A Surprising Switch from the Myers–Saito Cyclization to a Novel Biradical Cyclization in Enyne–Allenes: Formal Diels–Alder and Ene Reactions with High Synthetic Potential**

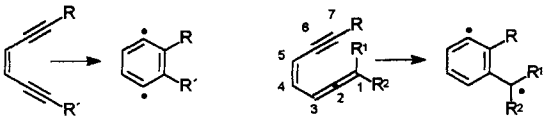
Michael Schmittel,* Manfred Keller, Susanne Kiau, and Marc Strittmatter

Abstract: If there is an aryl substituent on the acetylene terminus of enyne–allenes, then its reaction mode may be changed from the Myers–Saito cyclization to a novel C2–C6 cyclization resulting in a net intramolecular Diels–Alder or ene reaction. As a consequence, the thermal cyclization of readily accessible acyclic enyne–allenes can be utilized for the synthesis of complex benzofulvene and benzofluorene derivatives. Kinetic results of the C2–C6 cyclization reaction indicate a two-step reaction pathway with a benzofulvene biradical intermediate.

Keywords
allenes · biradicals · cycloaromatizations · enynes · reaction mechanisms

Introduction

Ever since the disclosure of the spectacular structures and mode of action of the natural enediyne antitumor antibiotics,[1] the thermal cycloaromatization of enediynes and enyne-cumulenes by the Bergman[2] and the Myers–Saito[3] cyclizations to afford reactive biradicals has been extensively investigated (Scheme 1).

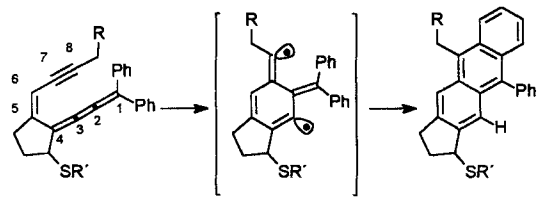


Scheme 1. The Bergman and Myers–Saito cyclizations.

Much current research is devoted to the total synthesis of the natural enediynes[1] and to the preparation of simple model compounds[4] with analogous antitumor and antibiotic activity. Furthermore, the combination of such biradical cycloaromatization protocols and subsequent radical cyclizations provides an elegant approach to polycyclic ring systems,[5, 6] particularly for the preparation of polyphenylenes and oligo(acenes).

In the natural antitumor antibiotic neocarcinostatin an enyne[3]cumulene core is responsible for the thermal formation of a highly reactive σ,σ-biradical.[3] The search for structural simplifications has led to the exploration of the much simpler enyne–allenes,[7, 8] the thermal reaction of which produces σ,π-biradicals,[3b] which are less reactive than the σ,σ-biradicals resulting from enediynes or enyne[3]cumulenes. Nevertheless, Nicolaou[9] and Saito[10] were able to demonstrate the DNA-cleaving properties of phosphine oxide-substituted enyne–allenes, thus indicating their potential use as anticancer drugs.

Since then enyne-cumulene[11, 12] and enyne–allene[6] model compounds have been synthesized and their thermal reactions investigated by several groups. In spite of the use of different triggering modes, namely light,[13] oxidation with SeO_2,[14] acid,[15] or base,[16] only Myers–Saito analogous products formed by the reaction between C2 and C7 have been reported, though enyne–allenes may offer a wide variety of other cyclization modes as well.[17] The only evidence for systems that do not follow the Myers–Saito format has been reported by Brückner.[15] He discovered that enyne[3]cumulene **1** undergoes cyclization with bond formation between C2 and C7 to produce **2** in 10% yield via a postulated intermediate biradical (Scheme 2).



1 **2**

Scheme 2. Brückner's postulated reaction mechanism for cyclization of enyne[3]-cumulene **1** via a postulated intermediate biradical to produce **2**.

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[**] Thermal and electron-transfer-induced reactions of enediynes and enyne–allenes, Part 8; for Part 7, see ref. [41].

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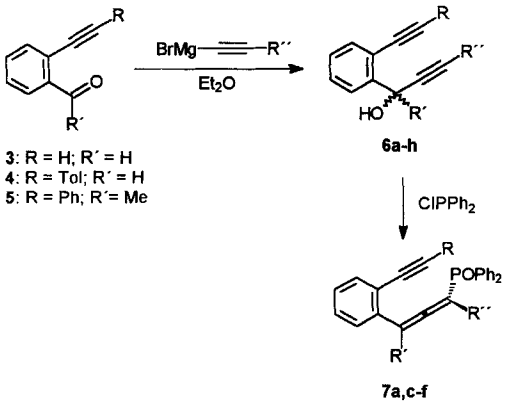
In preliminary communications reporting our investigations on the thermal reactions of enyne–allenes, we have very recently disclosed a remarkable switch from the well-known Myers–Saito C2–C7 cycloaromatization[3, 7] to an unprecedented C2–C6 cyclization affording benzofulvenes in high yield.[18, 19] We report the details in this paper. It seems that the C2–C6 cyclization is a fairly general thermal reaction for enyne–allenes because, shortly after our first report, related C2–C6 cyclizations were also observed by two other groups.[20, 21]

Results

Synthesis of enyne–allenes 7: Our efforts to trigger the Myers–Saito cyclization through electron transfer initiation[22] depended decisively on the availability of thermally stable enyne–allenes. Therefore, two well-known methods of increasing the thermal stability were tested by synthesizing the so-called "masked" enyne–allenes **7**. Here the ene moiety is made part of an aromatic system, and an aryl group is attached at the alkyne terminus. A convenient three- or four-step synthesis was devised for all enyne–allenes **7** starting from readily accessible precursors (Scheme 3). The alkynylated starting compounds **3**–**5** were



Scheme 3. Synthesis of enyne–allenes **7** starting from readily accessible precursors.

synthesized in high yields using the Pd^0-catalyzed coupling of RC≡CH with *o*-bromobenzaldehyde and *o*-bromoacetophenone.[23] Further reaction with various acetylides R″C≡CMgBr, prepared from the reaction of the corresponding acetylenes with EtMgBr, resulted in the formation of propargyl alcohols **6a–h**. In the final key step **6a–h** were treated with chlorodiphenylphosphine to afford the diphenylphosphine oxide-substituted enyne–allenes **7a,c–f** after a [2,3]-sigmatropic rearrangement of the intermediate propargylic phosphinite.[3b] Because of their thermal instability, we were not able to isolate the enyne–allenes **7b,g** and **h**, but rather their follow-up products (Table 1).

Enyne–allenes **7a,c–f** were stable at ambient temperature and could be purified by column chromatography. Their structural identity was deduced from their characteristic IR, ^1H NMR, and ^{13}C NMR spectroscopic data as well as by high-resolution mass spectroscopy. In the IR spectra of **7c–f** the C≡C stretching absorption was observed in a range typical for disubstituted acetylenes. In contrast, for **7a** the absorption occurred at 2105 cm^{-1}, which indicates a terminal acetylene. Additionally, the enyne–allenes exhibited a strong C=C=C stretching absorption between 1923 and 1932 cm^{-1} and a ^{13}C NMR resonance for the central carbon of the allene moiety between $\delta = 207$ and 220 (Table 2).

Table 1. Preparation of propargylic alcohols **6** and enyne–allenes **7**.

R	R′	R″	Alcohol	Yield	Enyne–allene	Yield
H	H	*n*Bu	**6a**	50%	**7a**	30%
H	H	Ph	**6b**	84%	**7b**	not isolated [a]
Tol	H	*n*Bu	**6c**	66%	**7c**	58%
Tol	H	cyclopropyl	**6d**	40%	**7d**	34%
Tol	H	Ph	**6e**	64%	**7e**	51%
Tol	H	Mes	**6f**	71% [b]	**7f**	66% [b]
Ph	Me	*n*Bu	**6g**	62%	**7g**	not isolated [a]
Ph	Me	*p*An	**6h**	65%	**7h**	not isolated [a]

[a] Not isolable at room temperature because of rapid thermal cycloaromatization. [b] See ref. [19].

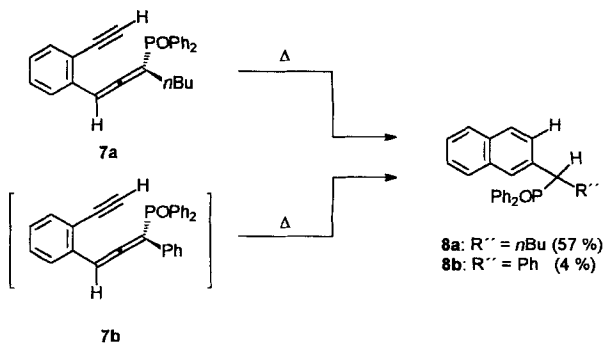
Table 2. Characteristic spectroscopic data of enyne–allenes **7**.

Enyne–allenes	$\tilde{\nu}$(C≡C) [cm^{-1}]	$\tilde{\nu}$(C=C=C) [cm^{-1}]	^{13}C NMR [δ]
7a	2105	1925	209.4
7c	2214	1932	208.8
7d	2227	1931	207.6
7e	2212	1923	220.5
7f [a]	2204	1928	210.2

[a] See ref. [19].

Thermolysis of enyne–allenes 7: In order to investigate their thermal behavior, the isolated enyne–allenes were heated with excess 1,4-cyclohexadiene, a hydrogen donor, in toluene for several hours. Whilst thermal rearrangement of **7a** (90 °C, 1 h) afforded 57% of the Myers–Saito cyclization product **8a**, we obtained the Myers–Saito cyclization product **8b** (4%) directly from the reaction of the propargyl alcohol **6b** with chlorodiphenylphosphine. Isolation of enyne–allene **7b** was not possible even at −30 °C. Obviously, the thermal instability of **7b** is a result of the phenyl substituent at the allene terminus, which is expected to lower the transition-state energy of the Myers–Saito biradical cyclization (Scheme 4).

Surprisingly, the simple switch from a hydrogen to an aryl group at the acetylene terminus redirected the course of the reaction from the Myers–Saito cycloaromatization to an un-



Scheme 4. Formation of the Myers-Saito cyclization products **8a,b**.

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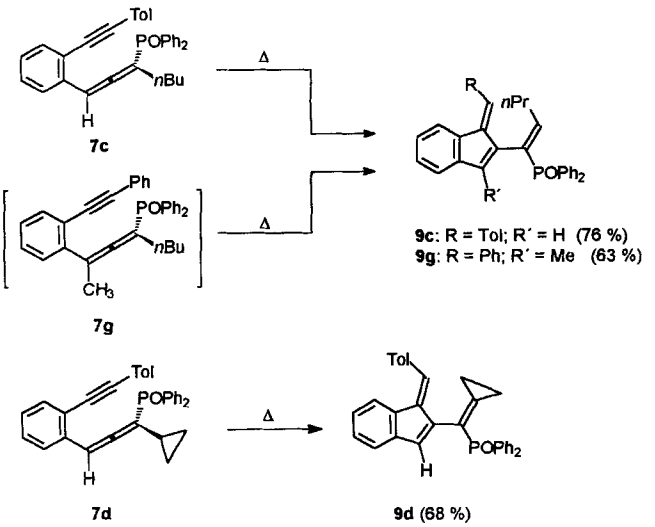
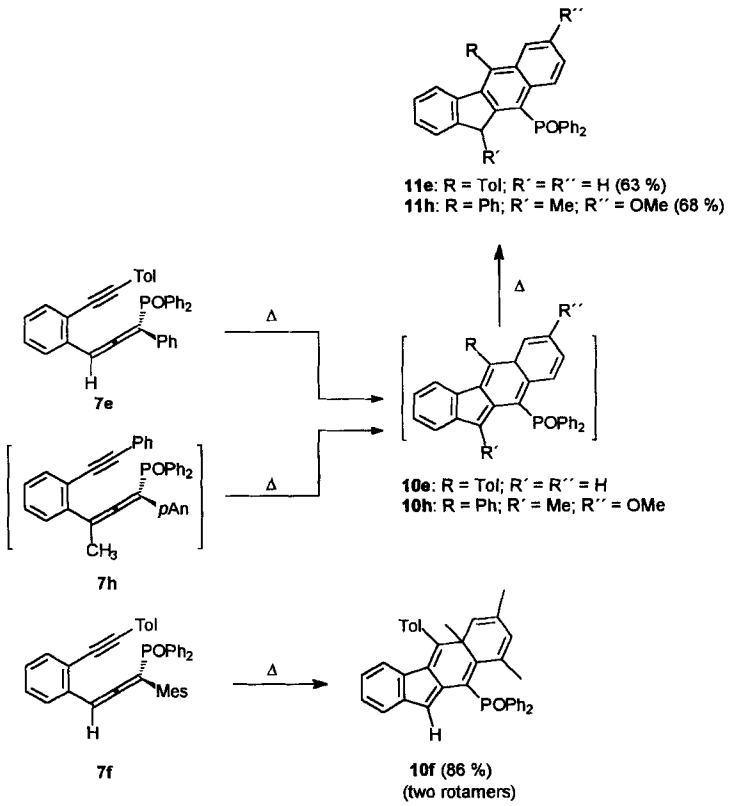
precedented C2–C6-cyclization, a formal ene or Diels–Alder reaction. For example, when enyne–allenes **7c** and **7d** were heated in toluene for 2 h at 100 °C in the presence of excess 1,4-cyclohexadiene, the benzofulvenes **9c** (76%) and **9d** (68%) were formed (Scheme 5). Enyne–allene **7g** could not be isolated on account of its thermal instability. Instead, benzofulvene **9g** was obtained in 63% yield directly from the reaction of propargyl alcohol **6g** with chlorodiphenylphosphine (Scheme 5).



Scheme 5. Thermal reactions of **7c,g**, and **d**.



Scheme 6. Thermal reactions of **7e,h**, and **f**.

Heating enyne–allene **7e** in toluene with excess 1,4-cyclohexadiene for 3 h at 105 °C afforded the benzofluorene derivative **11e** in 63% yield. In the absence of the hydrogen donor, the benzofulvene **10e** was detected by ^{1}H NMR spectroscopy after 2 h at 70 °C along with the unreacted enyne–allene **7e** and the benzofluorene **11e**.[24] Further heating transformed **10e** into the final product **11e**. A similar product, benzofluorene **11h**, was obtained directly from propargyl alcohol **6h** upon reaction with chlorodiphenylphosphine, presumably via the intermediate enyne–allene **7h** (Scheme 6). We should also mention at this point the thermal formation of benzofulvene **10f** in 86% yield from enyne–allene **7f**.[19]

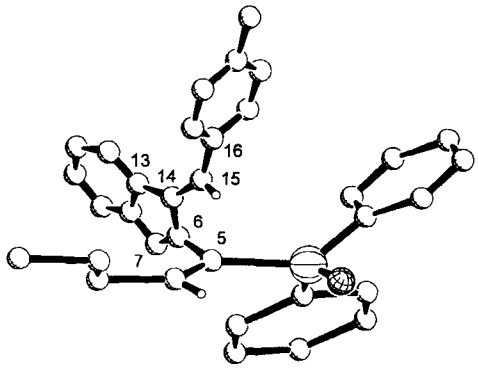


Figure 1. SCHAKAL representation of the crystal structure of **9c**.

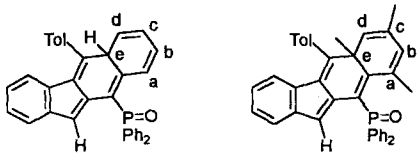
Structural identification of the cyclization products:

Benzofulvenes **9**: The benzofulvene structure of **9c**, **9d**, and **9g** was unambiguously established from 1D (^{1}H, ^{13}C, and ^{31}P) and 2D (C,H-correlation and H,H-COSY) NMR experiments. Additionally, we were able to verify the structure of **9c** by X-ray analysis (Figure 1).[25]

The bond lengths in the fulvene moiety (C6–C7 1.35, C14–C15 1.34, and C6–C14 1.48 Å) indicate the presence of localized double and single bonds. The C–C bond distance between the benzofulvene core and the $POPh_2$-substituted double bond C5–C6 is 1.49 Å, as expected for an allylic C–C single bond. The steric repulsion between the $POPh_2$ group and the benzofulvene is reduced by twisting both parts of the molecule to a dihedral angle of 96° (C7-C6-C5-P). Otherwise the bond lengths are in the expected range, as are most bond angles. A slight enlargement of the bond angles is observed about the tolyl-substituted double bond only (ϕ(C13-C14-C15) = 131° and ϕ(C14-C15-C16) = 128°) in order to minimize the steric repulsion between the tolyl group and the benzofulvene core.

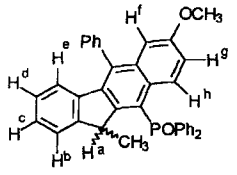
The configuration of both the tolyl- and the phosphine oxide-substituted double bond is (*E*). The O=P–C5=C6 angle is 16°, while the phenyl groups point towards the benzofulvene moiety.

Benzofulvene **10e**: The cross-conjugated structure of **10e** was deduced from the four characteristic ^{1}H NMR signals (H^a–H^d; δ = 5.20, 5.35, 6.12, 6.43), their coupling pattern, and a



comparison with the shifts for H^b and H^d in **10f** ($\delta = 5.40$, 5.87).[19] In the ^{13}C NMR spectrum a doublet ($J(P) = 56$ Hz) at $\delta = 48$ can be assigned to a CH (by 2D experiments) representing the bridgehead C^e in **10e**.

Fluorenes **11**: Despite exhaustive attempts, we have not yet been sucessful in obtaining crystals for X-ray analysis. Thus, the designation of their structural identity has to rely on data from NMR investigations. Although the assignment of the ^1H NMR signals of these polyaromatic compounds proved to be difficult, we were able to verify their structures by H,H-COSY and H,C-COSY NMR experiments. The spectrum of **11h** showed a characteristic quartet at $\delta = 5.09$, which was assigned to proton H^a. We were also able to unambiguously assign the protons from H^b–H^h from H,H-COSY NMR experiments (Figure 2).



11h

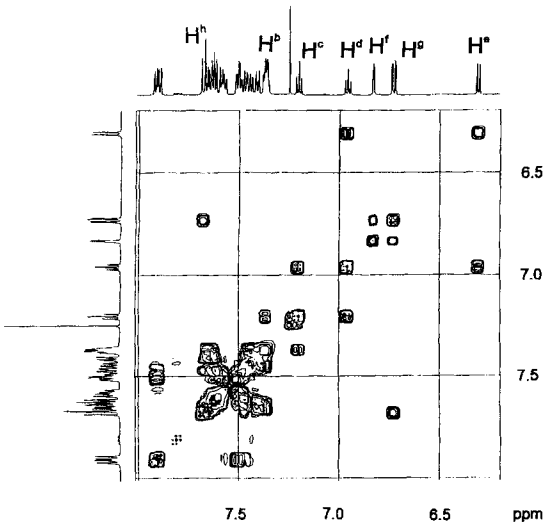


Figure 2. Part of the H,H-COSY NMR of benzofluorene **11h**.

The proton H^e resides in the shielding region of the adjacent phenyl ring and appears upfield at $\delta = 6.31$ (d, $^3J(H,H) = 7.9$ Hz). The assignment of the protons H^f, H^g, and H^h is supported by an additional long-range coupling between the hydrogens of the methoxy group and the protons H^f and H^g. A singlet was detected at $\delta = 29.95$ in the ^{31}P NMR spectrum; this is a characteristic shift of a phosphine oxide group. Additionally, the structure of the diphenylphosphine oxide moiety was established by its fragmentation pattern in the mass spectrum.

Kinetics: The kinetics of the thermolyses of **7a,c–f** were investigated by measuring the heat evolution as a function of a linear temperature gradient in a DSC[26] experiment and/or the decay of enyne–allene signals in the ^1H NMR spectrum at a defined temperature (Figure 3 and Table 3). Several independent DSC thermolyses were recorded to obtain reasonable accuracies in the activation data, because the large amount of data obtained

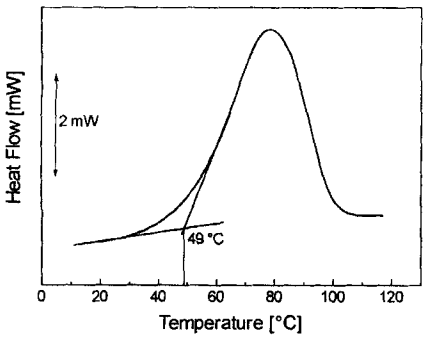


Figure 3. DSC of enyne–allene **7a** (0.2 M in mesitylene).

Table 3. Activation parameters for the thermal cyclization of enyne–allenes **7** in mesitylene (unless otherwise stated) determined by DSC and ^1H NMR experiments (in the presence of 2000 mol% 1,4-cyclohexadiene).

Reaction	$\Delta G^{\neq}$ [kcal mol^{-1}] at 80 °C [a]	k [sec^{-1}] at 73 °C [b]	$\Delta H^{\neq}$ [kcal mol^{-1}] [a]	$\Delta S^{\neq}$ [e.u.] [a]
7a → 8a	+24.3		+22.5	−5.0
	+24.3		+21.9	−6.8
	+24.2		+21.6	−7.2
7c → 9c	+26.4 [c]		+22.9 [c]	−9.8 [c]
	+26.7		+24.9	−5.3
	+26.7 [d]		+22.9 [d]	−8.7 [d]
		4.9×10^{-4} ([D$_6$]benzene)		
		3.4×10^{-4} ([D$_6$]DMSO)		
7d → 9d	+26.1		+20.1	−17.0
	+26.0		+21.1	−14.0
7e → 11e	+25.9	2.7×10^{-3} ([D$_6$]benzene)		
7f → 10f	+26.3	3.7×10^{-4} ([D$_6$]benzene)		

[a] Determined by DSC kinetics. [b] Determined by ^1H NMR kinetics. [c] Determined in DMSO. [d] Determined in DMSO/CF_3COOH 5:1.

in a single DSC experiment in general leads to unreasonably small standard deviations. Unfortunately, the DSC analyses of **7e** and **7f** provided an overlap of two weak exothermic signals indicative of a thermal follow-up reaction. Separation of the two processes by the curve-fitting routine used was unsuccessful, thus precluding the determination of the reaction order and the separation of $\Delta G^{\neq}$ into $\Delta H^{\neq}$ and $\Delta S^{\neq}$. Therefore, we followed their kinetics additionally by ^1H NMR at 73 °C. All kinetic traces followed a first-order decay pattern.

Discussion

Formal Ene and Diels–Alder Reactions: All the investigations described in this paper were prompted by the observation of a surprising switch from the Myers–Saito cycloaromatization of enyne–allene **7a** to a novel high yield C2–C6 cyclization in **7c**. This switch was triggered solely by replacing the hydrogen at the acetylene terminus by an aryl group. The product of this formal ene reaction, the benzofulvene derivative **9c**, was isolated in 76% yield, and its structure was unambiguously determined by X-ray analysis. In our preliminary contribution[18a] we suggested that the formal ene reaction proceeds via a novel benzofulvene biradical intermediate, in order to explain the different reactivity of **7a** and **7c** (Scheme 7).

The same reaction mode was also found for other alkyl-substituted enyne–allenes such as **7d** and **7g**, indicating that such

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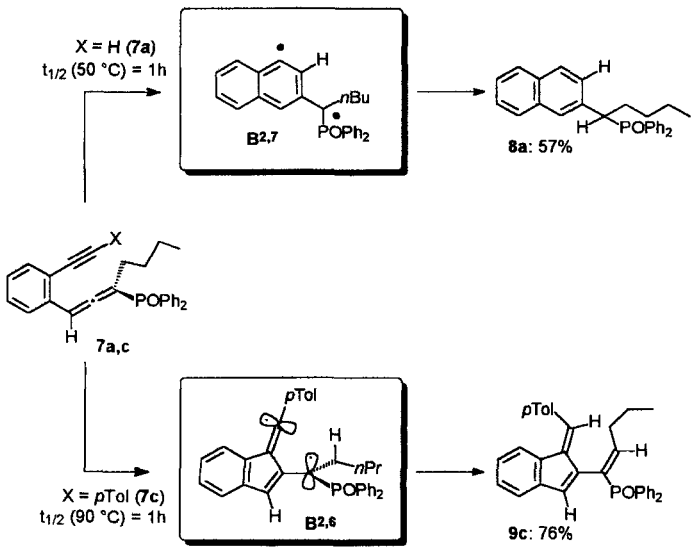
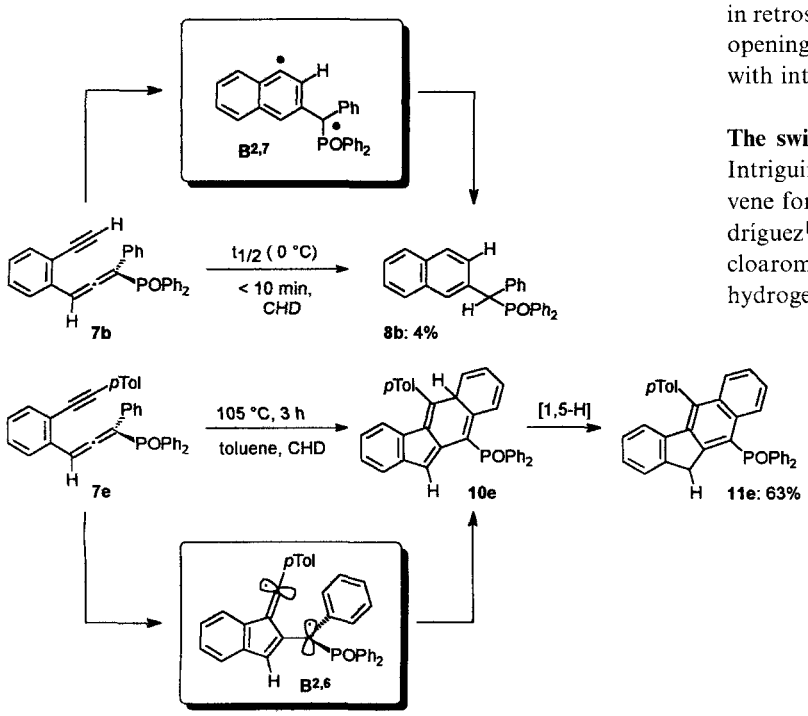


Scheme 7. The different reactivity of **7a** and **7c** may be a result of the formal ene reaction proceeding via a novel benzofulvene biradical intermediate.

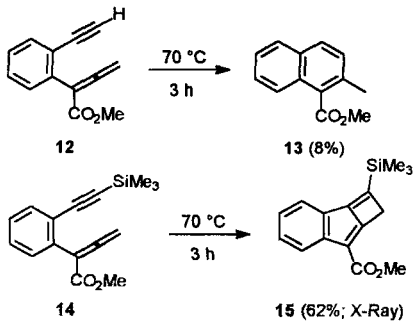
a reaction constitutes a general reaction motif.[18b] Even more impressively, when through the judicious choice of aryl instead of alkyl substituents at the allene terminus the formal ene reaction was rendered impossible, a C2–C6 cyclization reaction was observed again, this time leading to benzofulvene adducts that subsequently rearranged to the more stable benzofluorenes. However, when the aryl group at the alkyne terminus was replaced by hydrogen, the reaction mode switched back to the Myers–Saito cycloaromatization (Scheme 8).



Scheme 8. When the formal ene reaction was rendered impossible by the use of aryl instead of alkyl substituents at the allene terminus, a C2–C6 cyclization reaction leading to benzofulvene adducts (which subsequently rearranged to the more stable benzofluorenes) was observed; when the aryl group at the alkyne terminus was replaced by hydrogen, the reaction mode switched back to the Myers–Saito cycloaromatization.

The mechanism: Two mechanistic conclusions can be drawn directly from the kinetic data in Table 3: firstly, the failure to find any significant effect due to added acid definitely excludes a proton-catalyzed cyclization of **7c**. Secondly, the lack of a solvent effect on the cyclization rate of **7c** on switching from benzene to DMSO rules out a polar reaction mechanism. Hence, two mechanistic scenarios seem to be plausible for the formation of benzofulvene products **9** and benzofluorene products **11**: either a concerted, but certainly not synchronous pathway through ene and Diels–Alder reactions or a stepwise process via biradical $\mathbf{B}^{2,6}$. Importantly, two arguments against the one-step mechanism have emerged from the present investigations: firstly, the existence of a common biradical intermediate convincingly explains why formally different reactions such as an ene reaction and a Diels–Alder cycloaddition occur as alternative processes to the Myers–Saito cyclization. Secondly, a mere tenfold difference in rate constants for the cycloaddition of the mesityl-substituted enyne–allene **7f** compared to **7e** contradicts a concerted reaction pathway, but is readily explained by a stepwise process with formation of $\mathbf{B}^{2,6}$ constituting the rate-determining step. Indeed, to the best of our knowledge there are no reports in the literature of Diels–Alder cycloadditions across a mesityl group as part of a diene system; this is probably caused by steric hindrance. In addition, the intermediacy of a biradical has been rigorously established through our recent mechanistic investigations on phenylcyclopropyl-substituted enyne–allenes. Here the C2–C6 cyclization proved to be nonstereospecific.[27] Rate considerations have implied an approximate lifetime of the biradical of less than 10^{-8} s. In view of the short biradical lifetime, the lack of cyclopropyl ring opening in the reaction **7d** → **9d** was not surprising in retrospect, because the phenylmethylcyclopropyl radical ring opening, with a rate constant of $1.3 \times 10^6\ s^{-1}$, cannot compete with intramolecular hydrogen transfer.[28]

The switch from the Myers–Saito to the C2–C6 cyclization: Intriguingly, shortly after our first publication on the benzofulvene formation by an ene type reaction, Gillmann[20] and Rodríguez[21] also reported a switch from the Myers–Saito cycloaromatization to a C2–C6 cyclization. They replaced hydrogen by silyl substitutents, likewise at the alkyne terminus in enyne–allenes and in enyne–cumulenes. However, in their examples they did not observe either a ene or Diels–Alder reaction, but a formal [2+2] cycloaddition (Scheme 9).



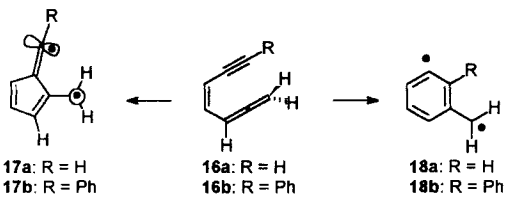
Scheme 9. Gillmann's reported formal [2+2] cycloaddition.

Although no mechanistic investigations were described for either contribution, it seems reasonable to assume a stepwise process for the formal [2+2] cycloadditions as well. In the light of the donor–acceptor substitution pattern, however, a zwitterion may dominate over a biradical mechanism.

Although the mechanistic situation, in terms of thermodynamics and kinetics, is far from being clear at present, the question still arises as to the reason why aryl and silyl substitution divert the reaction from the Myers–Saito reaction to the novel C2–C6 cyclization.

In all enyne–allenes **7** the C2–C7 distances in the *s-cis* conformation were calculated by AM1[29] to be around 330–350 pm. This is 130–150 pm greater than the C–C distance in the transition state of the Myers–Saito cycloaromatization, for which calculations have established a value of 196 pm.[30] In contrast, the C2–C6 distances in **7** are on average 50 pm smaller than those for C2–C7. As a consequence, there is less structural reorganization when moving towards the transition state of the C2–C6 than for the Myers–Saito cyclization.

Our AM1 calculations of biradical cyclizations of the two simple enyne–allenes **16a,b** identify fulvene biradicals **17** as minimum structures for the first time. Although AM1 calculations have not been explicitly parameterized for biradicals, they reproduce rather well the experimental heat of formation of 1,4-didehydrobenzene (with configuration interaction CI = 6).[31] From AM1 calculations for the α,3-didehydrotoluene **18a** we found $\Delta H_f^\circ = 110$ kcal mol^{-1}, which is close to the experimental values for α,3-didehydrotoluene ΔH_f°(exp.) = 103–109 kcal mol^{-1} determined in the gas phase.[32] This suggests that the energetics obtained for **16**, **17**, and **18** (Scheme 10) will be qualitatively correct.



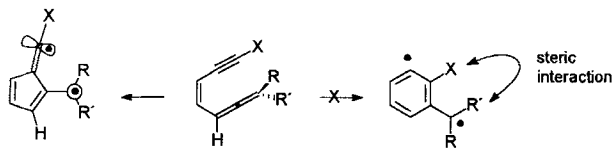
Scheme 10. Intermediate biradicals **17** and **18** obtained from compounds **16**.

According to AM1 calculations (Table 4), both fulvene biradicals **17a,b** have a singlet ground state, the higher SOMO of which is best represented as a planar fulvene methyl radical. The lower SOMO is best described as a vinyl radical with mainly σ character for **17a** and π character for **17b**. In the case of **17b**, the phenyl ring is orientated orthogonally to the plane of the fulvene system, thus aligning properly with the vinyl radical center for maximum stabilization. Such a stabilizing motif is known for simple arylvinyl radicals from ESR results[33].

Table 4. Energetic stabilization resulting from the presence of a phenyl ring.

	ΔH_f°(16) [kcal mol^{-1}]	ΔH_f°(17) [kcal mol^{-1}]	ΔH_f°(18) [kcal mol^{-1}]	ΔH_R(16→17) [kcal mol^{-1}]	ΔH_R(16→18) [kcal mol^{-1}]
a: R = H	114.2	134.7	110.3	20.5	−3.9
b: R = Ph	135.1	152.5	140.1	17.4	5.0

The enthalpy data in Table 4 suggests that the Myers–Saito cycloaromatization **16a**→**18a** is slighly exothermic (ΔH_R = −3.9 kcal mol^{-1}), which agrees with ab initio CASSCF and MRSDCI calculations (ΔH_R = −1.2 to 2.1 kcal mol^{-1}),[30] whilst it is endothermic for **16b**→**18b**. Since phenyl substitution in alkynes is known to cause destabilization of the alkyne,[34] we conclude that enyne–allene **16b** is also destabilized by the phenyl group. Hence, ΔH_R (**16b**→**18b**) = + 5 kcal mol^{-1} implies that the corresponding biradical **18b** becomes even more destabilized, presumably by the steric interaction of the two *ortho* substituents. This interaction should not be of any significance in the formation of the fulvene biradical. Obviously, such interaction will increase with increasing steric bulk of groups R and R′ (Scheme 11), as realized in by model compounds **7**.



Scheme 11. Destabilizing effect of two *ortho* substituents.

In contrast, the C2–C6 cyclization **16**→**17** becomes less endothermic by 3 kcal mol^{-1} on changing from R = H to Ph, presumably because the vinyl radical center can be stabilized by the attached phenyl group and steric effects are negligible. Nevertheless, for both substituents at the alkyne terminus, the Myers–Saito cycloaromatization is always thermodynamically much more favorable than the C2–C6 cyclization, simply because of the gain in resonance energy. But why do we see a switch between the two modes of cyclization with compounds **7a** and **7c** as well as with **7b** and **7e**? Obviously, the activation barrier for the C2–C6 cyclization of **16b** must fall below that of the Myers–Saito cycloaromatization (see Figure 4). This is currently being investigated by density functional theory calculations.[35]

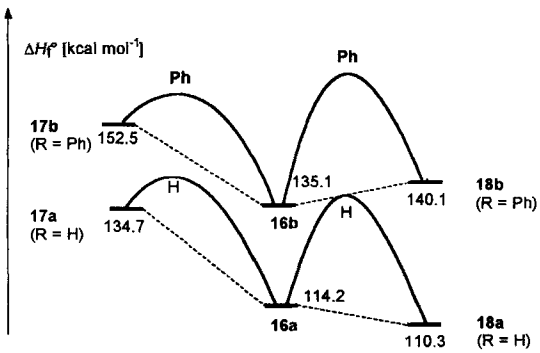


Figure 4. AM1 calculated reaction enthalpies for **16**→**17** or **18**. Activation barriers are not calculated; they are arbitrarily approximated from experimental data of structurally related compounds (Table 3) to qualitatively illustrate the switch of the reaction type.

To summarize, both the experimental data and calculations indicate the occurrence of a novel C2–C6 biradical cyclization as an alternative to the Myers–Saito cycloaromatization of enyne–allenes triggered by aryl substitution at the alkyne terminus. Interestingly, a related reaction switching operates for the

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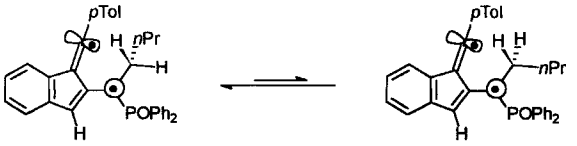
thermal rearrangement of 4-alkynylcyclobutenones, where enyne–ketenes have been postulated as intermediates.[36] If such a biradical intermediate is operative, however, we have to explain the highly stereoselective formation of an (*E*)-phosphine oxide-substituted double bond in **9c,g**. It is significant that AM1 calculations of biradical **19** indicate that the global minimum conformation (*ac*)-**19** (*anticlinal*) is characterized by a hydrogen that is only 240 pm away from the vinyl radical site, the transfer of which will lead to the (*E*) double bond. The other hydrogen is much further away ($d = 360$ pm). The alternative conformation (*sp*)-**19** (*synperiplanar*), which would lead to the (*Z*) double bond, has a much higher energy—approximately 8 kcal mol^{-1} (Scheme 12).



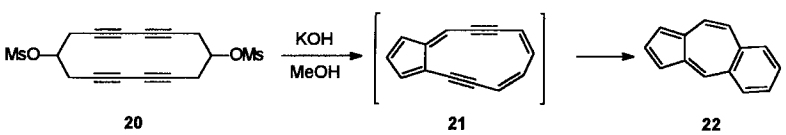
ac-**19ac** *sp*-**19**

Scheme 12. Anticlinal (*ac*)-**19** (minimum) and synperiplanar (*sp*)-**19** conformations of biradical **19**.

A C2–C6 biradical cyclization is also in agreement with the almost identical activation data for the formal ene (of **7c**) vs. Diels–Alder (of **7e**) reaction, although in the latter the presence of a phenyl substituent at the allene would suggest a significant rate increase at the first glance. Apparently, stabilization of the allene functionality in **7e** by the phenyl group is of the same magnitude as the stabilization of the radical center by the phenyl group in the transition state of the C2–C6 cyclization, which should therefore exhibit only little biradical character. This assumption also agrees with the situation in the Bergman cyclization. Very little biradical character was found for the transition state here too.[37]

The marked acceleration of the thermal C2–C6 cyclization of methyl-substituted enyne–allenes **7g** and **7h** vs. the hydrogen-substituted **7c** and **7e** is most probably caused by a ground-state effect.[18b] As already pointed out by Saito,[10] an increased *s-cis* to *s-trans* conformer ratio as well as some backward strain may cause a lower overall activation barrier for the cycloaromatization.

In conclusion, overwhelming evidence for a novel biradical cyclization in enyne–allenes has been described. The switch from the Myers–Saito cyclization is triggered by the presence of an aryl group at the alkyne terminus. Since this alternative thermal reaction mode could be also be triggered by other bulky radical stabilizing groups, the C2–C6 cyclization reaction may be quite general. Indeed, the seminal contribution of Sondheimer in 1966 may have been the first example of a C2–C6 cyclization, because a fulvene intermediate **21** was identified during the cyclization of **20** (Scheme 13).[38]



20 **21** **22**

Scheme 13. Possibly the first example of a C2–C6 cyclization: a fulvene intermediate **21** was identified by Sondheimer during the cyclization of **20**.

Experimental Section

General techniques: All reactions were carried out under N_2 using freshly distilled, anhydrous solvents, unless otherwise stated. Tetrahydrofuran (THF) and diethyl ether (Et_2O) were distilled from sodium/benzophenone, and triethylamine (NEt_3) from calcium hydride. All reactions were followed by thin-layer chromatography on Merck silica gel plates (60F-254). Merck silica gel (particle size 0.063–0.200 mm) was used for column chromatography. All yields correspond to analytically pure isolated material, unless otherwise stated. *o*-Ethinylbenzaldehyde (**3**) was prepared according to ref. [39]. ^{1}H and ^{13}C NMR spectra were recorded on Bruker AC-200, AM-250 or DMX-600 instruments and calibrated with tetramethylsilane as an internal reference (TMS, $\delta = 0.0$). The following abbreviations are used to indicate the multiplicities: s, singlet; d, doublet; t, triplet; q, quartet; q_i, quintet; m, multiplet. ^{31}P NMR were recorded on a Bruker AMX-400 instrument and calibrated with 85% phosphoric acid as an external reference ($\delta = 0.0$). IR spectra were recorded on a Perkin–Elmer 1605 series FT-IR spectrometer. Melting points were recorded on a Büchi melting point apparatus and are uncorrected. High resolution mass spectra (HRMS) were recorded on a Finnigan MAT-90 mass spectrometer with electronic ionization (EI; 70 eV).

2-(4-Tolylethinyl)benzaldehyde (**4**): A solution of *p*-iodotoluene (1.45 g, 6.65 mmol), tetrakis(triphenylphosphine)palladium(0) (228 mg, 190 μmol) and copper(I) iodide (170 mg, 590 μmol) in NEt_3 (30 mL) was treated with *o*-ethinylbenzaldehyde[39] (0.10 g, 6.95 mmol) at 60 °C. The reaction mixture was stirred at 50 °C for 1 h and quenched by adding water (50 mL). The organic layer was separated and the aqueous layer extracted with diethyl ether. The combined organic layers were dried ($MgSO_4$), filtered and concentrated. Purification of the residue by column chromatography (trichloromethane/cyclohexane 1:1; $R_f = 0.62$) afforded **4** (1.38 g, 94%) as yellow crystals. M.p. 38 °C; IR (KBr): $\tilde{\nu}$ = 3059, 3027, 2920, 2845, 2745 (CHO), 2214, 1698 (C=O), 1593, 1510, 1264, 1193, 817, 761 cm^{-1}; ^{1}H NMR (250 MHz, $CDCl_3$): δ = 2.31 (s, 3H), 7.13 (d, ^3J(H,H) = 8.0 Hz, 2H), 7.38 (d, ^3J(H,H) = 8.0 Hz, 1H), 7.39 (d, ^3J(H,H) = 8.0 Hz, 2H), 7.50 (t, ^3J(H,H) = 8.0 Hz, 1H), 7.54 (t, ^3J(H,H) = 8.0 Hz, 1H), 7.88 (d, ^3J(H,H) = 8.0 Hz, 1H), 10.57 (s, 1H); ^{13}C NMR (63 MHz, $CDCl_3$): δ = 20.6, 83.3, 98.6, 118.2, 123.5, 126.1, 127.3, 128.3, 130.5, 132.1, 132.7, 134.7, 138.3, 190.8; $C_{16}H_{12}O$ (220.1): calcd C 87.25, H 5.49, found C 87.25, H 5.50.

2-(Phenylethinyl)acetophenone (**5**): A solution of *o*-bromoacetophenone (4.97 g, 25.0 mmol) and phenylacetylene (3.83 g, 37.5 mmol) in NEt_3 (120 mL) was treated with dichlorobis(triphenylphosphine)palladium(II) (180 mg, 300 μmol) and copper(I) iodide (100 mg, 500 μmol). After the reaction mixture had been stirred at 90 °C for 15 h, water (200 mL) was added. The organic layer was then separated and the aqueous layer extracted with pentane (3 × 200 mL). The combined organic layers were dried ($MgSO_4$), filtered, and concentrated. Purification of the residue by column chromatography (methylene chloride/cyclohexane 1:1; $R_f = 0.3$) furnished **5** (4.52 g, 82%) as a brown oil. IR (neat): $\tilde{\nu}$ = 3060, 2925, 2850, 2214 (C≡C), 1683 (C=O), 1592, 1561, 1493, 1357, 757 cm^{-1}; ^{1}H NMR (250 MHz, $CDCl_3$): δ = 2.80 (s, 3H, CH_3), 7.35–7.57 (m, 7H, Ar–H), 7.63 (m, 1H), 7.76 (m, 1H); ^{13}C NMR (63 MHz, $CDCl_3$): δ = 30.0, 88.5, 95.0, 121.7, 122.8, 128.3, 128.5, 128.7, 128.8, 131.3, 131.5, 133.9, 140.7, 200.2; HRMS calcd for $C_{16}H_{12}O$ [M^+]: 220.0888, found 220.0894.

Compound 6a: The Grignard reagent was prepared from a mixture of magnesium (400 mg, 16.0 mmol) and 1-bromoethane (2.60 g, 15.0 mmol) in Et_2O (20 mL). After dropwise addition of a solution of 1-hexyne (1.23 g, 15.0 mmol) in Et_2O (10 mL) to the Grignard reagent, the mixture was refluxed until gas evolution ceased. The 1-hexinylmagnesium bromide formed was then treated with a solution of *o*-ethinylbenzaldehyde (**3**)[39] (980 mg, 8.00 mmol) in Et_2O (20 mL). After stirring at RT for 1 h, the mixture was quenched with saturated aqueous NH_4Cl. The organic layer was separated and the aqueous layer extracted with Et_2O (3 × 50 mL). The combined organic layers were dried ($MgSO_4$), filtered, and concentrated. Purification of the residue by column chromatography (trichloromethane/cyclohexane 1:1; $R_f = 0.62$) provided **6a** (810 mg, 50%) as a yellow oil. IR (neat): $\tilde{\nu}$ = 3401 (OH), 3293, 3066, 2933, 2872, 2224 (C≡C), 2105, 1448, 1379, 1002 (C–O), 759 cm^{-1}; ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.77 (t, ^3J(H,H) = 7.2 Hz, 3H), 1.20 (sext,

^3J(H,H) = 7.2 Hz, 2H), 1.35 (q_i, ^3J(H,H) = 7.2 Hz, 2H), 2.12 (td, ^3J(H,H) = 7.2 Hz, ^4J(H,H) = 2.0 Hz, 2H), 3.04 (s, 1H, OH), 3.25 (s, 1H), 5.76 (t, ^5J(H,H) = 2.0 Hz, 1H), 7.12 (td, ^3J(H,H) = 7.8 Hz, ^4J(H,H) = 1.5 Hz, 1H), 7.24 (td, ^3J(H,H) = 7.8 Hz, ^4J(H,H) = 1.5 Hz, 1H), 7.36 (dd, ^3J(H,H) = 7.8 Hz, ^4J(H,H) = 1.5 Hz, 1H); ^{13}C NMR (63 MHz, $CDCl_3$): δ = 13.2, 18.1, 21.5, 30.2, 62.4, 79.0, 80.7, 82.2, 87.0, 119.8, 126.2, 127.5, 128.9, 132.5, 143.1; HRMS calcd for $C_{15}H_{15}O$ ($M^+ - H$) 211.1123, found 211.1120.

Compound 6b: As described above for the synthesis of **6a**, **3**[39] (6.00 g, 46.0 mmol) and 2-phenylethinylmagnesium bromide (92.0 mmol) were brought to reaction. The crude product was purified by recrystallization from petroleum ether at −20 °C and column chromatography (ethyl acetate/cyclohexane 1:1, R_f = 0.42) to afford **6b** (9.00 g, 84%) as a pale yellow oil. IR (neat): $\tilde{\nu}$ = 3401 (OH), 3294 (≡CH), 3063, 2926, 2872, 2231 (C≡C), 2104 (C≡CH), 1596, 1488, 1379, 1273, 1031, 757 cm^{-1}; ^{1}H NMR (250 MHz, $CDCl_3$): δ = 2.61 (d, ^3J(H,H) = 5.2 Hz, 1H, OH), 3.25 (s, 1H), 6.00 (d, ^3J(H,H) = 5.2 Hz, 1H), 7.10 (m, 1H), 7.14–7.19 (m, 3H), 7.24 (m, 1H), 7.30–7.38 (m, 2H), 7.39 (dd, ^3J(H,H) = 7.5 Hz, ^4J(H,H) = 1.6 Hz 1H), 7.72 (dd, ^4J(H,H) = 8.1 Hz, ^3J(H,H) = 1.6 Hz, 1H); ^{13}C NMR (63 MHz, $CDCl_3$): δ = 62.3, 80.0, 81.8, 85.5, 87.1, 119.3, 121.4, 125.8,127.2, 127.5, 127.6, 128.4, 130.1, 132.1, 141.9; HRMS calcd for $C_{17}H_{11}O$ ($M^+ - H$) 231.0810, found 231.0807.

Compound 6c: As described above for the synthesis of **6a**, **4** (1.39 g, 6.32 mmol) and 1-hexinylmagnesium bromide (9.36 mmol) were brought to reaction. The crude product was purified by column chromatography (ethyl acetate/cyclohexane 1:3; R_f = 0.38) to furnish **6c** (1.25 g, 66%) as a yellow oil. IR (neat): $\tilde{\nu}$ = 3379 (OH), 3028, 2956, 2876, 2216 (C≡C), 1598, 1511, 1454, 1056 (C–O), 817, 758 cm^{-1}; ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.75 (t, ^3J(H,H) = 7.2 Hz, 3H), 1.31 (m, 4H), 2.13 (t, ^3J(H,H) = 7.2 Hz, 2H), 2.21 (s, 3H), 2.88 (s, 1H, OH), 5.83 (s, 1H), 7.04 (d, ^3J(H,H) = 8.0 Hz, 2H), 7.15 (td, ^3J(H,H) = 7.8 Hz, ^4J(H,H) = 1.5 Hz, 1H), 7.21 (td, ^3J(H,H) = 7.8 Hz, ^4J(H,H) = 1.5 Hz, 1H), 7.33 (d, ^3J(H,H) = 8.0 Hz, 2H), 7.40 (dd, ^3J(H,H) = 7.8 Hz, ^4J(H,H) = 1.5 Hz, 1H), 7.63 (dd, ^3J(H,H) = 7.8 Hz, ^4J(H,H) = 1.5 Hz, 1H); ^{13}C NMR (63 MHz, $CDCl_3$): δ = 13.2, 18.2, 21.1, 21.6, 30.3, 63.0, 79.2, 85.8, 87.0, 94.7, 119.5, 121.1, 125.2, 127.6, 128.3, 128.8, 131.1, 131.9, 138.3, 142.6; HMRS calcd for $C_{22}H_{21}O$ ($M^+ - H$): 301.1592, found 301.1591.

Compound 6d: As described for the synthesis of **6a**, **4** (2.50 g, 11.4 mmol) and 2-cyclopropylethinylmagnesium bromide (16.5 mmol) were brought to reaction. The resulting crude product was purified by column chromatography (ethyl acetate/cyclohexane 1:2; R_f = 0.38) to afford **6d** (1.30 g, 40%) as a yellow oil. IR (neat or film): $\tilde{\nu}$ = 3408 (OH), 3062, 2923, 2872, 2235 (C≡C), 1511, 1449, 1050, 1004, 980, 893, 817, 761 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$): δ = 0.61–0.65 (m, 4H), 1.18 (m, 1H), 2.25 (s, 3H), 2.70 (d, ^3J(H,H) = 4.4 Hz, 1H, OH), 5.78 (d, ^3J(H,H) = 4.4 Hz, 1H), 7.05 (d, ^3J(H,H) = 8.0 Hz, 2H), 7.16 (td, ^3J(H,H) = 8.0 Hz, ^4J(H,H) = 1.8 Hz, 1H), 7.23 (td, ^3J(H,H) = 8.0 Hz, ^4J(H,H) = 1.8 Hz, 1H), 7.33 (d, ^3J(H,H) = 8.0 Hz, 2H), 7.40 (dd, ^3J(H,H) = 8.0 Hz, ^4J(H,H) = 1.8 Hz, 1H), 7.57 (dd, ^3J(H,H) = 8.0 Hz, ^4J(H,H) = 1.8 Hz, 1H); ^{13}C NMR (63 MHz, $CDCl_3$): δ = −0.7, 8.0, 21.2, 63.0, 74.4, 85.8, 90.1, 84.7, 119.5, 121.1, 126.3, 127.7, 128.2, 128.8, 131.0, 131.9, 138.4, 142.5; HRMS calcd for $C_{21}H_{18}O$ ($M^+ - H$): 285.1279, found 285.1278.

Compound 6e: As described for the synthesis of **6a**, **4** (1.50 g, 6.82 mmol) and 2-phenyl-ethinylmagnesium bromide (7.84 mmol) were brought to reaction. The remaining residue was purified by column chromatography (ethyl acetate/cyclohexane 1:3; R_f = 0.21) to furnish **6e** (1.40 g, 64%) as brown crystals. M.p. 81 °C; IR (KBr): $\tilde{\nu}$ = 3394 (OH), 3060, 2925, 2850, 2215 (C≡C), 1598, 1510, 1443, 1034 (C–O), 817, 756 cm^{-1}; ^{1}H NMR (250 MHz, $CDCl_3$): δ = 2.21 (s, 3H), 6.04 (s, 1H), 7.00 (d, ^3J(H,H) = 8.0 Hz, 2H), 7.14–7.20 (m, 3H), 7.20 (td, ^3J(H,H) = 7.0 Hz, ^4J(H,H) = 1.8 Hz, 1H), 7.29–7.33 (m, 2H), 7.31 (d, ^3J(H,H) = 8.0 Hz, 2H), 7.37 (td, ^3J(H,H) = 7.0 Hz, ^4J(H,H) = 1.5 Hz, 1H), 7.42 (dd, ^3J(H,H) = 7.0 Hz, ^4J(H,H) = 1.8 Hz, 1H), 7.64 (dd, ^3J(H,H) = 7.0 Hz, ^4J(H,H) = 1.5 Hz, 1H); ^{13}C NMR (63 MHz, $CDCl_3$): δ = 21.4, 63.6, 88.4, 86.3, 86.9, 95.2, 119.6, 121.5, 122.4, 126.6, 128.1, 128.3, 128.6, 129.1, 131.4, 131.6, 132.2, 138.7, 142.1; HMRS calcd for $C_{24}H_{17}O$ ($M^+ - H$): 321.1279, found 321.1277.

Compound 6g: As described for the synthesis of **6a**, **5** (3.54 g, 16.1 mmol) and 1-hexinylmagnesium bromide (24.0 mmol) were brought to reaction. The crude product was purified by column chromatography (methylene chloride/cyclohexane 1:1; R_f = 0.2) to furnish **6g** (3.01 g, 62%) as a brown oil. IR (neat): $\tilde{\nu}$ = 3426 (O–H), 3059, 2957, 2844, 2243 (C≡C), 1599, 1571, 1492, 757 cm^{-1}; ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.79 (t, ^3J(H,H) = 7.2 Hz, 3H), 1.27–1.46 (m, 4H), 2.00 (s, 3H), 2.20 (t, ^3J(H,H) = 6.9 Hz, 3H), 3.56 (s, 1H), 7.24–7.37 (m, 5H), 7.53–7.60 (m, 3H), 7.75–7.77 (m, 1H); ^{13}C NMR (50 MHz, $CDCl_3$): δ = 13.6, 18.6, 22.0, 30.5, 30.7, 69.7, 83.5, 85.4, 88.6, 96.3, 119.9, 123.1, 124.9, 127.3, 128.4, 128.5, 131.3, 134.0, 147.0; HRMS calcd for $C_{22}H_{19}O$ ($M^+ - H$): 301.1592, found 301.1592.

Compound 6h: As described for the synthesis of **6a**, **5** (1.54 g, 7.00 mmol) and (*o*-methoxyphenyl)ethinylmagnesium bromide (8.00 mmol) were brought to reaction. The crude product was purified by column chromatography (methylene chloride/cyclohexane 1:1; R_f = 0.2) to afford **6h** (1.62 g, 65%) as a brown oil; IR (neat): $\tilde{\nu}$ = 3443 (O–H), 3060, 2927, 2849, 2229 (C≡C), 1605, 1570, 1509 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$): δ = 2.09 (s, 3H), 3.61 (s, 1H), 3.75 (s, 3H), 6.73 (m, 2H), 7.24–7.60 (m, 10H), 7.78 (m, 1H); ^{13}C NMR (50 MHz, $CDCl_3$): δ = 30.2, 55.2, 69.8, 84.4, 88.6, 91.0, 96.5, 113.7, 114.9, 120.2, 123.1, 124.7, 127.4, 128.4, 128.5, 131.4, 133.2, 134.1, 146.6, 159.5; HRMS calcd for $C_{25}H_{19}O_2$ ($M^+ - H$): 351.1385, found 351.1381.

Compound 7a: A mixture of **6a** (486 mg, 2.29 mmol) and NEt_3 (358 µL, 2.98 mmol) in THF (10 mL) was cooled to −70 °C and treated with chlorodiphenylphosphine (526 µL, 2.87 mmol). The yellow suspension was allowed to warm to −40 °C and stirring was continued for 1.5 h. After the reaction had been quenched by addition of water (20 mL), the organic layer was separated and the aqueous layer extracted with Et_2O (3 × 30 mL). The combined organic layers were dried ($MgSO_4$), filtered and concentrated. Purification of the residue by column chromatography (Et_2O, R_f = 0.22) afforded **7a** (271 mg, 30%). M.p. 29–33 °C (decomp.); IR (KBr): $\tilde{\nu}$ = 3295, 3049, 2942, 2861, 2105, 1925 (C=C=C), 1478, 1431 (P–Ph), 1185 (P=O), 1120, 914, 732, 703 cm^{-1}; ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.82 (t, ^3J(H,H) = 7.2 Hz, 3H), 1.32 (sext, ^3J(H,H) = 7.2 Hz, 2H), 1.55 (q_i, ^3J(H,H) = 7.2 Hz, 2H), 2.40 (m, 2H), 3.22 (s, 1H), 6.66 (td, ^3J(H,H) = 11.2 Hz, ^4J(H,H) = 3.4 Hz, 1H), 7.10 (td, ^3J(H,H) = 7.8 Hz, ^4J(H,H) = 1.5 Hz, 1H), 7.17 (m, 2H), 7.27–7.54 (m, 7H), 7.62–7.83 (m, 4H); ^{13}C NMR (63 MHz, $CDCl_3$): δ = 13.3, 21.9, 27.4, 30.1, 80.9, 81.8, 94.9 (d, J(P) = 14 Hz), 102.7 (d, J(P) = 101 Hz), 119.4, 125.8, 126.6, 127.6, 128.0, 128.1, 128.4, 130.9, 131.1, 131.1, 131.2, 131.3, 131.5, 131.6, 132.0, 132.6, 134.4, 209.4 (d, J(P) = 6 Hz); HRMS calcd for $C_{27}H_{25}OP$ [M^+]: 396.1643, found 396.1638.

Compound 7c: As described above for the synthesis of **7a** a mixture of **6c** (840 mg, 2.78 mmol) and NEt_3 (500 µL, 4.16 mmol) was treated with chlorodiphenylphosphine (710 µL, 3.87 mmol). The remaining residue was purified by column chromatography (Et_2O, R_f = 0.42) to furnish **7c** (780 mg, 58%) as yellow crystals. M.p. 35 °C (decomp.); IR (KBr): $\tilde{\nu}$ = 3057, 2955, 2871, 2214 (C≡C), 1932 (C=C=C), 1510, 1481, 1438 (P–Ph), 1185 (P=O), 1118, 817, 755, 724, 696 cm^{-1}; ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.75 (t, ^3J(H,H) = 7.2 Hz, 3H), 1.25 (sext, ^3J(H,H) = 7.2 Hz, 2H), 1.50 (q_i, ^3J(H,H) = 7.2 Hz, 2H), 2.29 (s, 3H), 2.33 (m, 2H), 6.67 (td, ^3J(H,H) = 8.1 Hz, ^4J(H,H) = 3.3 Hz, 1H), 7.05 (d, ^3J(H,H) = 8.0 Hz, 2H), 7.33 (d, ^3J(H,H) = 8.0 Hz, 2H), 7.00–7.21 (m, 3H), 7.22–7.42 (m, 7H), 7.54–7.75 (m, 4H); ^{13}C NMR (63 MHz, $CDCl_3$): δ = 13.6, 21.2, 22.1, 27.5, 30.3, 86.2, 94.2, 95.2 (d, ^3J(H,P) = 13 Hz), 102.8 (d, ^3J(H,P) = 98 Hz), 119.6, 120.7, 126.0, 126.8, 127.8, 128.0, 128.1, 128.2, 128.8, 128.9, 131.1, 131.2, 131.4, 131.5, 131.6, 131.7, 132.0, 134.0, 138.4, 208.8 (d, ^3J(H,P) = 7 Hz,); HRMS calcd for $C_{34}H_{31}OP$ [M^+]: 486.2110 , found 486.2113.

Compound 7d: A mixture of **6d** (90.0 mg, 320 µmol), 1,5-diazabicyclo-[4.3.0]non-5-ene (69.6 µL, 850 µmol) and silver benzoate (185 mg, 810 µmol) in DMF (10 mL) was cooled to −78 °C and treated with chlorodiphenylphosphine (149 µL, 810 µmol). The reaction mixture was allowed to warm to room temperature over 6 h. After the reaction had been quenched by addition of water (20 mL), the organic layer was separated and the aqueous layer extracted with Et_2O (3 × 30 mL). The combined organic layers were dried ($MgSO_4$), filtered and concentrated. Purification of the residue by column chromatography (Et_2O, R_f = 0.20) afforded **7d** (50.0 mg, 34%) as yellow crystals. M.p. 46 °–48 °C (decomp.); IR (KBr): $\tilde{\nu}$ = 3060, 3008, 2924, 2854, 2227 (C≡C), 1931 (C=C=C), 1510, 1438 (P–Ph), 1193, 1120, 908, 817, 732, 702 cm^{-1}; ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.61 (m, 2H), 0.84 (m, 2H), 1.58 (m, 1H), 2.35 (s, 3H), 6.76 (dd, ^3J(H,H) = 10.7 Hz, ^4J(H,H) = 1.3 Hz,

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1H), 7.14 (d, ^3J(H,H) = 8.3 Hz, 2H), 7.10–7.22 (m, 2H), 7.39 (d, ^3J(H,H) = 8.3 Hz, 2H), 7.31–7.43 (m, 7H), 7.67–7.88 (m, 4H); ^{13}C NMR (63 MHz, $CDCl_3$): δ = 8.6, 21.1, 29.3, 86.1, 94.3, 97.0 (d, J(P) = 14 Hz), 107.0 (d, J(P) = 100 Hz), 119.5, 121.0, 125.9, 127.0, 127.7, 127.8, 127.9, 128.0, 128.8, 129.6, 131.0, 131.1, 131.3, 131.5, 131.5, 131.6, 131.9, 132.0, 133.5, 138.3, 207.6 (d, J(P) = 7 Hz); HRMS calcd for $C_{33}H_{26}PO$ (M^+ – H) 469.1721, found 469.1721.

Compound 7e: As described for the synthesis of **7a** a mixture of **6e** (300 mg, 930 μmol) and NEt_3 (180 μL, 1.50 mmol) was treated with chlorodiphenylphosphine (260 μL, 1.40 mmol). The remaining residue was purified by column chromatography (Et_2O, R_f = 0.50) to furnish **7e** (240 mg, 51%) as yellow crystals. M.p. 67 °C (decomp.); IR (KBr): $\tilde{\nu}$ = 3062, 2978, 2949, 2212 (C≡C), 1923 (C=C=C), 1594, 1509, 1480, 1438 (P–Ph), 1197 (P=O), 1120, 817, 769, 732, 700 cm^{-1}; ^{1}H NMR (250 MHz, $CDCl_3$): δ = 2.38 (s, 3H), 6.90 (d, ^3J(H,H) = 11.9 Hz, 1H), 7.16 (d, ^3J(H,H) = 8.0 Hz, 2H), 7.16–7.55 (m, 17H), 7.65–7.85 (m, 4H); ^{13}C NMR (63 MHz, $CDCl_3$): δ = 21.0, 88.9, 93.3, 96.4 (d, ^3J(H,P) = 12 Hz), 104.8 (d, ^3J(H,H) = 75 Hz), 119.7, 123.9, 126.4, 127.2, 127.9, 128.0, 128.1, 128.2, 128.3, 128.7, 129.2, 129.4, 129.9, 131.4, 131.5, 131.6, 131.7, 131.8, 132.4, 135.2, 138.4, 220.5 (d, ^3J(H, P) = 6 Hz); HRMS calcd for $C_{36}H_{26}PO$ (M^+ – H): 505.1721, found 505.1721.

Compound 8a: A mixture of **7a** (520 mg, 1.31 mmol) and 1,4-cyclohexadiene (500 μL, 5.00 mmol) in toluene (10 mL) was heated to 90 °C for 1 h. After evaporation of the solvent the crude residue was purified by column chromatography (cyclohexane/ethyl acetate 1:1; R_f = 0.19) to furnish **8a** (330 mg, 57%) as pale yellow crystals. M.p. 170 °C (decomp.); IR (KBr): $\tilde{\nu}$ = 3055, 2988, 2836, 1599, 1437 (P–Ph), 1176 (P=O), 1118, 1099, 736, 723, 698 cm^{-1}; ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.63 (t, ^3J(H,H) = 7.2 Hz, 3H), 1.01–1.15 (m, 4H), 1.87 (m, 1H, 12-H), 2.16 (m, 1H, 12-H), 3.50 (m, 1H, 11-H), 7.04 (m, 2H), 7.16 (dd, ^3J(H,H) = 7.8 Hz, ^4J(H,H) = 1.5 Hz, 1H), 7.28–7.48 (m, 8H), 7.57 (s, 1H), 7.60–7.70 (m, 3H), 7.84 (m, 2H); ^{13}C NMR (63 MHz, $CDCl_3$): δ = 13.4, 21.8, 28.5, 29.6 (d, J(P) = 13 Hz), 46.6 (d, J(P) = 67 Hz), 124.6, 124.8, 126.5, 126.8, 127.0, 127.4, 127.6, 127.7, 127.9, 129.9, 130.2, 130.3, 130.7, 131.0, 131.3, 132.2, 132.6; HRMS calcd for $C_{27}H_{27}PO$ [M^+]: 398.1799, found 398.1801.

Compound 8b: A mixture of **6b** (220 mg, 948 μmol), 1,4-cyclohexadiene (1.90 mL, 19.0 mmol) and NEt_3 (600 μL, 4.75 mmol) in toluene/THF (1:1; 100 mL) was cooled to –78 °C and treated with chlorodiphenylphosphine (600 μL, 3.56 mmol). The reaction mixture was allowed to warm to –40 °C and stirred for 18 hours. After the reaction had been quenched with water (100 mL), the organic layer was separated and the aqueous layer extracted with Et_2O (2 × 50 mL). The combined organic layers were dried ($MgSO_4$), filtered, and concentrated. Purification of the residue by column chromatography (Et_2O, R_f = 0.50) afforded **8b** (9.80 mg, 4%) as pink crystals. M.p. > 250 °C (decomp.); IR (CCl_4): $\tilde{\nu}$ = 3364, 2964, 2926, 2855, 1597, 1493, 1438, 1183, 1114, 1032; ^{1}H NMR (250 MHz, $CDCl_3$): δ = 4.83 (d, ^3J(H,H) = 8.6 Hz, 1H), 7.08–7.14 (m, 3H), 7.22–7.34 (m, 5H), 7.38–7.43 (m, 5H), 7.52–7.63 (m, 6H), 7.73–7.86 (m, 2H), 7.95 (s, 1H); ^{13}C NMR (63 MHz, $CDCl_3$): δ = 52.5 (d, J(P) = 66 Hz), 124.8, 125.9, 126.4, 126.8, 126.9, 127.0, 127.1, 127.2, 127.3, 127.4, 127.5, 127.5, 128.6, 128.8, 128.9, 130.2, 130.3, 130.4, 130.5, 130.5, 130.6, 130.8, 130.9, 131.2, 132.3, 133.8, 133.9; HRMS calcd for $C_{29}H_{23}PO$ [M^+]: 418.1486, found 418.1490.

Compound 9c: A mixture of **7c** (302 mg, 620 μmol) and 1,4-cyclohexadiene (50.0 μL, 500 μmol) in toluene (20 mL) was heated to 100 °C for 2 h. After evaporation of the solvent the crude residue was purified by column chromatography (cyclohexane/ethyl acetate 1:1; R_f = 0.13) to provide **9c** (231 mg, 76%) as pale yellow crystals. M.p. 114 °C (decomp.); IR (KBr): $\tilde{\nu}$ = 3055, 2959, 2928, 2870, 1622, 1509, 1437 (P–Ph), 1190 (P=O), 1118, 749, 724, 698 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$): δ = 0.83 (t, ^3J(H,H) = 7.4 Hz, 3H), 1.44 (sext, ^3J(H,H) = 7.4 Hz, 2H), 2.11 (qd, ^3J(H,H) = 7.4 Hz, ^4J(H, P) = 2.3 Hz, 2H), 2.29 (s, 3H), 6.24 (d, ^4J(H, P) = 2.3 Hz, 1H), 6.56 (s, 1H), 6.81 (ddd, ^3J(H,H) = 7.7 Hz, ^3J(H,H) = 6.1 Hz, ^4J(H,H) = 2.3 Hz, 1H), 6.96 (d, ^3J(H,H) = 8.0 Hz, 2H), 7.02 (ddd, ^3J(H,H) = 6.8 Hz, ^3J(H,H) = 6.1 Hz, ^4J(H,H) = 0.7 Hz, 1H), 7.02 (dd, ^3J(H,H) = 6.8 Hz, ^3J(H,H) = 2.3 Hz, 1H), 7.05 (d, ^3J(H,H) = 8.0 Hz, 2H), 7.14 (dt, ^3J(H,P) = 19.1 Hz, ^3J(H,H) = 7.4 Hz, 1H), 7.23 (s, 2H), 7.31 (dd, ^3J(H,H) = 7.7 Hz, ^4J(H,H) = 0.7 Hz, 1H), 7.36 (m, 4H), 7.65 (m, 4H); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 13.9, 21.3, 22.0, 33.1 (d, J(P) = 26 Hz), 120.7, 123.0, 124.8, 127.7, 128.3, 128.9, 129.0, 130.0, 131.2, 131.7, 132.1, 133.2, 134.0, 134.6, 137.4 (d, J(P) = 40 Hz), 138.0, 138.2, 139.4, 143.1, 151.3 (d, J(P) = 12 Hz); ^{31}P NMR (162 MHz, $CDCl_3$): δ = 26.1 (s); HRMS calcd for $C_{34}H_{31}OP$ [M^+]: 486.2112, found 486.2111.

Compound 9d: A mixture of **7d** (50.0 mg, 110 μmol) and 1,4-cyclohexadiene (1.48 mL, 14.8 mmol) in toluene (20 mL) was heated to 100 °C for 2 h. After evaporation of the solvent the crude residue was purified by column chromatography (cyclohexane/ethyl acetate 1:1; R_f = 0.17) to furnish **9d** (35.0 mg, 68%) as yellow crystals. M.p. 163 °C; IR (KBr): $\tilde{\nu}$ = 3051, 3020, 2984, 2918, 1630, 1508, 1436 (P–Ph), 1184 (P=O), 744, 723, 697, 542 cm^{-1}; ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.93 (m, 2H), 1.28 (m, 2H), 2.33 (s, 3H), 6.79 (td, ^3J(H,H) = 7.0 Hz, ^4J(H,H) = 2.0 Hz), 6.83 (d, ^4J(H, P) = 2.3 Hz, 1H), 7.07 (td, ^3J(H,H) = 7.0 Hz, ^4J(H,H) = 1.3 Hz, 1H), 7.09 (m, 2H), 7.18 (d, ^3J(H,H) = 7.6 Hz, 2H), 7.28 (d, ^3J(H,H) = 7.6 Hz, 2H), 7.36–7.46 (m, 7H), 7.47 (td, ^3J(H,H) = 7.0 Hz, ^4J(H,H) = 2.0 Hz), 7.73 (dd, ^3J(H,H) = 7.6 Hz, ^4J(H,H) = 2.0 Hz, 2H), 7.79 (dd, ^3J(H,H) = 7.6 Hz, ^4J(H,H) = 2.0 Hz, 2H); ^{13}C NMR (63 MHz, $CDCl_3$): δ = 4.3 (d, J(P) = 14 Hz), 6.4, 21.4, 121.0, 123.0, 124.8, 127.8, 128.2, 128.4, 129.1, 129.2, 131.1, 131.6, 131.6, 131.9, 132.0 , 133.5, 133.6, 134.3, 138.3, 138.4, 138.6, 139.3, 143.3, 147.4, $C_{33}H_{26}PO$ (470.6) calcd C 84.23, H 5.78; found C 84.08, H 6.01.

Compound 9g: A mixture of **6g** (243 mg, 800 μmol), lithiumdiisopropylamide (1.00 mL, 820 μmol) and 1,4-cyclohexadiene (0.16 mL, 1.60 mmol) in THF (5 mL) was cooled to –78 °C and treated with chlorodiphenylphosphine (150 μL, 800 μmol). After 6 h the reaction mixture was allowed to warm to –40 °C and then stirred for 18 h. After the reaction had been quenched with water (5 mL), the organic layer was separated and the aqueous layer extracted with methylene chloride (3 × 20 mL). The combined organic layers were dried ($MgSO_4$), filtered, and concentrated. Purification of the residue by column chromatography (ethylacetate/cyclohexane 1:1; R_f = 0.3) afforded **9g** (122 mg, 63%) as a bright yellow oil. IR (neat): $\tilde{\nu}$ = 3058, 2958, 2929, 1620, 1598, 1437 (P–Ph), 1180 (P=O), 909, 728, 697 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$): δ = 0.88 (t, ^3J(H,H) = 7.4 Hz, 3H), 1.46 (q_i, ^3J(H,H) = 7.4 Hz, 2H), 1.64 (d, ^5J(H, P) = 2.7 Hz, 3H), 2.12 (dq, ^3J(H,H) = 7.4 Hz, ^4J(H,P) = 2.7 Hz, 2H), 6.61 (s, 1H), 6.93 (t, ^3J(H,H) = 7.3 Hz, 1H), 7.11 (d, ^3J(H,H) = 6.9 Hz, 2H), 7.15 (d, ^3J(H,H) = 7.3 Hz, 1H), 7.19 (t, ^3J(H,H) = 7.4 Hz, 1H), 7.23 (dt, ^3J(H,P) = 18.5 Hz, ^3J(H,H) = 7.4 Hz, 1H), 7.28–7.33 (m, 4H), 7.35–7.41 (m, 4H), 7.42–7.50 (m, 2H), 7.74–7.82 (m, 4H); ^{13}C NMR (151 MHz, $CDCl_3$): δ = 11.3, 14.0, 21.8, 32.8, 118.5, 122.7, 125.0, 127.6, 127.7, 128.0, 128.1, 128.9, 131.3, 131.5, 132.0, 132.1, 132.3, 134.2, 136.6, 139.3, 139.9, 144.5, 151.4; ^{31}P NMR (162 MHz, $CDCl_3$): δ = 23.16 (s); HRMS calcd for $C_{34}H_{31}OP$ [M^+]: 486.2112, found 486.2110.

Compound 11e: A mixture of **7e** (355 mg, 702 μmol) and 1,4-cyclohexadiene (1.23 g, 12.3 mmol) in toluene (20 mL) was heated at 105 °C for 3 h. After evaporation of the solvent, the crude residue was purified by column chromatography (cyclohexane/ethyl acetate 1:1; R_f = 0.65) to afford **11e** (224 mg, 63%) as pale yellow crystals. M.p. 112 °C (decomp.); IR (KBr): $\tilde{\nu}$ = 3026, 2919, 2870, 1501, 1436 (P–Ph), 1391, 1328, 1181 (P=O), 1117, 904, 808, 762, 725, 696 cm^{-1}; ^{1}H NMR (250 MHz, $CDCl_3$): δ = 2.46 (s, 3H), 3.99 (s, 2H), 6.34 (d, ^3J(H,H) = 7.2 Hz, 1H), 6.90 (td, ^3J(H,H) = 7.2 Hz, ^3J(H,H) = 1.5 Hz, 1H), 7.04 (td, ^3J(H,H) = 7.2 Hz, ^3J(H,H) = 1.5 Hz, 1H), 7.08–7.25 (m, 6H), 7.36–7.53 (m, 8H), 7.65–7.71 (m, 4H), 8.22 (d, ^3J(H,H) = 9.3 Hz, 1H); ^{13}C NMR (63 MHz, $CDCl_3$): δ = 21.1, 38.6, 123.3, 124.0, 124.9, 125.3, 126.0, 126.8, 127.0, 128.3, 128.5, 129.0, 129.6, 131.5, 131.6, 131.6, 131.7, 132.3, 133.4, 135.0, 135.4, 137.4, 137.6, 138.0, 139.1 143.9, 149.5; $C_{35}H_{27}OP$ (494.6): calcd C 85.36, H 5.37; found C 85.71, H 5.29.

Compound 11h: A mixture of **6h** (560 mg, 1.61 mmol), lithiumdiisopropylamide (4.2 mL, 1.8 mmol) and 1,4-cyclohexadiene (1.60 mL, 16.0 mmol) in THF (5 mL) was cooled to –40 °C and treated with chlorodiphenylphosphine (332 μL, 1.61 mmol). After the mixture had been stirred at –40 °C for 18 h, the reaction was quenched by the addition of water (20 mL). The organic layer was separated and the aqueous layer was then extracted with methylene chloride (3 × 50 mL). The combined organic layers were dried ($MgSO_4$), filtered, and concentrated. Purification of the residue by column chromatography (ethyl acetate/*n*-pentane 1:1; R_f = 0.2) afforded **11h** (597 mg, 68%) as yellow crystals. M.p. 148–149 °C; IR (CCl_4): $\tilde{\nu}$ = 3061, 2933, 2853, 1619, 1509, 1438 (P–Ph), 1180 (P=O), 908 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$): δ = 1.41 (d, ^3J(H,H) = 7.1 Hz, 3H), 3.59 (s, 3H), 5.09 (q, ^3J(H,H) = 7.1 Hz, 1H), 6.31 (d, ^3J(H,H) = 7.9 Hz, 1H), 6.73 (dd, ^3J(H,H) =

9.4 Hz, ^4J(H,H) = 2.8 Hz, 1H), 6.83 (m, 1H), 6.96 (t, ^3J(H,H) = 7.9 Hz, 1H), 7.21 (t, ^3J(H,H) = 7.9 Hz, 1H), 7.35–7.39 (m, 3H), 7.41–7.53 (m, 5H), 7.56–7.66 (m, 6H), 7.68 (d, ^3J(H,H) = 9.4 Hz), 7.89–7.93 (m, 2H); ^{13}C NMR (151 MHz, $CDCl_3$): δ = 24.3, 42.9, 54.9, 106.2, 116.8, 123.6, 123.7, 126.3, 127.8, 128.1, 128.5, 128.6, 128.7, 128.8, 129.1, 129.4, 129.5, 129.7, 131.3, 131.5, 131.6, 131.9, 132.2, 138.7, 151.3, 155.9, 156.9; ^{31}P NMR (162 MHz, $CDCl_3$): δ = 29.95 (s); HRMS calcd for $C_{37}H_{29}O_2P$ [M^+]: 536.1903, found 536.1906.

Crystal structure determination of 9c: Enraf Nonius CAD4 diffractometer, ω–2θ scan mode using $Cu_{K\alpha}$ (λ = 1.54178 Å) radiation with a graphite monochromator; 5929 reflections measured, 5697 unique, giving 5697 with $I > 2\sigma(I)$. $C_{34}H_{31}OP$, M = 486.6. Monoclinic, a = 14.3820 Å, b = 9.2890 Å, c = 21.1651 Å, β = 98.980°, V = 2792.9 Å^3, space group $P121/c1$, Z = 4, ρ_{calcd} = 1.157 mg mm^{-3}, yellow rhombic crystals. Crystal size: 0.5 × 0.35 × 0.25 mm.

DSC analysis: DSC measurements were carried out on differential scanning calorimeters Dupont 910 and Perkin Elmer 2C. In general, a 0.2 M solution of the enyne–allene (for details see Table 3) was heated in homemade capsules from −30 to 150 °C at a rate of 5 K min^{-1} and the heat evolution was recorded.[26] The kinetic reaction order and rate constants were extracted from the experimental data through comparison with a simulated DSC trace, the activation enthalpy and entropy of which were varied. (program written by E. Hickl, Freiburg).

^{1}H NMR kinetics: The effective temperature in the NMR spectrometer was determined by calibration with the chemical shifts of glycol and methanol.[40] The enyne–allenes were heated in 4×10^{-2} M solution in [D_6]benzene in the presence of *m*-nitroacetophenone as an internal standard (in the absence of 1,4-CHD). The disappearance of two or more significant hydrogen absorptions of the enyne–allene was followed over at least 2 halflives using about 10 data points. Independent of which signal was analyzed, the data fitted a clean first-order kinetic decay curve, exhibiting identical rate constants and standard deviations.

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