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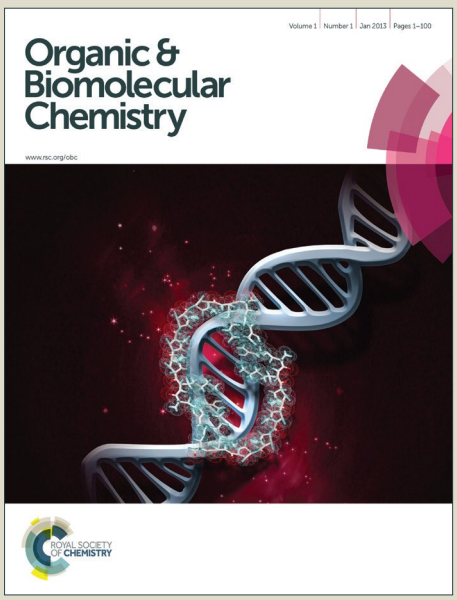

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PtI_2-Catalyzed Cyclization of 3-Acyloxy-1,5-enynes with the Elimination of HOAc and a Benzyl Shift: Synthesis of Unsymmetrical *m*-Terphenyls

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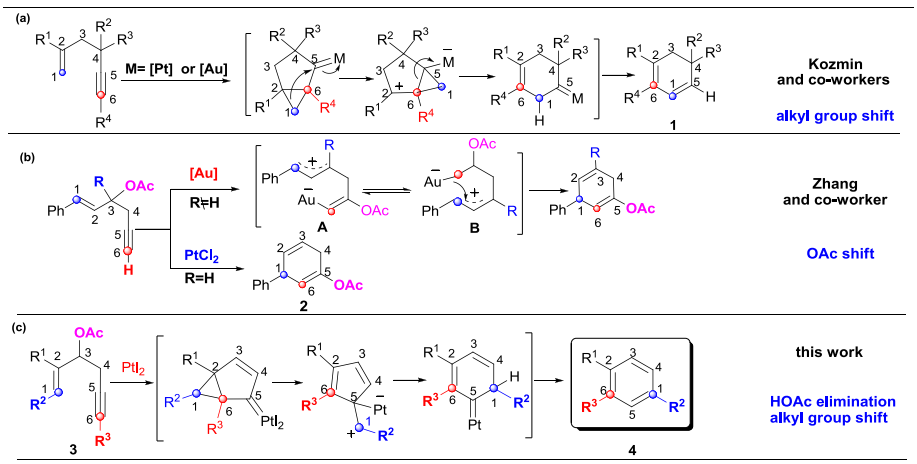
A novel cyclization of 3-acyloxy-1,5-enynes was developed in the presence of PtI_2 for the synthesis of substituted unsymmetrical *m*-terphenyls in good to excellent yields. Two unique steps were involved in this transformation, which includes the elimination of HOAc and the benzyl group migration. DFT calculations indicated that the rate-determining step was the migration of the benzylic carbocation to form a zwitterionic intermediate, which 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 one of the most studied and have been efficiently converted into cyclic products including bicyclo[3.1.0]hexenes,[3] cyclohexadienes **1** reported by Kozmin group, in which a Pt-catalyzed cyclization reaction was developed with the migration of the aryl group at the terminal of alkyne (Scheme 1a),[4] methylenecyclopentenes,[5] substituted benzene derivatives[6] and heterobicycle alkenes[7]. In 2006, Zhang's research group reported that the gold-catalyzed unique cycloisomerization of 3-acyloxy-1-en-5-yne yielded the 1-acyloxycyclohexa-1,4-dienes and acyloxy aromatic compound. The authors proposed that the phenyl group on the end of alkene could provide further stabilization to the carbon cation, permitting an efficient migration of the OAc group, and the alkenyl-gold intermediate was generated in situ. However, 3-acyloxy-1-en-5-yne derived from *trans*-cinnamaldehyde was unsuccessful with Au catalysts, but could be converted into cyclohexadiene **2** in 60% yield when 20 mol% $PtCl_2$ was 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 and followed by a Sonogashira coupling reaction and hydroxyl protection. Then a simple methodology was developed



Scheme 1 Intramolecular cyclization of 1,5-enynes

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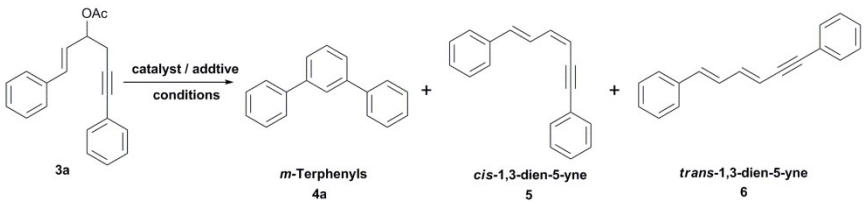
through using 3-acyloxy-1-en-5-ynes (ACEs) **3** as starting materials to synthesize various *m*-terphenyls **4** (Scheme 1c). Given an insight on the *m*-terphenyl product, we observed that a new centre benzene ring was herein constructed via the cyclization and consecutive aromatization of 1,5-enynes without the need of additional oxidation.[8] Notably, in the product **4**, the original substituent (R^1) on the alkene terminal (C1 position) of 1,5-enyne and the substituent (R^2) on the alkyne terminal (C6 position) are located at the *meta*-position of the newly formed centre cycle (Scheme 1c). In other words, the possible migration of 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 block for the synthesis of sterically demanding aryl ligands,[12] cyclophanes,[13] and potential host material 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 diversified *m*-terphenyls frameworks. For example, the Grignard reaction is employed by sequential treatment of 1,3-dichlorobenzene with *n*-BuLi and followed by *p*-tolyl-magnesium bromide to synthesize the symmetric terphenyls in early studies.[15] Then the transition-metal catalyzed coupling reactions are developed to become one of 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 derivatives. For example, Liu et. al reported a 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 his coworkers described a gold-catalyzed cyclo-aromatization of related 2,4-dien-6-yne carboxylic acids to synthesis of 2,3-disubstituted phenols and unsymmetrical *bi*- and terphenyls. However, the scope of substrates is limited due to the need of 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.

Table 1. Optimization studies of the cyclization of **3a**



Entry	Catalyst/ additive (mol%)	Condition	Yield of **4a** (%)[a]	Total yield of **5** and **6** (%)
1	$PtCl_2$ (20)	PhMe/ 110 ℃/ 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 ℃/ 45 min	--	21(**5**/**6**=2/1)
8	$FeCl_3.6H_2O$ (50)	PhMe/ 30 ℃/ 24 h	--	48 (**5**/**6**=1/1)
9	ZnI_2 (20)	PhMe/110 ℃/ 20 min	--	37 (**5**/**6**=2/3)
10	$PtCl_2$ (20)	CH_3CN/ 80 ℃ / 67 h	35 (conv. >99)	--
11	$PtCl_2$ (20)	THF/ 60 ℃ / 24 h	< 5	--
12	PtI_2 (10)	PhMe/ 110 ℃/ 80 min	85 (conv. >99)	--
13	PtI_2 (10)/ PPh_3 (50)	PhMe/ 110 ℃/ 48 h	No reaction	
14	PtI_2 (10)/ COD (50)	PhMe/ 110 ℃/ 48 h	< 5	--
15	PtI_2 (5)	PhMe/ 110 ℃/ 9 h	78 (conv. >99)	--
16	PtI_2 (2)	PhMe/ 110 ℃/ 33 h	<73 (conv. >99)	--
17	**PtI_2 (5)/ N-Phenyl-maleimide (50)**	**PhMe/ 110 ℃/ 5 h**	**92** (conv. >99)	--
18	PtI_2 (5)/ NMP (100)	PhMe/ 110 ℃/ 26 h	< 5	--

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

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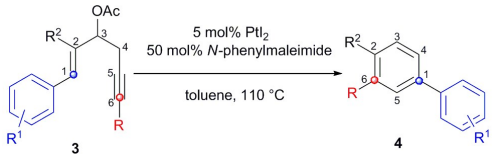
In our initial study, we chose 20 mol% $PtCl_2$ as π-acid metal catalyst and 3-acyloxy-1-en-5-yne **3a** as substrate to react at 110 ℃ in toluene. Without any detection of cyclohexadiene or acetoxyl arenes, the enyne **3a** underwent tandem cyclization and aromatization, resulting in the unexpected *m*-terphenyl **4a** (X-ray diffraction analysis of **4a** see supporting information) in 50% yield (entry 1, Table 1). Gold (I) and, gold (III) catalysts, whether with the ligand or not, display no effective 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 with different proportions. Other Lewis acid catalysts, such as $AgSbF_6$, $FeCl_3.6H_2O$[19] or ZnI_2, furnished the 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 Pt catalyst. As a result, this reaction gave a lower efficiency in CH_3CN and THF than that in toluene (Table 1, entries 10, 11). But to our delight, using 10 mol% PtI_2 to catalyze this reaction, the noticeably improved yield of *m*-terphenyl **4a** was obtained with high 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 PtI_2 catalyst from 10 mol% to 5 or 2 mol% even with prolonging reaction time 9 h and 33 h, respectively (entries 15 and 16). It should be noted that the conversion rate of this reaction was high up to above 99% by ^1H NMR trace but with low isolated yield of *m*-terphenyl in the case of the catalyst $PtCl_2$ and PtI_2 (entries 1, 10 and 16). This phenomenon could be explained by the easily 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 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 platinum metal catalyst in toluene, and thus shortened the reaction time and reduced the possible oligomer formation or decomposition of this enyne substrate under the reaction condition. However, when a 5-membered lactam structural compound, *N*-methyl pyrrolidinone, was used as additive, no reaction occurred (entry 18). Overall, the optimal reaction conditions were 5 mol% PtI_2 as catalyst, 50 mol% *N*-phenylmaleimide as additive, toluene as the solvent and a reaction temperature of 110 ℃.

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 with OH at 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.

Table 2. Scope of platinum catalyzed transformation of 1,5-enynes



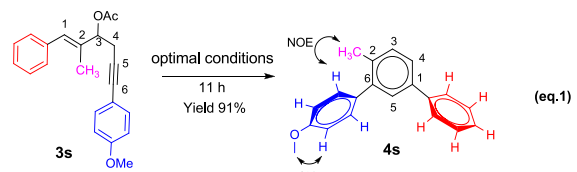
Entry	Substrate	t (h)	Yield (%) [a]
1	**3a**, R^1 = H, R^2= H, R= Ph	5	92
2	**3b**, R^1 = H, R^2= H, R= *p*-F-C_6H_4	24	87
3	**3c**, R^1 = H, R^2= H, R= *o*-F-C_6H_4	24	87
4	**3d**, R^1 = H, R^2= H, R= *m*-Cl-C_6H_4	24	90
5	**3e**, R^1 = H, R^2= H, R= *p*-I-C_6H_4	42	80
6	**3f**, R^1 = H, R^2= H, R= *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[b]	**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

Standard procedure: Under the 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 complete disappearance of **3** traced by TLC. Solvent was removed under reduced pressure and the crude mixture was purified by flash chromatography on silica gel; [a] Isolated yield; [b] 10 mol% PtI_2 without additive.

Under the optimized reaction conditions, we next examined the scope of cyclization of 3-acyloxy-1-en-5-yne bearing 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, alkyl substituents at the C6-position and aryl group at 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 C6-position or *p*-Cl, *p*-Br and *m*-Me phenyl group at C1-position could generate the desired products in high yields, respectively (Table 2, entries 2-6, 9-11). Additionally, substrates bearing an electron-deficient *p*-nitro- and

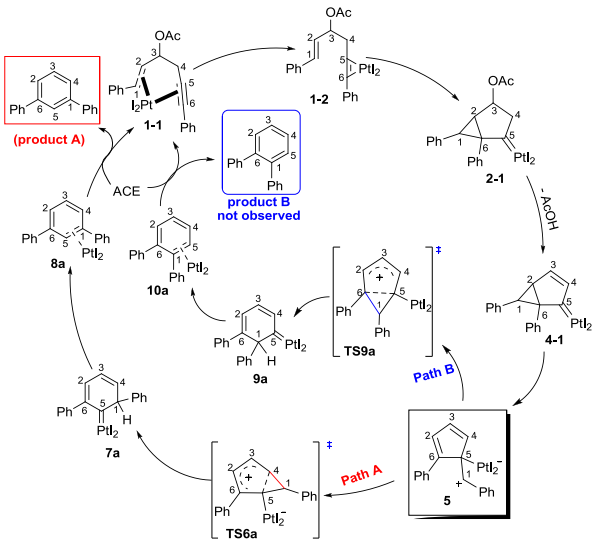
m-cyanophenyl group were well-tolerated and afforded the corresponding *m*-terphenyls in good yields (Table 2, entries 7-8). More interestingly, the substrates with electron-donating substituent at the alkene C2-position could also react to give the cyclization products with excellent yields up to 97% (entries 13-14). Nevertheless, the substrate with electron-withdrawing group (Br) at the C2-position of alkene furnished no cyclic product with most of the raw material recovered (entry 15). It could be rationalized by weakened nucleophilicity of alkene with the electronic-withdrawing group (Br). Additionally, all other substrates with heteroaromatic group thiophenyl- or large sterically hindrance group naphthalenyl-, or even small methyl group on the terminal of alkyne could also proceed 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 condition. Through a series of NMR spectroscopy experiments (DEPT, NOESY, HMBC and HMQC (see supporting information), it was confirmed that the Me- (pink) at the original C2 position of alkene and *p*-$MeOC_6H_4$- (blue) at the original C6 of terminal of the alkyne moiety are located at the *ortho*-position of the newly aromatic ring in **4s** (eq.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- (red) in the *m*-terphenyls **4t** (eq. 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, C4-C5 bonds and the generation of the new C1-C5, C1-C4, 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 derivates which continuously stimulated our research enthusiasm.



Scheme 2 The cyclization of enyne **3s** and **3t**

On the basis of the above all experimental results, we proposed possible pathways for the cyclization of 3-acyloxy-1,5-enynes (ACEs) (Scheme 3). After the Pt(II)-catalyst coordinates with the double and triple bonds of 1,5-enyne in **1-1**, the compound isomerizes to PtI_2-ACE π-complex **1-2** and 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 bond to generate the zwitterionic intermediate **5**.[23] Then the reaction may proceed through two paths, which lead to the regioselectivity of the transformation. In path **A**, zwitterionic intermediate **5** isomerizes to **TS6a** via the second cyclopropanation and 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**. Along pathway **A**, [1,2]-Ph group shift in **7a** leads to the formation of complex **8a**,[10] which releases the product **A** (**4a**) by coordinating with another molecular ACE, forming the **1-1**, and thus completing the whole catalytic cycle and starting the next cycle. Similarly, along pathway **B**, [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**.



Scheme 3 Possible mechanism

To understand the origins of regioselectivities in this cyclization reaction, Gibbs energy profiles of 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 benzyl carbocation via **TS5a**, which is confirmed to connect with the intermediates **4a-1** and **5a** on the energy profile (See Figure S2), is found to be the rate-determining step of the catalytic cycle. This step has an energy barrier of 22.4 kcal/mol. The following cyclopropanation of the zwitterionic intermediate **5a** is the regioselectivity-determining step. The computed energy barrier of bond-formation from C1 to C4 (**TS6a**) is lower than that of from C1 to C6 by 2.0 kcal/mol (**TS9a**), indicating that the formation of carbene **7a** is kinetically favored. The 2.0 kcal/mol difference between the activation barriers of 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.

DFT computed energy surface of proposed pathways for the PtI_2-catalyzed cyclization of ACE **b**, which bears a Me group at the C1-position, were also carried out (see Schemes S2).

Nevertheless, in the regioselective step of 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 2-methylbiphenyl product. This is also consistent with our experimental observations.

Two factors mainly affect the relative stability of **TS6** and **TS9**. One is the electronic effect as shown in Figure 2 and the other is the steric hindrance between two substituents at C1- and C6-position. 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 bigger sterically hindrance leads to the higher energy, while these two Ph substituents are apart in **TS6a**, and thus the energy is lower. However, in the case of R = CH_3 (**Fig. 2**), the replacement of bulky Ph group by small methyl group greatly decreases the sterically hindrance in **TS9b**. Consequently, **TS9b** is lower than **TS6b** in energy. Compared to the benzyl carbocation **5a**, NPA indicate that the electronegative atom C6 atom in the ethyl carbocation **5b** tends to attack the C1 atom for the favored **TS9b** formation. Hence, based on these calculations, we predicted that *o*-methylbiphenyls would be mainly generated via **TS9b** and followed by ring expanation and 1,2-H shift.

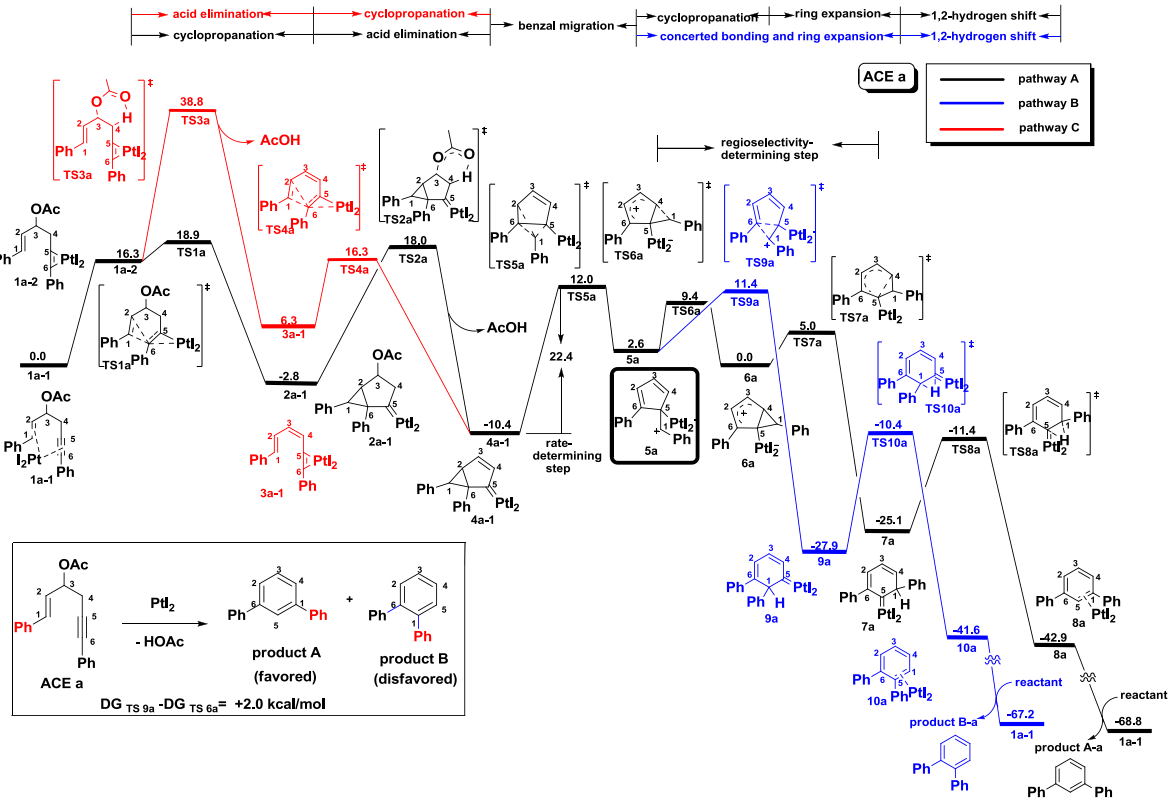


Fig. 1 Gibbs free energy profiles of the PtI_2-catalyzed cyclization of **ACE a**. Energies are in kcal/mol and calculated using B3LYP/SDD-6-311+G(d,p)/SMD(toluene)//B3LYP/SDD-6-31G(d)method with DFT-D3(BJ) dispersion correction.

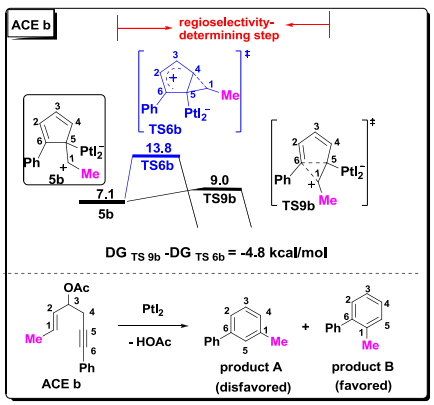


Fig. 2 Gibbs energy profile of the regioselectivity-determining step for PtI_2-catalyzed cyclization of **ACE b**.

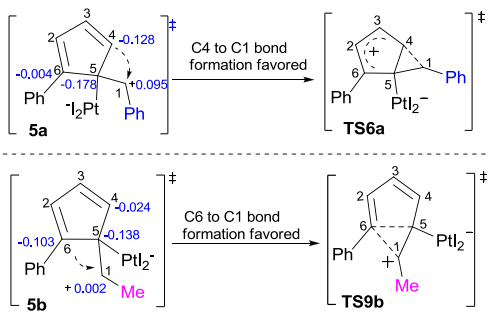
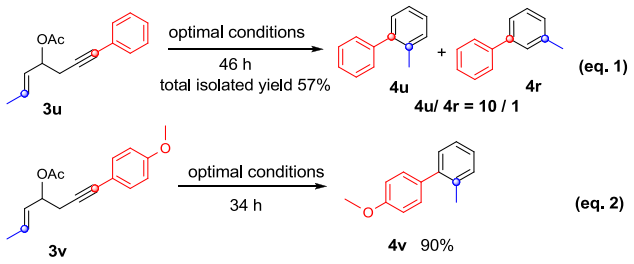


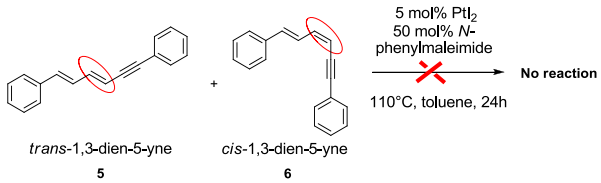
Fig.3 NPA charges of **5a** and **5b**



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

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 small methyl group at the C1-position of 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** (eq. 1, Scheme 4). While the enyne **3v** with electron-donating group (MeO) arene substituted alkyne could be transformed to a single product, 4'-methoxy-2-methylbiphenyl **4v** in 90% isolated yield under the standard reaction conditions (eq. 2, Scheme 4). The MeO- group as 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 favored pathway **A** showed in figure 1, the pathway **C** was also considered, in which acid elimination occurs prior to cyclopropanation with a very high energy barrier of 38.8 kcal/mol (red part in Figure 1, path **C**) than that required in pathway **A** (18.9 kcal/mol) (from **1a-1** to **TS3a-1**). Therefore, the pathway **C** should be ruled out from the favored pathways. Simultaneously, this 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 condition.[26] Consequently, no desired cyclization reaction occurred. It may be ascribed to the conjugated effect of 1,3-dien-5-yne which reduced the nucleophilicity of double bond and makes it difficult to attack the platinum-activated alkyne group to form the 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 production was also considered and then excluded by comparing the calculated results (see Scheme S3). In pathway **D**, elimination of acetic acid takes place at the last aromatization step. The energy barrier of the rate-determining benzyl migration is 30.2 kcal/mol, 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** (eq. 2, Scheme 2), which supports the deduction that the elimination of DOAc occurred prior to the migration of 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 calculation. The activation barrier of [1,2]-phenyl shift (**TS13a**, $\Delta G^{\neq}$ = 24.2 kcal/mol) is much higher than that of [1,2]-H shift (**TS10a**, $\Delta G^{\neq}$ = 17.5 kcal/mol), and also higher than that of the rate-determining benzal migration step (**Fig. 4**). This implies that [1,2]-H shift is advantageous over [1,2]-phenyl shift.[27] This is because the phenyl group can stabilize the transition state through 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 the [1,2]-phenyl migration is difficult and [1,2]-H migration is preferred. Furthermore, they gave the same explanation for this migratory tendency.[10d] Our calculation also indicates that product **4r** or **4u** cannot be obtained via [1,2]-Me shift due to the higher activation barrier energy than the favored [1,2]-H shift, even higher than the rate-determining ethyl migration step (see Scheme S5).

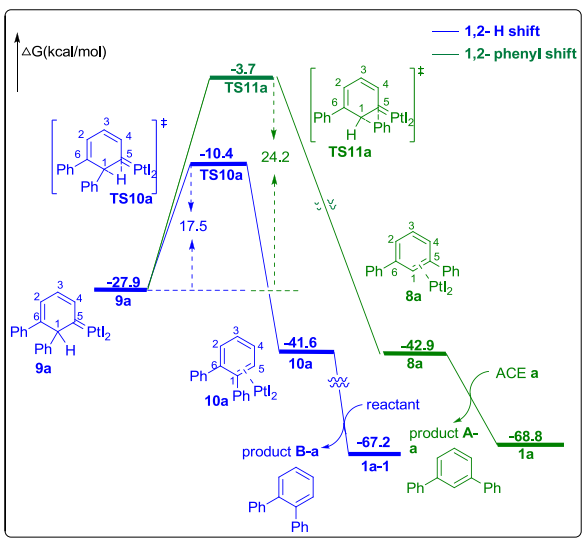
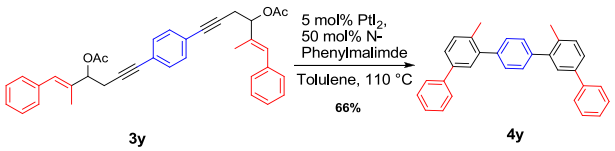


Fig. 4 Gibbs free energy profiles of 1,2-phenyl shift (in green line) and 1,2-hydrogen shift (in blue line) from intermediate **9a**, Energies (in kcal/mol) are relative to **1a-1** in **Fig.1**; Calculated using B3LYP/SDD-6-311+G(d,p)/SMD(toluene)//B3LYP/SDD -6-31G(d) method with DFT-D3(BJ) dispersion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

Finally, this methodology was applied to synthesize the multi-phenyl compound. [28] As shown in Scheme 6, starting from simple and commercial material *alpha*-methylcinnamaldehyde, we firstly prepared the substrate **3y** through the 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.



Scheme 6 The *m*-quinquephenyl synthesis

Conclusions

In conclusion, we developed a novel cyclization methodology of 1,5-enynes catalyzed by the PtI_2 for the synthesis of various substituted unsymmetrical *m*-terphenyls in good to excellent yield. 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-enynes substrates with R = Ph in the alkene part, these reactions are favor to proceed through pathway **A** via initial intramolecular cyclopropanation and acid elimination to give the α, β-unsaturated Pt-carbene. Subsequently, the benzylic carbocation migrate to form a zwitterionic intermediate, then proceeding the second cyclopropanation and followed by ring expansion to form the Pt-carbene isomer, the facile [1,2]-H shift rather than [1,2]-phenyl shift furnishes the *m*-terphenyls 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 the [1,2]-H shift of Pt-carbene isomer instead of [1,2]-methyl shift occur to generate the major *o*-methylphenyls products. DFT calculations indicated that the rate-determining step was 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. Additionally, the elimination step of HOAc was also given an intensive investigation through DFT. And this methodology could be applied to synthesize quinquephenyl compound, which provide a possible simple pathway to construct the photoelectric materials. The in-depth understanding of the cyclic models will be helpful to future design of the new substrates and reactions.

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