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PtI_2-catalyzed cyclization of 3-acyloxy-1,5-enynes with the elimination of HOAc and a benzyl shift: synthesis of unsymmetrical *m*-terphenyls†

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A novel cyclization of 3-acyloxy-1,5-enynes is developed in the presence of PtI_2 for the synthesis of substituted unsymmetrical *m*-terphenyls in good to excellent yields. Two unique steps are involved in this transformation, which includes the elimination of HOAc and benzyl group migration. DFT calculations indicated that the rate-determining step is the migration of the benzylic carbocation to form a zwitterionic intermediate followed by the elimination of HOAc. The subsequent cyclopropanation of the zwitterionic intermediate is the regioselectivity-determining step.

Introduction

Transition metal-catalyzed cycloisomerization of enynes has emerged as a powerful tool for the synthesis of carbocyclic compounds. In this active research field, Au catalysts are widely used because of their unique "π-acidity".[1] Comparably less attention is paid to the application of Pt(II) catalysts.[2] Among a series of applicable enyne substrates, 1,5-enynes are among the most studied and have been efficiently converted into cyclic products including bicyclo[3.1.0]hexenes,[3] cyclohexadienes **1** reported by Kozmin's group, in which a Pt-catalyzed cyclization reaction was developed with the migration of the aryl group at the terminal of the alkyne (Scheme 1a),[4] methylenecyclopentenes,[5] substituted benzene derivatives[6] and heterobicyclic alkenes.[7] In 2006, Zhang's research group reported that the gold-catalyzed unique cycloisomerization of 3-acyloxy-1-en-5-yne yielded 1-acyloxycyclohexa-1,4-dienes and acyloxy aromatic compounds. The authors proposed that the phenyl group at the end of the alkene could provide further stabilization to the carbon cation, allowing efficient migration of the OAc group, and the alkenyl-gold intermediate was generated *in situ*. However, the synthesis of 3-acyloxy-1-en-5-yne from *trans*-cinnamaldehyde was unsuccessful with Au catalysts, but it could be converted into cyclohexadiene **2** in 60% yield when 20 mol% $PtCl_2$ is used as an alternative catalyst (Scheme 1b), and they observed that the substrates with internal C–C triple bonds did not yield the desired products in their gold catalytic system.

Results and discussion

Based on our previous work,[9] we could obtain a series of aryl substituted 3-acyloxyl-1-en-5-yne products **3** through a Barbier-type propargylation reaction of various cinnamaldehydes followed by a Sonogashira coupling reaction and hydroxyl protection. Then a simple methodology was developed by using 3-acyloxy-1-en-5-ynes (ACEs) **3** as starting materials to synthesize various *m*-terphenyls **4** (Scheme 1c). Gaining insight into the *m*-terphenyl product, we observed that a new central benzene ring was constructed *via* the cyclization and consecutive aromatization of 1,5-enynes without the need for additional oxidation.[8] Notably, in the product **4**, the original substituent (R^1) on the alkene terminal (C1 position) of 1,5-enynes and the substituent (R^2) on the alkyne terminal (C6 position) are located at the *meta*-position of the newly formed central cyclic ring (Scheme 1c). In other words, the possible migration of the alkyl group involved in this cyclization is completely different from the previous reports.[10] Furthermore, diversified *m*-terphenyls, which possess interesting biological properties[11] and are the important building blocks for the synthesis of sterically demanding aryl ligands[12] and cyclophanes,[13] and potential host materials for organic light-emitting devices (OLEDs),[14] can be easily and efficiently synthesized by using various substituted patterns of the enynes in our methodology. In the past few decades, various approaches have been established to construct these diversi-

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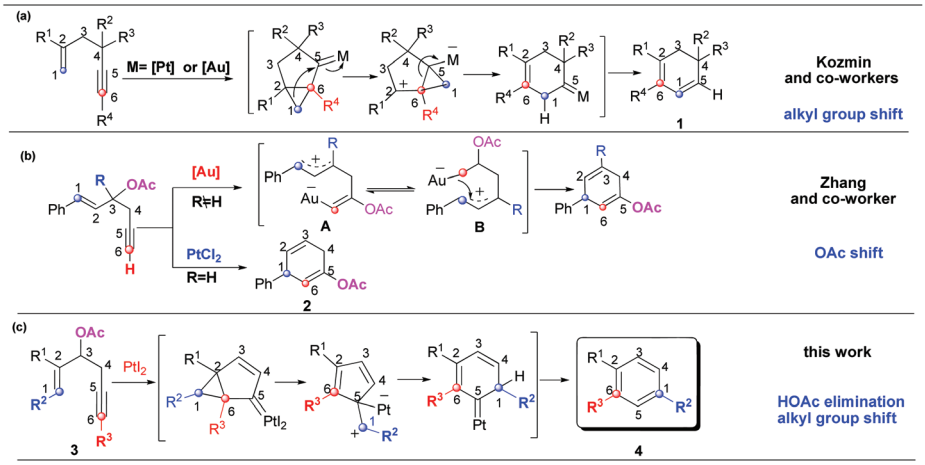


Scheme 1 Intramolecular cyclization of 1,5-enynes.

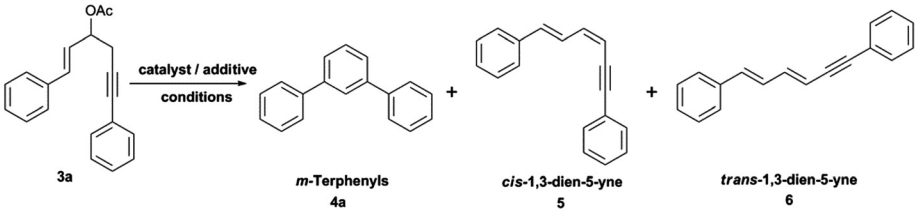
fied *m*-terphenyl frameworks. For example, the Grignard reaction is performed by sequential treatment of 1,3-dichlorobenzene with *n*-BuLi and then with *p*-tolyl-magnesium bromide to synthesize symmetric terphenyls in early studies.[15] Then transition-metal catalyzed coupling reactions are developed to become among the most popular tools, especially Suzuki–Miyaura cross-coupling.[16] In recent years, the cyclization reactions of enyne substrates were also explored to construct unsymmetrical *m*-terphenyl and its derivatives. For example, Liu *et al.* reported facile synthesis of 1,3-disubstituted benzenes through cyclization of alkynyl aldehydes and 2-substituted allylsilanes *via* gold-catalyzed tandem allylation and cyclization of enynes.[17] Aguilar and coworkers described a gold-catalyzed cyclo-aromatization of related 2,4-dien-6-yne carboxylic acids to synthesize 2,3-disubstituted phenols and unsymmetrical bi- and terphenyls. However, the scope of substrates is limited due to the need for a strong electron-donating group linked to the triple bond directly.[18] Therefore, it is still highly desirable to develop simple, highly efficient and regioselective methods for the synthesis of *m*-terphenyls.

In our initial study, we chose 20 mol% $PtCl_2$ as the π-acid metal catalyst and 3-acyloxy-1-en-5-yne **3a** as the substrate to react at 110 °C in toluene. Without any detection of cyclohexadiene or acetoxyl arenes, the enyne **3a** underwent tandem cyclization and aromatization, resulting in the unexpected *m*-terphenyl **4a** (X-ray diffraction analysis of **4a** see ESI†) in 50% yield (entry 1, Table 1). Gold(I) and gold(III) catalysts, whether with the ligand or not, display no effectiveness for the cyclization of 3-acyloxy-1,5-enyne (entries 2–6). In most cases, only *trans*-/*cis*-1, 3-dien-5-yne **5**/**6** were obtained in different proportions. Other Lewis acid catalysts, such as $AgSbF_6$, $FeCl_3{\cdot}6H_2O$[19] or ZnI_2, furnished similar results (see entries 7–9, Table 1). Because no desired cyclization products were obtained when employing other metal catalysts, we then focused on the investigation of other experimental parameters in the presence of a Pt catalyst. As a result, this reaction showed a lower efficiency in CH_3CN and THF than that in toluene (Table 1, entries 10 and 11). But to our delight, using 10 mol% PtI_2 to catalyze this reaction, a noticeably improved yield of *m*-terphenyl **4a** was obtained up to 85% (entry 12). Nevertheless, the addition of the ligands PPh_3 and 1,5-cyclooctadiene (COD) failed to promote the desired transformation under the investigated reaction conditions (entries 13 and 14), and the isolated yields of **4a** decreased when reducing the amount of the PtI_2 catalyst from 10 mol% to 5 or 2 mol% even with prolonging reaction times 9 h and 33 h, respectively (entries 15 and 16). It should be noted that the conversion rate of this reaction was high above 99% by ^1H NMR but with low isolated yield of *m*-terphenyl in the case of the catalysts $PtCl_2$ and PtI_2 (entries 1, 10 and 16). This phenomenon could be explained by the easy oligomerization or decomposition of this enyne substrate under the reaction conditions. Interestingly, when introducing 50 mol% *N*-phenylmaleimide to the reaction system with 5 mol% of the PtI_2 catalyst, this reaction could afford the desired product **4a** in 92% yield (entry 17). It was presumed that the additive *N*-phenylmaleimide acts as a ligand[20] to improve the solubility of the platinum metal catalyst in toluene, and thus it shortened the reaction time and reduced the possible oligomer formation or decomposition of this enyne substrate under the reaction conditions. However, when a 5-membered lactam structural compound, *N*-methyl pyrrolidinone, was used as an additive, no reaction occurred (entry 18). Overall, the optimal reaction conditions were 5 mol% PtI_2 as the catalyst, 50 mol% *N*-phenylmaleimide as the additive, toluene as the solvent and a reaction temperature of 110 °C.

Besides the above screening experiments, we had also examined several other 1,5-enynes with various hydroxyl protecting groups[21] such as OTBS, OCH_3 and even OH at the C3-position (Table S1†) to understand the effect of the leaving group at the C3-position on the reaction. As a result, the acetyl group is the best hydroxyl protecting group in our methodology.

Under the optimized reaction conditions, we next examined the scope of cyclization of 3-acyloxy-1-en-5-ynes bearing

Table 1 Optimization studies of the cyclization of **3a**[a]



Entry	Catalyst/additive (mol%)	Conditions	Yield of **4a** [b](%)	Total yield of **5** and **6** (%)
1	$PtCl_2$ (20)	PhMe/110 °C/1.5 h	50 (conv. >99)	—
2	AuCl (5)	DCM/48 h	No reaction	
3	PPh_3AuCl (5)	DCM/48 h	No reaction	
4	$AuCl_3$ (5)	DCM/48 h	No reaction	
5	PPh_3AuNTf_2 (5)	DCM/r.t./60 min	—	35(**5**/**6** = 1/1)
6	PPh_3AuOTf (5)	DCM/r.t./60 min	—	41 (**5**/**6** = 1/4)
7	$AgSbF_6$ (5)	DCE/60 °C/45 min	—	21(**5**/**6** = 2/1)
8	$FeCl_3{\cdot}6H_2O$ (50)	PhMe/30 °C/24 h	—	48 (**5**/**6** = 1/1)
9	ZnI_2 (20)	PhMe/110 °C/20 min	—	37 (**5**/**6** = 2/3)
10	$PtCl_2$ (20)	CH_3CN/80 °C/67 h	35 (conv. >99)	—
11	$PtCl_2$ (20)	THF/60 °C/24 h	<5	—
12	PtI_2 (10)	PhMe/110 °C/80 min	85 (conv. >99)	—
13	PtI_2 (10)/PPh_3 (50)	PhMe/110 °C/48 h	No reaction	
14	PtI_2 (10)/COD (50)	PhMe/110 °C/48 h	<5	—
15	PtI_2 (5)	PhMe/110 °C/9 h	78 (conv. >99)	—
16	PtI_2 (2)	PhMe/110 °C/33 h	<73 (conv. >99)	—
17	**PtI_2 (5)/*N*-Phenyl-maleimide (50)**	**PhMe/110 °C/5 h**	**92** (conv. >99)	**—**
18	PtI_2 (5)/NMP (100)	PhMe/110 °C/26 h	<5	—

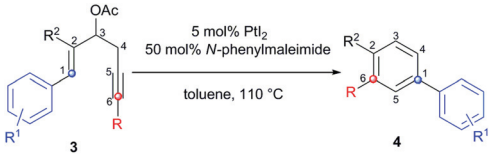
[a] Standard procedure: under a N_2 atmosphere, a platinum catalyst with or without an additive was added to a solution of 3-OAc-1-en-5-yne **3a** (0.1 mmol, 29 mg) in an anhydrous solvent (2 mL). The reaction was carried out under the given reaction conditions and the products were subsequently detected by TLC. [b] Isolated yield.

various substituents. As shown in Table 2, the present method could be applied to a variety of 3-acyloxy-1-en-5-ynes with aryl, heteroaryl, and alkyl substituents at the C6-position and an aryl group at the C1-position to give the corresponding *m*-terphenyls in high or excellent yields. In detail, 1,5-enynes bearing a *p*-F, *o*-F, *m*-Cl, *p*-I and *p*-MeO phenyl group at the C6-position or a *p*-Cl, *p*-Br and *m*-Me phenyl group at the C1-position could generate the desired products in high yields, respectively (Table 2, entries 2–6, 9–11). In addition, substrates bearing an electron-deficient *p*-nitro- and *m*-cyanophenyl group were well-tolerated and they afforded the corresponding *m*-terphenyls in good yields (Table 2, entries 7 and 8). More interestingly, the substrates with an electron-donating substituent at the alkene C2-position could also react to give cyclization products with excellent yields up to 97% (entries 13 and 14). Nevertheless, the substrate with an electron-withdrawing group (Br) at the C2-position of the alkene furnished no cyclic product with most of the raw material recovered (entry 15). It could be rationalized by the weakened nucleophilicity of the alkene with the electronic-withdrawing group (Br). In addition, all other substrates with a heteroaromatic group, thiophenyl, or a large group causing steric hindrance, naphthalenyl, or even a small methyl group on the terminal of the alkyne could also react smoothly under the standard reaction conditions and give the corresponding *m*-terphenyls in good yields (Table 2, entries 16–18).

To further ascertain the possible group migration of 1,5-enynes in our methodology, we designed two special 1,5-enyne substrates, **3s** and **3t**. As shown in Scheme 2, the corresponding products **4s** and **4t** were obtained under the optimal reaction conditions. Through a series of NMR spectroscopy experiments (DEPT, NOESY, HMBC and HMQC; see ESI†), it was confirmed that the Me (pink) at the original C2 position of the alkene and *p*-$MeOC_6H_4$ (blue) at the original C6 of the terminal of the alkyne moiety are located at the *ortho*-position of the newly formed aromatic ring in **4s** (eqn(1), Scheme 2),[4,5] and the deuterated labeling study of **3t** showed that only one deuterium atom exists in the newly formed central benzene ring which is adjacent to the *p*-BrC_6H_4 group (red) in the *m*-terphenyls **4t** (eqn (2), Scheme 2). Take a further look at the structures of **4s** and **4t**, obviously, the construction of this new central benzene ring from 1,5-enynes requires the cleavage of C1–C2 and C4–C5 bonds and the generation of new C1–C5, C1–C4, and C2–C6 bonds. Besides, a series of possible alkyl group migration was involved in this reaction to obtain the final *m*-terphenyls. In a word, there is an interesting skeletal rearrangement in the cyclization of 1,5-enyne derivatives which continuously stimulated our research enthusiasm.

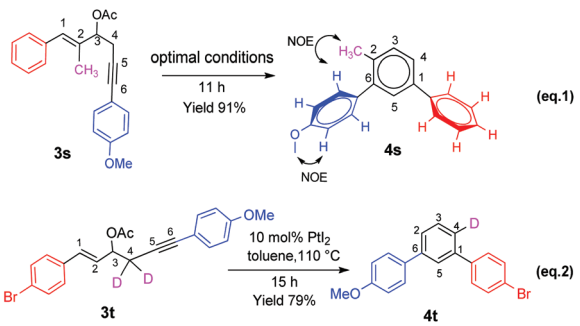
On the basis of all the above experimental results, we proposed possible pathways for the cyclization of 3-acyloxy-1,5-enynes (ACEs) (Scheme 3). After the Pt(II)-catalyst coordinates

Table 2 Scope of platinum catalyzed transformation of 1,5-enynes[a]



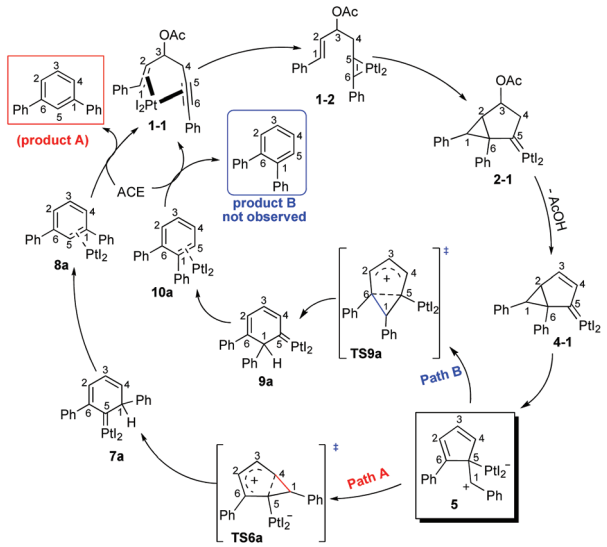
Entry	Substrate	t (h)	Yield[b](%)
1	**3a**, R^1 = H, R^2 = H, R = Ph	5	92
2	**3b**, R^1 = H, R^2 = H, R = *p*-F-C_6H_4	24	87
3	**3c**, R^1 = H, R^2 = H, R = *o*-F-C_6H_4	24	87
4	**3d**, R^1 = H, R^2 = H, R = *m*-Cl-C_6H_4	24	90
5	**3e**, R^1 = H, R^2 = H, R = *p*-I-C_6H_4	42	80
6	**3f**, R^1 = H, R^2 = H, R = *p*-CH_3O-C_6H_4	18	90
7	**3g**, R1 = H, R^2 = H, R = *m*-CN-C_6H_4	49	69
8	**3h**, R^1 = H, R^2 = H, R = *p*-NO_2-C_6H_4	24	75
9	**3i**, R^1 = 4-Cl, R^2 = H, R = Ph	24	82
10	**3j**, R^1 = 4-Br, R^2 = H, R = Ph	48	93
11[c]	**3k**, R^1 = 4-Br, R^2 = H, R = *p*-CH_3O-C_6H_4	16	79
12	**3l**, R^1 = 3-CH_3, R^2 = H, R = Ph	19	84
13	**3m**, R^1 = H, R^2 = CH_3, R = Ph	4	97
14	**3n**, R^1 = H, R^2 = C_6H_{13}, R = Ph	4	92
15	**3o**, R^1 = H, R^2 = Br, R = Ph	72	—
16	**3p**, R^1 = H, R^2 = H, R = 2-thiophenyl	6	56
17	**3q**, R^1 = H, R^2 = H, R = 1-naphthalenyl	6	87
18	**3r**, R^1 = H, R^2 = H, R = CH_3	23	79

[a] Standard procedure: under a N_2 atmosphere, PtI_2 (5 mol%, 2.2 mg) and *N*-phenylmaleimide (50 mol%, 8.6 mg) were added to a solution of 3-OAc-1-en-5-yne **3** (0.1 mmol) in anhydrous toluene (2 mL). The reaction mixture was stirred at 110 °C until the complete disappearance of **3** traced by TLC. The solvent was removed under reduced pressure and the crude mixture was purified by flash chromatography on silica gel. [b] Isolated yield. [c] 10 mol% PtI_2 without an additive.



Scheme 2 The cyclization of enynes **3s** and **3t**.

to the double and triple bonds of the 1,5-enyne in **1-1**, the compound isomerizes to PtI_2-ACE π-complex **1-2** followed by intramolecular cyclopropanation[3] to form the cyclopropyl metal carbene **2-1**. Then the elimination of acetic acid gives the α, β-unsaturated Pt-carbene **4-1**.[22] Subsequently, the alkyl-group cation (RCH^+) migrates to the carbene C5 with the cleavage of C1–C6 and C1–C2 bonds to generate the zwitterionic intermediate **5**.[23] Then the reaction may proceed through two pathways, which leads to the regioselectivity determination of



Scheme 3 Possible mechanism.

the transformation. In path **A**, zwitterionic intermediate **5** isomerizes to **TS6a** *via* the second cyclopropanation followed by ring expansion to form the Pt-carbene isomer **7a**. Alternatively, another pathway should also be considered for the zwitterionic intermediate **5**, the new C1–C6 bond-formation and ring expansion transform **5** to the carbene isomer **TS9a** in pathway **B**. In pathway **A**, a [1,2]-H group shift in **7a** leads to the formation of complex **8a**,[10] which releases the product **A** (**4a**) by coordinating to another molecular ACE, forming **1-1**, and thus completing the whole catalytic cycle and starting the next cycle. Similarly, in pathway **B**, the [1,2]-H shift in **9a** affords the complex **10a**, followed by the release of the product **B** and the regeneration of the PtI_2-ACE π-complex **1-1**.

To understand the origin of regioselectivity in this cyclization reaction, Gibbs energy profiles of the possible reaction pathways of PtI_2-catalyzed cyclization of ACE substrate **a** (R═Ph) are computed with density functional theory (DFT) methods (Fig. 1). DFT calculations indicated that pathway **A** is the most preferred mechanism for the generation of *m*-terphenyl products. The migration of the benzyl carbocation *via* **TS5a**, which is confirmed to connect with the intermediates **4a-1** and **5a** in the energy profile (see Fig. S2†), is found to be the rate-determining step of the catalytic cycle. This step has an energy barrier of 22.4 kcal mol^{-1}. The following cyclopropanation of the zwitterionic intermediate **5a** is the regioselectivity-determining step. The computed energy barrier for bond-formation from C1 to C4 (**TS6a**) is lower than that from C1 to C6 by 2.0 kcal mol^{-1} (**TS9a**), indicating that the formation of carbene **7a** is kinetically favored. The 2.0 kcal mol^{-1} difference between the activation barriers in the regioisomeric cyclopropanation and the ring expansion of TSs (**TS6a** and **TS9a**) suggests a regioselective ratio greater than 20 : 1 (*m*-terphenyl–*o*-terphenyl).[24] This computed result is consistent with experimental results.

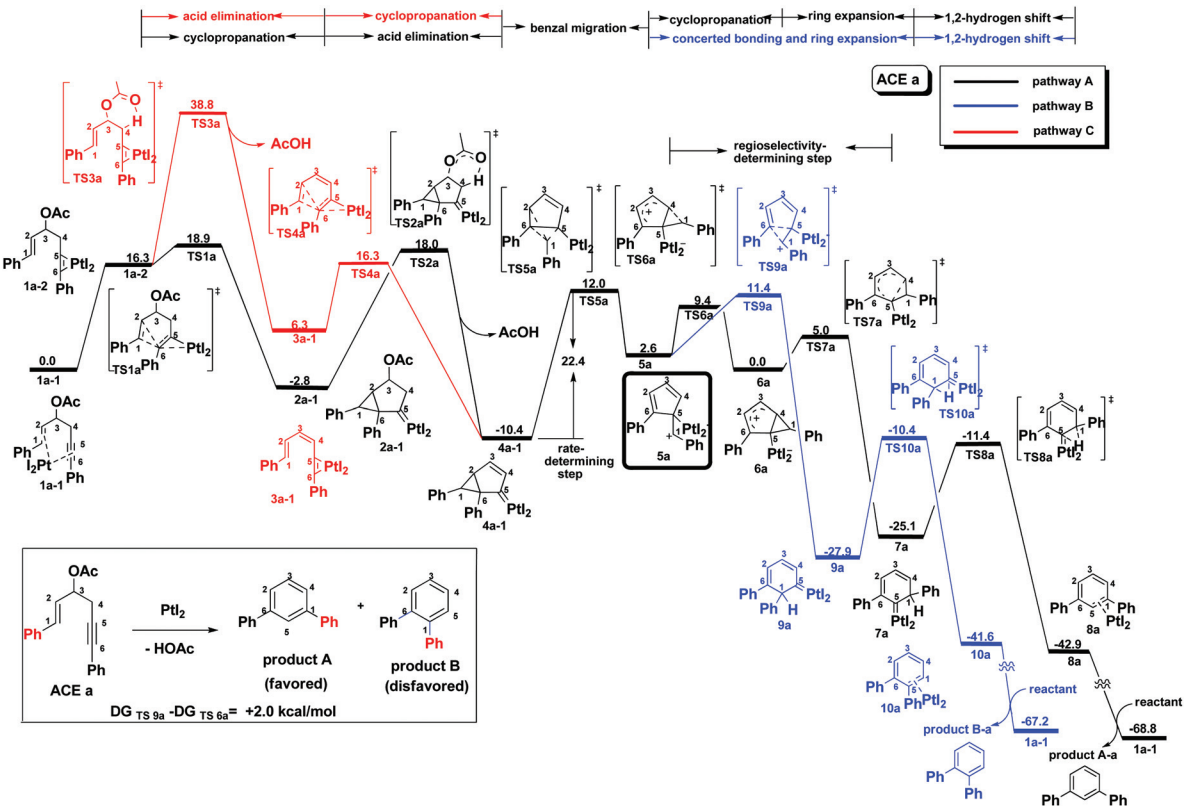


Fig. 1 Gibbs free energy profiles of the PtI_2-catalyzed cyclization of **ACE a**. Energies are in kcal mol^{-1} and calculated using the B3LYP/SDD-6-311+G(d,p)/SMD(toluene)//B3LYP/SDD-6-31G(d) method with DFT-D3(BJ) dispersion correction.

DFT computation for the energy surface in the proposed pathways for the PtI_2-catalyzed cyclization of ACE **b**, which bears a Me group at the C1-position, was also carried out (see Scheme S2†). Nevertheless, in the regioselective step with substrate ACE **b** (Fig. 2), the formation of the C1–C6 bond (**TS9b**) is advantageous over the formation of the C1–C4 bond (**TS6b**), thus leading to the major product 2-methylbiphenyl. This is also consistent with our experimental observations.

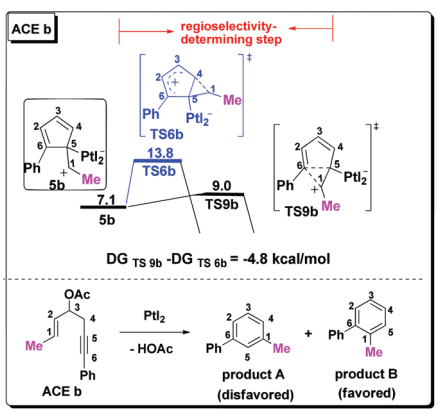


Fig. 2 Gibbs energy profile of the regioselectivity-determining step for PtI_2-catalyzed cyclization of **ACE b**.

Two factors mainly affect the relative stability of **TS6** and **TS9**. One is the electronic effect as shown in Fig. 2 and the other is the steric hindrance between two substituents at C1- and C6-positions. The natural population analysis (NPA)[25] calculations (Fig. 3) indicate that the C1 atom of **5a** is positively charged, thus the C1 atom is inclined to bind to the more electronegative C4 atom in **5a**. Moreover, two bulky Ph substituents are adjacent in **TS9a** (Scheme 3), and thus the greater steric hindrance leads to higher energy, while these two Ph substituents are far apart in **TS6a**, and thus the energy is lower. However, in the case of R = CH_3 (Fig. 2), the replace-

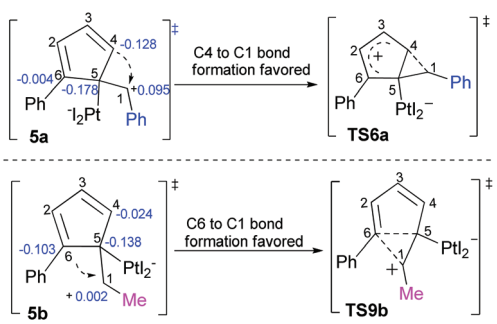
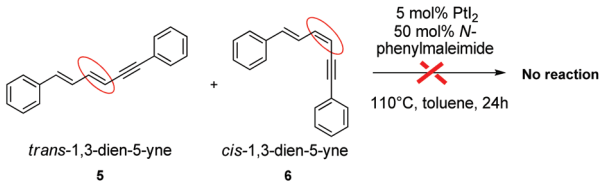


Fig. 3 NPA charges of **5a** and **5b**.

ment of the bulky Ph group by a small methyl group greatly decreases the steric hindrance in **TS9b**. Consequently, **TS9b** is lower than **TS6b** in energy. Compared to the benzyl carbocation **5a**, NPA indicates that the electronegative atom C6 in the ethyl carbocation **5b** tends to attack the C1 atom for the favorable **TS9b** formation. Hence, based on these calculations, we predicted that *o*-methylbiphenyls would be mainly generated *via* **TS9b** followed by ring expansion and a 1,2-H shift.

To test whether our calculation prediction was correct or not, we synthesized the substrates **3u** and **3v** which could generate the proposed intermediate **5b**. Consistent with the results of DFT and NPA calculations, *o*-methylbiphenyls rather than *m*-methylbiphenyls as major products were detected when using the 1,5-enyne substrates with a small methyl group at the C1-position of the alkene. For substrate **3u**, a mixture of *o*-methylbiphenyl and *m*-methylbiphenyl products was obtained in 57% total isolated yield with 10 : 1 ratio of **4u**/**4r** (eqn (1), Scheme 4). While for the enyne **3v** with an electron-donating group (MeO) the arene substituted alkyne could be transformed to a single product, 4′-methoxy-2-methylbiphenyl **4v**, in 90% isolated yield under the standard reaction conditions (eqn (2), Scheme 4). The MeO-group as an electron-donating group would change the charge distribution of the proposed intermediate, which may further affect the regioselectivities. Other enyne substrates could also afford the biphenyl derivatives (see Scheme S1†). These results demonstrated that substituents of the alkene moiety or alkyne terminal have a crucial effect on the regioselectivity or chemoselectivity of this cyclization reaction.

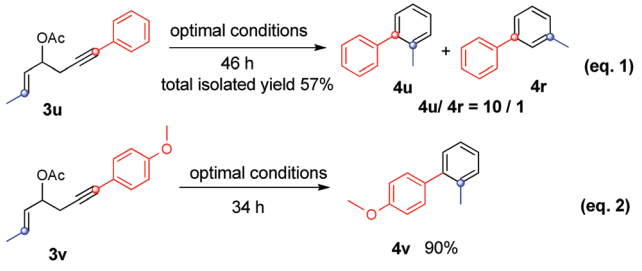
Besides the favorable pathway **A** shown in Fig. 1, pathway **C** was also considered, in which acid elimination occurs prior to cyclopropanation with a very high energy barrier of 38.8 kcal mol^{-1} (the red part in Fig. 1, path **C**) compared to that required in pathway **A** (18.9 kcal mol^{-1}) (from **1a-1** to **TS3a-1**). Therefore, pathway **C** should be ruled out from the favorable pathways. Simultaneously, these calculation results are confirmed by the experiment (Scheme 5). For example, a mixture of *trans*-**6** or *cis*-1,3-dien-5-yne **5** substrates was tested under the optimal reaction conditions.[26] Consequently, no desired cyclization reaction occurred. It may be ascribed to the conjugated effect of 1,3-dien-5-ynes which reduced the nucleophilicity of the double bond and makes it difficult to attack the platinum-activated alkyne group to form a cyclic ring. This result suggested that the acid elimination occurred after the formation of cyclopropyl metal carbene **2-1**. Undoubtedly, the OAc group plays a key role in the enyne cyclization.



Scheme 5 The controlled experiment of 1,3-dien-5-yne.

The possible pathway **D** for the formation of *m*-terphenyls was also considered and then excluded by comparing the calculated results (see Scheme S3†). In pathway **D**, elimination of acetic acid takes place in the last aromatization step. The energy barrier for the rate-determining benzyl migration is 30.2 kcal mol^{-1}, which is much higher than that of the rate-determining step of pathway **A**. On the other hand, no predicted D-migration product was detected in the deuterated labeling study of **3t** (eqn (2), Scheme 2), which supports the deduction that the elimination of DOAc occurred prior to the migration of the benzyl carbocation[10] (see Scheme S4†).

Discrimination of the two reaction pathways, that is [1,2]-H shift or [1,2]-alkyl migration from the carbene complex intermediate **9a**, could be explained by DFT calculations. The activation barrier of the [1,2]-phenyl shift (**TS11a**, $\Delta G^{\neq}$ = 24.2 kcal mol^{-1}) is much higher than that of the [1,2]-H shift (**TS10a**,



Scheme 4 *O*-methylbiphenyls as major products in the cyclization of 1,5-enyne derivatives. (a) Optimal conditions: 5 mol% PtI_2, 50 mol% *N*-phenylmaleimide, toluene, 110 °C. (b) The ratios of these cyclic products and their isomers were detected by proton NMR.

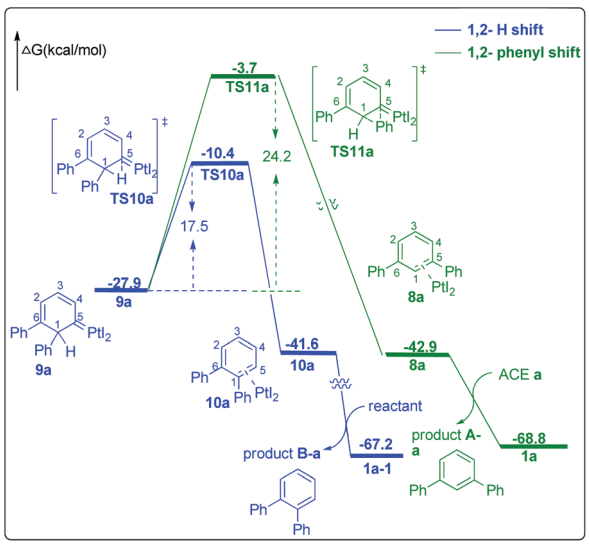
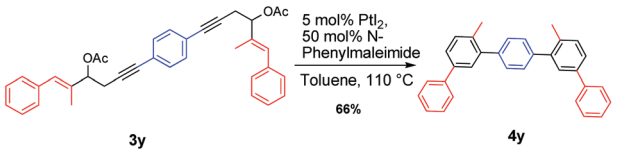


Fig. 4 Gibbs free energy profiles of the 1,2-phenyl shift (in green line) and 1,2-hydrogen shift (in blue line) from intermediate **9a**, energies (in kcal mol^{-1}) are relative to **1a-1** in Fig. 1; calculated using the B3LYP/SDD-6-311+G(d,p)/SMD(toluene)//B3LYP/SDD-6-31G(d) method with DFT-D3(BJ) dispersion correction.



Scheme 6 The *m*-quinquephenyl synthesis.

$\Delta G^{\neq}$ = 17.5 kcal mol^{-1}), and also higher than that of the rate-determining benzyl migration step (Fig. 4). This implies that the [1,2]-H shift is advantageous over the [1,2]-phenyl shift.[27] This is because the phenyl group can stabilize the transition state through the conjugation effect. Besides, the benzylic C–H bond is weaker than the ordinary C–H bond in the previous reports. For example, Yu and co-workers reported their DFT and experimental investigations of the mechanisms and regiochemistry of $PtCl_2$-catalyzed C–H functionalization reactions. They also disclosed that [1,2]-phenyl migration is difficult and [1,2]-H migration is preferred. Furthermore, they gave the same explanation for this migration tendency.[10d] Our calculation also indicates that product **4r** or **4u** cannot be obtained *via* a [1,2]-Me shift due to its higher activation barrier energy than the favored [1,2]-H shift, even higher than the rate-determining ethyl migration step (see Scheme S5†).

Finally, this methodology was applied to synthesize a multiphenyl compound.[28] As shown in Scheme 6, starting from a simple and commercial material alpha-methylcinnamaldehyde, we first prepared the substrate **3y** through Barbier-type propargylation and subsequent double Sonogashira coupling reaction with *para*-diiodobenzene, and thus successfully synthesized the dimethyl substituted quinquephenyl **4y** in 66% yield *via* PtI_2-catalyzed cyclization of 1,5-enynes.

Conclusions

In conclusion, we developed a novel cyclization methodology for 1,5-enynes catalyzed by PtI_2 for the synthesis of various substituted unsymmetrical *m*-terphenyls in good to excellent yields. The OAc group at the C3-position of the 1,5-enyne substrates plays a key role in the cyclization process, and a plausible mechanism was proposed to rationalize the transformation. For 1,5-enyne substrates with R = Ph in the alkene part, these reactions are favored to proceed through pathway **A** *via* initial intramolecular cyclopropanation and acid elimination to give an α, β-unsaturated Pt-carbene. Subsequently, the benzylic carbocation migrates to form a zwitterionic intermediate followed by the second cyclopropanation and ring expansion to form the Pt-carbene isomer; a facile [1,2]-H shift rather than a [1,2]-phenyl shift furnishes the *m*-terphenyl products. For substrates with R = Me, alternatively, another pathway **B** is favored, in which the relevant zwitterionic intermediate undergoes a concerted bond-formation and ring expansion; then a [1,2]-H shift of the Pt-carbene isomer instead of a [1,2]-methyl shift occurs to generate the major *o*-methylphenyl products. DFT calculations indicated that the rate-determining step is the migration of the benzylic carbocation to form a zwitterionic intermediate, which occurred after the elimination of HOAc. The following cyclopropanation of the zwitterionic intermediate is the regioselectivity-determining step. In addition, the elimination step of HOAc was also intensively investigated through DFT. This methodology could be applied to synthesize the quinquephenyl compound, providing a possible simple pathway to construct photoelectric materials. In-depth understanding of cyclic models will be helpful for future design of new substrates and reactions.

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Notes and references

1 Selected reviews on transition-metal-catalyzed cycloisomerization reactions: (*a*) E. Jimenez-Nunez and A. M. Echavarren, *Chem. Rev.*, 2008, **108**, 3326–3350; (*b*) V. Michelet, P. Y. Toullec and J. P. Genet, *Angew. Chem., Int. Ed.*, 2008, **47**, 4268–4315.

2 Selected recent reviews on gold and platinum catalysis: (*a*) L. M. Zhang, J. W. Sun and S. A. Kozmin, *Adv. Synth. Catal.*, 2006, **348**, 2271–2296; (*b*) A. Furstner, *Chem. Soc. Rev.*, 2009, **38**, 3208–3221; (*c*) A. S. K. Hashmi, *Angew. Chem., Int. Ed.*, 2010, **49**, 5232–5241; (*d*) A. Furstner, *Acc. Chem. Res.*, 2014, **47**, 925–938; (*e*) C. Obradors and A. M. Echavarren, *Acc. Chem. Res.*, 2014, **47**, 902–912.

3 Selected examples for Pt-or Au-catalyzed 1,5-enyne cyclizations to bicyclo[3.1.0]hexanes: (*a*) V. Mamane, T. Gress, H. Krause and A. Furstner, *J. Am. Chem. Soc.*, 2004, **126**, 8654–8655; (*b*) M. R. Luzung, J. P. Markham and F. D. Toste, *J. Am. Chem. Soc.*, 2004, **126**, 10858–10859; (*c*) C. Nieto-Oberhuber, M. P. Munoz, E. Bunuel, C. Nevado, D. J. Cardenas and A. M. Echavarren, *Angew. Chem., Int. Ed.*, 2004, **43**, 2402–2406; (*d*) N. Marion, P. de Fremont, G. Lemiere, E. D. Stevens, L. Fensterbank, M. Malacria and S. P. Nolan, *Chem. Commun.*, 2006, 2048–2050; (*e*) V. Lopez-Carrillo, N. Huguet, A. Mosquera and A. M. Echavarren, *Chem. – Eur. J.*, 2011, **17**, 10972–10978.

4 (*a*) L. M. Zhang and S. A. Kozmin, *J. Am. Chem. Soc.*, 2004, **126**, 11806–11807; (*b*) J. W. Sun, M. P. Conley, L. M. Zhang and S. A. Kozmin, *J. Am. Chem. Soc.*, 2006, **128**, 9705–9710.
5 F. Gagosz, *Org. Lett.*, 2005, **7**, 4129–4132.
6 (*a*) S. F. Kirsch, J. T. Binder, B. Crone, A. Duschek, T. T. Haug, C. Liebert and H. Menz, *Angew. Chem., Int. Ed.*, 2007, **46**, 2310–2313; (*b*) A. S. K. Hashmi and M. Wolfle, *Tetrahedron*, 2009, **65**, 9021–9029; (*c*) A. S. K. Hashmi, W. B. Yang, F. Rominger and C. Invest, *Angew. Chem., Int. Ed.*, 2011, **50**, 5761–5764; (*d*) A. S. K. Hashmi, W. B. Yang and F. Rominger, *Chem. – Eur. J.*, 2012, **18**, 6576–6580; (*e*) C. Li, Y. Zeng, H. Zhang, J. Feng, Y. Zhang and J. Wang, *Angew. Chem., Int. Ed.*, 2010, **49**, 6413.
7 L. M. Zhang and S. A. Kozmin, *J. Am. Chem. Soc.*, 2005, **127**, 6962–6963.
8 S. Z. Wang and L. M. Zhang, *J. Am. Chem. Soc.*, 2006, **128**, 14274–14275.
9 (*a*) Y. Zhang, H. Zhang, L. Y. Liu, X. Wang, W. X. Chang and J. Li, *Chem. J. Chin. Univ.*, 2012, **33**, 2447–2451; (*b*) X. Wang, L. Liu, W. Chang and J. Li, *Eur. J. Org. Chem.*, 2010, 5391–5396; (*c*) X. Wang, L. Liu, W. Chang and J. Li, *Sci. China., Ser B: Chem.*, 2009, **52**, 1314.
10 For a review on 1,2-alkyl migration in reactions catalyzed by π-acids, see: (*a*) B. Crone and S. F. Kirsch, *Chem. – Eur. J.*, 2008, **14**, 3514–3522; (*b*) D. J. Gorin and F. D. Toste, *Nature*, 2007, **446**, 395–403; (*c*) P. Pyykkö, *Angew. Chem., Int. Ed.*, 2004, **43**, 4412–4456. For selected relative ref. 4–6, and 8; (*d*) Y. Wang, W. Liao, G. Huang, Y. Xia and Z. X. Yu, *J. Org. Chem.*, 2014, **79**, 5684–5696; (*e*) H. Kusama, K. Ishida, H. Funami and N. Iwasawa, *Angew. Chem., Int. Ed.*, 2008, **47**, 4903–4905; (*f*) H. Kusama, E. Watanabe, K. Ishida and N. Iwasawa, *Chem. – Asian. J.*, 2011, **6**, 2273–2277.
11 For selected examples, see: (*a*) H. Kikuchi, Y. Matsuo, Y. Katou, Y. Kubohara and Y. Oshima, *Tetrahedron*, 2012, **68**, 8884–8889; (*b*) D. A. Patrick, M. A. Ismail, R. K. Arafa, T. Wenzler, X. Zhu, T. Pandharkar, S. K. Jones, K. A. Werbovetz, R. Brun, D. W. Boykin and R. R. Tidwell, *J. Med. Chem.*, 2013, **56**, 5473–5494.
12 For selected examples, see: (*a*) D. L. Kays, *Dalton Trans.*, 2011, **40**, 769–778; (*b*) B. M. Gridley, T. J. Blundell, G. J. Moxey, W. Lewis, A. J. Blake and D. L. Kays, *Chem. Commun.*, 2013, **49**, 9752–9754.
13 For selected examples, see: (*a*) Q. T. Fan, C. C. Wang, Y. Han, J. F. Zhu, W. Hieringer, J. Kuttner, G. Hilt and J. M. Gottfried, *Angew. Chem., Int. Ed.*, 2013, **52**, 4668–4672; (*b*) W.-J. Hu, X.-L. Zhao, M.-L. Ma, F. Guo, X.-Q. Mi, B. Jiang and K. Wen, *Eur. J. Org. Chem.*, 2012, 1448–1454.
14 Selected papers: (*a*) H. Sasabe, Y. J. Pu, K. Nakayama and J. Kido, *Chem. Commun.*, 2009, 6655–6657; (*b*) H. Sasabe, Y. Seino, M. Kimura and J. Kido, *Chem. Mater.*, 2012, **24**, 1404–1406.
15 C. J. F. Du, H. Hart and K. K. D. Ng, *J. Org. Chem.*, 1986, **51**, 3162–3165.
16 For selected examples, see: (*a*) J. M. A. Miguez, L. A. Adrio, A. Sousa-Pedrares, J. M. Vila and K. K. Hii, *J. Org. Chem.*, 2007, **72**, 7771–7774; (*b*) D. Qiu, S. Wang, S. Tang, H. Meng, L. Jin, F. Mo, Y. Zhang and J. Wang, *J. Org. Chem.*, 2014, **79**, 1979–1988.
17 S. Bhunia, S. M. Abu Sohel, C. C. Yang, S. F. Lush, F. M. Shen and R. S. Liu, *J. Organomet. Chem.*, 2009, **694**, 566–570.
18 P. Garcia-Garcia, M. A. Fernandez-Rodriguez and E. Aguilar, *Angew. Chem., Int. Ed.*, 2009, **48**, 5534–5537.
19 $FeCl_3$ catalyzed 1,6-enyne cyclization, see: C. Nieto-Oberhuber, M. P. Munoz, S. Lopez, E. Jimenez-Nuner, C. Nevado, E. Herrero-Gomez, M. Raducan and A. M. Echavarren, *Chem. – Eur. J.*, 2006, **12**, 1677–1693.
20 (*a*) For *N*-phenylmaleimide as a ligand coordinated to platinum(0) complex, see M. Reinhard and M. Gerard, *WO* 9525734, 1995; (*b*) The exact function of *N*-phenylmaleimide in our reaction system remains unclear currently, see Fig. S1 in ESI† for details.
21 (*a*) For 3-OTBS-1-en-5-yne cyclization to benzene derivatives, see: **6a–6d**; gold catalyzed 3-hydroxylated 5-en-1-yne isomerization to benzene derivatives, see (**5**) (*b*) C. M. Grise, E. M. Rodrigue and L. Barriault, *Tetrahedron*, 2008, **64**, 797–808; (*c*) G. J. Li and Y. H. Liu, *J. Org. Chem.*, 2010, **75**, 2903–2909. Gold catalyzed 3-OH-1-en-yne cyclization to benzene derivatives: (*d*) Y. A. Qiu, W. Q. Kong, C. L. Fu and S. M. Ma, *Org. Lett.*, 2012, **14**, 6198–6201.
22 Reaction of α, β-unsaturated platinum carbene intermediates: (*a*) P. A. Allegretti and E. M. Ferreira, *J. Am. Chem. Soc.*, 2013, **135**, 17266–17269; (*b*) K. Saito, H. Sogou, T. Suga, H. Kusama and N. Iwasawa, *J. Am. Chem. Soc.*, 2011, **133**, 689–691.
23 Consecutive 1,3-cationic alkylidene migration of nonclassical carbocation intermediates was proposed in the paper, see: Q. Zhou and Y. Li, *J. Am. Chem. Soc.*, 2014, **136**, 1505–1513.
24 P. Liu, P. McCarren, P. H. Y. Cheong, T. F. Jamison and K. N. Houk, *J. Am. Chem. Soc.*, 2010, **132**, 2050–2057.
25 A. E. Reed, R. B. Weinstock and F. Weinhold, *J. Chem. Phys.*, 1985, **83**, 735–746.
26 π-Acid metal catalyzed 1,3-dien-5-yne cyclization: (*a*) J. W. Dankwardt, *Tetrahedron Lett.*, 2001, **42**, 5809–5812; (*b*) J. J. Lian, C. C. Lin, H. K. Chang, P. C. Chen and R. S. Liu, *J. Am. Chem. Soc.*, 2006, **128**, 9661–9667; (*c*) P. Garcia-Garcia, A. Martinez, A. M. Sanjuan, M. A. Fernandez-Rodriguez and R. Sanz, *Org. Lett.*, 2011, **13**, 4970–4973; (*d*) A. M. Sanjuan, P. Garcia-Garcia, M. A. Fernandez-Rodriguez and R. Sanz, *Adv. Synth. Catal.*, 2013, **355**, 1955–1962.
27 For both free carbenes and metal carbenes, generally, the inherent migratory aptitude follows the order H > aryl > alkyl. For reviews, see: **10a**; (*a*) A. Nickon, *Acc. Chem. Res.*, 1993, **26**, 84; (*b*) M. T. H. Liu, *Acc. Chem. Res.*, 1994, **27**, 287.
28 Selected paper on *m*-quinquephenyl synthesis: (*a*) G. F. Woods and F. T. Reed, *J. Am. Chem. Soc.*, 1948, **71**, 1348–1350; (*b*) M. Bennett, N. B. Sunshine and G. F. Woods, *J. Org. Chem.*, 1963, **28**, 2514–2517. For a report on potential functionality research, see: (*c*) A. S. M. C. Rodrigues, M. A. A. Rocha and L. M. N. B. F. Santos, *J. Chem. Thermodyn.*, 2013, **63**, 78–83.