有机化学 DOI: 10.6023/cjoc201904028 研究论文
Chinese Journal of Organic Chemistry ARTICLE

4-二甲氨基吡啶促进的一锅法合成高选择性螺环丙烷吡唑啉酮衍生物

梁 杰 马会芳 阿布拉江•克依木*
(新疆大学化学化工学院 石油天然气精细化工教育部&新疆维吾尔自治区重点实验室 乌鲁木齐 830046)

摘要 发展了一种 4-二甲氨基吡啶(DMAP)促进的高立体选择性合成多取代螺环丙烷吡唑啉酮的方法. 该反应以吡唑啉酮、芳醛和溴乙酸酯为原料, DMAP 作为碱, 经三组分一锅反应, 合成一系列收率高且非对映选择性好的目标化合物. 该反应具有操作简单、产率高以及非对映选择性好等优点. 该合成方法对于螺环丙烷的研究具有重要的价值.
关键词 一锅法合成; 多组分反应; 螺环丙烷; 吡唑酮; 4-二甲氨基吡啶(DMAP)

High-Selective One-Pot Synthesis of Spirocyclopropane Pyrazolones Promoted by 4-Dimethylaminopyridine

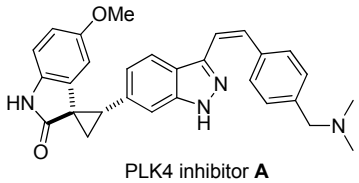
Liang, Jie Ma, Huifang Ablajan, Keyume*
(*Key Laboratory of Oil & Gas Fine Chemicals*, *Ministry of Education & Xinjiang Uyghur Autonomous Region*, *College of Chemistry and Chemical Engineering*, *Xinjiang University*, *Urumqi 830046*)

Abstract A 4-dimethylaminopyridine (DMAP)-promoted high stereoselectivity method for the synthesis of polysubstituted spiropropane pyrazolone was developed. A series of target compounds were synthesized from using pyrazolone, aromatic aldehyde and bromoacetate as raw materials, and DMAP as a base with high yield via three-component one-pot reaction. This reaction has the advantages of simple operation, high yield and good diastereotopic selectivity. In addition, this synthetic method is of great value for the study of spiropropane.
Keywords one-pot synthesis; multicomponent reactions; spirocyclopropane; pyrazolones; 4-dimethylaminopyridine (DMAP)

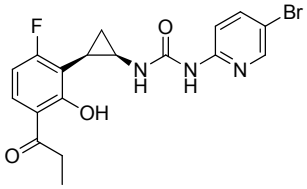
1 Introduction

The syntheses of multi-substituted spirocyclopropane ring systems have aroused much attention due to their various biological and pharmacological activities,[1] such as anticancer, antifungal, antitumor, insecticidal, *etc*. This oxindole derivative **A** exhibits PLK4 inhibitors activity,[2] and the cyclopropane compound **B** has high anti-HIV-1 activity.[3] The structure occurs widely as a basic skeleton in natural products,[4] and they are often used as versatile starting materials for the production of natural and synthetic compounds.[5] Spirocyclopropane derivatives feature intrinsic ring strain, and those are attractive for using in organic synthesis.[6]

In recent decades, many asymmetric cyclopropanation reactions have been reported, such as Simmons-Smith cyclopropanation,[7] Michael-initiated ring-closure of ylides with electron-deficient olefins,[8] transition-metal-catalyzed decomposition of diazoalkanes,[9] base-catalyzed α-halogenation with olefins[10] and miscellaneous reactions.[11]



PLK4 inhibitor **A**

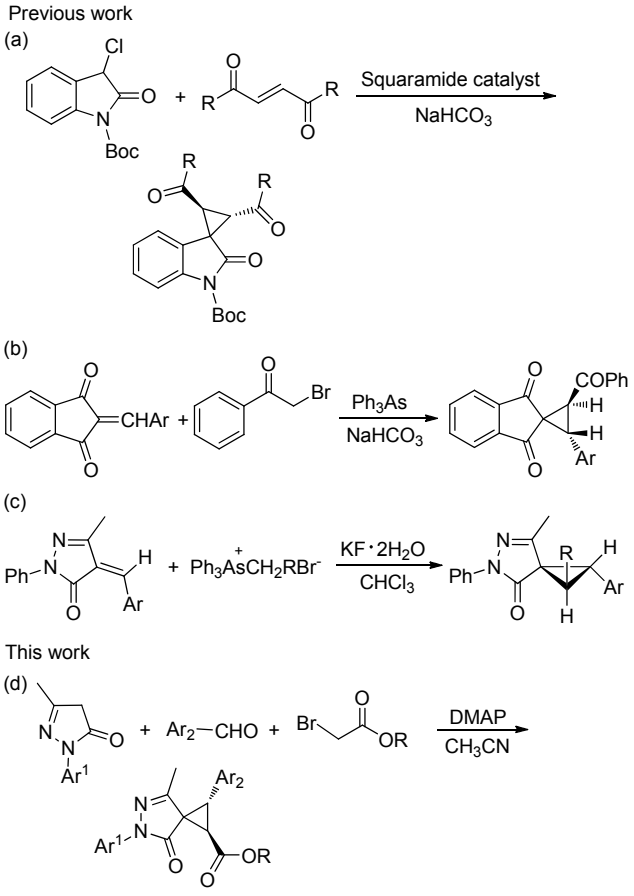


anti-HIV-1 activity
B

Figure 1 Bioactive compounds containing cyclopropane unit

* Corresponding author. E-mail: ablajan209@hotmail.com
Received April 10, 2019; revised June 11, 2019; published online July 9, 2019.
Project supported by the National Natural Science Foundation of China (Nos. 21961038, 21462041).
国家自然科学基金(Nos. 21961038, 21462041)资助项目.

Electron-deficient olefins and ylides were used to prepare enantioenriched cyclopropanes, using sulfonium,[12] sulfoximines,[13] chloroallyl amides,[14] phosphonates,[15] phosphorus ylides[16] and pyridinium ylide.[17] Asymmetric organocatalytic reaction of unsaturated 1,4-diketones and 3-chlorooxindoles generated a series of spiro-oxindoles with higher enantioselectivities (Scheme 1a).[18] Triphenylarsine has been used as a catalyst for the synthesis of cyclopropane-indan-diones using the cyclopropanation of alkene with phenacyl bromide (Scheme 1b).[19] Furthermore, the reaction of 4-arylidene-3-methyl-1-phenyl-pyrazolin-5-one with arsonium salt was resulted in spiro-cyclopropane-pyrazoles in the presence of KF•$2H_2O$ (Scheme 1c).[20] The stereoselective construction of spiro-pyrazolone-cyclopropane-oxindoles derivertives from the reaction of arylidenepyrazolones with 3-chlorooxindoles was reported using DIPEA as catalyst.[21] However, those methods have yet to be improved for preparing highly stereoselective cyclopropanes or mixtures of *cis*-*trans* isomers. Indeed, the catalysts used in those reactions are expensive and poisonous, and the product obtained by multi-step process does not meet the requirements of green chemistry.



Scheme 1 Synthesis of spirocyclopropanes.

Multicomponent reactions (MCRs) effectively combine more reactants to form a new molecule with several chemical bonds in a single route, and it has received much attention due to its environmental safety, economy steps and simple work-up.[22] Based on the importance of spirocyclopropane rings containing heterocycle moiety, it is very challenging to develop an efficient and simple method for the synthesis of spirocyclopropane linked to pyrazole. Herein we described a simple one-pot synthesis of multi-substituted spirocyclopropane pyrazolones using 4-dimethylaminopyridine oxide (DMAP) as a base (Scheme 1d).

2 Results and discussion

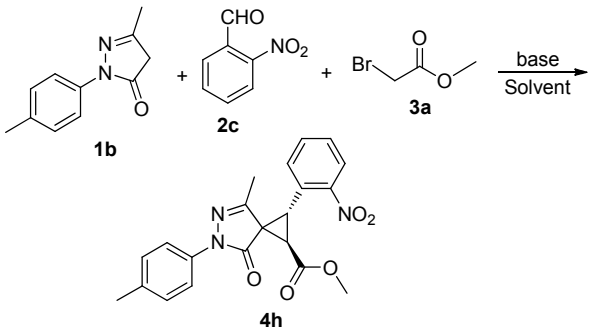
Our study on the one-pot reaction of pyrazolone **1b**, aromatic aldehyde **2c**, and bromoacetic ester **3a** with different bases was commenced. On the basis of other work,[23] the product was also anticipated to be *trans*-4,5-dihydro-1*H*-furo[2,3-*c*]pyrazole-5-carboxylate. However, the reaction product was further confirmed and verified as a *trans*-spirocyclopropane **4h** by NMR, HRMS and IR spectra. In addition, single crystal structure of product **4c** was carried out, which further confirmed the structure of the product (Figure 1).

Initially, the model reaction to optimize the reaction conditions was examined (Table 1). At first, several bases were selected and screened using acetonitrile as solvent (Entries 1～8). Obviously, the model reaction did not proceed well in the absence of base (Entry 1). As shown in Table 1, the corresponding product **4h** was generated with lower yields and diastereoselectivities in presence of inorganic base NaOH and Cs_2CO_3 (Entries 2 and 3). Then, various organic bases (Entries 4～8) were investigated. When using organic base, the yield and diastereoselectivity of compound **4h** got improved. Compound **4h** was obtained in the highest yield of 86% with excellent diastereoselectivity (94∶6) using DMAP as base (Entry 8). Subsequently, the reaction conditions were optimized by screening different solvents. The yield was 65% in CH_2Cl_2 (Entry 9), and the worst result was obtained in H_2O (Entry 10). Compound **4h** was obtained with 78% yield and good diastereoselectivity (88∶12) in solvents of $CH_3CO_2C_2H_5$ (Entry 11). Further comparisons considered reaction time and temperature (Entries 12～14). No significant change was found when running the reaction for 15 h or longer (Entry 12). Decreasing the reaction temperature from 81 ℃ to 25 ℃ and 60 ℃ resulted in incomplete reaction with 68% and 36% yields (Entries 13 and 14). These results further indicated that the reaction was completed at the boiling point of CH_3CN. Furthermore, the impact of base loading was examined. The result showed that reducing the base loading from 100 mol% to 50 mol% significantly decreased the reaction yield (Entry 15).

Once the reaction conditions had been optimized (Table 1, Entry 8), the scope of this tandem reaction was explored with a wide array of pyrazolone **1** (0.5 mmol), aryl aldehyde **2** (0.5 mmol), and bromoacetic ester **3** (0.5 mmol). The results summarized in Table 2 show that all the reactions proceeded well to afford the desired products in

goodtoexcellent yields (58%～89%) with excellent diastereoselectivities (6∶1 to >25∶1 *dr*).

Table 1 Optimization of the reaction conditions[a]

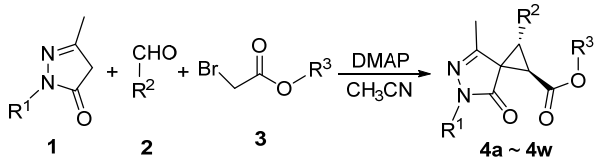


Entry	Base	Solvent	Temp./℃	Yield[b]/%	*trans*[c]/*cis*
1	No base	CH_3CN	81	NR	NR
2	NaOH	CH_3CN	81	41	45∶55
3	Cs_2CO_3	CH_3CN	81	48	48∶52
4	Pyridine	CH_3CN	81	82[c]	72∶28
5	TEBA	CH_3CN	81	56	80∶20
6	CTAB	CH_3CN	81	60	85∶15
7	DABCO	CH_3CN	81	70	72∶28
8	DMAP	CH_3CN	81	86	94∶6
9	DMAP	CH_2Cl_2	81	65	40∶60
10	DMAP	H_2O	100	Trace	NR
11	DMAP	CH_3CO_2Et	81	78	88∶12
12	DMAP	CH_3CN	81	86[d]	94∶6
13	DMAP	CH_3CN	25	36	46∶54
14	DMAP	CH_3CN	60	68	79∶21
15	DMAP	CH_3CN	81	50[e]	90∶10

[a] Reaction conditions: **1b** (0.5 mmol), **2c** (0.5 mmol), **3a** (0.5 mmol), solvent (5 mL), and base (0.5 mmol), reflux for 10 h. [b] Isolated yield. [c] Determined by ^{1}H NMR. [d] Reflux for 15 h. [e] 50 mol% DMAP

The effect of substituent in different positions on the aromatic aldehyde was first explored, and the corresponding products were obtained in moderate yield for compounds **4a**～**4e**. As shown in Table 2, aromatic aldehydes with adjacent substituents showed higher yields and diastereoselectivity than *para*-position substituents. 4-Cl and 2-Cl groups gave **4a** and **4d** in 62% and 85% yields, respectively. **4d** had the higher *dr* (12∶1) than **4a** (6∶1). When an electron donating group as CH_3 or OCH_3 is linked to aromatic aldehyde, the reaction is not ideal, so we can not get the pure product. Pyrazolones with 4-Me, 4-Cl, and the same aromatic aldehyde as above proceeded with 4-Cl and 4-Br (**4f**～**4g**, **4l**～**4m**) generated much lower yields than those of products containing 2-NO_2, 2-Cl and 2,4-Cl_2 (**4h**～**4i**, **4o**). As for the diastereoselectivity, **4h**～**4i** and **4o** were obtained with excellent diastereoselectivity (>15∶1). However, compounds **4k** and **4n** were obtained in 65% and 58% yields, and the structure of **4n** product converted to *trans*-isomers totally (>25∶1). Furthermore, the influence of pyrazolone on the reaction was further explored. Using pyrazolone bearing 2-Cl under standard conditions with different aromatic aldehydes, **4p**～**4s** were obtained in 77%～83% yields. *tert*-Butyl bromoacetate was then used to prepare compounds **4t**, **4u**, **4v**, and **4w** in 85%～89% yield with excellent diastereoselectivities (>25∶1 *dr*), giving slightly better yields and *dr* than the methyl bromoacetate. To summarize, multi-substituted spirocyclopropanes have been obtained easily via one-pot reaction route in high yield and with excellent diastereoselectivities.

Table 2 Substrate scope[a]



Entry	R^1	R^2	R^3	**4**	Yield[b]/%	*trans*/*cis*[c]
1	Ph	4-ClC_6H_4	Me	**4a**	62	6∶1
2	Ph	4-BrC_6H_4	Me	**4b**	67	8∶1
3	Ph	2-$O_2NC_6H_4$	Me	**4c**	84	11∶1
4	Ph	2-ClC_6H_4	Me	**4d**	85	12∶1
5	Ph	2,4-$Cl_2C_6H_4$	Me	**4e**	79	10∶1
6	4-$CH_3C_6H_4$	4-ClC_6H_4	Me	**4f**	62	15∶1
7	4-$CH_3C_6H_4$	4-BrC_6H_4	Me	**4g**	65	11∶1
8	4-$CH_3C_6H_4$	2-$O_2NC_6H_4$	Me	**4h**	86	18∶1
9	4-$CH_3C_6H_4$	2-ClC_6H_4	Me	**4i**	86	17∶1
10	4-$CH_3C_6H_4$	2,4-$Cl_2C_6H_4$	Me	**4j**	80	15∶1
11	4-$CH_3C_6H_4$	Ph	Me	**4k**	65	6∶1
12	4-ClC_6H_4	4-ClC_6H_4	Me	**4l**	62	9∶1
13	4-ClC_6H_4	4-BrC_6H_4	Me	**4m**	66	8∶1
14	4-ClC_6H_4	2-$O_2NC_6H_4$	Me	**4n**	58	>25∶1
15	4-ClC_6H_4	2,4-$Cl_2C_6H_4$	Me	**4o**	82	15∶1
16	2-ClC_6H_4	4-ClC_6H_4	Me	**4p**	77	11∶1
17	2-ClC_6H_4	4-BrC_6H_4	Me	**4q**	78	12∶1
18	2-ClC_6H_4	2-$O_2NC_6H_4$	Me	**4r**	83	18∶1
19	2-ClC_6H_4	2,4-$Cl_2C_6H_4$	Me	**4s**	80	13∶1
20	Ph	2,4-$Cl_2C_6H_4$	$C(Me)_3$	**4t**	89	>25∶1
21	4-$CH_3C_6H_4$	2-$O_2NC_6H_4$	$C(Me)_3$	**4u**	87	>25∶1
22	2-ClC_6H_4	2-$O_2NC_6H_4$	$C(Me)_3$	**4v**	87	>25∶1
23	4-ClC_6H_4	2,4-$Cl_2C_6H_4$	$C(Me)_3$	**4w**	85	>25∶1

[a] Reaction conditions: pyrazolone **1** (0.5 mmol), aryl aldehyde **2** (0.5 mmol), bromoacetic esters **3** (0.5 mmol), and DMAP (0.5 mmol) in 5 mL of CH_3CN, and refluxing for 10 h. [b] Isolated yield. [c] Determined by ^{1}H NMR.

Compound **4** was analyzed using NMR, HRMS, and IR spectroscopies. Single-crystal X-ray diffraction (Figure 2) was used to confirm the structure of compound **4c**.

A plausible reaction mechanism for the synthesis of compound **4** by the one-pot multicomponent tandem reaction is shown in Scheme 2. At first, *N*-alkyl pyridinium **A** was obtained by the reaction of bromoacetic esters with DMAP. Intermediate **C** was smoothly formed by Knoevenagel condensation of the pyrazolones and aromatic aldehydes. The second step is Michael addition between intermediates **A** and **C** to generate the zwitterion **D**. An intramolecular cyclization finally results the ultimate compound **4**. The reaction mechanism further explains that

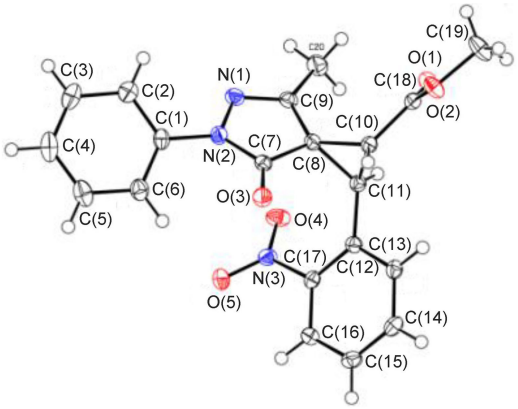
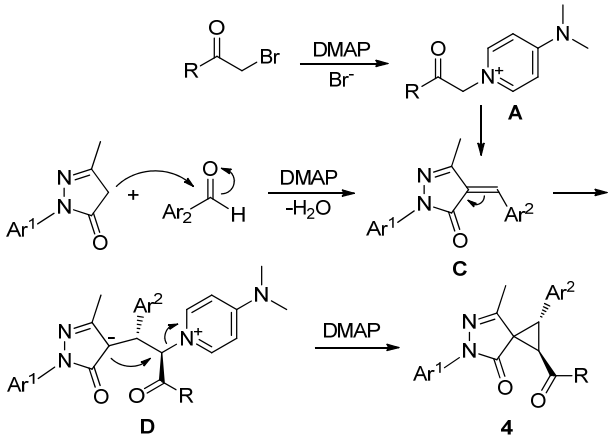


Figure 2 X-ray crystal structures of compound **4c**

the stereoselectivity at the spirocyclic carbon is affected by the structure of the reac tants and reaction intermediates.



Scheme 2 Plausible reaction mechanism for the formation of spiropyrazolone cyclopropanes

3 Conclusions

In summary, a simple and efficient approach for the synthesis of multi-substituted spirocyclo-propanepyrazolones has been developed. Those derivatives were obtained in good yields and excellent diastereoselectivities via one-pot three-component cascade spirocyclopropanation reactions of bromoacetic esters, pyrazolones and aromatic aldehydes using DMAP as base. DMAP plays a significance role in forming a stabilized intermediate and in acquiring a good leaving group for the Micheal-initiated ring-closure reaction. This methodology has the advantages of easy operation, high isolated yields, and convenient work-up. This novel and effective methodology for the synthesis of spirocyclopropanes containing pyrazole in a stereoselective fashion will lead to works assessing and researching the biological and pharmacological activities of these fused nitrogen-containing heterocyclic compounds.

4 Experimental section

4.1 General method

Reagents and solvents were from Aladdin, TCI or Acros, and used without further purification. The progress of the reaction was examined by TLC using analytical-grade silica gel plates (GF-254). Column chromatography was carried out using silica gel (300～400 mesh). Infrared (IR) spectra were recorded on a Bruker Equinox 55 spectrophotometer using samples as KBr pellets. NMR spectra (^{1}H NMR at 400 MHz, ^{13}C NMR at 100 MHz) were obtained on a Bruker Inova-400 instrument using $CDCl_3$ as solvent. Chemical shifts were relative to TMS as an internal standard. High-resolution mass spectrometry (HRMS) were obtained using a Micromass Q-TOF Global Tandem Mass Spectrometer.

4.2 General procedure for the synthesis of 4a～4w

A mixture of bromoacetic esters (0.5 mmol), pyrazolone (0.5 mmol), aromatic aldehyde (0.5 mmol) and DMAP (0.5 mmol) in acetonitrile (5 mL) was refluxed for 10 h. After completion of the reaction, as monitored by thin-layer chromatography (TLC), the reaction mixture was cooled to room temperature and the solvent was evaporated under reduced pressure. Finally, compounds **4a**～**4w** were separated by purification through column chromatography (silica gel 300−400 mesh) using CH_2Cl_2 and petroleum ether (V∶V=2∶1～5∶1) as the eluent.

4.3 Characterization of the compounds

Methyl 2-(4-chlorophenyl)-4-methyl-7-oxo-6-phenyl-5,6-diazaspiro[2.4]hept-4-ene-1-carboxylate (**4a**): Light yellow solid, m.p. 190～192 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.81 (dd, J=8.8, 1.1 Hz, 2H), 7.39～7.27 (m, 4H), 7.24 (d, J=8.3 Hz, 2H), 7.15 (dd, J=10.6, 4.3 Hz, 1H), 3.96～3.76 (m, 4H), 3.35 (d, J=8.7 Hz, 1H), 2.22 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 168.08, 167.04, 156.09, 138.06, 134.20, 130.57, 129.29, 128.78, 128.53, 125.06, 118.55, 52.93, 44.85, 38.72, 37.43, 15.15; IR (film) v: 3083, 3024, 2958, 2843, 1721, 1721, 1592, 1524, 1452, 1381, 1352, 1262, 1163, 865, 771, 735, 699, 534, 508 cm^{-1}; HRMS (TOF MS ES$^+$) calcd for $C_{20}H_{18}ClN_2O_3$ $[M+H]^+$ 369.1006, found 369.1002.

Methyl 2-(4-bromophenyl)-4-methyl-7-oxo-6-phenyl-5,6-diazaspiro[2.4]hept-4-ene-1-carboxylate (**4b**): Light yellow solid, m.p. 188～190 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.88～7.75 (m, 2H), 7.49～7.41 (m, 2H), 7.38～7.30 (m, 2H), 7.21～7.11 (m, 3H), 3.87 (d, J=8.7 Hz, 1H), 3.83 (s, 3H), 3.35 (d, J=8.7 Hz, 1H), 2.22 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 168.02, 166.99, 156.02, 138.03, 131.43, 130.85, 129.81, 128.74, 125.02, 122.37, 118.52, 52.89, 44.76, 38.73, 37.34, 15.10; IR (film) v: 3084, 3021, 2957, 2840, 1734, 1704, 1575, 1520, 1453, 1376, 1342, 1272, 1174, 871, 766, 734, 695, 534, 502 cm^{-1}; HRMS (TOF MS ES$^+$) calcd for $C_{20}H_{18}BrN_2O_3$ $[M+H]^+$ 413.0500, found 413.0504.

Methyl 4-methyl-2-(2-nitrophenyl)-7-oxo-6-phenyl-5,6-diazaspiro[2.4]hept-4-ene-1-carboxylate (**4c**): yellow solid, m.p. 183～185 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.05 (dd, J=8.2, 1.2 Hz, 1H), 7.78～7.71 (m, 2H), 7.65 (td, J=7.6, 1.3 Hz, 1H), 7.55 (d, J=7.7 Hz, 1H), 7.49 (m, 1H), 7.35～7.28 (m, 2H), 7.13 (m, 1H), 4.22 (d, J=8.6 Hz,

1H), 3.84 (s, 3H), 3.33 (d, J=8.7 Hz, 1H), 2.28 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 167.77, 167.18, 156.69, 148.77, 137.92, 133.28, 132.06, 129.38, 128.68, 127.59, 125.14, 118.82, 52.95, 44.59, 37.83, 36.62, 14.94; IR (film) v: 3064, 3030, 2965, 2824, 1755, 1710, 1581, 1532, 1464, 1387, 1339, 1259, 1166, 880, 726, 731, 691, 535, 509 cm^{-1}; HRMS (TOF MS ES$^+$) calcd for $C_{20}H_{18}N_3O_5$ [M+H]$^+$ 380.1241, found 380.1236.

Methyl 2-(2-chlorophenyl)-4-methyl-7-oxo-6-phenyl-5,6-diazaspiro[2.4]hept-4-ene-1-carboxylate (**4d**): yellow solid, m.p. 172～174 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.91～7.74 (m, 2H), 7.43～7.26 (m, 6H), 7.15 (t, J=7.4 Hz, 1H), 3.98～3.80 (m, 4H), 3.35 (d, J=8.6 Hz, 1H), 2.28 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 168.00, 167.04, 156.16, 138.14, 135.11, 130.74, 129.55, 129.17, 128.64, 126.51, 124.86, 118.62, 52.80, 44.33, 37.42, 15.02; IR (film) v: 3080, 3020, 2950, 2842, 1736, 1704, 1595, 1501, 1443, 1373, 1332, 1270, 1172, 873, 756, 736, 691, 538, 507 cm^{-1}; HRMS (TOF MS ES$^+$) calcd for $C_{20}H_{18}ClN_2O_3$ [M+H]$^+$ 369.1000, found 369.0996.

Methyl 2-(2,4-dichlorophenyl)-4-methyl-7-oxo-6-phenyl-5,6-diazaspiro[2.4]hept-4-ene-1-carboxylate (**4e**): Light yellow solid, m.p. 158～160 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.02～7.64 (m, 2H), 7.39～7.23 (m, 5H), 7.18～7.10 (m, 1H), 3.90～3.75 (m, 4H), 3.29 (d, J=8.6 Hz, 1H), 2.26 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 167.84, 166.99, 156.10, 138.13, 135.83, 134.83, 131.65, 129.23, 128.79, 128.44, 127.02, 125.10, 118.71, 52.97, 44.29, 37.34, 36.77, 15.10; IR (film) v: 3085, 3017, 2957, 2839, 1731, 11697, 1601, 1510, 1442, 1374, 1342, 1275, 1162, 773, 762, 741, 694, 543, 508 cm^{-1}; HRMS (TOF MS ES$^+$) calcd for $C_{20}H_{17}Cl_2N_2O_3$ [M+H]$^+$ 403.0616, found 403.0614.

Methyl 2-(4-chlorophenyl)-4-methyl-7-oxo-6-(p-tolyl)-5,6-diazaspiro[2.4]hept-4-ene-1-carboxylate (**4f**): Light yellow solid, m.p. 175～177 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.68 (d, J=8.6 Hz, 2H), 7.31～7.27 (m, 2H), 7.23 (d, J=8.4 Hz, 2H), 7.14 (d, J=8.3 Hz, 2H), 3.87 (d, J=8.6 Hz, 1H), 3.83 (s, 3H), 3.34 (d, J=8.7 Hz, 1H), 2.31 (s, 3H), 2.21 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 168.12, 166.84, 155.92, 135.64, 134.72, 134.13, 130.56, 129.31, 128.50, 118.56, 52.91, 44.80, 38.62, 37.36, 20.90, 15.13; IR (film) v: 3085, 3013, 2954, 2824, 1754, 1715, 1588, 1563, 1464, 1399, 1343, 1235, 1162, 884, 722, 735, 693, 534, 502 cm^{-1}; HRMS (TOF MS ES$^+$) calcd for $C_{21}H_{20}ClN_2O_3$ [M+H]$^+$ 383.1157, found 383.1151.

Methyl 2-(4-bromophenyl)-4-methyl-7-oxo-6-(*p*-tolyl)-5,6-diazaspiro[2.4]hept-4-ene-1-carboxylate (**4g**): Light yellow solid, m.p. 169～170 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.70～7.65 (m, 2H), 7.47～7.42 (m, 2H), 7.15 (m, 4H), 3.87～3.82 (m, 4H), 3.34 (d, J=8.6 Hz, 1H), 2.31 (s, 3H), 2.21 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 168.12, 166.85, 155.89, 135.67, 134.74, 131.45, 130.89, 129.92, 129.28, 122.37, 118.59, 52.90, 44.76, 38.68, 37.33, 20.91, 15.13; IR (film) v: 3065, 3028, 3036, 2954, 2935, 1752, 1688, 1575, 1506, 1445, 1378, 1333, 1293, 1166, 964, 856, 745, 684, 506 cm^{-1}; HRMS (TOF MS ES$^+$) calcd for $C_{21}H_{20}BrN_2O_3$ [M + H]$^+$ 427.0651, found 427.0647.

Methyl 4-methyl-2-(2-nitrophenyl)-7-oxo-6-(*p*-tolyl)-5,6-diazaspiro[2.4]hept-4-ene-1-carboxylate (**4h**): yellow solid, m.p. 180～183 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.05 (dd, J=8.2, 1.2 Hz, 1H), 7.69～7.58 (m, 3H), 7.55 (d, J=7.7 Hz, 1H), 7.49 (t, J=7.8 Hz, 1H), 7.12 (d, J=8.2 Hz, 2H), 4.22 (d, J=8.7 Hz, 1H), 3.85 (s, 3H), 3.32 (d, J=8.7 Hz, 1H), 2.30 (s, 3H), 2.28 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 167.84, 167.01, 156.57, 148.78, 135.53, 134.82, 133.31, 132.10, 129.29, 127.68, 125.18, 118.89, 52.97, 44.56, 37.79, 36.58, 20.89, 14.96; IR (film) v: 3032, 3013, 2952, 2855, 1734, 1708, 1577, 1516, 1452, 1345, 1272, 1200, 1174, 821, 790, 729, 506 cm^{-1}; HRMS (TOF MS ES$^+$) calcd for $C_{21}H_{20}N_3O_5$ [M+H]$^+$ 394.1397, found 394.1394.

Methyl 2-(2-chlorophenyl)-4-methyl-7-oxo-6-(*p*-tolyl)-5,6-diazaspiro[2.4]hept-4-ene-1-carboxylate (**4i**): Light yellow solid, m.p. 165～168 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.82～7.63 (m, 2H), 7.44～7.24 (m, 4H), 7.16 (dd, J=8.8, 0.6 Hz, 2H), 4.00～3.74 (m, 4H), 3.35 (d, J=8.6 Hz, 1H), 2.32 (s, 3H), 2.29 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 168.10, 166.93, 156.05, 135.86, 135.17, 134.54, 130.83, 129.75, 129.55, 129.22, 126.57, 118.69, 52.84, 44.37, 37.42, 20.90, 15.08; IR (film) v: 3017, 2998, 2948, 2864, 1739, 1701, 1597, 1512, 1449, 1332, 1270, 1203, 1161, 821, 740, 696, 509 cm^{-1}; HRMS (TOF MS ES$^+$) calcd for $C_{21}H_{20}ClN_2O_3$ [M+H]$^+$ 383.1157, found 383.1153.

Methyl 2-(2,4-dichlorophenyl)-4-methyl-7-oxo-6-(p-tolyl)-5,6-diazaspiro[2.4]hept-4-ene-1-carboxylate (**4j**): yellow solid, m.p. 158～160 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.75～7.63 (m, 2H), 7.35～7.23 (m, 3H), 7.20～7.12 (m, 2H), 3.82 (d, J=8.5 Hz, 4H), 3.29 (d, J=8.5 Hz, 1H), 2.32 (s, 3H), 2.26 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 167.76, 166.71, 155.79, 135.72, 134.62, 131.59, 129.14, 128.46, 126.89, 118.61, 52.81, 44.15, 37.16, 36.60, 20.82, 14.97; IR (film) v: 3019, 2955, 2925, 2861, 1738, 1695, 1592, 1511, 1450, 1329, 1277, 1103, 971, 871, 813, 649, 505 cm^{-1}; HRMS (TOF MS ES$^+$) calcd for $C_{21}H_{19}Cl_2N_2O_3$ [M + H]$^+$ 417.0767, found 417.0763.

Methyl 4-methyl-7-oxo-2-phenyl-6-(*p*-tolyl)-5,6-diazaspiro[2.4]hept-4-ene-1-carboxylate (**4k**): yellow solid, m.p. 118～120 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.80 (d, J=8.5 Hz, 2H), 7.47～7.26 (m, 5H), 7.20 (d, J=8.3 Hz, 2H), 3.96 (d, J=8.6 Hz, 1H), 3.82 (s, 3H), 3.32 (d, J=8.6 Hz, 1H), 2.35 (s, 3H), 1.37 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 168.55, 166.16, 156.05, 135.99, 134.60, 132.66, 129.33, 129.00, 128.52, 118.59, 52.82, 43.23, 40.15, 35.26, 20.93, 14.77; IR (film) v: 3029, 2956, 2924, 2851, 1745, 1685, 1588, 1521, 1454, 1323, 1267, 1110, 971, 873, 811, 644, 506 cm^{-1}; HRMS (TOF MS ES$^+$) calcd for $C_{21}H_{21}N_2O_3$ [M+H]$^+$ 349.1552, found 349.1550.

Methyl 2,6-bis(4-chlorophenyl)-4-methyl-7-oxo-5,6-diazaspiro[2.4]hept-4-ene-1- carboxylate (**4l**): Light yellow solid, m.p. 178～180 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ:

7.95～7.61 (m, 2H), 7.43～7.27 (m, 4H), 7.23 (d, J=8.3 Hz, 2H), 3.92～3.87 (m, 1H), 3.83 (s, 3H), 3.35 (d, J=8.7 Hz, 1H), 2.21 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 167.94, 167.01, 156.43, 136.65, 134.30, 130.55, 130.08, 129.12, 128.80, 128.57, 119.60, 52.97, 44.84, 38.89, 37.53, 15.16; IR (film) v: 3101, 3012, 2953, 2924, 2853, 1754, 1698, 1583, 1493, 1455, 1337, 1275, 1173, 1087, 835, 732, 695, 503 cm^{-1}; HRMS (TOF MS ES$^+$) calcd for $C_{20}H_{17}Cl_2N_2O_3$ [M+H]$^+$ 403.0616, found 403.0614.

Methyl 2-(4-bromophenyl)-6-(4-chlorophenyl)-4-methyl-7-oxo-5,6-diazaspiro[2.4]hept-4-ene-1-carboxylate (**4m**): Light yellow solid, m.p. 170～172 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.87～7.70 (m, 2H), 7.45 (d, J=8.5 Hz, 2H), 7.38～7.27 (m, 2H), 7.17 (d, J=8.3 Hz, 2H), 3.87 (d, J=8.7 Hz, 1H), 3.83 (s, 3H), 3.35 (d, J=8.7 Hz, 1H), 2.21 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 167.92, 166.99, 156.42, 136.64, 131.50, 130.86, 130.10, 129.65, 128.81, 122.51, 119.60, 52.98, 44.78, 38.93, 37.47, 15.16; IR (film) v: 3100, 3022, 2913, 2954 2832, 1755, 1687, 1598, 1483, 1445, 1335, 1254, 1177, 1083, 830, 730, 693, 504 cm^{-1}; HRMS (TOF MS ES$^+$) calcd for $C_{20}H_{17}BrClN_2O_3$ [M+H]$^+$ 447.0105, found 447.0101.

Methyl 6-(4-chlorophenyl)-4-methyl-2-(2-nitrophenyl)-7-oxo-5,6-diazaspiro[2.4]hept-4-ene-1-carboxylate (**4n**): yellow solid, m.p. 185～187 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.06 (dd, J=8.2, 1.3 Hz, 1H), 7.75～7.60 (m, 3H), 7.58～7.49 (m, 2H), 7.20～7.04 (m, 2H), 4.22 (d, J=8.6 Hz, 1H), 3.86 (s, 3H), 3.32 (d, J=8.6 Hz, 1H), 2.28 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 167.87, 167.01, 156.56, 148.81, 135.52, 134.85, 133.30, 132.09, 129.30, 128.76, 127.70, 125.22, 119.87, 118.92, 52.98, 44.57, 37.79, 36.58, 20.91, 14.97; IR (film) v: 3110, 3032, 2920, 2955, 2838, 1752, 1682, 1579, 1486, 1455, 1340, 1239, 1169, 1079, 832, 732, 691, 507 cm^{-1}; HRMS (TOF MS ES$^+$) calcd for $C_{20}H_{17}ClN_3O_5$ [M+H]$^+$ 414.0856, found 414.0853.

Methyl 6-(4-chlorophenyl)-2-(2,4-dichlorophenyl)-4-methyl-7-oxo-5,6-diazaspiro[2.4]hept-4-ene-1-carboxylate (**4o**): Light yellow solid, m.p. 165～167 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.87～7.67 (m, 2H), 7.39～7.19 (m, 5H), 3.83 (d, J=8.2 Hz, 4H), 3.27 (d, J=8.6 Hz, 1H), 2.24 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 167.58, 166.85, 156.32, 136.61, 135.69, 134.83, 131.50, 129.99, 129.14, 128.68, 128.18, 126.94, 119.62, 52.89, 44.16, 37.34, 36.81, 14.97; IR (film) v: 3113, 3001, 2952, 2923, 2851, 1744, 1697, 1593, 1491, 1451, 1330, 1275, 1171, 1090, 836, 738, 693, 509 cm^{-1}; HRMS (TOF MS ES$^+$) calcd for $C_{20}H_{16}Cl_3N_2O_3$ [M+H]$^+$ 437.0227, found 437.0223.

Methyl 6-(2-chlorophenyl)-2-(4-chlorophenyl)-4-methyl-7-oxo-5,6-diazaspiro[2.4]hept-4-ene-1-carboxylate (**4p**): Light yellow solid, m.p. 159～161 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.45～7.41 (m, 1H), 7.37～7.33 (m, 1H), 7.30～7.25 (m, 6H), 3.95～3.81 (m, 4H), 3.37 (d, J=8.6 Hz, 1H), 2.19 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 168.10, 167.57, 156.19, 134.44, 134.20, 131.67, 130.50, 129.73, 129.58, 129.37, 129.16, 128.75, 128.44, 127.39, 52.95, 43.71, 38.76, 37.04, 15.19; IR (film) v: 3103, 3024, 2955, 2923, 2864, 1744, 1716, 1594, 1523, 1482, 1452, 1343, 1334, 1268, 1198, 1087, 865, 766, 733, 545 cm^{-1}; HRMS (TOF MS ES$^+$) calcd for $C_{20}H_{17}Cl_2N_2O_3$ [M+H]$^+$ 403.0610, found 403.0605.

Methyl 2-(4-bromophenyl)-6-(2-chlorophenyl)-4-methyl-7-oxo-5,6-diazaspiro[2.4]hept-4-ene-1-carboxylate (**4q**): Light yellow solid, m.p. 169～170 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.43 (dt, J=4.5, 2.0 Hz, 3H), 7.37～7.33 (m, 1H), 7.33～7.26 (m, 2H), 7.19 (d, J=8.6 Hz, 2H), 3.95～3.80 (m, 4H), 3.37 (d, J=8.6 Hz, 1H), 2.19 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 168.08, 167.56, 156.18, 134.44, 131.66, 131.38, 130.92, 130.40, 129.78, 128.75, 127.40, 122.41, 52.96, 43.65, 38.80, 36.98, 15.19; IR (film) v: 3105, 3026, 2965, 2923, 2865, 1724, 1723, 1593, 1525, 1485, 1489, 1323, 1332, 1263, 1198, 1085, 866, 767, 736, 543 cm^{-1}; HRMS (TOF MS ES$^+$) calcd for $C_{20}H_{17}BrClN_2O_3$ [M+H]$^+$ 447.0105, found 447.0099.

Methyl 6-(2-chlorophenyl)-4-methyl-2-(2-nitrophenyl)-7-oxo-5,6-diazaspiro[2.4]hept-4-ene-1-carboxylate (**4r**): yellow solid, m.p. 182～184 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.06 (dd, J=8.2, 1.3 Hz, 1H), 7.60 (td, J=7.7, 1.3 Hz, 1H), 7.54 (s, 1H), 7.49～7.42 (m, 1H), 7.38 (d, J=2.3 Hz, 1H), 7.31 (s, 1H), 7.29～7.23 (m, 2H), 4.28 (d, J=8.6 Hz, 1H), 3.92～3.80 (m, 3H), 3.35 (d, J=8.6 Hz, 1H), 2.27 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 167.78, 156.97, 148.65, 134.40, 133.38, 132.30, 131.68, 130.28, 129.73, 129.44, 128.68, 127.74, 127.42, 125.22, 53.04, 43.35, 37.61, 36.80, 15.05; IR (film) v: 3101, 3023, 2952, 2926, 2860, 1737, 1711, 1596, 1525, 1487, 1450, 1348, 1330, 1270, 1183, 1092, 852, 764, 738, 549 cm^{-1}; HRMS (TOF MS ES$^+$) calcd for $C_{20}H_{17}ClN_3O_5$ [M+H]$^+$ 414.0851, found 414.0847.

Methyl 6-(2-chlorophenyl)-2-(2,4-dichlorophenyl)-4-methyl-7-oxo-5,6-diazaspiro[2.4]hept-4-ene-1-carboxylate (**4s**): Light yellow solid, m.p. 160～161 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.43 (dd, J=5.0, 4.4 Hz, 1H), 7.40～7.31 (m, 2H), 7.32～7.19 (m, 4H), 3.86 (s, 4H), 3.32 (d, J=8.5 Hz, 1H), 2.23 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 167.74, 167.38, 156.07, 135.73, 134.77, 134.38, 131.55, 130.34, 129.51, 129.06, 128.43, 128.22, 127.25, 126.81, 77.26, 76.94, 76.62, 52.89, 43.01, 36.80, 15.00; IR (film) v: 3095, 3032, 2894, 2952, 2862, 1738, 1721, 1585, 1555, 1459, 1457, 1343, 1334, 1286, 1175, 1089, 856, 765, 732, 541 cm^{-1}; HRMS (TOF MS ES$^+$) calcd for $C_{20}H_{16}Cl_3N_2O_3$ [M+H]$^+$ 437.0226, found 437.0221.

tert-Butyl 2-(2,4-dichlorophenyl)-4-methyl-7-oxo-6-phenyl-5,6-diazaspiro[2.4]hept-4-ene-1-carboxylate (**4t**): Light yellow solid, m.p. 151～153 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.94～7.81 (m, 2H), 7.39～7.22 (m, 5H), 7.19～7.10 (m, 1H), 3.81 (d, J=8.8 Hz, 1H), 3.25 (d, J=8.6 Hz, 1H), 2.29 (s, 3H), 1.55 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 167.11, 166.08, 156.24, 138.20, 135.81, 134.55, 131.68, 129.04, 128.66, 126.82, 124.86, 118.45, 83.13, 44.24, 38.67, 36.57, 27.94, 15.08; IR (film) v: 3077, 3002, 2979, 2933, 1734, 1707, 1594, 1502, 1486, 1438, 1372, 1333, 1206, 1148, 1051, 833, 752, 691, 498 cm^{-1}; HRMS (TOF MS ES$^+$) calcd for $C_{23}H_{23}Cl_2N_2O_3$ [M+H]$^+$

445.1080, found 445.1075.

tert-Butyl 4-methyl-2-(2-nitrophenyl)-7-oxo-6-(*p*-tolyl)-5,6-diazaspiro[2.4]hept-4-ene-1-carboxylate (**4u**): yellow solid, m.p. 177～179 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.98 (d, J=8.1 Hz, 1H), 7.68 (d, J=8.4 Hz, 2H), 7.64～7.48 (m, 2H), 7.42 (t, J=7.7 Hz, 1H), 7.12 (d, J=8.6 Hz, 2H), 4.16 (d, J=8.7 Hz, 1H), 3.27 (d, J=8.7 Hz, 1H), 2.30 (d, J=6.2 Hz, 6H), 1.54 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 167.16, 166.10, 156.74, 148.83, 135.68, 134.49, 133.09, 132.10, 129.12, 127.80, 124.94, 118.61, 83.15, 44.54, 39.15, 36.35, 27.91, 20.80, 14.96; IR (film) v: 3081, 3031, 2969, 2925, 2859, 1732, 1706, 1577, 1518, 1448, 1371, 1342, 1212, 1152, 960, 816, 731, 507 cm^{-1}; HRMS (TOF MS ES$^+$) calcd for $C_{24}H_{26}N_3O_5$ $[M+H]^+$ 436.1867, found 436.1863.

tert-Butyl 6-(2-chlorophenyl)-4-methyl-2-(2-nitro phenyl)-7-oxo-5,6-diazaspiro[2.4]hept-4-ene-1-carboxylate (**4v**): yellow solid, m.p. 165～167 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.04 (dd, J=8.2, 1.2 Hz, 1H), 7.57 (m, 2H), 7.47–7.14 (m, 5H), 4.23 (d, J=8.7 Hz, 1H), 3.28 (d, J=8.7 Hz, 1H), 2.27 (s, 3H), 1.54 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 167.88, 166.06, 157.12, 148.65, 134.42, 133.15, 132.25, 131.57, 130.17, 129.57, 129.21, 128.60, 127.83, 127.28, 125.01, 83.21, 43.27, 38.96, 36.58, 27.93, 15.00; IR (film) v: 3078, 3018, 2982, 2932, 2863, 1715, 1579, 1529, 1485, 1438, 1369, 1341, 1207, 1153, 1061, 838, 737, 542 cm^{-1}; HRMS (TOF MS ES$^+$) calcd for $C_{23}H_{23}ClN_3O_5$ $[M+H]^+$ 456.1326, found 456.1322.

tert-Butyl 6-(4-chlorophenyl)-2-(2,4-dichlorophenyl)-4-methyl-7-oxo-5,6-diazaspiro[2.4]hept-4-ene-1-carboxylate (**4w**): Light yellow solid, m.p. 158～160 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.08～7.75 (m, 2H), 7.41 (d, J=1.9 Hz, 1H), 7.32 (m, 4H), 3.69 (d, J=8.7 Hz, 1H), 3.20 (d, J=8.7 Hz, 1H), 1.49 (s, 9H), 1.36 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 168.08, 163.89, 155.57, 136.9, 135.21, 130.60, 130.19, 129.76, 129.53, 128.72, 127.27, 119.50, 83.10, 42.86, 38.00, 36.71, 27.92, 14.34; IR (film) v: 3034, 3004, 2974, 2928, 1740, 1701, 1594, 1495, 1450, 1370, 1308, 1220, 1148, 1090, 828, 798, 540, 490 cm^{-1}; HRMS (TOF MS ES$^+$) calcd for $C_{23}H_{22}Cl_3N_2O_3$ $[M+H]^+$ 479.0690, found 479.0687.

辅助材料(Supporting Information) 化合物 **4a**～**4w** 的核磁共振氢谱、碳谱. 这些材料可以免费从本刊网站(http://sioc- journal.cn/)上下载.

References

[1] (a) Kinder, F. R. J.; Wang, R.-M.; Bauta, W. E.; Bair, K. W. M. *Bioorg. Med. Chem. Lett.* **1996**, *6*, 1029.
(b) Wessjohann, L. A.; Brandt, W. *Chem. Rev.* **2003**, *103*, 1625.
(c) Chen, D. Y.-K.; Pouwer, R. H.; Richard, J.-A. *Chem. Soc. Rev.* **2012**, *41*, 4631.
(d) Djerassi, C.; Doss, G. A. *New J. Chem.* **1990**, *14*, 713.
(e) Donaldson, W. A. *Tetrahedron* **2001**, *57*, 8589.
(f) Faust, R. *Angew. Chem.* **2001**, *113*, 2312.
(g) Qian, P.; Du, B. G.; Song, R. C.; Wu, X. D.; Mei, H. B.; Han, J. L.; Pan, Y. *J. Org. Chem.* **2016**, *81*, 6546.

[2] Sampson, P. B.; Liu, Y.; Patel, N. K.; Feher, M.; Forrest, B. *J. Med. Chem.* **2015**, **58**, 130.

[3] Sahlberg, C.; Engelhardt, P. *J. Med. Chem.* **1999**, *42*, 4150.

[4] McMorris, T. C.; Kelner, M. J.; Wang, W.; Yu, J.; Estes, L. A.; Taetle, R. *J. Nat. Prod.* **1996**, *59*, 896.

[5] (a) Cordero, F. M.; Pisaneschi, F.; Salvati, M.; Paschetta, V.; Ollivier, J.; Salaun, J.; Brandi, A. *J. Org. Chem.* **2003**, *68*, 3271.
(b) Basavaiah, D.; Rao, A. J.; Satyanarayana, T. *Chem. Rev.* **2003**, *103*, 811.

[6] (a) Lebel, H.; Marcoux, J. F.; Molinaro, C.; Charette, A. B. *Chem. Rev.* **2003**, *103*, 977.
(b) Kulinkovich, O. G.; Meijere, D. A. *Chem. Rev.* **2000**, *100*, 2789.
(c) Mukherjee, P.; Das, A. R. *J. Org. Chem.* **2017**, *82*, 2794.

[7] Papageorgiou, C. D.; Cubillo de Dios, M. A.; Ley, S. V.; Gaunt, M. J. *Angew. Chem. Int. Ed.* **2004**, *43*, 4641.

[8] (a) Sun, X. L.; Tang, Y. *Acc. Chem. Res.* **2008**, *41*, 937.
(b) Kakei, H.; Sone, T.; Sohtome, Y.; Matsunaga, S.; Shibasaki, M. *J. Am. Chem. Soc.* **2007**, *129*, 13410.
(c) Wang, J.; Liu, X. H.; Dong, S. X.; Lin, L. L.; Feng, X. M. *J. Org. Chem.* **2013**, *78*, 6322.
(d) Guo, J.; Liu, Y. B.; Li, X. Q.; Liu, X. H.; Lin, L. L.; Feng, X. M. *Chem. Sci.* **2016**, *7*, 2717.

[9] (a) Sawada, T.; Nakada, M. *Org. Lett.* **2013**, *15*, 1004.
(b) Lindsay; V. N. G.; Nicolas, C.; Charette, A. B. *J. Am. Chem. Soc.* **2011**, *133*, 8972.
(c) Xu, X.; Zhu, S.; Cui, X.; Wojtas, L.; Zhang, X. P. *Angew. Chem.* **2013**, *125*, 12073.
(d) Xu, Z.-H.; Zhu, S.-N.; Sun, X.-L.; Tang, Y.; Dai, L.-X. *Chem. Commun.* **2007**, *38*, 1960.

[10] (a) Arai, S.; Nakayama, K.; Hatano, K.; Shioiri, T. *J. Org. Chem.* **1998**, *63*, 9572.
(b) Miyagawa, T.; Tatenuma, T.; Tadokoro, M.; Satoh, T. *Tetrahedron*, **2008**, *64*, 5279.

[11] (a) Newcomb, E. T.; Ferreira, E. M. *Org. Lett.* **2013**, *15*, 1772.
(b) Robinson, A.; Aggarwal, V. K. *Angew. Chem.* **2010**, *122*, 6823.

[12] Yuan, Z.-B.; Fang, X.-X.; Li, X.-Y.; Wu, J.; Yao, H.-Q.; Lin, A.-J. *J. Org. Chem.* **2015**, *80*, 1112.

[13] Pyne, S. G.; Dong, Z.; Skelton, B. W.; White, A. H. *J. Org. Chem.* **1997**, *62*, 2337.

[14] Hanessian, S.; Andreotti, D.; Gomtsyan, A. *J. Am. Chem. Soc.* **1995**, *117*, 10393.

[15] Kimber, M. C.; Taylor, D. K. *J. Org. Chem.* **2002**, *67*, 3142.

[16] Avery, T. D.; Jenkins, N. F.; Kimber, M. C.; Lupton, D. W.; Taylor, D. K. *Chem. Commun.* **2002**, *33*, 28.

[17] Wang, Q.; Song, X. K.; Chen, J.; Yan, C. G. *J. Comb. Chem.* **2009**, *11*, 1007.

[18] Ošeka, M.; Noole, A.; Žari, S.; Öeren, M.; Järving, I.; Lopp, M.; Kanger, T. *Eur. J. Org. Chem.* **2014**, *17*, 3599.

[19] Ren, Z. J.; Cao, W. G.; Tong, W. Q.; Chen, J.; Deng, H. M.; Wu, D. Y. *Synth. Commun.* **2008**, *38*, 2200.

[20] Ren, Z. J.; Cao, W. G.; Chen, J.; Chen, Y. L.; Deng, H. M.; Shao, M.; Wu, D. Y. *Tetrahedron* **2008**, *64*, 5156.

[21] Li, J. H.; Feng, T. F.; Du, D. M. *J. Org. Chem.* **2015**, *80*, 11369.

[22] (a) Ablajan, K.; Zeynepgul, E.; Wang, L. J.; Feng, J. *Tetrahedron* **2014**, *70*, 3976.
(b) Wang, L. J.; Ablajan, K.; Feng, J. *Ultrason. Sonochem.* **2015**, *22*, 113.
(c) Li, W. B.; Reyhangul, R.; Ablajan, K.; Zulpiya, G. *Tetrahedron* **2017**, *73*, 164.

[23] (a) Khan, A.; Lal, M.; Sidick Basha, R. *Synthesis* **2013**, *45*, 406.
(b) Wang, Q.-F.; Hou, H.; Hui, L.; Yan, C.-G. *J. Org. Chem.* **2009**, *74*, 7403.
(c) Chuang, C.-P.; Chen, K.-P. *Tetrahedron* **2012**, *68*, 1401.

(Li, L.; Fan, Y.)

