): calcd. C 41.68, H 3.50, N 4.86; found C 41.62, H 3.26, N 4.76.

4-Methoxyimino-1-(1*H*-pyrrol-2-yl)pent-1-en-3-one (10o): From 3-methoxyiminobutan-2-one (**8b**)[33] (2.4 g, 20.8 mmol) and pyrrole-2-carbaldehyde (2.0 g, 21.0 mmol) dissolved in methanol (20 mL). The colour of the solution turned red. The crude solid was recrystallized from methanol. Yellow solid, 1.9 g (9.9 mmol, 47.1%), m.p. 48.5 °C, b.p. 134 °C (0.003 mbar). ^1H NMR (300 MHz, $CDCl_3$): δ = 2.0 [s, 3 H, $H_3CC(N)$], 4.1 (s, 3 H, OCH_3), 6.3 (br. m, 1 H, $CH_{pyrrole}$), 6.7 (m, 1 H, $CH_{pyrrole}$), 6.9 (m, 1 H, $CH_{pyrrole}$), 7.2 (d, ^3J = 15.9 Hz, 1 H, $H_{olef.}$), 7,7 (d, ^3J = 15.9 Hz, $H_{olef.}$), 9.0 (br., 1 H, NH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 9.1 [$H_3CC(N)$], 63.0 (OCH_3), 111.3 ($C_{pyrrole}$), 114.1 ($C_{pyrrole}$), 115.6 ($C_{pyrrole}$), 122.9 ($C_{olef.}$), 129.5 (*ipso*-$C_{pyrrole}$), 132.9 ($C_{olef.}$), 156.1 (C=N), 186.3 (C=O) ppm. IR (film): $\tilde{\nu}$ = 3317 (br., $NH_{pyrrole}$), 3121 (w, $CH_{arom.}$), 2997 (w, $CH_{aliph.}$), 2933 (s, $CH_{aliph.}$), 2818 (w, CH), 1651 (vs, $C{=}O_{ketone}$), 1585 (s, $C{=}C_{olef.}$), 1557 (vs, br., C=C), 1539 (m, C=C), 1435 (m, $CH_{aliph.}$), 1337 (m, C–H), 1265 (s), 1202 (m), 1126 (m), 1067 (vs), 1034 (s), 989 (s), 931 (m), 868 (s), 856 (m), 737 (s), 662 (m, CH), 600 (s), 536 (m), 446 (m) cm^{-1}. MS (ESI, CH_3OH): *m*/*z* (%) = 193 (80) $[M + H]^+$, 215 (42) $[M + Na]^+$, 316 (80), 407 (100) $[M_2 + Na]^+$. $C_{10}H_{12}N_2O_2$ (192.21): calcd. C 62.49, H 6.29, N 14.57; found C 62.41, H 6.20, N 14.56.

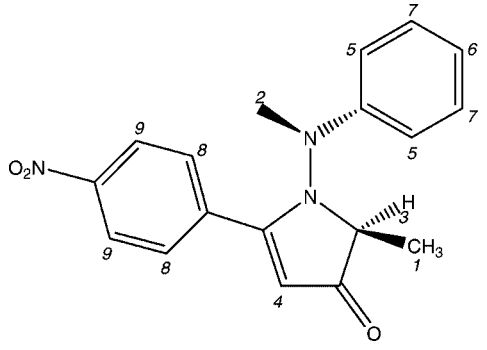
X-ray Crystal Structure Analysis of 10o:[38] Formula $C_{10}H_{12}N_2O_2$, M = 192.22, yellow crystal, 0.15 × 0.10 × 0.10 mm, a = 5.645(1), b = 8.433(1), c = 11.434(1) Å, α = 84.26(1), β = 76.72(1), γ = 73.07(1)°, V = 506.5(1) Å^3, $\rho_{calcd.}$ = 1.260 g cm^{-3}, μ = 0.735 mm^{-1}, empirical absorption correction (0.898 ≤ T ≤ 0.930), Z = 2, triclinic, space group $P\bar{1}$ (No. 2), λ = 1.54178 Å, T = 223 K, ω and φ scans, 4432 reflections collected (±h, ±k, ±l), [(sin θ)/λ] = 0.59 Å^{-1}, 1611 independent (R_{int} = 0.047) and 1299 observed reflections [$I \geq 2\sigma(I)$], 132 refined parameters, R = 0.041, wR_2 = 0.125, max. residual electron density 0.17 (–0.14) e Å^{-3}, hydrogen atoms calculated and refined as riding atoms.

1,4-Bis(4-methoxyimino-3-oxopent-1-en-1-yl)benzene (11a): 3-Methoxyiminobutan-2-one (**8b**)[33] (10.0 g, 86.9 mmol) was treated with an aqueous solution (10%) of potassium hydroxide (55 mL, 100 mmol) to give the enolate. The enolate was treated dropwise with a solution of terephthalaldehyde (5.0 g, 37.3 mmol) in ethanol (20 mL) at 0 °C. The solution was stirred at room temperature for 24 h, resulting in a bright brown solid. The product was filtered off (glass filter funnel D4) and washed with small amounts of cold ethanol. The crude product was purified by recrystallization from methanol. Yellow solid, 11.1 g (33.8 mmol; 90.6%), m.p. 195 °C (decomp.), b.p. 160–180 °C (0.002 mbar). ^1H NMR (300 MHz, $CDCl_3$): δ = 2.03 [s, 6 H, 2 × $H_3CC(N)$], 4.13 (s, 6 H, 2 × OCH_3), 7.64 (s, 4 H, $H_{olef./arom.}$), 7.70 (s, 4 H, $H_{olef./arom.}$) ppm. ^{13}C NMR (150 MHz, CD_2Cl_2): δ = 8.97 [$CH_3C(N)$], 63.55 (OCH_3), 121.87 ($C_{olef.}$), 129.20 (4 C, $C_{arom.}$), 137.20 (*ipso*-C), 141.76 ($C_{olef.}$), 156.24 (C=N), 186.53 (C=O) ppm. IR (KBr): $\tilde{\nu}$ = 3316 (w), 3032 (w, $CH_{arom.}$), 2988 (w, $CH_{aliph.}$), 2930 (w, C–$H_{aliph.}$), 2818 (w, $CH_{aliph.}$), 2124 (w), 1929 (w), 1663 (vs, $C{=}O_{ketone}$), 1597 (br. s, $C{=}C_{olef.}$), 1510 (m, C=C), 1418 (m, $CH_{aliph.}$), 1350 (sh.), 1315 (m, CH), 1294 (w), 1196 (m), 1067 (s), 1050 (vs), 1007 (m), 930 (m), 883 (m), 824 (m), 783 (w), 689 (s, C–H), 528 (m), 513 (m), 427 (w) cm^{-1}. MS (70 eV): *m*/*z* (%) = 328.0 (100) $[M]^+$, 297.0 (30), 269.1 (65), 228 (19), 184.0 (27), 156.0 (55), 128 (63), 100 (20), 72 (22). $C_{18}H_{20}N_2O_4$ (328.36): calcd. C 65.84, H 6.14, N 8.53; found C 65.86, H 5.95, N 8.47.

2,5-Bis(4-methoxyimino-3-oxopent-1-en-1-yl)thiophene (11b): 3-Methoxyiminobutan-2-one (**8b**)[33] (900 mg, 7.8 mmol) was treated with an aqueous solution (10%) of potassium hydroxide (6 mL) to give the enolate. The enolate was treated dropwise with a suspension of thiophene-2,5-dicarbaldehyde (500 mg, 3.6 mmol) in ethanol (5 mL) at 0 °C. Stirring was continued for 12 h at room temperature, resulting in an intensely yellow solid. This was filtered off and washed with small amounts of ethanol. Intensely yellow solid, 790 mg (2.4 mmol, 66.7%), m.p. 176 °C (decomp.). ^1H NMR (300 MHz, $CDCl_3$): δ = 2.02 [s, 6 H, 2 × $H_3CC(N)$], 4.13 (s, 6 H, 2 × OCH_3), 7.26 (s, 2 H, $H_{thio.}$), 7.48 (d, J = 15.6 Hz, 2 H, $H_{olef.}$), 7.76 (d, J = 15.7 Hz, 2 H, $H_{olef.}$) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 8.99 [$CH_3C(N)$], 63.32 (OCH_3), 121.17 ($C_{olef.}$), 132.51 ($C_{thiophene}$),134.65 ($C_{olefin.}$), 143.11 (*ipso*-C), 156.94 (C=N), 186.0 (C=O) ppm. IR (KBr): $\tilde{\nu}$ = 3305 (w), 3090 (sh.), 3080 (w), 2974 (w), 2937 (m, $CH_{aliph.}$), 2900 (sh.), 2820 (w, $CH_{aliph.}$), 1665 (vs, $C{=}O_{ketone}$), 1580 (vs, br., $C{=}C_{olef.}$), 1510 (m, C=C), 1450 (w), 1438

(w, $CH_{aliph.}$), 1377 (w), 1340 (m), 1281 (w), 1231 (m), 1190 (m), 1067 (s), 1051 (vs), 984 (m), 924 (m), 860 (s), 824 (s), 768 (w), 716 (w), 665 (m), 534 (m) cm^{-1}. MS (ESI, $CHCl_3$/MeOH): *m*/*z* (%) = 335 (80) $[M + H]^+$. $C_{16}H_{18}N_2O_4S$ (334.10): calcd. C 57.47, H 5.43, N 8.38; found C 57.22, H 5.33, N 8.19.

1-(Methylphenylamino)-2-methyl-5-(4-nitrophenyl)-1*H*-pyrrol-3-ol (12a): 4-(2-Methyl-2-phenylhydrazono)-1-(4-nitrophenyl)pent-1-en-3-one (**9b**) (320 mg, 1.0 mmol) was dissolved in dry dichloromethane (30 mL) and the solution cooled to –78 °C. After dropwise addition of trifluoromethanesulfonic acid (0.12 mL, 0.18 g, 1.2 mmol) the solution turned green, but brightened after about 5 min. A saturated sodium hydrogen carbonate solution (4.5 mL) was added at –78 °C. The solution was warmed to room temperature. The organic layer was washed with saturated sodium hydrogen carbonate solution (5 mL) until the aqueous layer became neutral. The organic layer was washed with water (20 mL), dried with $MgSO_4$ and 50% of the volume of the solvent was evaporated. TBME (20 mL) was added and the solvent completely removed. The residue was dried in vacuo. NMR spectroscopy of the crude product showed signals that we assigned to only two diastereomers (rotamers) of dihydropyrrole **12a′** (Scheme 11). The crude product was filtered through a short column (silica gel; TMBE). During the concentration of the solution a solid was formed, which was immediately dissolved in dichloromethane and analyzed by NMR spectroscopy. ^{1}H NMR (600 MHz, CD_2Cl_2, 298 K): δ = 1.54, 1.58 (2×s, 3 H, CCH_3, slightly broadened), 2.78, 3.07 [2×s, 3 H, $N(CH_3)$], 3.91, 4.31 (2×s, 1 H, 3-H, br.), 5.61, 5.63 (2×s, 1 H, 4-H), 6.85–6.92 (m, 2 H, 5-H), 7.05–7.06 (m, 1 H, 6-H), 7.26–7.34 (m, 2 H, 7-H), 7.62–7.74 (m, 2 H, 8-H), 8.17–8.20 (m, 2 H, 9-H).



Scheme 11. Numbering of **12a′** for NMR assignment.

General Procedure for the Cyclization of Azadienones with the Use of Trifluoromethanesulfonic Acid: A solution of trifluoromethanesulfonic acid (0.4 mL) in dry dichloromethane (150 mL) was cooled to –10 °C. A solution of the 1-azapenta-1,4-dienone (7.5 mmol) in dry dichloromethane (10 mL) was added dropwise with stirring (colour change). After complete addition stirring was continued until completion of the reaction (TLC control, eluent: TBME). Then the reaction mixture was treated with acetic anhydride (2 mL). After warming to room temperature and stirring for 10 min the solution was again cooled to –10 °C and a saturated solution of sodium hydrogen carbonate (10 mL) was added carefully. The added hydrogen carbonate initially solidified, so that the acidic reaction mixture was neutralized very slowly and in a controlled manner. The organic layer was washed with saturated sodium hydrogen carbonate solution (10 mL) until the aqueous layer became neutral. Then the organic layer was washed with water (20 mL), dried with $MgSO_4$ and 50% of the volume of the solvent evaporated. TMBE (20 mL) was added and the solvent was evaporated completely. The remaining crude product was dried in vacuo. The NMR spectra of the crude product showed only the signals of the corresponding pyrrole, however, sometimes it decomposed rapidly. When possible the substances were purified by recrystallization or column chromatography for CHN analysis.

1-(Methylphenylamino)-2-methyl-5-phenyl-1*H*-pyrrol-3-yl Acetate (13): From trifluoromethanesulfonic acid (0.1 mL) and 4-(2-methyl-2-phenylhydrazono)-1-phenylpent-1-en-3-one (**9a**) (500 mg, 1.8 mmol). The reaction mixture was treated with acetic anhydride (1.9 mL). The crude product was purified by column filtration (silica gel, TMBE). A small amount of a byproduct (methylaniline; 3.9%) was formed according to GC analysis that couldn′t be removed. Crude yield 560 mg (1.74 mmol, 96.7%). R_f (TLC) = 0.48 (silica gel, TBME), R_t (GC) = 21.08 min [40–10/min–280(5)], purity: 96.1%. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 1.88 (s, 3 H, H_3CCN), 2.26 [s, 3 H, $OC(O)CH_3$], 3.25 (s, 3 H, NCH_3), 6.26 (s, 1 H, $H_{pyrrole}$), 6.47–6.48 (m, 2 H, *o*-$H_{arom.}$), 6.82–6.85 (m, 1 H, $H_{arom.}$), 7.14–7.17 (m, 1 H, $H_{arom.}$), 7.20–7.37 (m, 6 H, $H_{arom.}$) ppm. ^{13}C NMR (150 MHz, CD_2Cl_2): δ = 8.39 (CH_3CN), 20.79 (H_3CCOO), 40.04 (NCH_3), 100.03 ($HC_{pyrrole}$), 111.36 (*o*-$C_{N–Ph.}$), 118.83 (C_q), 119.03 ($C_{arom.}$), 126.61 ($C_{arom.}$), 127.05 (*o*/*m*-$C_{arom.}$), 128.24 (*o*/*m*-$C_{arom.}$), 129.43 (*o*/*m*-$C_{arom.}$), 129.78 (C_q), 131.50 (C_q), 132.94 (C_q), 148.70 (*ipso*-$C_{N–Ph.}$), 169.10 [$H_3CC(O)O$] ppm. IR (Film): $\tilde{\nu}$ = 3066 (w, $CH_{arom.}$), 3031 (w, $CH_{arom.}$), 2962 (m, $CH_{aliph.}$), 2922 (w, $CH_{aliph.}$), 2818 (w, $CH_{aliph.}$), 2359 (w), 2251 (w), 1755 (s, C=O), 1598 (s, C=C), 1501 (vs), 1456 (w), 1369 (m), 1307 (w), 1219 (vs), 1146 (m), 1095 (m), 910, 806 (w), 752 (sh., CH), 734 (s), 692 (m). GC–MS (70 eV): *m*/*z* (%) = 320 (20) $[M]^+$, 248 (22), 172 (100) $[M – CH_3CO – NMePh]^+$, 107 (85), 106 (64), 77 (80), 51 (27), 43 (71).

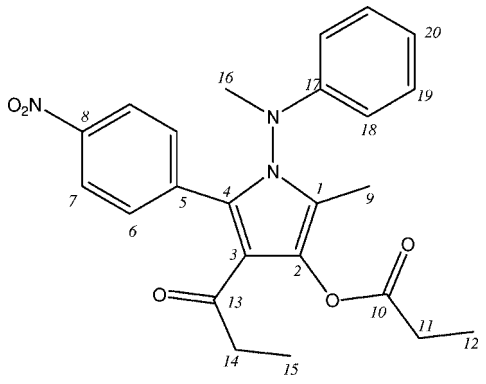
1-Methoxy-2-methyl-5-(1*H*-pyrrol-2-yl)-1*H*-pyrrol-3-yl Acetate (14): From trifluoromethanesulfonic acid (0.4 mL, 4.6 mmol) dissolved in dry dichloromethane (50 mL) and a solution of 4-methoxyimino-1-(1*H*-pyrrol-2-yl)pent-1-en-3-one (**10o**) (790 mg, 4.1 mmol) in dry dichloromethane (5.5 mL). The colour of the solution changed from yellow to orange to brown. The product was purified by column chromatography (SiO_2, TBME), resulting in a spectroscopically pure substance that decomposed rapidly. Brown gum, rapidly darkening to give a black tar, crude yield 561 mg (2.4 mmol, 58.4%), R_f (TLC) = 0.59 (silica gel, TBME). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.08 (s, 3 H, H_3CCN), 2.17 [s, 3 H, $OC(O)CH_3$], 3.69 (s, 3 H, OCH_3), 5.85–6.66 (m, 4 H, $H_{pyrrole}$), 8.62 (br., 1 H, NH) ppm. ^{13}C NMR (100 MHz, CD_2Cl_2): δ = 7.35 (CH_3CN), 20.73 (H_3CCOO), 65.51 ($NOCH_3$), 94.26 ($C_{pyrrole}$), 100.12 ($C_{pyrrole}$), 106.05 ($C_{pyrrole}$), 109.21 ($C_{pyrrole}$), 117.46 ($C_{pyrrole}$), 130.16 ($C_{pyrrole}$), 168.47 [$H_3CC(O)O$] ppm. MS (70 eV): *m*/*z* (%) = 234 (26) $[M]^+$, 203 (16) $[M – OCH_3]^+$, 161 (100), 91 (23). MS (ESI, $CHCl_3$/CH_3OH): *m*/*z* (%) = 257 (100) $[M + Na]^+$, daughters: 226 (50) $[M – OCH_3 + Na]^+$, 183 (72) $[M – OCH_3 – H_3CCO + Na]^+$. MS (MicroTOF): *m*/*z* (%): calcd. 257.0897 $[M + Na]^+$; found 257.0904 $[M + Na]^+$.

4-Benzoyl-3-benzoyloxy-2-methyl-1-(methylphenylamino)-5-phenyl-1*H*-pyrrole (15a): 4-(2-Methyl-2-phenylhydrazono)-1-phenylpent-1-en-3-one (**9a**) (334 mg, 1.2 mmol) was added dropwise to a solution of trifluoromethanesulfonic acid (0.3 mL, 3.4 mmol) at –78 °C to give a dark green solution. At the end of the addition the reaction mixture was slightly green. Stirring at –78 °C was continued for 10 min before the mixture was treated with a solution of benzoic anhydride (565 mg, 2.5 mmol) in dichloromethane (10 mL). The colourless solution was warmed to room temperature and stirring at room temperature was continued for 8 h. The reaction mixture was then treated with saturated sodium hydrogen carbonate solution. After aqueous work up the product was purified by column

chromatography (SiO_2, TBME/pentane = 1:1), but it was not possible to separate it from the derivative that is unsubstituted in the 4-position. Yellow oil, 88 mg (1.9 mmol, 15.0%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.04 (s, 3 H, CCH_3), 3.28 (NCH_3), 6.56–6.57 (m, 2 H, *o*-$H_{N-Ph.}$), 7.07–7.57 (m, 10 H, $H_{arom.}$), 7.64–7.66 (m, 2 H, $H_{arom.}$), 7.75–7.77 (m, 2 H, $H_{arom.}$), 7.84–7.87 (m, 2 H, $H_{arom.}$), 8.00–8.03 (m, 2 H, $H_{arom.}$) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 8.46 (CCH_3), 40.44 (NCH_3), 110.46 (C_q), 114.30, 120.23, 127.61–130.11 ($C_{arom.}$, $C_{pyrrole}$), 131.66, 132.13 (C_q), 132.80, 133.34 (C_q), 138.36, 138.73 ($C_{arom.}$, $C_{pyrrole}$), 151.81 (*ipso*-$C_{N-Ph.}$), 164.75 (CO_2Ph), 195.11 (PhC=O) ppm.

3-Acetoxy-4-acetyl-2-methyl-1-(methylphenylamino)-5-(4-nitrophenyl)-1*H*-pyrrole (15b): From trifluoromethanesulfonic acid (0.2 mL, 2.3 mmol) and 4-(2-methyl-2-phenylhydrazono)-1-(4-nitrophenyl)pent-1-en-3-one (**9b**) (507 mg, 1.5 mmol). The crude product was purified by column chromatography (SiO_2, TBME). Yellow solid, 474 mg (1.2 mmol, 75.3%), m.p. > 88 °C (decomp.). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.9 (s, 3 H, $NCCH_3$), 2.1 (s, 3 H,H_3CCO), 2.4 (s, 3 H, H_3CCO), 3.2 (s, 3 H, NCH_3), 6.37–6.40 (m, 2 H, *o*-$H_{N-Ph.}$), 6.85–6. 9 (m, 1 H, *p*-$H_{N-Ph.}$), 7.22–7.25 (m, 2 H, *m*-$H_{N-Ph.}$), 7.43–7.45 (m, 2 H, $H_{nitroarom.}$), 8.11–8.15 (m, 2 H, $H_{nitroarom.}$) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 8.1 (H_3CCN), 20.6 (H_3CCOO), 30.1 (H_3CC_{ketone}), 40.5 (NCH_3), 111.3 (*o*-$C_{N-Ph.}$), 114.9 (C_q), 120.1 (*p*-$C_{N-Ph.}$), 121.3 (C_q), 123.0 (2 C, $C_{nitroarom.}$), 129.6 (*m*-$C_{N-Ph.}$), 131.5 (2 C; $C_{nitroarom.}$), 131.9 (C_q), 132.2 (C_q), 137.2 (C_q), 147.7 (C_q), 147.9 (C_q), 169.13 (O=C_{ester}), 192.5 (O=C_{ketone}) ppm. MS (ESI, $CHCl_3$/CH_3OH, 38 eV): *m*/*z* (%) = 430 (100) $[M + Na]^+$, 408 (13) $[M + H]^+$.

1-(Methylphenylamino)-2-methyl-5-(4-nitrophenyl)-4-propionyl-3-propionyloxy-1*H*-pyrrole (15c): From trifluoromethanesulfonic acid (0.2 mL, 2.3 mmol) and 4-(2-methyl-2-phenylhydrazono)-1-(4-nitrophenyl)pent-1-en-3-one (**9b**) (547 mg, 1.7 mmol). The brown reaction mixture was stirred for 1 h at –78 °C before being treated with propionic anhydride (0.5 mL, 0.5 g, 3.9 mmol) to give a green solution. After work up with sodium hydrogen carbonate and evaporation of the solvent the crude product (an orange gum) was purified by column chromatography (SiO_2, TBME/pentane = 1:2). The solid decomposed rapidly. The substance was dissolved in chloroform and a ^{1}H NMR spectrum (600 MHz) recorded immediately. Orange gum, rapidly decomposing, crude yield 303 mg (0.7 mmol, 41.2%). R_f (TLC) = 0.32 (silica gel, TBME). ^{1}H NMR (600 MHz, $CDCl_3$): δ = 1.00 (t, ^3J = 7.3 Hz, 3 H, H_3C-12), 1.31 (t, ^3J = 7.5 Hz, 3 H, H_3C-15), 1.89 (s, 3 H, H_3C-9), 2.43 (q, ^3J = 7.3 Hz, 2 H, H_2C-11), 2.68 (q, ^3J = 7.5 Hz, 2 H, H_2C-14), 3.18 (s, 3 H, NCH_3), 6.38–6.39 (m, 2 H, HC-18), 6.87–6.89 (m, 1 H, HC-20), 7.23–7.26 (m, 2 H, HC-19), 7.43–7.44 (m, 2 H, HC-6), 8.11–8.13 (m, 2 H, HC-7) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 7.89 (C-9), 8.19 (C-12), 8.97 (C-15), 27.36 (C-14), 35.30 (C-11), 40.46 (NCH_3), 111.24 (C-18), 114.63 (C_q), 120.06 (C-20), 121.17 (C_q), 122.97 (C-7), 129.56 (C-19), 131.31 (C-6), 131.61 (C_q), 131.73 (C_q), 137.37 (C_q), 147.57 (C_q), 147.84 (C_q), 172.70 (C-10), 196.01 (C-13) ppm (Scheme 12).



Scheme 12. Numbering of **15c** for NMR assignment.

3-Acetoxy-4-acetyl-5-(2-bromophenyl)-1-methoxy-2-methyl-1*H*-pyrrole (16a): 1-(2-Bromophenyl)-4-methoxyiminopent-1-en-3-one (**10h**) (2.0 g, 7.1 mmol) was dissolved in dichloromethane (100 mL) and added dropwise to a solution of trifluoromethanesulfonic acid (4 mL, 48.8 mmol) in dichloromethane (500 mL). The reaction mixture was treated with acetic anhydride (15 mL). After aqueous work up a highly viscous, colourless liquid was obtained. Yield 1.91 g (5.2 mmol, 73.2%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.9 (s, 3 H, $NCCH_3$), 2.3 (s, 3 H, CH_3CO_2), 2.4 [s, 3 H, CH_3C(O)], 3.7 (s, 3 H, OCH_3), 7.51–7.71 (m, 3 H, $H_{arom.}$), 7.7–7.8 (m, 1 H, $H_{arom.}$) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 7.39 ($H_3CC_{pyrrole}$), 21.12 (H_3CCOO), 29.67 (H_3CCO_{ketone}), 66.74 (OCH_3), 112.17 ($C_{pyrrole}$), 116.81 ($C_{pyrrole}$), 126.35 (C_q), 127.76 (CH), 128.62 (C_q), 129.86 (C_q), 131.34 (CH), 131.88 (C_q), 133.34 (2 C, $C_{arom.}$), 169.96 (CO_2CH_3), 192.51 (H_3C=O) ppm. MS (ESI, MicroTOF, CH_3OH): *m*/*z* (%) = 366.03 $[M + H]^+$, 388.01 (100) $[M + Na]^+$. $C_{16}H_{16}BrNO_4$ (366.21): calcd. C 52.48, H 4.40, N 3.82; found C 53.06, H 5.06, N 3.47.

3-Acetoxy-4-acetyl-5-(4-chlorophenyl)-1-methoxy-2-methyl-1*H*-pyrrole (16b): From 1-(4-chlorophenyl)-4-methoxyiminopent-1-en-3-one (**10i**) (0.55 g, 2.3 mmol) and a solution of trifluoromethanesulfonic acid (0.3 mL) in dichloromethane. The reaction mixture was treated with acetic anhydride (2 mL) at –78 °C. The reaction mixture was warmed to –10 °C and treated with sodium hydrogen carbonate solution followed by aqueous work up. The product was purified by Kugelrohr distillation. Yellow, very viscous oil, 0.53 g (1.6 mmol, 71.6%), b.p. 200 °C (0.009 mbar). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.95 (s, 3 H, $NCCH_3$), 2.08 (s, 3 H, CH_3CO_2), 2.25 [s, 3 H, CH_3C(O)], 3.50 (s, 3 H, OCH_3), 7.36 (m, 4 H, $H_{arom.}$) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 7.02 ($H_3CC_{pyrrole}$), 20.63 (H_3CCOO), 30.00 (H_3CCO_{ketone}), 65.85 (OCH_3), 111.74 ($C_{pyrrole}$), 116.38 ($C_{pyrrole}$), 127.46 ($C_{pyrrole}$), 128.05 ($C_{pyrrole}$), 128.52 (*o*/*m*-$C_{arom.}$), 129.53 (*ipso*-$C_{arom.}$), 132.10 (*o*/*m*-$C_{arom.}$), 135.06 (*ipso*-$C_{arom.}$), 169.49 (CO_2CH_3), 192.67 (H_3C=O) ppm. IR (film): $\tilde{\nu}$ = 3025 (w, $CH_{arom.}$), 2941 (m, $CH_{aliph.}$), 1764 (vs, C=O), 1658 (vs), 1602 (m), 1522 (s), 1473 (s), 1431 (s), 1410 (s), 1367 (s), 1261 (m), 1206 (vs), 1130 (m), 1111 (m), 1016 (m), 962 (w), 907 (w), 843 (sh.), 814 (vs), 731 (s) cm^{-1}. MS (ESI, MicroTOF, CH_3OH): calcd. 344.0660 $[M + Na]^+$; found 344.0661. $C_{16}H_{16}ClNO_4$ (321.76): calcd. C 59.73, H 5.01, N 4.35; found C 59.53, H 4.99, N 4.25.

3-Acetoxy-4-acetyl-1-methoxy-2-methyl-5-(4-nitrophenyl)-1*H*-pyrrole (16c): 1-(4-Nitrophenyl)-4-methoxyiminopent-1-en-3-one (**10j**) (0.75 g, 3.0 mmol) was added dropwise to a solution of trifluoromethanesulfonic acid (0.5 mL) in dichloromethane. The dark-coloured reaction mixture was treated with acetic anhydride (2 mL) at –78 °C. The reaction mixture was warmed to –10 °C and treated with sodium hydrogen carbonate solution followed by aqueous work up. The product was purified by column chromatography (SiO_2, TBME). Viscous reddish gum, 0.56 g (1.7 mmol, 56.7%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.08 (s, 3 H, $NCCH_3$), 2.10 (s, 3 H, CH_3CO_2), 2.26 [s, 3 H, CH_3C(O)], 3.51 (s, 3 H, OCH_3), 7.60–7.64 (m, 2 H, $H_{arom.}$), 8.17–8.20 (m, 2 H, $H_{arom.}$) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 7.17 ($H_3CC_{pyrrole}$), 20.52 (H_3CCOO), 30.06 (H_3CCO_{ketone}), 66.04 (OCH_3), 112.27 ($C_{pyrrole}$), 117.47 ($C_{pyrrole}$), 123.05 (*o*/*m*-$C_{arom.}$), 125.94 ($C_{pyrrole}$), 129.71 ($C_{pyrrole}$), 131.51 (*o*/*m*-$C_{arom.}$), 135.28 (*ipso*-$C_{arom.}$), 147.45 (*ipso*-$C_{arom.}$), 169.05 (CO_2CH_3), 192.23 (H_3C=O) ppm. IR (film): $\tilde{\nu}$ = 3098 (w, $CH_{arom.}$), 2988 (m, $CH_{aliph.}$), 2941 (w, $CH_{aliph.}$), 1771 (s, C=O), 1665 (m),

1601 (m), 1589 (s, C=C), 1474 (w), 1429 (w), 1394 (w), 1346 (vs), 1267 (w), 1202 (s), 1109 (m), 1090 (m), 1045 (w), 1013 (w), 961 (w), 903 (w), 858 (m), 833 (s), 733 (m) cm^{-1}. MS (ESI, MicroTOF): calcd. 355.0901 $[M + Na]^+$; found 355.0909. $C_{16}H_{16}N_2O_6$ (332.31): calcd. C 57.83, H 4.85, N 8.43; found C 57.98, H 5.09, N 8.57.

3-Acetoxy-4-acetyl-1-methoxy-2-methyl-5-styryl-1*H*-pyrrole (16d): From a solution of trifluoromethanesulfonic acid (0.4 mL, 4.6 mmol) in dry dichloromethane (20 mL) and a solution of 2-methoxyimino-7-phenylhepta-4,6-dien-3-one (**3**) (0.63 g, 2.7 mmol) in dry dichloromethane (10 mL). The resulting reaction mixture was slowly warmed to –10 °C and treated with acetic anhydride (2.0 mL). After aqueous work up a yellow precipitate was obtained. In some experiments no precipitate was formed after evaporation of the solvent. In such cases the oil was dissolved in chloroform and the solvent was again removed in vacuo to give a yellow solid which was recrystallized from methanol. Yellow solid, 0.57 g (1.8 mmol, 67.4%), m.p. >68 °C (decomp.). ^1H NMR (300 MHz, $CDCl_3$): δ = 2.15 (s, 3 H, $NCCH_3$), 2.33 (s, 3 H, O_2CCH_3), 2.37 [s, 3 H, $(O)CCH_3$], 3.91 (s, 3 H, OCH_3), 7.23–7.37 (m, 3 H, $H_{arom.}$), 7.43 (d, J = 16.8 Hz, 1 H, $H_{olef.}$), 7.51–7.54 (m, 2 H, $H_{arom.}$), 7.69 (d, ^3J = 16.8 Hz, 1 H, $H_{olef.}$) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 7.4 (H_3CCN), 20.7 (H_3CCOO), 30.5 (H_3CCO_{ketone}), 65.0 (OCH_3), 111.2 ($C_{pyrrole}$), 115.6 ($C_{olef.}$), 117.7 ($C_{pyrrole}$), 126.3 ($C_{pyrrole}$), 126.6 (*o*/*m*-$C_{arom.}$), 127.9 (p-$C_{arom.}$), 128.6 (*o*/*m*-$C_{arom.}$), 129.8 ($C_{pyrrole}$), 132.3 ($C_{olef.}$), 137.6 (*ipso*-$C_{arom.}$), 168.9 ($O=C_{ester}$), 192.8 ($O=C_{ketone}$) ppm. IR (KBr): $\tilde{\nu}$ = 3304, 3022 (w, $CH_{arom.}$), 2936 (m, $CH_{aliph.}$), 2820 (m, $CH_{aliph.}$), 1659 (vs, C=O), 1585 (s, br., C=C), 1448 (m), 1356 (s, $CH_{aliph.}$), 1317 (w), 1213 (w), 1075 (m, br.), 915 (m), 853 (m), 756 (vs, $CH_{arom.}$), 689 (vs, $CH_{arom.}$) cm^{-1}. MS (ESI, $CHCl_3/CH_3OH$, 40 eV): *m*/*z* (%) = 649.6 (100) $[M_2 + Na]^+$, 627.6 (18) $[M_2 + H]^+$, 336.5 (55) $[M + Na]^+$, 314.5 (51) $[M + H]^+$. $C_{18}H_{19}NO_4$ (313.35): calcd. C 68.99, H 6.11, N 4.47; found C 68.12, H 5.90, N 4.29.

X-ray Crystal Structure Analysis of 16d:[38] Formula $C_{18}H_{19}NO_4$, M = 313.34, yellow crystal, 0.60 × 0.20 × 0.10 mm, a = 12.863(1), b = 7.990(2), c = 16.695(2) Å, β = 103.11(1)°, V = 1666.2(5) $Å^3$, $\rho_{calcd.}$ = 1.249 $g cm^{-3}$, μ = 0.725 mm^{-1}, empirical absorption correction (0.670 ≤ T ≤ 0.931), Z = 4, monoclinic, space group $P2_1/n$ (No. 14), λ = 1.54178 Å, T = 223 K, $\omega/2\theta$ scans, 3535 reflections collected (–h, –k, ±l), [(sin θ)/λ] = 0.62 $Å^{-1}$, 3382 independent (R_{int} = 0.016) and 2599 observed reflections [$I \geq 2\sigma(I)$], 213 refined parameters, R = 0.055, wR_2 = 0.172, max. residual electron density 0.55 (–0.48) $e Å^{-3}$, hydrogen atoms calculated and refined as riding atoms.

3-Acetoxy-4-acetyl-1-methoxy-2-methyl-5-(3-thienyl)-1*H*-pyrrole (16e): From trifluoromethanesulfonic acid (0.4 mL, 4.6 mmol) and 4-methoxyimino-1-(3-thienyl)pent-1-en-3-one (**10m**) (0.450 g, 2.1 mmol), resulting in a red solution. The product was separated by column chromatography (SiO_2, TBME) from a byproduct showing a third acylation on the thiophene moiety. Colourless crystals, 0.370 g (1.3 mmol; 60.1%), m.p. 114–115 °C. ^1H NMR (400 MHz, $CDCl_3$): δ = 2.05 (s, 3 H, $NCCH_3$), 2.15 (s, 3 H, O_2CCH_3), 2.34 [s, 3 H, $(O)CCH_3$], 3.62 (s, 3 H, OCH_3), 7.24 (m, 1 H, $H_{thiophene}$), 7.41 (m, 1 H, $H_{thiophene}$), 7.55 (m, 1 H, $H_{thiophene}$) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 6.9 (H_3CCN), 20.6 (H_3CCOO), 29.6 (H_3CCO_{ketone}), 65.7 (OCH_3), 111.8 ($C_{pyrrole}$), 116.3 ($C_{pyrrole}$), 124.4 ($C_{pyrrole}$), 125.2 ($HC_{thiophene}$), 127.0 ($HC_{thiophene}$), 128.4 (C_q), 129.3 ($HC_{thiophene}$), 129.4 (C_q), 169.6 ($O=C_{ester}$), 192.8 ($O=C_{ketone}$) ppm. IR (KBr): $\tilde{\nu}$ = 3437 (br.), 3097 (m), 2995 (w), 2951 (w, $CH_{aliph.}$), 2926 (w), 1759 (m, C=O), 1645 (vs), 1435 (m), 1414 (m), 1367 (m), 1259 (w), 1207 (vs), 1132 (w), 1093 (w), 1013 (w), 978 (m), 932 (m), 864 (w), 800 (m), 686 (w) cm^{-1}. MS (ESI, MicroTOF, CH_3OH): calcd. 316.0614 $[M + Na]^+$; found 316.0616. $C_{14}H_{15}NO_4S$ (293.34): calcd. C 57.32, H 5.15, N 4.77; found C 57.07, H 5.00, N 4.86.

X-ray Crystal Structure Analysis of 16e:[38] Formula $C_{14}H_{15}NO_4S$, M = 293.33, colourless crystal, 0.45 × 0.25 × 0.25 mm, a = 10.830(1), b = 8.581(1), c = 15.654(1) Å, β = 100.81(1)°, V = 1428.9(2) $Å^3$, $\rho_{calcd.}$ = 1.363 $g cm^{-3}$, μ = 2.135 mm^{-1}, empirical absorption correction (0.447 ≤ T ≤ 0.617), Z = 4, monoclinic, space group $P2_1/n$ (No. 14), λ = 1.54178 Å, T = 223 K, ω and φ scans, 8379 reflections collected (±h, ±k, ±l), [(sin θ)/λ] = 0.59 $Å^{-1}$, 2399 independent (R_{int} = 0.042) and 2098 observed reflections [$I \geq 2\sigma(I)$], 193 refined parameters, R = 0.041, wR_2 = 0.124, max. residual electron density 0.23 (–0.26) $e Å^{-3}$, sulfur atom disordered over two positions, hydrogen atoms calculated and refined as riding atoms.

4-Benzoyl-3-benzoyloxy-1-benzyloxy-2-methyl-5-phenyl-1*H*-pyrrole (16f): 4-(Benzyloxyimino)-1-phenylpent-1-en-3-one (**10a**) (660 mg, 2.4 mmol) was added dropwise to trifluoromethanesulfonic acid (0.4 mL, 4.6 mmol) at –78 °C to give an orange solution. At the end of the addition the reaction mixture turned slightly yellow. Stirring was continued for 10 min at –78 °C before the reaction mixture was treated with a solution of benzoic anhydride (1.1 g, 4.9 mmol) in dichloromethane (17 mL). The solution turned colourless. The mixture was warmed to room temperature and stirred for 1 h. Then the reaction mixture was again cooled to –10 °C and washed with sodium hydrogen carbonate solution. After aqueous work upthe product was purified by column filtration (SiO_2, TBME), but separation from a byproduct that was unsubstituted in the 4-position could not be achieved. Yellow oil, 0.96 g. ^1H NMR (400 MHz, $CDCl_3$): δ = 2.11 (s, 3 H, $NCCH_3$), 4.55 (s, 2 H, $PhCH_2$), 6.93–8.06 (m, 20 H, $H_{arom.}$) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 8.60 (CH_3), 81.35 (OCH_2Ph), 111.58 (C_q), 117.86, 125.82, 127.43, 128.30, 128.61, 129.01, 129.32, 129.58, 130.13, 130.57, 130.84, 131.20, 131.24, 132.21, 133.53, 134.01, 135.24, 139.77 ($C_{arom.}$, $C_{pyrrole}$), 165.65 (CO_2Ph), 191.57 (PhC=O) ppm. MS (ESI, $CH_3OH/CHCl_3$, 50 eV): *m*/*z* (%) = 511 (63) $[M + Na]^+$, 489 (100) $[M + H]^+$, 407 (6) $[M – PhC=O + Na]^+$, 385 (95) $[M – PhC=O + H]^+$.

4-Acetyl-3-acetoxy-1-benzyloxy-2-methyl-5-phenyl-1*H*-pyrrole (16g): 4-(Benzyloxyimino)-1-phenylpent-1-en-3-one (**10a**) (0.51 g, 1.8 mmol) was added dropwise to trifluoromethanesulfonic acid (0.3 mL, 3.4 mmol) at –78 °C to give a yellow solution. Stirring at –78 °C was continued for 10 min and then the reaction mixture was treated with acetic anhydride (3.5 mL, 3.6 mmol) to give a red solution. The reaction mixture was warmed to –10 °C and treated with sodium hydrogen carbonate solution followed by aqueous work up. The product was purified by column chromatography (silica gel, TBME) to give a red oil, 0.44 g (1.2 mmol, 67.3%). ^1H NMR (400 MHz, $CDCl_3$): δ = 2.00 (s, 3 H, $NCCH_3$), 2.08 (CH_3), 2.33 (CH_3), 4.60 (s, 2 H, $PhCH_2$), 6.13–6.92 (m, 2 H, $H_{arom.}$), 7.23–7.34 (m, 3 H, $H_{arom.}$), 7.47–7.51 (m, 5 H, $H_{arom.}$) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 8.60 (CH_3), 20.72 (H_3CCOO), 29.96 (H_3CCO_{ketone}), 80.70 (OCH_2Ph), 111.67 ($C_{pyrrole}$), 116.71 ($C_{pyrrole}$), 128.33 (2 C), 128.55 (2 C), 128.97 (*p*-$C_{arom.}$), 129.30 (*p*-$C_{arom.}$), 129.41 (C_q), 129.44 (C_q), 129.62 (2 C), 129.99 (C_q), 131.11 (2 C), 132.76 ($C_{arom.}$,$C_{pyrrole}$), 169.68 (CO_2CH_3), 193.19 ($H_3C=O$) ppm. IR (film): $\tilde{\nu}$ = 3065 (w), 3032 (w, $CH_{arom.}$), 2955 (sh., $CH_{aliph.}$), 2930 (m, $CH_{aliph.}$), 1827 (s), 1769 (vs), 1657 (s), 1599 (w), 1526 (w), 1474 (m), 1431 (m), 1402 (s), 1369 (s, $CH_{aliph.}$), 1258 (w), 1209 (s, br.), 1126 (s, br), 1092 (m), 997 (m), 954 (w), 910 (m, br), 770 (sh.), 754 (m, $CH_{arom.}$), 702 (s, $CH_{arom.}$) cm^{-1}. MS (ESI, MicroTOF, CH_3OH): calcd. 386.1363 ($C_{22}H_{21}NO_4Na^+$); found 386.1357.

1-Methoxy-2-methyl-5-phenyl-4-propionyl-3-(propionyloxy)-1*H*-pyrrole (16h): 4-Methoxyimino-1-phenylpent-1-en-3-one (**10f**) (1.0 g,

4.9 mmol) were added dropwise to trifluoromethanesulfonic acid (0.5 mL, 5.7 mmol) at –78 °C. The reaction mixture was warmed to room temperature and again cooled to –78 °C before it was treated with propionic anhydride (0.6 mL, 0.6 g, 4.9 mmol). The product was purified by column filtration (silica gel, petroleum ether/TBME = 5:1). Viscous brown gum, rapidly decomposing. Crude yield 0.41 g (1.3 mmol, 26.5%). R_f (TLC) 0.10 (silica gel, TBME). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.91 (t, ^3J = 7.3 Hz, 3 H), 1.29 (t, ^3J = 7.6 Hz, 3 H), 2.15 (s, 3 H, $NCCH_3$), 2.26 (q, ^3J = 7.3 Hz, 2 H, CH_2), 2.64 (q, ^3J = 7.6 Hz, 2 H), 2.93 (s, 3 H, OCH_3), 7.42–7.50 (m, 5 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 7.06 (CH_3), 8.26 (CH_3), 9.04 ($NCCH_3$), 27.40 (CH_2), 34.92 (CH_2), 65.77 (OCH_3), 111.47 (C_q), 115.91 (C_q), 128.24 (*o*/*m*-$C_{arom.}$), 128.8 (*p*-$C_{arom.}$), 129.0 (C_q), 129.4 (C_q), 129.5 (C_q), 130.7 (*o*/*m*-$C_{arom.}$), 173.1 (O=C_{ester}), 196.6 (O=C_{ketone}) ppm. MS (70 eV): *m*/*z* (%) = 315 (45) $[M]^+$, 286 (3), 259 (100) $[M - C_2H_5C(O)]^+$, 228 (99) $[C_{13}H_{10}NO_3]^+$, 210 (31) $[C_{14}H_{12}NO]^+$, 199 (16), 182 (19), 159 (13), 141 (24), 129 (33), 57 (67).

1,4-Bis[4-acetoxy-3-acetyl-1-methoxy-5-methyl-1*H*-pyrrol-2-yl]benzene (17a): From a solution of trifluoromethanesulfonic acid (4.0 mL, 45.8 mmol) in dichloromethane (500 mL) and a solution of 1,4-bis(4-methoxyimino-3-oxopent-1-en-1-yl)benzene (**11a**) (2.0 g, 6.1 mmol) in dichloromethane (100 mL). The reaction mixture was treated with acetic anhydride (20 mL) and neutralized by addition of a saturated sodium hydrogen carbonate solution (2 × 80 mL). After aqueous work up the solvent was completely removed. The ^{1}H NMR spectrum of the crude product showed only the signals of the resulting pyrrole. For the elemental analysis the substance was recrystallized from methanol. Ochre-brown solid, 2.87 g (5.8 mmol, 95%) (crude product), 1.33 g (2.7 mmol, 44%) after second recrystallization, m.p. 216 °C (decomp.). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.05 (s, 6 H, 2 × H_3C-6), 2.18 (s, 6 H, 2 × H_3C-10), 2.34 (s, 6 H, 2 × H_3C-13), 3.61 (s, 6 H, 2 × OCH_3), 7.60 (s, 4 H, $H_{arom.}$) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 7.10 (H_3CCN), 20.70 (H_3CCOO), 29.88 (H_3CC_{ketone}), 65.77 (OCH_3), 111.90 ($C_{pyrrole}$), 116.50 ($C_{pyrrole}$), 128.65 (C_q), 129.60 (C_q), 129.72 (C_q), 130.72 (4 × $C_{arom.}$), 169.58 (OC=O), 192.81 (C=O) ppm. IR (KBr): $\tilde{\nu}$ = 3022 (sh., $CH_{arom.}$), 2995 (s, $CH_{aliph.}$), 2939 (m, $CH_{aliph.}$), 2882 (sh., $CH_{aliph.}$), 1778 (vs), 1761 (m), 1666 (vs), 1597 (s, C=C), 1544 (m), 1473 (m), 1423 (s, C-$H_{aliph.}$), 1396, 1365, 1319 (w), 1253 (m), 1211 (vs), 1132 (w), 1095 (w), 1047 (w), 1012 (s), 966 (w), 906 (s), 864 (s), 827 (m), 810 (m) cm^{-1}. MS (ESI, $CHCl_3$/CH_3OH): *m*/*z* (%) = 535 (42) $[M + K]^+$, 519 (100) $[M + Na]^+$, 497 (50) $[M + H]^+$. MS (70 eV): *m*/*z* (%) = 496 (50) $[M]^+$, 454 (42) $[M - C_2H_2O]^+$, 423 (27) $[C_{23}H_{23}N_2O_6^{\cdot}]^+$, 381 (100) $[C_{21}H_{21}N_2O_5^{\cdot}]^+$, 350 (38), 307 (11), 127 (29), 113 (18), 57 (19). $C_{26}H_{28}N_2O_8$ (496.51): calcd. C 62.89, H 5.68, N 5.64; found C 62.46, H 5.52, N 5.55.

X-ray Crystal Structure Analysis of 17a:[38] Formula $C_{26}H_{28}N_2O_8$, M = 496.50, yellow-orange crystal, 0.50 × 0.50 × 0.35 mm, a = 20.421(2), b = 8.426(1), c = 15.953(1) Å, β = 109.25(1)°, V = 2591.5(4) Å^3, $\rho_{calcd.}$ = 1.273 g cm^{-3}, μ = 0.792 mm^{-1}, empirical absorption correction ($0.713 \leq T \leq 0.982$), Z = 4, monoclinic, space group $C2/c$ (No. 15), λ = 1.54178 Å, T = 223 K, $\omega/2\theta$ scans, 2720 reflections collected (+h, +k, ±l), [(sin θ)/λ] = 0.62 Å^{-1}, 2644 independent (R_{int} = 0.031) and 2402 observed reflections [$I \geq 2\sigma(I)$], 215 refined parameters, R = 0.054, wR_2 = 0.162, max. residual electron density 0.33 (–0.37) e Å^{-3}, the group O7 to C10 and O12 was refined with split positions, hydrogen atoms calculated and refined as riding atoms.

2,5-Bis[4-acetoxy-3-acetyl-1-methoxy-5-methyl-1*H*-pyrrol-2-yl]-thiophene (17b): From trifluoromethanesulfonic acid (0.1 mL, 1.2 mmol) and 2,5-bis(4-methoxyimino-3-oxopent-1-en-1-yl)thiophene (**11b**) (150 mg, 0.4 mmol). Complete purification by various methods could not be achieved. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.18 [s, 12 H, 4 × H_3C, (2 × CH_3CN, 2 × H_3CC_{ester})], 2.33 (s, 6 H, 2 × H_3C, H_3CC_{ketone}), 3.79 (s, 6 H, 2 × OCH_3), 7.36 (s, 2 H, $H_{thiophene}$) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 7.1 (H_3CCN), 20.6 (H_3CCOO), 29.6 (H_3CC_{ketone}), 66.1 (OCH_3), 113.0 ($C_{pyrrole}$), 117.6 ($C_{pyrrole}$), 120.7 (C_q), 129.6 (C_q), 130.5 ($HC_{thiophene}$), 131.2 (C_q), 169.3 (OC=O), 192.5 (C=O) ppm. MS (ESI, $CHCl_3$/CH_3OH, cone 35 eV): *m*/*z* (%) = 503 (50) $[M + H]^+$, 525 (100) $[M + Na]^+$. MS (MicroTOF): calcd. 525.1296 $[M + Na]^+$; found 525.1302 $[M + Na]^+$.

Supporting Information (see footnote on the first page of this article): Quantum chemical data for Figure S1 and S2 and graphical representations of the transition states **1-TS** (charge distribution and relevant orbitals, Figure 2).

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