Base Induced Cyclobutenone Rearrangements and Its Application in the Synthesis of Aromatic Amines

Xiaodan Han, Jianping Fu, Juwu Hu, Wei Xiong, Huibin Wang, Lei Wu

PII: S0040-4039(19)31087-1
DOI: https://doi.org/10.1016/j.tetlet.2019.151304
Reference: TETL 151304

To appear in: *Tetrahedron Letters*

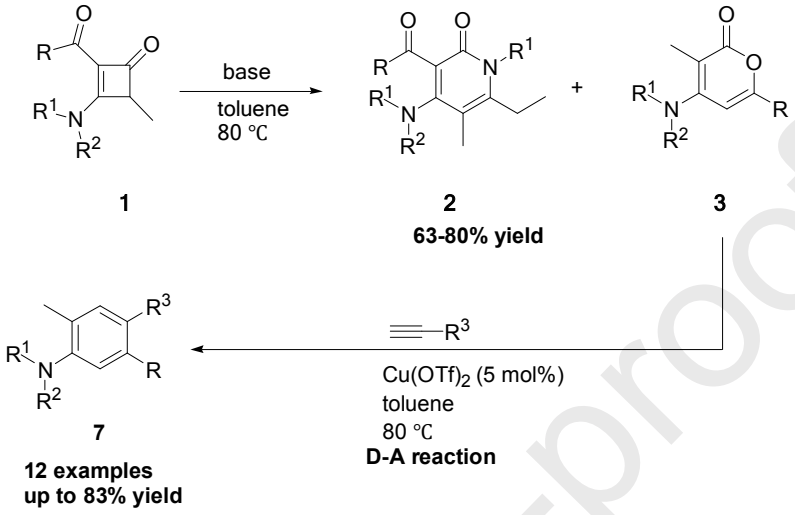
Received Date: 20 August 2019
Revised Date: 10 October 2019
Accepted Date: 18 October 2019

Please cite this article as: Han, X., Fu, J., Hu, J., Xiong, W., Wang, H., Wu, L., Base Induced Cyclobutenone Rearrangements and Its Application in the Synthesis of Aromatic Amines, *Tetrahedron Letters* (2019), doi: https://doi.org/10.1016/j.tetlet.2019.151304

Base Induced Cyclobutenone Rearrangements and Its Application in the Synthesis of Aromatic Amines

Xiaodan Han, Jianping Fu, Juwu Hu, * Wei Xiong, * Huibin Wang, Lei Wu
Department of Applied Chemistry, Jiang Xi Academic of Sciences, Nanchang, 330096, People's Republic of China

E-mail: hjw19771985@163.com



- **easily available starting materials**
- **a divergent synthesis approach**
- **D-A reaction was realized in good yields and in a highly regioselective manner under mild conditions**

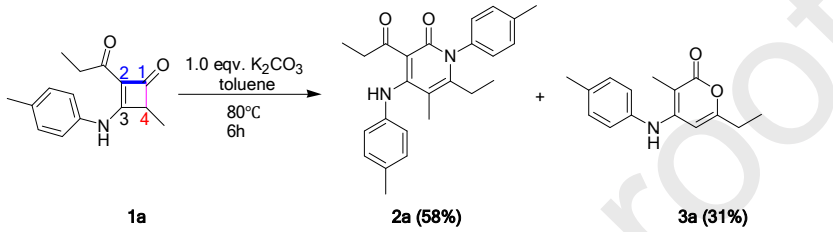
Abstract: A series of fully substituted 2-pyridone **2** and functionalized α-pyrones **3** are synthesized starting from cyclobutenones **1** under a base-promoter in toluene at 80 ℃. This rearrangement is complimentary to the previously reported ring expansion of cyclobutenones, providing a divergent synthesis of corresponding products from the same precursor **1**. In addition, α-pyrones **3** has also been applied to the synthesis of aromatic amines **7** in good yields (64–83%) and in a highly regioselective manner via D-A reaction under mild conditions.

Keywords: substituted pyridones; α-pyrones ; D-A reaction; aromatic amines

Cyclobutenones are extremely versatile synthetic intermediates and have seen a rapid development in the construction of a wide range of organic compounds including several bioactive natural products and drugs[1]. Owing to their inherent high ring strain, the ring-opening/rearrangement reactions of cyclobutenone triggered by numerous reaction conditions, primarily involving thermolysis[2], photolysis[3], and transition metal-catalyzed[4] have been recognized as one of the most direct, effective, atom-economical and rapid methods for chemical transformations. Over the past decades, the ring-opening reactions of cyclobutenone have been well studied[5] and they have successfully paved the way for the synthesis of ring-expanded products, e.g. aromatics [6], quinones[7], pyrone[8], indole alkaloids[9], cycloheptadienone[10] . To date, this type reactions of cyclobutenone are still a topical area of continuing interest. Recently, series of 3-aminocyclobut-2-en-1-ones **1** incorporating acyl and amino groups have been easily prepared by our group[11] , which were proven very useful, especially in the synthesis of persubstituted phenols [12]and 4-quinolones[11]. Encouraged by these results and our continued interest in the synthesis of highly valuable carbo- and heterocycles from cyclobutenone derivatives, we further explored the reaction behavior of 3-aminocyclobut-2-en-1-ones **1** and found it was sensitive to base conditions. We now wish to report a simple and efficient access to 2-pyridones **2** and/or α-pyrones **3** relying upon utilization of 3-aminocyclobut-2-en-1-ones **1** in the presence of base-promoter and present a mechanism involved in the

ring-opening/recyclization process.

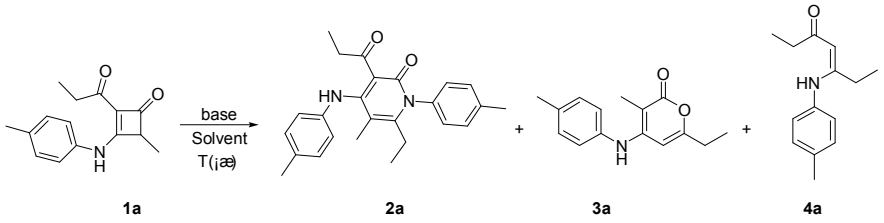
At the outset of our study, 3-aminocyclobut-2-en-1-one **1a** was prepared and tried the thermal cyclization reaction by heating from 50 ℃ to 110 ℃ in toluene. Regrettably, no reaction occurred in the absence of catalyst. After many attempts, it was found when **1a** was subjected to K_2CO_3 (1.0 eqv.) in toluene at 80 ℃ for a period of time, two different products were obtained (Scheme 1). The structure of **2a** was unambiguously established by its spectra, analytical data and X-ray crystallographic analysis. According to our previous work[12], **3a** was named 6-ethyl-3-methyl-4-p-tolylamino-pyran-2-one. This result intrigued us to explore the precious reaction conditions to prepare 2-pyridone 2 and/or α-pyrones derivatives **3** selectively from 3-aminocyclobut-2-en-1-one **1** since those compounds with 2-pyridone or α-pyrone structure have emerged not only as key units in many natural product and pharmaceuticals but also as important intermediates for various biologically active molecules[13].



Scheme 1

Then, we examined the ring-opening/rearrangement of 3-aminocyclobut-2-en-1-one **1a** to **2a** and **3a** by varying reaction conditions and the results were summarized in table 1. Selecting K_2CO_3 (1.0 eqv.) as a base, the reaction of **1a** afforded **2a** in 58% isolated yield within 6 h in toluene at 80 ℃ along with α-pyrones **3a** in 31% yield (Table 1, entry 1). Increasing the amount of K_2CO_3 from 1.0 to 1.5 equivment made considerable effect on the yield of product **2a** and the reaction time was shortened to 4 h (Table 1, entry 2). A further increase in the amount of K_2CO_3 to 2.0 eqv. was not required (Table 1, entry 3). Moreover, the reaction temperature was also found to be an important factor for this transformation. By lowing the temperature to RT, the reaction did not take place (Table 1, entry 4). Higher temperature resulted in a sharply decline in the yield of **2a** compared to entry 2, whereas the yield of **3a** increased up to 78% (Table 1, entry 5). Addition of other carbonates, such as Cs_2CO_3 and Na_2CO_3 were less effective for improvement of **2a** yield (Table 1, entries 6-7). In particular, it should be noted that when hydroxide (KOH, NaOH, LiOH) was utilized to replace K_2CO_3 for this reaction, the product **2a** was not observed even if the reaction time was prolonged and in the meantime, α-pyrone **3a** was obtained as the major product in high yields, concominated by a by-product enamine **4a** (Table 1, entries 8-10). Subsequently, we moved on to screen the reaction solvent. Among the solvents tested, CH_3CN gave **2a** as the main product in 71% yield (Table 1, entry11); When the reaction was carried out in DMF or 1,4-dioxane or H_2O, instead of **2a**, α-pyrones **3a** was obtained as the major product in moderate yields (Table 1, entries 12-14); In comparison, no **2a** and/or **3a** could be detected with anhydrous toluene as the solvent (Table 1, entry15). Thus, the most suitable reaction conditions for the formation of **2a** or **3a** was established by simple changing the base promoter in toluene at 80 ℃.

Table 1. Optimization of reaction conditions for the synthesis of 2-pyridone **2a**[a] and α-pyrone **3a**[b]



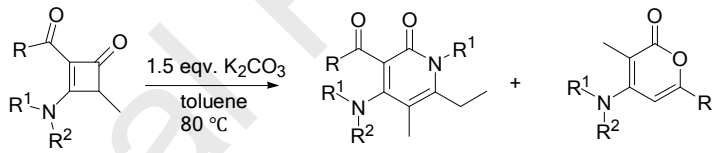
Entry	Base (eqv.)	Solvent	T (℃)	**2a**[c] Yield (%)	**3a**[d] Yield (%)	**4a**[e] Yield (%)
1	K_2CO_3 (1.0)	toluene	80	58	31	0

2	**K_2CO_3 (1.5)**	**toluene**	**80**	**79**	**15**	**0**
3	K_2CO_3 (2.0)	toluene	80	68	20	0
4	K_2CO_3 (1.5)	toluene	rt	0	0	0
5	K_2CO_3 (1.5)	toluene	90	19	78	0
6	Cs_2CO_3(1.5)	toluene	80	77	17	0
7	Na_2CO_3(1.5)	toluene	80	36	33	0
8	**KOH (1.5)**	**toluene**	**80**	**0**	**96**	**trace**
9	NaOH(1.5)	toluene	80	0	90	9
10	LiOH(1.5)	toluene	80	0	87	11
11	K_2CO_3 (1.5)	CH_3CN	80	71	25	0
12	K_2CO_3 (1.5)	DMF	80	0	58	0
13	K_2CO_3 (1.5)	1,4-dioxane	80	0	61	0
14	K_2CO_3 (1.5)	H_2O	80	trace	65	0
15	K_2CO_3 (1.5)	anhydrous toluene	80	0	0	0

[a/b]Reaction conditions: **1a** (1.0 mmol), solvent (5.0 mL). [c/d/e]Isolated yields

To generalized this approach, several kinds of 3-aminocyclobut-2-en-1-ones **1** were studied for the synthesis of fully substituted 2-pyridone **2** in the presence of 1.5 eqv. K_2CO_3 at 80 ℃ in toluene. As shown in Table 2, substituted **1** having aryl group on the nitrogen atom can participate in the ring-opening/recyclization process to afford the major product 2-pyridone **2a-h** in moderate yields (Table 2, entries 1-8). However, the reaction of **1i** (R = OMe) under the same optimized reaction conditions failed to produce even trace of **2i** or **3i** (Table 2, entry 9). Using **1j** (R^1 = *n*-butyl group) as substrate, the reaction gave α-pyrone **3j** in good yield whereas the yield of 2-pyridone **2j** dropped to trace amounts (Table 2, entry 10). As for **1k** (R^1 = piperidyl), the corresponding product **2k** was not observed and α-pyrone **3k** was obtained in 87% yield (Table 2, entry 11). Notably, no formation of **2l** and/or **3l** was detected in case of a pyridine group at R^1 (Table 3, entry 12), which is due to the conversion of **1l** to naphthyridine **5** (Scheme 2)[9]. The structure of **5** was confirmed by its spectral data (^{1}HNMR, ^{13}CNMR and HRMS) and finally by the X-ray crystallographic data.

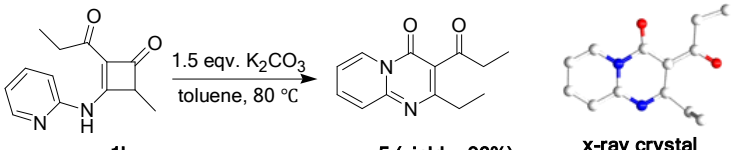
Table 2. Ring-expanding reaction of **1** with K_2CO_3 in toluene[a]



1 **2** **3**

Entry	**1**	R	R^1	R^2	**2** Yield[b] (%)	**3** Yield[c] (%)
1	**1a**	Et	4-MeC_6H_4	H	79(**2a**)	15(**3a**)
2	**1b**	Et	C_6H_5	H	74(**2b**)	19(**3b**)
3[d]	**1c**	Et	4-ClC_6H_4	H	73(**2c**)	20(**3c**)
4	**1d**	Et	4-$MeOC_6H_4$	H	77(**2d**)	16(**3d**)
5	**1e**	Et	2-MeC_6H_4	H	71(**2e**)	25(**3e**)
6	**1f**	Et	2,4-$Me_2C_6H_3$	H	63(**2f**)	30(**3f**)
7[e]	**1g**	Et	4-$CF_3C_6H_4$	H	75(**2g**)	17(**3g**)
8	**1h**	Me	4-MeC_6H_4	H	80(**2h**)	11(**3h**)
9	**1i**	OMe	4-MeC_6H_4	H	0(**2i**)	0(**3i**)
10	**1j**	Et	*n*-butyl	H	trace(**2j**)	82(**3j**)
11	**1k**	Et	$(CH_2)_5$	-	0(**2k**)	87(**3k**)
12[f]	**1l**	Et	C_5H_4N	H	0(**2l**)	0(**3l**)

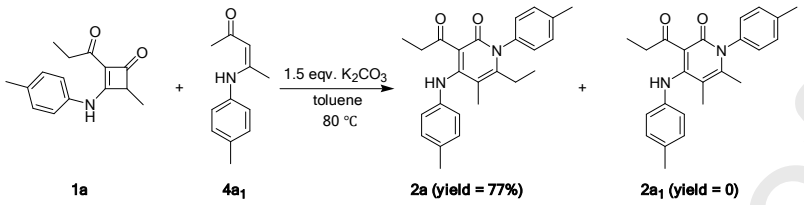
[a]Reaction conditions: 1 (1.0 mmol), K_2CO_3 (1.5 mmol), toluene (5 mL), 80 ℃, 5 h. [b/c]Isolated yields. [d/e] Reaction conditions: 1 (1.0 mmol), K_2CO_3 (1.5 mmol), toluene (5 mL), 60 ℃, 10 h. [f]Substrate **1l** was converted to naphthyridine **5** in 96% yield.



1l **5 (yield = 96%)** **x-ray crystal structure of 5**

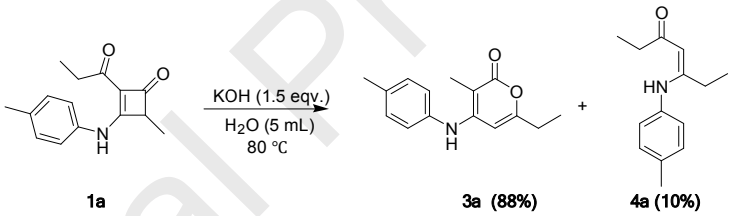
Scheme 2

To obtain deeper insight into the reaction mechanism, some supplementary experiments were conducted. First, we were interested in whether an enamine moiety captured in the reaction of **1** with hydroxides (table 1, entries 8-10), would be able to insert into the four-membered ring. Consequently, we tried the reaction of **1a** with **4a$_1$** under the same reaction conditions as in Table 2. As a result, the reaction gave **2a** in 77% yield and no **2a$_1$** was produced (Scheme 3), which can be inferred enamine **4a** was not involved in the formation of 2-pyridone **2a**.

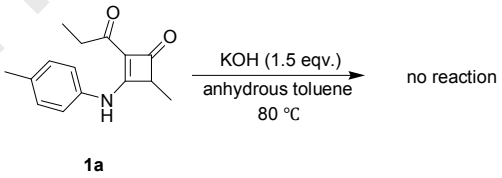


Scheme 3

Further evidence for this mechanism was provided by reactions of **1a** with different base-promoters in anhydrous toluene and H_2O.The experiments showed that only a trace or no **2a** was detected and **3a** was generated as the main product from **1a** in 65% and 88% yields when the reactions were carried out in H_2O at 80 ℃ in the presence of K_2CO_3 (1.5 eqv.) for 8 h and KOH (1.5 eqv.) for 5 h (Table 1, entry 14; Scheme 4), respectively. Additionally, no reaction occurred when **1a** was treated with K_2CO_3 or KOH in anhydrous toluene under other identical conditions (Table 1, entry 15; Scheme 5), while most of **1a** remained. These results clearly indicate that a wetted condition even a trace amount of water (Table 1, entries 1-13) and the basicity of the promoter have a significant bearing on the outcome of this reaction.

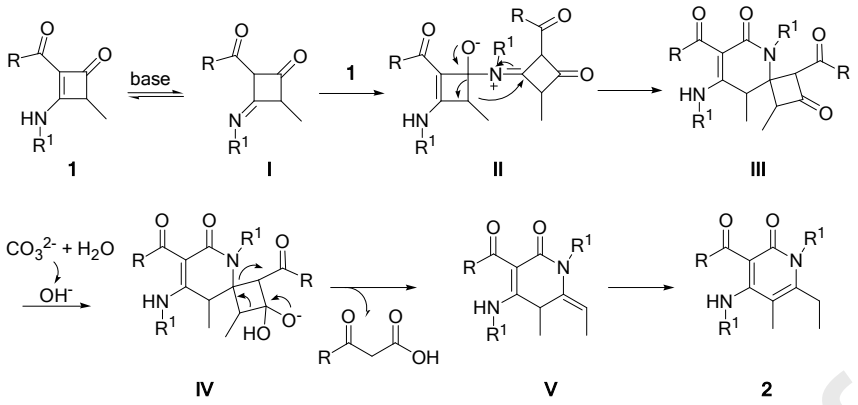


Scheme 4



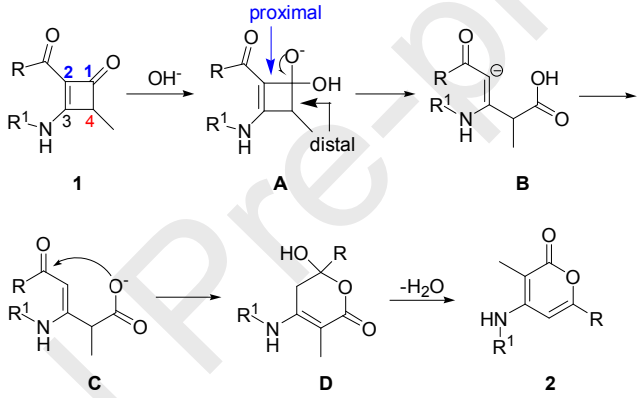
Scheme 5

On the basis of all of the results described and the related reports on the OH/NH_2-initiated ring-opening reaction of cyclobutenones[14-17], we considered OH^- as a promoter, which comes from KOH solution or hydrolysis of potassium carbonate in a wetted condition, to initiate the reaction. Therefore, plausible mechanisms for the synthesis of 2-pyridones 2 and α-pyrones **3** from 3-aminocyclobut-2-en-1-ones **1** were proposed in Scheme 6 and Scheme 7. The synthesis of 2-pyridones **2** with K_2CO_3 as a base [14a,17b]: under a base reagent, cyclobutenones **1** undergoes a tautomerism to form imines **I**. **I** acts as a nucleophile and rapidly reacts with another molecule of cyclobutenones **1** to form [4+2] cycloaddition product **III** via 1,2-addition(III)/ring-opening(IV) and concomitant intramolecular cyclization (**II**). Then 1,2-addition of OH^- to the carbonyl moiety in **III** initiated ring opening of cyclobutanone (**IV**), accompanied by elimination of β-carbonyl carboxylic acid to give intermediate **V**, which eventually led to product 2-pyridones **2** after double bond inward shift. (**Scheme 6**).



Scheme 6 possible mechanism for the formation of 2-pyridones **2**

A proposed mechanism for α-pyrones **3** synthesis with KOH as a base promoter is depicted in Scheme 7[15, 18]: firstly, OH^- attacks the carbonyl moiety of substrate **1(A),** leading to ring opening predominantly at the C_1-C_2 bond and the formation of intermediate vinyl anion **B**[19], which is consistent with the description of Roberts and co-workers[15a]. Followed by a proton transfer, the intermediate **C** occurs an intramolecular *O*-nucleophilic addition to furnish a cyclic intermediate **D**. Finally, **D** removes a molecule of water, giving rise to the product α-pyrones **3** (Scheme 7).



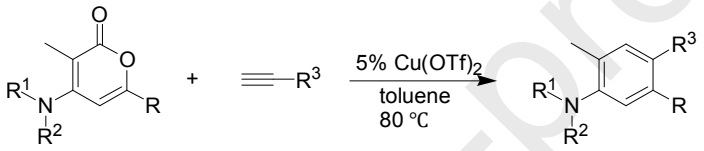
Scheme 7 possible mechanism for the formation of α-pyrones **3**

When hydroxides was used instead of K_2CO_3 as a promoter in the reaction system under otherwise identical conditions as those in table 2, α-pyrones **3** can be obtained as the mjor product in excellent yields, which was introduced by Han's formerly report [12] and no longer elaborated in this paper. To extend the synthetic value of the protocol, our interest was focused on the synthetic use of α-pyrones **3**, which has often been taken as a potentially useful scaffold for the synthesis of complex heterocyclic compounds[20]. Eventually, we found that aromatic amines **7** could be obtained from the prepared α-pyrones **3** as a diene component in Diels–Alder reactions with terminal alkynes **6** in the presence of 5% $Cu(OTf)_2$ in toluene at 80 ℃ for 7 h, followed by the extrusion of CO_2 (Table 3). Despite the traditional methods for aromatic compounds via D-A reaction of pyrone with alkynes/ alkenes have been presented, they often suffer from harsh reaction conditions (e.g. high temperatures ≥150 ℃, expensive catalyst and ligands), poor yields and low regioselectivities[23]. From the previous observations, it is anticipated that the above D-A reactions will be further improved and afford the expected product under mild conditions. We detailed herein, the development of this concept into an efficient approach for generating functionalised aromatic amines in good yields and in a highly regioselective manner.

As can be seen from Table 3, the reactions of α-pyrones **3a-f** bearing aryl moiety at R^1, including

electron-rich (Table 3, entry 1 and entries 4-6), phenyl (Table 3, entry2), electron-deficient (Table 3, entry 3) *N*-aryl groups reacted well with but-3-yn-2-one **6a** (1.0 mmol) to afford aromatic amines **7a–f** in moderate yields (64–73%). The presence of a Me group instead of Et at R also showed good reaction activity in the D-A reaction and gave **7h** in 69% yield (Table 3, entry 7). Compounds **7**'s structure was determined by its spectral and analytical data, and further confirmed by the X-ray diffraction of **7a** (Figure 1). Similarly, the present procedure applied to α-pyrones **3j-k** bearing a *n*-butyl or piperidyl group on the nitrogen atom, providing **7j** and **7k** in good yields (Table 3, entries 8-9). Subsequently, we examined the reactivity of other terminal alkynes. To our delight, the reactions of **3a** with **6b**, **6c** and **6d** gave rise to aromatic amines derivatives (**7l**, **7m** and **7n**) in 83%, 57% and 51% yields, respectively (Table 3, entries 10-12). However, when 1-pentyne (**6d**) was applied, no reaction occurred (Table 3, entry 13). Given the results have suggested that the electronic properties of substituents in terminal alkynes **6** has an important effect on the reactivity of our reaction.

Table 3. D-A reaction of 2-pyrones 3 with terminal alkynes 6[a]



3 **6** **7**

Entry	**1**	R	R^1	R^2	R^3	**Product** 7	7 Yield[b] (%)
1	**3a**	Et	4-MeC_6H_4	H	$COCH_3$**(6a)**	**7a**	73
2	**3b**	Et	C_6H_5	H	$COCH_3$	**7b**	71
3	**3c**	Et	4-ClC_6H_4	H	$COCH_3$	**7c**	67
4	**3d**	Et	4-$MeOC_6H_4$	H	$COCH_3$	**7d**	76
5	**3e**	Et	2-MeC_6H_4	H	$COCH_3$	**7e**	73
6	**3f**	Et	2,4-$Me_2C_6H_3$	H	$COCH_3$	**7f**	64
7	**3h**	Me	4-MeC_6H_4	H	$COCH_3$	**7h**	69
8	**3j**	Et	*n*-butyl	H	$COCH_3$	**7j**	66
9	**3k**	Et	$(CH_2)_5$	-	$COCH_3$	**7k**	78
10	**3a**	Et	4-$CH_3C_6H_4$	H	CHO**(6b)**	**7l**	83
11	**3a**	Et	4-$CH_3C_6H_4$	H	C_6H_5**(6c)**	**7m**	57
12	**3a**	Et	4-$CH_3C_6H_4$	H	4-MeC_6H_5**(6d)**	**7n**	51
13	**3a**	Et	4-$CH_3C_6H_4$	H	C_3H_7 **(6e)**	**7o**	0

[a]Reaction conditions: 1 (1.0 mmol), 6 (1 mmol), $Cu(OTf)_2$ (5 mmol%), toluene (5 mL), 80 ℃, 7 h. [b]Isolated yields.

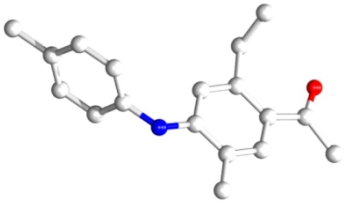


Figure 1. ORTEP drawing of **7a**

In conclusion, we have developed a divergent synthesis of 2-pyridones **2** and α-pyrones **3** in good yields starting from the same precursor 3-aminocyclobut-2-en-1-ones **1** upon regulation of base conditions. Also a catalytic amount of $Cu(OTf)_2$-catalyzed Diels-Alder reaction of α-pyrones **3** with terminal alkynes to furnish aromatic amines **7** has been detailed. Contrasting with the so far reported Diels-Alder reactions of α-pyrones with alkynes, this method features low-cost, short reaction time, mild reaction conditions, operational simplicity, as well

as high regioselectivity.

Acknowledgments

We are grateful to the National Natural Science Foundation of China (Grants 21562023 and 21862007) and the Jiangxi Provincial Science & Technology Department (20171BBF60074) for financial support.

Supplementary data

The supporting information of detailed experimental procedures, CIF data for **2a** and full characterization data for **2a-h**, **3a-k**, **4a**, **5** and **7a-n** is available free of charge on the line.

References

[1] a) X. Yan, X. Hu. *J. Org. Chem*. **2014**, *79*, 5282. b) T. Kondo, Y. Taguchi, Y. Kaneko, M. Niimi, T. Mitsudo. *Angew. Chem. Int. Ed*. **2004**, *43*, 5369. c) T. Kondo, M. Niimi, M. Nomura, K. Wada, T. Mitsudo. *Tetrahedron Letters*. **2007**, *48*, 2837. d) N. A. Magomedov, P. L. Ruggiero, Y. C. Tang. *J. Am. Chem. Soc*. **2004**, *126*, 1624. e) T. Hamura, T. Suzuki, T. Matsumoto, K. Suzuki. *Angew. Chem. Int. Ed*. **2006**, *45*, 6294. f) E. F. Plow, C. S. Cierniewski, Z. Xiao, T. A. Haas, T. V. Byzova. *Thromb. Haemostasis*. **2001**, *86*, 34. g) C. J. Helal, Z. Kang, J. C. Lucas, B. R. Bohall. *Org. Lett*. **2004**, *6*, 1853. h) K. Seio, T. Miyashita, K. Sato, M. Sekine. *Eur. J. Org. Chem*. **2005**, 5163. i) J. Li, Y. Han, T. B. Freedman, S. Zhu, D. J. Kerwood, Y. Y. Luk. *Tetrahedron Letters*. **2008**, *49*, 2128.

[2] a) D. C. Harrowven, D. D. Pascoe, I. L. Guy. *Angew. Chem*. **2007**, *119*, 429. b) S. Niwayama, E. A. Kallel, C. Sheu, K. N. Houk. *J. Org. Chem*. **1996**, *61*, 2517. c) N. M. Goudgaon, J. Shi, R. F. Schinazi. *Tetrahedron Letters*. **1998**, *39*, 1869.

[3] a) J. E. Baldwin, M. C. McDaniel. *J. Am. Chem. Soc*. **1968***, 90*, 6118. b) A. Hassner, S. Naidorf. *Tetrahedron Letters*. **1986**, *27*, 6389. c) D. C. Harrowven, M. Mohamed, T. P. Goncalves, R. J. Whitby, D. Bolien, H. F. Sneddon. *Angew. Chem. Int. Ed.* **2012**, *51*, 4405.

[4] a) M. A. Huffman, L. S. Liebeskind. *J. Am. Chem. Soc*. **1990**, *112*, 8617. b) A. L. Auvinet, J. P. Harrity. *Angew. Chem. Int. Ed.* **2011**, *50*, 2769. c) P. H. Chen, J. Sieber, C. H. Senanayake, G. Dong. *Chem. Sci*. **2015**, *6*, 5440.

[5] P. H. Chen, G. Dong. *Chem. Eur. J*. **2016**, *22*, 18290.

[6] a) S. L. Xu, H. W. Moore. *J. Org. Chem*. **1992**, *57*, 326. b) D. J. Krysan, A. Gurski, L. S. Liebeskind. *J. Am. Chem. Soc*. **1992**, *114*, 1412.

[7] L. S. Liebeskind, S. Iyer, C. F. Jewel. *J. Org. Chem*. **1986**, *51*, 3065.

[8] a) P. Mingo, S. J. Zhang, L. S. Liebeskind. *J. Org. Chem*. **1999**, *64*, 2145. b) T. Kondo, Y. Taguchi, Y. Kaneko, M. Niimi, T. Mitsudo. *Angew. Chem. Int. Ed*. **2004**, *43*, 5369.

[9] a) L. S. Liebeskind, J. Y. Wang. *Tetrahedron*. **1993**, *49*, 5461. b) B. R. Yerxa, H. W. Moore. *Tet. Lett*, **1992**, *33*, 7811.

[10] M. A. Huffman, L. S. Liebeskind. *J. Am. Chem. Soc*.**1993**, *115*, 4895.

[11] Y. L. Zhao, S. C.Yang, C. H. Di, X. D. Han, Q. L. *Chem. Commun*. **2010**, *46*, 7614.

[12] X. D. Han, Y. L. Zhao, J. Meng, C. Q. Ren, Q. Liu. *J. Org. Chem.* **2012**, *77*, 5173.

[13] a) Z. Lv, C. Sheng, T. Wang, Y. Zhang, J. Liu, J. Feng, H. Sun, H. Zhong, C. Niu, and K. Li. *J. Med. Chem*. **2010**, *53*, 6. b) C. G. Savarin, J. A. Murry and P. G. Dormer. *Org. Lett*. **2002**, *4*(12), 2071. c) C. J. Schaefer, D. W. Ruhrmund, L. Pan, S. D. Seiwert, K. Kossen. *European Respiratory Review*. **2011**, *20*, 85. d) a) M. E.Wall, M. C. Wani, C. E.Cook, K. H. Palmer, A. T. McPhail, G. A. Sim. *J. Am. Chem. Soc.* **1966**, *88*, 3888. e) M. Di Braccio, G. Grossi, G. Roma, C. Marzano, F. Baccichetti, M. Simonato and F. Bordin, *Il Farmaco*, **2003**, *58*, 1083. f) G. P. McGlacken and I. J. S. Fairlamb. *Nat. Prod. Rep*. **2005**, *22*, 369. g) Y. Kamano, T. Nogawa, A. Yamashita, M. Hayashi, M. Inoue, P. Draˇ sar and G. R. Pettit. *J. Nat. Prod.* **2002**, *65*, 1001. h) M. Torres, S. Gil and M. Parra. *Current Organic Chemistry*, **2005**, *9*, 1757. i) T. Sengupta, K. S. Gayen, P. Pandit and D. K. Maiti. *Chem. Eur. J.* **2012**, *18*, 1905. j) T. Sengupta, K. S. Gayen, P. Pandit and D. K. Maiti. *Chem. Eur. J.* **2012**, *18*, 1905. k) M. T. Cocco, C. Congiu, V. Onnis. *Eur. J. Med. Chem*. **2000**, *35*, 545. l) P. S. Dragovich, T. J. Prins, R. Zhou, E. L. Brown, F. C. Maldonado, S. A. Fuhrman, L. S. Zalman, T. Tuntland, C. A. Lee, A. K. Patick, D. A. Matthews, T. F. Hendrickson, M. B. Kosa, B. Liu, M. R. Batugo, J.-P. R. Gleeson, S. K. Sakata, L. Chen, M. C. Guzman, J. W. Meador, R. A. Ferre, S. T. Worland. *J. Med. Chem.* **2002**, *45*(8), 1607.

[14] a) P. Chen, G. Dong. *Chem. Eur. J.* **2016**, *22*, 18290. b) E. F. Silversmith, Y. Kitahara, M. C. Caserio, J. D. Roberts. *J. Am.*

Chem. Soc. **1958**, *80*, 5840. c) Y. Li, X. Su, W. Zhou, W. Li, J. Zhang. *Chem. Eur. J*. **2015**, *21*, 1. d) Y. Yamamoto, M. Ohno, S. Eguchi. *Tetrahedron.* **1994**, *20*, 7783. e) L. Skattebol, J. D. Roberts. *J. Am. Chem. Soc.* **1958**, *80*, 4085. f) N. A. Magomedov, P. L. Ruggiero, Y. Tang. *J. Am. Chem. Soc.* **2004**, *126*, 1624. g) D. Bellue, B. Ernst. *Angew. Chem. Int. Ed. Engl*. **1988**, *27*, 797. h) J. Ficini, S. Falou, J. d'Angelo. *Tetrahedron Letters*. **1977**, *22*, 1931.

[15] a) J. D. Roberts, G. B. Kline, H. E. Simmons. *J. Am. Chem. Soc.* **1953**, *75*, 4765. b) E. F. Silversmith, Y. Kitahara, M. C. Caserio, J. D. Roberts. *J. Am. Chem. Soc*. **1958**, *80*, 5840.

[16] J. C. Bradley, T. Durst. *Can. J. Chem*. **1995**, *73*, 1660.

[17] a) A. Gokhale, P. Schiess. *Helv. Chim. Acta*. **1998**, *81*, 251. b) B. S. Li, Y. Wang, Z. Jin, P. Zheng, R. Ganguly, Y. R. Chi. *Nat. Commun*. **2015**, *6*, 6207. c) B. S. Li, Y. Wang, Z. Jin, Y. R. Chi. *Chem. Sci.* **2015**, *6*, 6008. d) T. Matsumoto, T. Hamura, Y. Kuriyama, K. Suzuki. *Tetrahedron Lett*. **1997**, *38*, 8985.

[18] E. F. Silversmith, Y. Kitahara, M. C. Caserio, J. D. Roberts. *J. Am. Chem. Soc*. **1958**, *80*, 5840.

[19] a) A. A. Bothner-By. *ibid*. **1955**, *77*, 3293. b) S. I. Miller, R. M. Noyes. *ibid*. **1952**, *74*, 629. c) T. L. Jacobs, W. R. Scott, Jr. *ibid*. **1953**, *75*, 5497. d) W. E. Truce, J. A. Simms, M. M. Boudakian. *ibid*. **1956**, *78*, 595. e) D. Y. Curtin, J. W. Crump. *ibid*. **1958**, *80*, 1922. f) D. Y. Curtin, H. W. Johnson, Jr. and E. G. Steiner. *ibid*. **1955**, *77*, 4566. g) E. F. Silversmith, J. D. Roberts. *J. Am. Chem. Soc*. **1956**, *78*, 4023. h) J. D. Roberts, G. B. Kline, H. E. Simmons. *J. Am. Chem. Soc.* **1953**, *75*, 4765.

[20] a) H. Okarnura, T. Iwagawa, M. Nakatani. *Tetrahedron Letters.* **1995**. *36*, 5939. b) L. R. Marrison, J. M. Dickinson, R. Ahmed and I. J. S. Fairlamb. *Tetrahedron Letters*. **2002**, *43*, 8853.

[21] P. Carlo, A. Echavarren, P. Prados. *J. Org. Chem.* **1983**, *48*, 5373.

[22] P. Zhao, C. M. Beaudry. *Angew. Chem. Int. Ed*. **2014**, *53*, 1.

[23] a) P. M. Delaney, D. L. Browne, H. Adams, A. Plant, J. P. A. Harrity. *Tetrahedron*, **2008**, *64*, 866. b) V. M. Muzalevskiv, V. G. Nenaldenko, A. V. Shastin, E, S. Balenkova. *Synthesis*. **2008**, *18*, 2899. c) J. J. Lee, G. A. Kraus. *Tetrahedron Letters*. **2009**, *13*, 2734. d) D. A. Evans, T. Lectka, and S. J. Miller. *Tetrahedron Letters*. **1993**, *34*, 7027.

Declaration of interests

☒ The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

☐The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:

Highlights:

1. It provides a divergent way to form different products from the same precursor .
2. The reaction was successfully realized upon regulation of base promoters.
3. Also a D-A reaction to furnish aromatic amines 7 has been elaborated.
4. The D-A method features mild reaction condition, high yield and regioselectivity.