有机化学 DOI: 10.6023/cjoc202303031 研究论文
Chinese Journal of Organic Chemistry ARTICLE

偶氮次甲基亚胺与氮杂二烯前体的[4＋3]环加成反应构建功能化四氮杂䓬衍生物

张晓轲*,a,c 郑相如 b 王朝永*,a
(a 重庆大学附属涪陵医院中心实验室 重庆 408000)
(b 重庆医科大学附属第三医院 重庆 401120)
(c 遵义医科大学 贵州 563006)

摘要 四氮杂䓬衍生物具有良好的生物活性，目前，对于该骨架的构建方法非常有限，因此，建立了一种通过氢氧化钾促进 α-卤代乙酰腙原位形成 1,2-氮杂二烯中间体，与偶氮次甲基亚胺环合反应合成高度取代的四氮杂䓬衍生物的新方法. 该方法表现出良好的官能团耐受性和底物普适性.

关键词 α-卤代乙酰腙；偶氮次甲基亚胺；四氮杂䓬衍生物；氮杂二烯前体

Strategy to Construct Functionalized Tetrazepine Derivatives via [4＋3] Annulation Reaction of Azomethine Imine with Azadiene Precursor

Zhang, Xiaoke*,a,c Zheng, Xiangru b Wang, Chaoyong*,a
(a *Central Laboratory*, *Chongqing University Fuling Hospital*, *Chongqing 408000*)
(b *The Third Affiliated Hospital of Chongqing Medical University*, *Chongqing 401120*)
(c *Zunyi Medical University*, *Guizhou 563006*)

Abstract Tetrazepine derivative exhibits good biological activities. Only a limited method has been devoted to constructing these frameworks to date. Therefore, an efficient and novel way was established for the synthesis of functionalized tetrazepine scaffolds through the cycloaddition reaction of azomethine imine with 1,2-azadiene formed *in situ* by α-halogeno hydrazones in the presence of KOH. This transformation shows excellent functional group tolerance and substrate scope.

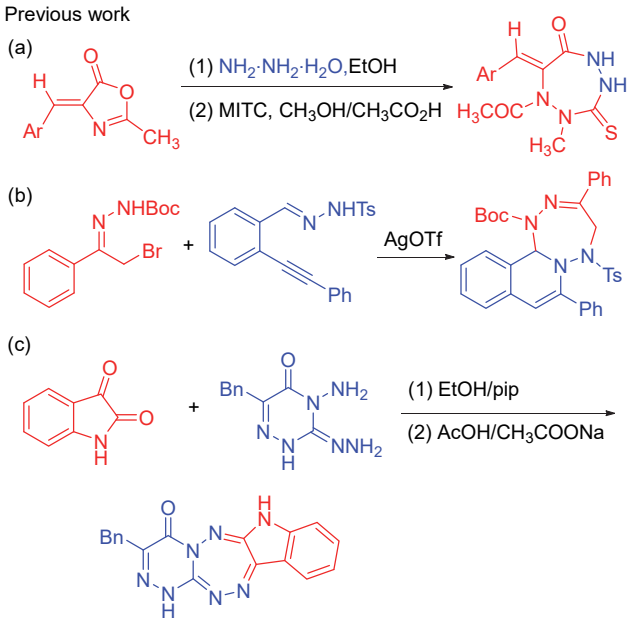
Keywords α-halogeno hydrazone; azomethine imine; tetrazepine derivative; azadiene precursor

1 Introduction

Nitrogen-containing heterocyclic skeletons show interesting medicinally significant biological activities.[1] For example, di-nitrogen fused heterocyclic derivatives with broad-spectrum inhibitory activity have been reported.[2] Triazepine frameworks possess antipsychotic, analgesic, and antisecretory activities.[3] Tetrazepine derivatives are promising candidates as the antimicrobial, hypnotic agent.[4-5] Therefore, a wide range of powerful strategies have been developed to construct these compounds bearing multiple nitrogen atoms. For instance, Tetrazepine scaffolds were prepared through the condensation between hydrazine hydrate and carbonyl, multistep synthesis, or annulation.[5-6] However, compared to five or six-membered rings, these methods for synthesizing seven-membered fused heterocyclic skeletons containing four or more heteroatoms are very rare, which is limited by the enthalpic and entropic factors.[7] Recently, Kumari's group[8] disclosed an efficient approach to provide l,2,4,5-tetraazaperhydroepin by two steps using 2-methyl oxazolin-5-one as substrate in the presence of hydrazine hydrate and methyl isothiocyanate (MITC) (Scheme 1a). Gong and coworkers[9] realized an [4＋3] annulation reaction between α-halogeno hydrazones and *C,N*-cyclic azomethine imines giving biologically important tetrazepine derivatives

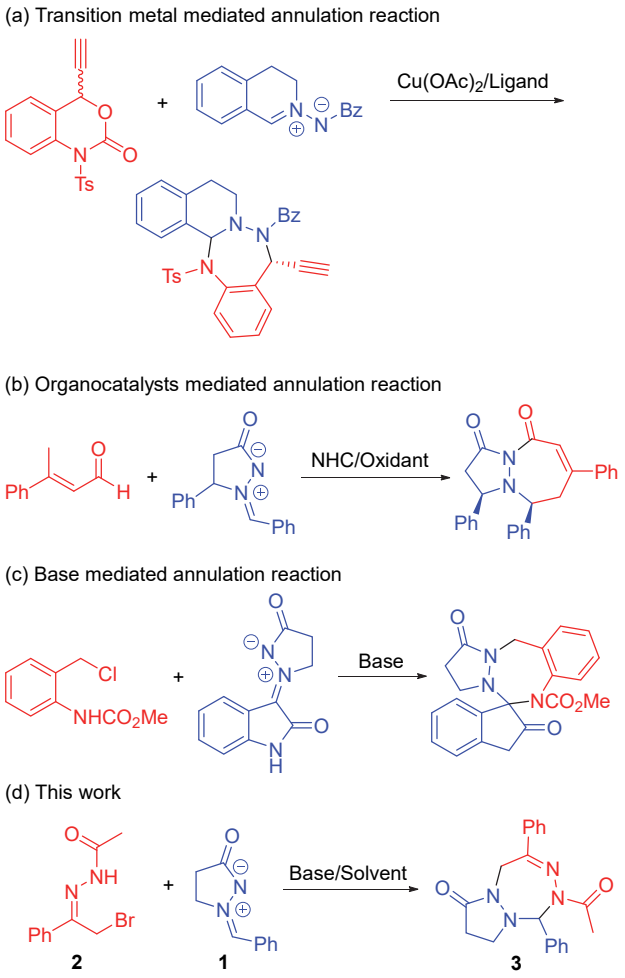
* Corresponding authors. E-mail: cqwchy@sina.com; xiaokezhang53@163.com
Received March 21, 2023; revised May 15, 2023; published online June 6, 2023.
Project supported by the Guizhou Provincial Science and Technology Plan Program (No. QKHJC-ZK[2023]-495) and the Chongqing Natural Science Foundation (No. cstc2021jcyj-bsh0010).
贵州省科技厅基础研究计划(No. QKHJC-ZK[2023]-495)和重庆市自然科学基金(No. cstc2021jcyj-bsh0010)资助项目.

(Scheme 1b). In addition, 1,2,4-triazine skeletons which show antimicrobial and cytotoxic activities, have been obtained by Zoorob's group[5c] through a condensation reaction (Scheme 1c). Although some methods have been developed, exploring a practical and efficient strategy constructing heterocyclic skeletons with multiple heteroatoms is of great value.



Scheme 1 Synthesis of seven-membered heterocyclic skeleton bearing four heteroatoms

Azomethine imine has been proven as an attractive building block,[10] since Huisgen *et al.*[10a] revealed the concept of 1,3-dipolar annulation in 1960. For example, a [3+2] cycloaddition reaction of azomethine imine could offer the tricyclic chromenopyrazole, spirocyclic amine, and cyclopenta[*c*]pyrazole.[11] Besides, tricyclic dinitrogen-fused, quinazoline-based, and [2,3]-fused indoline *O*-heterocycle, tricyclic 1,2,4-hexahydrotriazine, and isoquinoline-fused triazine scaffold could be generated by the [3+3] annulation of azomethine imine with ynone, Morita-Baylis-Hillman carbonate, vinyl aziridine, indole, and azaoxallyl cation.[12] Meanwhile, various seven-membered rings could be achieved through [4+3] cycloaddition. These methods were divided into the following issue: (1) Transition metal-mediated annulation reaction.[13] In 2018, Jiang and co-workers[13b] reported a decarboxylative cycloaddition strategy catalyzed by $Cu(OAc)_2$ using *C,N*-cyclic azomethine imine and allenylidene precursor as substrates (Scheme 2a). (2) Organocatalyst-mediated annulation reaction.[14] *N*-Heterocyclic carbene-mediated annulation of enal with azomethine imine has been developed for the synthesis of bioactive dinitrogen-fused heterocycle in the presence of oxidant (Scheme 2b).[14f] (3) Base-mediated annulation reaction.[15] Hu's group[15a] established a way to provide triazepine derivatives through [3+4] annulation of isatin *N,N'*-cyclic azomethine imine with *aza-o*QMs promoted by cesium carbonate (Scheme 2c).



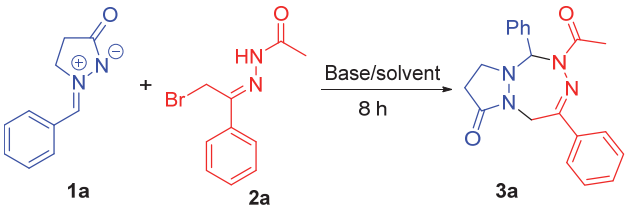
Scheme 2 Annulation of azomethine imines with C4 synthons

α-Halogeno hydrazone is a promising molecular block to construct *N*-containing heterocycle framework through [4+1], [4+2], and [4+3] annulation reactions.[16] To date, the cycloaddition reactions of azadiene precursors with dipoles have been rarely developed. For instance, Xiao's group[14h] disclosed the annulation of *C,N*-cyclic azomethine imine with azoalkene precursor affording the tetrazepine derivatives. In 2016, Zhao's group[17] reported a method to construct 1,2,4,5-oxatriazepine via an annulation of nitrone with *α*-halogeno hydrazones. In the same year, the [4+3] cycloaddition of phthalazinium dicyanomethanides was found by Guo's group.[14i] Later, Zhai's group[18] utilized pyridinium 1,4-zwitterionic thiolates and *α*-halogeno hydrazones as substrates furnishing 1,4,5-thiadiazepines skeletons. Besides, the cycloaddition of *C,N*-cyclic azomethine imines formed *in situ* with *α*-halogeno hydrazones offering tetrazepine derivatives has been developed.[9] Encouraged by the above research, we envisioned that tetrazepine framework could be obtained through [4+3] cycloaddition reaction utilizing azomethine imines and *α*-halogeno hydrazone as substrates (Scheme 2d).

2 Results and discussion

Initially, azomethine imine **1a** and *N'*-(2-bromo-1-phenylethylidene) acetohydrazide **2a** were selected as model substrates which were dissolved in dichloromethane (DCM) at room temperature with Na_2CO_3 as an additive. After 8 h, this process was completed, and the expected product **3a** was obtained with a low yield (Entry 1). In order to further improve the yield of **3a**, the reaction condition has been optimized. As shown in Table 1, the chemical yield of this cycloaddition product was dramatically influenced by the base. When different inorganic bases were used, **3a** was produced in 36%～79% yields (Table 1, Entries 2～6). In addition, organic base triethylamine (TEA), 1,4-diazabicyclo[2.2.2]octane (TEDA) could not promote this process (Table 1, Entries 7～8). Moreover, a similar result was obtained using K_2CO_3 or KOH as an additive affording **3a** in 73%, 79% yields, respectively (Table 1, Entry 3 and Entry 5). Meanwhile, the strength of screened bases has a significant effect on the chemical yields of **3a** (Table 1, Entries 2～6). Based on these results, KOH was a better choice for this process. Next, the solvent was screened. Using Et_2O as a solvent, **3a** was provided in 57% yield (Table 1, Entry 9). Compared with *N*,*N*-dimethylformamide (DMF) as a solvent, the yield increased using $CHCl_3$ or MeCN (Table 1, Entries 10～12). To our delight, when this reaction was performed in tetrahydrofuran (THF), **3a** was provided in 91% yield (Table 1, Entry 13). Furthermore, increasing or decreasing temperature could not improve the yield of **3a** (Table 1, Entries 15～16). Therefore, the optimal reaction conditions for this transformation were that *n*(**1a**)∶*n*(**2a**)∶*n*(KOH) was 1.5∶1∶2, and THF was used as solvent.

Table 1 Optimization of reaction conditions[a]



Entry	Base	Solvent	Yield[b]/%
1	Na_2CO_3	CH_2Cl_2	36
2	Cs_2CO_3	CH_2Cl_2	51
3	K_2CO_3	CH_2Cl_2	73
4	Na_2CO_3	CH_2Cl_2	64
5	KOH	CH_2Cl_2	79
6	KO^{t}Bu	CH_2Cl_2	42
7	TEDA	CH_2Cl_2	Trace
8	TEA	CH_2Cl_2	Trace
9	KOH	Et_2O	57
10	KOH	$CHCl_3$	72
11	KOH	MeCN	75
12	KOH	DMF	63
13	KOH	THF	91
14	KOH	EtOAc	60
15[c]	KOH	THF	56
16[d]	KOH	THF	89

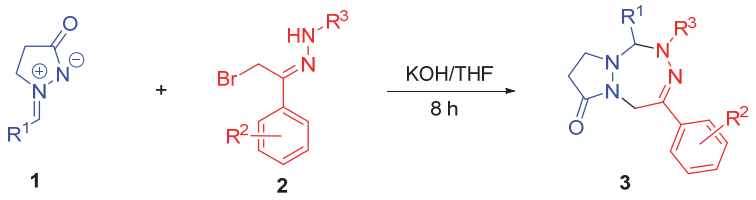
[a] Reaction conditions: **1a** (0.15 mmol), **2a** (0.1 mmol), and base (0.2 mmol) were reacted in solvent (2 mL) at room temperature. [b] Isolated yield based on **2a**. [c] Reaction was performed at 0 ℃. [d] Reaction was performed at 70 ℃.

With the optimized experimental conditions in hand, the scope of substrate was examined. These representative results were summarized in Table 2. Obviously, the azomethine imine containing Cl substituent on the phenyl ring provided a better yield of cycloaddition product **3b**. Thus, it was selected as a model substrate. *α*-Halogeno hydrazones bearing different kinds of substituents, such as Br, F, NO_2, CN, and Cl could efficiently react with azomethine imine bearing Cl substituent on the phenyl ring under the optimized conditions, delivering the expected products in good to excellent yields (79%～88%). Strong electron absorption ability made the yield of **3d** slightly decreased. Meanwhile, the substrate featuring Cl or Br on the 3 or 4 position of phenyl ring was also tolerated with this transformation, offering the corresponding annulation products **3g** and **3h** in 81% and 82% yields, respectively. Significantly, the halogen substituted aryl rings provide an opportunity for cross-coupling type transformations (**3c**, **3d**, **3f**, **3g**, **3h**, **3i**). It was observed that disubstituted *α*-halogeno hydrazone could undergo [4＋3] cycloaddition reaction forming the desired **3i** in 79% yield. Furthermore, **1** bearing electron donating group such as Me, OMe, could also be applied to this transformation, the cycloaddition product **3j**, **3k** were obtained in 85%～87% yields. Moreover, tetrazepine skeleton bearing naphthyl **3l** could be achieved via this process. Subsequently, substrate scope of azomethine imines was tested. Employing Br, CF_3, Me, MeO in place of Cl of **1** also furnished the expected **3m**, **3n**, **3o** and **3p** in good yields. Fused substituted azomethine imine also performed well, affording **3q** in 57% yield, where the naphthalene influenced the progress of cyclization leading to the low yield. It is noteworthy that using *α*-halogeno *p*-toluene-sulfonyl hydrazone as C4 synthon to react with nitrone could not give the [4＋3] annulation product.[17] To our surprise, azadiene could be generated by *α*-halogeno *p*-toluenesulfonyl hydrazone *in situ* which underwent [4＋3] annulation with azomethine imines furnishing the analogue of tetrazepine derivatives in 46%～67% yields in this process.

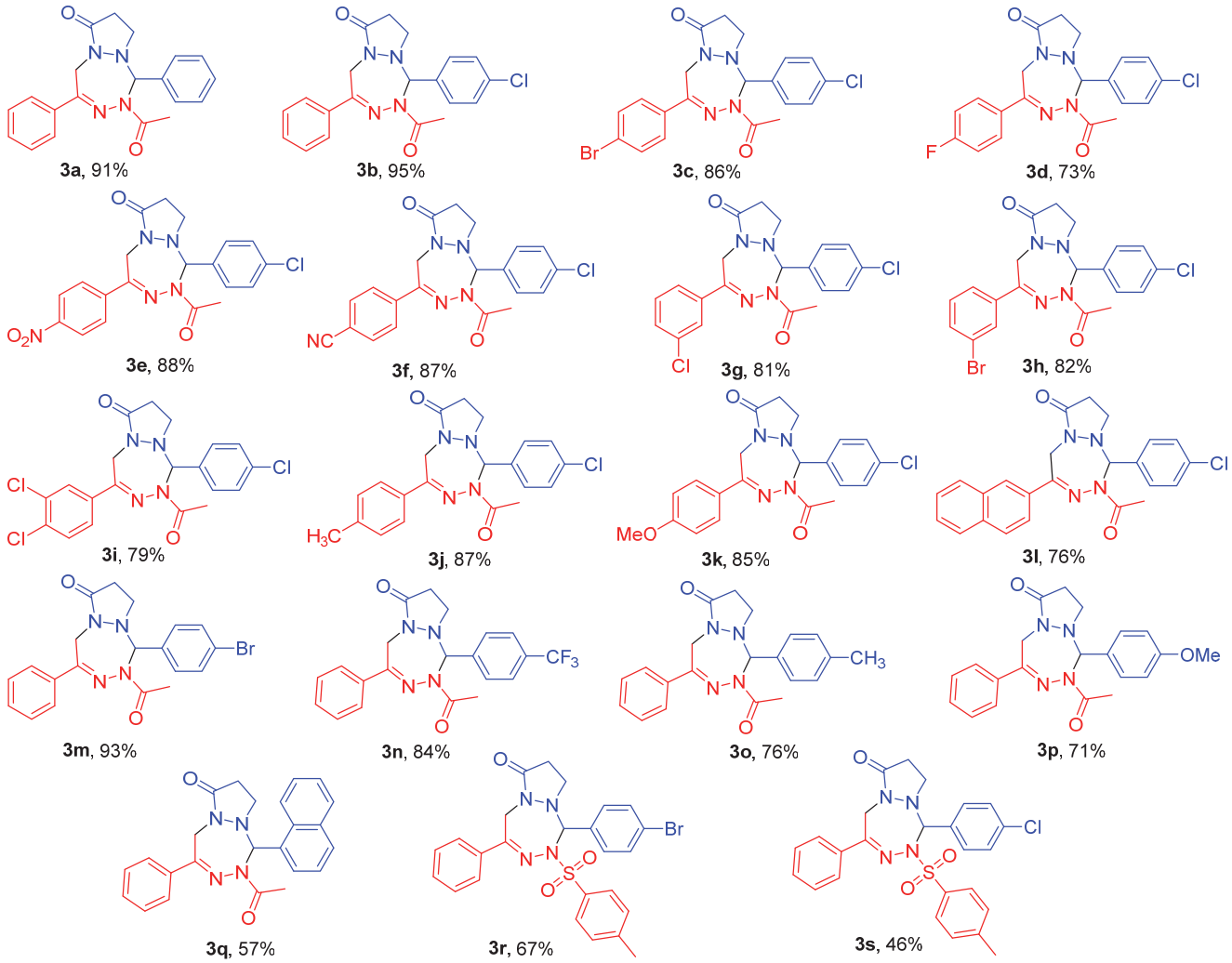
A postulated reaction pathway was illustrated in Scheme 3. KOH-trigged 1,4-elimination of *α*-halo hydrazone **2a** generated the 1,2-diazadiene intermediate **Int 1** *in situ*.[16-19] The azomethine imine **1a** then trapped the 1,2-diazadiene intermediate **Int 1** affording the tetrazepine derivative through continuous C—N bond formation.

To further demonstrate the application of this transformation. A gram-scale experiment has been performed (Scheme 4). *α*-Halo hydrazone **2a** (5 mmol) and azomethine imine **1a** (7.5 mmol) were treated with KOH (10 mmol) under optimal reaction condition, providing **3a** (1.55 g) in 89% yield.

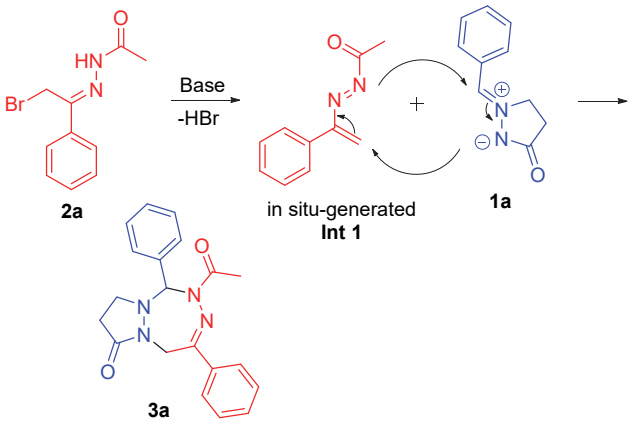
Table 2 Scope with various α-halogeno hydrazones and azomethine imines[a]



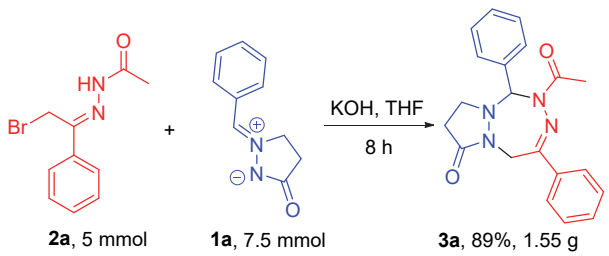
1 2 3



[a] Reaction conditions: **1** (0.15 mmol), **2** (0.1 mmol), and KOH (0.2 mmol) were reacted in THF (2 mL) at room temperature. [b] Isolated yield based on **2**.



Scheme 3 Postulated reaction pathway



Scheme 4 Gram-scale experiment of this process

3 Conclusions

In conclusion, the [4+3] annulation reaction of α-halo hydrazone with azomethine imine promoted by KOH has been realized affording tetrazepine derivatives through the

simultaneous construction of C—N bond process with good to excellent yield. This transformation was performed under precise metal-free, catalyst-free condition, and exhibited a broad substrate compatibility. It is noteworthy that *α*-halogeno *p*-toluenesulfonyl hydrazone was also tolerated in this transformation. Further applications of tetrazepine derivatives in pharmacology will be explored.

4 Experimental section

4.1 General information

All reactions were carried out in the air. All reagents were purchased from commercial suppliers and used without further purification unless otherwise noted. Thin-layer chromatography was performed using silica gel GF254 precoated plates (0.20～0.25 mm thickness) with a fluorescent indicator. Visualization on thin-layer chromatography (TLC) was achieved by UV light (254 nm). Column chromatography was performed on silica gel 90, 200～300 mesh. ^{1}H NMR and ^{13}C NMR (400 and 101 MHz, respectively) spectra were recorded on a Bruker Avance 400 spectrometer. ^{1}H NMR chemical shifts were relative to tetramethylsilane (TMS) with the solvent resonance employed as the internal standard ($CDCl_3$, δ 7.26 ppm). ^{13}C NMR chemical shifts were relative to tetramethylsilane (TMS) with the solvent resonance as the internal standard ($CDCl_3$, δ 77.16). High resolution mass spectra (HRMS) were obtained using a fourier transfer ion cyclotron resonance (FTICR) mass spectrometer and electrospray ionization (ESI).

4.2 General synthesis of 1,2,4,5-tetrazepine derivatives

To the solution of azomethine imine **1** (0.15 mmol) in THF, *N*-acetyl-*α*-chlorohydrazone **2** (0.1 mmol) and KOH (0.2 mmol) were added at room temperature. The mixture was stirred at room temperature for 8 h. After **2** completed monitored by TLC, the solvent was removed under reduced pressure. The crude product was purified by column chromatography [*V*(petroleum) ∶ *V*(EtOAc) = 4 ∶ 1] to give the expected **3**.

2-Acetyl-1,4-diphenyl-2,5,8,9-tetrahydro-1*H*,7*H*-pyrazolo[1,2-*a*][1,2,4,5]tetrazepin-7-one (**3a**): Colorless oil, 31 mg, 91% yield. ^{1}H NMR (400 MHz, Chloroform-*d*) *δ*: 7.49 (d, *J*=4.0 Hz, 2H), 7.44 (d, *J*=8.0 Hz, 2H), 7.37～7.29 (m, 5H), 7.25 (d, *J*=8.0 Hz, 1H), 7.20 (s, 1H), 5.34 (d, *J*=16.0 Hz, 1H), 3.74～3.66 (m, 2H), 3.35 (q, *J*=8.0 Hz, 1H), 2.71～2.65 (m, 2H), 2.57 (s, 3H); ^{13}C NMR (101 MHz, Chloroform-*d*) *δ*: 175.5, 169.0, 151.5, 136.6, 135.1, 130.2, 128.5, 128.4, 128.2, 126.6, 126.5, 76.5, 49.4, 45.4, 31.0, 22.0; HRMS (ESI) calcd for $C_{20}H_{21}N_4O_2$ $[M+H]^+$ 349.1659, found 349.1656.

2-Acetyl-1-(4-chlorophenyl)-4-phenyl-2,5,8,9-tetrahydro-1*H*,7*H*-pyrazolo[1,2-*a*][1,2,4,5]tetrazepin-7-one (**3b**): Colorless oil, 36 mg, 95% yield. ^{1}H NMR (400 MHz, DMSO-d_6) *δ*: 7.59 (d, *J*=8.0 Hz, 2H), 7.41～7.32 (m, 7H), 7.08 (s, 1H), 5.14 (d, *J*=20.0 Hz, 1H), 3.74～3.66 (m, 2H), 3.33～3.18 (m, 1H), 2.55～2.46 (m, 2H), 2.44 (s, 3H); ^{13}C NMR (101 MHz, DMSO-d_6) *δ*: 174.8, 169.8, 151.2, 136.4, 135.1, 133.0, 130.7, 129.0, 128.9, 128.8, 126.6, 76.6, 49.6, 45.5, 30.4, 22.1; HRMS (ESI) calcd for $C_{20}H_{19}ClN_4O_2Na$ $[M+Na]^+$ 405.1089, found 405.1081.

2-Acetyl-4-(4-bromophenyl)-1-(4-chlorophenyl)-2,5,8,9-tetrahydro-1*H*,7*H*-pyrazolo[1,2-*a*][1,2,4,5]tetrazepin-7-one (**3c**): Colorless oil, 39 mg, 86% yield. ^{1}H NMR (400 MHz, Chloroform-*d*) *δ*: 7.45 (d, *J*=8.0 Hz, 2H), 7.39～7.35 (m, 4H), 7.28 (d, *J*=8.0 Hz, 2H), 7.14 (s, 1H), 5.31 (d, *J*=16.0 Hz, 1H), 3.74～3.69 (m, 1H), 3.60 (d, *J*=20.0 Hz, 1H), 3.33 (q, *J*=12.0 Hz, 1H), 2.69～2.64 (m, 2H), 2.55 (s, 3H); ^{13}C NMR (101 MHz, Chloroform-*d*) *δ*: 175.3, 169.1, 150.4, 135.1, 134.2, 133.6, 131.7, 128.8, 128.0, 127.8, 125.0, 76.1, 49.4, 45.0, 30.9, 21.9; HRMS (ESI) calcd for $C_{20}H_{18}BrClN_4O_2Na$ $[M+Na]^+$ 483.0194, found 483.0198.

2-Acetyl-1-(4-chlorophenyl)-4-(4-fluorophenyl)-2,5,8,9-tetrahydro-1*H*,7*H*-pyrazolo[1,2-*a*][1,2,4,5]tetrazepin-7-one (**3d**): Colorless oil, 29 mg, 73% yield. ^{1}H NMR (400 MHz, Chloroform-*d*) *δ*: 7.47～7.44 (m, 2H), 7.32 (d, *J*=8.0 Hz, 2H), 7.23 (d, *J*=8.0 Hz, 2H), 7.09 (s, 1H), 6.96 (t, *J*=8.0 Hz, 2H), 5.27 (d, *J*=16.0 Hz, 1H), 3.68～3.63 (m, 1H), 3.55 (d, *J*=20.0 Hz, 1H), 3.28 (q, *J*=12.0 Hz, 1H), 2.64～2.59 (m, 2H), 2.49 (s, 3H); ^{13}C NMR (101 MHz, Chloroform-*d*) *δ*: 175.3, 169.1, 165.2, 162.7, 150.5, 135.2, 134.2, 130.9 (d, *J*=4.0 Hz), 128.7 (d, *J*=29.0 Hz), 128.5 (d, *J*=27.0 Hz),115.6 (d, *J*=22.0 Hz), 76.1, 49.4, 45.2, 30.9, 21.9; HRMS (ESI) calcd for $C_{20}H_{18}ClFN_4O_2Na$ $[M+Na]^+$ 423.0995, found 423.0991.

2-Acetyl-1-(4-chlorophenyl)-4-(4-nitrophenyl)-2,5,8,9-tetrahydro-1*H*,7*H*-pyrazolo[1,2-*a*][1,2,4,5]tetrazepin-7-one (**3e**): Colorless oil, 37 mg, 88% yield. ^{1}H NMR (400 MHz, Chloroform-*d*) *δ*: 8.19 (d, *J*=8.0 Hz, 2H), 7.68 (d, *J*=8.0 Hz, 2H), 7.37～7.27 (m, 4H), 7.18 (s, 1H), 5.34 (d, *J*=16.0 Hz, 1H), 3.78～3.67 (m, 2H), 3.34 (q, *J*=12.0 Hz, 1H), 2.72～2.66 (m, 2H), 2.60 (s, 3H); ^{13}C NMR (101 MHz, Chloroform-*d*) *δ*: 175.3, 169.1, 148.6, 148.6, 140.6, 134.9, 134.5, 128.9, 127.9, 127.1, 123.7, 76.2, 49.4, 45.0, 30.8, 21.9; HRMS (ESI) calcd for $C_{20}H_{18}ClN_5O_4Na$ $[M+Na]^+$ 450.0940, found 450.0943.

4-(2-Acetyl-1-(4-chlorophenyl)-7-oxo-2,5,8,9-tetrahydro-1*H*,7*H*-pyrazolo[1,2-*a*][1,2,4,5]tetrazepin-4-yl)benzonitrile (**3f**): Colorless oil, 35 mg, 87% yield. ^{1}H NMR (400 MHz, Chloroform-*d*) *δ*: 7.62 (s, 4H), 7.36～7.27 (m, 4H), 7.17 (s, 1H), 5.31 (d, *J*=16.0 Hz, 1H), 3.76～3.71 (m, 1H), 3.65 (d, *J*=16.0 Hz, 1H), 3.33 (q, *J*=12.0 Hz, 1H), 2.71～2.64 (m, 2H), 2.58 (s, 3H); ^{13}C NMR (101 MHz, Chloroform-*d*) *δ*: 175.3, 169.0, 148.9, 138.9, 134.9, 134.4, 132.3, 128.9, 127.9, 126.8, 118.0, 113.7, 76.2, 49.4, 44.9, 30.8, 21.9; HRMS (ESI) calcd for $C_{21}H_{18}ClN_5O_2Na$ $[M+Na]^+$ 430.1041, found 430.1040.

2-Acetyl-4-(3-chlorophenyl)-1-(4-chlorophenyl)-2,5,8,9-tetrahydro-1*H*,7*H*-pyrazolo[1,2-*a*][1,2,4,5]tetrazepin-7-one (**3g**): Colorless oil, 33 mg, 81% yield. ^{1}H NMR (400 MHz, Chloroform-*d*) *δ*: 7.51 (s, 1H), 7.37～7.24 (m, 7H), 7.15 (s, 1H), 5.31 (d, *J*=16.0 Hz, 1H), 3.74～3.69 (m, 1H), 3.62 (d, *J*=16.0 Hz, 1H), 3.33 (q, *J*=12.0 Hz, 1H), 2.70～2.64

(m, 2H), 2.58 (s, 3H); ^{13}C NMR (101 MHz, Chloroform-*d*) *δ*: 175.3, 169.0, 149.8, 136.4, 135.1, 134.6, 134.3, 130.4, 129.8, 128.8, 128.0, 126.4, 124.4, 76.1, 49.4, 45.1, 30.9, 22.0; HRMS (ESI) calcd for $C_{20}H_{18}Cl_2N_4O_2Na$ $[M+Na]^+$ 439.0699, found 439.0695.

2-Acetyl-4-(3-bromophenyl)-1-(4-chlorophenyl)-2,5,8,9-tetrahydro-1*H*,7*H*-pyrazolo[1,2-*a*][1,2,4,5]tetrazepin-7-one (**3h**): Colorless oil, 38 mg, 82% yield. ^{1}H NMR (400 MHz, Chloroform-*d*) *δ*: 7.66 (s, 1H), 7.51 (d, *J*=8.0 Hz, 1H), 7.42 (d, *J*=8.0 Hz, 1H), 7.36 (d, *J*=8.0 Hz, 2H), 7.30 (d, *J*=8.0 Hz, 2H), 7.20 (t, *J*=8.0 Hz, 1H), 7.15 (s, 1H), 5.30 (d, *J*=16.0 Hz, 1H), 3.75～3.69 (m, 1H), 3.61 (d, *J*=20.0 Hz, 1H), 3.33 (q, *J*=12.0 Hz, 1H), 2.70～2.64 (m, 2H), 2.57 (s, 3H); ^{13}C NMR (101 MHz, Chloroform-*d*) *δ*: 175.4, 169.1, 149.7, 136.7, 135.1, 134.3, 133.3, 130.0, 129.3, 128.8, 128.0, 124.9, 122.7, 76.1, 49.4, 45.1, 30.9, 22.0; HRMS (ESI) calcd for $C_{20}H_{18}ClBrN_4O_2Na$ $[M+Na]^+$ 483.0194, found 483.0191.

2-Acetyl-1-(4-chlorophenyl)-4-(3,4-dichlorophenyl)-2,5,8,9-tetrahydro-1*H*,7*H*-pyrazolo[1,2-*a*][1,2,4,5]tetrazepin-7-one (**3i**): Colorless oil, 35 mg, 79% yield. ^{1}H NMR (400 MHz, Chloroform-*d*) *δ*: 7.61 (d, *J*=4.0 Hz, 1H), 7.41～7.27 (m, 6H), 7.15 (s, 1H), 5.28 (d, *J*=16.0 Hz, 1H), 3.75～3.69 (m, 1H), 3.60 (d, *J*=16.0 Hz, 1H), 3.37～3.29 (m, 1H), 2.70～2.63 (m, 2H), 2.57 (s, 3H); ^{13}C NMR (101 MHz, Chloroform-*d*) *δ*: 175.3, 169.1, 148.8, 135.0, 134.7, 134.5, 134.4, 133.0, 130.5, 128.9, 128.1, 128.0, 125.3, 76.2, 49.4, 44.9, 30.8, 21.9; HRMS (ESI) calcd for $C_{20}H_{17}Cl_3N_4O_2Na$ $[M+Na]^+$ 473.0309, found 473.0308.

2-Acetyl-1-(4-chlorophenyl)-4-(*p*-tolyl)-2,5,8,9-tetrahydro-1*H*,7*H*-pyrazolo[1,2-*a*][1,2,4,5]tetrazepin-7-one (**3j**): Colorless oil, 34 mg, 87% yield. ^{1}H NMR (400 MHz, Chloroform-*d*) *δ*: 7.34 (dd, *J*=16.0, 8.0 Hz, 4H), 7.22 (d, *J*=8.0 Hz, 2H), 7.09～7.07 (m, 3H), 5.31 (d, *J*=16.0 Hz, 1H), 3.67～3.62 (m, 1H), 3.54 (d, *J*=16.0 Hz, 1H), 3.28 (q, *J*=12.0 Hz, 1H), 2.63～2.59 (m, 2H), 2.49 (s, 3H), 2.28 (s, 3H); ^{13}C NMR (101 MHz, Chloroform-*d*) *δ*: 175.4, 169.1, 151.8, 140.8, 135.3, 134.1, 131.9, 129.2, 128.7, 128.2, 126.4, 76.0, 49.4, 45.2, 31.0, 21.9, 21.2; HRMS (ESI) calcd for $C_{21}H_{21}ClN_4O_2Na$ $[M+Na]^+$ 419.1245, found 419.1240.

2-Acetyl-1-(4-chlorophenyl)-4-(4-methoxyphenyl)-2,5,8,9-tetrahydro-1*H*,7*H*-pyrazolo[1,2-*a*][1,2,4,5]tetrazepin-7-one (**3k**): Colorless oil, 35 mg, 85% yield. ^{1}H NMR (400 MHz, DMSO-d_6) *δ*: 7.56 (d, *J*=8.0 Hz, 2H), 7.37 (q, *J*=8.0 Hz, 4H), 7.05 (s, 1H), 6.88 (d, *J*=8.0 Hz, 2H), 5.14 (d, *J*=16.0 Hz, 1H), 3.72 (s, 3H), 3.68～3.64 (m, 2H), 3.38～3.16 (m, 1H), 2.51～2.46 (m, 2H), 2.41 (s, 3H); ^{13}C NMR (101 MHz, DMSO-d_6) *δ*: 174.6, 169.9, 161.4, 151.2, 136.5, 132.9, 129.0, 128.8, 128.3, 127.2, 114.3, 76.6, 55.7, 49.6, 45.3, 30.3, 22.1; HRMS (ESI) calcd for $C_{21}H_{21}ClN_4O_3Na$ $[M+Na]^+$ 435.1194, found 435.1192.

2-Acetyl-1-(4-chlorophenyl)-4-(naphthalen-2-yl)-2,5,8,9-tetrahydro-1*H*,7*H*-pyrazolo[1,2-*a*][1,2,4,5]tetrazepin-7-one (**3l**): Colorless oil, 33 mg, 76% yield. ^{1}H NMR (400 MHz, Chloroform-*d*) *δ*: 7.79～7.72 (m, 5H), 7.46～7.43 (m, 2H), 7.35 (d, *J*=12.0 Hz, 2H), 7.22 (d, *J*=8.0 Hz, 2H), 7.13 (s, 1H), 5.51 (d, *J*=20.0 Hz, 1H), 3.72～3.65 (m, 2H), 3.31 (q, *J*=12.0 Hz, 1H), 2.67～2.61 (m, 2H), 2.58 (s, 3H); ^{13}C NMR (101 MHz, Chloroform-*d*) *δ*: 175.4, 169.0, 151.0, 135.2, 134.1, 133.9, 132.5, 132.0, 128.7, 128.5, 128.2, 128.1, 127.5, 127.3, 126.6, 126.4, 123.2, 76.0, 49.4, 45.0, 31.0, 22.0; HRMS (ESI) calcd for $C_{24}H_{21}ClN_4O_2Na$ $[M+Na]^+$ 455.1245, found 455.1244.

2-Acetyl-1-(4-bromophenyl)-4-phenyl-2,5,8,9-tetrahydro-1*H*,7*H*-pyrazolo[1,2-*a*][1,2,4,5]tetrazepin-7-one (**3m**): Colorless oil, 40 mg, 93% yield. ^{1}H NMR (400 MHz, Chloroform-*d*) *δ*: 7.47～7.45 (m, 2H), 7.40～7.21 (m, 7H), 7.07 (s, 1H), 5.32 (d, *J*=16.0 Hz, 1H), 3.68～3.63 (m, 1H), 3.58 (d, *J*=20.0 Hz, 1H), 3.28 (q, *J*=8.0 Hz, 1H), 2.64～2.59 (m, 2H), 2.51 (s, 3H); ^{13}C NMR (101 MHz, Chloroform-*d*) *δ*: 175.4, 169.0, 151.7, 135.8, 134.8, 131.7, 130.4, 128.5, 128.4, 126.4, 122.4, 76.1, 49.4, 45.3, 30.9, 21.9; HRMS (ESI) calcd for $C_{20}H_{19}BrN_4O_2Na$ $[M+Na]^+$ 449.0584, found 449.0584.

2-Acetyl-4-phenyl-1-(4-(trifluoromethyl)phenyl)-2,5,8,9-tetrahydro-1*H*,7*H*-pyrazolo[1,2-*a*][1,2,4,5]tetrazepin-7-one (**3n**): Colorless oil, 35 mg, 84% yield. ^{1}H NMR (400 MHz, Chloroform-*d*) *δ*: 7.59 (s, 4H), 7.51～7.49 (m, 2H), 7.39～7.35 (m, 1H), 7.34～7.31 (m, 2H), 7.25 (d, *J*=20.0 Hz, 1H), 5.39 (d, *J*=16.0 Hz, 1H), 3.77～3.70 (m, 1H), 3.61 (d, *J*=16.0 Hz, 1H), 3.37 (q, *J*=12.0 Hz, 1H), 2.72～2.67 (m, 2H), 2.58 (s, 3H); ^{13}C NMR (101 MHz, Chloroform-*d*) *δ*: 175.4, 169.1, 151.8, 140.9, 134.7, 130.5, 128.5, 127.2, 126.4, 125.6, 125.5, 76.1, 49.5, 45.3, 30.9, 21.9; HRMS (ESI) calcd for $C_{21}H_{19}F_3N_4O_2Na$ $[M+Na]^+$ 439.1352, found 439.1357.

2-Acetyl-4-phenyl-1-(*p*-tolyl)-2,5,8,9-tetrahydro-1*H*,7*H*-pyrazolo[1,2-*a*][1,2,4,5]tetrazepin-7-one (**3o**): Colorless oil, 27 mg, 76% yield. ^{1}H NMR (400 MHz, Chloroform-*d*) *δ*: 7.47 (d, *J*=8.0 Hz, 2H), 7.33～7.22 (m, 5H), 7.11～7.05 (m, 3H), 5.29 (d, *J*=16.0 Hz, 1H), 3.67～3.63 (m, 2H), 3.32～3.25 (m, 1H), 2.66～2.57 (m, 2H), 2.52 (s, 3H), 2.23 (s, 3H); ^{13}C NMR (101 MHz, Chloroform-*d*) *δ*: 175.6, 168.9, 151.3, 138.0, 135.2, 133.5, 130.1, 129.2, 128.4, 126.5, 126.5, 76.4, 49.4, 45.3, 31.1, 22.0, 20.9; HRMS (ESI) calcd for $C_{21}H_{22}N_4O_2Na$ $[M+Na]^+$ 385.1635, found 385.1637.

2-Acetyl-1-(4-methoxyphenyl)-4-phenyl-2,5,8,9-tetrahydro-1*H*,7*H*-pyrazolo[1,2-*a*][1,2,4,5]tetrazepin-7-one (**3p**): Colorless oil, 27 mg, 71% yield. ^{1}H NMR (400 MHz, Chloroform-*d*) *δ*: 7.48～7.46 (m, 2H), 7.35～7.22 (m, 5H), 7.09 (s, 1H), 6.79～6.77 (m, 2H), 5.30 (d, *J*=20.0 Hz, 1H), 3.71 (s, 3H), 3.68～3.62 (m, 2H), 3.32～3.25 (m, 1H), 2.65～2.59 (m, 2H), 2.51 (s, 3H); ^{13}C NMR (101 MHz, Chloroform-*d*) *δ*: 175.5, 169.0, 159.3, 151.4, 135.2, 130.2, 128.4, 128.4, 127.9, 126.5, 113.8, 76.2, 55.1, 49.4, 45.3, 31.1, 22.0; HRMS (ESI) calcd for $C_{21}H_{22}N_4O_3Na$ $[M+Na]^+$ 401.1584, found 401.1582.

2-Acetyl-1-(naphthalen-1-yl)-4-phenyl-2,5,8,9-tetrahydro-1*H*,7*H*-pyrazolo[1,2-*a*][1,2,4,5]tetrazepin-7-one (**3q**): Colorless oil, 22 mg, 57% yield. ^{1}H NMR (400 MHz, Chloroform-*d*) *δ*: 8.09 (d, *J*=8.0 Hz, 1H), 7.84～7.67 (m,

3H), 7.51～7.41 (m, 3H), 7.30～7.21 (m, 2H), 7.18～7.05 (m, 4H), 5.34 (d, J=16.0 Hz, 1H), 4.24 (d, J=16.0 Hz, 1H), 3.74～3.68 (m, 1H), 3.58～3.33 (m, 1H), 2.82～2.74 (m, 1H), 2.56～2.50 (m, 1H), 2.26 (s, 3H); ^{13}C NMR (101 MHz, Chloroform-*d*) δ: 173.5, 171.3, 157.1, 134.1, 133.8, 132.1, 130.5, 130.2, 129.8, 128.8, 128.3, 126.7, 126.4, 126.2, 125.8, 124.2, 122.9, 50.3, 46.8, 30.5, 29.6, 21.7; HRMS (ESI) calcd for $C_{24}H_{22}N_4O_2Na$ $[M+Na]^+$ 421.1635, found 421.1638.

1-(4-Bromophenyl)-4-phenyl-2-tosyl-2,5,8,9-tetrahydro-1*H*,7*H*-pyrazolo[1,2-*a*][1,2,4,5]tetrazepin-7-one (**3r**): Colorless oil, 36 mg, 67% yield. ^{1}H NMR (400 MHz, Chloroform-*d*) δ: 7.87 (d, J=8.0 Hz, 2H), 7.41～7.38 (m, 2H), 7.34～7.22 (m, 7H), 7.01 (d, J=8.0 Hz, 2H), 6.47 (s, 1H), 5.25 (d, J=20.0 Hz, 1H), 3.70～3.64 (td, J=9.0, 3.6 Hz, 1H), 3.56～3.48 (m, 1H), 3.36 (d, J=20.0 Hz, 1H), 2.72～2.66 (m, 2H), 2.43 (s, 3H); ^{13}C NMR (101 MHz, Chloroform-*d*) δ: 168.7, 151.4, 144.9, 134.9, 134.4, 134.0, 131.5, 130.3, 129.6, 129.1, 128.7, 128.4, 126.5, 122.7, 81.2, 48.8, 45.0, 31.0, 21.7; HRMS (ESI) calcd for $C_{25}H_{23}BrN_4O_3SNa$ $[M+Na]^+$ 561.0566, found 561.0562.

1-(4-Chlorophenyl)-4-phenyl-2-tosyl-2,5,8,9-tetrahydro-1*H*,7*H*-pyrazolo[1,2-*a*][1,2,4,5]tetrazepin-7-one (**3s**): Colorless oil, 23 mg, 46% yield. ^{1}H NMR (400 MHz, Chloroform-*d*) δ: 7.85 (d, J=8.0 Hz, 2H), 7.37 (d, J=8.0 Hz, 2H), 7.30～7.20 (m, 5H), 7.05 (s, 4H), 6.47 (s, 1H), 5.25～5.20 (m, 1H), 3.67～3.62 (m, 1H), 3.49 (q, J=8.0 Hz, 1H), 3.34 (d, J=16.0 Hz, 1H), 2.70～2.67 (m, 2H), 2.40 (s, 3H); ^{13}C NMR (101 MHz, Chloroform-*d*) δ: 168.7, 151.4, 144.8, 134.4, 134.4, 134.4, 134.0, 130.3, 129.6, 128.7, 128.7, 128.5, 128.4, 126.5, 81.2, 48.8, 45.0, 31.0, 21.6; HRMS (ESI) calcd for $C_{25}H_{23}ClN_4O_3SNa$ $[M+Na]^+$ 517.1072, found 517.1078.

Supporting Information The ^{1}H NMR and ^{13}C NMR of **3**. The Supporting Information is available free of charge via the Internet at http://sioc-journal.cn/.

References

[1] For some selected examples: (a) Hu, X.; Li, D.; Chu, C.; Li, X.; Wang, X. H.; Jia, Y.; Hua, H. M.; Xu, F. X. *Int. J. Mol. Sci.* **2018**, *19*, 3403.
(b) Xiao, Y.; Gong, Q.; Wang, W. H.; Liu, F.; Kong, Q. H.; Pan, F.; Zhang, X. K.; Yu, C. Y.; Hu, S. S.; Fan, F.; Li, S. H.; Liu, Y. *Cancer Cell Int.* **2020**, *20*, 371.
(c) Dong, G. Q.; Liu, Y.; Wu, Y.; Tu, J.; Chen, S. Q.; Liu, N.; Sheng, C. Q. *Chem. Commun.* **2018**, *54*, 13535.
(d) Fu, D. J.; Li, J.; Yu, B. *Eur. J. Med. Chem.* **2021**, *214*, 113254.
(e) Abdel-Halim, M.; Sigler, S.; Racheed, N. A. S.; Hefnawy, A.; Fathalla, R. K.; Hammam, M. A.; Maher, A.; Maxuitenko, Y. L.; Keeton, A. B.; Hartmann, R. W.; Engel, M.; Piazza, G. A.; Abadi, A. H. *J. Med. Chem.* **2021**, *64*, 4462.

[2] (a) Krueger, B. W.; Fischer, R.; Bertram, H. J.; Bretschneider, T.; Boehm, S.; Krebs, A.; Schenke, T.; Santel, H. J.; Lurssen, K.; Schmidt, R. R.; Erdelen, C.; Wachendorff-Neumann, U.; Stendel, W. *EP0508126*, **1992**.
(b) Muehlebach, M.; Cederbaum, F.; Cornes, D.; Friedmann, A. A.; Glock, J.; Hall, G.; Indolese, A. F.; Kloer, D. P.; Goupil, G. L.; Maetzke, T.; Meier, H.; Schneider, R.; Stoller, A.; Szczepanski, H.; Wendeborna, S.; Widmer, H. *Pest. Manage. Sci.* **2011**, *67*, 1499.
(c) Kamata, M.; Yamashita, T.; Tokkyo Koho, J. K. *JP 2009196966*, **2009**.
(d) Kamata, M.; Yamashita, T.; Kina, A.; Tawada, M.; Endo, S.; Mizukami, A.; Sasaki, M.; Tani, A.; Nakano, Y.; Watanabe, Y.; Furuyama, N.; Funami, M.; Amano, N.; Fukatsu, K. *Bioorg. Med. Chem. Lett.* **2012**, *22*, 4769.

[3] (a) Kodato, S. I.; Wada, H.; Saito, S.; Takeda, M.; Nishibata, Y.; Aoe, K.; Date, T.; Onoda, Y.; Tamaki, H. *Chem. Pharm. Bull.* **1987**, *35*, 80.
(b) Mashevskaya, I. V.; Makhmudov, R. R.; Kuslina, L. V.; Mokrushin, I. G.; Shurov, S. N.; Maslivets, A. N. *Pharm. Chem. J.* **2012**, *45*, 660.
(c) Ibrahim, S. M.; Baraka, M. M.; El-Sabbagh, O. I.; Kothayer, H. *Med. Chem. Res.* **2013**, *22*, 1488.

[4] Almerico, A. M.; Mingoia, F.; Diana, P.; Barraja, P.; Lauria, A.; Montalbano, A.; Cirrincione, G.; Dattolo, G. *J. Med. Chem.* **2005**, *48*, 2859.

[5] (a) Gupta, C. M.; Bhaduri, A. P.; Khanna, N. M. *J. Med. Chem.* **1968**, *11*, 392.
(b) Ghorab, M. M.; Heiba, H. I.; El-gawish, M. A. *Phosphorus, Sulfur Silicon Relat. Elem.* **1995**, *106*, 85.
(c) Hamama, W. S.; El-Bana, G. G.; Shaaban, S.; Zoorob, H. H. *J. Heterocycl. Chem.* **2018**, *55*, 971.

[6] (a) Maggio, B.; Raffa, D.; Raimondi, M. V.; Cascioferro, S.; Plescia, F.; Tolomeo, M.; Barbusca, E.; Cannizzo, G.; Mancuso, S.; Daidone, G. *Eur. J. Med. Chem.* **2008**, *43*, 2386.
(b) Maggio, B.; Raffa, D.; Raimondi, M. V. *ARKIVOC* **2006**, *xv*, 120.
(c) Vahedi, H.; Rajabzadeh, G.; Farvandi, F. *Chin. Chem. Lett.* **2010**, *21*, 1419.
(d) Darehkordi, A.; Khorasani, F. N.; Mohammadi, M.; Kazemi, E. *Monatsh. Chem.* **2020**, *151*, 1835.

[7] For selected examples, see: (a) Zhou, M. B.; Song, R. J.; Wang, C. Y.; Li, J. H. *Angew. Chem., Int. Ed.* **2013**, *52*, 10805.
(b) Feng, J. J.; Lin, T. Y.; Wu, H. H.; Zhang, J. L. *J. Am. Chem. Soc.* **2015**, *137*, 3787.
(c) Liu, L. L.; Chiu, P. *Chem. Commun.* **2011**, *47*, 3416.
(d) Gao, H. Y.; Wu, X. X.; Zhang, J. L. *Chem. Commun.* **2010**, *46*, 8764.

[8] Kumari, Y. B. *Heterocycl. Commun.* **2007**, *13*, 177.

[9] Li, Z. F.; Li, S. K.; Kan, T. J.; Wang, X. Y.; Xin, X.; Hou, Y. L.; Gong, P. *Adv. Synth. Catal.* **2020**, *362*, 2626.

[10] (a) Huisgen, R.; Fleischmann, R.; Eckell, A. *Tetrahedron Lett.* **1960**, *1*, 1.
(b) Breugst, M.; Reissig, H. U. *Angew. Chem., Int. Ed.* **2020**, *59*, 12293.
(c) Yue, G. Z.; Liu, B. *Chin. J. Org. Chem.* **2020**, *40*, 3132 (in Chinese).
(乐贵洲, 刘波, 有机化学, **2020**, *40*, 3132.)

[11] (a) Bakthadoss, M.; Agarwal, V. *ChemistrySelect* **2018**, *3*, 6960.
(b) Choi, A.; Castle, J.; Saruengkhanphasit, R.; Coldham, I. *Synthesis* **2020**, 1273.
(c) Sandmeier, T.; Sievertsen, N.; Carreira, E. M. *Helv. Chim. Acta* **2020**, *103*, e2000058.

[12] (a) Li, Z.; Yu, H.; Liu, Y.; Zhou, L.; Sun, Z.; Guo, H. *Adv. Synth. Catal.* **2016**, *358*, 1880.
(b) Zhou, L.; Yuan, C.; Zhang, C.; Zhang, L.; Gao, Z.; Wang, C.; Liu, H.; Wu, Y.; Guo, H. *Adv. Synth. Catal.* **2017**, *359*, 2316.
(c) Zhu, C. Z.; Feng, J. J.; Zhang, J. *Chem. Commun.* **2017**, *53*, 4688.
(d) Yu, L.; Zhong, Y.; Yu, J.; Gan, L.; Cai, Z.; Wang, R.; Jiang, X. *Chem. Commun.* **2018**, *54*, 2353.
(e) Cheng, X.; Cao, X.; Xuan, J.; Xiao, W. J. *Org. Lett.* **2018**, *20*, 52.

[13] (a) Wei, L.; Wang, Z. F.; Yao, L.; Qiu, G. F.; Tao, H. Y.; Li, H.; Wang, C. J. *Adv. Synth. Catal.* **2016**, *358*, 3955.
(b) Wang, Y. F.; Zhu, L. P.; Wang, M. R.; Xiong, J.; Chen, N. N.; Feng, X.; Xu, Z. Q.; Jiang, X. X. *Org. Lett.* **2018**, *20*, 6506.

[14] (a) Li, Z.; Feng, Y. L.; Hou, Z. F.; Zhang, L.; Yang, W. J.; Wu, Y.; Xiao, Y. M.; Guo, H. C. *RSC Adv.* **2015**, *5*, 34481.
(b) Mei, G. J.; Zhu, Z. Q.; Zhao, J. J.; Bian, C. Y.; Chen, J.; Chen, R. W.; Shi, F. *Chem. Commun.* **2017**, *53*, 2768.
(c) Li, C.; Wang, C. S.; Li, T. Z.; Mei, G. J.; Shi, F. *Org. Lett.* **2019**, *21*, 598.
(d) Yuan, C. H.; Zhou, L. J.; Xia, M. R.; Sun, Z. H.; Wang, D. Q.; Guo, H. C. *Org. Lett.* **2016**, 18, 5644.
(e) Na, R.; Jing, C.; Xu, Q.; Jiang, H.; Wu, X.; Shi, J. *J. Am. Chem. Soc.* **2011**, *133*, 13341.
(f) Wang, M.; Huang, Z. J.; Xu, J. F.; Chi, Y. R. *J. Am. Chem. Soc.* **2014**, *136*, 1214.
(g) Na, R.; Jing, C. F.; Xu, Q. H.; Jiang, H.; Wu, X.; Shi, J. Y.; Zhong, J. C.; Wang, M.; Benitez, D.; Tkatchouk, E.; Goddard, W. A.; Guo, H. C.; Kwon, O. *J. Am. Chem. Soc.* **2011**, *133*, 13337.
(h) Hu, X. Q.; Chen, J. R.; Gao, S.; Feng, B.; Lu, L. Q.; Xiao, W. J. *Chem. Commun.* **2013**, *49*, 7905.
(i) Yang, W. J.; Yuan, C. H.; Liu, Y.; Mao, B. M.; Sun, Z. H.; Guo, H. C. *J. Org. Chem.* **2016**, *81*, 7597.

[15] (a) Jin, Q.; Zhang, J.; Jiang, C.; Zhang, D.; Gao, M.; Hu, S. *J. Org. Chem.* **2018**, *83*, 8410.
(b) Hu, X. Q.; Chen, J. R.; Gao, S.; Feng, B.; Lu, L. Q.; Xiao, W. J. *Chem. Commun.* **2013**, *49*, 7906.
(c) Zhi, Y.; Zhao, K.; Shu, T.; Enders, D. *Synthesis* **2016**, *48*, 240.
(d) Chen, L.; Yang, G. M.; Wang, J.; Jia, Q. F.; Wei, J.; Du, Z. Y. *RSC Adv.* **2015**, *5*, 76697.

[16] For selected examples, see: (a) Zhang, X. K.; Pan, Y.; Wang, H. B.; Liang, C.; Ma, X. F.; Jiao, W.; Shao, H. W. *Adv. Synth. Catal.* **2021**, *363*, 459.
(b) Chen, J. R.; Dong, W. R.; Candy, M.; Pan, F. F.; Jörres, M.; Bolm, C. *J. Am. Chem. Soc.* **2012**, *134*, 6924.
(c) Huang, R.; Chang, X.; Li, J.; Wang, C. J. *J. Am. Chem. Soc.* **2016**, *138*, 3998.
(d) Quan, B. X.; Zhuo, J. R.; Zhao, J. Q.; Zhang, M. L.; Zhou, M. Q.; Zhang, X. M.; Yuan, W. C. *Org. Biomol. Chem.* **2020**, *18*, 1886.
(f) Chen, B.; Chu, W. D.; Liu, Q. Z. *RSC Adv.* **2019**, *9*, 1487.
(g) Huang, R.; Chang, X.; Li, J.; Wang, C. J. *J. Am. Chem. Soc.* **2016**, *138*, 3998.
(h) Yin, W. H.; Fang, L.; Wang, Z. Y.; Gao, F.; Li, Z. F.; Wang, Z. Y. *Org. Lett.* **2020**, *21*, 7361.
(i) Cao, W. B.; Xu, X. P.; Ji, S. J. *Org. Biomol. Chem.* **2017**, *15*, 1651.
(j) Zhong, X. G.; Lv, J.; Luo, S. *Org. Lett.* **2015**, *17*, 1561.
(k) Deng, Y. M.; Pei, C.; Arman, H.; Dong, K. Y.; Xu, X. F.; Doyle, M. P. *Org. Lett.* **2016**, *18*, 5884.

[17] Zhao, H. W.; Pang, H. L.; Tian, T.; Li, B.; Chen, X. Q.; Song, X. Q.; Meng, W.; Yang, Z.; Liu, Y. Y.; Zhao, Y. D. *Adv. Synth. Catal.* **2016**, *358*, 1826.

[18] Cheng, B.; Li, Y. T.; Wang, T. M.; Zhang, X. P.; Li, H.; Li, Y.; Zhai, H. B. *Chem. Commun.* **2019**, *55*, 14606.

[19] Zhang, X. K.; Wang, H. B.; Li, Z. W.; Shu, Y.; Gan, S. Zhang, X. F.; Shao, H. W.; Wang, C. Y. *ACS Omega* **2022**, *7*, 40963.

(Cheng, F.)

