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Synthesis of Pyrroles through a 4π-Electrocyclic Ring-Closure Reaction of 1-Azapentadienyl Cations

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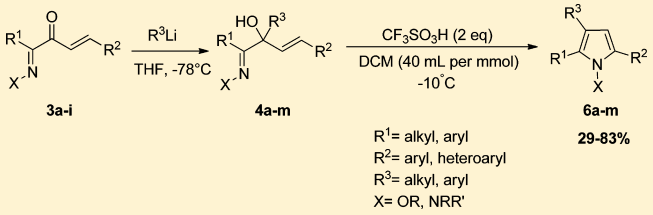
Supporting Information

ABSTRACT: 1-Azapenta-1,4-diene-3-ols **4a−m** are easily accessible from 1-azapenta-1,4-dien-3-ones **3a−i** and organolithium compounds. Treatment of the compounds **4a−m** with strong acid (triflic acid) generates 1-azapentadienyl cations in situ upon protonation at the hydroxyl oxygen atom and subsequent water elimination. The intermediate cations undergo facile 4π-electrocyclization under ambient condition to give diversely substituted pyrroles **6a−m** in moderate to good yield. The product pyrrole **6k** could be characterized by X-ray diffraction. Quantum chemical calculations were performed to elucidate the mechanism of this reaction with respect to starting compounds, transition states, and products. They support the proposed mechanism of a 4π-conrotatory Möbius-type electrocyclic ring-closure reaction.



INTRODUCTION

Pyrrole is a structural unit of immense importance occurring as a building block of many physiologically important natural products such as heme, chlorophyll, and vitamin B12 among others.[1] It has also been extensively used in the synthesis of a variety of pharmaceutical agents[2] along with its application in the field of material science[3] for conducting polymers,[4] molecular optics,[5] etc. Many substituted pyrroles have been isolated mainly from marine sources, and they show important biological properties.[6] This general importance is still inspiring synthetic chemists to find new ways to synthesize pyrrole and its derivatives. There is a whole range of methods available for the synthesis of pyrrole.[1a,7] Multicomponent reactions[8] and metal-catalyzed reactions[9] are two of the predominantly applied strategies among others.

As part of a continuing project investigating the influence of heteroatoms on the reactivity of positively and negatively charged polyenyl species, we have been able to demonstrate computationally and experimentally that 1-azapentadienyl cations[10] are quite reactive intermediates that stabilize themselves by undergoing a facile conrotatory 4π-electrocyclization reaction to give pyrroles. 1-Azapentadienyl cations might be considered to be vinylogous 1-azaallyl cations, which were studied by Creary et al.[11] For the generation of these reactive intermediates **1** we used 1-azapentadienyl derivatives (and also 1-oxapentadienyl cations for the corresponding furans) with an appropriate leaving group (acetate) at the 5-position (Scheme 1).[12]

Later we also showed that 1-azapenta-1,4-diene-3-ones **3** can be conveniently activated to undergo cyclization reactions upon treatment with a strong Brønsted acid to give 1-aza-3-hydroxypentadienyl cations, which cyclize to variably substituted hydroxy pyrroles (aza-Nazarov reaction,[13] Scheme 2).[14]

Whereas the products of a classical Nazarov cyclization are characterized by a cyclopentenone structure, the products of an aza-Nazarov ring-forming reaction always contain a hydroxy function in the 3-position, which in the case of pyrroles is the reason for the substantial instability of such compounds. We bypassed this problem by working up the reaction mixture using acetic anhydride in order to isolate the much more stable acetates instead of the hydroxy pyrroles (Scheme 2).

However, the formation of this 3-hydroxy- or 3-acetoxy group may be regarded to be a certain limitation of this cyclization method. Thus, a more general control in terms of the substitution pattern at this position seemed to be desirable. Substituent redundancy in the final product is also a common problem with the multicomponent approach for the formation of pyrroles.[8]

In order to circumvent this limitation we became interested in the generation of 1-azapentadienyl cations **1** from 1-azapenta-1,4-diene-3-ols **4** by use of strong Brønsted acids ("super acid","superelectrophilic conditions"). This led us to propose that compounds of type **4**, with a hydroxyl group at the 3-position acting as leaving group upon protonation, might be the substrate of choice (Scheme 3).

Herein we report a highly versatile linear approach to form pyrroles through a conrotatory 4π-electrocyclization reaction.

RESULTS

Synthesis of the Precursor and Model Reaction. We envisaged 1-azapenta-1,4-diene-3-one **3a** as a suitable precursor for the synthesis of the required 1-azapenta-1,4-diene-3-ol **4a** from an 1,2-addition of an organometallic reagent, e.g.,

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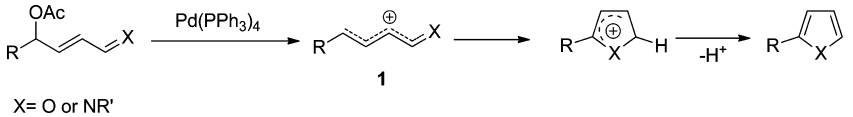
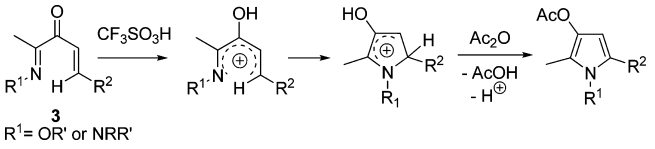
Scheme 1. Cyclization of 1-Aza- or 1-Oxapentadienyl Cation 1 upon Cleavage of an Acetate Leaving Group from the 5-Position of an Appropriately Substituted 1-Aza- or 1-Oxapenta-1,3-diene



Scheme 2. Cyclization of 1-Azapenta-1,4-diene-3-ones 3 to Pyrroles upon Treatment with Strong Brønsted Acid



methyllithium or others to the carbonyl group. As published earlier, compound **3a** was efficiently synthesized through a two-step procedure involving condensation of a 1,2-diketone with a substituted hydroxylamine or hydrazine followed by aldol condensation with an aldehyde.[14] The required starting compound for the ring-closure reaction, 1-azapenta-1,4-diene-3-ol **4a**, was obtained in 68% yield by treatment of **3a** with MeLi (1.6 M in hexane) in THF at −78 °C (Scheme 4). This reaction proceeded in high regio- and chemoselectivity as the 1,2-addition product of MeLi to the carbonyl group was observed exclusively without any product of 1,4-addition or addition to the C═N bond.

This precursor **4a** was screened with respect to a range of Brønsted acids and reaction conditions for the intended cyclization reaction (Table 1). The use of concd H_2SO_4 did not give a clean reaction. The use of polyphosphoric acid (PPA) also gave an intractable mixture of products. Interestingly, CH_3CO_2H did not force any reaction even at high temperature. Then we turned our attention to the "super acid" triflic acid. We found that the alcohol **4a** underwent a clean reaction in 15 min at −10 °C when 1 or more than 1 equiv of triflic acid was used in dilute dichloromethane solution to give **6a** as the sole product in 20−40% yield (Schemes 5, Table 1, entries 4−6). Best yields were obtained with 2 equiv of acid in dilute solution (0.025 M) (entry 6). However, 5 equiv of acid gave no detectable product (entry 7).

In the presence of 1.2 equiv of trifluoroacetic acid an unexpected product **7** was obtained, containing formally two molecules of $\mathbf{5a}^+$ (Table 1, entry 8 and Scheme 6). Substoichiometric amounts of triflic acid (0.4 equiv, entry 9) also gave compound **7** as the only product. This can be rationalized by the fact that at any point of time during the reaction pyrrole **6a** and uncyclized pentadienyl cation $\mathbf{5a}^+$ coexist in the reaction medium and react to give **7** by electrophilic aromatic substitution at C-4 position of the pyrrole **6a**.

Scheme 4. Synthesis of the Cyclization Precursor, 1-Azapenta-1,4-diene-3-ol 4a

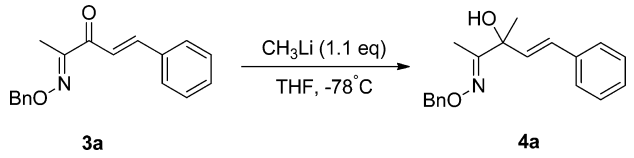
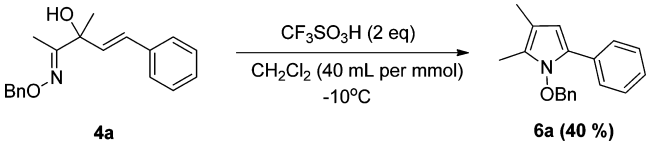


Table 1. Optimization Attempts for the Cyclization of 4a

entry	acid used	amount of acid (equiv)	reaction conditions[a]	product	yield (%)
1	concd H_2SO_4	1.2	CH_2Cl_2	intractable mix.	
2	PPA	excess	CH_2Cl_2	intractable mix.	
3	CH_3COOH	1.2	CH_2Cl_2	no reaction[b]	
4	CF_3SO_3H	1	CH_2Cl_2 (0.025 M)	**6a**	32
5	CF_3SO_3H	2	CH_2Cl_2 (0.2 M)	**6a**	<20[c]
6	CF_3SO_3H	2	CH_2Cl_2 (0.025 M)	**6a**	40
7	CF_3SO_3H	5	CH_2Cl_2 (0.025 M)	**6a**	
8	CF_3COOH	1.2	CH_2Cl_2	**7**	67
9	CF_3SO_3H	0.4	CH_2Cl_2	**7**	53

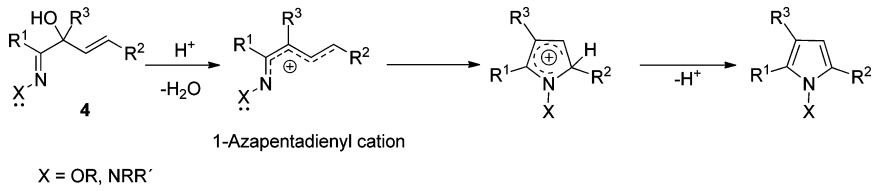
[a]All reactions were carried out at −10 °C. [b]No reaction was observed even at elevated temp; starting material could be recovered. [c]The product pyrrole **6a** could not be purified completely in this case.

Scheme 5. Optimized Reaction Conditions for the Synthesis of Pyrrole 6a from 4a



We conclude from these optimization experiments that the key to the success of this reaction is the availability of a sufficient amount of protons in the reaction medium at any time during the reaction in order to protonate all the substrate molecules almost simultaneously. This condition can be assured only in the presence of at least stoichiometric amounts of a very strong acid.

Scheme 3. Synthesis of Pyrroles from 3-Hydroxy-1-aza-penta-1,4-dienes



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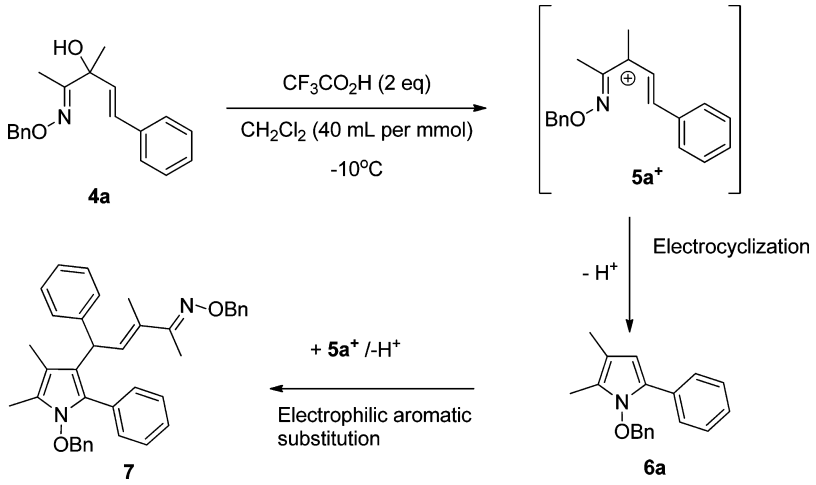
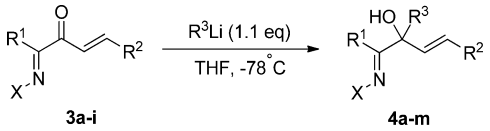
Scheme 6. Reaction of Precursor 4a with Trifluoroacetic Acid (TFA)



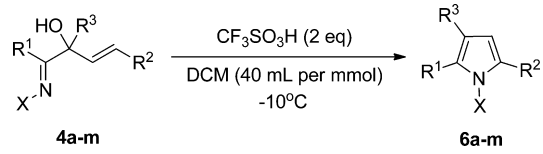
Scope of the Reaction. In order to study the scope of the ring-forming reaction under these optimized reaction conditions, we synthesized a large number of compounds **4b–m**. Different substituents R^1, R^2, and X were introduced by the appropriate choice of the precursors **3a–i**.[14] Varying substituents R^3 came from the respective organometallic species R^3Li. All compounds **4b–m** were efficiently obtained in moderate to good yields exactly under the reaction condition mentioned in Scheme 7 (Table 2).

Scheme 7. Synthesis of 1-Azapenta-1,4-diene-3-ols 4a–m



Upon protonation using 2 equiv of triflic acid in dilute dichloromethane solution at −10 °C, all substrates **4a–m** reacted to give pyrroles in moderate to good yields (Scheme 8, Table 3), thus allowing the controlled introduction of various alkyl and aryl substituents at C2 and C3, of aryl and heteroaryl groups at C5, and of alkoxy and amino groups at N1 of the pyrrole skeleton. The aryl substituents R^2 may carry either electron-withdrawing or electron-donating groups in the 2- or 4-position. It is worth noting that pyrroles having alkyl chains at the 3-position are key units found in many functional organic materials.[15] The reaction worked with similar facility when oximes (entries 1–10) or hydrazones were used (entries 11–13). The yield was generally found to be higher in cases with aryl groups (entries 8 and 10) at the C-3 position as compared to those with an alkyl group at the same position. In the alkyl cases we observed the formation of byproducts in larger quantities compared to the aryl examples, possibly an indication of competing polymerization.

Scheme 8. Acid-Promoted Cyclization Reaction of Compounds 4a–m



In general the pyrroles were easily identified by ^1H (proton at C4 at 6.0 to 6.8 ppm) and ^{13}C NMR (C3, C4 at 100–110 ppm) spectroscopy. The structure of the compound **6k** was also confirmed by single crystal X-ray analysis (Figure 1).

Table 2. Yields and Substitution Patterns of 1-Azapenta-1,4-diene-3-ols 4a–m from the Corresponding 1-Azapenta-1,4-diene-3-ones 3a–i

entry	starting compound	product	X	R^1	R^2	R^3	yield (%)
1	**3a**	**4a**	OBn	Me	Ph	Me	68
2	**3b**	**4b**	OBn	Me	2-Br-Ph	Me	57
3	**3c**	**4c**	OBn	Me	2-OCH_3-Ph	Me	61
4	**3d**	**4d**	OBn	Me	4-Cl-Ph	Me	64
5	**3e**	**4e**	OBn	Me	4-Me-Ph	Me	68
6	**3b**	**4f**	OBn	Me	2-Br-Ph	*n*-Bu	51
7	**3b**	**4g**	OBn	Me	2-Br-Ph	*i*-Pr	45
8	**3b**	**4h**	OBn	Me	2-Br-Ph	Ph	46
9	**3f**	**4i**	OBn	Me	2-thienyl	Me	63
10	**3d**	**4j**	OBn	Me	4-Cl-Ph	4-Me-Ph	60
11	**3g**	**4k**	N(Me)Ph	Me	Ph	Me	51
12	**3h**	**4l**	N(Me)Ph	Me	4-Me-Ph	Me	65
13	**3i**	**4m**	1-indolinyl	Ph	Ph	Me	79

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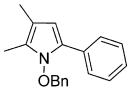
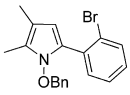
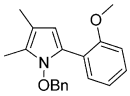
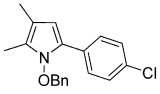
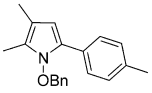
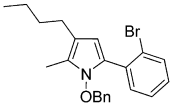
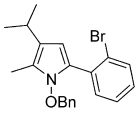
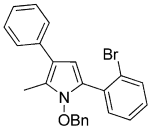
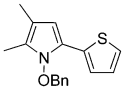
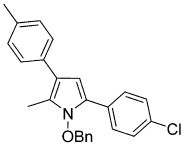
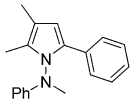
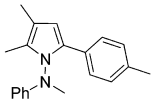
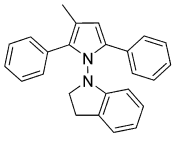
Table 3. Yields and Structures of the Pyrroles 7a−m

Entry	Precursor	Product	Structure of the Product	Yield (%)
1	**4a**	**6a**		40
2	**4b**	**6b**		53
3	**4c**	**6c**		29
4	**4d**	**6d**		30
5	**4e**	**6e**		32
6	**4f**	**6f**		50
7	**4g**	**6g**		30
8	**4h**	**6h**		83
9	**4i**	**6i**		36
10	**4j**	**6j**		64
11	**4k**	**6k**		54
12	**4l**	**6l**		67
13	**4m**	**6m**		33

DISCUSSION

The proposed mechanism of the reaction is depicted in Scheme 9. The hydroxyl group of the 1-azapenta-1,4-diene-3-ol **4** gets protonated in the presence of acid, and the H_2O molecule is eliminated to generate the delocalized 1-azapentadienyl cation $\mathbf{5}^+$, the precursor for the cyclization. This cation has to undergo several conformational changes through C−C bond rotation to attain the required "U"-conformation, the active conformation for the electrocyclization. Then this cation undergoes the 4π conrotatory electrocyclization to form the pyrrolium cation **8**, which upon proton elimination with aromatization gives the pyrrole **6**.

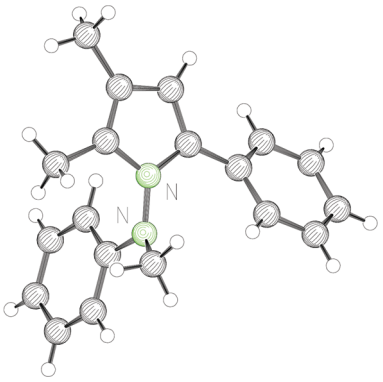


Figure 1. Molecular structure of **6k** as obtained by X-ray diffraction.

This suggested mechanism is well supported by quantum chemical calculation at the B3LYP/6-311G(d,p)//B3LYP/6-311G(d,p) and the SCS-MP2/6-311G(d,p)//B3LYP/6-311G-(d,p) level of theory.[16−19] For the first step of the reaction sequence, the gas phase protonation, quantum chemical calculations indicate a preferred *O*-protonation over *N*-protonation of the model substrate **4n** ($R^1 = R^3 = Me$, R^2 = Ph, X = OCH_3) by approximately 4 kcal/mol. This *O*-protonated species is expected to lose easily a molecule of water to generate the cation $\mathbf{5n}^+$, the 1-azapentadienyl cation (Scheme 9).

For the second reaction step, the electrocyclization, the W-shaped conformer $\mathbf{W\text{-}5n}^+$ has to undergo two consecutive bond rotations in order to attain the appropriate conformation (Scheme 10). The rotational barrier from $\mathbf{W\text{-}5n}^+$ to the sickle-shaped $\mathbf{S\text{-}5n}^+$ through rotation about C2−C3 (**TS** $\mathbf{W\text{-}5n}^+\mathbf{\text{-}S\text{-}5n}^+$) was calculated to be 8.4 kcal/mol. $\mathbf{S\text{-}5n}^+$ then undergoes the next conformational change through rotation about C3−C4 with a barrier of 19.4 kcal/mol to convert into the U-shaped conformer $\mathbf{U\text{-}5n}^+$ (**TS** $\mathbf{S\text{-}5n}^+\mathbf{\text{-}U\text{-}5n}^+$) required for electrocyclization. The cyclization of this cation $\mathbf{U\text{-}5n}^+$ to pyrrolium cation $\mathbf{8n}^+$ was found to be highly exothermic (ca. 24 kcal/mol) with a very low activation barrier of only 0.04 kcal/mol (**TS** $\mathbf{U\text{-}5n}^+\mathbf{\text{-}8n}^+$) (Scheme 10). These calculated barriers correspond well with the observed feasibility of the reaction and the reaction conditions (−10 °C, short reaction times). The calculated exothermicity of the reaction matches well with the observations made earlier by us[12] for the cyclization of 1-azapentadienyl cation and calculations by Sorensen and Rauk for the cyclization of pentadienyl cations (15−35 kcal/mol).[20] Whereas the relative energies of the open-chain conformers coincide well at both levels of theory, surprisingly large differences are found for the relative energies of the transition state and for the cyclic product.

The transition state **TS** $\mathbf{U\text{-}5n}^+\mathbf{\text{-}8n}^+$ of the cyclization is nonplanar with dihedral angles of N1−C2−C3−C4 = 17.98° and C2−C3−C4−C5 = 9.44° (Figure 2). The partially formed C−N bond in the transition state **TS** has a length of 2.17 Å.

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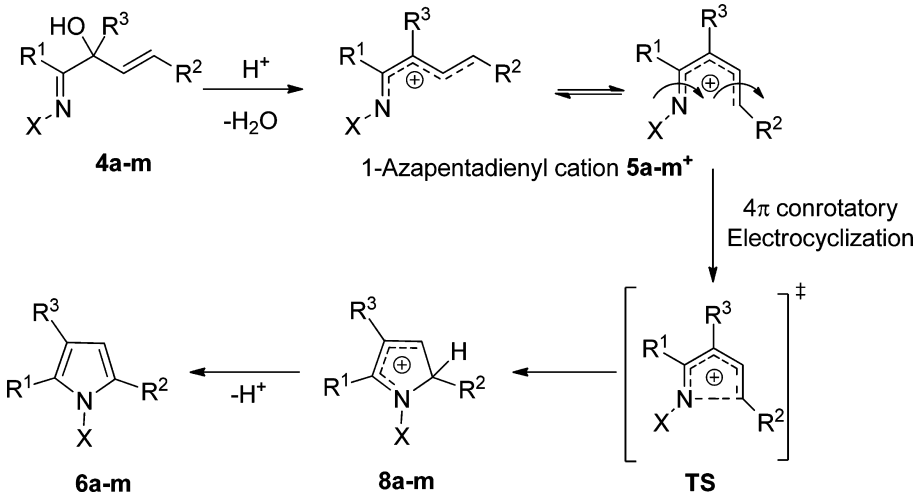
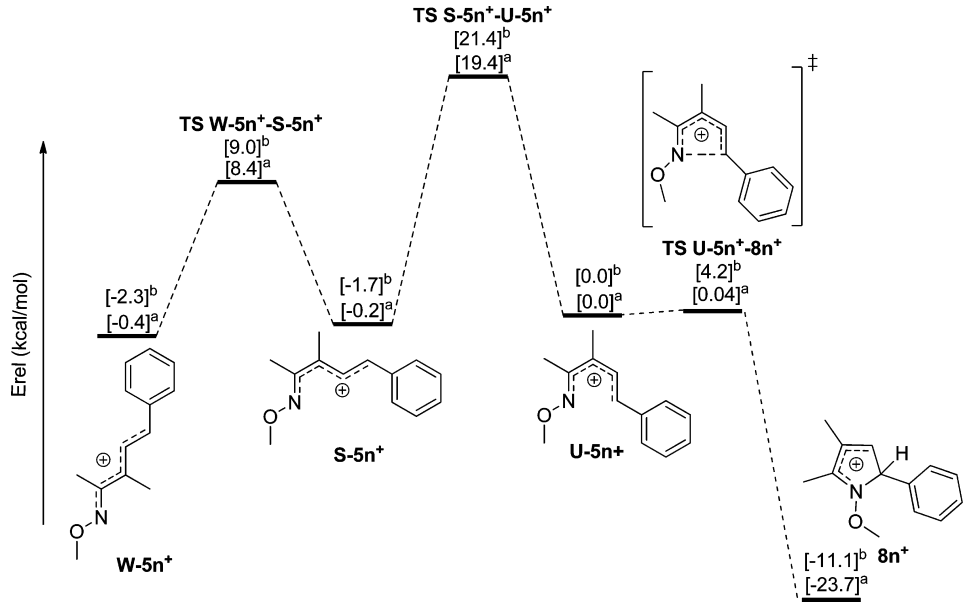
Scheme 9. Proposed Reaction Mechanism for the Cyclization of Compounds 4 To Give Pyrroles 6



Scheme 10. SCS-MP2 Energy Profile for the Cyclization of Cation W-5n+ to Pyrrolium Cation 8n+



[a]SCS-MP2/6-311G(d,p)//B3LYP/6-311G(d,p)+ZPE (kcal/mol).

[b]B3LYP/6-311G(d,p)// B3LYP/6-311G(d,p)+ZPE (kcal/mol).

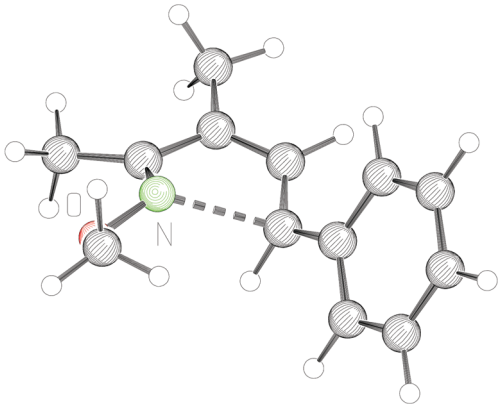


Figure 2. Calculated transition state **TS U-5n+-8n+** for the cyclization (B3LYP/6-311G(d,p)).

This indicates an early transition state, a characteristic feature for the highly exothermic reactions according to Hammond's postulate. Houk et al. have reported that the conrotatory electrocyclization of the pentadienyl cation to the cyclopentenyl cation proceeds through a transition state with a partially formed C−C bond (2.27 Å).[21]

The nature of the electrocyclization reaction was investigated by analyzing the transition state **U-5n+-8n+** with respect to NBO charges at the termini of the 1-azapentadienyl cation and to NICS values. The NBO charge separation between the atoms N1 and C5 was found to be only 0.16 e, which indicates little ionic character for the reaction. The lowest NICS value[22] for the unsymmetrical transition state with respect to an axis perpendicular to the plane of the ensuing heterocycle was calculated to be −7.2 [(B3LYP/6-311G(d,p)], which is strongly indicative of the Möbius type[23] aromatic character (Figure 3). Upon comparing the optimized geometries of the

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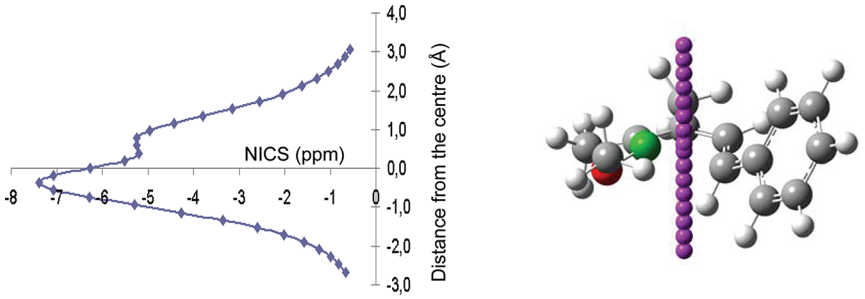

Figure 3. Calculated NICS values for the transition structure **TS U-5n$^+$-8n$^+$** (left). Measuring points are along an axis perpendicular to the center of the developing cyclic moiety (right).

open chain, transition state, and cyclic structure, it can be seen that the reaction is conrotatory in nature. We conclude that this ring-forming reaction shows all of the features of a Möbius aromatic conrotatory 4π electrocyclic ring-closure reaction.

CONCLUSION

In summary we have been able to demonstrate for the first time the synthetic use of 1-aza-3-hydroxy-penta-1,4-dienes **4** for the preparation of variably substituted *N*-alkoxy- and *N*-amino pyrroles **6**. The starting compounds **4** are easily accessible by treatment of 1-aza-penta-1,4-dien-3-ones **3** with various lithium compounds attacking the carbonyl function of **3** in a strongly chemoselective manner. Treatment of **4** with trifluoromethanesulfonic acid (triflic acid) yields the pyrroles **6** in moderate to good yield upon aqueous workup. Mechanistically, we suggest the intermediate formation of highly reactive 1-azapentadienyl cations after protonation at the hydroxyl group of **4** by the super acid and subsequent loss of water. Then, the 1-azapentadienyl cations undergo a pericyclic ring-closure reaction leading to the pyrroles **6** after proton loss and aromatization. High level quantum chemical calculations have been used to investigate the reaction mechanism theoretically. They indicate a conrotatory 4π electrocyclic ring-closure reaction. The calculated nonplanar transition state for the cyclization possesses Möbius-type aromatic character as indicated by NBO charges and NICS calculations. Further applications of this new methodology with regard to the use for the preparation of more complicated pyrrole derivatives are being currently investigated.

EXPERIMENTAL SECTION

Melting points are uncorrected. ^{1}H, ^{13}C, GCOSY, GHSQC, GHMBC, and 1D-NOE NMR spectroscopy: TMS (^{1}H) (0.00 ppm) and $CDCl_3$ (^{13}C) (77.0 ppm) were used as internal references. When necessary, the experiments were carried out with complete exclusion of moisture. Compounds **3** were prepared according to a literature procedure.[14]

General Procedure for the Formation of (1*E*,4*E*)-4-(Alkoxyimino)-1-aryl-pent-1-en-3-one 3. One equivalent of 3-benzyloxyimino-butan-2-one[14] was dissolved in the minimum amount of methanol, and 0.5 equiv of KOH (30% in methanol) was added. To this solution was added 1.1 equiv of aldehyde, and the mixture was stirred at room temperature. Usually after some time, a solid precipitated out of the solution. For completion, the reaction mixture was left to stir overnight at room temperature. Then, the solid was filtered off and washed with cold methanol to remove soluble impurities. In case the precipitate was not formed, the reaction mixture was cooled to 0 °C to allow precipitation. The crude products were purified by recrystallization.

(1E,4E)-4-((Benzyloxy)imino)-1-(2-methoxyphenyl)-pent-1-en-3-one **3c**. Compound **3c** was obtained from 3-benzyloxyimino-butan-2-one (0.382 g, 2 mmol) and 2-methoxybenzaldehyde (0.285 g, 2.1 mmol) according to the general procedure. The subsequent recrystallization from methanol gave the pure product (0.4 g, 1.3 mmol, 65%) as a pale yellow solid (mp 76−78 °C). ^{1}H NMR (300 MHz, CD_2Cl_2): δ (ppm) 1.95 (s, 3H, CH_3), 3.80 (s, 3H, OCH_3), 5.25 (s, 2H, OCH_2), 6.85−6.96 (m, 2H, CH_{ar}), 7.24−7.37 (m, 6H, CH_{ar}), 7.54 (dd, 1H, J = 7.8, 1.7 Hz, CH_{ar}), 7.61 (d, 1H, J = 16.2 Hz, CH_{ol}), 7.92 (d, 1H, J = 16.2 Hz, CH_{ol}). ^{13}C NMR (75 MHz, CD_2Cl_2): δ (ppm) 9.4 (CH_3), 55.9 (OCH_3), 77.9 (OCH_2), 111.6 ($CH_{ar/ol}$), 121.0 ($CH_{ar/ol}$), 121.5 ($CH_{ar/ol}$), 124.3 (C_q), 128.6 ($CH_{ar/ol}$), 128.8 ($CH_{ar/ol}$), 128.84 ($CH_{ar/ol}$), 129.0 ($CH_{ar/ol}$), 132.1 ($CH_{ar/ol}$), 137.7 (C_q), 138.3 ($CH_{ar/ol}$), 156.8 (C_q), 159.2 (C=N), 187.1 (C=O). IR (neat) $\tilde{\nu}$: 3069 (w), 3055 (w), 2982 (w), 2873 (w), 1672 (vs), 1493 (s), 1457 (s), 1376 (s), 1232 (s), 1212 (s), 1134 (m), 1082 (s), 1027 (m), 968 (m), 875 (s), 866 (s), 726 (s), 717 (s), 673 (m), 664 (m), 652 (s), 623 (s). HRMS (ESI): calcd for $C_{19}H_{19}NO_3Na$ 332.1263; found 332.1257. Anal. Calcd for $C_{19}H_{19}NO_3$: C, 73.77; H, 6.19; N, 4.53. Found: C, 73.72; H, 6.18; N, 4.53.

(1E,4E)-4-((Benzyloxy)imino)-1-(4-chlorophenyl)-pent-1-en-3-one **3d**. Compound **3d** was obtained from 3-benzyloxyimino-butan-2-one (0.382 g, 2 mmol) and 4-chlorobenzaldehyde (0.294 g, 2.1 mmol) according to the general procedure. The subsequent recrystallization from methanol gave the pure product **3d** (0.363 g, 1.16 mmol, 58%) as a white solid (mp 122−123 °C). ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm) 1.98 (s, 3H, CH_3), 5.26 (s, 2H, OCH_2), 7.25−7.28 (m, 3H, CH_{ar}), 7.31−7.33 (m, 4H, CH_{ar}), 7.43 (d, 2H, J = 8.6 Hz, CH_{ar}), 7.50 (d, 1H, J = 16.0 Hz, CH_{ol}), 7.57 (d, 1H, J = 16.0 Hz, CH_{ol}). ^{13}C NMR (75 MHz, $CDCl_3$): δ (ppm) 9.4 (CH_3), 77.6 (OCH_2), 121.1 ($CH_{ar/ol}$), 128.29 ($CH_{ar/ol}$), 128.31 ($CH_{ar/ol}$), 128.5 ($CH_{ar/ol}$), 129.1 ($CH_{ar/ol}$), 129.7 ($CH_{ar/ol}$), 133.6 ($CH_{ar/ol}$), 136.2 (C_q), 136.9 (C_q), 141.6 ($CH_{ar/ol}$), 156.4 (C=N), 186.5 (C=O). IR (neat) $\tilde{\nu}$: 3073 (w), 3048 (w), 2933 (w), 2843 (w), 1676 (vs), 1482 (s), 1457 (s), 1365 (s), 1231 (s), 1214 (s), 1135 (m), 1091 (s), 1027 (m), 978 (m), 876 (s), 864 (s), 727 (s), 717 (s), 665 (m), 647 (m), 622 (s), 613 (s). HRMS (ESI): calcd for $C_{18}H_{16}NO_2ClNa$ 336.0767; found 336.0762. Anal. Calcd for $C_{18}H_{16}NO_2Cl$: C, 68.90; H, 5.14; N, 4.46. Found: C, 68.86; H, 5.18; N, 4.40.

(1E,4E)-4-(Phenoxyimino)-1-(thiophen-2-yl)-pent-1-en-3-one **3f**. Compound **3f** was obtained from 3-benzyloxyimino-butan-2-one (1.0 g, 5.24 mmol) and 2-thiophene carbaldehyde (0.59 g, 0.49 mL, 5.24 mmol) according to the general procedure. Pure product **3f** (0.863 g, 3.03 mmol, 58%) was obtained by recrystallization from CH_2Cl_2 as a white solid (mp 84 °C). ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 1.95 (s, 3H, CH_3), 5.23 (s, 2H, OCH_2), 6.95 (dd, 1H, J = 5.1, 3.7 Hz, CH_{ar}), 7.19−7.21 (m, 1H, CH_{ar}), 7.27−7.35 (m, 7H, CH_{ar}), 7.72 (d, 1H, J = 15.7 Hz, CH_{ol}). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 9.4 (CH_3), 77.6 (OCH_2), 119.8 ($CH_{ar/ol}$), 128.25 ($CH_{ar/ol}$), 128.29 ($CH_{ar/ol}$), 128.5 ($CH_{ar/ol}$), 128.55 ($CH_{ar/ol}$), 128.7 ($CH_{ar/ol}$), 131.8 ($CH_{ar/ol}$), 135.5 ($CH_{ar/ol}$), 136.9 (C_q), 140.7 (C_q), 156.2 (C=N), 186.4 (C=O). IR (neat) $\tilde{\nu}$: 3069 (w), 3057 (w), 2843 (w), 2361 (m), 1671 (vs), 1487 (s), 1446 (s), 1375 (m), 1245 (s), 1214 (m), 1163 (m), 1097 (s), 1046 (m), 978 (m), 863 (s), 747 (s), 717 (s), 664 (m), 642 (m), 639 (s), 616 (m). HRMS (ESI): calcd for $C_{16}H_{15}NO_2SNa$ 308.0721; found 308.0718. Anal. Calcd for $C_{16}H_{15}NO_2S$: C, 67.34; H, 5.30; N, 4.91. Found: C, 67.12; H, 5.42; N, 4.83.

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(1E,4E)-4-(2-Methyl-2-phenylhydrazono)-1-(p-tolyl)-pent-1-en-3-one ***3h.*** Compound **3h** was obtained from the hydrazone (*E*)-3-(2-methyl-2-phenylhydrazono)butan-2-one[14] (1.0 g, 5.26 mmol) and 4-methylbenzaldehyde (0.693 g, 5.78 mmol) according to the general procedure. The subsequent recrystallization from methanol gave the pure product as a yellow solid (mp 97−99 °C) in 44% yield. ^{1}H NMR (300 MHz, CD_2Cl_2): δ (ppm) 2.05 (s, 3H, CH_3), 2.29 (s, 3H, PhCH_3), 3.44 (s, 3H, NCH_3), 6.95−7.00 (m, 1H, CH_{ar}), 7.14 (d, 2H, J = 8.1 Hz, CH_{ar}), 7.18−7.20 (m, 2H, CH_{ar}), 7.26−7.31 (m, 2H, CH_{ar}), 7.47 (d, 2H, J = 8.1 Hz, CH_{ar}), 7.56 (d, 1H, J = 16.0 Hz, CH_{ol}), 7.90 (d, 1H, J = 16.0 Hz, CH_{ol}). ^{13}C NMR (75 MHz, CD_2Cl_2): δ (ppm) 15.0 (CH_3), 21.6 (PhCH_3), 43.6 (NCH_3), 117.5 (C$H_{ar/ol}$), 120.9 (C$H_{ar/ol}$), 122.7 (C$H_{ar/ol}$), 128.7 (C$H_{ar/ol}$), 129.4 (C$H_{ar/ol}$), 129.9 (C$H_{ar/ol}$), 133.2 (C_q), 140.9 (C_q), 141.5 (C$H_{ar/ol}$), 149.7 (C_q), 150.0 (C═N), 188.7 (C═O). IR (neat) $\tilde{\nu}$: 3061 (w), 3028 (w), 2918 (w), 1651 (m), 1593 (m), 1557 (m), 1491 (m), 1348 (w), 1306 (m), 1277 (m), 1206 (m), 1177 (m), 1103 (m), 1059 (m), 1028 (m), 997 (m), 874 (m), 806 (m), 743 (s). HRMS (ESI): calcd for $C_{19}H_{20}N_2ONa$ 315.1473; found 315.1468. Anal. Calcd for $C_{19}H_{20}N_2O$: C, 78.05; H, 6.89; N, 9.58. Found: C, 77.99; H, 7.03; N, 9.55.

(1E,3E)-1-(Indolin-1-ylimino)-1,4-diphenyl-but-3-en-2-one ***3i.*** To a dry Schlenk flask was added *t*-BuOK (0.112 g, 1 mmol) was added and dissolved in abs THF (10 mL). Then, the ketophosphonate (*E*)-dimethyl(3-(indolin-1-ylimino)-2-oxo-3-phenylpropyl) phosphonate[13h] (0.372 g, 1 mmol) was dissolved in 2 mL of THF and added to the base. This reaction mixture was stirred at RT for 1 h followed by the addition of benzaldehyde (0.12 mL, 1.1 mmol), dissolved in 1 mL of THF. The progress of the reaction was monitored by TLC. After the completion of the reaction, the solvent was evaporated in vacuo. The residue was then dissolved in CH_2Cl_2, washed with brine, dried over $MgSO_4$, and concentrated to obtain the crude product. The subsequent recrystallization gave 0.25 g (0.72 mmol, 72%) of **3i** as a yellow solid (mp 127−128 °C). ^{1}H NMR (300 MHz, CD_2Cl_2): δ (ppm) 2.93 (t, 2H, J = 8.2 Hz, NCH_2CH_2), 3.22 (t, 2H, J = 8.2 Hz, NCH_2CH_2), 6.92 (td, J = 7.4, 0.7 Hz, 1H, CH_{ar}), 7.06 (d, J = 7.3 Hz, 1H, CH_{ar}), 7.22−7.26 (m, 3H, CH_{ar}), 7.30−7.36 (m, 7H, CH_{ar}), 7.59 (d, J = 7.3 Hz, 2H, CH_{ar}), 7.63 (d, J = 16.0 Hz, 1H, CH_{ol}), 8.12 (d, J = 16.0 Hz, 1H, CH_{ol}). ^{13}C NMR (75 MHz, CD_2Cl_2): δ (ppm) 26.9 (NCH_2CH_2), 52.4 (NCH_2CH_2), 110.2 (C$H_{ar/ol}$), 121.0 (C$H_{ar/ol}$), 122.1 (C$H_{ar/ol}$), 124.1 (C$H_{ar/ol}$), 126.5 (C$H_{ar/ol}$), 127.1 (C$H_{ar/ol}$), 127.21 (C$H_{ar/ol}$), 127.22 (C$H_{ar/ol}$), 127.5 (C$H_{ar/ol}$), 127.8 (C$H_{ar/ol}$), 128.7 (C$H_{ar/ol}$), 129.3 (C_q), 133.5 (C_q), 134.8 (C_q), 139.9 (C$H_{ar/ol}$), 140.5 (C_q), 146.9 (C_q), 187.4 (C═O). IR (neat) $\tilde{\nu}$: 3458 (m), 3421 (m), 2359 (w), 2180 (w), 2154 (w), 1653 (s), 1607 (s), 1547 (s), 1481 (m), 1325 (m), 1302 (s), 1269 (s), 1240 (m), 1163 (m), 1126 (m), 1115 (m), 1103 (s), 1065 (s), 1011 (m), 957 (s), 829 (s), 750 (m), 716 (m), 696 (m). HRMS (ESI): calcd for $C_{24}H_{20}N_2OH$: 353.1654; found 353.1648.

General Procedure for the Preparation of (2*E*,4*E*)-5-(2-Aryl)-3-hydroxy-3-alkyl-pent-4-en-2-one *O*-Benzyl Oxime (4). To a clean dry Schlenk flask was transferred dry THF (10 mL per mmol). To this was added 1-azapenta-1,4-diene-3-one **3** (1 equiv), and the mixture was cooled to −78 °C. Then the corresponding organolithium species (1.1 equiv) was added to the mixture dropwise. Then the reaction mixture was stirred at the same temperature. The progress of the reaction was monitored by TLC. Once the reaction was complete the mixture was quenched with satd aq NH_4Cl solution, diluted with CH_2Cl_2, and washed three times with water. The combined organic layers were dried with Na_2SO_4 and concentrated in vacuo. Finally, the alcohol **4** was purified by column chromatography.

(2E,4E)-3-Hydroxy-3-methyl-5-phenyl-pent-4-en-2-one O-Benzyl Oxime ***(4a).*** This compound was obtained from the corresponding ketone **3a** (0.279 g, 1 mmol) and methyllithium (1.6 M in Et_2O) (0.7 mL, 1.1 mmol) according to the general procedure. The subsequent chromatographic purification (Et_2O/pentane, 1:3) gave 0.2 g (0.68 mmol, 68%) of **4a** as a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm) 1.46 (s, 3H, CH_3COH), 1.83 (s, 3H, CH_3CN), 3.90 (s, br, 1H, OH), 5.06 (s, 2H, OCH_2Ph), 6.16 (d, 1H, J = 16.0 Hz, CH_{olef}), 6.58 (d, 1H, J = 16.0 Hz, CH_{olef}), 7.16−7.31 (m, 10H, CH_{arom}); ^{13}C NMR (75 MHz, $CDCl_3$): δ (ppm) 11.4 (CH_3OH), 25.9(CH_3CN), 74.4 (C_q, COH), 76.1 (CH_2), 126.6 (C$H_{arom/olef}$), 127.7 (C$H_{arom/olef}$), 127.8 (C$H_{arom/olef}$), 128.2 (C$H_{arom/olef}$), 128.4 (C$H_{arom/olef}$), 128.5 (C$H_{arom/olef}$), 129.4 (C$H_{arom/olef}$), 132.8 (C$H_{arom/olef}$), 136.6 (C_q), 137.6 (C_q), 159.4 (CH_3CN). IR (neat) $\tilde{\nu}$: 3451 (M), 3063 (M), 3046 (M), 3030 (M), 2980 (M), 2930 (M), 2868 (M), 2361 (S), 2334 (S), 1497 (M), 1466 (M), 1454 (M), 1437 (M), 1368 (M), 1244 (M), 1207 (M), 1180 (M), 1109 (M), 1082 (M), 1022 (M), 968 (M), 881 (M), 866 (M), 822 (M), 746 (M), 714 (M), 696 (M), 677 (M), 652 (M), 611 (M), 586 (M), 581 (M), 573 (M), 552 (M), 542 (M), 536 (M), 527 (M). HRMS (ESI): calcd for $C_{19}H_{21}NO_2Na$ 318.1470; found 318.1465.

(2E,4E)-5-(2-Bromophenyl)-3-hydroxy-3-methyl-pent-4-en-2-one O-Benzyl Oxime ***(4b).*** This compound was obtained from the corresponding ketone **3b** (0.359 g, 1 mmol) and methyllithium (1.6 M in Et_2O) (0.7 mL, 1.1 mmol) according to the general procedure. The subsequent chromatographic purification (Et_2O/pentane, 1:3) gave 0.21 g (0.57 mmol, 57%) of **4b** as a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm) 1.48 (s, 3H, CH_3COH), 1.85 (s, 3H, CH_3CN), 3.81 (s, br, 1H, OH), 5.06 (s, 2H, OCH_2Ph), 6.07 (d, 1H, J = 15.9 Hz, CH_{olef}), 6.91 (d, 1H, J = 15.9 Hz, CH_{olef}), 6.99−7.04 (m, 1H, CH_{arom}), 7.17 (t, 1H, J = 7.5 Hz, CH_{arom}), 7.22−7.29 (m, 5H, CH_{arom}), 7.39 (d, 1H, J = 7.8 Hz, CH_{arom}), 7.46 (d, 1H, J = 8.0 Hz, CH_{arom}); ^{13}C NMR (75 MHz, $CDCl_3$): δ (ppm) 11.4 (CH_3OH), 25.7(CH_3CN), 74.7 (C_q, COH), 76.3 (CH_2), 123.9 (C_q), 127.2 (C$H_{arom/olef}$), 127.4 (C$H_{arom/olef}$), 127.9 (C$H_{arom/olef}$), 128.2 (C$H_{arom/olef}$), 128.4 (C$H_{arom/olef}$), 128.6 (C$H_{arom/olef}$), 129.0 (C$H_{arom/olef}$), 132.9 (C$H_{arom/olef}$), 136.1 (C$H_{arom/olef}$), 136.7 (C_q), 137.6 (C_q), 159.0 (CH_3CN). IR (neat) $\tilde{\nu}$: 3451 (w), 3063 (w), 3046 (w), 3030 (w), 2980 (w), 2930 (w), 2868 (w), 2361 (S), 1466 (M), 1454 (M), 1437 (M), 1368 (S), 1244 (M), 1207 (M), 1180 (M), 1109 (M), 1082 (M), 1022 (VS), 968 (VS), 881 (M), 866 (M), 822 (M), 746 (VS), 714 (M), 696 (VS), 677 (M), 652 (M), 611 (M), 586 (M), 581 (M), 573 (M), 552 (M), 542 (M), 536 (M), 527 (M). HRMS (ESI): calcd for $C_{19}H_{20}BrNO_2Na$ 396.0575; found 396.0563. Anal. Calcd for $C_{19}H_{20}BrNO_2$: C, 60.97; H, 5.39; N, 3.74. Found: C, 60.77; H, 5.78; N, 3.56

(2E,4E)-3-Hydroxy-5-(2-methoxyphenyl)-3-methyl-pent-4-en-2-one O-Benzyl Oxime ***(4c).*** This compound was obtained from corresponding ketone **3c** (0.309 g, 1 mmol) and methyllithium (1.6 M in Et_2O) (0.7 mL, 1.1 mmol) according to the general procedure. The subsequent chromatographic purification (Et_2O/pentane, 1:3) gave 0.19 g (0.61 mmol, 61%) of **4c** as a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm) 1.47 (s, 3H, CH_3COH), 1.84 (s, 3H, CH_3CN), 3.76 (s, 3H, OCH_3), 3.83 (s, br, 1H, OH), 5.06 (s, 2H, OC H_2Ph), 6.18 (d, 1H, J = 16.2 Hz, CH_{olef}), 6.79 (d, 1H, J = 8.2 Hz, CH_{arom}), 6.85 (d, 1H, J = 7.5 Hz, CH_{arom}), 6.92 (d, 1H, J = 16.2 Hz, CH_{olef}), 7.14 (d, 1H, J = 7.8 Hz, CH_{arom}), 7.29−7.31 (m, 5H, CH_{arom}), 7.34 (d, 1H, J = 7.7 Hz, CH_{arom}); ^{13}C NMR (75 MHz, $CDCl_3$): δ (ppm) 11.4 (CH_3), 25.8 (CH_3), 55.4 (OCH_3), 74.9 (C_q, COH), 76.2 (OCH_2Ph), 110.8 (C$H_{arom/olef}$), 120.6 (C$H_{arom/olef}$), 125.5 (C$H_{arom/olef}$), 126.9 (C$H_{arom/olef}$), 127.8 (C$H_{arom/olef}$), 128.1 (C$H_{arom/olef}$), 128.3 (C$H_{arom/olef}$), 128.7 (C$H_{arom/olef}$), 133.3 (C_q), 137.6 (C_q), 156.8 (C_q), 159.5 (C_q). IR (neat) $\tilde{\nu}$: 3449 (W), 3032 (W), 2978 (W), 2932 (W), 2837 (W), 1607 (S), 1578 (W), 1510 (VS), 1454 (W), 1368 (W), 1304 (W), 1246 (VS), 1175 (S), 1105 (S), 1030 (S), 972 (S), 930 (W), 851 (W), 816 (W), 741 (W), 698 (W), 608 (VS). HRMS (ESI): calcd for $C_{20}H_{23}NO_3Na$ 348.1576; found 348.1574.

(2E,4E)-5-(4-Chlorophenyl)-3-hydroxy-3-methyl-pent-4-en-2-one O-Benzyl Oxime ***(4d).*** This compound was obtained from the corresponding ketone **3d** (0.313 g, 1 mmol) and methyllithium (1.6 M in Et_2O) (1.1 mmol) according to the general procedure. The subsequent chromatographic purification (Et_2O/pentane, 1:3) gave 0.21 g (0.64 mmol, 64%) of **4d** as a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm) 1.45 (s, 3H, CH_3), 1.83 (s, 3H, CH_3), 3.85 (s, 1H, COH), 5.06 (s, 2H, OC H_2Ph), 6.14 (d, 1H, J = 16.0 Hz, CH_{olef}), 6.54 (d, 1H, J = 16.0 Hz, CH_{olef}), 7.20−7.29 (m, 9H, CH_{arom}); ^{13}C NMR (75 MHz, $CDCl_3$): δ (ppm) 11.4 (CH_3), 26.0 (CH_3), 74.6 (C_q, COH), 76.3 (CH_2Ph), 127.8 (C$H_{arom/olef}$), 127.9 (C$H_{arom/olef}$), 128.2 (C$H_{arom/olef}$), 128.4 (C$H_{arom/olef}$), 128.7 (C$H_{arom/olef}$), 133.4 (C$H_{arom/olef}$), 133.5 (C$H_{arom/olef}$), 135.1 (C_q), 137.5 (C_q), 159.2

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(C_q). IR (neat) $\tilde{\nu}$: 3314 (W), 3037 (W), 2918 (W), 2862 (W), 1690 (W), 1616 (W), 1504 (W), 1454 (W), 1368 (S), 1219 (W), 1179 (W), 1129 (S), 1008 (W), 969 (W), 813 (W), 779 (W), 698 (W). HRMS (ESI): calcd for $C_{19}H_{20}NO_2ClNa$ 352.1080; found 352.1075.

*(2E,4E)-3-Hydroxy-3-methyl-5-(p-tolyl)-pent-4-en-2-one O-Benzyl Oxime (**4e**).* This compound was obtained from the corresponding ketone **3e** (0. 293 g, 1 mmol) and methyllithium (1.6 M in Et_2O) (0.7 mL, 1.1 mmol) according to the general procedure. The subsequent chromatographic purification (Et_2O/pentane, 1:3) gave 0.21 g (0.68 mmol, 68%) of **4e** as a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm) 1.43 (s, 3H, CH_3COH), 1.80 (s, 3H, CH_3CN), 2.23 (s, 3H, PhCH_3), 3.81 (s, 1H, O*H*), 5.03 (s, 2H, OCH_2Ph), 6.09 (d, 1H, *J* = 16.0 Hz, CH_{olef}), 6.52 (d, 1H, *J* = 16.0 Hz, CH_{olef}), 7.01 (d, 2H, *J* = 8.0 Hz, CH_{arom}), 7.17 (d, 2H, *J* = 8.0 Hz, CH_{arom}), 7.20−7.23 (m, 1H, CH_{arom}), 7.25−7.27 (m, 5H, CH_{arom}); ^{13}C NMR (75 MHz, $CDCl_3$): δ (ppm) 11.4 (CH_3OH), 21.1 (PhCH_3) 26.0(CH_3CN), 74.7 (C_q, *C*OH), 76.2 (CH_2), 126.6 ($CH_{arom/olef}$), 127.9 ($CH_{arom/olef}$), 128.2 ($CH_{arom/olef}$), 128.4 ($CH_{arom/olef}$), 129.3 ($CH_{arom/olef}$), 129.3 ($CH_{arom/olef}$), 131.9 ($CH_{arom/olef}$), 133.8 (C_q), 137.6 (C_q), 137.7 (C_q), 159.6 (C_q). IR (neat) $\tilde{\nu}$: 3304 (W), 3030 (W), 2928 (W), 2862 (W), 1690 (W), 1611 (W), 1514 (W), 1454 (W), 1368 (S), 1209 (W), 1179 (W), 1109 (S), 1018 (W), 974 (W), 802 (W), 743 (W), 698 (W). HRMS (ESI): calcd for $C_{20}H_{23}NO_2Na$ 332.1626; found 332.1625.

*(E)-3-((E)-2-Bromostyryl)-3-hydroxy-heptan-2-one O-Benzyl Oxime (**4f**).* This compound was obtained from the corresponding ketone **3b** (0.354 g, 1 mmol) and *n*-butyllithium (1.6 M in hexane) (0.7 mL, 1.1 mmol) according to the general procedure. The subsequent chromatographic purification (Et_2O/pentane, 1:10) gave 0.19 g (0.51 mmol, 51%) of **4f** as a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm) 0.81 (t, 3H, *J* = 7.2 Hz, CH_2CH_3), 0.98−1.10 (m, 1H, $CH_2CH_2CH_3$), 1.24 (m, 2H, $CH_2CH_2CH_3$), 1.33−1.40 (m, 1H, COHCH_2), 1.68−1.73 (m, 2H, COHCH_2), 1.82 (s, 3H, CH_3CN), 3.97 (s, 1H, CO*H*), 5.05 (s, 2H, OCH_2Ph), 6.07 (d, 1H, *J* = 15.9 Hz, CH_{olef}), 6.94 (d, 1H, *J* = 15.9 Hz, CH_{olef}), 7.00 (dd, 1H, *J* = 7.7, 1.2 Hz, C H_{arom}), 7.12−7.15 (m, 1H, CH_{arom}), 7.18−7.23 (m, 2H, CH_{arom}), 7.24−7.26 (m, 2H, CH_{arom}), 7.37 (dd, 1H, *J* = 7.8, 1.4 Hz, C H_{arom}), 7.44 (dd, 1H, *J* = 8.0, 1.2 Hz, C H_{arom}); ^{13}C NMR (75 MHz, $CDCl_3$): δ (ppm) 11.5 (CH_3), 14.1 (CH_2CH_3), 22.9 (CH_2CH_2), 25.3 (CH_3CN), 37.8 (CH_2COH), 76.2 (CH_2OPh), 77.0 (C_qOH), 123.9 (C_q), 127.2 ($CH_{arom/olef}$), 127.4 ($CH_{arom/olef}$), 127.8 ($CH_{arom/olef}$), 128.1 ($CH_{arom/olef}$), 128.4 ($CH_{arom/olef}$), 128.7 ($CH_{arom/olef}$), 128.8 ($CH_{arom/olef}$), 132.9 ($CH_{arom/olef}$), 135.6 ($CH_{arom/olef}$), 136.9 (C_q), 137.6 (C_q), 158.3 (C =N). IR (neat) $\tilde{\nu}$: 3478 (W), 2955 (W), 2930 (W), 2870 (W), 2359 (W), 1497 (W), 1466 (M), 1454 (M), 1369 (M), 1209 (W), 1159 (W), 1022 (S), 970 (W), 916 (W), 750 (W), 698 (W), 631 (S), 538 (VS), 525 (VS). HRMS (ESI): calcd for $C_{22}H_{26}BrNO_2Na$ 440.1024; found 440.1018.

*(2E,4E)-5-(2-Bromophenyl)-3-hydroxy-3-isopropyl-pent-4-en-2-one O-Benzyl Oxime (**4g**).* This compound was obtained from the corresponding ketone **3b** (0.354 g, 1 mmol) and isopropyllithium (1.3 M in THF) (0.84 mL, 1.1 mmol) according to the general procedure. The subsequent chromatographic purification (Et_2O/pentane, 1:20) gave 0.17 g (0.45 mmol, 45%) of **4g** as a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm) 0.7 (d, 3H, *J* = 6.5 Hz, CHCH_3), 0.9 (d, 3H, *J* = 6.7 Hz, CHCH_3), 1.83 (s, 3H, CH_3CN), 1.98 (h, 1H, *J* = 6.7 Hz, C*H*(CH_3)$_2$), 3.95 (s, 1H, CO*H*), 5.05 (s, 2H, OC*H* $_2$Ph), 6.07 (d, 1H, *J* = 15.8 Hz, CH_{olef}), 6.97−7.02 (m, 2H, C$H_{arom/olef}$), 7.13−7.20 (m, 2H, CH_{arom}), 7.37 (d, 2H, *J* = 7.7 Hz, CH_{arom}), 7.45 (d, 2H, *J* = 8.0 Hz, CH_{arom}); ^{13}C NMR (75 MHz, $CDCl_3$): δ (ppm) 11.5 (CH(CH_3)$_2$), 16.3 (CH_3), 16.3 (CH_3), 33.6 (CH_3CN), 76.2 (CH_2OPh), 79.3 (C_qOH), 123.2 (C_q), 127.2 ($CH_{arom/olef}$), 127.4 ($CH_{arom/olef}$), 127.8 ($CH_{arom/olef}$), 128.0 ($CH_{arom/olef}$), 128.3(CH $_{arom/olef}$), 128.7 ($CH_{arom/olef}$), 129.3 ($CH_{arom/olef}$), 132.9 (CH $_{arom/olef}$), 135.0 ($CH_{arom/olef}$), 137.1 (C_q), 137.6 (C_q), 158.5 (C =N). IR (neat) $\tilde{\nu}$: 3478 (W), 2965 (W), 1466 (M), 1454 (M), 1369 (M), 1240 (W), 1163 (M), 1022 (S), 972 (S), 750 (S), 700 (M), 630 (S). HRMS (ESI): calcd for $C_{21}H_{24}BrNO_2Na$ 424.0888; found 424.0875.

*(2E,4E)-5-(2-Bromophenyl)-3-hydroxy-3-phenyl-pent-4-en-2-one O-Benzyl Oxime (**4h**).* This compound was obtained from the corresponding ketone **3b** (0.500 g, 1.45 mmol) and phenyllithium (1.9 M in Et_2O) (0.33 mL, 1.6 mmol) according to the general procedure. The subsequent chromatographic purification (Et_2O/pentane, 1:3) gave 0.28 g (0.67 mmol, 46%) of **4h** as a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm) 1.76 (s, 3H, CH_3), 4.26 (s, 1H, CO*H*), 5.11 (s, 2H, OCH_2Ph), 6.60 (d, 1H, *J* = 15.8 Hz, CH_{olef}), 7.06 (d, 1H, *J* = 15.8 Hz, CH_{olef}), 7.00−7.06 (m, 1H, CH_{arom}), 7.16−7.31 (m, 11H, CH_{arom}), 7.46−7.48 (m, 2H, CH_{arom}); ^{13}C NMR (75 MHz, $CDCl_3$): δ (ppm) 11.4 (CH_3), 12.9 (CH_3), 76.4 (C_q, COH), 78.9 (CH_2Ph), 126.8 ($CH_{arom/olef}$), 127.9 ($CH_{arom/olef}$), 128.2 ($CH_{arom/olef}$), 128.4 ($CH_{arom/olef}$), 129.0 ($CH_{arom/olef}$), 132.8 ($CH_{arom/olef}$), 136.0 (C_q), 137.6 (C_q), 159.3 (C_q). IR (neat) $\tilde{\nu}$: 3478 (W), 2965 (W), 1466 (W), 1454 (W), 1369 (W), 1240 (W), 1204 (W), 1167 (W), 1022 (M), 972 (W), 932 (W), 750 (M),700 (M),658 (W), 631 (M),608 (W), 528 (VS), 509 (S). HRMS (ESI): calcd for $C_{24}H_{21}BrNO_2NaH$ 460.0711; found 460.0710.

*(2E,4E)-3-Hydroxy-3-methyl-5-(thiophen-2-yl)-pent-4-en-2-one O-Benzyl Oxime (**4i**).* This compound was obtained from the corresponding ketone **3f** (0.285 g, 1 mmol) and methyllithium (1.6 M in Et_2O) (0.7 mL, 1.1 mmol) according to the general procedure. The subsequent chromatographic purification (Et_2O/pentane, 1:10) gave 0.19 g (0.63 mmol, 63%) of **4i** as a colorless oil. ^{1}H NMR (300 MHz, C_6D_6): δ (ppm) 1.45 (s, 3H, CH_3), 1.80 (s, 3H, CH_3), 3.47 (br, 1H, CO*H*), 5.11 (s, 2H, OCH_2Ph), 6.29 (d, 1H, *J* = 15.7 Hz, CH_{olef}), 6,76−6.82 (m, 1H, CH_{arom}), 7.02 (d, 1H, *J* = 15.7 Hz, CH_{olef}), 7.18−7.27 (m, 4H, CH_{arom}), 7.36−7.38 (m, 4H, CH_{arom}); ^{13}C NMR (75 MHz, C_6D_6): δ (ppm) 11.0 (CH $_3$), 26.3 (CH_3), 74.7 (C_q, COH), 76.4 (CH_2Ph), 122.8 ($CH_{arom/olef}$), 124.5 (CH $_{arom/olef}$), 126.4 ($CH_{arom/olef}$), 127.6 ($CH_{arom/olef}$), 128.1 (CH $_{arom/olef}$), 128.6 ($CH_{arom/olef}$), 128.6 ($CH_{arom/olef}$), 133.2 (CH $_{arom/olef}$), 138.2 (C_q), 142.3 (C_q), 159.8 (C_q). IR (neat) $\tilde{\nu}$: 3447 (M), 3032 (M), 2980 (M), 2930 (M), 2872 (M), 1643 (M), 1454 (M), 1368 (M), 1179 (M), 1107 (M), 1018 (M), 959 (M), 856 (M), 737 (M), 696 (S), 631 (S), 538 (S), 527 (VS). HRMS (ESI): calcd for $C_{17}H_{19}NO_2SNa$ 324.1034; found 324.1029. Anal. Calcd for $C_{17}H_{19}NO_2S$: C, 67.74; H, 6.35; N, 4.65. Found: C, 67.81; H, 6.17; N, 4.74.

*(2E,4E)-5-(4-Chlorophenyl)-3-hydroxy-3-(p-tolyl)-pent-4-en-2-one O-Benzyl Oxime (**4j**).* This compound was obtained from the corresponding ketone **3d** and *p*-tolyl lithium. *p*-Tolyl lithium was generated *in situ* by metal−halogen exchange of *p*-bromotoluene using *n*-butyl lithium (1.6 M in hexane) by adding *n*-BuLi (0.7 mL, 1.1 equiv) to a solution of *p*-bromotoluene (0.188 g, 1.1 mmol,1.1 equiv) in THF (10 mL) cooled to −78 °C. To this solution of *p*-tolyl lithium in THF, ketone **3d** (0.313 g, 1 mmol as a solution in THF) was added dropwise. Then, the general procedure was followed with regard to the monitoring of the progress and the work up of the reaction. The subsequent chromatographic purification (Et_2O/pentane, 1:3) gave 0.24 g (0.60 mmol, 60%) of **4j** as a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm) 1.74 (s, 3H, CH_3), 2.25 (s, 3H, tol-CH_3), 4.22 (s, 1H, CH_3O*H*), 5.11 (s, 2H, OCH_2Ph), 6.62 (d, 1H, *J* = 15.8 Hz, CH_{olef}), 6.71 (d, 1H, *J* = 15.8 Hz, CH_{olef}), 7.05 (d, 2H, *J* = 7.8 Hz, CH_{arom}), 7.15−7.30 (m, 11H, CH_{arom}); ^{13}C NMR (75 MHz, $CDCl_3$): δ (ppm) 12.8 (CH_3), 21.1 (CH_3), 76.3 (C_q, COH), 78.6 (OCH_2Ph), 126.7 ($CH_{arom/olef}$), 127.9 ($CH_{arom/olef}$), 127.9 ($CH_{arom/olef}$), 128.2 ($CH_{arom/olef}$), 128.4 ($CH_{arom/olef}$), 128.7 ($CH_{arom/olef}$), 129.2 ($CH_{arom/olef}$), 129.2 ($CH_{arom/olef}$), 131.4 ($CH_{arom/olef}$), 133.3 (C_q), 135.3 (C_q), 137.6 (C_q), 137.7 (C_q), 139.6 (C_q), 158.7 (C_q). IR (neat) $\tilde{\nu}$: 3439 (M), 3030 (M), 2924 (M), 2870 (M), 1510 (M), 1491 (M), 1454 (M), 1368 M), 1179 (M), 1092 (M), 1013 (M), 974 (M), 905 (M), 858 (M), 818 (M), 752 (M), 725 (M), 698 (M), 631 (M), 608 (M). HRMS (ESI): calcd for $C_{25}H_{24}NO_2ClNa$ 428.1393; found 428.1388.

*(1E,4E)-3-Methyl-4-(2-methyl-2-phenylhydrazono)-1-phenyl-pent-1-en-3-ol (**4k**).* This compound was obtained from the corresponding ketone **3g** (0.278 g, 1 mmol) and methyllithium (1.6 M in Et_2O) (0.7 mL, 1.1 mmol) according to the general procedure. The subsequent chromatographic purification (Et_2O/pentane, 1:3) gave 0.15 g (0.51 mmol, 51%) of **4k** as light yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm) 1.53 (s, 3H, CH_3), 1.90 (s, 3H, CH_3), 2.97 (s, 3H, CH_3), 5.39 (br, 1H, O*H*), 6.23 (d, 1H, *J* = 16.0 Hz, CH_{olef}), 6.71 (d, 1H, *J* = 16.0 Hz, CH_{olef}), 6.79−6.86 (m, 3H, CH_{arom}), 7.16−7.27

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(m, 5H, CH_{arom}), 7.32−7.35 (m, 2H, CH_{arom}). ^{13}C NMR (75 MHz, $CDCl_3$): δ (ppm) 14.5 (CH_3), 26.0 (CH_3), 43.1 (CH_3), 75.1 (C_q, COH), 115.9 ($CH_{arom/olef}$), 120.8 ($CH_{arom/olef}$), 126.7 ($CH_{arom/olef}$), 127.8 ($CH_{arom/olef}$), 128.6 ($CH_{arom/olef}$), 128.9 ($CH_{arom/olef}$), 129.9 ($CH_{arom/olef}$), 132.8 ($CH_{arom/olef}$), 136.7 (C_q), 151.1 (C_q), 171.7 (C_q). IR (neat) $\tilde{\nu}$: 3387 (W), 3059 (W), 3026 (W), 2976 (W), 2926 (W), 1599 (VS), 1493 (VS), 1449 (S), 1368 (S), 1296 (S), 1182 (S), 1070 (S), 1028 (S), 970 (S), 746 (S), 692 (VS), 617 (VS). HRMS (ESI): calcd for $C_{19}H_{22}N_2OH$ 295.1810; found 295.1797.

(1E,4E)-3-Methyl-4-(2-methyl-2-phenylhydrazono)-1-(p-tolyl)-pent-1-en-3-ol (**4l**). This compound was obtained from the corresponding ketone **3h** (0.292 g, 1 mmol) and methyllithium (1.6 M in Et_2O) (0.7 mL, 1.1 mmol) according to the general procedure. The subsequent chromatographic purification (Et_2O/pentane, 1:10) gave 0.20 g (0.65 mmol, 65%) of **4l** as light yellow oil. ^1H NMR (300 MHz, C_6D_6): δ (ppm) 1.22 (s, 3H, CH_3), 1.37 (s, 3H, CH_3), 1.81 (s, 3H, CH_3), 2.42 (s, 3H, NCH_3), 5.03 (br, 1H, OH), 6.03 (d, 1H, J = 15.9 Hz, CH_{olef}), 6.53−6.59 (m, 1H, CH_{arom}), 6.60−6.64 (m, 2H, CH_{arom}), 6.66−6.70 (m, 3H, $CH_{arom/olef}$), 6.85−6.90 (m, 2H, CH_{arom}), 6.94 (d, 2H, J = 8.2 Hz, CH_{arom}); ^{13}C NMR (75 MHz, C_6D_6): δ (ppm) 12.8 (CH_3), 19.8 (CH_3), 25.3 (CH_3), 41.8 (CH_3), 74.2 (C_q, COH), 114.9 ($CH_{arom/olef}$), 119.6 ($CH_{arom/olef}$), 125.6 ($CH_{arom/olef}$), 127.8 ($CH_{arom/olef}$), 128.2 ($CH_{arom/olef}$), 128.5 ($CH_{arom/olef}$), 131.3 ($CH_{arom/olef}$), 133.2 (C_q), 136.1 (C_q), 150.4 (C_q), 170.9 (C_q). IR (neat) $\tilde{\nu}$: 3357 (W), 3064 (W), 3025 (W), 2976 (W), 2936 (W), 1601 (VS), 1492 (VS), 1459 (S), 1375 (S), 1296 (S), 1182 (S), 1070 (S), 1037 (S), 970 (S), 746 (S), 692 (VS), 620 (VS). HRMS (ESI): calcd for $C_{20}H_{24}N_2ONa$ 331.1786; found 331.1781

(1E,3E)-1-(Indolin-1-ylimino)-2-methyl-1,4-diphenyl-but-3-en-2-ol (**4m**). This compound was obtained from the corresponding ketone **3i** (0.17 g, 0.48 mmol) and methyllithium (1.6 M in Et_2O) (0.28 mL, 0.53 mmol) according to the general procedure. The subsequent chromatographic purification (Et_2O/pentane, 1:10) gave 0.14 g (0.38 mmol, 79%) of **4m** as light yellow oil. ^1H NMR (300 MHz, $CDCl_3$): δ (ppm) 1.76 (s, 3H, CH_3OH), 2.43 (t, J = 8.3 Hz, 2H, NCH_2CH_2), 2.68−2.88 (m, 2H, NCH_2CH_2), 5.25 (s, 1H, CH_3OH), 6.57 (d, 1H, J = 15.9 Hz, CH_{olef}), 6.90−6.99 (m, 2H, CH_{arom}), 7.06−7.16 (m, 5H, CH_{arom}), 7.19−7.26 (m, 5H, CH_{arom}), 7.37−7.40 (m, 3H, CH_{arom}); ^{13}C NMR (75 MHz, $CDCl_3$): δ (ppm) 27.7 (CH_3), 28.1 (NCH_2CH_2), 54.6 (NCH_2CH_2), 75.8 (C_q, COH), 111.3 ($CH_{arom/olef}$), 121.4 ($CH_{arom/olef}$), 124.7 ($CH_{arom/olef}$), 126.9 ($CH_{arom/olef}$), 127.2 ($CH_{arom/olef}$), 127.7 (C_q), 128.0 ($CH_{arom/olef}$), 128.1 ($CH_{arom/olef}$), 134.9 (C_q), 136.4 (C_q), 137.7 (C_q), 151.4 (C_q), 153.3 (C_q). IR (neat) $\tilde{\nu}$: 3391 (W), 3026 (W), 2972 (W), 2924 (W), 2858 (M), 1614 (M), 1593 (M), 1479 (VS), 1462 (M), 1371 (M), 1265 (M), 1207 (M), 1180 (M), 1153 (M), 1117 (M), 1072 (M), 1016 (M), 986 (M), 889 (M), 853 (M), 746 (VS), 704 (S), 691 (VS). HRMS (ESI): calcd for $C_{25}H_{24}N_2ONa$ 391.1786; found 391.1781.

General Method for the Synthesis of Pyrroles 6a−m. To a clean, dry Schlenk flask was added dry CH_2Cl_2 (40 mL per mmol of the substrate), and the mixture was cooled down to −10 °C using salt−ice mixture. Then CF_3SO_3H (2 equiv) was added followed by the dropwise addition of the substrate **4** (1 equiv as a solution in DCM). Usually the reaction mixture turned to brown or red after the addition of the substrate. Soon this color slowly faded. The progress of the reaction was monitored by TLC. After the completion, the reaction mixture was quenched with satd aq $NaHCO_3$ solution and washed a couple of times with water. Then the organic phase was dried with $MgSO_4$ and concentrated in vacuo. The product pyrrole was purified using silica gel column chromatography.

1-(Benzyloxy)-2,3-dimethyl-5-phenyl-pyrrole (**6a**). This compound was obtained from **4a** (0.295 g, 1 mmol) according to the general procedure. The subsequent chromatographic purification (Et_2O/pentane, 1:10) gave 0.11 g (0.40 mmol, 40%) of **6a** as a colorless oil. ^1H NMR (300 MHz, $CDCl_3$): δ (ppm) 2.11 (s, 3H, CH_3), 2.14 (s, 3H, CH_3), 4.63 (s, 2H, CH_2), 6.30 (s, 1H, $CH_{pyrrole}$), 7.15−7.18 (m, 6H, CH_{arom}), 7.26−7.32 (m, 2H, CH_{arom}), 7.95−7.98 (m, 2H, CH_{arom}).^{13}C NMR (75 MHz, $CDCl_3$): δ (ppm) 8.7 (CH_3), 11.2 (CH_3), 80.1 (CH_2), 104.7 ($CH_{pyrrole}$), 111.0 (C_q), 123.2 (C_q), 126.0 (CH_{arom}), 126.2 (CH_{arom}), 126.3 (C_q), 128.4 (CH_{arom}), 128.5 (CH_{arom}), 129.0 (CH_{arom}), 129.7 (CH_{arom}), 131.7 (C_q), 133.9 (C_q). IR (neat) $\tilde{\nu}$: 3063 (M), 3026 (M), 2914 (M), 2862 (M), 1601 (M), 1512 (M), 1452 (M), 1383 (M), 1217 (M), 1177 (M), 1157 (M), 1119 (M), 1076 (M), 1030 (M), 982 (M), 964 (M), 949 (M), 908 (M), 847 (M), 789 (M), 748 (M), 735 (M), 692 (M), 652 (M). HRMS (ESI): calcd for $C_{19}H_{19}NONa$ 300.1364; found 300.1356. Anal. Calcd for $C_{19}H_{19}NO$: C, 82.28; H, 6.90; N, 5.05. Found: C, 82.07; H, 7.23; N, 5.46.

1-(Benzyloxy)-5-(2-bromophenyl)-2,3-dimethyl-pyrrole (**6b**). This compound was obtained from **4b** (0.2 g, 0.54 mmol) according to the general procedure. The subsequent chromatographic purification (Et_2O/pentane, 1:10) gave 0.1 g (0.28 mmol, 53%) of **6b** as a colorless oil. ^1H NMR (300 MHz, C_6D_6): δ (ppm) 2.08 (s, 3H, CH_3), 2.14 (s, 3H, CH_3), 4.50 (s, 2H, CH_2), 6.47 (s, 1H, $CH_{pyrrole}$), 6.78−6.83 (m, 1H, CH_{arom}), 7.00−7.03 (m, 3H, CH_{arom}), 7.08−7.11 (m, 3H, CH_{arom}), 7.62−7.67 (m, 2H, CH_{arom}). ^{13}C NMR (75 MHz, C_6D_6): δ (ppm) 8.7 (CH_3), 11.4 (CH_3), 80.8 (CH_2), 108.7 ($CH_{pyrrole}$), 110.5 (C_q), 121.3 (C_q), 122.4 (C_q), 123.4 (C_q), 125.9 (CH_{arom}), 127.3 (CH_{arom}), 127.4 (CH_{arom}), 127.9 (CH_{arom}), 128.5 (CH_{arom}), 131.3 (CH_{arom}), 131.5 (C_q), 132.1 (CH_{arom}), 132.8 (C_q). IR (neat) $\tilde{\nu}$: 3063 (w), 3032 (w), 2920 (w), 2862 (w), 1597 (w), 1558 (w), 1510 (w), 1454 (w), 1435 (w), 1379 (w), 1256 (w), 1213 (w), 1177 (w), 1119 (w), 1082 (w), 1043 (w), 1026 (m), 966 (w), 953 (w), 907 (w), 849 (w), 793 (w), 748 (S), 737 (m), 716 (w), 696 (m), 683 (w), 637 (w), 608 (w), 586 (w), 527 (w). HRMS (ESI): calcd for $C_{19}H_{18}NOBrNa$ 378.0469; found 378.0464.

1-(Benzyloxy)-5-(2-methoxyphenyl)-2,3-dimethyl-pyrrole (**6c**). This compound was obtained from **4c** (0.325 g, 1 mmol) according to the general procedure. The subsequent chromatographic purification (Et_2O/pentane, 1:3) gave 0.1 g (0.29 mmol, 29%) of **6c** as a colorless oil. ^1H NMR (300 MHz, C_6D_6): δ (ppm) 1.97 (s, 3H, CH_3), 2.12 (s, 3H, CH_3), 3.77 (s, 3H, OCH_3), 4.63 (s, 2H, CH_2), 6.07 (s, 1H, $CH_{pyrrole}$), 6.88−6.95 (m, 2H, CH_{arom}), 7.03−7.06 (m, 2H, CH_{arom}), 7.20−7.24 (m, 4H, CH_{arom}), 7.55 (dd, 1H, J = 7.6, 1.7 Hz, CH_{arom}).^{13}C NMR (75 MHz, C_6D_6): δ (ppm) 8.7 (CH_3), 11.4 (CH_3), 55.5 (OCH_3), 80.1 (CH_2), 104.7 ($CH_{pyrrole}$), 111. (C_q), 114.4 (CH_{arom}), 122.3 (CH_{arom}), 125.4 (C_q), 126.7 (CH_{arom}), 127.9 (CH_{arom}), 128.6 (CH_{arom}), 128.9 (CH_{arom}),129.8 (CH_{arom}), 134.7 (C_q), 158.7(C_q). IR (neat) $\tilde{\nu}$: 3032 (w), 2936 (w), 2916 (w), 2835 (w), 1611 (m), 1572 (m), 1526 (v), 1454 (m), 1441 (m), 1377 (m), 1285 (M), 1246 (v), 1223 (w), 1177 (M), 1119 (w), 1105 (w), 1076 (w), 1032 (m), 966 (W), 951 (W), 908 (W), 831 (M), 808 (m), 781 (m), 754 (m), 737 (m), 696 (m), 621 (m), 604 (m), 590 (m). HRMS (ESI): calcd for $C_{20}H_{21}NO_2Na$ 330.1470; found 330.1465.

1-(Benzyloxy)-5-(4-chlorophenyl)-2,3-dimethyl-pyrrole (**6d**). This compound was obtained from **4d** (0.2 g, 0.61 mmol) according to the general procedure. The subsequent chromatographic purification (Et_2O/pentane, 1:3) gave 0.06 g (0.2 mmol, 30%) of **6d** as white solid (mp 87−89 °C). ^1H NMR (300 MHz, C_6D_6): δ (ppm) 2.07 (s, 3H, CH_3), 2.11 (s, 3H, CH_3), 4.49 (s, 2H, CH_2), 6.16 (s, 1H, $CH_{pyrrole}$), 7.08−7.14 (m, 5H, CH_{arom}), 7.24−7.27 (m, 2H, CH_{arom}), 7.64−7.67 (m, 2H, CH_{arom}). ^{13}C NMR (75 MHz, C_6D_6): δ (ppm) 8.69 (CH_3), 11.5 (CH_3), 80.2 (CH_2), 105.9 ($CH_{pyrrole}$), 111.5 (C_q), 123.8 (C_q), 125.3 (C_q), 127.4 (CH_{arom}), 128.6 (CH_{arom}), 128.9 (CH_{arom}), 129.1 (CH_{arom}), 129.8 (CH_{arom}), 130.9 (C_q), 131.7 (C_q), 134.2 (C_q). IR (neat) $\tilde{\nu}$: 3067 (W), 3032 (W), 2916 (W), 2862 (W), 1597 (W), 1512 (S), 1454 (W), 1414 (W), 1393 (W), 1377 (W), 1219 (W), 1177 (W), 1092 (S), 1013 (W), 964 (W), 951 (W), 908 (W), 833 (W), 785 (S), 760 (S), 745 (S), 735 (S), 696 (S), 631 (S). HRMS (ESI): calcd for $C_{19}H_{18}NOClH$ 312.1155; found 312.1150. Anal. Calcd for $C_{19}H_{18}NOCl$: C, 73.19; H, 5.82; N, 4.49. Found: C, 73.14; H, 5.93; N, 4.49.

1-(Benzyloxy)-2,3-dimethyl-5-(p-tolyl)-pyrrole (**6e**). This compound was obtained from **4e** (0.2 g, 0.65 mmol) according to the general procedure. The subsequent chromatographic purification (Et_2O/pentane, 1:10) gave 0.06 g (0.23 mmol, 32%) of **6e** as white solid (mp 54−56 °C). ^1H NMR (300 MHz, $CDCl_3$): δ (ppm) 2.13 (s, 3H, CH_3), 2.16 (s, 3H, CH_3), 2.25 (s, 3H, CH_3), 4.62 (s, 2H, OCH_2Ph), 6.52 (s, 1H, $CH_{pyrrole}$), 7.13−7.18 (m, 7H, CH_{arom}), 7.92 (d, 2H, J = 8.2 Hz, CH_{arom}). ^{13}C NMR (75 MHz, $CDCl_3$): δ (ppm)

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8.7 (CH_3), 11.6 (CH_3), 21.1 (CH_3), 80.0 (OCH_2Ph), 105.2 ($CH_{pyrrole}$), 111.1 (C_q), 122.9 (C_q), 126.4 (CH_{arom}), 126.7, 128.6 (CH_{arom}), 128.9 (CH_{arom}), 129.6 (CH_{arom}), 129.7 (CH_{arom}), 129.9 (C_q), 134.7 (C_q), 135.5 (C_q). IR (neat) $\tilde{\nu}$: 3034 (W), 2913 (W), 2884 (W), 2858 (W), 1524 (M) 1452 (M), 1375 (M), 1225 (W), 1207 (W), 1177 (W), 1107 (W), 988 (W), 964 (M), 947 (M), 910 (M), 851 (M), 822 (S) 783 (M) 754 (M) 737 696 (M). HRMS (ESI): calcd for $C_{20}H_{21}NOH$ 292.1701; found 292.1696.

*1-(Benzyloxy)-5-(2-bromophenyl)-3-butyl-2-methyl-pyrrole (**6f**).* This compound was obtained from **4f** (0.19 g, 0.46 mmol) according to the general procedure. The subsequent chromatographic purification (Et_2O/pentane, 1:20) gave 0.09 g (0.23 mmol, 50%) of **6f** as oil. ^{1}H NMR (300 MHz, C_6D_6): δ (ppm) 1.03 (t, 3H, J = 7.3 Hz, CH_3CH_2), 1.43−1.55 (m, 2H, CH_2), 1.65−1.75 (m, 2H, CH_2), 2.10 (s, 3H, CH_3), 2.56 (t, 2H, J = 7.5 Hz, CH_2CH_2), 4.51 (s, 2H, CH_2), 6.53 (s, 1H, $CH_{pyrrole}$), 6.78−6.83 (m, 1H, CH_{arom}), 6.99−7.03 (m, 3H, CH_{arom}), 7.09−7.11 (m, 3H, CH_{arom}), 7.63−7.69 (m, 2H, CH_{arom}). ^{13}C NMR (75 MHz, C_6D_6): δ (ppm) 8.8 (CH_3), 14.3 (CH_3CH_2), 22.8 (CH_2), 26.4 (CH_2), 33.7 (CH_2), 80.7 (CH_2OPh), 107.8 ($CH_{pyrrole}$), 115.9 (C_q), 122.3 (C_q), 123.7 (C_q), 124.5 (C_q), 127.1 (CH_{arom}), 128.2 (CH_{arom}), 128.5 (CH_{arom}), 128.9 (CH_{arom}), 129.9 (CH_{arom}), 132.6 (CH_{arom}), 133.3 (C_q), 133.6 (CH_{arom}), 134.5 (C_q). IR (neat) $\tilde{\nu}$: 3063 (w), 3032 (W), 2955 (W), 2926 (W), 2855 (W), 1595 (W), 1558 (W), 1454 (W), 1377 (W), 1213 (W), 1161 (W), 1119 (W), 1084 (W), 1026 (W), 959 (W), 907 (W), 849 (W), 799 (W), 750 (m),716 (W), 694 (m), 637 (m), 611 (m), 511 (w), 501 (m), 492 (m), 476 (M). HRMS (ESI): Calcd. for $C_{22}H_{24}NOBrNa$ 420.0939; found 420.0935. Anal. Calcd for $C_{22}H_{24}NOBr$: C, 66.33; H, 6.07; N, 3.52. Found: C, 67.07; H, 6.05; N, 3.46.

*1-(Benzyloxy)-5-(2-bromophenyl)-3-isopropyl-2-methyl-pyrrole (**6g**).* This compound was obtained from **4g** (0.16 g, 0.4 mmol) according to the general procedure. The subsequent chromatographic purification (Et_2O/pentane, 1:20) gave 0.045 g (0.14 mmol, 30%) of **6g** as oil. ^{1}H NMR (300 MHz, C_6D_6): δ (ppm) 1.37 (d, 6H, J = 6.9 Hz, $CH(CH_3)_2$), 2.10 (s, 3H, CH_3), 2.90 (hept, 1H, J = 6.9 Hz, $CH(CH_3)_2$), 4.49 (s, 2H, OCH_2Ph), 6.54 (s, 1H, $CH_{pyrrole}$), 6.80 (ddd, 1H, J = 8.0, 7.4, 1.7 Hz, CH_{arom}), 6.98−7.03 (m, 3H, CH_{arom}), 7.07−7.11 (m, 3H, CH_{arom}), 7.65 (ddd, 2H, J = 7.9, 4.0, 1.4 Hz, CH_{arom}). ^{13}C NMR (75 MHz, C_6D_6): δ (ppm) 8.7 (CH_3), 24.2 (CH_3), 26.0 ($CH(CH_3)_2$), 80.7 (CH_2OPh), 104.9 ($CH_{pyrrole}$), 121.2 (C_q), 122.3 (C_q), 123.7 (C_q), 124.4 (C_q), 127.1 (CH_{arom}), 128.2 (CH_{arom}), 128.5 (CH_{arom}), 128.9 (CH_{arom}), 129.9 (CH_{arom}), 132.6 (CH_{arom}), 133.4 (C_q), 133.6 (CH_{arom}), 134.5 (C_q). IR (neat) $\tilde{\nu}$: 3059 (W), 3030 (W), 2957 (M), 2922 (W), 2866 (W), 1589 (M), 1508 (M), 1456 (S), 1381 (M), 1211 (M), 1161 (M), 1024 (M), 957 (M), 901 (S), 802 (M), 750 (VS), 731 (M), 700 (M), 683 (M), 637 (M), 610 (M). HRMS (ESI): calcd for $C_{21}H_{22}NOBrH$ 386.0943; found 386.0938.

*1-(Benzyloxy)-5-(2-bromophenyl)-2-methyl-3-phenyl-pyrrole (**6h**).* This compound was obtained from **4h** (0.24 g, 0.55 mmol) according to the general procedure. The subsequent chromatographic purification (Et_2O/pentane, 1:20) gave 0.19 g (0.45 mmol, 83%) of **6h**. ^{1}H NMR (300 MHz, C_6D_6): δ (ppm) 2.27 (s, 3H, CH_3), 4.50 (s, 2H, OCH_2Ph), 6.80 (s, 1H, $CH_{pyrrole}$), 6.80−6.86 (m, 1H, CH_{arom}), 6.98−7.05 (m, 3H, CH_{arom}), 7.07−7.11 (m, 3H, CH_{arom}), 7.20−7.26 (m, 1H, CH_{arom}), 7.40 (t, 2H, J = 7.6 Hz, CH_{arom}), 7.62−7.67 (m, 4H, CH_{arom}). ^{13}C NMR (75 MHz, C_6D_6): δ (ppm) 10.4 (CH_3), 80.9 (OCH_2Ph), 107.1 ($CH_{pyrrole}$), 117.6 (C_q), 123.0 (C_q), 124.0 (C_q), 125.7 (CH_{arom}), 127.1 (CH_{arom}), 128.0 (CH_{arom}), 128.6 (CH_{arom}), 128.7 (CH_{arom}), 128.8 (CH_{arom}), 129.1 (CH_{arom}), 129.9 (CH_{arom}), 132.7 (CH_{arom}), 132.8 (C_q), 133.6 (CH_{arom}), 134.1 (C_q), 137.3 (C_q). IR (neat) $\tilde{\nu}$: 3032 (W), 2943 (W), 2882 (W), 1603 (S), 1560 (W), 1520 (W), 1491 (S), 1454 (S), 1379 (W), 1364 (W), 1258 (W), 1229 (W), 1213 (W), 1173 (W), 1152 (W), 1119 (W), 1070 (W), 1045 (W), 1026 (S), 984 (W), 951 (M), 907 (M), 849 (W), 804 (W), 758 (VS), 748 (VS), 739 (VS), 719 (W), 694 (VS), 683 (W), 629 (W), 611 (W), 542 (W), 530 (W), 519 (W), 500 (W). HRMS (ESI): calcd for $C_{24}H_{20}NOBrNa$ 440.0626; found 440.0611. Anal. Calcd For $C_{24}H_{20}NOBr$: C, 68.91; H, 4.82; N, 3.35. Found: C, 68.80; H, 5.06; N, 3.32.

*1-(Benzyloxy)-2,3-dimethyl-5-(thiophen-2-yl)-pyrrole (**6i**).* This compound was obtained from **4i** (0.18 g, 0.60 mmol) according to the general procedure. The subsequent chromatographic purification (Et_2O/pentane, 1:20) gave 0.06 g (0.22 mmol, 36%) of **6i** as yellow solid (mp 58−60 °C). ^{1}H NMR (300 MHz, C_6D_6): δ (ppm) 2.03 (s, 3H, CH_3), 2.08 (s, 3H, CH_3), 4.72 (s, 2H, OCH_2Ph), 6.34 (s, 1H, CH_{arom}), 6.90 (s, 1H, CH_{arom}), 6.91 (d, 1H, J = 1.4 Hz, CH_{arom}), 7.16 (d, 1H, J = 2.1 Hz, CH_{arom}), 7.18−7.19 (m, 2H, CH_{arom}), 7.24−7.26 (m, 2H, CH_{arom}), 7.43 (dd, 1H, J = 2.9, 1.4 Hz, CH_{arom}). ^{13}C NMR (75 MHz, C_6D_6): δ (ppm) 8.6 (CH_3), 11.4 (CH_3), 80.1 (OCH_2Ph), 105.2 (CH_{arom}), 111.4 (C_q), 121.2 (C_q), 122.4 (CH_{arom}), 122.8 (CH_{arom}), 122.9, 127.5 (CH_{arom}), 128.6 (CH_{arom}), 128.9 (CH_{arom}), 129.6 (CH_{arom}), 134.2 (C_q), 134.6 (C_q). IR (neat) $\tilde{\nu}$: 3105 (M), 3069 (M), 3038 (M), 2945 (M), 2918 (M), 2882 (M), 2858 (M), 1528 (M), 1499 (M), 1481 (M), 1464 (M), 1452 (M), 1398 (M), 1366 (M), 1335 (M), 1227 (M), 1215 (M), 1196 (M), 1175 (M), 1113 (M), 1078 (M), 1030 (M), 982 (M), 972 (M), 951 (S), 926 (M), 908 (S), 843 (S), 814 (S), 777 (S), 768 (S), 758 (S), 745 (S), 735 (S), 692 (S), 637 (M), 602 (M). HRMS (ESI): calcd for $C_{17}H_{17}NOSH$ 284.1109; found 284.1104.

*1-(Benzyloxy)-5-(4-chlorophenyl)-2-methyl-3-(p-tolyl)-pyrrole (**6j**).* This compound was obtained from **4j** (0.18 g, 0.45 mmol) according to the general procedure. The subsequent chromatographic purification (Et_2O/pentane, 1:20) gave 0.11 g (0.29 mmol, 64%) of **6j** as white solid (mp 123−124 °C). ^{1}H NMR (300 MHz, C_6D_6): δ (ppm) 2.29 (s, 3H, CH_3), 2.34 (s, 3H, CH_3), 4.49 (s, 2H, OCH_2Ph), 6.56 (s, 1H, $CH_{pyrrole}$), 7.08−7.14 (m, 5H, CH_{arom}), 7.26−7.29 (m, 5H, CH_{arom}), 7.55 (d, 2H, J = 8.0 Hz, CH_{arom}), 7.67 (d, 2H, J = 8.0 Hz, CH_{arom}). ^{13}C NMR (75 MHz, C_6D_6): δ (ppm) 10.0 (CH_3), 21.2 (CH_3), 80.4 (OCH_2Ph), 104.4 ($CH_{pyrrole}$), 118.7 (C_q), 123.9 (C_q), 126.2 (C_q), 127.8 (CH_{arom}), 127.9 (CH_{arom}), 128.7 (CH_{arom}), 129.0 (CH_{arom}), 129.2 (CH_{arom}), 129.6 (CH_{arom}), 129.9 (CH_{arom}), 130.5 (C_q), 132.2 (C_q), 133.9 (C_q), 134.3 (C_q), 135.2 (C_q). IR (neat) $\tilde{\nu}$: 3073 (W), 3032 (W), 2920 (W), 2887 (W), 1616 (W), 1597 (W), 1585 (W), 1562 (W), 1524 (W), 1499 (S), 1476 (M), 1456 (M), 1429 (M), 1408 (M), 1381 (M), 1238 (M), 1213 (M), 1180 (M), 1148 (M), 1105 (M), 1090 (M), 1028 (M), 1011 (M), 991 (M), 978 (M), 951 (M), 914 (M), 849 (M), 833 (S), 824 (S), 781 (VS), 772 (S), 750 (S), 737 (VS), 698 (S), 677 (M), 642 (M), 613 (M), 600 (M). HRMS (ESI): calcd for $C_{25}H_{22}NOClNa$ 410.1288; found 410.1284. Anal. Calcd for $C_{25}H_{22}NOCl$: C, 77.41; H, 5.72; N, 3.61. Found: C, 77.46; H, 5.84; N, 3.35.

*2,3-Dimethyl-5-phenyl-pyrrol-1-methylphenylamine (**6k**).* This compound was obtained from **4k** (0.12 g, 0.41 mmol) according to the general procedure. The subsequent chromatographic purification (Et_2O/pentane, 1:10) gave 0.06 g (0.22 mmol, 54%) of **6k** as a white solid (mp 77−78 °C). ^{1}H NMR (300 MHz, C_6D_6): δ (ppm) 1.87 (s, 3H, CH_3), 2.16 (s, 3H, CH_3), 2.88 (s, 3H, NCH_3), 6.43 (s, 1H, $CH_{pyrrole}$), 6.51−6.54 (m, 2H, CH_{arom}), 6.79−6.85 (m, 1H, CH_{arom}), 7.04−7.09 (m, 2H, CH_{arom}), 7.16−7.21 (m, 3H, CH_{arom}), 7.63−7.67 (m, 2H, CH_{arom}). ^{13}C NMR (75 MHz, C_6D_6): δ (ppm) 9.4 (CH_3), 11.6 (CH_3), 39.6 (NCH_3), 108.5 ($CH_{pyrrole}$), 111.6 (CH_{arom}), 114.6 (C_q), 119.0 (CH_{arom}), 126.4 (CH_{arom}), 126.6 (C_q), 127.0 (CH_{arom}), 128.7 (CH_{arom}), 129.8 (CH_{arom}), 131.4 (C_q), 133.0 (C_q), 149.4 (C_q). IR (neat) $\tilde{\nu}$: 3014 (W), 2898 (W), 2869 (W), 1609 (M), 1526 (M), 1493 (S), 1477 (W), 1293 (W), 1264 (W), 1190 (W), 1164 (W), 1103 (W), 1022 (W), 989 (W), 874 (W), 869 (W), 820 (W), 804 (S), 756 (S), 692 (M), 664 (W), 644 (W). HRMS (ESI): calcd for $C_{19}H_{20}N_2Na$ 299.1524; found 299.1519.

*X-ray Crystal Structure Analysis of **6k**.* Formula $C_{19}H_{20}N_2$, MW = 276.37, colorless crystal 0.30 × 0.13 × 0.07 mm^3, a = 18.0934(3) Å, b = 8.1573(2) Å, c = 21.2642(4) Å, α = 90.000, β = 99.461(2), γ = 90.000, V = 3095.76(11) Å^3, ρ_{calc} = 1.186 g cm^{-3}, μ = 0.07 mm^{-1}, empirical absorption correction (0.979 ≤ T ≤ 0.995), Z = 8, monoclinic, space group $C2/c$ (No. 15), λ = 0.71073 Å, T = 223(2) K, ω and j scans, 11067 reflections collected ((±h, ±k, ±l), [(sin θ)/λ] = 0.59 Å^{-1}, 2683 independent (R_{int} = 0.045 and 2291 observed reflections [$I > 2\sigma(I)$], 193 refined parameters, R = 0.052, R_w^2 = 0.138, max (min) residual electron density 0.24 (−0.19) e Å^{-3}, hydrogen atoms calculated and refined as riding atoms.

*2,3-Dimethyl-5-(p-tolyl)-pyrrol-1-methylphenylamine (**6l**).* This compound was obtained from **4l** (0.2 g, 0.65 mmol) according to the general procedure. The subsequent chromatographic purification (Et_2O/pentane, 1:20) gave 0.11 g (0.43 mmol, 67%) of **6l** as a yellow solid (mp 82−84 °C). ^{1}H NMR (300 MHz, C_6D_6): δ (ppm) 1.49 (s, 3H, CH_3), 1.75 (s, 3H, CH_3), 1.78 (s, 3H, CH_3), 2.51 (s, 3H, CH_3), 6.02 (s, 1H, $CH_{pyrrole}$), 6.12−6.15 (m, 2H, CH_{arom}), 6.40−6.44 (m, 1H, CH_{arom}), 6.59 (d, 2H, J = 8.0 Hz, CH_{arom}), 6.76−6.82 (m, 2H, CH_{arom}), 7.16 (d, 2H, J = 8.0 Hz, CH_{arom}). ^{13}C NMR (75 MHz, C_6D_6): δ (ppm) 8.0 (CH_3), 10.3 (CH_3), 19.6 (CH_3), 38.2 (N-CH_3), 106.6 ($CH_{pyrrole}$), 110.7 (CH_{arom}), 113.0 (C_q), 117.6 (CH_{arom}), 124.8 (C_q), 125.7 (CH_{arom}), 128.0 (CH_{arom}), 128.3 (C_q), 128.9 (C_q), 130.2 (C_q), 134.4 (C_q), 148.1 (C_q). IR (neat) $\tilde{\nu}$: 3024 (W), 2918 (W), 2860 (W), 1599 (M), 1526 (M), 1499 (S), 1477 (W), 1294 (W), 1254 (W), 1190 (W), 1155 (W), 1113 (W), 1032 (W), 989 (W), 874 (W), 839 (W), 820 (W), 800 (S), 746 (S), 692 (M), 656 (W), 642 (W), 583 (W), 546 (W). HRMS (ESI): calcd for $C_{20}H_{22}N_2Na$ 313.1681; found 313.1675. Anal. Calcd for $C_{20}H_{22}N_2$: C, 82.72; H, 7.64; N, 9.65. Found: C, 82.27; H, 7.86; N, 9.35

*1-(3-Methyl-2,5-diphenyl-pyrrol-1-yl)indoline (**6m**).* This compound was obtained from **4m** (0.13 g, 0.35 mmol) according to the general procedure. The subsequent chromatographic purification (Et_2O/pentane, 1:20) gave 0.04 g (0.12 mmol, 33%) of **6m** as a light yellow oil. ^{1}H NMR (300 MHz, C_6D_6): δ (ppm) 2.28 (s, 3H, CH_3), 2.34−2.48 (m, 2H, NCH_2CH_2), 3.35−3.50 (m, 2H, NCH_2CH_2), 6.52 (s, 1H, $CH_{pyrrole}$), 6.66 (d, 1H, J = 7.8 Hz, CH_{arom}), 6.73−6.78 (m, 1H, CH_{arom}), 6.84 (d, 1H, J = 7.8 Hz, CH_{arom}), 7.03−7.10 (m, 3H, CH_{arom}), 7.10−7.13 (m, 2H, CH_{arom}), 7.18−7.23 (m, 2H, CH_{arom}), 7.37−7.40 (m, 2H, CH_{arom}), 7.70−7.73 (m, 2H, CH_{arom}).^{13}C NMR (75 MHz, C_6D_6): δ (ppm) 12.3 (CH_3), 27.4 (NCH_2CH_2), 53.9 (NCH_2CH_2), 108.6 ($CH_{pyrrole}$), 109.9 (C_q), 117.2 (CH_{arom}), 119.8 (CH_{arom}), 125.1 (CH_{arom}), 126.3, 126.9 (CH_{arom}), 127.3 (CH_{arom}), 127.8 (CH_{arom}), 128.1 (CH_{arom}), 128.2 (CH_{arom}), 128.6 (CH_{arom}), 131.1(CH_{arom}), 132.5 (C_q), 132.7(C_q), 133.2(C_q), 134.6(C_q), 152.6(C_q). IR (neat) $\tilde{\nu}$: 3051 (M), 2928 (M), 2870 (M), 1601 (VS), 1489 (VS), 1468 (M), 1458 (M), 1443 (M), 1327 (M), 1271 (S), 1233 (M), 1171 (M), 1097 (M), 1074 (M), 916 (M), 812 (M), 793 (M), 748 (VS), 729 (M), 694 (VS), 675 (M), 642 (M), 619 (M), 611 (M), 513 (S). HRMS (ESI): calcd for $C_{25}H_{22}N_2H$ 351.1861; found 351.1856.

*(2E,3E)-5-(1-(Benzyloxy)-4,5-dimethyl-2-phenyl-pyrrol-3-yl)-3-methyl-5-phenyl-pent-3-en-2-one O-Benzyl Oxime (**7**).* This compound was obtained from alcohol **4a** according to the general procedure for the cyclization. To a clean dry Schlenk flask was transferred 40 mL of dry CH_2Cl_2. This was cooled to −10 °C, and then CF_3CO_2H (0.15 mL, 2 mmol) was added. To this solution alcohol **4a** (0.295 g, 1 mmol) was added dropwise as a solution in dry CH_2Cl_2. The reaction was stirred for 1 h and then quenched with satd. $NaHCO_3$ solution. Then the phases were separated, and the organic phase was washed twice with H_2O, dried with $MgSO_4$, and concentrated in vacuo. The product was purified using column chromatography (Et_2O/pentane 1:10) to give 0.185 g (67%) of **7** as a colorless oil. ^{1}H NMR (300 MHz, C_6D_6): δ (ppm) 1.90 (s, 3H, CH_3), 1.99 (s, 3H, CH_3), 2.03 (s, 3H, CH_3), 2.10 (s, 3H, CH_3), 4.49 (s, 2H, OCH_2Ph), 5.22 (s, 2H, OCH_2Ph), 5.52 (d, 1H, J = 9.3 Hz, CH), 6.56 (dq, 1H, J = 9.3, 1.4 Hz, CH), 6.95−6.98 (m, 2H, CH_{arom}), 7.06−7.12 (m, 5H, CH_{arom}), 7.15−7.22 (m, 5H, CH_{arom}), 7.31 (t, 2H, J = 7.5 Hz, CH_{arom}), 7.38 (d, 2H, J = 6.8 Hz, CH_{arom}), 7.51 (d, 2H, J = 8.0 Hz, CH_{arom}), 7.63 (d, 2H, J = 6.9 Hz, CH_{arom}). ^{13}C NMR (75 MHz, C_6D_6): δ (ppm) 8.5 (CH_3), 10.5 (CH_3), 10.6 (CH_3), 12.6 (CH_3), 40.7 (CH), 76.1 (OCH_2Ph), 79.8 (OCH_2Ph), 109.4 (CH_{arom}), 117.3 (C_q), 122.5 (C_q), 125.5 (C_q), 126.0 (CH_{arom}), 126.8 (CH_{arom}), 127.5 (CH_{arom}), 127.8 (CH_{arom}), 128.2 (CH_{arom}), 128.3 (CH_{arom}), 128.4 (CH_{arom}), 128.7 (CH_{arom}), 129.6 (CH_{arom}), 130.0 (CH_{arom}), 134.3 (CH_{arom}), 133.4 (C_q), 134.19 (C_q), 134.22 (C_q), 138.58 (C_q), 144.6 (C_q), 156.4 (C_q). IR (neat) $\tilde{\nu}$: 3065 (W), 3028 (W), 2926 (W), 2862 (M), 1692 (M), 1603 (M), 1530 (M), 1447 (M), 1373 (M), 1329 (M), 1209 (M), 1016 (M), 980 (S), 953 (M), 905 (M), 883 (S), 766 (M), 750 (VS), 716 (M), 698 (VS), 608 (M). HRMS (ESI): calcd for $C_{38}H_{38}N_2O_2Na$ 577.2831; found 577.2837.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Spectral characteristics of the synthesized compounds; ^{1}H and ^{13}C spectra for the new compounds; Cartesian coordinates and SCS-MP2/6-311G(d,p)//B3LYP/6-311G(d,p)+ZPE energies for the calculated structures and thermal ellipsoid plots for the crystal structure (50% ellipsoid probability). This material is available free of charge via the Internet at http://pubs.acs.org.

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■ REFERENCES

(1) (a) Sundberg, R. J. In *Comprehensive Heterocyclic Chemistry II*; Katritzky, A. R., Rees, C. W., Scriven, E. F. V., Eds.; Oxford: U.K., 1996; Vol. 2. For selected examples, see: (b) Aiello, A.; D'Esposito, M.; Fattorusso, E.; Menna, M.; Mueller, W. E. G.; Perovic-Ottstadt, S.; Schroeder, H. C. *Bioorg. Med. Chem.* **2006**, *14*, 17. (c) Lewer, P.; Chapin, E. L.; Graupner, P. R.; Gilbert, J. R.; Peacock, C. *J. Nat. Prod.* **2003**, *66*, 143. (d) Fürstner, A. *Angew. Chem., Int. Ed.* **2003**, *42*, 3582. (e) Balme, G. *Angew. Chem., Int. Ed.* **2004**, *43*, 6238. (f) Bellina, F.; Rossi, R. *Tetrahedron* **2006**, *62*, 7213.

(2) For selected examples, see: (a) Clark, B. R.; Capon, R. J.; Lacey, E.; Tennant, S.; Gill, J. H. *Org. Lett.* **2006**, *8*, 701. (b) Bode, H. B.; Irschik, H.; Wenzel, S. C.; Reichenbach, H.; Mueller, R.; Hoefle, G. *J. Nat. Prod.* **2003**, *66*, 1203.

(3) (a) Curran, D.; Grimshaw, J.; Perera, S. D. *Chem. Soc. Rev.* **1991**, *20*, 391. For selected examples, see: (b) Ogawa, K.; Rasmussen, S. C. *Macromolecules* **2006**, *39*, 1771. (c) Facchetti, A.; Abbotto, A.; Beverina, L.; van der Boom, M. E.; Dutta, P.; Evmenenko, G.; Pagani, G. A.; Marks, T. J. *Chem. Mater.* **2003**, *15*, 1064.

(4) (a) Gimenez, I. F.; Alves, O. L. *J. Braz. Chem. Soc.* **1999**, *10*, 167. (b) Reynolds, J. R.; Poropatic, P. A.; Toyooka, R. L. *Macromolecules* **1987**, *20*, 958.

(5) (a) Nizurski-Mann, R. E.; Cava, M. P. *Heterocycles* **1992**, *34*, 2003. (b) Chou, S.-S. P.; Yeh, Y.-H. *Tetrahedron Lett.* **2001**, *42*, 1309.

(6) (a) Spivey, A. C.; Frampton, C. S.; Battersby, A. R. *J. Chem. Soc., Perkin Trans. 1* **1996**, 2103. (b) Jacobi, P. A.; Buddhu, S. C.; Fry, D.; Rajeswari, S. *J. Org. Chem.* **1997**, *62*, 2894. (c) Leung, S. H.; Nguyen, L. T.; Smith, K. M. *Heterocycl. Commun.* **1996**, *2*, 9.

(7) Ferreira, V. F.; de Souza, M. C. B. V.; Cunha, A. C.; Pereira, L. O. R.; Ferreira, M. L. G. *Org. Prep. Proced. Int.* **2001**, *33*, 411.

(8) For reviews on multicomponent reactions for the synthesis of pyrrole, see: (a) Estèvez, V.; Villacampa, M.; Menéndez, J. C. *Chem. Soc. Rev.* **2010**, *39*, 4402. (b) Balme, G.; Bouyssi, D.; Monteiro, N. *Heterocycles* **2007**, *73*, 87. (c) Balme, G. *Angew. Chem., Int. Ed.* **2004**, *43*, 6238.

(9) Dudnik, A. S.; Gevorgyan, V. *Catalysed Carbon-Heteroatom Bond Formation*; Yudin, A. K., Ed.; Wiley-VCH: Weinheim, 2010; p 227.

(10) (a) Severin, T.; Adam, R.; Lerche, H. *Chem. Ber.* **1975**, *108*, 1756−1767. (b) Severin, T.; Lerche, H. *Chem Ber.* **1976**, *109*, 1171−1178. (c) Severin, T.; Poehlmann, H. *Chem Ber.* **1977**, *110*, 491−499. (d) Trost, B. M.; Keinan, E. *J. Org. Chem.* **1980**, *45*, 2741−2746. (e) Enders, D.; Maaßen, R.; Han, S.-H. *Liebigs Ann.* **1996**, 1565−1574. (f) Cortés, R. D.; Silva, A. L.; Maldonado, L. A. *Tetrahedron Lett.* **1997**, *38*, 2207−2210. (g) Friedrich, M.; Wächtler, A.; de Meijere, A. *Synlett* **2002**, *4*, 619−621. (h) For a recent review see: Davies, R. L.; Tantillo, D. J. *Curr. Org. Chem.* **2010**, *14*, 1561−1577.

(11) Creary, X.; Burtch, E. A.; Jiang, Z *J. Org. Chem.* **2003**, *68*, 1117.
(12) Alickmann, D.; Fröhlich, R.; Maulitz, A. H.; Würthwein, E.-U. *Eur. J. Org. Chem.* **2002**, 1523.
(13) (a) Ciufolini, M. A.; Roschangar, F. *Tetrahedron* **1997**, *53*, 11049. (b) Matoba, K.; Itoh, K.; Yamazaki, T.; Nagata, M. *Chem. Pharm. Bull.* **1981**, *29*, 2442. (c) Matoba, K.; Miyata, Y.; Yamazaki, T. *Chem. Pharm. Bull.* **1983**, *31*, 476. (d) Matoba, K.; Terada, T.; Sugiuara, M.; Yamazaki, T. *Heterocycles* **1987**, *26*, 55. (e) Aftfah, A.; Abu-Shuheil, M. Y.; Hill, J. *Tetrahedron* **1990**, *46*, 6483. (f) Klumpp, D. A.; Zhang, Y.; O'Connor, M. J.; Estevens, P. M.; Almeida, L. S. *Org. Lett.* **2007**, *9*, 3085. (g) Emayan, K.; Rees, C. W. *Bull. Soc. Chim. Belg.* **1997**, *106*, 605. (h) Ghavtadze, N.; Fröhlich, R.; Würthwein, E.-U. *Eur. J. Org. Chem.* **2008**, 3656. (i) Shimada, N.; Ashburn, B. O.; Basak, A. K.; Bow, W. F.; Vicic, D. A.; Tius, M. A. *Chem. Commun.* **2010**, *46*, 3774. (j) Solingapuram Sai, K. K.; O'Connor, M. J.; Klumpp, D. A. *Tetrahedron Lett.* **2011**, *52*, 2195. (k) For a review on aza-Nazarov reaction see: Nakanishi, W.; West, F. G. *Curr. Opin. Drug Discovery Dev.* **2009**, *6*, 732.
(14) Dieker, J.; Fröhlich, R.; Würthwein, E.-U. *Eur. J. Org. Chem.* **2006**, 5339.
(15) For selected recent examples, see: (a) Meltola, N. J.; Wahlroos, R.; Soini, A. E. *J. Fluoresc.* **2004**, *14*, 635. (b) Zotti, G.; Zecchin, S.; Schiavon, G.; Vercelli, B.; Berlin, A.; Grimoldi, S. *Macromol. Chem. Phys.* **2004**, *205*, 2026. (c) Xu, H.; Yu, G.; Xu, W.; Xu, Y.; Cui, G.; Zhang, D.; Liu, Y.; Zhu, D. *Langmuir* **2005**, *21*, 5391. (d) Foitzik, R. C.; Kaynak, A.; Beckmann, J.; Pfeffer, F. M. *Synth. Met.* **2005**, *155*, 185. (e) Zhao, W.; Carreira, E. M. *Chem.—Eur. J.* **2006**, *12*, 7254. (f) Foitzik, R. C.; Kaynak, A.; Pfeffer, F. M. *Synth. Met.* **2006**, *156*, 637. (g) Foitzik, R. C.; Kaynak, A.; Pfeffer, F. M.; Beckmann, J. *Synth. Met.* **2006**, *156*, 1333. (h) Jiao, L.; Hao, E.; Vicente, G. H.; Smith, K. M. *J. Org. Chem.* **2007**, *72*, 8119. (i) King, R. C. Y.; Boussoualem, M.; Roussel, F. *Polymer* **2007**, *48*, 4047. (j) Zotti, G.; Vercelli, B.; Berlin, A. *Chem. Mater.* **2008**, *20*, 397.
(16) All computations in this study have been performed using the Gaussian 03 suite of programs.[17] The Becke three-parameter exchange functional and the correlation functional of Lee, Yang, and Parr (B3LYP) with the 6-311G(d,p) basis set were used to compute the geometries and the normal mode vibration frequencies of the starting cation, the corresponding transition structure, and the product. For single-point energy calculations on DFT-optimized geometries the SCS-MP2 method was used.[18] The transition structures were localized starting with AM1 reaction pathway calculations using the MOPAC 2007 program.[19] The transition structures were further optimized at the DFT level with the Gaussian 03 package of programs using the option "mndofc" (opt) (ts, noeigentest, mndofc)), applying the B3LYP/6-311G(d,p) basis set. In order to verify the character of the stationary points, they were subjected to frequency analyses. In the discussion, *E* (0 K) energies are used, which contain zero-point corrections. The vibration related to the imaginary frequency corresponds to the nuclear motion along the reaction coordinate under study. Intrinsic reaction coordinate (IRC) calculations were performed in order to unambiguously connect transition structure with reactant and product. Bond orders and atomic charges were calculated with the natural bond orbital (NBO) method as implemented in the Gaussian 03 program.
(17) Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Montgomery, J. A.; Vreven, T., Jr.; Kudin, K. N.; Burant, J. C.; Millam, J. M.; Iyengar, S. S.; Tomasi, J.; Barone, V.; Mennucci, B.; Cossi, M.; Scalmani, G.; Rega, N.; Petersson, G. A.; Nakatsuji, H.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Klene, M.; Li, X.; Knox, J. E.; Hratchian, H. P.; Cross, J. B.; Adamo, C.; Jaramillo, J.; Gomperts, R.; Stratmann, R. E.; Yazyev, O.; Austin, A. J.; Cammi, R.; Pomelli, C.; Ochterski, J. W.; Ayala, P. Y.; Morokuma, K.; Voth, G. A.; Salvador, P.; Dannenberg, J. J.; Zakrzewski, V. G.; Dapprich, S.; Daniels, A. D.; Strain, M. C.; Farkas, O.; Malick, D. K.; Rabuck, A. D.; Raghavachari, K.; Foresman, J. B.; Ortiz, J. V.; Cui, Q.; Baboul, A. G.; Clifford, S.; Cioslowski, J.; Stefanov, B. B.; Liu, G.; Liashenko, A.; Piskorz, P.; Komaromi, I.; Martin, R. L.; Fox, D. J.; Keith, T.; Al-Laham, M. A.; Peng, C. Y.; Nanayakkara, A.; Challacombe, M.; Gill, P. M. W.; Johnson, B.; Chen, W.; Wong, M. W.; Gonzalez, C.; Pople, J. A. *Gaussian 03, Revision C.01*; Gaussian, Inc.: Wallingford, CT, 2004.
(18) Grimme, S. *J. Chem. Phys.* **2003**, *118*, 9095.
(19) (a) Stewart, J. J. P. *MOPAC2007*; Stewart Computational Chemistry: Colorado Springs, CO, 2007; http://OpenMOPAC.net. (b) Stewart, J. J. P. *J. Mol. Modeling* **2007**, *13*, 1173.
(20) Sorensen, T. S.; Rauk, A. *Carbocations in Pericyclic Reactions*; Marchand, A. P., Lehr, R. E., Eds.; Academic Press: New York, 1977; Vol. *II*, p 21.
(21) Houk, K. N.; Li, Y.; Evansek, D. J. *Angew. Chem., Int. Ed.* **1992**, *31*, 682.
(22) For NICS values, see: Schleyer, P. v. R.; Maerker, C.; Dransfeld, A.; Jiao, H.; van Eikema Hommes, N. J. R. *J. Am. Chem. Soc.* **1996**, *118*, 6317−6318.
(23) (a) Heilbronner, E. *Tetrahedron Lett.* **1964**, *5*, 1923. (b) Zimmerman, H. E. *J. Am. Chem. Soc.* **1966**, *88*, 1564. (c) Zimmerman, H. E. *Acc. Chem. Res.* **1971**, *4*, 272. (d) Rzepa, H. S. *Chem. Rev.* **2005**, *105*, 3697. (e) Herges, R. *Chem. Rev.* **2006**, *106*, 4820.