Tetrahedron 66 (2010) 8095–8100

Contents lists available at ScienceDirect

Tetrahedron

journal homepage: www.elsevier.com/locate/tet

Facile synthesis of highly functionalized six-membered heterocycles via PPh_3-catalyzed [4+2] annulations of activated terminal alkynes and hetero-dienes: scope, mechanism, and application

Qiongmei Zhang, Tong Fang, Xiaofeng Tong *

Key Laboratory for Advanced Materials and Institute of Fine Chemicals, East China University of Science and Technology, Shanghai 200237, China

ARTICLE INFO

Article history:
Received 1 June 2010
Received in revised form 13 July 2010
Accepted 16 July 2010
Available online 6 August 2010

Keywords:
PPh_3 Catalysis
Hetero-diene
[4+2] Annulations
Heterocycle
H-Transfer

ABSTRACT

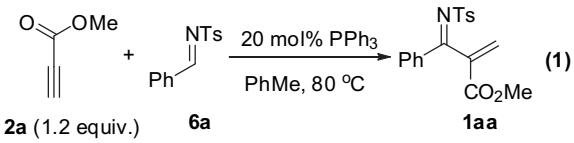
A novel [4+2] annulation between activated terminal alkynes and aza-dienes or oxo-dienes has been developed with the use of triphenylphosphine catalyst (20 mol %), which provides a facile method for synthesis of the corresponding highly functionalized dihydropyridines or dihydropyrans in good to excellent yields. The reaction mechanism has also been established, consisting formal hetero-Diels–Alder reaction catalyzed by PPh_3 and [1,3]-proton transfer, which exhibits a large isotopic effect.

1. Introduction

Heterocycles form, by far, the largest of the classical divisions of organic chemistry.[1] Among heterocyclic compounds, hydropyridines present ubiquitous structural motifs, which are frequently found in natural products and in compounds of interest for the pharmaceutical, agrochemical, and other chemical industries.[2] As another type of six-membered heterocycles, hydropyrans are also important core units within a multitude of biologically active natural products.[3] Although diverse synthetic approaches toward hydropyridines and hydropyrans have been developed, versatile, and flexible methodologies to construct these heterocycles with selective control of substitution patterns using readily accessible building blocks are still of pressing interest.

Recently we have reported the phosphine-catalyzed [4+2] annulations between aza-dienes **1** and 1-phenylprop-2-yn-1-one **2b**, which provide a facile entry to highly functionalized 1, 2-dihydropyridines **3** (part A, Scheme 1).[4] Further investigations also disclosed that 1,4-dihydropyridine [**3**] was a crucial intermediate for this transformation, which could be recognized as the formal aza-Diels–Alder adduct from aza-dienes **1** and alkynes **2**. As a continuation of the study on the phosphine-catalyzed cycloadditions,[5] we became interested in extending this reaction protocol to oxo-dienes **4**. Compounds **4** are believed to be possessed similar electrophilicity and reactivity as those of aza-dienes **1**. Thus we envisioned that similar oxo-Diels–Alder reaction of oxo-dienes **4** would also be promoted by phosphine catalyst, and highly functionalized dihydropyrans [**5**] would be produced consequently (part B, Scheme 1). This reaction represents, to our knowledge, a novel reaction mode for phosphine catalysis, although nucleophilic phosphine catalysis has been widely developed for cycloaddition chemistry, which regio- and stereoselectively generates carbo- and heterocyclic motifs.[6] In this Article, we report the formal triphenylphosphine-catalyzed hetero-Diels–Alder reactions[7] between hetero-dienes and activated terminal alkynes, as well as experiments for clarifying the mechanism of these novel [4+2] annulations.

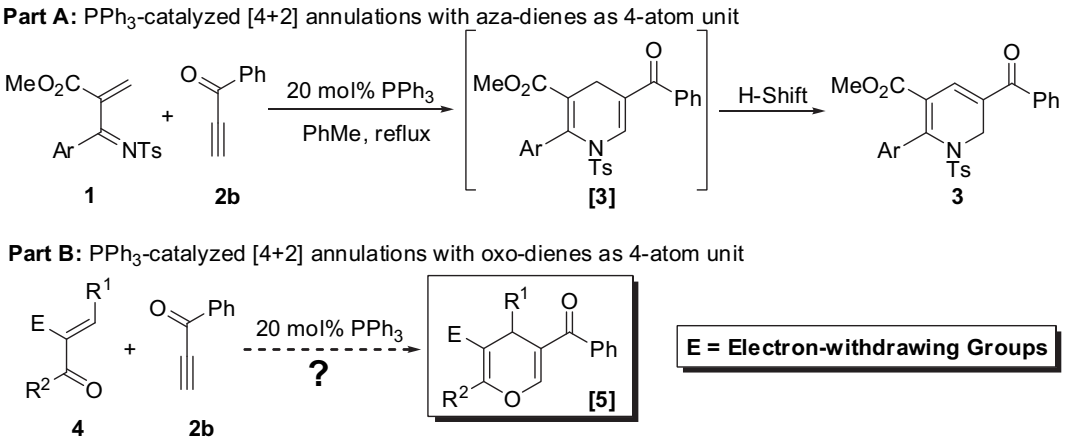
2. Results and discussions



2a (1.2 equiv.) **6a** **1aa** **(1)**

* Corresponding author. E-mail address: tongxf@ecust.edu.cn (X. Tong).

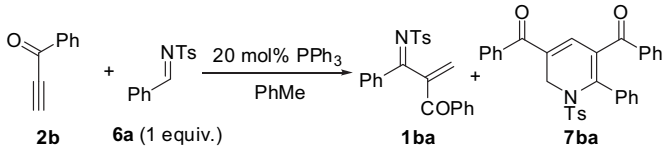
0040-4020/$ – see front matter © 2010 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tet.2010.07.043



Scheme 1. Design plan for PPh_3-catalyzed synthesis of dihydropyridines and dihydropyrans.

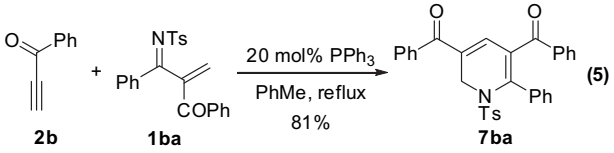
Very recently, we have discovered that aza-diene **1aa** can be readily obtained from methyl propiolate **2a** (1.2 equiv) and imine **6a** with 20 mol % PPh_3 as catalyst (Eq. 1).[8]

Surprisingly, when 1-phenylprop-2-yn-1-one **2b** rather than **2a** was used as the substrate, one unexpected compound **7ba** was obtained as major product with 53% isolated yield, while the corresponding aza-diene **1ba** was isolated only in 36% yield (Eq. 2, Scheme 2). The solid state structure of **7ba** was further determined by a single crystal X-ray diffraction analysis.[9] Single crystals of complex **7ba** were obtained from CH_2Cl_2/petroleum ether at room temperature. An ORTEP type view of **7ba** is shown in Figure 1.



Scheme 2. The relationship between **1ba** and **7ba**.

Contrarily, compound **1ba** would become favorable, accompanied by **7ba** (21% vs 14%) when the amount of **2b** was reduced to be 1.0 equiv (Eq. 3, Scheme 2). When 3 equiv of **2b** were used, compound **7ba** was found out to be the only product and **1ba** was not detected at all (Eq. 4, Scheme 2). These results strongly indicated that **1ba** probably worked as the intermediate for the formation of **7ba**. In fact, **1ba** smoothly reacted with **2b** (1.2 equiv) in the presence of PPh_3 (20 mol %) to afford **7ba** in 81% yield although higher reaction temperature was required (Eq. 5), which led us to discover a novel phosphine-catalyzed [4+2] annulations[10] between aza-dienes **1ba** and alkynes **2b**.



2.1. [4+2] Annulations between aza-dienes and alkynes

With these preliminary results in hand, we next examined the generality of the phosphine-catalyzed [4+2] annulations of aza-dienes and alkynes and the results are presented in Table 1. This

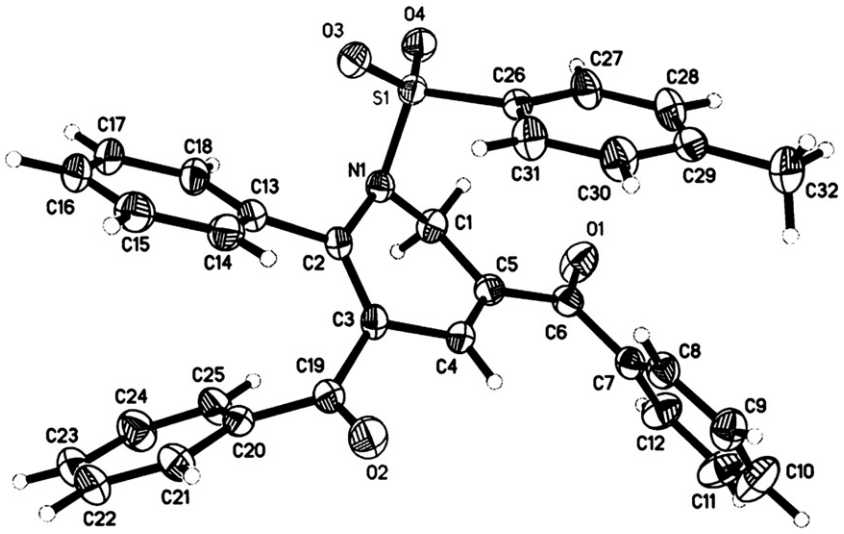
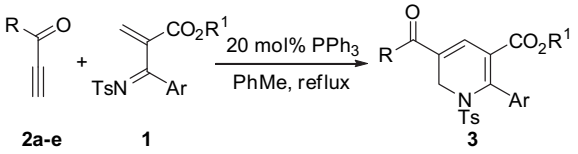


Figure 1. X-ray crystallography of **7ba**. Ellipsoids at 30% probability.

transformation strongly depended on the activated group of terminal alkyne. When methyl propiolate **2a** was employed as two-atom unit, no reaction occurred at all (entry 1, Table 1). Alkyl ketone **2e** resulted in complicated reactions with some unidentified products (entry 9, Table 1). However, aryl ketones **2b–d** readily underwent [4+2] annulations with a variety of aza-dienes to provide the corresponding 1,2-dihydropyridines **3** in good to excellent yields (entries 2–8, Table 1). The substituents on the phenyl ring seem to take some effects on the reaction performance although we don't have convincing explanations for these observations at this stage.

Table 1
PPh_3-catalyzed [4+2] annulations of alkynes and aza-dienes[a]

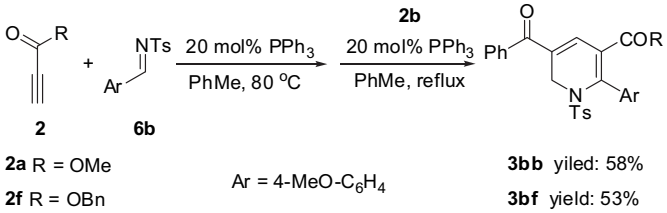


2a-e **1** **3**

Entry	**2** (R)	**1** (R^1, Ar)	**3**/Yield[b] (%)
1	**2a** (OMe)	**1aa** (Me, Ph)	**3aa** (ND)[d]
2	**2b** (Ph)	**1aa**	**3ba** (59)
3	**2b**	**1ab** (Me, 4-MeO/C_6H_4)	**3bb** (96)
4	**2b**	**1ac** (Me, 4-Br/C_6H_4)	**3bc** (86)
5	**2c** (4-MeO/C_6H_4)	**1ab**	**3cb** (59)
6	**2d** (4-Me/C_6H_4)	**1ac**	**3dc** (60)
7	**2c**	**1ac**	**3cc** (50)
8	**2b**	1fb (Bn, 4-MeO/C_6H_4)	**3bf** (63)
9[c]	**2e** (n-C_5H_{11})	**1aa**	**3ea** (—)

[a] Reaction conditions: the solution of **2** (0.6 mmol) in toluene (6 mL) was slowly added to the mixture of **1** (0.3 mmol) and PPh_3 (0.06 mmol) in toluene (6 mL) at 120 °C.
[b] Isolated yield.
[c] With unidentified products.
[d] ND=not detected.

In view of the conditions of Eq. 1 and Table 1, we found that these two reactions shared almost common conditions except the reaction temperature. This observation inspired us to explore the possibility of preparing compounds **3** in one-pot strategy with first step serving for the formation of aza-dienes **1** in situ and second step for [4+2] annulations with external **2b** (Scheme 3). One-pot tandem reactions are important for the efficient construction of complex chemical structures and therefore are an active research area in the synthetic community.[11] Fortunately, this one-pot strategy could be smoothly achieved through direct addition of compounds **2b** to the reaction systems, in which the compounds **1** were thought to be firstly formed catalyzed by 20 mol % PPh_3 with both of **6b** and propiolates as starting materials at 80 °C. And the corresponding [2+2+2] annulation products **3bb** and **3bf** were obtained in the yield of 58% and 53%, respectively. Obviously, these numbers were some lower compared to the yields of the corresponding products in Table 1. Furthermore, for better performance of the one-pot strategy, both additional 20 mol % amount of PPh_3 and elevated temperature (reflux) were required for the second step (Scheme 3).



2 **6b**

2a R = OMe
2f R = OBn

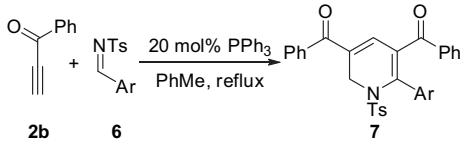
Ar = 4-MeO-C_6H_4

3bb yiled: 58%
3bf yield: 53%

Scheme 3. Synthesis of **3bb** and **3bf** in one-pot way.

Reconsidering the results presented in Scheme 2, it is easy to identify that formal [2+2+2] annulation can be achieved between **2b** and imine **6** when large excess of **2b** (3 equiv) is used. Further investigations of these novel [2+2+2] annulations were also undertaken under similar conditions. It was a pleasure to disclose that the [2+2+2] annulations proceeded smoothly with a range of substrates and 1,2-dihydropyridines **7** could also be easily obtained in good to excellent yields. The details are presented in Table 2.

Table 2
PPh_3-catalyzed [2+2+2] annulations of alkyne **2b** and imines **6**[a]



2b **6** **7**

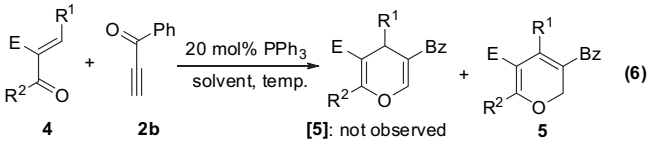
Entry	**6** (Ar)	**7**	Yield[b] (%)
1	**6a** (Ph)	**7ba**	75
2	**6b** (4-MeO/C_6H_4)	**7bb**	90
3	**6c** (4-Br/C_6H_4)	**7bc**	85
4	**6d** (4-Cl/C_6H_4)	**7bd**	67
5	**6e** (4-Me/C_6H_4)	**7be**	59

[a] Reaction conditions: the solution of **2b** (1.5 mmol) in toluene (10 mL) was slowly added to the mixture of **6** (0.5 mmol) and PPh_3 (0.1 mmol) in toluene (10 mL) at 120 °C.
[b] Isolated yield.

2.2. [4+2] Annulations between oxo-dienes and alkynes

Upon the success of PPh_3-catalyzed [4+2] annulations of aza-dienes **1** and 1-phenylprop-2-yn-1-one **2b**, we would like to extend this reaction protocol to oxo-dienes **4** (Eq. 6, Table 3). This extension is conducted on the basis of the considerations that oxo-dienes **4** possess similar electrophilicity as that of aza-dienes **1** and might perform similar reactivity toward 1-phenylprop-2-yn-1-one **2b** in the presence of PPh_3 catalyst.

Table 3
Optimized conditions for PPh_3-catalyzed [4+2] annulations of **2b** and oxo-dienes **4**[a]



4 **2b** **[5]**: not observed **5** **(6)**

Entry	**4** (R^1, E, R^2)	T (°C)	Sol.	**5**/yield[b] (%)
1	**4a** (Ph, CO_2Et, Me)	120	PhMe	0 (**5ba**)
2	**4b** (Ph, COMe, Me)	120	PhMe	20 (**5bb**)
3	**4c** (Ph, CN, Ph)	120	PhMe	74 (**5bc**)
4	**4c** (Ph, CN, Ph)	80	PhMe	78 (**5bc**)
5	**4c** (Ph, CN, Ph)	rt	PhMe	88 (**5bc**)
6	**4c** (Ph, CN, Ph)	rt	DMF	95 (**5bc**)
7	**4c** (Ph, CN, Ph)	rt	CH_2Cl_2	80 (**5bc**)
8	**4c** (Ph, CN, Ph)	rt	MeCN	99 (**5bc**)
9	**4c** (Ph, CN, Ph)	rt	acetone	97 (**5bc**)
10[c]	**4c** (Ph, CN, Ph)	rt	MeCN	0 (**5bc**)

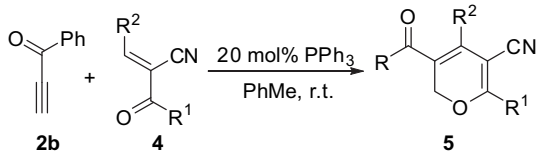
[a] Reaction conditions: the solution of **2b** (0.6 mmol) in toluene (10 mL) was slowly added to the mixture of **4** (0.5 mmol) and PPh_3 (0.1 mmol) in toluene (10 mL) within 1.5 h.
[b] Isolated yield.
[c] Without PPh_3 catalyst.

To our disappointment, no reaction took place at 120 °C in toluene and **4a** was recovered in 89% yield (entry 1, Table 3). We suspected that the electrophilicity of **4a** might be too weak relative to aza-dienes. Therefore, we turned our attention to the compounds **4b** and **4c**, which were activated by much stronger electron-withdrawing groups, keton- and cyano-, respectively. To our

delight, both **4b** and **4c** reacted with **2b** to give highly functionalized 2*H*-pyrans **5bb** and **5bc** in the yields of 20% and 74%, respectively (entries 2 and 3, Table 3). These results indicated that the electrophilicity of **4** played a determining role for the efficiency of this transformation and the best results would be achieved by applying oxo-dienes **4**, which were activated by strongly electron-withdrawing cyano-group. Even more, **4c** worked well at room temperature (entries 5–9, Table 3). It was noted that 4*H*-pyrane [**5**] could not be detected in reaction mixture. Solvent screening also disclosed that this transformation had little solvent effect; a wide range of solvents could be employed to give excellent yields (entries 5–9, Table 3). However, toluene solvent was found to be the optimal one due to its more general substrate tolerance (vide infra). Furthermore, control experiments shown that this reaction did not occur at all without PPh_3 catalyst (entry 10, Table 3).[12]

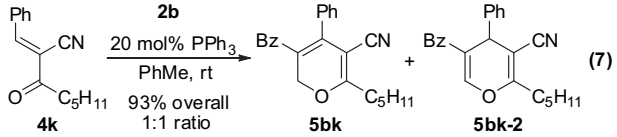
With the optimized conditions in hand, the scope of the PPh_3-catalyzed [4+2] annulations of oxo-dienes **4** and **2b** was further investigated (Table 4). In general, various highly functionalized 2*H*-pyrans were provided in good to excellent yields. Especially, hetero-aryl motifs, such as furan (entries 2 and 8) and thiophene (entries 5, 7, and 8) were successfully incorporated. Introduction of alkenyl was also a particular feature of this method (entry 6). Interestingly, the reaction of **2b** with oxo-diene **4k**, which attached a pentyl group on the R^1-position, offered not only the desired product **5bk** but also the compound **5bk-2** with a ratio of 1:1 (Eq. 7). Moreover, this method could be extended to the β-disubstituted oxo-dienes **4l** and **4m**, affording the products 4,4-dialkyl-4*H*-pyrans **5bl** and **5bm** (Eq. 8). As expected, the yields were much lower probably because the substituents at β-position reduced the electrophilicity of oxo-dienes for both steric and electronic reasons.

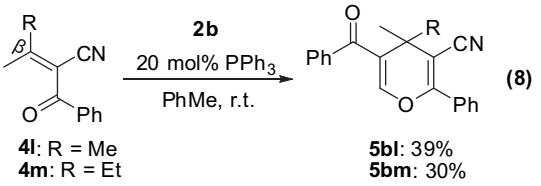
Table 4
PPh_3-catalyzed [4+2] annulations of **2b** with oxo-dienes **4**[a]



Entry	**4** (R^1, R^2)	**5**/Yield[b] (%)
1	**4c** (Ph, Ph)	88 (**5bc**)
2	**4d** (Ph, 2-furan)	99 (**5bd**)
3	**4e** (Ph, 4-Br/Ph)	99 (**5be**)
4	**4f** (Ph, 4-MeO/Ph)	83 (**5bf**)
5	**4g** (Ph, 2-thiophene)	90 (**5bg**)
6	**4h** (Ph, styrene)	89 (**5bh**)
7	**4i** (2-Thiophene, Ph)	99 (**5bi**)
8	**4j** (2-Thiophene, 2-furan)	84 (**5bj**)

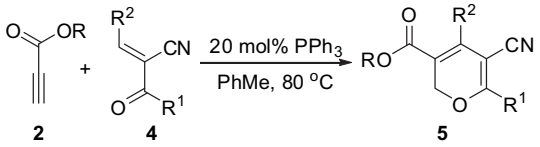
[a] Reaction conditions: the solution of **2b** (0.6 mmol) in toluene (10 mL) was slowly added to the mixture of **4** (0.5 mmol) and PPh_3 (0.1 mmol) in toluene (10 mL) within 1.5 h.
[b] Isolated yield.





Compared to aza-dienes **1**, oxo-dienes **4** presented higher reactivity toward **2b** with much lower reaction temperature and higher yields. Thus we envisioned that propiolates **2a** and **2f** could react with oxo-dienes **4** to furnish [4+2] annulations as a two-atom unit (Table 5). We were delighted to find that the corresponding products **5** with a carboxylate group on pyran rings could also be obtained, although elevated temperature was required to complete the reaction.

Table 5
PPh_3-catalyzed [4+2] annulations of propiolates with oxo-dienes **4**[a]

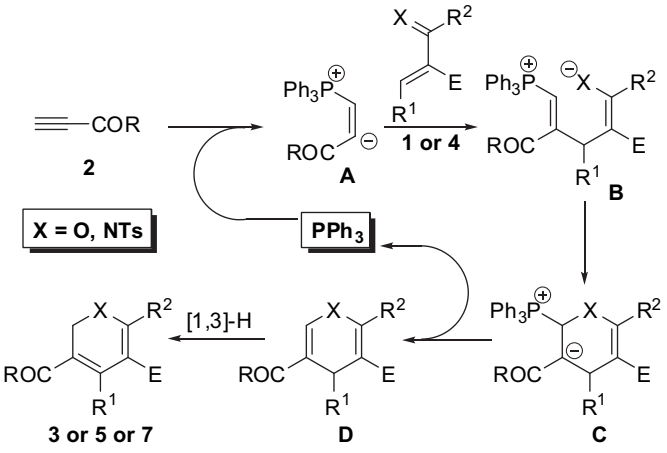


Entry	**2** (R)	**4** (R^1, R^2)	**5**/Yield[b] (%)
1	**2a** (Me)	**4c** (Ph, Ph)	96 (**5ac**)
2	**2f** (Bn)	**4c**	71 (**5fc**)
3	**2a**	**4e** (Ph, 4-Br/Ph)	37 (**5ae**)
4	**2a**	**4f** (Ph, 4-MeO/Ph)	65 (**5af**)
5	**2a**	**4g** (Ph, 2-thiophene)	69 (**5ag**)
6	**2a**	**4h** (Ph, styrene)	51 (**5ah**)
7	**2a**	**4i** (2-Thiophene, Ph)	71 (**5ai**)
8	**2a**	**4k** (C_5H_{11}, Ph)	63 (**5ak**)

[a] Reaction conditions: the solution of **2** (1.0 mmol) in toluene (10 mL) was slowly added to the mixture of **4** (0.5 mmol) and PPh_3 (0.1 mmol) at 80 °C in toluene (10 mL) within 1.5 h.
[b] Isolated yield.

2.3. Mechanistic considerations

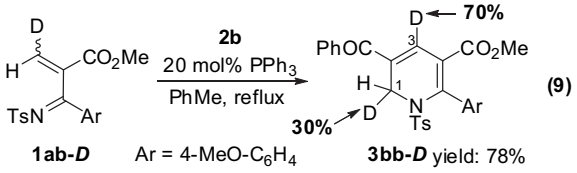
A proposed mechanism for the PPh_3-catalyzed annulations between **2** and hetero-dienes is depicted in Scheme 4. Addition of PPh_3 to activated terminal alkyne **2** generates intermediate **A**,[13] which undergoes Michael-addition reaction with hetero-diene **1** or **4** to produce intermediate **B**. Then the formed hetero-atomic anion of **B** undergoes 6-*endo* cyclization followed by elimination of PPh_3 to yield six-membered heterocycle **D**.[14] In the end, the final product can be obtained via [1,3]-proton transfer process.



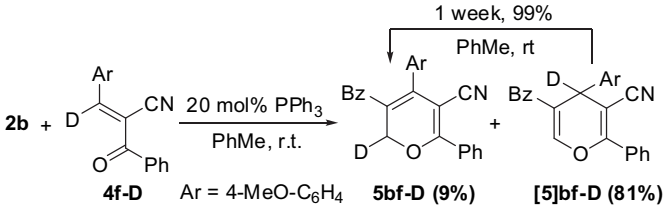
Scheme 4. Proposed mechanism for PPh_3-catalyzed [4+2] annulations.

On the basis of this proposed mechanism and the catalytic results (Tables 1–5 and Eqs. 1–8), some features of this reaction protocol have been observed and summarized as follows: (1) Intermediate **A** works as nucleophile and its nucleophilicity seems to be strongly determined by the activated groups of alkynes. When the activated group is carboxylate, the corresponding intermediate **A** (R=OMe,

Scheme 4) is a too weak nucleophile to undergo Michael-addition reaction with aza-dienes. Contrarily, the intermediate **A** (R=Ph) attaching benzoyl group shows higher reactivity toward hetero-dienes. We postulate that benzoyl group possibly exhibits two positive effects to stabilize the carboanion of intermediate **A**: one is the stronger electron-withdrawing ability; the other is the larger conjugated systems afforded by phenyl group. However we do not have further evidences to support this at present. (2) Hetero-dienes also play important roles for Michael-addition step. The more electrophilicity hetero-dienes exhibit, the more readily would Michael-addition step occur. For example, oxo-diene **4a** is inert for [4+2] annulations as two-atom unit, while oxo-dienes **4c**–**j** can smoothly react with **2b** even at room temperature. (3) The reaction pathway involving intermediate **D** is possible, which is evidenced by the isolation of some stable 4*H*-pyran products, such as **5bl** and **5bm**. (4) [1,3]-Proton transfer process might be driven by the conjugating requirement provided by aryl and/or cyano groups on dihydropyran and dihydropyridine ring. This transfer process would be partially inhibited in the case of **5bk**–**2**, whose alkyl substituent (*n*-pentyl) at 2-position is believed to partially reduce the conjugated effect.



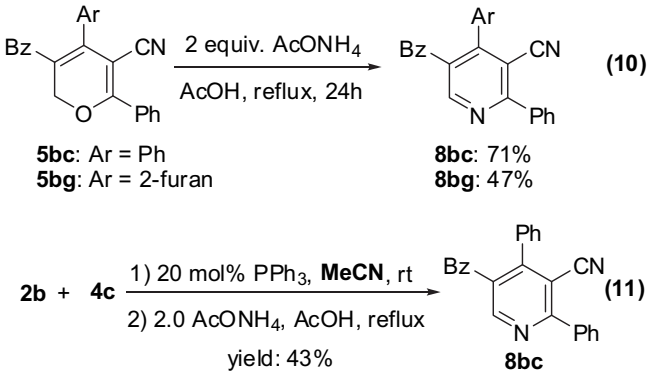
In order to get more details about the reaction mechanism, we conducted some control experiments with the deuterium-labeled substrates. When compound **1ab**-**D** was subjected to the [4+2] annulations with **2b**, the deuterium atom was found out to be fully incorporated into the products **3bb**-**D** with 30% **D** at C1 atom and 70% **D** at C3 atom (Eq. 9). These results strongly indicated that the [1,3]-proton transfer process, with a K_D:K_H=2.3 isotope effect, was involved in the reaction pathway. Interestingly, when the deuterium-labeled oxo-diene **4f**-**D** was employed, the distribution of products shifted in favor of 4*H*-pyran [**5**]**bf**-**D**, which would be completely transformed into 2*H*-pyran **5bf**-**D** within 1 week (Scheme 5). These results clearly showed that [1,3]-proton transfer process in dihydropyran system took place much more slowly relative to that in dihydropyridine, exhibiting a larger isotope effect (K_D:K_H=9).



Scheme 5. Deuterium labeling studies.

2.4. Synthetic transformation

In order to demonstrate the synthetic utility of the present method, we developed a procedure to synthesize 2,3,4,5-tetra-substituent pyridine via the treatment of 2*H*-pyrans with 2 equiv of ammonium acetate in acetic acid solvent.[15] As a result, nicotinonitrile-like pyridine derivatives[16] **8bc** and **8bg** could be readily obtained in moderate yield (Eq. 10, Scheme 6). In fact, pyridine **8bc** was also obtained in 43% yield through a one-pot way, whereas the ammonium acetate reagent and acetic acid solvent were directly added into the reaction systems after the completion of PPh_3-catalyzed annulations of **2b** and **4c** in acetonitrile solvent (Eq. 11, Scheme 6).



Scheme 6. Synthetic utility of 2*H*-pyrans.

3. Conclusions

In summary, we report a new PPh_3-catalyzed [4+2] annalution of activated terminal alkynes and aza-dienes or oxo-dienes, which allows the efficient construction of highly functionalized 2*H*-dihydropyridines and dihydropyrans, respectively. The [4+2] annulations can also tolerate the dienes with β-disubstituted alkenes although the yields are somewhat lower. The reaction mechanism has been proposed with two-step sequences, initial PPh_3-catalyzed [4+2] annalution and subsequent [1,3]-proton transfer. In some cases, the intermediated products from PPh_3-catalyzed [4+2] annalution can be separately obtained. Deuterium labeling studies also provide strong evidences to support the involving [1,3]-proton transfer process, which exhibits a large isotopic effect in both dihydropyridine and dihydropyran systems. The flexibility for direct synthesis of pyridine derivatives in one-pot way through initial PPh_3-catalyzed [4+2] annulations in acetonitrile solvent, followed by the addition of ammonium acetate and acetate acid, has also been demonstrated.

4. Experimental section

4.1. General

Unless otherwise noted, all reactions were carried out under a nitrogen atmosphere using a standard syringe, cannula, and septa apparatus. The commercially available reagents were used without further purification. NMR spectra were run at 400 (^{1}H) or 100 MHz (^{13}C) in $CDCl_3$.

4.2. Typical procedure for PPh_3-catalyzed synthesis of 3ba

Aza-diene **1aa** (0.3 mmol), PPh_3 (15.7 mg, 20 mmol %) were added to toluene (6 mL) in there-neck bottle. The mixture was stirred at 120 °C under nitrogen atmosphere. To this reaction mixture the solution of 1-arylpropynones **2b** (0.6 mmol) in toluene (6 mL) was slowly added within 1 h. The reaction mixture was monitored by TLC. Once the reaction was finished, the reaction mixture was cooled down to room temperature. The contents were transferred to a round-bottom flask, and volatiles were removed in vacuo. Then the mixture was directly subjected to silica gel column

chromatography (petroleum ether/EtOAc 15:1 to 5:1 gradient) to give the product **3ba**.

4.3. Typical procedure for PPh_3-catalyzed synthesis of 5bc

Oxo-diene **4c** (0.5 mmol), PPh_3 (26.2 mg, 20 mmol %) were added to toluene (10 mL) in one-neck bottle. The mixture was stirred at room temperature under nitrogen atmosphere. To this reaction mixture the solution of terminal alkynes **2b** (0.6 mmol) in toluene (10 mL) was slowly added within 1.5 h. The reaction was monitored by TLC. When the reaction was finished, the mixture was directly subjected to silica gel column chromatography (petroleum ether/EtOAc 30:1 to 10:1 gradient) to give the product **5bc**.

4.4. Typical procedure for synthesis of 8bc

2*H*-Pyran **5bc** (0.2 mmol), ammonium acetate (30.8 mg, 0.4 mmol), and acetic acid (3 mL) was added into one-necked bottle. The reaction mixture was heated and reflux for 24 h. The mixture then was cooled down to room temperature. Water (30 mL) and CH_2Cl_2 (30 mL) were added. The organic layer was separated and dried over Na_2SO_4. The solvent was removed under vacuum to obtain a liquid, which was purified via FCG to give product **8bc**.

Spectral data of compounds **3aa**, **5bc**, and **8bc** are listed below. Other spectral data and copies of the ^1H and ^{13}C NMR spectra of all compounds are given in the Supplementary data.

*4.4.1. Compound **3ba**.* ^1H NMR (400 MHz, $CDCl_3$): δ 7.53–7.38 (m, 10H), 7.31 (d, J=7.2 Hz, 2H), 7.19 (d, J=8.0 Hz, 2H), 6.89 (s, 1H), 4.91 (s, 2H), 3.45 (s, 3H), 2.36 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 192.5, 167.1, 150.7, 144.6, 137.3, 135.3, 135.2, 131.9, 130.7, 130.0, 129.7, 128.7, 128.3, 127.9, 127.0, 126.7, 120.3, 51.8, 45.6, 21.5; MS (EI-m/z): 473 (M^+); HRMS calcd for $C_{27}H_{23}NO_5S$ 473.1297. Found 473.1296.

*4.4.2. Compound **5bc**.* Yellow solid, mp: 102–103 °C. ^1H NMR (400 MHz, $CDCl_3$): δ 8.10–8.08 (m, 2H), 7.63–7.60 (m, 1H), 7.56–7.53 (m, 4H), 7.31–7.23 (m, 3H), 7.17–7.14 (m, 5H), 5.24 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 194.9, 170.4, 141.1, 137.1, 134.2, 133.0, 132.5, 130.7, 129.9, 129.8, 129.5, 129.1, 128.8, 128.2, 128.0, 119.3, 117.6, 90.8, 69.3. MS (m/z): 363 (M^+); HRMS calcd for $C_{25}H_{17}NO_2$ 363.1259. Found 363.1260.

*4.4.3. Compound **8bc**.* ^1H NMR (400 MHz, $CDCl_3$): δ 8.92 (s, 1H), 8.03–8.00 (m, 2H), 7.64–7.56 (m, 5H), 7.48–7.47(m, 1H), 7.36–7.30 (m, 7H); ^{13}C NMR (100 MHz, $CDCl_3$): δ194.4, 163.4, 153.6, 150.9, 137.0, 136.3, 134.0, 133.8, 133.3, 130.7, 129.9, 129.7, 129.3, 129.1, 128.7, 128.6, 128.5, 116.4, 107.9. MS (m/z):360 (M^+); HRMS calcd for $C_{25}H_{16}N_2O$ 360.1263. Found 360.1261.

Acknowledgements

This work is supported by the Fundamental Research Funds for the Central Universities. Special gratitude also goes to Prof. Xingyi Wang and Ms. Shuzhen Jiang for their support.

Supplementary data

Supplementary data (copies of NMR spectra) associated with this article can be found, in the online version, at doi:10.1016/j.tet.2010.07.043.

References and notes

1. For reviews see: (a) Martins, M. A. P.; Frizzo, C. P.; Moreira, D. N.; Buriol, L.; Machado, P. *Chem. Rev.* **2009**, *109*, 4140; (b) Martins, M. A. P.; Frizzo, C. P.; Moreira, D. N.; Zanatta, N.; Bonacorso, H. G. *Chem. Rev.* **2008**, *108*, 2015; (c) Druzhinin, S. V.; Balenkova, E. S.; Nenajdenko, V. G. *Tetrahedron* **2007**, *63*, 7753; (d) Martins, M. A. P.; Cunico, W.; Pereira, C. M. P.; Flores, A. F. C.; Bonacorso, H. G.; Zanatta, N. *Curr. Org. Synth.* **2004**, *1*, 39.
2. For reviews see: (a) *Progress in Heterocyclic Chemistry*; Gribble, G. W., Joule, J. A., Eds.; Elsevier: Oxford, 2008; Vol. 20; (b) Lavilla, R. *J. Chem. Soc., Faraday Trans.* **2002**, 1141; (c) Simon, C.; Constantieux, T.; Rodriguez, J. *Eur. J. Org. Chem.* **2004**, 4957.
3. For reviews see: (a) Faulkner, D. J. *Nat. Prod. Rep.* **2000**, *17*, 7; (b) Larrosa, I.; Romea, P.; Urpi, F. *Tetrahedron* **2008**, *64*, 2683; (c) Clarke, P. A.; Santos, S. *Eur. J. Org. Chem.* **2006**, 2045; (d) Nakata, T. *Chem. Rev.* **2005**, *105*, 4314; (e) Wong, H. N. C.; Yu, P.; Yick, C. Y. *Pure Appl. Chem.* **1999**, *71*, 1041; (f) Kuthan, J.; Sebek, P.; Boehm, S. *Adv. Heterocycl. Chem.* **1995**, *62*, 19.
4. Liu, H.; Zhang, Q.; Wang, L.; Tong, X. *Chem. Commun.* **2010**, 312.
5. Zhang, Q.; Yang, L.; Tong, X. *J. Am. Chem. Soc.* **2010**, *132*, 2550.
6. For reviews, see: (a) Lu, X.; Zhang, C.; Xu, Z. *Acc. Chem. Res.* **2001**, *34*, 535; (b) Methot, J. L.; Roush, W. R. *Adv. Synth. Catal.* **2004**, *346*, 1035; (c) Lu, X.; Du, Y.; Lu, C. *Pure Appl. Chem.* **2005**, *77*, 1985; (d) Nair, V.; Menon, S. R.; Sreekanth, A. R.; Abhilash, N.; Biji, A. T. *Acc. Chem. Res.* **2006**, *39*, 520; (e) Ye, L.; Zhou, J.; Tang, Y. *Chem. Soc. Rev.* **2008**, *37*, 1140; (f) Kwong, C. K.; Fu, M. Y.; Lam, C. S.; Toy, P. H. *Synthesis* **2008**, 2307.
7. For reviews see: (a) Weinreb, S. M.; Scola, P. M. *Chem. Rev.* **1989**, *89*, 1525; (b) Reymond, S.; Cossy, J. *Chem. Rev.* **2008**, *108*, 5359; (c) Behforouz, M.; Ahmadian, M. *Tetrahedron* **2000**, *56*, 5259; (d) Takao, K.-I.; Munakata, R.; Tadano, K.-I. *Chem. Rev.* **2005**, *105*, 4779.
8. Liu, H.; Zhang, Q.; Wang, L.; Tong, X. *Chem.—Eur. J.* **2010**, *16*, 1968.
9. CCDC 739301 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.
10. For representative examples of phospine-catalyzed [4+2] cycloadditions, see: (a) Zhu, X.-F.; Lan, J.; Kwon, O. *J. Am. Chem. Soc.* **2003**, *125*, 4716; (b) Wurz, R. P.; Fu, G. C. *J. Am. Chem. Soc.* **2005**, *127*, 12234; (c) Tran, Y. S.; Kwon, O. *J. Am. Chem. Soc.* **2007**, *129*, 12632.
11. For reviews, see: (a) Bruggink, A.; Schoevaart, R.; Kieboom, T. *Org. Process Res. Dev.* **2003**, *7*, 622; (b) Ajamian, A.; Gleason, J. L. *Angew. Chem., Int. Ed.* **2004**, *43*, 3754; (c) Wasilke, J.-C.; Obrey, S. J.; Baker, R. T.; Bazan, G. C. *Chem. Rev.* **2005**, *105*, 1001; (d) Pellissier, H. *Tetrahedron* **2006**, *62*, 1619; (e) MacMillan, D. W. C.; Walji, A. M. *Synlett* **2007**, 1477; (f) Chapman, C. J.; Frost, C. G. *Synthesis* **2007**, 1.
12. This result convincingly rules out the other mechanistic consideration, consisting Diels–Alder reaction of oxo-diene with alkyne and [1,3]-proton transfer.
13. (a) Larpent, C.; Meignan, G.; Patin, H. *Tetrahedron Lett.* **1991**, *32*, 2615; (b) Lu, C.; Lu, X. *Org. Lett.* **2002**, *4*, 4677; (c) Trost, B. M.; Li, C. J. *J. Am. Chem. Soc.* **1994**, *116*, 3167; (d) Trost, B. M.; Li, C. J. *J. Am. Chem. Soc.* **1994**, *116*, 10819; (e) Trost, B. M.; Dake, G. R. *J. Org. Chem.* **1997**, *62*, 5670; (f) Dake, G. R.; Trost, B. M. *J. Am. Chem. Soc.* **1997**, *119*, 7595; (g) Dureen, M. A.; Stephan, D. W. *J. Am. Chem. Soc.* **2009**, *131*, 8396.
14. Guo, H.; Xu, Q.; Kwon, O. *J. Am. Chem. Soc.* **2009**, *131*, 6318.
15. (a) Reinhoudt, D. N.; Dijkstra, P. J. *Pure Appl. Chem.* **1988**, *60*, 477; (b) Shibuya, J.; Nabeshima, M.; Nagano, H.; Maeda, K. *J. Chem. Soc., Perkin Trans. 2* **1988**, 1607; (c) Dijkstra, P. J.; Hertog, H. J.; Eerden, J.; Harkema, S.; Reinhoudt, D. N. *J. Org. Chem.* **1988**, *53*, 375.
16. (a) Katritzky, A. R.; Denisenko, A.; Arend, M. *J. Org. Chem.* **1999**, *64*, 6076; (b) Palacios, F.; Alonso, C.; Rubiales, G. *J. Org. Chem.* **1997**, *62*, 1146; (c) Reich, S. H.; Melnick, M.; Pino, M. J.; Fuhry, M. A. N.; Trippe, A. J.; Appelt, K.; Davies, J. F., II; Wu, B. W.; Musick, L. *J. Med. Chem.* **1996**, *39*, 2781; (d) Katsuyama, I.; Ogawa, S.; Yamaguchi, Y.; Funabiki, K.; Matsui, M.; Muramatsu, H.; Shibata, K. *Synthesis* **1997**, 1321.