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Ring-Closure Reactions of 1,2-Diaza-4,5-benzoheptatrienyl Metal Compounds: Experiment and Theory†

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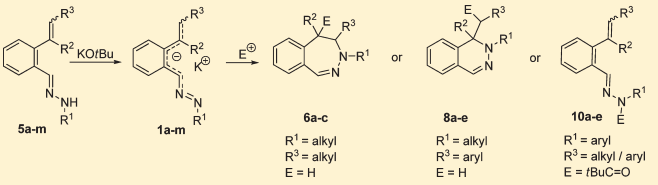
Supporting Information

ABSTRACT: 2-Alkenylbenzylidene hydrazones **5a**−**m**, which are accessible in good to excellent yields in a four-step synthesis, are converted into 1,2-diaza-4,5-benzoheptatrienyl metal compounds **1a**−**m** by treatment with KO-*t*-Bu as base. These metal compounds undergo the various types of reactions in good yields and exclusively depending on the nature of substituents R^1 and R^3. Thus, metal compounds **1a**−**c** carrying alkyl substituents R^1 and R^3 form 3*H*-benzodiazepines **6a**−**c** after electrophilic quench of the intermediate cyclic anion **7** in a 7-*endo*-*trig* electrocyclic reaction with a möbius aromatic transition structure **1**$^-$-**TS**. Similarly, a benzothienyl derivative **5n** is converted into diazepine **6d**. Potassium compounds **1d**−**h**, which are *N*-methyl and aryl substituted at R^3, form 1,2-dihydrophthalazines **8a**−**e** in a predominantly charge-controlled 6-*exo*-*trig* cyclization reaction. In contrast, aryl−aryl-substituted systems **5i**−**m** did not lead to cyclic products upon deprotonation, but the intermediate open-chain metal compounds **1i**−**m** were trapped by acid chlorides at N1 to yield the hydrazides **10a**−**e**. We interpret thermodynamics and kinetics of these reactions in the context of the Baldwin rules on the basis of quantum chemical calculations and discuss the transition structures considering the results of NICS and NBO-charge calculations. Examples of the products **6**, **8**, and **10** could be characterized by X-ray diffraction.



INTRODUCTION

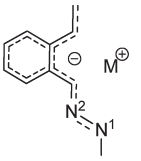
1,2-Diaza-4,5-benzoheptatrienyl anions **1**, specifically their alkali metal compounds (Scheme 1), are potential precursors for competing 4-*exo*-, 5-*endo*-, 5-*exo*-, 6-*endo*-, 6-*exo*-, and 7-*endo*-*trig* cyclization reactions (Scheme 2). They may be understood as homologues of heteroallyl anions like enolates and azaenolates.[1] According to the perturbation theory,[2] heteroatoms disturb the electronic structure of polyenyl anions. Thus, if an electronegative heteroatom like nitrogen is in an odd position (large coefficient of the HOMO), a stabilizing effect, excluding cyclization reactions is observed, otherwise, with the electronegative heteroatom in an even position (node of the HOMO), a destabilizing influence, which may lead to ring-forming reactions.[3−5]

The compounds studied here are anionic, conjugated heptatrienyl systems, specifically their alkali metal compounds with an 4,5-annulated aromatic moiety and two nitrogen atoms introduced in the chain in position 1 and 2. The ambiguous character of N1 in odd and N2 in even position turns anion **1** into a very interesting model compound. It is known from the literature that the *N*-methylene-*N*′-monoalkyl hydrazone subunit has three competing nucleophilic centers (N1, N2, C3) offering various possibilities for unusual reactions.[6]

It may be anticipated that such an electronically unbalanced system may be very susceptible to varying substituent effects. Therefore, we assumed that the reactivity of these compounds might be manipulated by the appropriate choice of the electronic properties of substituents.[7]

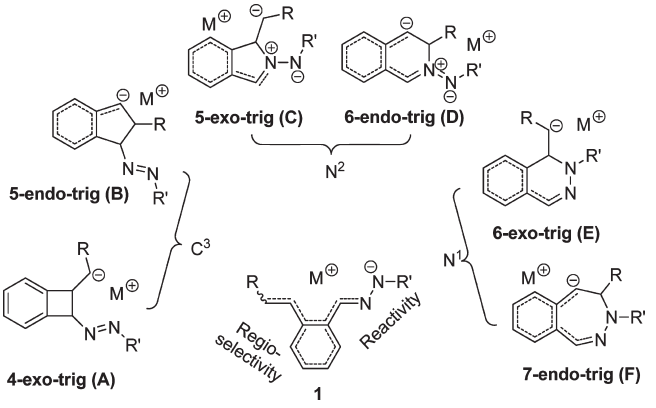
Open-chain mono- and diazaheptatrienyl metal compounds have been utilized as powerful building blocks in the synthesis of highly complex mono- and polycyclic, functionalized heterocyclic

Scheme 1. 1,2-Diaza-4,5-benzoheptatrienyl Metal Compounds 1



1 (M = Li, K)

Scheme 2. Possible Cyclization Reactions of Metal Compounds 1



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Scheme 3. General Synthesis of Hydrazones 5

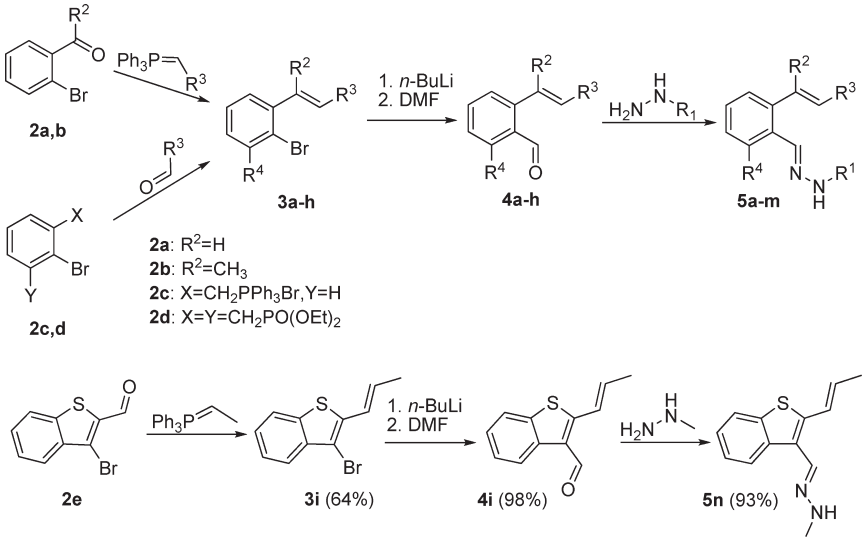

Table 1. Yields and Substitution Patterns of Bromoarenes 3 and Aldehydes 4

no.	yield (%)	no.	yield (%)	R^2	R^3	R^4
3a	53	**4a**	97	H	H	H
3b	61	**4b**	69	Me	H	H
3c	62	**4c**	70	H	Me	H
3d	77	**4d**	70	H	Ph	H
3e	93	**4e**	82	H	Ph	styryl
3f	85	**4f**	83	H	4-Cl-Ph	H
3g	64	**4g**	96	Me	4-Cl-Ph	H
3h	87	**4h**	74	H	4-OMe-Ph	H

Table 2. Yields and Substitution Pattern of Hydrazones 5 from Aldehydes 4

no.	R^1	R^2	R^3	R^4	yield (%)
5a	Me	H	H	H	98
5b	Me	Me	H	H	99
5c	Me	H	Me	H	91
5d	Me	H	Ph	H	96
5e	Me	H	Ph	styryl	66
5f	Me	H	4-Cl-Ph	H	95
5g	Me	Me	4-Cl-Ph	H	98
5h	Me	H	4-OMe-Ph	H	89
5i	Ph	H	H	H	98
5j	Ph	H	Me	H	82
5k	Ph	H	Ph	H	96
5l	4-F-Ph	H	H	H	62
5m	4-F-Ph	H	Ph	H	37

compounds. Previous investigations on this topic have shown that reactions of such metal compounds may lead to the formation of five- (indenes,[8] imidazoles[9]), six- (naphthalenes,[10] pyridines,[4] isoquinolines[7]), and seven-membered rings (benzazepines[11]).

In 1976, when Baldwin formulated rules that should allow chemists to predict ring-forming reactions, he was aware of the ambiguous character of 4-*exo-trig*, 5-*exo-trig*, 6-*endo-trig*, 6-*exo-trig*, and 7-*endo-trig* ring-forming reactions and quoted all of them "favored".[12] A few years later, a great number of studies were undertaken to fill the general rules with examples, adjustments for special types of reactions or particular cases, and experimental approval or disapproval.[13] There are still new aspects appearing that proove the high complexity of this topic.[14]

The rules originate from a careful analysis of "the stereochemical requirements of the transition states" and hence facilities and trajectories of ring-closure reactions.[12] These influences, interpreted as kinetic terms, are supposed to be predominant over the thermodynamics of competing cyclic products.

RESULTS AND DISCUSSION

1,2-Diazaheptatrienyl lithium or potassium compounds **1a**−**n** may be generated by deprotonation of the corresponding hydrazones **5a**−**n** with strong bases like LiTMP, LDA, KO-*t*-Bu, or even potassium as reductive electron base.[15,16]

For the synthesis of the hydrazones **5a**−**m**, a three-step procedure starting from carbonyl compounds **2a,b** was developed, which were converted into the 2-alkenylbromoarenes **3a**−**h** by Wittig (**3a**−**d**,**f**−**i**) or Wittig−Horner (**3e**) olefinations. Then, the aldehydes **4a**−**i** were synthesized by lithiation of **3a**−**i** and formylation using *N*,*N*-dimethylformamide (Scheme 3, Table 1).[17] Finally, condensation of aldehydes **4a**−**i** with mono substituted hydrazines in the presence of molecular sieves gave the 2-alkenylbenzylidene hydrazones **5a**−**m** and benzothienyl hydrazone **5n**.[18]

All hydrazones **5a**−**n** were obtained spectroscopically pure; however, they could not be crystallized. They hydrolyzed easily during column chromatography and decomposed during distillation. Thus, in agreement with known procedures, we decided to use the crude material for further reactions (Table 2).[8,19]

Under standard reaction conditions, the metal compounds **1** were generated by treatment of the 2-alkenyl-1-*N*-methylene-*N*′-alkyl or aryl hydrazones **5a**−**n** with 1.5 equiv of KO-*t*-Bu in anhydrous THF under argon atmosphere at ambient temperature. In all examples, intense red to purple colorings indicated the formation of anions **1**.

Reactions of the Potassium Compounds 1a−c and 1n Carrying Aliphatic Substituents (R^1 and R^3) at N1 and C7. The deprotonation of substrates **5a**−**c** and **5n** carrying alkyl substituents at R^1 and R^3 led after aqueous workup to the

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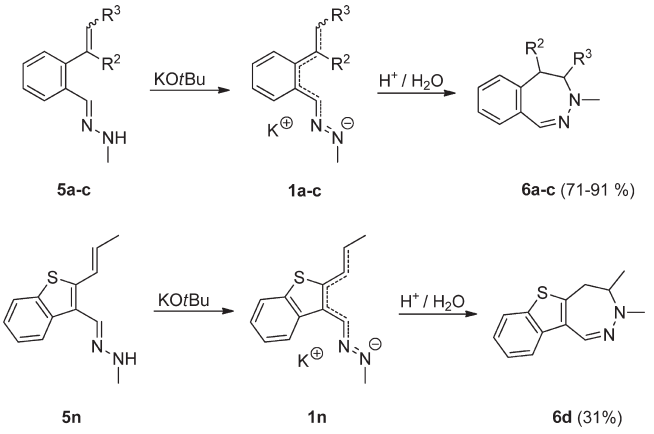
Table 3. Yields and Substitution Pattern of 4,5-Dihydro-3*H*-benzo[*d*][1,2]diazepines 6a−c

no.	R^2	R^3	yield (%)
6a	H	H	71
6b	Me	H	75
6c	H	Me	91

Scheme 4. Deprotonation of Hydrazones 5a−c,n and Ring-Closure Reactions To Give 4,5-Dihydro-3*H*-benzo[*d*]-[1,2]diazepines 6a−c and the Benzothienyl Derivative 6d



formation of 4,5-dihydro-3*H*-benzo[*d*][1,2]diazepines **6a−c** (Table 3), which were obtained in moderate to good yields, and to the corresponding benzothienyl compound **6d** (Scheme 4). These novel substances could be isolated and fully characterized by spectroscopic methods. We also were able to grow single crystals of **6d** and to characterize them by X-ray diffraction (Figure 1).

On the basis of quantum chemical calculations[20] on model anion **1a**$^-$ (without counterion or solvent effects) carried out at the SCS-MP2/6-311+G(d,p)//B3LYP/6-31+G(d,p) level[21,22] (corrected for zero-point energies) of various conformers of the starting anion **1a**$^-$, the transition state **1a**$^-$**-TS**, and product **7a**$^-$, we propose the following mechanism for the formation of diazepinyl anions **7a−c** and **7n**. Once a reasonable helical conformation (in,in′-cis) of the open-chain anion **1a**$^-$ is adopted, the n−π orbitals of the terminal electron-rich atoms overlap and the C−N bond is being formed by a 7-*endo-trig* cyclization. The mutual relationship of these structures was checked by IRC reaction path analysis. The computational results show that the product **7a**$^-$ is 7.2 kcal/mol lower in energy than the open-chain species **1a**$^-$. The activation barrier is quite low with only 1.3 kcal/mol. As expected, less sterically hindered isomeric forms of **1a**$^-$ are lower in energy; however, most barriers of rotation are expected to be easily surmounted under the reaction conditions (counterion, room temperature).[23,24] One should note, however, that the rotation about the iminic CN bond[25] has a relatively high calculated activation barrier of 24.6 kcal/mol. In order to get an idea of possible solvent effects, single-point SCRF-CPCM-(UAKS) calculations using tetrahydrofuran as solvent were performed on the same level of theory. As the data in Scheme 5 indicate, such effects have only minor effects on the kinetics and the thermodynamics of the reaction.[26]

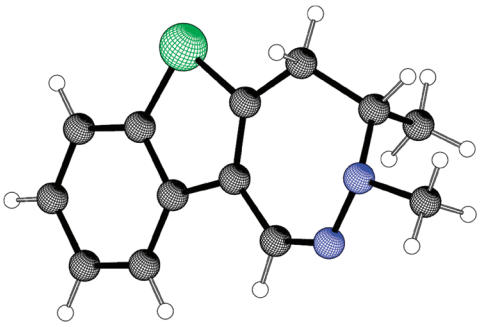
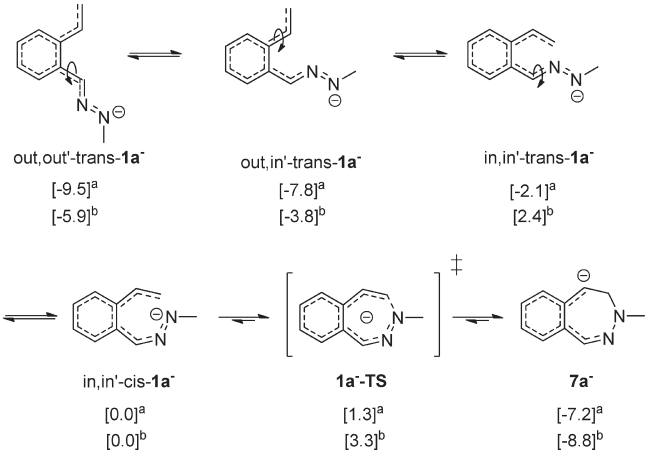


Figure 1. Molecular structure of **6d** as obtained by X-ray diffraction.

Scheme 5. Computational Simulation of the 7-*Endo-Trig* Cyclization of the Anion 1a$^-$ To Give Anion 7a$^-$ as a Model Reaction for the Formation of Type 6 Compounds for the Gas Phase and SCRF-CPCM(UAKS) Solution-Phase Simulations (THF) (Relative Energies: SCS-MP2/6-311+G(d,p)// B3LYP/6-31+G(d,p) (Corrected for Zero-Point Energies) [kcal/mol]; See the Supporting Information for Optimized Structures)



[a] Gas phase data. [b] SCRF-CPCM(UAKS) data for tetrahydrofuran as solvent.

The mode of this cyclization reaction is discussed on the basis of geometries, charges (determined by the natural bond orbital method (NBO[27])), and NICS[28] values (B3LYP/6-311+G(d,p)).

The transition structure **1a**$^-$**-TS** of this conrotatory 8π electron 7-*endo-trig* cyclization process is helically shaped (deviation from plane N1−N2−C3−C4, 4.7°; N2−C3−C4−C6, 17.5°; C3−C4−C5−C6, 11.0°; C4−C5−C6−C7, 13.9°; Σ 47.1°), indicating Möbius aromaticity. The line shape of the calculated NICS values along an axis perpendicular to the TS structure with a lowest value of −8.0 ppm (Figure 2) also indicates π^2 aromaticity.[29] The distance between the terminal atoms amounts to 2.09 Å. The NBO charge on the terminal carbon atom is −0.40e and on the nitrogen atom −0.35e, giving a total charge separation of only 0.05e. Thus, both the NICS value and low charge separation indicate a predominant pericyclic character of the bond-forming step with a strong binding interaction in the HOMO-1 and HOMO-2 (Figure 3).[30−32]

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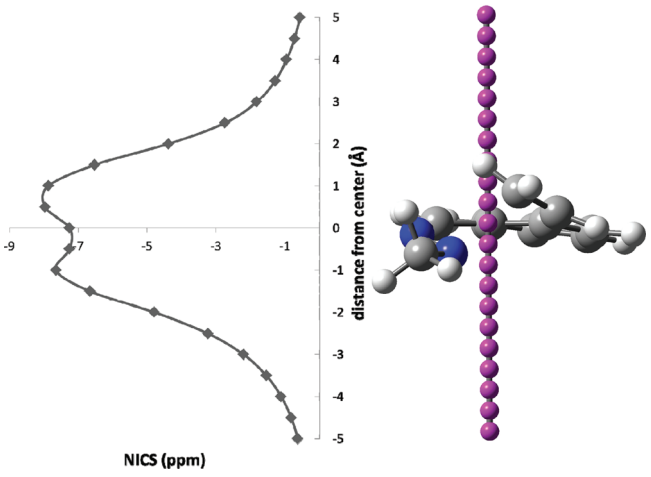


Figure 2. Calculated NICS values (ppm) for the anionic conrotatory 8π ring-closing transition structure **1a**$^-$**-TS** leading to benzodiazepinyl anion **7a**$^-$. The measuring points along an axis perpendicular to the center of the cyclic moiety of the transition structure are shown in purple (B3LYP/6-311+G(d,p)).

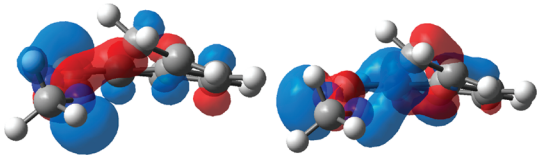
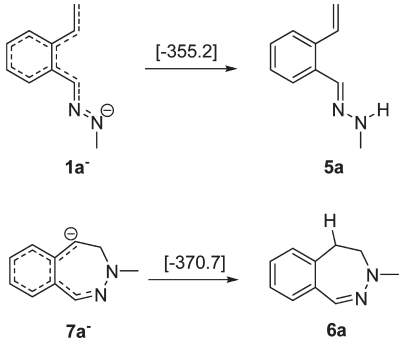


Figure 3. Molecular orbitals HOMO-1 (left) and HOMO-2 (right) of the anionic transition structure **1a**$^-$**-TS** (side view, isocontour value 0.05/0.05; B3LYP/6-31+G(d,p)).

Scheme 6. Calculated Proton Affinities of the Anions 1a$^-$ and 7a$^-$ (SCS-MP2/6-311+G(d,p)//B3LYP/6-31+G(d,p) (Corrected for Zero-Point Energies) [kcal/mol]



Very surprisingly, while optimizing the synthetic potential of this ring forming reaction we were not able to introduce other electrophiles but only protons into the final products **6**. In these experiments, various electrophiles were added to the reaction mixture after the cyclization was completed according to TLC reaction control. However, no other electrophile but a proton was observed in the final products **6**, whatever electrophile was used to trap the anionic reaction mixture.

This observation might be explained by a kind of base-induced autocatalytic proton-transfer reaction mechanism based on the relative basicity of the deprotonated starting material **1**, the resulting metal compound **7**, and that of KO-*t*-Bu. The proton affinities are expected to be of the following order:[16]

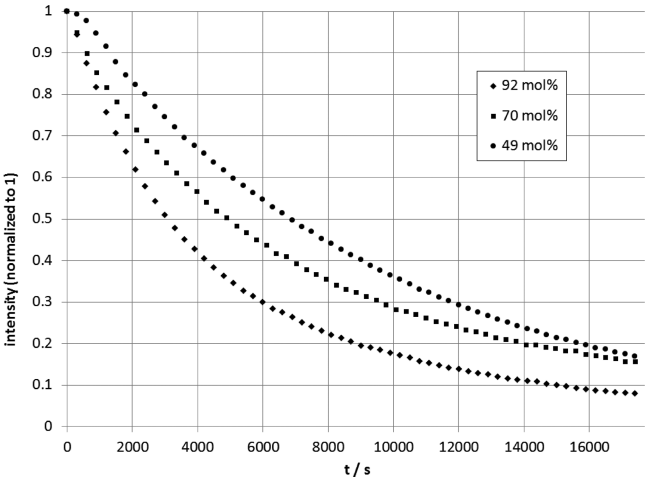


Figure 4. Conversion of **5a** in time-dependent NMR experiments with different substoichiometric loadings of base (●, 49 mol %; ■, 70 mol %; ♦, 92 mol %) (integral of one of the olefinic signals after different reaction times (s), normalized to 1).

$$7 > \text{KO-}t\text{-Bu} > \mathbf{1}$$

Quantum chemical calculations (SCS-MP2/6-311+G(d,p)//B3LYP/6-31+G(d,p)) show that the gas-phase proton affinity of the benzodiazepienyl anion **7a**$^-$ is considerably higher (15.5 kcal/mol) compared to that of the open-chain anion **1a**$^-$ (Scheme 6). Thus, under the reaction conditions, the intermediate benzodiazepinyl anion **7** obviously will be protonated either by hydrazone **5** (feeds one more anion **1**$^-$ into the catalytic cycle) or by *tert*-butyl alcohol (which regenerates the base) generating benzodiazepine **6** and keeping the proton-transfer cycle alive. To support this proposal on a simple and qualitative basis we performed a series of time-dependent NMR experiments with varying substoichiometric amounts of base.

In NMR tubes 0.175 M solutions (THF-d_8) of hydrazone **5a** were treated with substoichiometric amounts (49, 70, 92 mol %) of KO-*t*-Bu at room temperature under argon atmosphere. After the addition, ^{1}H NMR spectra were recorded every 5 min. The spectra showed slowly decreasing signals of hydrazone **5a** and signals of benzodiazepine **6a** increasing with the same rate. The decreasing intensities of one of the olefinic signals of **5a** are shown in Figure 4.

Interestingly, the experimental curves show higher conversion compared to the amount of base used with almost full consumption of the starting material. There is no direct evidence for the metal species **1a** or **7a** in the spectra. Obviously, both species **1a** and **7a** have short half-lives that keep the concentration under the detection limit of NMR spectroscopy. Thus, the deprotonation step, various conformational changes of the intermediate anion **1a**, its ring-closure reaction, and the reprotonation from *t*-BuOH or **5a** are fast at room temperature on the NMR time scale, which is in accordance with the low calculated barrier. In summary, the strong basicity of the cyclic anion **7** is causing the autocatalytic proton transfer in this reaction.

Reactions of the Potassium Compounds 1d−h Carrying Aliphatic Substituents R^1 at N1 and Aromatic Substituents R^3 at C7. Quite surprisingly, substrates **5d−h**, which are

Scheme 7. Deprotonation of Hydrazones 5d−h and Ring-Closure Reactions To Give 1,2-Dihydrophthalazines 8a−e

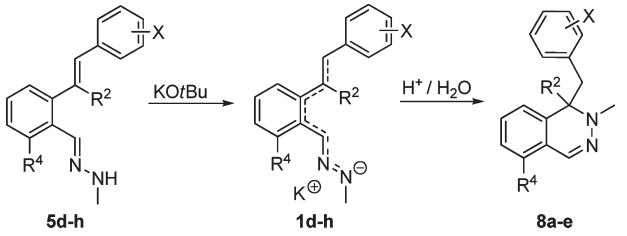


Table 4. Yields and Substitution Pattern of 8a−e

no.	R2	X	R^4	yield (%)
8a	H	H	H	80
8b	H	H	Styryl	84
8c	H	4-Cl	H	97
8d	Me	4-Cl	H	43
8e	H	4-OMe	H	75

N-methyl substituted (R^1) and aryl-substituted at R^3, reacted quite differently compared to the bis-alkyl-substituted substrates discussed so far. Treatment with 1.5 equiv of KO-*t*-Bu as base at room temperature in dry THF under argon atmosphere and subsequent aqueous workup led to formation of 1,2-dihydrophthalazines **8a−e** in moderate to good yields (Scheme 7, Table 4). These new compounds were isolated and characterized using NMR spectroscopy and in the case of **8a** by X-ray diffraction (Figure 5).

We propose the following mechanism for the *6-exo-trig* cyclization forming 1,2-dihydrophthalazine derivatives **8a−e**. Treatment of 2-alkenylbenzylidene hydrazines **5d−h** with KO-*t*-Bu generates the reactive diazaheptatrienyl anions **1d−h**. The terminal nitrogen atom N1 has a sufficient nucleophilicity to attack the electron deficient olefinic α-carbon in a *6-exo-trig* cyclization mode.[6] After the ring closure, the negative charge is well stabilized in the benzylic position of the aromatic substituent R^3. Proton quench of the anion generates the observed 1,2-dihydrophthalazines **8a−e**.

According to quantum chemical calculations (SCS-MP2/6-311+G(d,p)//B3LYP/6-31+G(d,p)), the reaction of model anion out,in′-cis-$\mathbf{1d}^-$ (E_{rel} = 0.0 kcal/mol) to give the cyclic isomer $\mathbf{9a}^-$ is exothermic (−5.6 kcal/mol) with a low activation barrier of only 3.3 kcal/mol. Other isomers of $\mathbf{1d}^-$, e.g., the out, out′-trans conformer (−6.0 kcal/mol) are, as expected, lower in energy (Scheme 8). The transformations of $\mathbf{1d}^-$ include rotations about C3−C4 and N2−C3 of the 1,2-diazaheptatrienyl moiety. The gas phase energy required for rotation about the N2−C3 bond is calculated to be quite high at 22.2 kcal/mol but presumably is lowered by solvent and counterion effects.[23,24] Calculations involving solvent effects (SCRF-CPCM(UAKS), THF) show mostly only minor effects on the relative energies. However, it should be noted that the relative SCRF energy of the cyclic product $\mathbf{9a}^-$ with its relatively localized negative charge is significantly lower[26] compared to the gas phase.

NICS calculations (B3LYP/6-311+G(d,p)) indicate no aromaticity of the transition state $\mathbf{1d}^-$**-TS** with a NICS value of −2.1 ppm (Figure 6). The NBO charges at the terminal bond-forming atoms amount to −0.34e on nitrogen and −0.15e on carbon giving a total charge separation of 0.19e. The distance between these atoms is 2.12 Å. The olefinic side chain is bent out of plane with a deviation of 115°. We conclude that 1,2-dihydrophthalazines **8** are formed in a preferentially charge-controlled reaction.

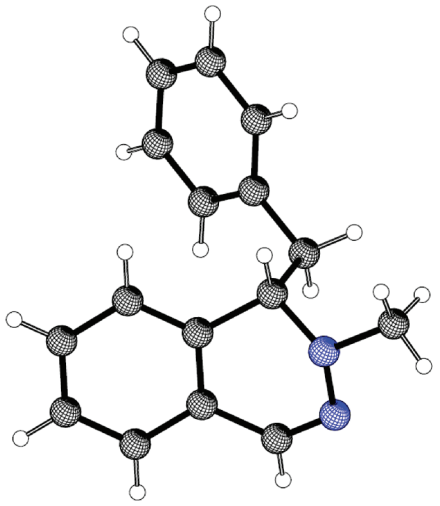


Figure 5. Molecular structure of **8a** as obtained by X-ray diffraction.

Similarly to the reactions of substrates with aliphatic substituents R^3, we were not able to use electrophiles other than protons in order to quench the cyclic anions **9**. After the cyclization was completed according to TLC control, various electrophiles were added to the mixture. However, only protonated products **8** were observed.

In accord with the previous explanations, we state that compounds **5d−h** are deprotonated whereby the cyclic anions **9** are generated. As a strong base, **9** is protonated by either precursor **5** or *tert*-butyl alcohol to give 1,2-dihydrophthalazines **8**.

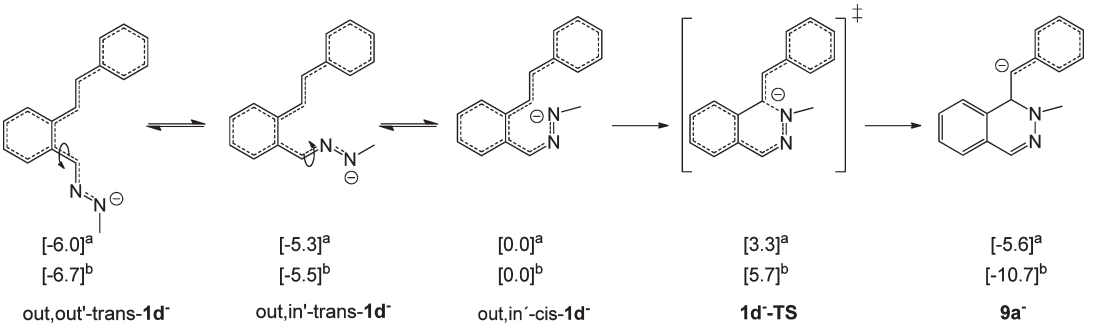
Reactions of the Potassium Compounds 1i−m Carrying Aromatic Substituents R^1 at N1. The last series of compounds studied here covers substrates **5i−m**, which are *N*-aryl substituted (R^1). Treatment with KO-*t*-Bu and trapping with acid chlorides as electrophiles under exactly the same conditions as above gave open-chain *N*-acylated diazaheptatriene compounds **10a−e** in good yields (Table 5). Compounds **10a,c,d** are crystalline and could by analyzed by single-crystal X-ray diffraction.

As here again an intense color is observed during the deprotonation we assume that compounds **5i−m** form the intermediate metal compounds **1i−m** in the course of the reaction. The anionic species formed are well stabilized by the *N*-aryl substituents, especially those with electron-withdrawing groups. Therefore, these less reactive intermediates do not undergo cyclization reactions in contrast to the examples above. The electrophile attacks the intermediate anion at the terminal nitrogen atom, which is the most nucleophilic position.

Ring Formation in the Context of the Baldwin Rules. The discussion of these results in the context of the Baldwin rules is based on a computational treatment of all possible ring-forming reactions in combination with the experiments described above. We investigated 5-*exo-trig*, 5-*endo-trig*, 6-*exo-trig*, 6-*endo-trig*, and 7-*endo-trig* cyclization reactions calculationally for *N*-methyl R = phenyl/H precursors at the quantum chemical level SCS-MP2/6-311+G(d,p)//B3LYP/6-31+G(d,p)+ZPE. In contrast to the preceding sections, here the energies are given relative to the

dx.doi.org/10.1021/jo2001534 |*J. Org. Chem.* 2011, 76, 1979–1991

Scheme 8. Calculated 6-*Exo-Trig* Cyclization of 1d$^-$ as Model for the Formation of Type 8 Compounds from 5d−h for the Gas Phase and SCRF-CPCM(UAKS) Solution-Phase Simulations (THF) (Relative Energies: SCS-MP2/6-311+G(d,p)//B3LYP/6-31+G(d,p) (Corrected for Zero-Point Energies) [kcal/mol]; See the Supporting Information for Optimized Structures)



[a] Gas phase data. [b] SCRF-CPCM(UAKS) data for tetrahydrofuran as solvent.

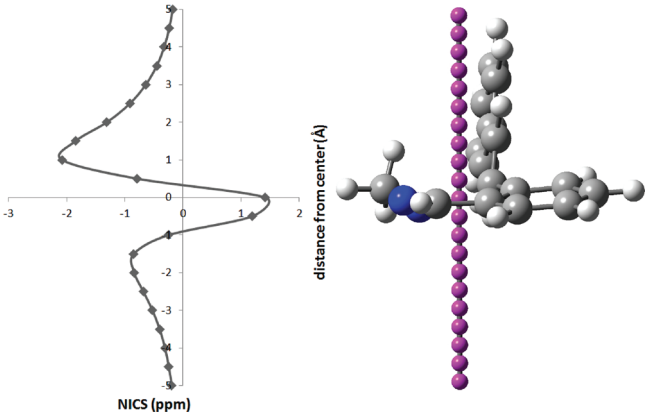
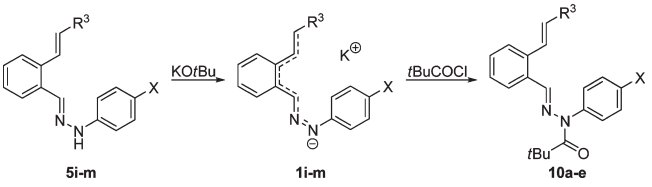


Figure 6. Calculated NICS values (ppm) for the ring-closing transition structure **1d**$^-$**-TS** leading to 1,2-dihydrophthalazinyl anion **9a**$^-$. The measuring points along an axis perpendicular to the center of the cyclic moiety of the transition structure are shown in purple.

Table 5. Yields and Substitution Patterns for Compounds 10a−e

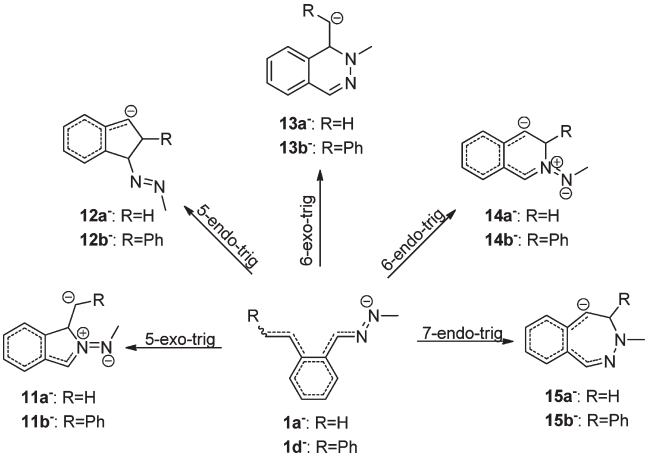


no.	X	R^3	yield (%)
10a	H	H	57
10b	H	Me	53
10c	H	Ph	57
10d	F	H	69
10e	F	Ph	69

global minimum structures (out,out′-trans) of the open chain anion **1a**$^-$, respectively, **1d**$^-$ (Table 6), again neglecting counterions and solvent effects.

In general, the calculational results are consistent with the experimental findings. As expected and in accordance with the qualitative Baldwin rules, the formation of the five-membered ring systems **11**$^-$ and **12**$^-$ is unfavorable. Thus, the structures **11a**$^-$ and **13a**$^-$ (5-*exo-trig* and 6-*exo-trig*) do not correspond to minima on the potential energy hypersurface but open up upon geometry optimization to give conformers of **1a**$^-$. The nonconjugated carbanionic center in these structures is certainly an unfavorable feature compared to the delocalized structure of **1a**$^-$. Similarly, the five-membered ring systems **12**$^-$ (5-*endo-trig*),

Table 6. Comparison of 5-*Exo-Trig*, 5-*Endo-Trig*, 6-*Exo-Trig*, 6-*Endo-Trig*, and 7-*Endo-Trig* Ring-Forming Reactions of Anion 1a$^-$ and 1d$^-$. (Activation Barriers (E_{rel} TS) and Reaction Energies (E_{rel} Cycle) with Regard to the Global Minimum Structures of the Open-Chain Form (E_{rel} = 0.0 kcal/mol)): SCS-MP2/6-311+G(d,p)//B3LYP/6-31+G(d,p) (Corrected for Zero-Point Energies) [kcal/mol]; See the Supporting Information for Optimized Structures)



reaction	product	E_{rel} TS	E_{rel} cycle	product	E_{rel} TS	E_{rel} cycle
5-*exo-trig*	**11a**$^-$[a]			**11b**$^-$[a]		
5-*endo-trig*	**12a**$^-$	30.1	15.7	**12b**$^-$	25.7	9.1
6-*exo-trig*	**13a**$^-$[a]			**13b**$^-$	9.3	**0.4**
6-*endo-trig*	**14a**$^-$	24.2	22.4	**14b**$^-$	21.1	19.2
7-*endo-trig*	**15a**$^-$	10.8	**2.3**	**15b**$^-$	6.3	4.1

[a] Structure of the drawing does not correspond to a minimum on the energy hypersurface.

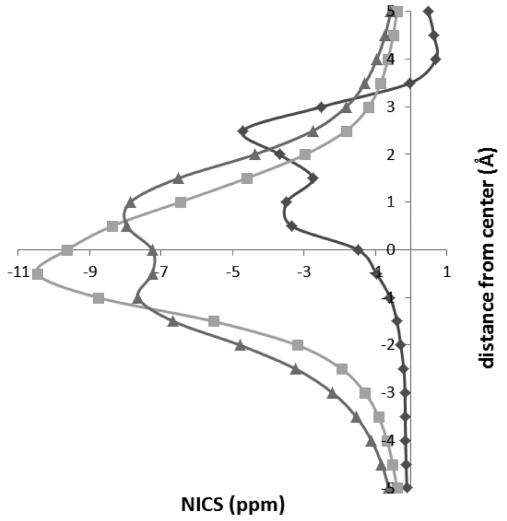


Figure 7. NICS values (ppm) for the transition states of three competing *endo-trig* ring-closure reactions (R^3 = H); ♦, 5-*endo-trig* (**1a**$^-$ → **12a**$^-$); ■, 6-*endo-trig* (**1a**$^-$ → **14a**$^-$); ▲, 7-*endo-trig* (**1a**$^-$ → **15a**$^-$).

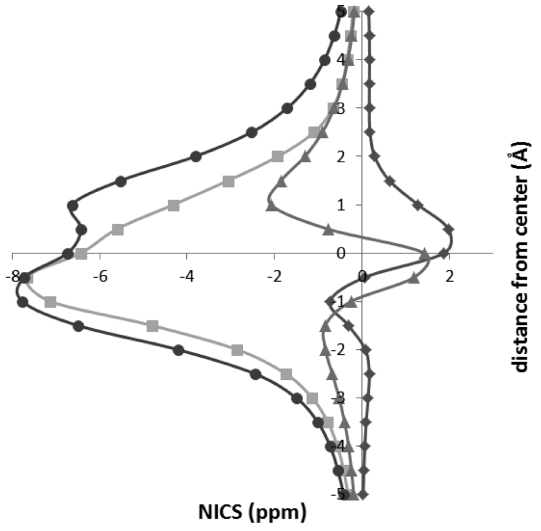
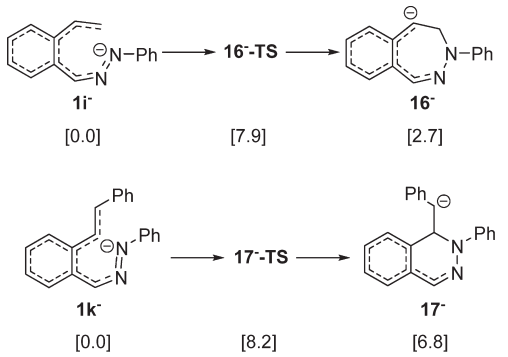


Figure 8. NICS values (ppm) for the transition states of competing ring formations (R^3 = Ph); ♦ 5-*endo-trig* (**1b**$^-$ → **12b**$^-$); ▲, 6-*exo-trig* (**1b**$^-$ → **13b**$^-$); ■, 6-endotrig (**1b**$^-$ → **14b**$^-$); ● 7-endotrig(**1b**$^-$ → **15b**$^-$).

although corresponding to minima on the energy hyper surface, are unfavorable and only accessible via high kinetic barriers in endothermic reactions. NICS calculations indicate a charge controlled, nonpericyclic cyclization mode (Figures 7 and 8). In **13b**$^-$ (6-*exo-trig*), the effect of the phenyl substituent is clearly visible, as it is stabilizing the anionic center, leading to an overall thermoneutral reaction with a low barrier in agreement with the experiments leading to **8a**−**e**. Both 6-*endo-trig* systems **14a**$^-$ and **14b**$^-$ show high calculated barriers and are significantly endothermic. As in the systems **11**$^-$, the dipolar N−N subunit is suspected to be the reason for the relative instability. For **14**$^-$, very low NICS values of the TS clearly indicate a pericyclic ring formation. In contrast to **14**$^-$, the 7-*endo-trig* cyclizations giving **15a**$^-$ and **15b**$^-$ are clearly favored as also seen experimentally for **6a**−**d**. The transition structure is quite low in energy with 10.8 kcal/mol for **15a**$^-$ and 6.3 kcal/mol for **15b**$^-$. The ring closure reactions

Scheme 9. Ring-Closure Reactions of the *N*-Aryl Derivatives 1i$^-$ and 1k$^-$ (Relative Energies: SCS-MP2/6-311+G(d,p)//B3LYP/6-31+G(d,p) Level (Corrected for Zero-Point Energies) [kcal/mol]; See the Supporting Information for Optimized Structures)



of these anionic systems are calculated to be only slightly endothermic. From the NICS results the reaction mode is identified as a π^2 Möbius aromatic electrocyclization involving 8π electrons.

Finally, we investigated as alternative reaction pathways to the experimentally not occurring ring closure reactions of **5i**−**m** via the anions **1i**−**m** the 6-*exo-trig* and 7-*endo-trig* cyclizations of the *N*-phenyl-substituted substrate **1i**$^-$ and **1k**$^-$ (SCS-MP2/6-311+G(d,p)//B3LYP/6-31+G(d,p), Scheme 9). Both reactions show only minor activation barriers, but both products are calculated to be higher in energy compared to the indicated conformations of the starting anions. We conclude from this data, that here the stabilizing substituent effect of the aryl group(s) precludes the experimental realization of otherwise feasible ring closure reactions in the context of the Baldwin rules.

■ CONCLUSION

In summary, we have shown that diazaheptatrienyl metal compounds **1** are precursors for three competing reaction pathways, whose realization exclusively depends on the electronic nature of attached substituents. The first pathway allows access to benzodiazepines **6** through an electrocyclic 8π electron Möbius-type 7-*endo-trig* ring-closure reaction, which is realized if hydrogen or alkyl groups are attached to the vinyl moiety of **1**. We could identify and investigate a base-catalyzed proton-transfer mechanism by use of time dependent NMR methods. Following a second reaction pathway, 1,2-dihydrophthalazines **8** are accessible through an ionic 6-*exo-trig* ring-closure reaction in case aryl groups are used as substituents of substrate **1**. The third reaction pathway allows the synthesis of large, highly unsaturated and conjugated *N*-carbonyl-*N*-aryl-*N*′-(2-alkenylbenzylidene) hydrazides **10** and is applicable in the case of well stabilized, doubly aromatic substituted precursors **1**. Comprehensive quantum-chemical calculations have been carried out to investigate the reaction mechanisms as well as the thermodynamic and kinetic properties of intermediates and transition structures.

The broad variety of cyclic and open-chain products is in agreement with the initial hypothesis that the reactivity of the model compound **1** can be manipulated by the appropriate choice of the electronic properties of the substituents attached.

■ EXPERIMENTAL SECTION

Melting points are uncorrected. ^{1}H, ^{13}C NMR spectroscopy: TMS (^{1}H) (0.00 ppm), $CDCl_3$ (^{1}H) (7.26 ppm), C_6D_6 (1H) (7.16 ppm),

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$CDCl_3$ (^{13}C) (77.0 ppm) and C_6D_6 (^{13}C) (128.1 ppm) were used as internal reference. When necessary, the experiments were carried out with complete exclusion of moisture.

Preparation of Olefins 3a−i. Compounds **3a−i and 4a−i** were prepared according to reference[17] if not marked otherwise.

The spectroscopic data of the following compounds are in agreement with literature data: 2-vinylbromobenzene **3a**,[17] 1-bromo-2-(prop-1-en-2-yl)benzene **3b**,[33] (*E*/*Z*)-1-bromo-2-(prop-1-enyl)benzene **3c**, (*E*/*Z*)-1-bromo-2-styrylbenzene **3d**,[34] (*E*/*Z*)-2-bromo-4′-chlorostilbene **3f**,[14d] (*E*/*Z*)-2-bromo-4′-methoxystilbene **3h**,[35] 2-vinylbenzaldehyde **4a**,[17] 2-(prop-1-en-2-yl)benzaldehyde **4b**,[33] (*E*/*Z*)-2-(prop-1-enyl)benzaldehyde **4c**,[34] (*E*/*Z*)-2-(*E*-*β*-4-methoxystyryl)benzaldehyde **4d**,[34] (*E*/*Z*)-2-(*β*-4′-methoxystyryl)benzaldehyde **4h**,[36] *N*-phenyl-*N*′-(2-(*E*/*Z*)-styrylbenzylidene)hydrazine **5k**.[37]

1-Bromo-2,6-E-di-β-styrylbenzene ***3e*** was prepared according to ref 38. A solution of 2.66 g (110.8 mmol) of NaH (60% in mineral oil) and 0.03 g (1.4 mmol) of 15-crown-5 ether in 200 mL of absolute THF was treated with 25.32 g (55.4 mmol) of 2-bromo-1,3-dimethylenebenzene-bis-diethylphosphate and 11.76 g (110.8 mmol) of benzaldehyde, dissolved in 100 mL of absolute THF at 0 °C and was stirred overnight. Then the mixture was diluted with diethyl ether, washed with brine, dried over $MgSO_4$, filtered, and concentrated. After recrystallization from EtOH and Kugelrohr distillation (100 °C/6 × 10^{-3} mbar) compound **3e** was obtained as colorless solid in 16.35 g (93%, 51.5 mmol) yield: mp 160−161 °C; IR (neat) $\tilde{\nu}$ = 3057, 3030, 3001, 1595, 1578, 1491, 1460, 1449, 1402, 1304, 1211, 1072, 1018, 961, 912, 866, 783, 750, 704, 689, 681; ^1H NMR (400 MHz, $CDCl_3$) δ 6.90 (d, J = 16.1 Hz, 2H), 7.19 (m, 3H), 7.23−7.32 (m, 4H), 7.41−7.52 (m, 8H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 124.7, 124.9, 125.8, 126.3, 127.0, 127.4, 127.7, 130.7, 136.0, 137.3; MS (GC/MS, 2.30e[5]) m/z 362 (90), 360 (100), 276 (20), 265 (25), 204 (55), 203 (95), 202 (50), 189 (20). Anal. Calcd for $C_{22}H_{17}Br$ (361.27): C, 73.14; H, 4.74. Found: C, 72.95; H, 4.68.

X-ray crystal structure analysis of **3e**:[39] formula $C_{22}H_{17}Br$, M = 361.27, colorless crystal 0.23 × 0.15 × 0.10 mm, a = 11.9102(5) Å, b = 19.4178(9) Å, c = 14.6074(7) Å, β = 91.028(2)°, V = 3377.7(3) Å^3, ρ_{calc} = 1.421 g cm^{-3}, μ = 3.266 mm^{-1}, empirical absorption correction (0.496 ≤ T ≤ 0.736), Z = 8, monoclinic, space group $P2_1/m$ (No. 11), λ = 1.54178 Å, T = 223(2) K, ω and φ scans, 29138 reflections collected (±h, ±k, ±l), [(sin θ)/λ] = 0.60 Å^{-1}, 6104 independent (R_{int} = 0.043) and 5295 observed reflections [$I \geq 2\,\sigma(I)$], 433 refined parameters, R = 0.046, wR^2 = 0.127, max (min) residual electron density 1.46 (−0.54) e Å^{-3}, hydrogen atoms calculated and refined as riding atoms.

(E/Z)-1-Bromo-2-(4′-chloro-α-methyl-β-styryl)benzene ***3g***. 4-Benzyltriphenylphosphonium chloride (24.52 g, 57.8 mmol) was dissolved in 200 mL of abs THF, cooled to 0 °C, and treated with 1 equiv (58.0 mmol, 36.3 mL) of *n*-BuLi (1.6 M in hexane). After 30 min, 11.53 g (57.8 mmol) of 2-bromoacetophenone was added dropwise. Then the mixture was allowed to warm to room temperature and was stirred overnight. The mixture was concentrated to 50 mL, the precipitate was filtered off. Subsequent concentration and vacuum distillation (118 °C/2.0× 10^{-2} mbar) gave 10.91 g (64%, 37.1 mmol) of **3g** with an *E*/*Z* ratio of 2.3/1. IR (neat) $\tilde{\nu}$ = 3053, 3026, 2970, 2909, 1589, 1489, 1470, 1431, 1404, 1094, 1024, 1013, 876, 814, 758, 731, 656, 625; ^1H NMR (400 MHz, $CDCl_3$) δ 2.10 (d, J = 1.6 Hz, 3H, *E*), 2.12 (d, J = 1.5 Hz, 3H, *Z*), 6.29 (d, J = 1.4 Hz, 1H, *Z*), 6.39 (d, J = 1.4 Hz, 1H, *E*), 6.71 (m, 2H, *E*), 6.97 (dt, J = 7.9, 2.2 Hz, 2H, *E*), 6.97−7.01 (m, 1H, *Z*), 7.04−7.10 (m, 1H, *E*, 2H, *Z*), 7.16−7.27 (m, 3H, *E*, 4H, *Z*), 7.51 (dd, J = 7.9, 2.2 Hz, 1H, *Z*), 7.52 (dd, J = 8.0, 1.4 Hz, 1H, *E*); ^{13}C NMR (101 MHz, $CDCl_3$) δ 19.5, 26.3, 122.2, 122.3, 126.9, 127.4, 128.1, 128.2, 128.4, 128.5, 128.6, 128.7, 129.2, 129.4, 129.7, 129.8, 130.3, 132.1, 132.9, 133.1, 135.5, 136.0, 138.9, 139.6, 142.9, 146.2; MS (GC/MS, 2.86e[7]) m/z 308 (30), 306 (25), 192 (100), 191 (30), 94 (35). Anal. Calcd for $C_{14}H_{10}BrCl$ (293.59): C, 57.27; H, 3.43. Found: C, 57.28; H, 3.32.

(E/Z)-3-Bromo-2-(prop-1-enyl)benzo[b]thiophene ***3i*** was prepared according to ref 17 from 3-bromobenzo[*b*]thiophene-2-carbaldehyde and ethyltriphenylphosphonium bromide. After purification by column chromatography (cyclohexane) **3i** was obtained as colorless oil in 5.01 g (84%, 19.8 mmol) yield in a *E*/*Z* ratio of 1/1. It was not possible to remove the minor impurity (2-(prop-1-enyl)benzo[*b*]thiophene) by column chromatography or distillation. Purity according to GC > 92%. IR (neat) ν(tilde) = 3059, 3026, 2963, 2909, 1450, 1433, 1321, 1302, 1252, 947, 907, 787, 772, 748, 723; ^1H NMR (400 MHz, C_6D_6) δ 1.48 (d, J = 6.8, 3H, *E*), 1.80 (d, J = 7.4, 3H, *Z*), 5.63 (dq, J = 11.6, 7.4, 1H, *Z*), 6.06 (m, 1H, *E*), 6.75−6.85 (m, br, 1H, *E*, 1H, *Z*), 6.94−7.02 (m, 2H), 7.05−7.14 (m, 2H), 7.31 (d, J = 8.0, 1H, *E*), 7.35 (d, J = 8.0, 1H, *Z*), 7.72 (d, J = 7.8, 1H, *E*), 7.78 (d, J = 7.9, 1H, *Z*); ^{13}C NMR (75 MHz, C_6D_6) δ 15.3, 18.5, 106.4, 108.7, 122.2, 122.4, 122.4, 123.2, 123.4, 123.9, 125.4, 125.4, 125.7, 125.8, 129.9, 131.2, 135.2, 136.6, 137.8, 138.0, 138.2, 139.2; HRMS (ESI) calcd for $C_{11}H_9BrSAg$ 358.8654, found 358.8657.

Preparation of Aldehydes 4a−i. *General Procedure (**A**) for the Formylation of 1-Bromo-2-Alkenylbenzene Derivatives.* The 2-formyl-1-styrylbenzenes were prepared referring to ref 17. A solution of 1-bromo-2-alkenylbenzene (1 equiv) in 50 mL of abs THF was treated with 1.1 equiv of *n*-BuLi (1.6 M in hexane) at −78 °C and stirred for 30 min. Subsequently, 1.5 equiv of dry DMF were added dropwise. While being stirred for 3 h, the mixture was allowed to warm to room temperature followed by dilution with TBME. The organic layer was washed with brine, dried over $MgSO_4$, filtered, and concentrated.

2,6-Bis(E-β-styryl)benzaldehyde ***4e*** was prepared according to general procedure A from **3e** (15.92 g, 43.9 mmol) and DMF (4.81 g, 65.9 mmol). Subsequent recrystallization from EtOH gave compound **4e** as a colorless solid: 11.22 g (82%, 36 mmol); mp 165−167 °C; IR (neat) $\tilde{\nu}$ = 3053, 3034, 1597, 1578, 1493, 1449, 984, 962, 899, 793, 746, 691; ^1H NMR (400 MHz, C_6D_6) δ 6.90 (d, J = 16.1, 2H), 7.23−7.17 (m, 6H), 7.35 (d, J = 7.7, 2H), 7.50−7.45 (m, 5H), 7.93 (d, J = 16.1, 2H), 10.56 (s, 1H); ^{13}C NMR (101 MHz, C_6D_6) δ 126.4, 127.1, 127.3, 128.3, 129.0, 131.7, 132.6, 134.3, 137.5, 140.9, 192.8; HRMS (ESI) calcd for $C_{23}H_{18}ONa$ 333.1250, found 333.1251. Anal. Calcd for $C_{23}H_{18}O$ (310.39): C, 89.00; H, 5.85. Found: C, 88.95; H, 5.86.

2-(E-β-4′-Chlorostyryl)benzaldehyde ***4f*** was prepared according to general procedure A from **3f** (3.79 g, 13.0 mmol) and DMF (1.43 g, 19.5 mmol). After distillation (126 °C/7.6 × 10^{-1} mbar), compound **4f** was obtained as a colorless oil: 2.61 g (83%, 10.8 mmol); IR (neat) $\tilde{\nu}$ = 3080, 3059, 3024, 2961, 2859, 2745, 1695, 1589, 1493, 1476, 1447, 1387, 1202, 1180, 1115, 899, 783, 698; ^1H NMR (300 MHz, $CDCl_3$) δ 6.78 (s, 2H), 6.98−6.91 (m, 2H), 7.16−7.04 (m, 4H), 7.33 (dd, J = 8.3, 2.3, 1H), 7.76 (d, J = 2.3, 1H), 10.08 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 125.1, 127.9, 128.5, 128.8, 129.2, 132.1, 133.9, 134.00, 134.4, 134.4, 135.4, 139.3, 190.5; HRMS (ESI) calcd for $C_{15}H_{11}ClONa$ 265.0391, found 265.0388. Anal. Calcd for $C_{15}H_{11}ClO$ (242.05): C, 74.23; H, 4.57. Found: C, 74.09; H, 4.67.

2-(E-α-Methyl-β-4′-chlorostyryl)benzaldehyde ***4g*** was prepared according to general procedure A from **3g** (3.34 g, 10.7 mmol) and DMF (1.17 g, 16.1 mmol). After distillation (121 °C/5.5 × 10^{-2} mbar), compound **4g** was obtained as a colorless oil: 2.63 g (96%, 10.3 mmol) in a *E*/*Z* ratio of 2.3/1; IR (neat) $\tilde{\nu}$ = 3065, 3028, 2970, 2911, 2845, 2745, 1694, 1595, 1491, 1447, 1402, 1269, 1192, 1094, 1013, 872, 827, 816, 770, 646; ^1H NMR (300 MHz, $CDCl_3$) δ 2.18 (d, J = 1.6 Hz, 3H, *E*), 2.22 (d, J = 1.5 Hz, 3H, *Z*), 6.26 (d, J = 1.2 Hz, 1H, *Z*), 6.56 (d, J = 1.4 Hz, 1H, *E*), 6.58−6.64 (m, 2H, *E*), 6.90−6.97 (m, 2H, *E*), 7.15−7.40 (m, 2H, *E*, 6H, *Z*), 7.52 (dd, J = 22.8, 1.5 Hz, 1H, *Z*), 7.52 (dd, J = 7.6, 1.5 Hz, 1H, *E*), 7.84 (dd, J = 7.8, 1.4 Hz, 1H, *E*), 7.86−7.90 (m, 1H, *Z*), 9.98 (d, J = 0.7 Hz, 1H, *E*), 10.14 (d, J = 0.6 Hz, 1H, *Z*); ^{13}C NMR (75 MHz, $CDCl_3$) δ 20.8, 28.5, 127.5, 127.9, 128.4, 128.4, 128.6, 128.6, 128.7, 128.8, 129.3, 129.8, 130.2, 130.3, 131.9, 132.4, 132.5, 132.9, 133.6, 133.7, 134.8, 135.5, 135.5, 135.8, 145.9, 149.1, 191.6, 192.0; HRMS (ESI) calcd

for $C_{16}H_{13}ClONa$ 297.0553, found 297.0609. Anal. Calcd for $C_{16}H_{13}ClO$ (256.07): C, 74.85; H, 5.10. Found: C, 74.79; H, 5.26.

2-(Prop-1-enyl)benzo[b]thiophene-3-carbaldehyde ***4i*** was prepared according to general procedure A from **3i** (1.87 g, 7.5 mmol) and DMF (822 mg, 11.3 mmol). After purification by column chromatography (cyclohexane 98%, TBME 2%), compound **4i** was obtained as a colorless solid: 1.17 g (76%, 5.9 mmol); mp 48−49 °C; IR (neat) $\tilde{\nu}$ = 3001, 2909, 2841, 2750, 1666, 1638, 1506, 1460, 1433, 1358, 1202, 1136, 1053, 939, 752, 731, 700; ^{1}H NMR (300 MHz, C_6D_6) δ 1.42 (dd, J = 6.8, 1.8, 3H), 6.05 (dq, J = 15.4, 6.8, 1H), 6.75 (dq, J = 15.4, 1.7, 1H), 7.04−6.98 (dd, J = 7.2, 1.2, 1H), 7.17 (ddd, J = 8.2, 7.2, 1.2, 1H), 7.35−7.30 (m, 1H), 8.84 (ddd, J = 8.2, 1.2, 0.7, 1H), 10.14 (s, 1H); ^{13}C NMR (75 MHz, C_6D_6) δ 18.6, 121.6, 121.9, 125.0, 126.0, 126.2, 128.9, 135.0, 137.0, 138.2, 156.4, 183.8; HRMS (ESI) calcd for $C_{12}H_{10}OSNa$ 225.0345, found 225.0345. Anal. Calcd for $C_{12}H_{10}OS$ (202.27): C, 71.25; H, 4.98. Found: C, 71.34; H, 5.14.

Preparation of Hydrazones 5a−n. General procedure B for the synthesis of (2-alkenylbenzylidene)hydrazine derivatives was performed referring to our previous work.[8] To dried molecular sieves (4 Å) in a Schlenk flask under argon atmosphere a solution of 5.0 mmol of aldehyde in 25 mL of dry dichloromethane was added and the mixture treated with 1 or 1.5 equiv of the respective hydrazine. The mixture was stirred overnight at room temperature. Subsequently, the slurry was filtered through a pad of silica, and the filtrate was diluted with TBME, washed with brine, dried over $MgSO_4$, filtered, and concentrated. The substances were used without further purification.

N-Methyl-N′-(2-vinylbenzylidene)hydrazine ***5a*** was obtained according to general procedure B from aldehyde **4a** (660 mg, 5.0 mmol) and methylhydrazine (345 mg, 7.5 mmol) as a colorless oil: 782 mg (98%, 4.8 mmol); bp 78 °C/3.0 × 10^{-2} mbar; IR (neat) $\tilde{\nu}$ = 3373, 3061, 2928, 2870, 1763, 1699, 1684, 1653, 1636, 1624, 1576, 1558, 1541, 1506, 1472, 1466, 1449, 1437, 1418, 1358, 1261, 1159, 1018, 989, 914, 820, 770, 752, 633; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.88 (d, J = 0.6 Hz, 3H), 5.25 (dd, J = 11.0, 1.4 Hz, 1H), 5.54 (dd, J = 17.4, 1.4 Hz, 1H), 7.03 (dd, J = 17.4, 11.0 Hz, 1H), 7.11−7.20 (m, 2H), 7.31−7.38 (m, 1H), 7.67 (m, 1H), 7.70 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 34.9, 116.6, 125.7, 126.6, 127.8, 127.8, 133.2, 133.3, 134.5, 135.9; HRMS (ESI) calcd for $C_{10}H_{13}N_2$ 161.1073, found 161.1076.

N-(2-(Prop-1-en-2-yl)benzylidene)-N′-methylhydrazine ***5b*** was obtained according to general procedure B from aldehyde **4b** (728 mg, 5.0 mmol) and methylhydrazine (345 mg, 7.5 mmol) as a light yellow oil: 857 mg (99%, 4.9 mmol); IR (neat) $\tilde{\nu}$ = 3416, 3078, 3063, 2968, 2855, 2795, 1638, 1605, 1584, 1559, 1489, 1474, 1435, 1371, 1348, 1304, 1277, 1221, 1150, 1117, 1082, 1042, 1016, 951, 899, 814, 756, 660, 633, 556, 515, 502 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.07 (dd, J = 1.5, 1.0 Hz, 3H), 2.95 (d, J = 0.5 Hz, 3H), 4.90 (dq, J = 1.9, 0.9 Hz, 1H), 5.26 (dq, J = 3.1, 1.5 Hz, 1H), 7.11−7.26 (m, 4H), 7.73 (s, 1H), 7.84−7.89 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 25.1, 34.9, 116.3, 124.8, 127.1, 127.5, 128.0, 132.5, 134.9, 142.6, 144.2; HRMS (ESI) calcd for $C_{11}H_{14}N_2Na$ 197.1055, found 197.1060.

N-Methyl-N′-(2-((E/Z)-prop-1-enyl)benzylidene)hydrazine ***5c***. According to general procedure B, **5c** was obtained from aldehyde **4c** (732 mg, 5.0 mmol) and methylhydrazine (345 mg, 7.5 mmol) as a light yellow oil: 797 mg (91%, 4.6 mmol) in a ratio E/Z of 2.5/1; ^{1}H NMR (400.13 MHz, CD_2Cl_2) δ 1.67 (dd, J = 7.0, 1.8 Hz, 3H, Z), 1.90 (dd, J = 6.7, 1.8 Hz, 3H, E), 2.92 (d, J = 0.4 Hz, 3H, Z), 2.95 (d, J = 0.4, 3H, E), 5.66 (br, 1H, E/Z), 5.88 (dq, J = 7.0, 11.4 Hz, 1H, Z), 6.04 (dq, J = 6.6, 15.5 Hz, 1H, E), 6.57 (ddd, J = 11.4, 1.7, 3.4 Hz, 1H, Z), 6.78 (ddd, J = 15.5, 1.6, 3.3 Hz, 1H, E), 7.10−7.24 (m, 2H, E/Z), 7.33−7.38 (m, 1H, E/Z), 7.62 (s, 1H, Z), 7.69−7.72 (m, 1H, E), 7.77 (s, 1H, E), 7.80−7.84 (m, 1H, Z); ^{13}C NMR (100.61 MHz, CD_2Cl_2) δ 14.6, 19.0, 35.0, 35.1, 124.8, 125.7, 127.0, 127.2, 127.2, 127.4, 127.9, 128.3, 128.4, 128.5, 128.9, 130.0, 133.3, 133.6, 134.4, 135.7, 136.4; HRMS (ESI) calcd for $C_{11}H_{14}N_2Na$ 197.1049, found 197.1043.

N-Methyl-N′-(2-(E/Z)-β-styrylbenzylidene)hydrazine ***5d***. According to general procedure B, **5d** was obtained from aldehyde **4d** (1.04 g, 5.0 mmol) and methylhydrazine (345 mg, 7.5 mmol) as a light yellow oil: 1.14 g (96%, 4.8 mmol) in an E/Z ratio of 2.3/1; bp 132 °C/3.0 × 10^{-2} mbar; IR (neat) $\tilde{\nu}$ = 3416, 3057, 3022, 2886, 2797, 1601, 1582, 1493, 1474, 1445, 1404, 1350, 1152, 1117, 1084, 1028, 957, 918, 878, 785, 760, 698, 667, 635; ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.76 (s, 3H, Z), 2.93 (s, 3H, E), 5.49 (br, 1H, E/Z), 6.59 (d, 1H, J = 12.2, Z), 6.66 (d, 1H, J = 12.2, E), 6.89 (d, 1H, J = 16.1, E), 6.99 − 7.70 (m, 10H, E/Z, 1H, E), 7.77 (s, 1H, Z), 7.78 (d, 1H, E); ^{13}C NMR (75.47 MHz, $CDCl_3$) δ 34.7, 35.1, 124.8, 126.2, 126.3, 126.4, 126.5, 126.6, 127.3, 127.5, 127.6, 127.7, 127.9, 128.2, 128.3, 128.7, 128.9, 129.1, 129.4, 131.3, 133.6, 133.9, 135.5, 135.8, 136.6, 137.6; HRMS (ESI) calcd for $C_{16}H_{17}N_2$ 237.1386, found 237.1384.

N-(2,6-Di-β-styryl)benzylidene-N′-methylhydrazine ***5e***. According to general procedure B, **5e** was obtained from aldehyde **4e** (1.55 g, 5.0 mmol) and methylhydrazine (345 mg, 7.5 mmol) as an orange solid: 1.37 g (66%, 3.3 mmol); mp 88−90 °C; IR (neat) $\tilde{\nu}$ = 3345, 3028, 2920, 2855, 1591, 1560, 1491, 1450, 1346, 1159, 1138, 1074, 961, 951, 851, 789, 748, 739, 691, 673, 656, 611; ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.06 (s, 3H), 6.98 (d, J = 16.2 Hz, 2H), 7.22−7.40 (m, 7H), 7.48−7.60 (m, 8H), 7.87 (s, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 35.1, 126.0, 126.6, 126.6, 127.6, 128.0, 128.7, 128.7, 130.4, 133.2, 137.0, 137.8; HRMS (ESI) calcd for $C_{24}H_{23}N_2$ 339.1856, found 339.1864. Anal. Calcd for $C_{24}H_{22}N_2$ (338.44): C, 85.17; H, 6.55; N, 8.28. Found: C, 84.90; H, 6.37; N, 8.14.

N-(2-(β-4′-Chlorostyryl)benzylidene)-N′-methylhydrazine ***5f***. According to general procedure B, **5f** was obtained from aldehyde **4f** (1.21 g, 5.0 mmol) and methylhydrazine (345 mg, 7.5 mmol) as a yellow resin: 1.29 g (95%, 4.8 mmol); IR (neat) $\tilde{\nu}$ = 3422, 3350, 3057, 2976, 2876, 2799, 1773, 1574, 1493, 1472, 1447, 1400, 1348, 1155, 1105, 1076, 918, 870, 812, 785, 772, 750, 696; ^{1}H NMR (300 MHz, C_6D_6) δ 2.31 (s, 1H), 6.47 (dd, J = 16.6, 12.1, 1H), 6.90 (dd, J = 7.7, 4.8, 2H), 7.11 (dd, J = 7.5, 1.5, 1H), 7.33 (s, 1H), 8.35 (s, 1H); ^{13}C NMR (75 MHz, C_6D_6) δ 34.12, 125.10, 127.41, 127.67, 127.68, 128.55, 129.35, 129.98, 131.29, 132.09, 133.85, 133.96, 136.55, 136.74; HRMS (ESI) calcd for $C_{16}H_{16}ClN_2$ 271.0997, found 271.0990.

N-(2-(α-Methyl-β-4′-chlorostyryl)benzylidene)-N′-methylhydrazine ***5g***. According to general procedure B, **5g** was obtained from aldehyde **4g** (1.28 g, 5.0 mmol) and methylhydrazine (345 mg, 7.5 mmol) as a yellow resin: 1.39 g (98%, 4.9 mmol) and a E/Z ratio of 2.5/1; IR (neat) $\tilde{\nu}$ = 3022, 2968, 2909, 2872, 2797, 1584, 1489, 1441, 1402, 1348, 1225, 1148, 1092, 1013, 951, 874, 814, 756, 692; ^{1}H NMR (300 MHz, C_6D_6) δ 2.09 (m, 3H, E, 3H, Z), 2.48 (s, 3H, E), 2.58 (s, 3H, Z), 4.95 (br, 1H, E, 1H, Z), 6.36 (s, 1H, Z), 6.40 (d, J = 1.3, 1H, E), 6.82−6.88 (m, 2H, E), 6.89−6.96 (m, 2H, E), 6.98− 7.29 (m, 4H, E, 8H, Z), 7.55 (s, 1H, E), 7.67 (s, 1H, Z), 8.44 (m, 1H, E, 1H, Z); ^{13}C NMR (75 MHz, C_6D_6) δ 20.7, 28.2, 34.5, 34.7, 125.5, 125.7, 127.0, 127.6, 127.6, 127.8, 128.3, 128.3, 128.6, 128.6, 128.7, 129.5, 129.9, 130.5, 130.6, 131.8, 132.5, 133.0, 133.6, 133.8, 135.9, 136.6, 138.5, 138.8, 140.3, 144.2; HRMS (ESI) calcd for $C_{17}H_{18}ClN_2$ 285.1153, found 285.1143.

N-(2-(β-4′-Methoxystyryl)benzylidene)-N′-methylhydrazine ***5h***. According to general procedure B, **5h** was obtained from aldehyde **4h** (1.19 g, 5.0 mmol) and methylhydrazine (345 mg, 7.5 mmol) as a light yellow resin: 1.19 g (89%, 4.5 mmol); IR (neat) $\tilde{\nu}$ = 3373, 3007, 2936, 2837, 1763, 1682, 1603, 1578, 1510, 1464, 1449, 1429, 1302, 1246, 1175, 1111, 1028, 962, 820, 752, 696; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.98 (s, 3H), 3.80 (d, J = 0.7 Hz, 3H), 5.67 (s, 1H), 6.80−6.98 (m, 3H), 7.23 (m, 2H), 7.38 (d, J = 16.1 Hz, 1H), 7.44 (d, J = 8.4 Hz, 2H), 7.48−7.58 (m, 1H), 7.69−7.78 (m, 1H), 7.85 (s, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 35.1, 55.4, 114.2, 124.1, 126.2, 126.6, 127.4, 127.9, 127.9, 130.4, 130.9, 133.3, 133.8, 135.8, 159.4; HRMS (ESI) calcd for $C_{17}H_{19}N_2O$ 267.1492, found 267.1491.

N-Phenyl-N′-(2-vinylbenzylidene)hydrazine ***5i***. According to general procedure B, **5i** was obtained from aldehyde **4a** (663 mg, 5.0 mmol) and phenylhydrazine (542 mg, 5.0 mmol) as a light yellow oil: 1.09 g (98%, 4.9 mmol) yield; IR (neat) $\tilde{\nu}$ = 3306, 3055, 3026, 2911, 1661, 1601, 1495, 1447, 1314, 1258, 1246, 1128, 1069, 1036, 883, 750, 694, 633; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.37 (dd, J = 11.0, 1.4 Hz, 1H), 5.61 (dd, J = 17.4, 1.4 Hz, 1H), 6.86 (tt, J = 7.4, 1.1, 1H), 7.09 (m, 2H), 7.16 (dd, J = 17.4, 11.0 Hz, 1H), 7.21−7.31 (m, 4H), 7.41−7.47 (m, 1H), 7.63 (s, 1H), 7.84−7.89 (m, 1H), 7.91 (s, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 112.7, 117.0, 120.1, 126.4, 126.9, 127.8, 128.3, 129.2, 129.3, 132.2, 134.6, 135.4, 136.3, 144.6; HRMS (ESI) calcd for $C_{15}H_{14}N_2Na$ 223.1230, found 223.1237.

N-Phenyl-N′-(2-((E/Z)-prop-1-enyl)benzylidene)hydrazine ***5j***. According to general procedure B, **5j** was obtained from aldehyde **4c** (730 mg, 5.0 mmol) and phenylhydrazine (540 mg, 5.0 mmol) as an orange resin: 968 mg (82%, 4.1 mmol) with an E/Z ratio of 2/1; bp 153 °C/8.0 × 10^{-2} mbar; IR (neat) $\tilde{\nu}$ = 3314, 3028, 2963, 2909, 1694, 1599, 1576, 1557, 1520, 1493, 1443, 1373, 1308, 1288, 1260, 1192, 1171, 1138, 1105, 1069, 993, 964, 945, 914, 881, 748, 691, 669, 650, 640, 615; ^{1}H NMR (300 MHz, C_6D_6) δ 1.56 (dd, J = 7.0, 1.8 Hz, 3H, Z), 1.76 (dd, J = 6.6, 1.8 Hz, 3H, E), 2.71 (s, 1H, Z), 4.44 (s, 1H, E), 5.75 (dq, J = 11.4, 7.0 Hz, 1H, Z), 5.90 (dq, J = 15.5, 6.6 Hz, 1H, E), 6.48−6.51 (m, 1H, E), 6.51−6.54 (m, 1H, Z), 6.56 (q, J = 1.8, 1H, E), 6.71−6.91 (m, 2H, E, 2H, Z), 6.98−7.19 (m, 6H, Z, 6H, E), 7.19−7.29 (m, 2H, Z, 1H, E), 7.34 (s, 1H, E), 7.36 (s, 1H, Z), 8.06 (m, 1H, E), 8.17−8.26 (m, 1H, Z); ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.0, 17.5, 111.00, 111.7, 117.8, 118.9, 124.3, 124.4, 125.2, 125.9, 125.9, 126.1, 126.5, 126.9, 127.0, 127.1, 127.3, 127.8, 127.9, 127.9, 128.2, 128.2, 128.6, 132.4, 134.2, 134.4, 134.4, 135.3; HRMS (ESI) $C_{16}H_{16}N_2Na$ calcd for 259.1206, found 259.1212.

N-(4-Fluorophenyl)-N′-(2-vinylbenzylidene)hydrazine ***5l***. According to general procedure B, **5l** was obtained from aldehyde **4a** (658 mg, 5.0 mmol) and 4-fluorophenylhydrazine (629 mg, 5.0 mmol) as a yellow resin: 1.15 g (62%, 3.1 mmol); IR (neat) $\tilde{\nu}$ = 3237, 3067, 2963, 1684, 1653, 1601, 1506, 1300, 1260, 1223, 1153, 1076, 1013, 918, 862, 797, 772, 689, 662, 648, 604; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.38 (dd, J = 11.0, 1.4 Hz, 1H), 5.62 (dd, J = 17.4, 1.4 Hz, 1H), 6.90−7.06 (m, 4H), 7.15 (dd, J = 17.4, 11.0, 1H), 7.24−7.32 (m, 2H), 7.41−7.47 (m, 1H), 7.59 (s, 1H), 7.82−7.88 (m, 1H), 7.94 (s, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 113.7 (d, 7.5 Hz), 115.5 (d, J = 22.6 Hz), 117.1 126.3, 126.9, 27.8, 128.4, 132.1, 134.5, 135.6, 136.3, 141.0 (d, J = 2.1 Hz), 157.3 (d, J = 237.0 Hz); HRMS (ESI) calcd for $C_{15}H_{13}FN_2Na$ 263.0955, found 263.0962.

N-(4-Fluorophenyl)-N′-(2-β-styrylbenzylidene)hydrazine ***5m***. According to general procedure B, after recrystallization from ethanol **5m** was obtained from aldehyde **4d** (1.03 g, 5.0 mmol) and 4-fluorophenylhydrazine (633 mg, 5.0 mmol) as a yellow solid: 0.59 g (37%, 1.9 mmol); mp 143 °C (ethanol); IR (neat) $\tilde{\nu}$ = 3291, 3048, 3022, 1595, 1553, 1510, 1493, 1479, 1447, 1416, 1354, 1290, 1256, 1209 (s, CF), 1152, 1126, 1088, 1074, 1045, 964, 916, 827, 802, 752, 729, 691, 652, 602; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.89−6.96 (m, 3H), 6.97−7.03 (m, 3H), 7.26−7.33 (m, 3H), 7.34−7.40 (m, 2H), 7.55 (m, 3H), 7.64 (d, J = 16.1, 1H), 7.74−7.79 (m, 1H), 7.98 (s, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 113.7 (d, J = 7.5 Hz), 115.8 (d, J = 22.6 Hz), 126.7, 126.9, 127.1, 127.3, 127.7, 127.8, 128.4, 128.8, 131.4, 132.4, 135.9, 136.2, 137.5, 140.9 (d, J = 2.2 Hz,), 157.3 (d, J = 237.4 Hz); HRMS (ESI) calcd for $C_{21}H_{17}FN_2Na$ 339.1268, found 339.1273.

1-Methyl-2-((2-prop-1-enyl)benzo[b]thiophen-3-yl)methylene)hydrazine ***5n***. According to general procedure B, **5n** was obtained from aldehyde **4i** (1.01 g, 5.0 mmol) and methylhydrazine (345 mg, 7.5 mmol) as a light yellow oil: 1.07 g (93%, 4.7 mmol); IR (neat) $\tilde{\nu}$ = 3393, 3316, 2963, 2909, 2868, 1589, 1458, 1433, 1369, 1200, 1155, 1121, 1080, 1018, 943, 758, 731; ^{1}H NMR (300 MHz, C_6D_6) δ 1.62 (dd, J = 6.8, 1.8, 3H), 2.53 (d, J = 0.5, 3H), 6.13 (dq, J = 15.4, 6.7, 1H), 6.91 (dq, J = 15.4, 1.7, 1H), 7.14−7.06 (m, 1H), 7.29 (ddd, J = 8.3, 7.1, 1.2, 1H), 7.52 (ddd, J = 8.0, 1.2, 0.7, 1H), 7.65 (s, 1H), 8.94 (ddd, J = 8.2, 1.2, 0.7, 1H); ^{13}C NMR (75 MHz, C_6D_6) δ 18.8, 34.9, 122.0, 123.8, 124.9, 125.3, 126.0, 127.3, 129.4, 130.3, 138.2, 139.3, 139.9; HRMS (ESI) calcd for $C_{13}H_{15}N_2S$ 231.0950, found 231.0951.

Synthesis of 4,5-Dihydro-3*H*-benzo[*d*][1,2]diazepines 6a−d. General procedure C for the deprotonation and further conversion of hydrazones **5a**−**n** was performed. To a solution of 2 mmol of hydrazone in 30 mL of abs THF, 1.5 equiv (3.0 mL, 3.0 mmol) of KO-*t*-Bu (1 M in THF) was added at room temperature. The solution was stirred for 16 h and was quenched subsequently with saturated NH_4Cl solution. After dilution with TBME, the mixture was washed with brine, dried over $MgSO_4$, filtered, and concentrated.

3-Methyl-4,5-dihydro-3H-benzo[d][1,2]diazepine ***6a***. According to general procedure C after deprotonation of hydrazone **5a** (321 mg, 2.0 mmol) and purification by HPLC (*n*-pentane 85%, TBME 10%, TEA 5%), **6a** was obtained as a colorless oil: 232 mg (71%, 1.4 mmol); bp of 115 °C/1 × 10^{-3} mbar; IR (neat) $\tilde{\nu}$ = 3061, 3017, 2955, 2909, 2855, 2791, 1558, 1495, 1445, 1400, 1310, 1258, 1204, 1150, 1117, 1022, 924, 874, 781, 756, 727, 698, 664, 633, 611; ^{1}H NMR (300 MHz, C_6D_6) δ 2.79−2.85 (m, 2H), 2.92 (ddd, J = 5.6, 3.7, 1.1, 2H), 2.95 (s, 3H), 6.80−6.85 (m, 1H), 6.92 (dd, J = 7.2, 2.0, 1H), 6.95−6.99 (m, 1H), 7.00−7.04 (m, 1H), 7.27 (s, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 37.8, 48.4, 54.2, 126.4, 127.6, 129.2, 132.2, 132.5, 135.3, 139.8; HRMS (ESI) calcd for $C_{10}H_{13}N_2$ 161.1073, found 161.1075. Anal. Calcd for $C_{10}H_{12}N_2$ (160.22): C, 74.97; H, 7.55; N,17.48. Found: C, 75.14; H, 7.80; N, 17.26.

3,5-Dimethyl-4,5-dihydro-3H-benzo[d][1,2]diazepine ***6b***. According to general procedure C after deprotonation of hydrazone **5b** (349 mg, 2.0 mmol) and purification by column chromatography (*n*-pentane 85%, TBME 10%, TEA 5%), **6b** was obtained as a colorless oil: 317 mg (91%, 1.82 mmol); IR (neat) $\tilde{\nu}$ = 3061, 3005, 2959, 2856, 1558, 1491, 1462, 1439, 1402, 1368, 1323, 1254, 1240, 1211, 1153, 1090, 1078, 1036, 997, 907, 808, 754, 698, 658, 633, 588, 549; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.24−1.29 (m, 3H), 3.15 (d, J = 12.5, 1H), 3.21 (s, 3H), 3.29 (ddd, J = 17.6, 12.7, 5.9 Hz, 2H), 7.07 (s, 1H), 7.12−7.30 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 22.3, 41.7, 49.0, 58.6, 126.3, 127.2, 128.7, 131.7, 132.2, 133.9, 145.2; HRMS (ESI) calcd for $C_{11}H_{15}N_2$ 175.1230, found 175.1232. Anal. Calcd for $C_{11}H_{14}N_2$ (174.24): C, 75.82; H, 8.10; N, 16.08. Found: C, 75.82; H, 8.20; N, 16.05.

3,4-Dimethyl-4,5-dihydro-3H-benzo[d][1,2]diazepine ***6c***. According to general procedure C after deprotonation of hydrazone **5c** (346 mg, 2.0 mmol) and purification by Kugelrohr distillation (143 °C/2 × 10^{-2} mbar), **6c** was obtained as a colorless oil: 264 mg (75%, 1.5 mmol); IR (neat) $\tilde{\nu}$ = 3060, 3016, 2974, 2929, 2868, 2806, 1583, 1556, 1492, 1444, 1400, 1375, 1350, 1319, 1263, 1251, 1205, 1157, 1124, 1109, 1072, 1026, 993, 947, 914, 879, 848, 804, 756, 730, 690, 667; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.92 (d, J = 6.8 Hz, 3H). 2.94 (dd, J = 15.8, 5.6 Hz, 1H), 3.19 (s, 3H), 3.31 (d, J = 15.8 Hz, 1H), 3.86−3.94 (m, 1H), 7.07−7.26 (m, 5H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 12.3, 42.7, 46.3, 56.7, 126.4, 127.4, 129.9, 130.5, 132.3, 133.9, 136.6; HRMS (ESI) calcd for $C_{11}H_{15}N_2$ 175.1235, found 175.1237. Anal. Calcd for $C_{11}H_{14}N_2$ (174.24): C, 75.82; H, 8.10; N, 16.08. Found: C, 75.57; H, 8.14; N, 16.13.

3,4-Dimethyl-4,5-dihydro-3H-thiopheno[d][1,2]diazepine ***6d***. According to general procedure C after deprotonation of hydrazone **5n** (463 mg, 2.0 mmol) and purification by column chromatography (cyclohexane 90%, TBME 10%), **6d** was obtained as a colorless solid: 142 mg (31%, 0.62 mmol); mp 75−78 °C; IR (neat) $\tilde{\nu}$ = 2984, 2916, 2872, 2799, 1558, 1535, 1460, 1449, 1437, 1395, 1377, 1350, 1319, 1240, 1177, 1155, 1111, 970, 945, 901, 868, 785, 752, 729, 675, 650, 606; ^{1}H NMR (300 MHz, C_6D_6) δ 0.88−0.70 (m, 3H); 2.64 (td, J = 4.9, 1.5, 1H), 3.03 (d, J = 4.9, 3H), 3.32−3.04 (m, 2H), 7.12−6.95 (m, 2H), 7.50−7.41 (m, 1H), 7.62−7.52 (m, 1H), 7.81 (s, 1H); ^{13}C NMR (75 MHz, C_6D_6) δ 10.5, 38.1, 47.5, 55.7, 121.2, 122.2, 124.5, 124.8, 127.2, 127.3, 139.3, 139.7, 140.3; HRMS (ESI) calcd for $C_{13}H_{15}N_2S$ 231.0950, found

231.0945. Anal. Calcd for $C_{13}H_{14}N_2S$ (230.32): C, 67.79; H, 6.31; N, 12.16. Found: C, 67.51; H, 5.99; N, 11.96.

X-ray crystal structure analysis of **6d**:[39] formula $C_{13}H_{14}N_2S$, M = 230.32, colorless crystal 0.43 × 0.15 × 0.02 mm, a = 8.6678(16) Å, b = 6.1892(4) Å, c = 21.9200(20) Å, β = 100.563(11)°, V = 1156.0(2) Å^3, ρ_{calc} = 1.323 g cm^{-3}, μ= 2.247 mm^{-1}, empirical absorption correction (0.445 ≤ T ≤ 0.956), Z = 4, monoclinic, space group $P2_1/n$ (No. 14), λ= 1.54178 Å, T = 223(2) K, ω and φ scans, 4773 reflections collected (±h, ±k, ±l), [(sinθ)/λ] = 0.60 Å^{-1}, 1676 independent (R_{int} = 0.075) and 1288 observed reflections [$I \geq 2\ \sigma(I)$], 147 refined parameters, R = 0.064, wR^2 = 0.186, max (min) residual electron density 0.36 (−0.31) e Å^{-3}, hydrogen atoms calculated and refined as riding atoms.

Synthesis of 2-Methyl-1,2-dihydrophthalazines 8a−e. *1-Benzyl-2-methyl-1,2-dihydrophthalazine* ***8a***. According to general procedure C after deprotonation of hydrazone **5d** (471 mg, 2.0 mmol) and purification by HPLC (*n*-pentane 85%, TBME 10%, TEA 5%), **8a** was obtained as a colorless solid: 380 mg (80%, 1.6 mmol); mp 51 °C; IR (neat) $\tilde{\nu}$ = 3026, 2945, 2855, 2808, 1605, 1541, 1495, 1450, 1439, 1371, 1333, 1285, 1234, 1161, 1123, 1103, 1074, 1013, 924, 883, 853, 802, 768, 748, 731, 694; ^{1}H NMR (300 MHz, C_6D_6) δ 2.82 (dd, J = 12.7, 9.4 Hz, 1H), 2.95 (dd, J = 12.7, 4.8 Hz, 1H), 3.16 (s, 3H), 4.21 (dd, J = 9.4, 4.8 Hz, 1H), 6.21−6.31 (m, 1H), 6.69−6.78 (m, 2H), 6.84−6.95 (m, 2H), 6.99−7.07 (m, 1H), 7.07−7.15 (m, 3H), 7.53 (s, 1H); ^{13}C NMR (75 MHz, C_6D_6) δ 33.2, 42.6, 62.2, 123.5, 125.7, 126.3, 126.5, 127.6, 128.3, 128.4, 130.2, 131.7, 135.1, 138.2; HRMS (ESI) calcd for $C_{16}H_{17}N_2$ 237.1392, found 237.1392. Anal. Calcd for $C_{16}H_{16}N_2$ (236.31): C, 81.32; H, 6.82; N, 11.85. Found: C, 81.06; H, 6.81; N, 11.54.

X-ray crystal structure analysis of **8a**:[39] formula $C_{16}H_{16}N_2$, M = 236.31, colorless crystal 0.30 × 0.25 × 0.15 mm, a = 5.5133(2) Å, b = 8.0665(3) Å, c = 25.6190(9) Å, V = 1280.60(8) Å^3, ρ_{calc} = 1.226 g cm^{-3}, μ= 0.073 mm^{-1}, empirical absorption correction (0.979 ≤ T ≤ 0.989), Z = 4, orthorhombic, space group $P2_12_12_1$ (No. 19), λ= 0.71073 Å, T = 223(2) K, ω and φ scans, 7616 reflections collected (±h, ±k, ±l), [(sinθ)/λ] = 0.67 Å^{-1}, 2941 independent (R_{int} = 0.053) and 2678 observed reflections [$I \geq 2\ \sigma(I)$], 164 refined parameters, R = 0.050, wR^2 = 0.177, Flack parameter 0(4), max (min) residual electron density 0.31 (−0.35) e Å^{-3}, hydrogen atoms calculated and refined as riding atoms.

1-Benzyl-2-methyl-5-β-styryl-1,2-dihydrophthalazine ***8b***. According to general procedure C after deprotonation of hydrazone **5e** (675 mg, 2.0 mmol) and purification by column chromatography (*n*-pentane 80%, TBME 20%), **8b** was obtained as a light red wax: 574 mg (84%, 1.7 mmol); IR (neat) $\tilde{\nu}$ = 3061, 3026, 2926, 2857, 1701, 1649, 1585, 1495, 1452, 1381, 1344, 1256, 1206, 1161, 1113, 1026, 959, 937, 746, 691; ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.78 (dd, J = 12.8, 9.6, 1H), 3.05 (dd, J = 12.8, 4.7, 1H), 3.26 (s, 3H), 4.34 (dd, J = 9.5, 4.7, 1H), 6.21 (d, J = 7.4, 1H), 6.85 (dd, J = 6.7, 2.8, 2H), 7.00−7.09 (m, 2H), 7.13−7.22 (m, 3H), 7.31 (dt, J = 4.5, 1.8, 1H), 7.39 (t, J = 7.4, 2H), 7.61−7.43 (m, 4H), 7.85 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 32.44, 42.68, 62.61, 121.83, 123.95, 125.2, 125.78, 126.18, 126.67, 127.99, 128.15, 128.79, 128.81, 129.88, 132.05, 132.08, 133.31, 133.33, 137.21, 137.68; HRMS (ESI) calcd for $C_{24}H_{23}N_2$ 339.1856, found 339.1857.

1-(4-Chlorobenzyl)-2-methyl-1,2-dihydrophthalazine ***8c***. According to general procedure C after deprotonation of hydrazone **5f** (541 mg, 2.0 mmol) and purification by HPLC (cyclohexane 85%, TBME 15%), **8c** was obtained as a colorless solid: 507 mg (97%, 1.9 mmol); mp of 83−85 °C; IR (neat) $\tilde{\nu}$ = 3026, 2947, 2855, 2808, 1495, 1450, 1373, 1285, 1234, 1163, 1123, 1103, 1013, 924, 804, 768, 748, 731, 694; ^{1}H NMR (599 MHz, benzene) δ 2.55 (dd, J = 12.8, 9.4, 1H), 2.63 (dd, J = 12.8, 4.7, 1H), 3.01 (s, 3H), 3.96 (dd, J = 9.4, 4.7, 1H), 6.04−6.10 (m, 1H), 6.27−6.34 (m, 2H), 6.75 (dd, J = 11.4, 4.3, 2H), 6.92 (td, J = 7.4, 1.2, 1H), 6.94−6.97 (m, 2H), 7.36 (s, 1H); ^{13}C NMR (151 MHz, benzene) δ 32.4, 42.5, 61.8, 123.6, 125.5, 126.4, 127.7, 128.3, 128.5, 131.2, 131.5, 132.2, 135.1, 136.6; HRMS (ESI) calcd for $C_{16}H_{16}ClN_2$ Cl 271.0997, found 271.0979. Anal. Calcd for $C_{16}H_{15}ClN_2$ (270.76): C, 70.98; H, 5.58; N, 10.35. Found: C, 70.82; H, 5.58; N, 10.05.

1-(4-Chlorobenzyl)-1,2-dimethyl-1,2-dihydrophthalazine ***8d***. According to general procedure C after deprotonation of hydrazone **5g** (567 mg, 2.0 mmol) and purification by column chromatography (cyclohexane 85%, TEA 15%), **8d** was obtained as a light yellow solid: 241 mg (43%, 0.9 mmol); mp of 66−72 °C; IR (neat) $\tilde{\nu}$ = 3061, 3030, 2967, 2930, 2878, 1489, 1447, 1379, 1354, 1200, 1092, 1080, 1016, 972, 908, 858, 849, 810, 795, 758, 745, 718; ^{1}H NMR (400 MHz, C_6D_6) δ 1.36 (s, 3H), 2.50 (d, J = 13.0, 1H), 3.02 (d, J = 13.0, 1H), 3.15 (s, 1H), 6.34−6.40 (m, 2H), 6.45 (d, J = 7.8, 1H), 6.85 (dd, J = 7.5, 1.1, 1H), 6.91 (td, J = 7.6, 1.4, 1H), 6.98−7.09 (m, 3H), 7.50 (d, J = 0.4, 1H); ^{13}C NMR (101 MHz, C_6D_6) δ 21.6, 36.2, 39.8, 60.2, 123.6, 124.2, 126.2, 127.4, 127.9, 128.8, 132.3, 132.3, 134.2, 135.0, 136.0; GC−MS m/z 284 (30), 282 (100), 267 (20), 240 (30), 132 (30), 130 (40), 89 (40). Anal. Calcd for $C_{17}H_{17}ClN_2$ (284.11): C, 71.70; H, 6.02; N, 9.84. Found: C, 71.65; H, 5.97; N, 9.62.

1-(4-Methoxybenzyl)-2-methyl-1,2-dihydrophthalazine ***8e***. According to general procedure C after deprotonation of hydrazone **5h** (537 mg, 2.0 mmol) and distillation (115 °C/1.0 × 10^{-3} mbar), **9e** was obtained as a colorless resin: 404 mg (75%, 1.5 mmol); IR (neat) $\tilde{\nu}$ = 3021, 2959, 2922, 2808, 1611, 1512, 1454, 1300, 1246, 1179, 1101, 1026, 1009, 912, 812, 752, 739; ^{1}H NMR (300 MHz, C_6D_6) δ 2.72 (dd, J = 12.9, 9.4 Hz, 1H), 2.84 (dd, J = 12.9, 4.8 Hz, 1H), 3.09 (s, 3H), 3.28 (s, 3H), 4.10 (dd, J = 9.4, 4.8 Hz, 1H), 6.20−6.27 (m, 1H), 6.52−6.60 (m, 2H), 6.61−6.70 (m, 2H), 6.77−6.87 (m, 2H), 6.96 (td, J = 7.5, 1.3 Hz, 1H), 7.44 (s, 1H); ^{13}C NMR (75 MHz, C_6D_6) δ 32.3, 42.6, 54.6, 62.3, 113.9, 123.5, 125.8, 126.6, 127.6, 129.9, 131.1, 131.9, 135.0, 158.7; MS (GC−MS) m/z 266 (100), 223 (85), 178 (25), 159 (45), 148 (28), 115 (40), 89 (25). Anal. Calcd for $C_{17}H_{18}N_2O$ (266.14): C, 76.66; H, 6.81; N, 10.52. Found: C, 76.43; H, 6.52; N, 10.15.

Synthesis of *N*-Aryl-*N*′-(2-alkenylbenzylidene)-*N*-trimethylacetyl Hydrazides 10a−e. General procedure D for the synthesis of *N*-(2-alkenylbenzylidene)-*N*′-phenyl-*N*′-trimethylacetyl hydrazides **10a−e** was performed. To a solution of the corresponding hydrazone in 30 mL of abs THF was added 1.5 equiv of KO-*t*-Bu (1 M in THF) at room temperature. The solution was stirred for 16 h, 1 equiv of trimethylacetyl chloride was added dropwise, and the mixture was stirred for additional 2 h. After dilution with TBME, the mixture was washed with brine, dried over $MgSO_4$, filtered, and concentrated.

N-Phenyl-N′-(2-vinylbenzylidene)-N-trimethylacetyl Hydrazide ***10a***. According to general procedure D after deprotonation of hydrazone **5i** (389 mg, 1.8 mmol), conversion with trimethylacetyl chloride (216 mg, 1.8 mmol), and recrystallization from ethanol, **10a** was obtained as a yellow solid: 314 mg (57%, 1.0 mmol); mp 109 °C; IR (neat) $\tilde{\nu}$ = 3088, 3067, 2970, 2930, 2872, 1665, 1655, 1603, 1589, 1558, 1476, 1449, 1393, 1319, 1287, 1233, 1188, 1175, 1163, 1115, 1086, 1070, 1018, 986, 928, 914, 903, 858, 810, 775, 752, 718, 694; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.48 (s, 9H), 5.13 (dd, 1H, J = 1.2, 11.0), 5.37 (dd, 1H, J = 1.2, 17.3), 6.56 (dd, 1H, J = 11.0, 17.4), 7.05−7.09 (m, 2H), 7.22−7.40 (m, 4H), 7.41 (s, 1H), 7.43−7.49 (m, 2H), 7.81−7.86 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 27.8, 40.6, 118.0, 125.9, 127.0, 127.9, 128.9, 129.4, 130.1, 131.6, 133.3, 137.3, 137.6, 138.5, 179.0; HRMS (ESI) calcd for $C_{20}H_{22}N_2ONa$ 329.1624, found 329.1632. Anal. Calcd for $C_{20}H_{22}N_2O$ (306.17): C, 78.40; H, 7.24; N, 9.14. Found: C, 78.27; H, 7.24; N, 9.08.

X-ray crystal structure analysis of **10a**:[39] formula $C_{20}H_{22}N_2O$, M = 306.40, colorless crystal 0.30 × 0.05 × 0.05 mm, a = 5.9552(4), b = 18.8208(12), c = 15.8660(13) Å, β = 97.527(3)°, V = 1763.0(2) Å^3, ρ_{calc} = 1.154 g cm^{-3}, μ= 0.559 mm^{-1}, empirical absorption correction (0.850 ≤ T ≤ 0.973), Z = 4, monoclinic, space group $P2_1/c$ (No. 14), λ= 1.54178 Å, T = 223(2) K, ω and φ scans, 11779 reflections collected (±h, ± k, ± l), [(sinθ)/λ] = 0.60 Å^{-1}, 2974 independent (R_{int} = 0.092) and 1982 observed reflections [$I \geq 2\ \sigma(I)$], 211 refined parameters, R = 0.091,

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wR^2 = 0.271, max (min) residual electron density 0.44 (−0.27) e Å^{-3}, hydrogen atoms calculated and refined as riding atoms.

N-((E/Z)-Prop-1-enylbenzylidene)-N′-phenyl-N′-trimethylacetyl Hydrazide ***10b***. According to general procedure C after deprotonation of hydrazone **5j** (486 mg, 2.0 mmol), conversion with trimethylacetyl chloride (241 mg, 2.0 mmol), and purification by HPLC (*n*-pentane 50%, TBME 47%, TEA 3%), **10b** was obtained as a colorless solid: 338 mg (53%, 1.1 mmol); mp 82 °C; IR (neat) $\tilde{\nu}$ = 3067, 2970, 2926, 2870, 1734, 1668, 1605, 1585, 1560, 1491, 1479, 1454, 1393, 1364, 1321, 1285, 1221, 1171, 1072, 964, 959, 926, 905, 818, 764, 735, 719, 706, 694, 652; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.45 (dd, 3H, J = 7.0, 1.7, *Z*), 1.53 (s, 9H, *E*/*Z*), 1.70 (dd, 3H, J = 6.6, 1.7, *E*), 5.63 (dq, 1H, J = 7.0, 11.4, *Z*), 5.84 (dq, 1H, J = 6.6, 15.5, *E*), 6.20 (dd, 1H, J = 11.4, 1.5, *Z*), 6.29 (dd, 1H, J = 15.6, 1.6, 3.3, *E*), 7.07−7.18 (m, 2H, *E*/*Z*), 7.01−7.34 (m, 3H, *E*/*Z*), 7.40−7.60 (m, 4H, *E*/*Z*), 7.81−7.90 (m, 1H, *E*), 8.00−8.02 (m, 1H, *Z*); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.5, 18.8, 26.6, 27.1, 40.5, 40.9, 125.5, 126.3, 127.1, 127.4, 127.5, 127.6, 127.7, 129.2, 129.2, 129.3, 129.4, 129.5, 129.5, 129.7, 130.1, 130.3, 130.4, 130.9, 131.7, 132.7, 137.9, 138.1, 138.2, 138.4, 174.4, 179.0; HRMS (ESI) calcd for $C_{21}H_{24}N_2ONa$ 343.1781, found 343.1787. Anal. Calcd for $C_{21}H_{24}N_2O$ (320.19): C, 78.71; H, 7.55; N, 8.74. Found: C, 78.65; H, 7.47; N, 8.40.

N-Phenyl-N′-((E/Z)-styrylbenzylidene)-N′-trimethylacetyl Hydrazide ***10c***. According to general procedure D after deprotonation of hydrazone **5k** (1.52 g, 5.1 mmol), conversion with trimethylacetyl chloride (613 mg, 5.1 mmol), and recrystallization from ethanol **10c** was obtained as a colorless solid: 1.10 g (57%, 2.9 mmol); mp 149 °C; IR (neat) $\tilde{\nu}$ = 3069, 2972, 2924, 1663, 1605, 1587, 1558, 1487, 1479, 1445, 1391, 1381, 1312, 1285, 1244, 1213, 1190, 1173, 1117, 1086, 1072, 1026, 961, 928, 905, 860, 775, 746, 714, 704, 633, 621; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.48 (s, 9H), 6.40 (s, 2H), 6.77−6.82 (m, 2H), 6.90−6.95 (m, 2H), 7.10−7.20 (m, 4H), 7.24−7.36 (m, 3H), 7.37−7.44 (m, 3H), 7.93−7.97 (m, 1H); ^{13}C NMR (100.61 MHz, $CDCl_3$) δ 26.8, 39.5, 124.5, 125.7, 126.5, 126.6, 127.0, 127.6, 127.9, 128.1, 128.4, 128.5, 128.8, 131.0, 131.4, 134.7, 136.0, 136.8, 138.2, 177.8; HRMS (ESI) calcd for $C_{26}H_{27}N_2O$ 383.2118, found 383.2122. Anal. Calcd $C_{26}H_{26}N_2O$ (382.20): C, 81.64; H, 6.85; N, 7.32. Found: C, 81.17; H, 6.86; N, 7.11.

X-ray crystal structure analysis of **10c**:[39] formula $C_{26}H_{26}N_2O$, M = 382.49, colorless crystal 0.30 × 0.25 × 0.02 mm, a = 10.3577(6) Å, b = 11.0416(6) Å, c = 19.1457(11) Å, V = 2189.6(2) Å^3, ρ_{calc} = 1.160 g cm^{-3}, μ = 0.549 mm^{-1}, empirical absorption correction (0.853 ≤ T ≤ 0.989), Z = 4, orthorhombic, space group $P2_12_12_1$ (No. 19), λ = 1.54178 Å, T = 223(2) K, ω and φ scans, 25132 reflections collected (±h, ±k, ±l), [(sinθ)/λ] = 0.60 Å^{-1}, 3734 independent (R_{int} = 0.105) and 2788 observed reflections [$I \geq 2\,\sigma(I)$], 265 refined parameters, R = 0.047, wR^2 = 0.102, Flack parameter −0.1(5), max (min) residual electron density 0.11 (−0.13) e Å^{-3}, hydrogen atoms calculated and refined as riding atoms.

N-(4-Fluorophenyl)-N′-(2-vinylbenzylidene)-N-trimethylacetyl Hydrazide ***10d***. According to general procedure D after deprotonation of hydrazone **5l** (319 mg, 1.4 mmol), conversion with trimethylacetyl chloride (169 mg, 1.4 mmol), and recrystallization from ethanol, **10d** was obtained as a colorless solid: 283 mg (69%, 0.9 mmol); mp 131 °C; IR (neat) $\tilde{\nu}$ = 3071, 2955, 2920, 2868, 1655, 1605, 1557, 1504, 1479, 1450, 1396, 1362, 1327, 1288, 1215 (s, CF), 1175, 1092, 991, 947, 920, 847, 826, 800, 781, 750, 727, 698, 623; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.54 (s, 9H), 5.26 (dd, 1H, J = 1.2, 11.0), 5.47 (dd, 1H, J = 1.2, 17.3), 6.66 (dd, 1H, J = 11.0, 17.4), 7.10−7.43 (m, 7H), 7.49 (s, 1H), 7.88−7.93 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 27.8, 40.7, 117.2 (d, J = 22.8), 118.3, 125.9, 127.1, 128.0, 129.6, 130.8, 130.9, 131.4, 133.2 (d, J = 3.4), 133.2, 137.7, 138.6, 162.5 (d, J = 162.5), 179.2; HRMS (ESI) calcd for $C_{20}H_{21}FN_2ONa$ 347.1530, found 347.1537. Anal. Calcd for $C_{20}H_{21}FN_2O$ (324.16): C, 74.05; H, 6.53; N, 8.64. Found: C, 73.99; H, 6.43; N, 8.52.

X-ray crystal structure analysis of **10d**:[39] formula $C_{20}H_{21}FN_2O$, M = 324.39, colorless crystal 0.35 × 0.35 × 0.05 mm, a = 8.8802(2) Å, b = 9.8243(2) Å, c = 10.8484(2) Å, α = 96.224(2)°, β = 96.788(1)°, γ = 109.107(1)°, V = 877.04(3) Å^3, ρ_{calc} = 1.228 g cm^{-3}, μ = 0.675 mm^{-1}, empirical absorption correction (0.798 ≤ T ≤ 0.967), Z = 2, triclinic, space group $P\bar{1}$ (No. 2), λ = 1.54178 Å, T = 223(2) K, ω and φ scans, 10825 reflections collected (±h, ±k, ±l), [(sinθ)/λ] = 0.60 Å^{-1}, 3165 independent (R_{int} = 0.044) and 2831 observed reflections [$I \geq 2\,\sigma(I)$], 220 refined parameters, R = 0.042, wR^2 = 0.113, max (min) residual electron density 0.15 (−0.19) e Å^{-3}, hydrogen atoms calculated and refined as riding atoms.

N-(4-Fluorophenyl)-N′-(2-β-styrylbenzylidene)-N′-trimethylacetyl Hydrazide ***10e***. According to general procedure D after deprotonation of hydrazone **5m** (321 mg, 1.0 mmol), conversion with trimethylacetyl chloride (132 mg, 1.1 mmol), and recrystallization from ethanol, **10e** was obtained as a colorless solid: 279 mg (69%, 0.7 mmol); mp 137−142 °C; IR (neat) $\tilde{\nu}$ = 3071, 2974, 2957, 2934, 1655, 1603, 1503, 1479, 1441, 1395, 1360, 1321, 1288, 1215 (s, CF), 1175, 1111, 1090, 1076, 1026, 1011, 959, 945, 916, 885, 845, 826, 795, 779, 772, 752, 725, 698; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.47 (s, 9H, *Z*), 1.54 (s, 9H, *E*), 6.43 (s, 1H, *Z*), 6.67−6.81 (m, 2H, *Z*/*E*), 6.89−7.64 (m, 12H, *Z*/*E*), 7.88−7.99 (m, 1H, *E*); ^{13}C NMR (75 MHz, $CDCl_3$) δ 26.7, 26.8, 39.5, 39.6, 115.7, 116.0, 116.3, 123.5, 124.5, 125.0, 125.4, 125.6, 126.0, 126.6, 126.7, 126.8, 127.1, 127.1, 127.7, 128.1, 128.5, 128.6, 128.7, 129.7, 129.8, 129.9, 130.0, 130.5, 130.7, 131.4, 131.8, 131.8, 134.7, 135.8, 136.3, 136.9, 138.0, 138.3, 161.2 (d, J = 248.1, *Z*), 161.5 (d, J = 249.1, *E*), 178.0, 178.1; HRMS (ESI) calcd for $C_{26}H_{25}FN_2ONa$ 423.1843, found 423.1844. Anal. Calcd for $C_{26}H_{25}FN_2O$ (400.20): C, 77.97; H, 6.29; N, 6.99. Found: C, 77.54; H, 6.23; N, 6.86.

■ ASSOCIATED CONTENT

Supporting Information. ^{1}H and ^{13}C spectra for the new compounds; optimized Cartesian coordinates (B3LYP/6-31+G(d,p) and SCS-MP2/6-311+G(d,p)//B3LYP/6-31+G-(d,p)+ZPE energies for the calculated structures; graphics of the crystal structures showing thermal ellipsoids with 50% probability. This material is available free of charge via the Internet at http://pubs.acs.org.

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DEDICATION

†Dedicated to Prof. Dr. Dieter Hoppe at the occasion of his 70th birthday.

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(20) All computations in this study have been performed using the Gaussian 03 suite of programs.[21] The Becke three-parameter exchange functional and the correlation functional of Lee, Yang, and Parr (B3LYP) with the 6-31+G(d,p) basis set were used to compute the geometries and the normal-mode vibration frequencies of the starting anions, the corresponding transition structures, and the products. For single-point energy calculations on DFT-optimized geometries, the SCS-MP2 method was used employing the 6-311+G(d,P) basis set.[22] Transition structures were localized starting with PM6 reaction pathway calculations using the MOPAC 2007 program. MOPAC2007: Stewart, J. J. P. Stewart Computational Chemistry, Colorado Springs, CO, 2007, HTTP://OpenMOPAC.net; Stewart, J. J. P. *J. Mol. Modeling* **2007**, *13*, 1173. The transition structures were further optimized at the DFT level with the Gaussian 03 package of programs using the option "mndofc" or "calcfc" (opt = (ts, noeigentest, mndofc) or opt = (ts, noeigentest, calcfc)), applying the B3LYP/6-31+G(d,p) basis set. In order to verify the character of the stationary points, they were subjected to frequency analyses. The energies discussed contain unscaled zero point corrections. The vibration related to the imaginary frequency corresponds to the nuclear motion along the reaction coordinate under study. In significant cases intrinsic reaction coordinate (IRC) calculations were performed in order to unambiguously connect transition structures with reactants and products. Bond orders and atomic charges were calculated with the natural bond orbital (NBO) method as implemented in the Gaussian 03 program.
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