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Aromaticity of the Bergman, Myers−Saito, Schmittel, and Directly Related Cyclizations of Enediynes

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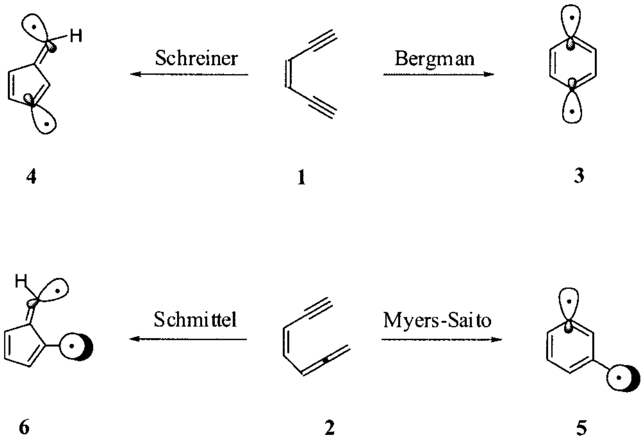
Aromaticity criteria (magnetic susceptibility exaltations, nucleus independent chemical shifts (NICS), and aromatic stabilization energy (ASE) evaluations) for enediyne and enyne-allene cyclizations evaluated at (UBS)-BLYP/6-31G* all agree that the degrees of cyclic electron delocalization of the benzenoid systems formed by the Bergman (**3**) and Myers−Saito reactions (**5**) are comparable to benzene. The reaction enthalpy differences between the parent cyclizations and their benzannelated analogues are not entirely due to disparities in gained ASE during the reactions. The alternative formation of fulvene biradicals is not accompanied by favorable aromatic effects.

Introduction

The pharmaceutical demand for cytotoxic antitumor drugs has stimulated detailed scrutiny of cyclization reactions of polyunsaturated hydrocarbons yielding biradicaloid intermediates. These species are able to abstract hydrogen atoms from DNA, leading to cell death.[1] Calicheamycin,[2] Dynemicin,[3] and Neocarzinostatin[4] are examples of such naturally occurring antitumor antibiotics. In addition to the well-known Bergman[5,6] ring closure, the Myers−Saito[7] and Schmittel cyclizations[8] are fundamentally important. In analogy to the Schmittel reaction, Schreiner et al.[9] recently suggested that the fulvene biradical **4** also might form from enediyne (**1**).

With the exception of **4**, all cyclizations depicted in Scheme 1 display the "nonperfect synchronization" phenomenon;[9−11] i.e., the corresponding transition states are product-like geometrically but reactant-like electronically, lacking biradical character. The transition state for the formation of the fulvene derivative **4**, however, is significantly biradicaloid.[9] Studying open-shell species such as biradicals experimentally and theoretically presents great challenges. Apart from computationally expensive multireference techniques such as complete active space self-consistent field (CASSCF) or multireference configuration interaction (MR-CI), density functional theory (DFT) is now well established to be a sufficiently accurate qualitative theoretical description of such biradicals.[12−17]

Scheme 1. Different Cyclizations of Enediyne (1) and Enyne-allene (3)



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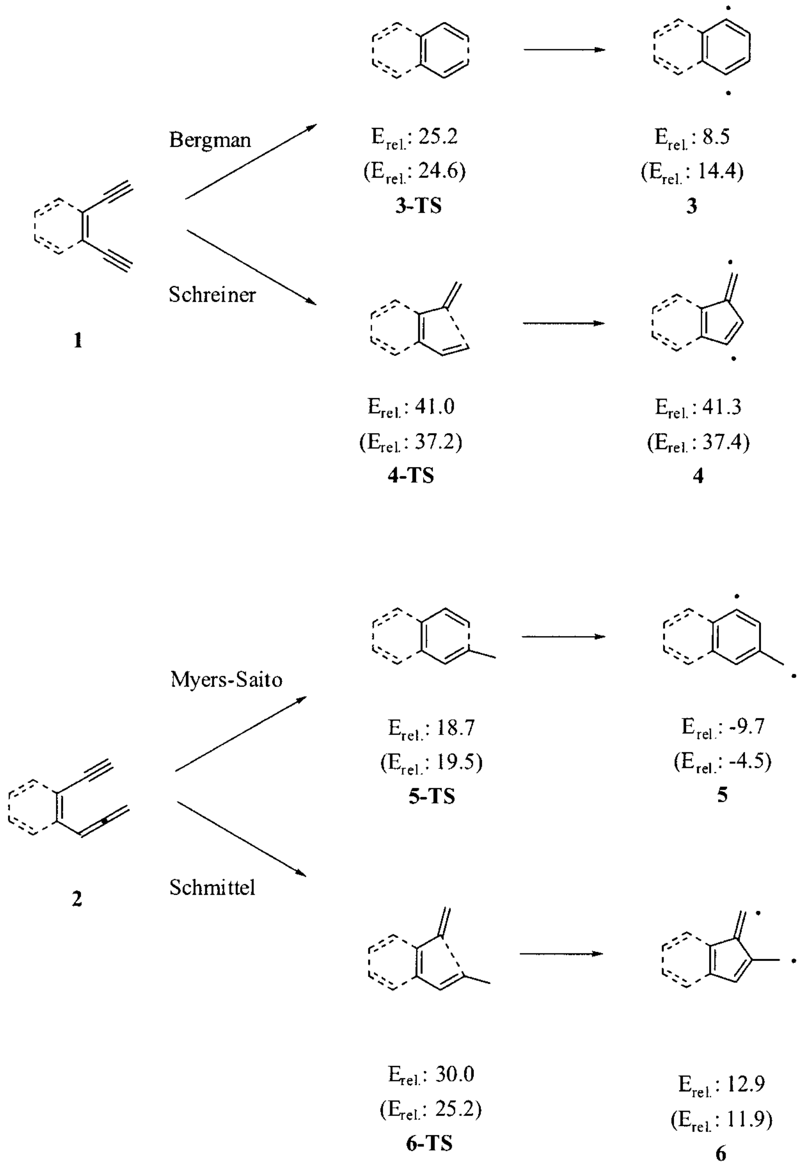
Scheme 2. Cyclization Reactions of Enediyne (1), Enyne-allene (2), and Their Benzannelated Counterparts[a]



[a] Benzannelated counterparts are indicated by an attached benzenoid ring sketched with dashed lines and are numbered according to the parent systems with a preceding "**B**". Relative barriers and reaction enthalpies ($\Delta_0 H$ in kcal/mol, values for the benzannelated versions are given in parentheses) computed at (UBS)-BLYP/6-31G* were taken from ref 9.[41]

Though the Bergman cyclization is intuitively regarded as an "aromatization reaction", the degree of cyclic electron delocalization[18,19] of the title reactions is not yet understood satisfyingly. Schreiner, Shaik, and co-workers[10] concluded that while *p*-benzyne (**3**) is strongly π-aromatic, the transition state (**3-TS**) for the Bergman cyclization is essentially nonaromatic in the π sense but significantly σ-aromatic; i.e., the cyclic delocalization is *in* the ring plane.[18,20] We report here an alternative and expanded approach to study the aromaticity of the parent Bergman, Schmittel, and Myers–Saito cyclizations together with the new enediyne fulvene mode as well as each of their benzannelated counterparts (Scheme 2). Though the effect of benzannelation is known to be important, its electronic consequences have not been elucidated fully.[9,17,21] Formation of the fulvene biradicals **4** and **6** (Scheme 2) is energetically less favorable than that of the benzannelated fulvene biradicals **B4** and **B6**. The parent Bergman and Myers–Saito biradicals, **3** and **5**, however, are energetically more feasible than their benzannelated analogues. The influence of aromatic stabilization on these energetic findings is evaluated in the present study.

The aromatic stabilization energy (ASE) with respect to hypothetical, nonaromatic reference systems characterizes systems with cyclic electron delocalization. The ASE can be evaluated by isodesmic or, better, homodes-

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Table 1. Computed Magnetic Susceptibilities, χ_M (ppm-cgs), Magnetic Susceptibility Exaltations (CSGT-BLYP/6-311+G//BLYP/6-31G*), Λ (ppm-cgs), and NICS Values (ppm) at GIAO−BLYP/6-311+G**//BLYP/6-31G* and SOS-DFT-IGLO/III//BLYP/6-31G* for Enediyne (1) and *o*-Diethynylbenzene (B1) Cyclizations**[a]

compound	χ_M	χ_M'	Λ	NICS type	NICS (0.0)	NICS (0.5)	NICS (1.0)	NICS (1.5)	NICS (2.0)
3-TS	−55.9			GIAO	−17.9	−15.9	−11.3	−7.0	−4.2
				IGLO total	−19.5	−17.5	−12.4	−7.7	−4.7
				C≡C (π)[b]	−9.0	−7.0	−3.6	−1.6	−0.6
				C=C (π)[b]	−6.1	−4.7	−2.3	−0.9	−0.3
				π (total)	−15.1	−11.7	−5.9	−2.5	−0.9
				C≡C (σ_1)[b]	−4.2	−4.0	−3.4	−2.6	−1.8
				C≡C (σ_2)[b]	0.8	0.2	−0.2	−0.2	−0.2
				C=C (σ)[b]	0.1	−0.4	−0.9	−0.9	−0.7
				σ (total)	+2.9	+1.2	−0.5	−0.9	−0.9
3	−48.9	−34.7	−14.2	GIAO	−19.0	−17.9	−13.8	−8.9	−5.4
B1	−74.9			GIAO					
					(−7.3)	(−8.5)	(−8.8)	(−7.1)	(−4.9)
B3-TS	−85.6			GIAO	−16.2	−14.5	−10.4	−6.5	−4.0
					(−7.9)	(−9.6)	(−9.7)	(−7.1)	(−4.6)
B3	−82.7	−55.0	−27.7	GIAO	−20.3	−19.4	−15.2	−9.9	−6.0
					(−9.7)	(−11.2)	(−11.0)	(−8.1)	(−5.3)
4-TS	−37.0			GIAO	−6.6	−5.2	−3.4	−2.1	−1.2
4	−35.4	−35.1	−0.3	GIAO	−6.5	−5.3	−3.6	−2.4	−1.5
B4-TS	−65.0			GIAO	−2.3	−1.8	−1.1	−0.5	−0.3
					(−7.5)	(−8.6)	(−8.7)	(−6.5)	(−4.3)
B4	−63.3	−55.4	−7.9	GIAO	−2.7	−2.1	−1.4	−0.9	−0.6
					(−7.2)	(−8.3)	(−8.5)	(−6.5)	(−4.3)

[a] NICS values for the annelated benzene rings are given in parentheses. [b] cf. Figure 1.

motic equations. Furthermore, aromatics sustain diatropic ring currents, which can be probed theoretically by means of nucleus-independent chemical shifts (NICS) as introduced by Schleyer et al.[22] Negative NICS denote net diatropic ring currents and positive NICS indicate net paratropic ring currents. A further refinement, "dissected NICS", gives a complete break-down of the individual contributions, e.g., differentiation of σ- and π-contributions in C−C double bonds, to the total NICS.[23] Another characteristic of aromatic compounds is their exalted diamagnetic susceptibility (Λ).[19,24−27] The latter is defined as the difference between the actually measured or computed magnetic susceptibility (χ_M) and the quantity estimated from an increment scheme (χ_M').[27]

$$\Lambda = \chi_M - \chi_M' \tag{1}$$

Methods. We employed the unrestricted broken-spin (UBS) method in which spatial and spin symmetries are broken by mixing the frontier molecular orbitals for all computations on open-shell singlets. This allows the inclusion of some static electron correlation and is an acceptably compromising treatment for open-shell singlets.[9,15] Geometries, optimized at RBLYP/6-31G* or UBS−BLYP/6-31G* for open-shell singlet species, were taken from refs 9 and 11. Note that open-shell species exhibit temperature-dependent paramagnetism due to the unpaired electrons, but the diamagnetic or paramagnetic susceptibility exaltations evaluated here are temperature independent and result from cyclic electron delocalization. We computed magnetic susceptibilities at (UBS)-BLYP/6-311+G** using the continuous set of gauge transformations (CSGT) procedure. NICS for the reactants (where applicable), transition states, and biradical intermediates were computed at (UBS)-BLYP/6-311+G** using the gauge-including atomic orbitals (GIAO) approach as implemented in Gaussian 98.[28] Dissected NICS values were obtained using the individual gauge for localized orbitals (IGLO) method[29] at IGLO-SOS-

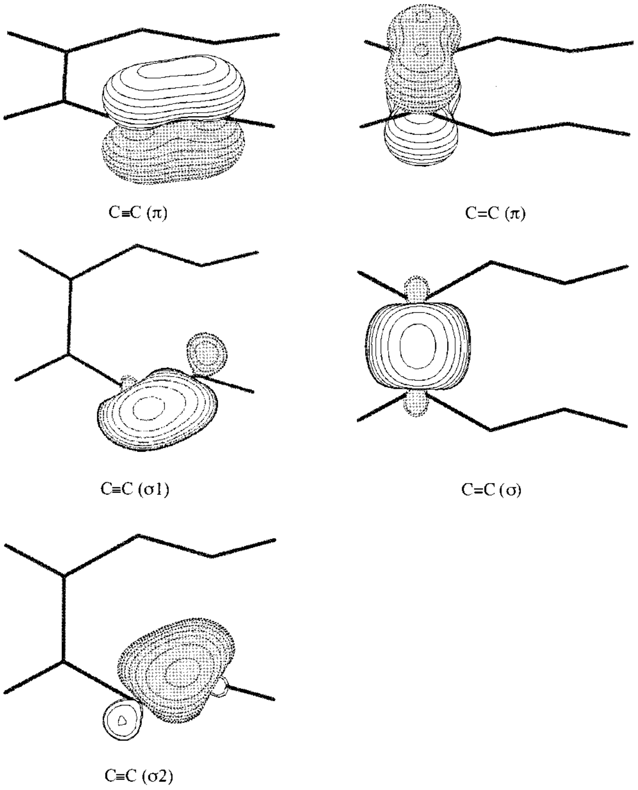
C≡C (π) C=C (π)
C≡C (σ1) C=C (σ)
C≡C (σ2)

Figure 1. Pipek−Mezey localized orbitals used for the dissected NICS computations.

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Table 2. NICS Values (GIAO-BLYP/631G*//BLYP/6-31G* and IGLO-SOS-DFPT/III) for Reference Compounds

compound	χ_M	χ_M'	Λ	NICS type	NICS (0.0)	NICS (0.5)	NICS (1.0)	NICS (1.5)	NICS (2.0)
benzene	−52.1	−41.1	−11.0	GIAO	−7.7	−9.4	−9.8	−7.3	−4.7
	(−54.8)[a]		(−13.7)[a]						
				IGLO	−8.8	−10.7	−10.6	−7.8	−5.2
				total					
				π	−20.7	−16.8	−9.6	−4.8	−2.4
				σ (C−C)	+14.0	+9.0	+2.1	−0.6	−1.2
naphthalene	−87.8	−61.4	−26.4	GIAO	−8.3	−10.2	−10.5	−7.9	−5.3
	(−91.9)[a]		(−30.5)[a]						
				IGLO					
				total	−8.9	−10.8	−10.8	−8.1	−5.5
				π	−20.3	−17.0	−10.1	−5.1	−2.3
				σ (C−C)	+13.3	+8.2	+1.8	−0.9	−1.5
fulvene	−41.6	−41.9	+0.3	GIAO	+1.6	+0.1	−1.9	−2.2	−1.6
	(−43.0)[a]		(−1.1)[a]						
				IGLO					
				total	+0.2	−1.7	−3.0	−2.7	−2.1
				π (ring)	−9.8	−4.9	+0.7	+1.8	+1.4
				π (exo)	−2.7	−1.7	−0.7	−0.3	−0.1
				σ (C−C, ring)	+14.5	+7.9	0.0	−1.6	−1.4
				σ (C−C, exo)	−0.1	−0.3	−0.5	−0.4	−0.3
				σ (C−H, ring)	−1.4	−2.4	−2.8	−2.0	−1.2
benzyl radical (**7**)	−51.7	−47.5	−4.2	GIAO	−3.5	−5.3	−6.3	−4.9	−3.2
				IGLO					
				total	−4.0	−5.3	−5.7	−4.3	−2.9
				π (ring)	−18.1	−14.5	−7.9	−3.5	−1.5
				π (exo)	+3.4	+3.5	+3.0	+2.2	+1.5
				σ CC_{ring}	+12.6	+8.2	+2.2	−0.4	−1.2
				σ CC_{exo}	+0.4	+0.2	0.0	0.0	0.0
2-methylenenaphthalene radical (**B7**)[b]	−82.9	−67.8	−15.1	GIAO	−3.5	−5.3	−6.2	−4.8	−3.2
					−5.4	−7.2	−8.2	−6.6	−4.5
				IGLO	−4.0	−5.7	−6.1	−4.6	−3.1
				total	−5.9	−7.5	−7.9	−6.0	−4.1
				$\pi_{same\ ring}$	−17.9	−14.6	−8.2	−3.7	−1.6
					−19.1	−15.7	−9.2	−4.5	−2.2
				$\pi_{annelated\ ring}$	−0.8	−0.6	−0.4	−0.3	−0.2
					+0.4	+0.6	+0.5	+0.4	+0.1
				π_{exo}	+3.6	+3.6	+3.1	+2.3	+1.6
					+1.5	+1.5	+1.3	+1.0	+0.8
				σ $CC_{same\ ring}$	+11.6	+7.6	+2.0	−0.4	−1.0
					+12.3	+8.1	+2.1	−0.4	−1.0
				σ $CC_{distant\ ring}$	+0.4	0.0	−0.3	−0.4	−0.4
					+0.6	+0.2	−0.3	−0.2	−0.2
				σ $CC_{distant\ ring}$	+0.3	+0.2	0.0	−0.1	0.0
					+0.1	+0.1	+0.1	0.0	0.0

[a] Taken from refs 25 and 26. [b] For each NICS entry, the value for the ring directly attached to the methylene group is given first and the values for the annelated ring are given underneath.

DFPT-PW91/IGLO-III(TZ2P) with the deMon-Master NMR module,[30] which uses the Pipek−Mezey localization procedure.[31]

The interaction of the spin of the unpaired electron(s) of an open-shell species with the applied external magnetic field alters the electronic structure and often leads to line broadening, which then prohibits meaningful NMR experiments with open-shell species.[32] Computation of magnetic shieldings and susceptibilities of such species, however, is possible[33] due to the separability of the nuclear/electron spin magnetic interaction terms in the Hamiltonian.[34] The wave function is determined during the SCF procedure, and the subsequently applied magnetic perturbation acts on this (nonmagnetically altered) wave function. The NMR open-shell calculations in GAUSSIAN 98[28] (GIAO and CSGT method) are truncated to the interaction terms that do not include the effects due to the spin of the unpaired electron(s). Hence, the two main factors (alteration of the electronic structure and line broadening) that are responsible for the impracticability of NMR experiments with open-shell species are excluded artificially in quantum chemical computations. The NMR module for the deMon program, however, has not been programmed to perform unrestricted broken

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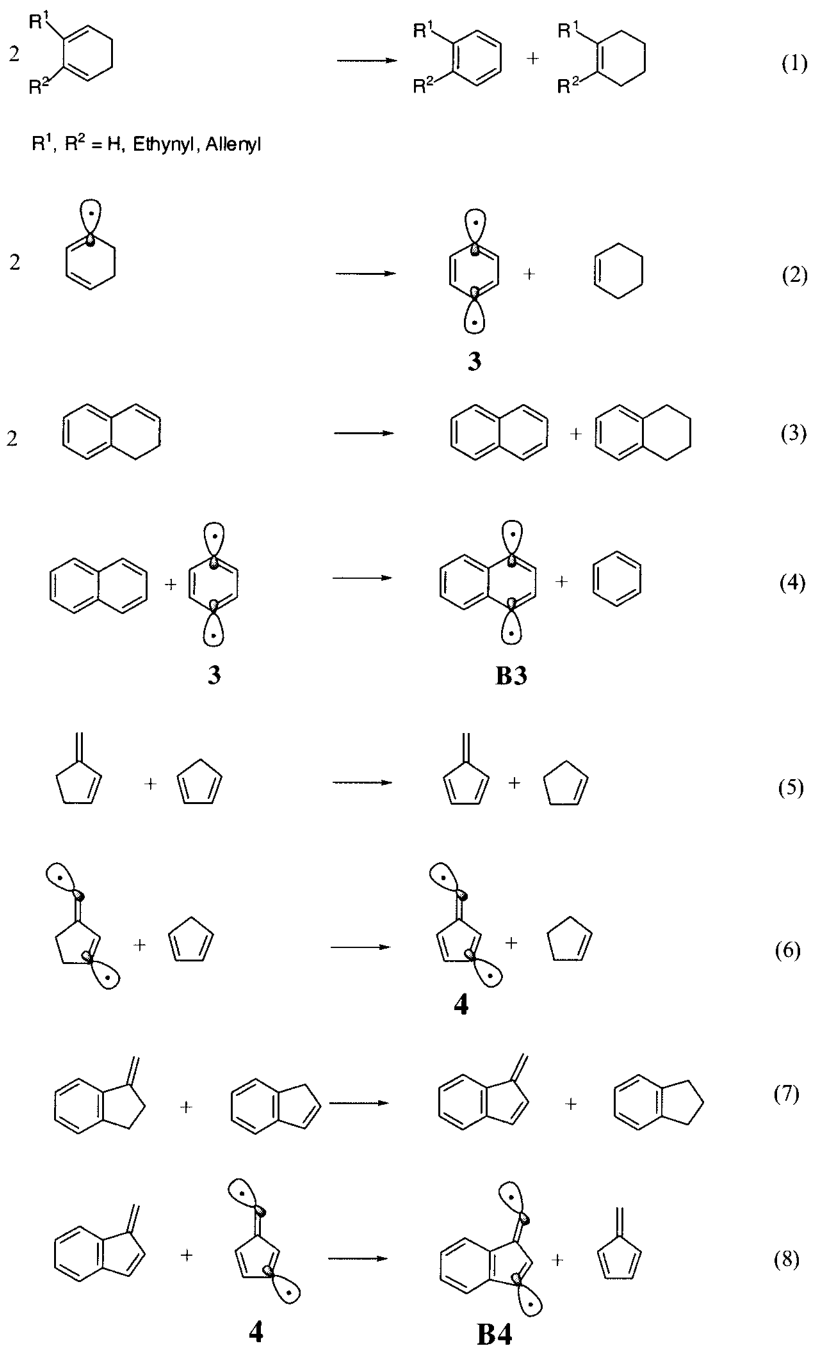
Scheme 3. Homodesmotic Equations to Evaluate Aromatic Stabilization Energies for the Intermediates Generated by Enediyne Cyclizations and for Suitable Reference Systems



spin computations; consequently, dissected NICS were not applied to open-shell species.

Results and Discussion

Enediynes. The characterization of the Bergman cyclization as an aromatization reaction is confirmed by the computed negative NICS values (Table 1). The dissection of NICS for **3-TS** reveals, as expected, three different contributions for the triple bonds and two different contributions for the double bond (Figure 1). Whereas the assignment of σ- and π-components for the double bond is straightforward, visualization of the Pipek–Mezey localized orbitals (Figure 1) clearly shows that the in-plane π- and σ-system of the triple bonds mix and are *indistinguishable*. The perpendicular π-system, nevertheless, appears as expected and adds, overall, −15.1 ppm to NICS(0) and −5.9 ppm to NICS(1) (Table 1). All triple-bond in-plane components total −3.3 ppm to NICS(0) and −3.6 ppm to NICS(1). Hence, we conclude, in contradistinction to an earlier study,[10] that cyclic electron delocalization in **3-TS** occurs predominately in the perpendicular π-system. It is unclear at this point why there is such a discrepancy between the various methods to evaluate the aromaticity of this TS, but it seems possible that the VB description favors π-localization somewhat.

In cases where dissected NICS is unavailable, NICS(1), i.e., at 1 Å above the ring plane, is generally recommended as the most reliable gauge,[23,35] since local effects of CC and CH sigma bonds become insignificant.

This is shown for benzene and naphthalene, in Table 2, where the NICS total at 1 Å is governed mainly by the π-contributions. Note that *p*-benzyne (**3**) also sustains a diatropic ring current with NICS(1) of −13.8 ppm, displaying π-aromaticity.

The magnetic susceptibility for **3** can be estimated from an increment scheme[25−27] ($\chi_{M}' = -34.7$ ppm-cgs) analogous to benzene under omission of two CH bonds. Comparison with the computed value ($\chi_{M} = -48.9$ ppm-cgs) reveals a diamagnetic exaltation of $\Lambda = -14.2$ ppm-cgs. For benzene we computed a diamagnetic exaltation of $\Lambda = -11.0$ ppm-cgs (exp. 13.7 ppm-cgs)[27] with respect to the increment value ($\chi_{M}' = 41.1$ ppm-cgs). Note that this approach is somewhat crude for open-shell singlet species, as it includes no correction for the two nonbonding, unpaired electrons and is only applicable because the NMR computations neglect any interaction with the spin of the unpaired electrons. This method is not valid for the transition state, as it is unclear which increments should be used.

NICS for the benzannelated version of the Bergman cyclization (Table 1) indicates diatropic ring currents in both species, **B3-TS** and **B3**, with the annelated rings resembling benzene-like values. The computed magnetic susceptibility for **B3** (Table 1) is diamagnetically exalted by −27.7 ppm-cgs with respect to the increment scheme value ($\chi_{M}' = -55.0$ ppm-cgs, Table 2). Naphthalene exhibits a similar exaltation ($\Lambda = -26.4$ ppm-cgs), and we conclude that **B3** and naphthalene have comparable degrees of aromaticity.

The computed barrier for the Bergman cyclization, 25.2 kcal/mol at BLYP/6-31G*, is in good agreement with experiment (28.2 kcal/mol), and the formation of intermediate **3** is 8.5 kcal/mol (exp. 8.5 kcal/mol) endothermic at (UBS)-BLYP/6-31G* with respect to enediyne **1**.[9] Benzannelation does not affect the height of the barrier (24.6 kcal/mol) significantly but increases the endothermicity substantially ($\Delta_0 H = 14.4$ kcal/mol; i.e., increased by 5.9 kcal/mol). We employed the homodesmotic equations depicted in Scheme 3 to evaluate the aromatic stabilization energies (ASE) and effects of aromaticity on enediyne cyclizations.

The ASE for **3** according to eq 2 is 33.1 kcal/mol (Table 3), which is close to the benzene value of 34.3 kcal/mol (eq 1, $R^1 = R^2 = H$) at (UBS)-BLYP/6-31G*. This confirms our conclusions based on magnetic criteria that *p*-benzyne (**3**) and benzene exhibit comparable degrees of aromaticity. Note that a biradical reference in eq 2 would be desirable, i.e., 1,3-cyclohexadien-1,4-diyl instead of 1,3-cyclohexadien-1-yl. The former species, however, cannot be optimized; ring opening to the open-chain diallene (1,2,4,5-hexatetraene) occurs inevitably. Stabilization due to coupling of the radical sites in **3** can be estimated by the singlet−triplet splitting, which is −3.8 kcal/mol for *p*-benzyne as well as for 1,4-didehydronaphthalene.[36] A stabilization of 29.3 kcal/mol remains for **3** when applying this correction to eq 2.

How much ASE does a system gain by aromatization of a second ring, annelated to a benzene moiety? Considering a ASE of 5.7 kcal/mol per p-electron in benzene (on the basis of eq 1), one might expect an additional ASE of 22.8 kcal/mol for the second ring in naphthalene as it adds four electrons to the π-system.[37−39] The ASE derived from eq 3, 20.6 kcal/mol (Table 3), deviates only by 1.2 kcal/mol from this linear extrapolation. Equation 4, exothermic by 0.2 kcal/mol (Table 4), indicates that **B3** totals 20.8 kcal/mol more ASE than **3**; i.e., the total ASE of **B3** is 53.9 kcal/mol. The starting material to yield **B3**, **B1**, has a total ASE of 36.3 kcal/mol according to eq 1 ($R^1 = R^2 = C_2H$). Therefore, the gain of ASE during Bergman cyclization of **B1** is only 17.6 kcal/mol. Correction for stabilization due to the two unpaired electrons reduces the ASE of **B3** to 50.1 kcal/mol and the gained ASE during cyclization to 13.8 kcal/mol. This is 15.5 kcal/mol less ASE compared to the parent Bergman cyclization. The actual increase in endothermicity between cyclization of enediynes (**1**) and its benzannelated analogue (**B1**), however, is only 5.9 kcal/mol. Therefore, benzannelation appears to be favorable, but the penalty for the reduced gain in ASE cannot be overcompensated.

Table 3. Aromatic Stabilization Energies (ASE) Evaluated at (UBS)-BLYP/6-31G*

compound	equation	ASE (kcal/mol)
3	2	33.1 (29.3)[a]
4	6	−2.4
5	10	28.4
6	12	0.4
B6 (fulvene ring)	14	0.4
benzene	1 ($R^1 = R^2 = H$)	34.3
diethynylbenzene (**B1**)	1 ($R^1 = R^2 = C_2H$)	36.3
1-allenyl-2-ethynylbenzene (**B2**)	1 ($R^1 = C_2H$, R^2 = allenyl)	34.2
naphthalene (second ring)	3	20.6
benzyl radical (**7**)	9	30.6
fulvene	5	−1.1
benzfulvene (fulvene ring)	7	0.4

[a] Corrected for interaction of the two unpaired electrons.

Table 4. Enthalpies of Homodesmotic Equations to Evaluate the Effect of Benzannelation on the Stabilization of the Biradical Cyclization Intermediates

equation	system	$\Delta_0 H$ (kcal/mol)
4	**3**/**B3**	−0.2
8	**4**/**B4**	+0.6
11	**5**/**B5**	−0.8
13	**6**/**B6**	+3.7

The alternative cyclization mode of **1** yields the fulvene biradical **4**. Since the parent fulvene is nonaromatic with a diamagnetic susceptibility exaltation of −1.1 ppm-cgs and NICS values close to zero (Table 2), no favorable aromatic effects are expected for the formation of **4**. The computed diamagnetic exaltation of **4** with respect to the increment value ($\chi_{M}' = -35.1$ ppm-cgs, Table 1) is −0.3 ppm-cgs. The NICS(0) values, −6.6 ppm for **4-TS** and −6.5 ppm for **4**, are negative rather than positive as found for fulvene (+1.6 ppm, Table 2). At points higher than 1 Å above the ring, the NICS values match well with those of fulvene (Table 2). NICS dissection for the parent fulvene reveals large paramagnetic σ-contributions and somewhat smaller diamagnetic π-contributions from the

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Table 5. Computed Magnetic Susceptibilities (CSGT-(UBS)-BLYP/6-311+G//(UBS)-BLYP/6-31G*), χ_M (ppm-cgs), Magnetic Susceptibility Exaltations, Λ (ppm-cgs), and NICS Values (ppm) at GIAO-(UBS)-BLYP/6-311+G**/(UBS)-BLYP/6-31G* and SOS-DFPT-IGLO/III-TZ2P//BLYP/6-31G* for the Reactants, Transition States, and Intermediates of Enyne-allene (2) and *o*-Ethynyl-allenylbenzene (B2) Cyclizations**[a]

compd	χ_M	χ_M'	Λ	NICS type	NICS (0.0)	NICS (0.5)	NICS (1.0)	NICS (1.5)	NICS (2.0)
5-TS	−52.0			GIAO	−9.3	−6.4	−4.9	−3.4	−2.2
				IGLO total	−10.1	−7.2	−5.5	−3.9	−2.6
				π (total)	−12.3	−9.2	−4.9	−2.2	−1.0
				π (ring)	−14.0	−10.6	−5.7	−2.6	−1.2
				σ (C−C, total)	+4.2	+3.9	+1.4	−0.2	−0.4
				σ (C−C, ring)	+4.0	+3.6	+1.1	−0.5	−0.7
5	−48.5	−44.3	−4.2	GIAO	−6.9	−7.4	−6.9	−4.9	−3.0
B2	−78.4			GIAO					
					(−7.0)	(−8.4)	(−8.6)	(−6.4)	(−4.2)
B5-TS	−83.0			GIAO	−7.7	−9.3	−7.7	−5.0	−3.0
					(−7.2)	(−8.6)	(−9.2)	(−7.2)	(−4.9)
B5	−73.3	−64.6	−8.7	GIAO	−8.4	−7.3	−5.7	−4.1	−2.8
					(−2.7)	(−4.8)	(−6.6)	(−5.6)	(−3.8)
6-TS	−45.8			GIAO	−5.7	−7.3	−5.9	−3.4	−1.9
				dissected total	−7.0	−8.8	−7.0	−4.1	−2.3
				π (total)	−11.7	−7.7	−2.8	−0.7	−0.2
				π (ring)	−12.9	−9.5	−4.7	−1.8	−0.8
				σ (C−C, total)	+7.1	+1.7	−1.7	−1.9	−1.2
				σ (C−C, ring)	+7.4	+2.0	−1.3	−1.5	−0.9
6	−36.0	−47.1	+11.1	GIAO	+1.0	−0.4	−1.8	−1.5	−0.9
B6-TS	−73.6			GIAO	−1.6	−1.4	−1.5	−1.1	−0.8
					(−6.2)	(−7.1)	(−7.7)	(−6.1)	(−4.1)
B6	−68.2	−67.4	−0.8	GIAO	+1.9	+0.5	−0.8	−0.7	−0.5
					(−3.8)	(−5.3)	(−6.4)	(−5.2)	(−3.6)

[a] NICS values for the annelated benzene rings are given in parentheses.

ring C−C bonds to NICS(0). At 1 Å above the ring plane, the σ- and π-contributions from the ring are diminished, and the computed NICS (total) are dominated by the contributions from the C−H bonds and the exocyclic C−C σ-bond. This shows that the local shielding effects dominate, and there is no significant diatropic ring current. Due to the open-shell character of **4** and **4-TS**, dissected NICS cannot be applied to these species to investigate further the more negative NICS values in the center and at 0.5 Å. However, in the parent fulvene the large σ- and π-contributions at these points effectively cancel. The two σ-radical centers in **4** and **4-TS** apparently affect this balance, and the overall NICS is somewhat negative. Neither of these two species nor fulvene are “aromatic”.

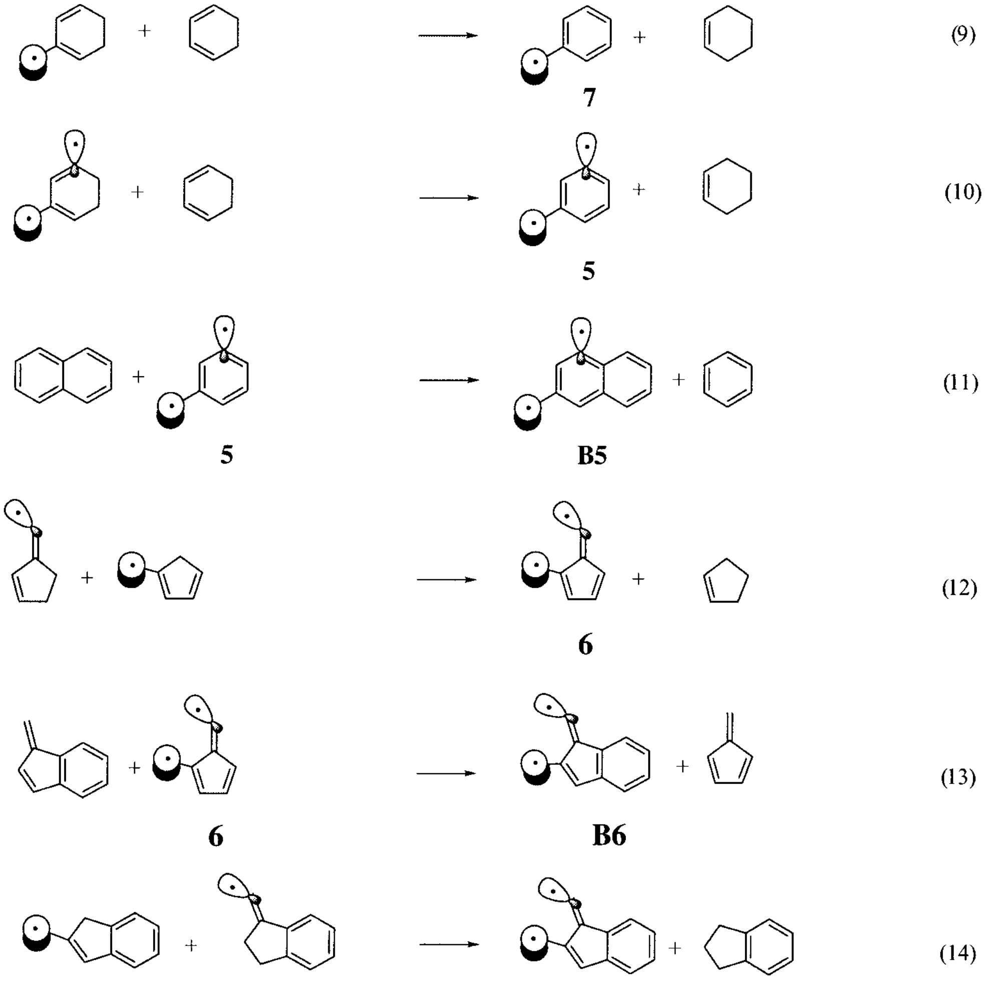
Equation 5, slightly endothermic (1.1 kcal/mol, Table 3), also corroborates fulvene as nonaromatic. We computed a similar endothermicity (2.4 kcal/mol, Table 3) for **4** using eq 6. It is evident from such ASE evaluations, NICS, and the computed paramagnetic susceptibility exaltations that **4** is nonaromatic, confirming chemical intuition. The dissection of NICS for the parent fulvene, however, clearly shows that despite the obvious overall conclusion, the details are more complex.

For the benzannelated counterparts **B4** and **B4-TS** we also computed negative NICS for the benzenoid rings, but only negligible values for the fulvene moieties (Table 1). Note that the fulvene moieties in these systems do not display the somewhat negative NICS shown for **4** and **4-TS**. Both the barrier and the overall endothermicity for the formation of **B4** from **B1** are reduced slightly compared to the formation of **4** from **1** (Scheme 2).[9] The formation of fulvene annelated to a benzenoid system is not accompanied by any favorable stabilization as documented by the negligible exothermicity of 0.4 kcal/mol (Table 2) for eq 7 (Scheme 3). This also implies that the cyclic electron delocalization and the stabilization of the benzenoid moiety remain unaffected. Analogously, eq 8 is essentially thermoneutral (+0.6 kcal/mol, Table 4). Hence, the computed decrease in endothermicity for the fulvene cyclization of **B1** compared to **1** is *not* due to aromaticity effects.

Enyne-allenes. The Myers−Saito cyclization is the only exothermic reaction (−9.7 kcal/mol at UBS-BLYP/6-31G*;[9] −15 ± 3 kcal/mol exp.,[4] Scheme 2) within the set discussed in the present paper. In contrast to the cyclizations of enediynes, enyne-allenes generate mixed σ,π- rather than σ,σ-biradicals. GIAO−NICS at 1.0 Å above the ring plane (−6.9 ppm for **5** and −4.9 ppm for **5-TS**, Table 5) are, in both cases, considerably negative, hinting at the presence of a diatropic ring current. Dissected NICS for **5-TS** reveals large π-contributions (Table 5) though smaller than those in benzene (Table 2). The local paramagnetic effects from the σ-bonds, however, are weaker compared to benzene (4.2 ppm in the center compared to 14.0 ppm in benzene). For **5**, where dissected NICS is not available, GIAO−NICS has a less negative value (−6.9 ppm) in the center compared to **5-TS** (−9.3 ppm) but abates less rapidly above the center.

Benzylic conjugation of a π-radical perturbs the cyclic electron delocalization in a benzenoid system such as **5**. This is reflected in reduced NICS (total) values for the benzyl radical **7** compared to benzene (Table 2). The π-contributions from the ring (−18.1 ppm) are substantial but slightly smaller than for benzene (−20.7 ppm) in the center; the localized exocyclic π-bond of **7** also adds paramagnetic contributions. Similarly, π-conjugation in the benzyl cation diminishes NICS (NICS(0): −3.3 ppm) and reduces the aromatic stabilization energy (by −7.7

Scheme 4. Homodesmotic Equations to Evaluate Aromatic Stabilization Energies for the Intermediates Generated by Enyne-allene Cyclizations and for Suitable Reference Systems



kcal/mol compared to benzene) as reported previously.[40] From this NICS pattern it is apparent that the extent of cyclic electron delocalization shrinks when conjugated to a benzylic radical center. A similar effect from the benzylic radical center in **5** is expected, and at 1 Å and higher above the ring plane, the NICS values match those of the benzylic radical almost exactly. Hence, **5** must have large π-contributions since NICS (total, 1.0 Å) is −6.9 ppm.

The computed magnetic susceptibilities, $\chi_M = -51.7$ ppm-cgs for **7** (Table 2) and −48.5 ppm-cgs for **5** (Table 5), also suggest diminished cyclic electron delocalization. The χ_M' values for the benzyl radical **7** (−47.5 ppm-cgs) and for **5** (−44.3 ppm-cgs) can be approximated from increments. Hence, the exaltations are estimated to be −4.2 ppm-cgs for both **7** and **5**, which is drastically reduced compared to benzene (−11.0 ppm-cgs, Table 2) or *p*-benzyne (**3**) (−14.2 ppm-cgs, Table 1).

We employed the homodesmotic equations depicted in Scheme 4 to evaluate the aromatic stabilization energies for all enyne-allene cyclization intermediates and adequate reference systems. According to eq 10, formation of **5** is facilitated by its large ASE of 28.4 kcal/mol (Table 3). This value is close to the ASE values for benzene (34.3 kcal/mol) and for the benzyl radical (**7**) (30.6 kcal/mol using eq 9). Hence, the perturbation of aromatic stabilization from either of the radical centers must be small.

NICS for the benzannelated transition state **B5-TS** indicates diatropic currents in both rings, but NICS in the center of the benzenoid ring in **B5** is diminished (Table 5). This compares well with the NICS evaluation of the 2-methylenenaphthalene radical (**B7**, Table 2): not only the ring directly attached to the methylene substituent but also the distant ring shows reduced NICS compared to benzene or naphthalene. Dissected NICS reveals paramagnetic effects from the exocyclic methylene group that even affect the distant ring. NICS computed at points above the ring centers in **B5**, however, are sufficiently negative (−5.7 and −6.6 ppm at 1 Å, Table 5) to indicate diatropic currents. The computed diamagnetic susceptibility exaltation for **B5** (−8.7 ppm-cgs, Table 5), however, is diminished compared to that for **B7** (−15.1 ppm-cgs, Table 2) and naphthalene (−26.4 ppm-cgs, Table 2).

Similar to the Bergman reaction, benzannelation for the Myers−Saito cyclization does not affect the height of the barrier but disfavors the biradical intermediate **B5**. The latter is only 4.5 kcal/mol lower in energy than *o*-ethynyl-allenylbenzene (**B2**) at (UBS)-BLYP/6-31G*

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[40] Mo, Y.; Jiao, H.; Lin, Z.; Schleyer, P. v. R. *Chem. Phys. Lett.* **1998**, *289*, 383−390.

[41] Reference 9 also reports relative energies for all transition states and intermediates evaluated at UBCCD/cc-pVDZ//(UBS)-UBLYP/6-31G*, which are in good agreement with the (UBS)-BLYP/6-31G* energies reported here. Since we use the (UBS)-BLYP/6-31G* level to evaluate aromatic stabilization energies (ASE), we have chosen to report only the DFT energies here.

(Scheme 2), a decrease in endothermicity of 5.2 kcal/mol compared to the parent cyclization. Equation 11 is essentially thermoneutral, $\Delta_0 H = -0.8$ kcal/mol (Table 4). Since the difference in ASE between benzene and naphthalene is 20.6 kcal/mol and eq 11 is exothermic by −0.8 kcal/mol, we estimate an ASE difference between **5** and **B5** of 21.4 kcal/mol. Therefore, **B5** is facilitated by an overall ASE of 49.8 kcal/mol and its precursor **B2** is facilitated by 34.2 kcal/mol ASE (eq 1, Table 3). Hence, the gain in stabilization from the Myers−Saito ring closure with an annelated benzene ring is 15.6 kcal/mol, i.e., a reduction of 12.8 kcal/mol compared to the parent reaction. The total decrease in exothermicity for the formation of **B5** from **B2** compared to **5** from **2**, though, is only about 5 kcal/mol. Analogous to the cyclization of enediynes (**1**) and 1,2-diethynylbenzene (**B1**), benzannelation appears to be beneficial, as addressed earlier by Wenthold and Lipton;[21] but the reduced gain of ASE during ring closure dominates, and the reaction, overall, is energetically less favorable than the parent version.

We computed only negligible NICS and a paramagnetic susceptibility exaltation of $\Lambda = +11.1$ ppm-cgs for the Schmittel fulvene biradical (**6**) (Table 5). In contrast, NICS for the transition state **6-TS** is substantially negative. Dissected NICS for **6-TS** reveals large contributions both from the σ- and π-bonds. The contributions from the ring π-bonds to NICS(1) are −4.7 ppm and the NICS(1) total is −7.0 ppm and −5.9 ppm using the IGLO and GIAO methods, respectively. These data indicate unambiguously the presence of a weak diatropic ring current in **6-TS**, which is no longer present in **6**. Equation 12 also indicates that there is no special stabilization for **6** (Table 3).

Benzannelation decreases the height of the barrier for the Schmittel cyclization (25.2 kcal/mol compared to 30.0 kcal/mol, Scheme 2), but the overall endothermicity is only reduced by 1 kcal/mol at (UBS)-BLYP/6-31G*.[9] Despite its benzenoid moiety, the intermediate **B6** is only slightly diamagnetically exalted ($\Lambda = -0.8$ ppm-cgs, Table 5). NICS for the fulvene ring is negligible in **B6-TS** and **B6** (Table 5). Note that the unexpectedly encountered diatropic ring current in **6-TS** is not present in **B6-TS**. The benzenoid ring in **B6**, similar to **B5**, exhibits smaller NICS values compared to **B6-TS**, **B2**, or benzene itself (Tables 2 and 5). Again, this is the result of long-range effects from conjugation with the π-radical. The homodesmotic eqs 13 and 14 (Scheme 4) are particularly instructive in this respect. The latter equation is essentially thermoneutral (−0.4 kcal/mol, Table 3) and indicates no special stabilization for the formation of a "Schmittel-type" fulvene attached to a benzenoid ring. Conjugation of the π-radical with the π-system of the benzene moiety already is included in the reference. In contrast, the π-radical in eq 13 is conjugated with the benzenoid system only on the right side of the equation and the endothermicity is 3.7 kcal/mol (Table 4). This is the order of magnitude expected for such perturbation due to long-range conjugation of a π-radical with a benzenoid system. We conclude that the Schmittel cyclization of **B2** reduces the ASE of the benzenoid ring by about 3.7 kcal/mol. As the reaction is actually slightly less endothermic compared to the parent system, other favorable effects override the loss of the ASE.

Conclusions

Our detailed study supports and quantifies the general assumption of aromaticity in the biradicals **3** and **5** generated by the Bergman and Myers−Saito reactions. According to our magnetic susceptibility, NICS, and aromatic stabilization evaluations, the degree of aromaticity in those biradicals is comparable to that in benzene. The aromatic stabilization energy (ASE) gained by the benzannelated versions of the Bergman (**B3**) and Myers−Saito (**B5**) cyclizations is only a fraction of the ASE for the parent systems. In both cases, the actual difference in reaction enthalpy between the benzannelated version and the parent cyclization is less than expected from ASE evaluations. Therefore, both cyclizations benefit from benzannelation, in principle, but the ASE toll is too large to make **B3** and **B5** energetically more feasible than **3** and **5**, each with respect to its precursor. The alternative formations of the fulvene biradicals **4** and **6** do not, as expected, benefit from aromatic stabilization. The degree of aromaticity in the annelated benzenoid ring remains essentially unaffected in **B4** but is perturbed in **B6** by long-range conjugation with the π-radical center.

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Supporting Information Available: Tables of energies and structures. This material is available free of charge via the Internet at http://pubs.acs.org.

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