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"On water" palladium catalyzed diastereoselective boronic acid addition to structurally diverse cyclopropane nitriles†

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An efficient palladium catalyzed diastereoselective addition of arylboronic acids to complex spirocyclopropyl dinitriles is developed in the presence of a catalytic amount of 4-dodecylbenzenesulphonic acid (DBSA) as a Brønsted acid surfactant in aqueous media. The protocol is also found to be highly effective when different types of nitrile compounds and organo-boron compounds are used. The overall reaction has been found to be very cost efficient since it requires low catalyst loading, mild thermal energy and short reaction time. Wide substrate scope, operational simplicity, good to excellent product yield, and use of green solvents make the reaction a practical route to transform nitrile into a keto functionality in biorelevant heterocyclic scaffolds. The scale-up synthesis of the target scaffolds can also be achieved with ease which also signifies the practicability of this protocol.

Introduction

The keto functionality can be found in numerous bioactive compounds[1] and natural products.[2] It is also one of the key functional groups in countless organic transformations.[3] Installation of a carbonyl group in organic scaffolds may be achieved *via* Friedel–Crafts acylation,[4] oxidation of secondary alcohols,[5] Weinreb ketone synthesis[6] and other protocols involving the addition of organometallic reagents (Grignard or organo-lithium reagents) to nitriles.[7] However, these methodologies cannot be useful to install a keto functionality in a complex organic molecule because of poor tolerance against harsh reaction conditions. Additionally, these methods are plagued with additional disadvantages such as stoichiometric amount of reagents, hazardous chemical compounds, tedious reaction conditions and poor chemo-selectivity. In view of the immense importance of the keto containing complex heterocyclic skeleton, we wish to transform the nitrile functionality present in our previously synthesized cyclopropane nitriles into the corresponding ketones under relatively mild conditions. Transition metal catalyzed formation of ketones can be realized as a practical route in synthetic chemistry due to their commercial importance along with catalytic efficacy. In the literature, there are only a handful examples of transition metal catalyzed synthesis of ketones,[8] and in most of the cases simple nitriles are used as substrates. The very first attempt was made by Larock *et al. via* the reaction between arylboronic acids and nitrile compounds in the presence of a palladium catalyst.[8a,b] Furthermore, Lu *et al.* extended the scope using different reactants.[8c] Recently, Sarkar *et al.* have performed this type of palladium catalyzed addition reaction with pyrazole tethered ligands for the synthesis of aryl ketones and 3-acylindoles.[8d] Murakami *et al.* and Miura *et al.* have parallelly established the reaction through the use of a rhodium catalyst.[8e–f,i–j] Some groups are also using the concept to synthesize small heterocyclic molecules *via* the metal catalyzed addition of arylboronic acid to nitriles followed by their inter- or intramolecular cyclization (Scheme 1).[9] But the majority of these procedures involve simple nitrile molecules, toxic organic solvents or binary solvents and drastic conditions. Thus, there is enough urgency for robust transition metal catalysis to obtain highly functionalized ketones. Herein, we wish to disclose a practical route to construct synthetically and biologically important ketones *via* the reaction between boronic acid with highly functionalized cyclopropane nitriles in the presence of a catalytic amount of DBSA as a Brønsted acid combined surfactant using water as the sole solvent.

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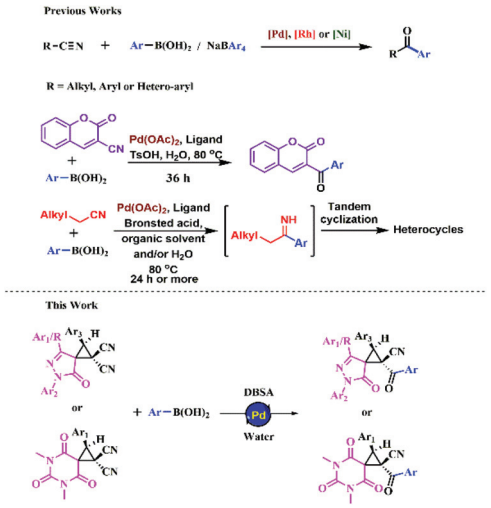
†Electronic supplementary information (ESI) available: Copies of ^{1}H and ^{13}C NMR spectra and X-ray crystallographic data for compounds **4a** and **5g**. CCDC 1952896 and 1952797. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/d0ob00077a

Results and discussion

We employed spirocyclopropylpyrazolone and barbiturate dicarbonitriles for this transformation. Initially, **1a** and



Scheme 1 Transition metal catalyzed transformation of nitriles into ketones.

phenylboronic acid (**3a**) were chosen as the model reactants for optimizing the reaction conditions. Several Brønsted acids (Table 1) and ligands (Table 2) were employed during this investigation. Initially, the reaction was performed in an aqueous medium in the presence of dioxane as a co-solvent at 100 °C using $Pd(OAc)_2$ and **L2** with 1.0 equivalent of **1a** and 2.0 equivalents of **3a** (Table 1, entry 1) in search of **4a′**. Despite the low conversion of the starting material, we isolated the newly formed compound. After complete characterization, it was found to be product **4a** from the reaction between boronic acid and one of the two nitriles of the starting spirocyclopropane. It is worth mentioning that no trace of **4a′** was obtained during this reaction which is supported by the fact that **4a** was observed as a single spot during TLC and also NMR studies revealed the absence of any isomeric peaks. On detecting the excellent diastereoselectivity of this reaction, we immediately

Table 2 Ligands used for optimization

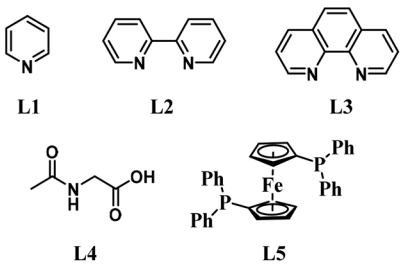
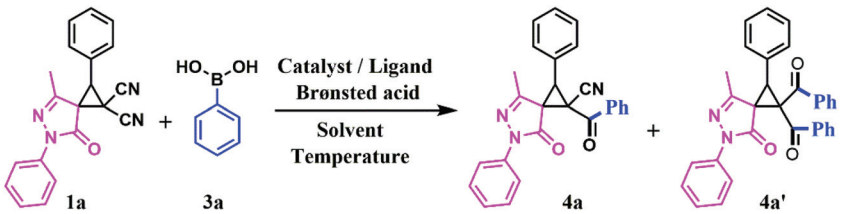


Table 1 Screening of catalysts, ligands, acids and solvents and optimization of reaction conditions[a]



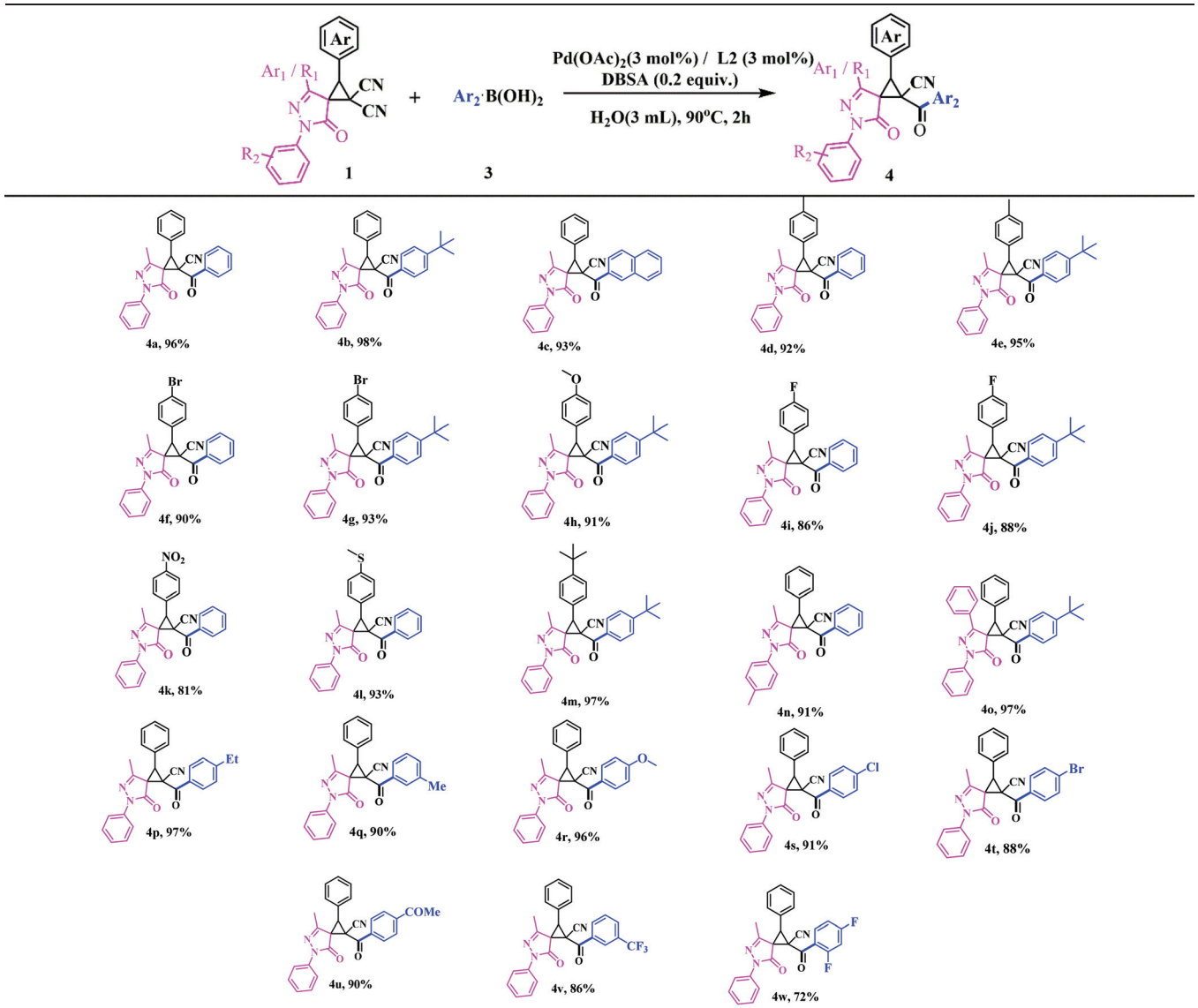
Entry	Catalyst (mol%)	Ligand (mol%)	Brønsted acid (equiv.)	Solvent	Temp. (°C)	Time (h)	Yield of **4a**[b] (%)
1[c]	$Pd(OAc)_2$ (5)	L2 (5)	AcOH (2.0)	1,4-Dioxane + H_2O (1 : 1)	100	3.0	20
2[c]	$Pd(OAc)_2$ (5)	L2 (5)	TfOH (2.0)	1,4-Dioxane + H_2O (1 : 1)	100	2.0	13
3[c]	$Pd(OAc)_2$ (5)	L2 (5)	AcOH (2.0)	1,4-Dioxane + H_2O (1 : 1)	100	3.0	20
4[c]	$Pd(OAc)_2$ (10)	L2 (10)	AcOH (2.0)	1,4-Dioxane + H_2O (1 : 1)	100	3.0	22
5[c]	$Pd(OAc)_2$ (5)	L2 (5)	AcOH (2.0)	DMSO + H_2O (2 : 1)	130	2.0	10
6[c]	$Pd(OAc)_2$ (5)	L2 (5)	AcOH (2.0)	NMP + H_2O (2 : 1)	130	2.0	12
7[c]	$Pd(OAc)_2$ (5)	L2 (5)	TFA (2.0)	1,4-Dioxane + H_2O (1 : 1)	100	3.0	10
8	$Pd(OAc)_2$ (5)	L2 (5)	AcOH (1.1)	1,4-Dioxane + H_2O (1 : 1)	100	3.0	34
9	$Pd(OAc)_2$ (5)	L2 (5)	TfOH (1.1)	1,4-Dioxane + H_2O (1 : 1)	100	2.0	25
10	$Pd(OAc)_2$ (5)	L2 (5)	PTSA (1.1)	1,4-Dioxane + H_2O (1 : 1)	100	2.0	40
11	$Pd(OAc)_2$ (5)	L2 (5)	PTSA (1.1)	1,4-Dioxane + H_2O (1 : 1)	90	2.0	52
12	$Pd(OAc)_2$ (5)	L2 (5)	PTSA (1.1)	THF + H_2O (1 : 1)	90	2.0	76
13	$Pd(OAc)_2$ (5)	L2 (5)	PTSA (1.1)	THF + H_2O (1 : 1)	80	4.0	54
14	$Pd(OAc)_2$ (5)	L2 (5)	DBSA (1.1)	H_2O	90	2.0	90
15	$Pd(OAc)_2$ (5)	L2 (5)	DBSA (0.2)	H_2O	90	2.0	94
16	**$Pd(OAc)_2$ (3)**	**L2 (3)**	**DBSA (0.2)**	**H_2O**	**90**	**2.0**	**96**
17	$Pd(OAc)_2$ (3)	L2 (3)	DBSA (2.0)	H_2O	90	2.0	88
18	$Pd(OAc)_2$ (2)	L2 (2)	DBSA (0.2)	H_2O	90	2.0	72
19	—	—	DBSA (0.2)	H_2O	Reflux	24.0	—
20	$FeCl_3$ (20)	—	DBSA (0.2)	H_2O	Reflux	20.0	—
21	$Yb(OTf)_3$ (20)	—	DBSA (0.2)	H_2O	Reflux	20.0	—
22	$Cu(OTf)_2$ (20)	—	DBSA (0.2)	H_2O	Reflux	20.0	—

[a] All the reactions were carried out with **1a** (0.5 mmol) and **2a** (0.6 mmol) in 3 mL of the solvent or solvent mixture. [b] Isolated yields of **4a** and **4a′** were not obtained in every case. [c] 2.0 equiv. of phenylboronic acid (**3a**) were used instead of 1.2 equiv.

began our investigation to optimize the reaction conditions for the formation of **4a** in a maximum yield as the diastereoselective reactions have great impact in synthetic organic chemistry.[10]

Then we modified the conditions by varying the amount of the catalyst, ligands, additives and solvent systems (Table 1, entries 2–7; Table S1 (see the ESI), entries 1 and2†) but all of them did not alter the diastereoselectivity and furnished **4a**. We then changed the amount of phenylboronic acid (1.2 equiv.) and the additive (1.1 equiv.) which increased the yield of **4a** to 34% (Table 1, entry 8). The use of triflic acid instead of acetic acid (Table 1, entry 9) however further decreased the yield. The use of *p*-toluenesulfonic acid (Table 1, entry 10) resulted a slight increase in the yield. Lowering of the temperature and use of THF as the solvent increased the yield to a great extent (Table 1, entries 11 and 12). Interestingly, when we used DBSA instead of *p*-toluenesulfonic acid (Table 1, entry 14), a further increase in the yield was observed. The absence of any co-solvent did not affect the reaction due to the surfactant property of DBSA. Generally, it forms micelles in water which act as reactors.[11] Furthermore, a catalytic amount of DBSA (Table 1, entry 15) was found to provide even better results.[12] Further deviation from these conditions either by changing the palladium catalyst or the ligand and other reagents lowered the yield (Table 1, entries 17 and 18; Table S1, entries 3–7 and 10–12†). The use of a mono-protected amino acid ligand (**L4**) and dppf (**L5**) along with palladium acetate was found to be unproductive (Table S1, entries 8

Table 3 Substrate scope for the synthesis of ketones from pyrazolo cyclopropane nitriles[a]



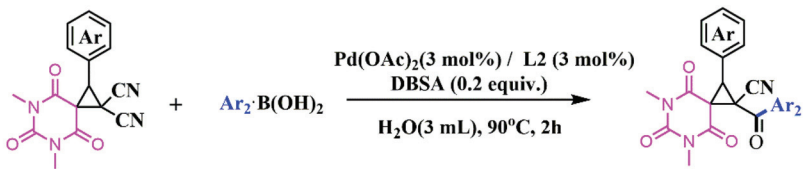
[a] Reaction conditions: 4-methyl-7-oxo-2,6-diaryl-5,6-diazaspiro[2.4]hept-4-ene-1,1-dicarbonitrile (**1a–i**) or 7-oxo-2,4,6-triphenyl-5,6-diazaspiro[2.4] hept-4-ene-1,1-dicarbonitrile (**1j**), arylboronic acid (1.2 mmol), 90 °C, 2 h.

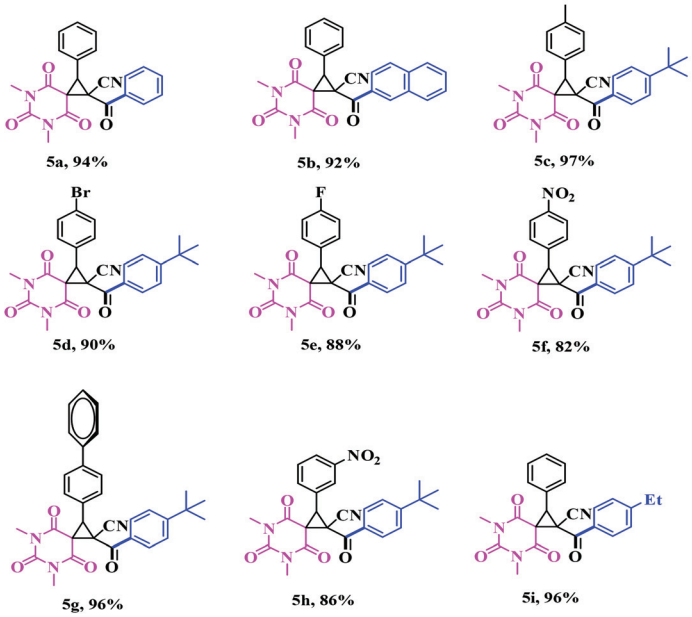
and 9†). Additionally, replacement of DBSA with aromatic and aliphatic carboxylic acids failed to afford **4a** (Table S1, entries 13 and 14†). The reaction was also carried out in the presence of Lewis acids such as $FeCl_3$, $Yb(OTf)_3$ and $Cu(OTf)_2$ and also in the absence of any metal catalyst (Table 1, entries 19–22) but all the attempts were in vain which essentially indicates the necessity of palladium salts as the effective catalyst for this particular transformation.

With these optimized conditions, we then started to investigate the extent and constraint of this protocol. For this objective, a wide variety of 4-methyl-7-oxo-2,6-diaryl-5,6-diazaspiro [2.4]hept-4-ene-1,1-dicarbonitrile (**1a–i**), 7-oxo-2,4,6-triphenyl-5,6-diazaspiro[2.4]hept-4-ene-1,1-dicarbonitrile (**1j**) and 5,7-dimethyl-4,6,8-trioxo-2-aryl-5,7-diazaspiro[2.5]-octane-1,1-dicarbonitrile (**2a–g**) possessing electron-donating and electron-withdrawing groups were prepared according to the literature.[13] Then these were employed for the reaction with 1.2 mmol arylboronic acid in the presence of 0.2 mmol DBSA using 3 mol% $Pd(OAc)_2$ and 3 mol% **L2** as the catalyst system in 3 mL water (Tables 3 and 4).

Every time, the reaction proceeded very smoothly. Furthermore, the reaction takes only 2 hours to consume the starting materials in all instances. In almost every case, we found that the desired ketones are produced in excellent yields (Tables 3 and 4). We also examined a vast variety of phenylboronic acid derivatives carrying both electron-donating and electron-withdrawing functionalities. Unfortunately, alkyl and heterocyclic boronic acids failed to produce the corresponding ketones under the optimized conditions. The reason may be the lower migratory aptitude of alkyl groups as compared to aryl groups present in boronic acid. In the case of the heterocyclic counterparts, the heterocyclic scaffold may inhibit the co-ordination of heteroaryl boronic acid with palladium. The reaction was found to be very compatible with the substrates containing bulky substituent groups like 4-*tert*-butyl phenyl and extended aromatic groups like naphthyl and biphenyl as well. However, it was found that the yields of the ketones carrying $-NO_2$, –F and $-CF_3$ groups (**4i–k**, **4v**, **4w**, **5e**, **5f**, and **5h**) are slightly lower than those of their other homologues. This may happen due to the lower solubility of their precursor nitriles (**1e**, **1f**, **2d**, **2e**, and **2g**) and phenylboronic acid derivatives (**3g** and **3k**) in aqueous media. All the synthesized compounds were well characterized through ^1H and ^{13}C NMR and IR spectroscopy. Finally, the structural motifs of the synthesized compounds were established through X-ray analysis of **4a** and **5g** (Fig. 1a and b) .

Table 4 Substrate scope for the synthesis of ketones from barbiturate cyclopropane nitriles[a]





[a] Reaction conditions: 5,7-dimethyl-4,6,8-trioxo-2-aryl-5,7-diazaspiro[2.5]-octane-1,1-dicarbonitrile (**2a–g**) (1.0 mmol), arylboronic acid (1.2 mmol), 90 °C, 2 h.

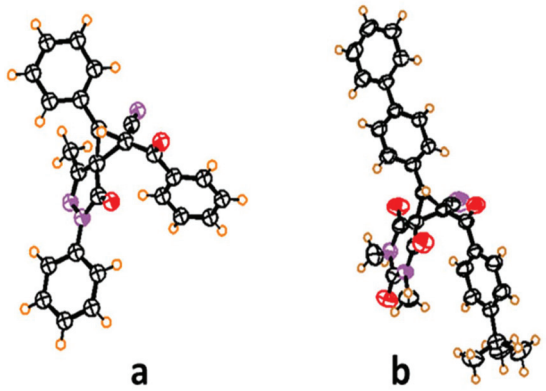
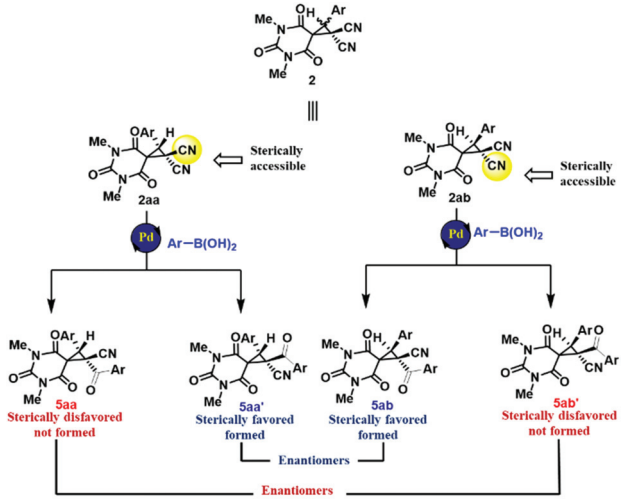
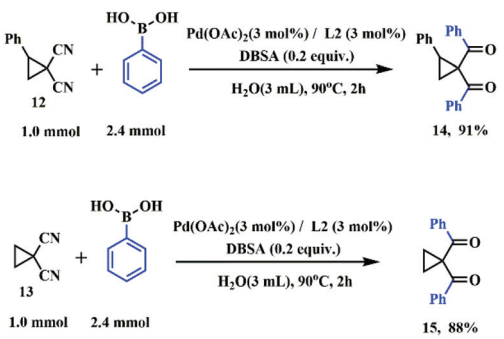


Fig. 1 (a) ORTEP diagram of compound **4a** (CCDC 1952896).† (b) ORTEP diagram of compound **5g** (CCDC 1952797).†

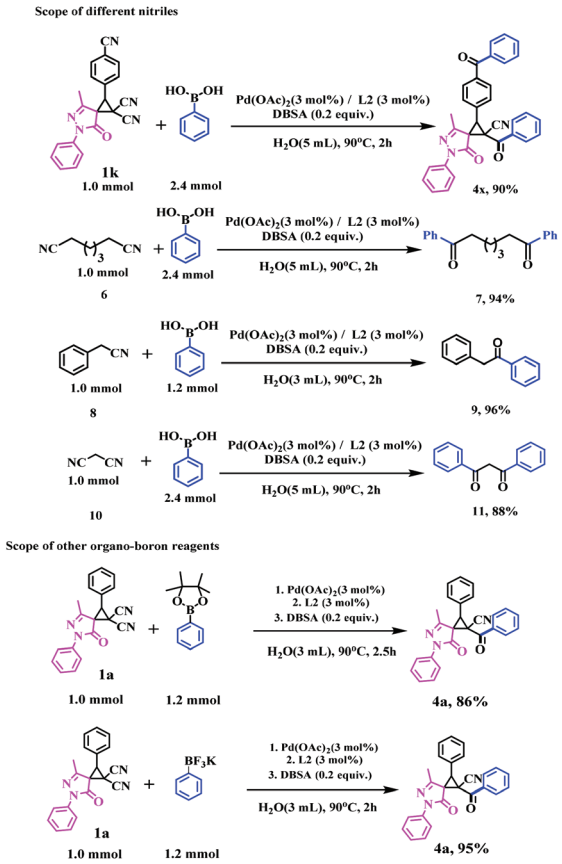


Scheme 3 Diastereoselectivity of the reaction.

We also performed some control experiments to establish the diastereoselectivity of the reaction using different nitrile compounds (Scheme 2). We took **1k** as our nitrile substrate where an aromatic nitrile group resides along with both cyclopropylic nitriles. Then the reaction with 2.4 equiv. of phenylboronic acid resulted in the transformation of one cyclopropylic nitrile along with the aromatic nitrile into the corresponding keto functionality. We also found that both of the nitrile groups of pimelonitrile (**6**) and malononitrile (**10**) can be converted to ketones through this protocol and the products **7** and **11** were obtained in 94% and 88% yields, respectively. Interestingly, when the amount of phenylboronic acid was reduced to half (1.2 equiv.), we obtained the same products from **1k**, **6** and **10** but the yields obtained were very low and almost half of the starting material remained unreacted. The yields obtained for the products **4x**, **7** and **11** were 43%, 46% and 33% respectively (see ESI, Scheme S2†). Additionally, phenyl acetonitrile can also be converted to 1,2-diphenylethan-1-one with an excellent yield. Interestingly, despite the efficacy of this protocol towards converting aromatic and aliphatic nitrile groups into the corresponding ketones, one of the two geminal nitriles of the starting spirocyclopropane always remained inactive during the reaction. This confirms that the diastereoselectivity lies inherently in the starting molecules which can be easily explained by considering the steric environment of the starting substrates (Scheme 3). Since **2** is present as an enantiomeric mixture of **2aa** and **2ab**, during the reaction, four stereoisomers can be obtained, at least theoretically. However, since the formation of isomers **5aa** and **5ab′** is sterically forbidden, they were not obtained during the reaction which is confirmed by analyzing NMR and X-ray data. Only **5aa′** and **5ab** were found to be the products which are essentially enantiomers with respect to each other. Interestingly, **5aa** and **5ab′**, bearing an enantiomeric relationship to each other, possess a diastereomeric relationship with **5aa′** and **5ab** respectively. Thus, it is quite clear that this reaction is indeed a diastereoselective reaction and affords only one diastereomer as an enantiomeric mixture. From (Scheme 3) and Scheme S1 (see the ESI)† it is evident that the structure of these cyclopropanes (**1** and **2**) plays a crucial role in this diastereoselective reaction, so we applied our protocol on 2-phenylcyclopropane-1,1-dicarbonitrile (**12**) and cyclopropane-1,1-dicarbonitrile (**13**) which are free of any steric hindrance. On reaction with 2.4 equiv. of phenylboronic acid, both of the nitrile groups of **12** and **13** were converted to ketones (**14** and **15**) with excellent yields (Scheme 4). We also performed this reaction with 1.2 equiv. of phenylboronic acid for cyclopropane **12** and **13**, which led to the same product but in a lower yield (see ESI, Scheme S2†). Furthermore, we investigated the suitability of other organo-boron compounds like aryl boron pinacolate and potassium aryl boron trifluoride salt in this protocol and they showed very impressive results (Scheme 2). We also obtained an optical image of the reaction mixture (Fig. 2) which confirms the formation of micelles promoted by DBSA. The formation of the micellar medium facilitates the reaction to occur in the hydrophobic interior[14] and eliminates water from the core which essentially improves the overall rate and yield of the reaction. Again, we performed



Scheme 4 Scope of the steric hindrance free cyclopropane nitriles.



Scheme 2 Control experiments.

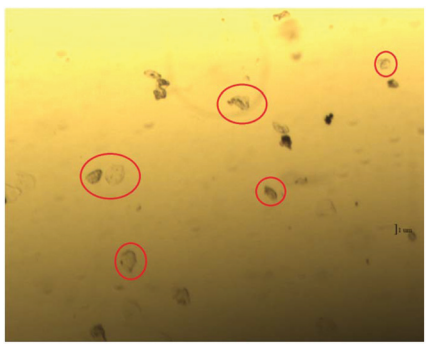


Fig. 2 Optical micrograph of the micellar medium.

DLS and TEM studies to identify the size distribution pattern and shape of micelles. The dynamic light scattering study discloses that the hydrodynamic radius of the micelles lies in in the 0.7–1 nm range (Fig. 3). The TEM image of a drop of DBSA solution further confirms this fact as small dark spots can be seen in the polymeric matrix arising from the micellar aggregation (Fig. 4).

To check the practical applicability of this protocol, we performed the gram-scale synthesis of **4a** and **5a** and they were obtained in 91% and 90% yields respectively (Scheme 5).

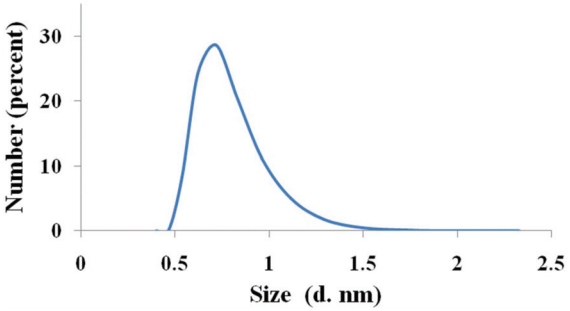


Fig. 3 Micellar size distribution as observed in the dynamic light scattering experiment.

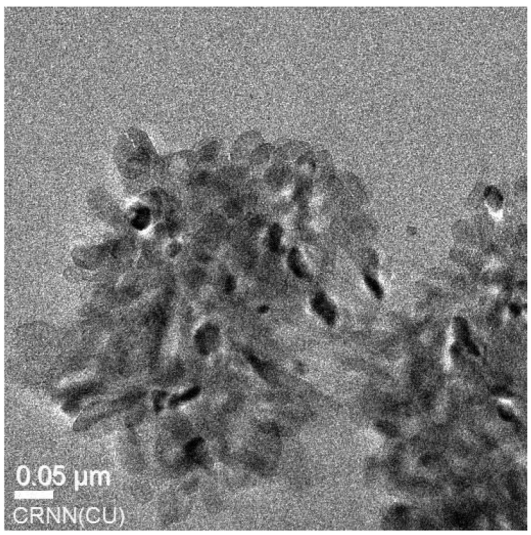
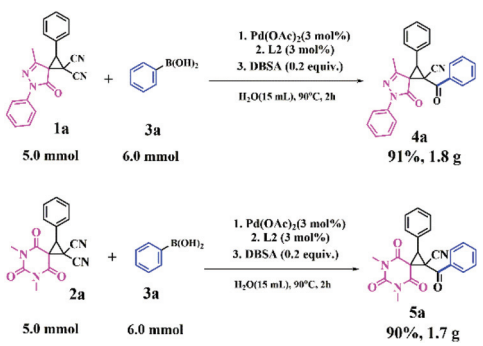
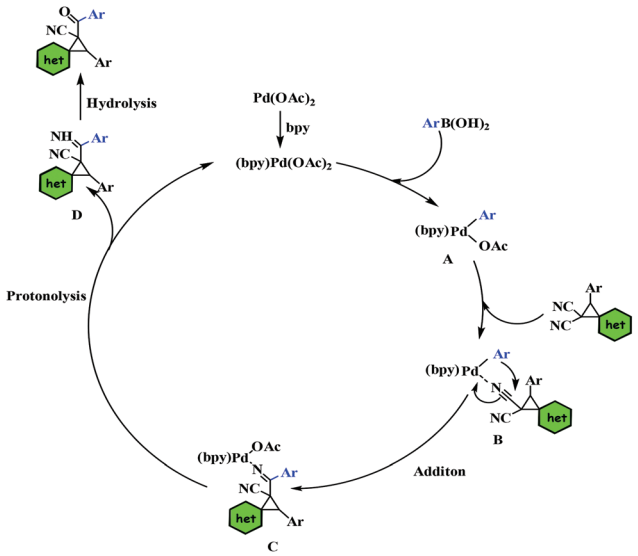


Fig. 4 Transmission electron microscopy image of the DBSA solution showing an ~0.7–1 nm sized micellar distribution (small dark spots).



Scheme 5 Scale-up synthesis of **4a** and **5a**.

According to the previous literature[8,15] and based on the above results, it is clear that transmetallation and co-ordination of Pd(II) complex species with nitriles are the key steps of this reaction. Hence the plausible reaction mechanism can be the transfer of aryl group to the C≡N bond forming intermediate **C**. Protonolysis of **C** produces **D** and regenerates the palla-



Scheme 6 Plausible mechanism of the reaction.

dium catalyst. Hydrolysis of **D** yields ketones as the products (Scheme 6).

Conclusion

In summary, we have developed a protocol for palladium catalyzed diastereoselective addition of arylboronic acids to complex cyclopropyl dinitriles which is the first case of these types of reactions involving such a complex scaffold. Moreover, this reaction is unique compared to the rest of the reactions of this category due to the use of catalytic DBSA in aqueous media. Additionally, the advantages offered by this reaction are: low catalyst loading, greener solvents, mild conditions and shorter reaction time. The extension and development of this protocol by inclusion of other suitable species instead of boronic acid are in progress.

Experimental

Materials, methods and general synthetic procedures

^{1}H-NMR and ^{13}C-NMR spectral analyses were carried out using 300 MHz, 400 MHz, 500 MHz, 75 MHz, 100 MHz, and 125 MHz instruments where tetramethylsilane (TMS) was used as an internal standard. Infrared spectra were recorded in KBr pellets in the reflection mode on a FTIR spectrophotometer. High resolution mass spectra were obtained using a mass spectrometer. Elemental analyses were performed using an autoanalyzer. Suitable single crystals of compounds **4a** and **5g** were mounted on an X-ray diffractometer equipped with a graphite monochromator. All the reactions were monitored by thin layer chromatography carried out on aluminium-blocked silica gel plates coated with silica gel GF_{254} under UV light and also by exposure to iodine vapor for detection. Melting points were recorded on a Köfler Block apparatus and are uncorrected. DBSA and organo-boron compounds were purchased from Sigma-Aldrich. For column chromatography, 100–200 mesh silica gel was used. All the organic solvents used in the reaction were appropriately dried and distilled prior to use.

General procedure for the synthesis of the required pyrazolone derivatives. Sodium acetate (574.0 mg, 7.0 mmol) was added in a suspension of aromatic hydrazine hydrochloride derivatives (7.0 mmol) in 8 mL of EtOH and 2 mL of water, and the mixture was stirred at rt for 5 min. Then, to the mixture, ethyl acetoacetate (911.0 mg, 7.0 mmol) or ethyl benzoylacetate (1345.5 mg, 7.0 mmol) was added, and the resultant mixture was heated to reflux for 3 h. After that, the mixture was poured dropwise onto crushed ice (50 g) with vigorous stirring, and the resulting precipitate was then filtered and crystallized from EtOH. The obtained pyrazolone derivatives were then used for the synthesis of pyranopyrazoles without further purification.[16]

General procedure for the synthesis of pyranopyrimidine-diones and pyranopyrazoles. Triethylamine (2 drops) was added to a mixture of aromatic aldehydes (4.0 mmol), malononitrile (264 mg, 4.0 mmol), and 1,3-dimethylbarbituric acid (624 mg, 4.0 mmol) or pyrazolones (4.0 mmol) in EtOH (8 mL), and the reaction mixture was refluxed for 15 min. The precipitate that was formed after cooling the reaction mixture to room temperature was filtered, washed with water (3 × 5 mL) and EtOH (2 × 5 mL), and finally crystallized from EtOH. The crystallized pure pyranopyrimidine-diones and pyranopyrazoles were then employed for the synthesis of spirocyclopropyl barbiturates and pyrazolones without further purification.[13]

General method for the synthesis of spirocyclopropyl-pyrazolones (1a–k) and barbiturates (2a–g). To a stirring suspension of PIDA (483.2 mg, 1.5 mmol) in 7 mL of DCM, I_2 (380.1 mg, 1.5 mmol) was added and stirred for 5 min at rt. Then, pyranopyrimidine-diones (3.0 mmol) or pyranopyrazoles (3.0 mmol) were added in this mixture, followed by the addition of triethylamine (6.0 mmol), and the resulting mixture was stirred for 30 min at rt. After completion of the reaction (monitored by TLC), the solvent was evaporated from the reaction mixture under reduced pressure and the resulting crude mass was triturated with MeOH (8 mL). The solid precipitate thus obtained was then filtered and washed with MeOH (3 × 5 mL) and finally crystallized from ethyl acetate to obtain the pure products.[13]

Procedure for the synthesis of 2-phenylcyclopropane-1,1-dicarbonitrile (12). A 25 mL oven dried RB flask was charged with styrene (412.5 mg, 3 mmol) and malononitrile (238.0 mg, 3.6 mmol). Then 6 mL of dry DCE was added to it and stirred. Next, $PhI(OAc)_2$ (1063.0 mg, 3.3 mmol) and K_2CO_3 (456.1 mg, 3.3 mmol) were added in the mixture and heated at 80 °C. After completion of the reaction (monitored by TLC), the mixture was cooled to room temperature and poured into 25 mL brine and extracted with DCM (3 × 15 mL). The solvent was removed under reduced pressure, and the residue was pur-

ified by flash silica gel column chromatography (EtOAc–petroleum ether = 1 : 10).[17]

Procedure for the synthesis of cyclopropane-1,1-dicarbonitrile (13). In a 100 mL RB flask, malononitrile (1 g, 15.2 mmol) and K_2CO_3 (5.5 g, 39.8 mmol) were dissolved in 40 mL anhydrous DCM. Then, 1,2-dibromoethane (3.85 g, 20.6 mmol) and crown ether 18-C-6 (0.7 g, 2.65 mmol) were added in this mixture and stirred for 48 hours under a nitrogen atmosphere. After completion of the reaction, the reaction mixture was filtered and concentrated under reduced pressure. Finally, it was purified by flash silica gel column chromatography.[18]

General procedure for the synthesis of 4a–o, 5a–h and 9. In a 25 mL oven-dried RB flask, 3 mol% $Pd(OAc)_2$ (6.74 mg) and 3 mol% 2,2′-bipyridine (4.68 mg) were taken. Then a solution of 0.2 mmol 4-dodecylbenzenesulfonic acid (65.3 mg) in 1.5 mL of distilled water was added and stirred for 5 minutes. After that, 1.0 mmol of **1**, **2** or **8** and 1.2 mmol arylboronic acid (**3**) were added in the RB flask sequentially under vigorous stirring and then another 1.5 mL of distilled water was added to mark up the volume. Next, the mixture was heated at 90 °C in an open atmosphere for 2 hours. After completion of the reaction (monitored by TLC), the mixture was allowed to cool to room temperature and then neutralized with 30 mL saturated $NaHCO_3$ solution and extracted with 3 × 15 mL ethyl acetate. Then the combined organic layers were washed with saturated brine and dried over anhydrous Na_2SO_4. After that, the solvent was reduced under vacuum and the product was purified by column chromatography in 100–200 mesh silica gel using a mixture of ethyl acetate in petroleum ether (1 : 19 to 3 : 17) as an eluent.

General procedure for the synthesis of 4p and 7. In a 25 mL oven-dried RB flask, 3 mol% $Pd(OAc)_2$ (13.4 mg) and 3 mol% 2,2′-bipyridine (10.0 mg) were taken. Then a solution of 0.4 mmol 4-dodecylbenzenesulfonic acid (130.6 mg) in 1.5 mL of distilled water was added and stirred for 5 minutes. After that, 1.0 mmol of **1j** or **6** and 2.4 mmol phenylboronic acid (**3a**) were added in the RB flask sequentially under vigorous stirring and then another 3.5 mL of distilled water was added to mark up the volume. Next, the mixture was heated at 90 °C in an open atmosphere for 2 hours. After completion of the reaction (monitored by TLC), the mixture was allowed to cool to room temperature and then neutralized with 30 mL saturated $NaHCO_3$ solution and extracted with 3 × 15 mL ethyl acetate. Then the combined organic layers were washed with saturated brine and dried over anhydrous Na_2SO_4. After that, the solvent was reduced under vacuum and the product was purified by column chromatography in 100–200 mesh silica gel using a mixture of ethyl acetate in petroleum ether as an eluent.

Synthesis of 4a and 5a on a 5 mmol scale. In a 50 mL oven-dried RB flask, 3 mol% $Pd(OAc)_2$ (33.6 mg) and 3 mol% 2,2′-bipyridine (23.4 mg) were taken. Then a solution of 1.0 mmol 4-dodecylbenzenesulfonic acid (327.0 mg) in 5 mL of distilled water was added and stirred for 5 minutes. After that, 5.0 mmol of **1a** or **2a** and 6.0 mmol arylboronic acid (**3a**) were added in the RB flask sequentially under vigorous stirring and then another 10 mL of distilled water was added to mark up the volume. Next, the mixture was heated at 90 °C in an open atmosphere for 2 hours. After completion of the reaction (monitored by TLC), the mixture was allowed to cool to room temperature and then neutralized with 50 mL saturated $NaHCO_3$ solution and extracted with 3 × 20 mL ethyl acetate. Then the combined organic layers were washed with saturated brine and dried over anhydrous Na_2SO_4. After that, the solvent was reduced under vacuum and the product was purified by column chromatography in 100–200 mesh silica gel using a mixture of ethyl acetate in petroleum ether as an eluent to afford **4a** (91%) and **5a** (90%) as pure products.

Characterization data for the products 4a–w and 5a–i

1-Benzoyl-4-methyl-7-oxo-2,6-diphenyl-5,6-diazaspiro[2.4]hept-4-ene-1-carbonitrile (4a). Off-white solid (389.2 mg, 96%); mp: 184–186 °C; ^{1}H NMR (300 MHz; $CDCl_3$; Me_4Si): δ 7.95–7.88 (m, 2H), 7.76–7.69 (m, 2H), 7.64 (t, J = 7.4 Hz, 1H), 7.50 (t, J = 7.6 Hz, 7H), 7.37 (t, J = 7.9 Hz, 2H), 7.20 (t, J = 7.4 Hz, 1H), 4.27 (s, 1H), 2.00 (s, 3H); ^{13}C{^{1}H}NMR (75 MHz; $CDCl_3$; Me_4Si): δ 183.2, 165.4, 153.1, 137.1, 134.6, 132.8, 129.1, 129.0, 128.9, 128.8, 128.6, 125.4, 118.5, 118.4, 118.3, 113.7, 46.2, 39.9, 36.6, 16.4; IR (KBr): 2961, 2230, 1718, 1550, 1487, 1328, 1257, 1161, 1110, 1015, 834 cm^{-1}; anal. calcd for [$C_{26}H_{19}N_3O_2$]: C 77.02; H 4.72; N 10.36; O 7.89. Found: C 77.05; H 4.74; N 10.34; O 7.90.

1-(4-(*tert*-Butyl)benzoyl)-4-methyl-7-oxo-2,6-diphenyl-5,6-diazaspiro[2.4]hept-4-ene-1-carbonitrile (4b). White (452.3 mg, 98%); mp: 168–170 °C; ^{1}H NMR (300 MHz; $CDCl_3$; Me_4Si): δ 7.85 (d, J = 8.6 Hz, 2H), 7.70 (d, J = 7.6 Hz, 2H), 7.50 (dd, J = 5.3, 3.4 Hz, 7H), 7.37 (t, J = 7.9 Hz, 2H), 7.20 (t, J = 7.4 Hz, 1H), 4.26 (s, 1H), 2.00 (s, 3H), 1.32 (s, 9H); ^{13}C{^{1}H}NMR (75 MHz; DMSO-d_6; Me_4Si): δ 183.3, 165.8, 158.8, 153.1, 137.3, 130.4, 129.8, 129.27, 129.2, 129.1, 129.0, 128.7, 126.5, 125.7, 118.8, 114.3, 46.4, 36.6, 35.2, 30.7, 30.6, 16.4; IR (KBr): 2946, 2232, 1721, 1558, 1481, 1323, 1247, 1149, 1101, 1010, 823 cm^{-1}; anal. calcd for [$C_{30}H_{27}N_3O_2$]: C 78.07; H 5.90; N 9.10; O 6.93. Found: C 78.05; H 5.91; N 9.07; O 6.91.

1-(2-Naphthoyl)-4-methyl-7-oxo-2,6-diphenyl-5,6-diazaspiro[2.4]hept-4-ene-1-carbonitrile (4c). Off-white (423.6 mg, 93%); mp: 192–193 °C; ^{1}H NMR (300 MHz; $CDCl_3$; Me_4Si): δ 8.44 (s, 1H), 7.95–7.84 (m, 4H), 7.72–7.49 (m, 9H), 7.31 (t, J = 7.9 Hz, 2H), 7.15 (t, J = 7.4 Hz, 1H), 4.34 (s, 1H), 2.06 (s, 3H); ^{13}C{^{1}H} NMR (75 MHz; $CDCl_3$; Me_4Si): δ 184.3, 166.6, 154.3, 138.1, 136.9, 133.0, 132.12, 131.2, 130.6, 130.3, 130.2, 130.09, 130.0, 129.6, 129.5, 128.5, 128.0, 126.4, 124.3, 119.5, 114.8, 47.4, 41.1, 37.8, 17.5; IR (KBr): 2964, 2223, 1711, 1564, 1489, 1321, 1240, 1154, 1108, 1012, 765 cm^{-1}; anal. calcd for [$C_{30}H_{21}N_3O_2$]: C 79.10; H 4.65; N 9.22; O 7.02. Found: C 79.11; H 4.63; N 9.23; O 7.01.

1-Benzoyl-4-methyl-7-oxo-6-phenyl-2-(*p*-tolyl)-5,6-diazaspiro[2.4]hept-4-ene-1-carbonitrile (4d). Yellow (385.9 mg, 92%); mp: 190–191 °C; ^{1}H NMR (300 MHz; $CDCl_3$; Me_4Si): δ 7.91 (d, J = 7.2 Hz, 2H), 7.73 (d, J = 7.7 Hz, 2H), 7.63 (t, J = 7.4 Hz, 1H), 7.49 (t, J = 7.6 Hz, 2H), 7.35 (dt, J = 23.9, 8.0 Hz, 6H), 7.20 (t, J = 7.4 Hz, 1H), 4.23 (s, 1H), 2.44 (s, 3H), 2.02 (s, 3H); ^{13}C{^{1}H}NMR (75 MHz; $CDCl_3$; Me_4Si): δ 183.6, 165.8, 153.6, 139.3, 137.5,

134.9, 133.2, 129.9, 129.3, 129.2, 128.97, 128.9, 128.8, 125.7, 125.6, 118.7, 114.1, 46.6, 40.2, 37.0, 21.2, 16.8; IR (KBr): 2992, 2242, 1710, 1510, 1372, 1334, 1167, 1012, 812 cm^{-1}; anal. calcd for $[C_{27}H_{21}N_3O_2]$: C 77.31; H 5.05; N 10.02; O 7.63. Found: C 77.29; H 5.03; N 10.03; O 7.65.

1-(4-(*tert*-Butyl)benzoyl)-4-methyl-7-oxo-6-phenyl-2-(*p*-tolyl)-5,6-diazaspiro[2.4]hept-4-ene-1-carbonitrile (4e). Yellow (451.8 mg, 95%); mp: 185 °C; ^{1}H NMR (300 MHz; $CDCl_3$; Me_4Si): δ 7.83 (d, J = 8.6 Hz, 2H), 7.70 (d, J = 7.7 Hz, 2H), 7.49 (d, J = 8.6 Hz, 2H), 7.42–7.29 (m, 6H), 7.20 (t, J = 7.4 Hz, 1H), 4.21 (s, 1H), 2.43 (s, 3H), 2.00 (s, 3H), 1.31 (s, 9H); $^{13}C\{^1H\}$ NMR (75 MHz; $CDCl_3$; Me_4Si): δ 183.2, 165.9, 158.9, 153.7, 139.2, 137.5, 130.7, 129.9, 129.3, 129.0, 128.9, 128.8, 128.7, 126.3, 125.8, 125.6, 118.8, 114.3, 46.6, 40.2, 37.2, 35.3, 30.8, 21.2, 16.8; IR (KBr): 2995, 2237, 1710, 1508, 1378, 1330, 1161, 1002, 821 cm^{-1}; anal. calcd for $[C_{31}H_{29}N_3O_2]$: C 78.29; H 6.15; N 8.84; O 6.73. Found: C 78.30; H 6.13; N 8.85; O 6.72.

1-Benzoyl-2-(4-bromophenyl)-4-methyl-7-oxo-6-phenyl-5,6-diazaspiro[2.4]hept-4-ene-1-carbonitrile (4f). Yellow (435.9 mg, 90%); mp: 162 °C; ^{1}H NMR (300 MHz; $CDCl_3$; Me_4Si): δ 8.11 (td, J = 8.6, 6.4 Hz, 1H), 7.87–7.80 (m, 2H), 7.51–7.35 (m, 8H), 7.21 (t, J = 7.4 Hz, 1H), 7.10–7.02 (m, 1H), 6.89–6.79 (m, 1H), 4.31 (s, 1H), 1.89 (s, 3H); $^{13}C\{^1H\}$NMR (75 MHz; DMSO-d_6; Me_4Si): δ 183.5, 165.6, 152.7, 137.3, 135.4, 132.7, 132.1, 129.6, 129.0, 128.6, 128.5, 125.6, 122.7, 118.6, 114.0, 16.5; IR (KBr): 2952, 2237, 1712, 1560, 1497, 1324, 1256, 1162, 1116, 1001, 840 cm^{-1}; anal. calcd for $[C_{26}H_{18}BrN_3O_2]$: C 64.47; H 3.75; Br 16.50; N 8.68; O 6.61. Found: C 64.48; H 3.73; Br 16.51; N 8.67; O 6.63.

2-(4-Bromophenyl)-1-(4-(*tert*-butyl)benzoyl)-4-methyl-7-oxo-6-phenyl-5,6-diazaspiro[2.4]hept-4-ene-1-carbonitrile (4g). Yellow (502.6 mg, 93%); mp: 158–159 °C; ^{1}H NMR (300 MHz; $CDCl_3$; Me_4Si): δ 7.81 (d, J = 8.6 Hz, 2H), 7.66 (t, J = 8.6 Hz, 4H), 7.49 (d, J = 8.6 Hz, 2H), 7.37 (dd, J = 14.4, 8.0 Hz, 4H), 7.20 (t, J = 7.4 Hz, 1H), 4.16 (s, 1H), 2.03 (s, 3H), 1.31 (s, 9H); $^{13}C\{^1H\}$NMR (75 MHz; $CDCl_3$; Me_4Si): δ 182.8, 165.6, 159.3, 153.1, 137.4, 132.6, 132.5, 131.2, 130.5, 129.0, 128.98, 128.9, 128.1, 126.4, 125.8, 123.7, 118.9, 114.0, 46.4, 39.5, 37.0, 35.4, 30.9, 16.9; IR (KBr): 2958, 2232, 1716, 1559, 1495, 1331, 1254, 1168, 1113, 1009, 844 cm^{-1}; anal. calcd for $[C_{30}H_{26}BrN_3O_2]$: C 66.67; H 4.85; Br 14.78; N 7.78; O 5.92. Found: C 66.65; H 4.86; Br 14.77; N 7.77; O 5.94.

1-(4-(*tert*-Butyl)benzoyl)-2-(4-methoxyphenyl)-4-methyl-7-oxo-6-phenyl-5,6-diazaspiro[2.4]hept-4-ene-1-carbonitrile (4h). Yellow (447.3 mg, 91%); mp: 155 °C; ^{1}H NMR (300 MHz; $CDCl_3$; Me_4Si): δ 7.84 (d, J = 8.5 Hz, 2H), 7.70 (d, J = 7.8 Hz, 2H), 7.52–7.33 (m, 6H), 7.20 (t, J = 7.4 Hz, 1H), 7.01 (d, J = 8.7 Hz, 2H), 4.19 (s, 1H), 3.88 (s, 3H), 2.02 (s, 3H), 1.31 (s, 9H); $^{13}C\{^1H\}$ NMR (75 MHz; $CDCl_3$; Me_4Si): δ 183.9, 166.6, 160.9, 159.7, 154.4, 138.2, 131.4, 129.5, 127.0, 126.3, 121.4, 119.6, 115.3, 115.0, 56.0, 47.4, 40.7, 38.0, 36.0, 31.5, 17.5; IR (KBr): 2955, 2230, 1712, 1651, 1552, 1492, 1329, 1251, 1166, 1111, 1011, 768 cm^{-1} anal. calcd for $[C_{31}H_{29}N_3O_3]$: C 75.74; H 5.95; N 8.55; O 9.76. Found: C 75.75; H 5.93; N 8.54; O 9.79.

1-Benzoyl-2-(4-fluorophenyl)-4-methyl-7-oxo-6-phenyl-5,6-diazaspiro[2.4]hept-4-ene-1-carbonitrile (4i). White (364.1 mg, 86%); mp: 192–193 °C; ^{1}H NMR (300 MHz; $CDCl_3$; Me_4Si): δ 7.90 (d, J = 7.2 Hz, 2H), 7.71 (d, J = 7.7 Hz, 2H), 7.64 (t, J = 7.4 Hz, 1H), 7.49 (dd, J = 9.9, 5.5 Hz, 4H), 7.37 (t, J = 7.9 Hz, 2H), 7.20 (t, J = 8.4 Hz, 3H), 4.21 (s, 1H), 2.03 (s, 3H); $^{13}C\{^1H\}$NMR (75 MHz; $CDCl_3$; Me_4Si): δ 183.2, 165.5, 164.6, 161.3, 153.0, 137.3, 134.9, 132.9, 131.3, 131.2, 129.2, 128.8, 125.7, 124.6, 118.6, 116.5, 116.2, 113.8, 46.4, 39.3, 36.9, 16.7; IR (KBr): 2968, 2231, 1712, 1559, 1495, 1331, 1254, 1168, 1113, 1009, 834 cm^{-1}; anal. calcd for $[C_{26}H_{18}FN_3O_2]$: C 73.75; H 4.28; F 4.49; N 9.92; O 7.56. Found: C 73.74; H 4.26; F 4.51; N 9.91; O 7.58.

1-(4-(*tert*-Butyl)benzoyl)-2-(4-fluorophenyl)-4-methyl-7-oxo-6-phenyl-5,6-diazaspiro[2.4]hept-4-ene-1-carbonitrile (4j). Yellow (422.0 mg, 88%); mp: 184–185 °C; ^{1}H NMR (300 MHz; $CDCl_3$; Me_4Si): 7.80 (d, J = 8.5 Hz, 2H), 7.66 (d, J = 7.7 Hz, 2H), 7.51–7.44 (m, 4H), 7.34 (t, J = 7.9 Hz, 2H), 7.18 (t, J = 8.4 Hz, 3H), 4.17 (s, 1H), 1.99 (s, 3H), 1.28 (s, 9H); $^{13}C\{^1H\}$NMR (75 MHz; $CDCl_3$; Me_4Si): δ 182.8, 165.6, 164.6, 161.3, 159.1, 153.1, 137.3, 131.4, 131.3, 130.4, 128.9, 128.8, 128.7, 126.3, 125.7, 124.8, 118.8, 116.5, 116.2, 114.0, 46.4, 39.3, 37.0, 35.3, 30.8, 16.7; IR (KBr): 2988, 2237, 1709, 1562, 1491, 1339, 1256, 1165, 1109, 1015, 847 cm^{-1}; anal. calcd for $[C_{30}H_{26}FN_3O_2]$: C 75.14; H 5.47; F 3.96; N 8.76; O 6.67. Found: C 75.15; H 5.46; F 3.98; N 8.75; O 6.66.

1-Benzoyl-4-methyl-2-(4-nitrophenyl)-7-oxo-6-phenyl-5,6-diazaspiro[2.4]hept-4-ene-1-carbonitrile (4k). Yellow (364.8 mg, 81%); mp: 201–202 °C; ^{1}H NMR (300 MHz; $CDCl_3$; Me_4Si): δ 8.27 (d, J = 8.5 Hz, 2H), 7.78 (d, J = 7.5 Hz, 2H), 7.58 (dt, J = 19.0, 9.4 Hz, 5H), 7.41 (t, J = 7.6 Hz, 2H), 7.27 (t, J = 7.8 Hz, 2H), 7.11 (t, J = 7.3 Hz, 1H), 4.17 (s, 1H), 1.92 (s, 3H); $^{13}C\{^1H\}$ NMR (75 MHz; $CDCl_3$; Me_4Si): δ 182.7, 165.0, 152.1, 148.3, 137.1, 136.0, 135.2, 132.6, 130.6, 129.3, 128.79, 128.7, 125.9, 124.39, 124.3, 118.69, 118.6, 113.4, 46.2, 38.8, 36.4, 16.7; IR (KBr): 2968, 2231, 1712, 1559, 1495, 1345, 1250, 1168, 1113, 1009, 834 cm^{-1}; anal. calcd for $[C_{26}H_{18}N_4O_4]$: C 69.33; H 4.03; N 12.44; O 14.21. Found: C 69.34; H 4.01; N 12.46; O 14.20.

1-Benzoyl-4-methyl-2-(4-(methylthio)phenyl)-7-oxo-6-phenyl-5,6-diazaspiro[2.4]hept-4-ene-1-carbonitrile (4l). Yellow (419.9 mg, 93%); mp: 146–147 °C; ^{1}H NMR (300 MHz; $CDCl_3$; Me_4Si): δ 7.90–7.84 (m, 2H), 7.68 (d, J = 7.7 Hz, 2H), 7.61 (t, J = 7.4 Hz, 1H), 7.48 (d, J = 7.9 Hz, 2H), 7.42–7.29 (m, 6H), 7.18 (t, J = 7.4 Hz, 1H), 4.17 (s, 1H), 2.52 (s, 3H), 2.01 (s, 3H); $^{13}C\{^1H\}$ NMR (75 MHz; $CDCl_3$; Me_4Si): δ 183.1, 165.3, 153.0, 140.3, 137.0, 134.6, 132.7, 129.4, 128.9, 128.5, 126.1, 125.3, 124.6, 118.4, 113.6, 46.2, 39.5, 36.6, 16.5, 14.8; IR (KBr): 2962, 2229, 1708, 1551, 1331, 1254, 1178, 1123, 1012, 843 cm^{-1}; anal. calcd for $[C_{27}H_{21}N_3O_2S]$: C 71.82; H 4.69; N 9.31; O 7.09; S 7.10. Found: C 71.84; H 4.67; N 9.30; O 7.08; S 7.11.

1-(4-(*tert*-Butyl)benzoyl)-2-(4-(*tert*-butyl)phenyl)-4-methyl-7-oxo-6-phenyl-5,6-diazaspiro[2.4]hept-4-ene-1-carbonitrile (4m). Yellow (502.1 mg, 97%); mp: 175–176 °C; ^{1}H NMR (500 MHz; $CDCl_3$; Me_4Si): δ 7.83–7.81 (m, 2H), 7.70–7.68 (m, 2H), 7.49–7.46 (m, 4H), 7.42 (d, J = 8.0 Hz, 2H), 7.35–7.32 (m, 2H), 7.17 (m, 1H), 4.19 (s, 1H), 1.97 (s, 3H), 1.35 (s, 9H), 1.29 (s, 9H); $^{13}C\{^1H\}$NMR (100 MHz; $CDCl_3$; Me_4Si): δ 183.3, 166.1, 159.1, 153.8, 152.7, 137.7, 130.9, 129.2, 129.07, 129.04, 129.0,

126.4, 126.3, 126.0, 125.7, 119.0, 114.5, 46.7, 40.3, 37.3, 35.4, 34.9, 31.3, 31.0, 16.9; IR (KBr): 2957, 2229, 1715, 1535, 1490, 1331, 1251, 1172, 1107, 1013, 835 cm^{-1}; anal. calcd for $[C_{34}H_{35}N_3O_2]$: C 78.89; H 6.82; N 8.12; O 6.18. Found: C 78.91; H 6.83; N 8.10; O 6.17.

1-Benzoyl-4-methyl-7-oxo-2-phenyl-6-(*p*-tolyl)-5,6-diazaspiro[2.4]hept-4-ene-1-carbonitrile (4n). Yellow (381.7 mg, 91%); mp: 183–184 °C; ^{1}H NMR (300 MHz; $CDCl_3$; Me_4Si): δ 7.78 (d, J = 7.2 Hz, 2H), 7.46 (d, J = 8.1 Hz, 3H), 7.37 (s, 7H), 7.03 (d, J = 8.1 Hz, 2H), 4.13 (s, 1H), 2.21 (s, 3H), 1.87 (s, 3H); $^{13}C\{^1H\}$NMR (75 MHz; $CDCl_3$; Me_4Si): δ 183.5, 165.4, 153.2, 135.4, 134.9, 134.8, 133.0, 129.4, 129.3, 129.1, 129.0, 128.8, 118.7, 113.9, 46.4, 40.0, 36.7, 20.8, 16.6; IR (KBr): 2998, 2245, 1713, 1511, 1374, 1329, 1165, 1007, 819 cm^{-1}; anal. calcd for $[C_{27}H_{21}N_3O_2]$: C 77.31; H 5.05; N 10.02; O 7.63. Found: C 77.33; H 5.04; N 10.01; O 7.64.

1-(4-(*tert*-Butyl)benzoyl)-7-oxo-2,4,6-triphenyl-5,6-diazaspiro[2.4]hept-4-ene-1-carbonitrile (4o). Yellow (507.9 mg, 97%); mp: 178–180 °C; ^{1}H NMR (300 MHz; $CDCl_3$; Me_4Si): δ 8.04 (d, J = 7.8 Hz, 2H), 7.53 (d, J = 8.6 Hz, 2H), 7.47–7.29 (m, 11H), 7.22 (t, J = 3.7 Hz, 1H), 7.15 (t, J = 7.7 Hz, 2H), 6.88 (d, J = 7.3 Hz, 2H), 4.75 (s, 1H), 1.30 (s, 9H); $^{13}C\{^1H\}$NMR (125 MHz; $CDCl_3$; Me_4Si): δ 183.1, 163.7, 159.8, 154.4, 138.1, 130.7, 130.5, 129.6, 129.4, 129.2, 129.1, 129.0, 128.5, 128.0, 127.8, 126.2, 125.9, 119.0, 112.6, 44.8, 40.4, 37.2, 35.6, 31.1; IR (KBr): 2989, 2242, 1711, 1512, 1364, 1322, 1164, 1005, 809 cm^{-1}; anal. calcd for $[C_{35}H_{29}N_3O_2]$: C 80.28; H 5.58; N 8.02; O 6.11. Found: C 80.31; H 5.59; N 8.01; O 6.10.

1-(4-Ethylbenzoyl)-4-methyl-7-oxo-2,6-diphenyl-5,6-diazaspiro[2.4]hept-4-ene-1-carbonitrile (4p). White solid (420.1 mg, 97%); mp: 180–181 °C; ^{1}H NMR (300 MHz; $CDCl_3$; Me_4Si): δ 7.90 (d, J = 8.3 Hz, 2H), 7.51–7.40 (m, 5H), 7.34 (d, J = 8.3 Hz, 2H), 4.34 (s, 1H), 3.36 (s, 3H), 3.19 (s, 3H), 2.73 (q, J = 7.6 Hz, 2H), 1.26 (t, J = 7.6 Hz, 3H); $^{13}C\{^1H\}$NMR (75 MHz; $CDCl_3$; Me_4Si): δ 183.65, 166.39, 154.11, 152.95, 138.07, 131.44, 130.05, 129.86, 129.81, 129.71, 129.52, 129.45, 129.41, 126.23, 119.34, 117.30, 114.77, 78.01, 77.58, 77.16, 47.08, 40.82, 37.55, 29.62, 17.36, 15.45; IR (KBr): 2967, 2226, 1722, 1547, 1482, 1318, 1251, 1159, 1113, 1021, 830 cm^{-1}; anal. calcd for $[C_{28}H_{23}N_3O_2]$: C 77.58; H 5.35; N 9.69; O 7.38. Found: C 77.60; H 5.33; N 9.70; O 7.39.

4-Methyl-1-(3-methylbenzoyl)-7-oxo-2,6-diphenyl-5,6-diazaspiro[2.4]hept-4-ene-1-carbonitrile (4q). White gummy liquid (377.5 mg, 90%); ^{1}H NMR (300 MHz; $CDCl_3$; Me_4Si): δ 7.71 (dd, J = 8.4, 7.2 Hz, 3H), 7.61 (d, J = 7.6 Hz, 1H), 7.52–7.44 (m, 5H), 7.41 (d, J = 7.6 Hz, 1H), 7.38–7.30 (m, 3H), 7.22–7.15 (m, 1H), 4.23 (s, 1H), 2.36 (s, 3H), 1.98 (s, 3H); $^{13}C\{^1H\}$NMR (75 MHz; $CDCl_3$; Me_4Si): δ 183.74, 165.90, 153.60, 139.41, 137.50, 135.91, 133.12, 129.56, 129.53, 129.38, 129.31, 129.10, 128.96, 126.07, 125.77, 118.84, 114.12, 77.50, 77.07, 76.65, 46.61, 40.29, 37.03, 21.36, 16.83; IR (KBr): 2972, 2230, 1725, 1545, 1487, 1312, 1247, 1153, 1117, 1024, 837 cm^{-1}; anal. calcd for $[C_{27}H_{21}N_3O_2]$: C 77.31; H 5.05; N 10.02; O 7.63. Found: C 77.333; H 5.07; N 10.01; O 7.61.

1-(4-Methoxybenzoyl)-4-methyl-7-oxo-2,6-diphenyl-5,6-diazaspiro[2.4]hept-4-ene-1-carbonitrile (4r). White solid (418.0 mg, 96%); mp: 195–196 °C; ^{1}H NMR (300 MHz; $CDCl_3$; Me_4Si): δ 7.92–7.85 (m, 2H), 7.76 (dd, J = 8.7, 1.0 Hz, 2H), 7.53–7.46 (m, 5H), 7.41–7.34 (m, 2H), 7.24–7.17 (m, 1H), 6.99–6.92 (m, 2H), 4.26 (s, 1H), 3.85 (s, 3H), 1.99 (s, 3H); $^{13}C\{^1H\}$NMR (75 MHz; $CDCl_3$; Me_4Si): δ 181.82, 165.87, 164.98, 153.61, 137.60, 131.45, 129.55, 129.34, 129.29, 129.07, 128.97, 126.17, 125.69, 118.75, 114.66, 114.41, 77.52, 77.09, 76.67, 55.69, 46.57, 40.35, 36.99, 16.87; IR (KBr): 2970, 2232, 1726, 1542, 1480, 1328, 1248, 1162, 1117, 1027, 831 cm^{-1}; anal. calcd for $[C_{27}H_{21}N_3O_3]$: C 74.47; H 4.86; N 9.65; O 11.02. Found: C 74.49; H 4.84; N 9.63; O 11.05.

1-(4-Chlorobenzoyl)-4-methyl-7-oxo-2,6-diphenyl-5,6-diazaspiro[2.4]hept-4-ene-1-carbonitrile (4s). White solid (400.2 mg, 91%); mp: 177–178 °C; ^{1}H NMR (300 MHz; $CDCl_3$; Me_4Si): δ 7.88–7.81 (m, 2H), 7.74 (dd, J = 8.7, 1.1 Hz, 2H), 7.50 (s, 6H), 7.47 (s, 1H), 7.39 (t, J = 7.9 Hz, 2H), 7.22 (t, J = 7.4 Hz, 1H), 4.25 (s, 1H), 1.98 (s, 3H); $^{13}C\{^1H\}$NMR (75 MHz; $CDCl_3$; Me_4Si): δ 182.61, 165.70, 153.47, 141.78, 137.43, 131.53, 130.21, 129.78, 129.47, 129.37, 129.03, 128.69, 125.88, 118.71, 113.87, 77.48, 77.05, 76.63, 46.61, 40.34, 36.72, 16.82; IR (KBr): 2972, 2235, 1729, 1537, 1469, 1320, 1253, 1168, 1121, 1022, 835 cm^{-1}; anal. calcd for $[C_{26}H_{18}ClN_3O_2]$: C 70.99; H 4.12; Cl 8.06; N 9.55; O 7.27. Found: C 70.97; H 4.14; Cl 8.08; N 9.54; O 7.26.

1-(4-Bromobenzoyl)-4-methyl-7-oxo-2,6-diphenyl-5,6-diazaspiro[2.4]hept-4-ene-1-carbonitrile (4t). Yellow solid (426.2 mg, 88%); mp: 160–162 °C; ^{1}H NMR (300 MHz; $CDCl_3$; Me_4Si): δ 7.80–7.70 (m, 4H), 7.65 (d, J = 8.7 Hz, 2H), 7.50 (s, 5H), 7.39 (t, J = 7.9 Hz, 2H), 7.23 (t, J = 7.4 Hz, 1H), 4.25 (s, 1H), 1.98 (s, 3H); $^{13}C\{^1H\}$NMR (75 MHz; $CDCl_3$; Me_4Si): δ 182.98, 165.80, 153.57, 137.53, 132.88, 132.04, 130.77, 130.32, 129.57, 129.48, 129.15, 128.78, 126.00, 118.83, 113.96, 77.58, 77.16, 76.74, 46.72, 40.44, 36.80, 16.93; IR (KBr): 2974, 2231, 1726, 1535, 1470, 1321, 1251, 1166, 1126, 1032, 834 cm^{-1}; anal. calcd for $[C_{26}H_{18}BrN_3O_2]$: C 64.47; H 3.75; Br 16.50; N 8.68; O 6.61. Found: C 64.46; H 3.76; Br 16.51; N 8.68; O 6.60.

1-(4-Acetylbenzoyl)-4-methyl-7-oxo-2,6-diphenyl-5,6-diazaspiro[2.4]hept-4-ene-1-carbonitrile (4u). Yellow gummy liquid (402.7 mg, 90%); ^{1}H NMR (300 MHz; $CDCl_3$; Me_4Si): δ 7.99 (q, J = 8.6 Hz, 4H), 7.74–7.68 (m, 2H), 7.48 (s, 5H), 7.34 (dd, J = 10.7, 5.2 Hz, 2H), 7.18 (t, J = 7.4 Hz, 1H), 4.24 (s, 1H), 2.59 (s, 3H), 1.97 (s, 3H); $^{13}C\{^1H\}$NMR (75 MHz; $CDCl_3$; Me_4Si): δ 196.92, 183.36, 165.71, 153.47, 141.36, 137.43, 136.16, 129.52, 129.47, 129.39, 129.15, 129.03, 129.01, 128.63, 125.87, 118.68, 113.75, 77.51, 77.09, 76.66, 46.70, 40.39, 36.85, 26.91, 16.80; IR (KBr): 2975, 2239, 1721, 1585, 1486, 1310, 1245, 1150, 1121, 1026, 841 cm^{-1}; anal. calcd for $[C_{28}H_{21}N_3O_3]$: C 75.15; H 4.73; N 9.39; O 10.73. Found: C 75.17; H 4.75; N 9.37; O 10.71.

4-Methyl-7-oxo-2,6-diphenyl-1-(3-(trifluoromethyl)benzoyl)-5,6-diazaspiro[2.4]hept-4-ene-1-carbonitrile (4v). Yellow gummy liquid (407.2 mg, 86%); ^{1}H NMR (300 MHz; $CDCl_3$; Me_4Si): δ 8.20 (s, 1H), 7.96 (d, J = 7.9 Hz, 1H), 7.86 (d, J = 7.9 Hz, 1H), 7.72–7.67 (m, 2H), 7.62 (t, J = 7.9 Hz, 1H), 7.49 (s, 5H), 7.36 (dd, J = 10.7, 5.2 Hz, 2H), 7.19 (t, J = 7.4 Hz, 1H), 4.25 (s, 1H), 1.98 (s, 3H); $^{13}C\{^1H\}$NMR (75 MHz; $CDCl_3$; Me_4Si): δ 165.67, 153.43, 137.30, 133.70, 131.60, 130.05, 129.58, 129.45, 129.42, 129.01, 128.49, 125.97, 118.80, 113.59, 77.47, 77.05,

76.62, 46.67, 40.34, 36.63, 16.76; IR (KBr): 2980, 2247, 1725, 1587, 1490, 1319, 1254, 1159, 1120, 1030, 844 cm^{-1}; anal. calcd for $[C_{27}H_{18}F_3N_3O_2]$: C 68.50; H 3.83; F 12.04; N 8.88; O 6.76. Found: C 68.48; H 3.84; F 12.06; N 8.89; O 6.75.

1-(2,4-Difluorobenzoyl)-4-methyl-7-oxo-2,6-diphenyl-5,6-diazaspiro[2.4]hept-4-ene-1-carbonitrile (4w). White solid (346.6 mg, 72%); mp: 171–172 °C; ^1H NMR (300 MHz; $CDCl_3$; Me_4Si): 8.18–8.08 (m, 1H), 7.86 (dd, J = 8.7, 1.0 Hz, 2H), 7.50–7.38 (m, 7H), 7.23 (t, J = 7.4 Hz, 1H), 7.12–7.04 (m, 1H), 6.92–6.82 (m, 1H), 4.33 (s, 1H), 1.91 (s, 3H); $^{13}C\{^1H\}$NMR (75 MHz; $CDCl_3$; Me_4Si): δ 180.1, 166.5, 154.1, 137.6, 134.2, 129.39, 129.3, 129.2, 190.0, 125.6, 113.6, 113.3, 105.2, 104.8, 46.5, 40.9, 29.7, 16.5; IR (KBr): 2981, 2235, 1730, 1532, 1471, 1325, 1255, 1161, 1132, 1037, 843 cm^{-1}; anal. calcd for $[C_{26}H_{17}F_2N_3O_2]$: C 70.74; H 3.88; F 8.61; N 9.52; O 7.25. Found: C 70.75; H 3.86; F 8.63; N 9.51; O 7.26.

1-Benzoyl-5,7-dimethyl-4,6,8-trioxo-2-phenyl-5,7-diazaspiro [2.5]octane-1-carbonitrile (5a). Yellow (364.1 mg, 94%); mp: 220–222 °C; ^1H NMR (400 MHz; $CDCl_3$; Me_4Si): δ 7.97 (d, J = 7.6 Hz, 2H), 7.64 (t, J = 7.2 Hz, 1H), 7.52–7.40 (m, 7H), 4.31 (s, 1H), 3.34 (s, 3H), 3.16 (s, 3H); $^{13}C\{^1H\}$NMR (100 MHz; $CDCl_3$; Me_4Si): δ 184.2, 163.8, 160.5, 150.4, 135.0, 133.4, 129.3, 129.1, 129.0, 128.8, 128.7, 112.8, 44.5, 42.3, 40.8, 29.4; IR (KBr): 3412, 2951, 2231, 1680, 1429, 1262, 1120, 842, 747, 497 cm^{-1}; anal. calcd for $[C_{22}H_{17}N_3O_4]$: C 68.21; H 4.42; N 10.85; O 16.52. Found: C 68.20; H 4.41; N 10.87; O 16.51.

1-(2-Naphthoyl)-5,7-dimethyl-4,6,8-trioxo-2-phenyl-5,7-diazaspiro[2.5]octane-1-carbonitrile (5b). Yellow (402.4 mg, 92%); mp: 210–212 °C; ^1H NMR (300 MHz; $CDCl_3$; Me_4Si): δ 8.54 (s, 1H), 8.00–7.87 (m, 4H), 7.68–7.52 (m, 4H), 7.49–7.42 (m, 1H), 4.41 (s, 1H), 3.38 (s, 3H), 3.14 (s, 3H); $^{13}C\{^1H\}$NMR (125 MHz; $CDCl_3$; Me_4Si): δ 184.3, 163.9, 160.6, 150.5, 136.3, 132.4, 131.2, 130.8, 130.0, 129.7, 129.5, 129.1, 129.0, 128.9, 128.0, 127.5, 127.1, 123.7, 112.9, 44.6, 42.4, 41.1, 29.46, 29.4; IR (KBr): 3425, 2957, 2242, 1699, 1431, 1265, 1125, 842, 745, 486 cm^{-1}; anal. calcd for $[C_{26}H_{19}N_3O_4]$: C 71.39; H 4.38; N 9.61; O 14.63. Found: C 71.40; H 4.37; N 9.63; O 14.62.

1-(4-(*tert*-Butyl)benzoyl)-5,7-dimethyl-4,6,8-trioxo-2-(*p*-tolyl)-5,7-diazaspiro[2.5]octane-1-carbonitrile (5c). Yellow (443.8 mg, 97%); mp: 164–166 °C; ^1H NMR (300 MHz; $CDCl_3$; Me_4Si): δ 7.94 (d, J = 8.6 Hz, 2H), 7.54 (d, J = 8.6 Hz, 2H), 7.41 (d, J = 7.9 Hz, 2H), 7.26 (d, J = 8.0 Hz, 2H), 4.33 (s, 1H), 3.37 (s, 3H), 3.22 (s, 3H), 2.40 (s, 3H), 1.36 (s, 9H); $^{13}C\{^1H\}$NMR (75 MHz; $CDCl_3$; Me_4Si): δ 183.8, 163.8, 160.5, 159.0, 150.4, 138.9, 130.7, 129.6, 128.8, 126.2, 125.6, 112.9, 44.5, 40.9, 35.3, 30.9, 29.3, 29.2, 21.2; IR (KBr): 3420, 2970, 2231, 1680, 1429, 1376, 1258, 1122, 848, 741, 492 cm^{-1}; anal. calcd for $[C_{27}H_{27}N_3O_4]$: C 70.88; H 5.95; N 9.18; O 13.99. Found: C 70.89; H 5.93; N 9.17; O 14.00.

2-(4-Bromophenyl)-1-(4-(*tert*-butyl)benzoyl)-5,7-dimethyl-4,6,8-trioxo-5,7-diazaspiro[2.5]octane-1-carbonitrile (5d). Yellow (470.1 mg, 90%); mp: 204–206 °C; ^1H NMR (300 MHz; $CDCl_3$; Me_4Si): δ 7.90 (d, J = 8.6 Hz, 2H), 7.56 (t, J = 8.2 Hz, 4H), 7.38 (d, J = 8.1 Hz, 2H), 4.28 (s, 1H), 3.38 (s, 3H), 3.18 (s, 3H), 1.35 (s, 9H); $^{13}C\{^1H\}$NMR (75 MHz; $CDCl_3$; Me_4Si): δ 182.9, 163.1, 160.0, 158.9, 149.9, 131.7, 131.6, 130.2, 130.1, 130.0, 128.49, 128.4, 127.5, 126.0, 122.9, 112.3, 42.8, 41.6, 40.5, 35.0, 30.5, 28.9; IR (KBr): 3417, 2943, 2234, 1675, 1421, 1257, 1117, 839, 741, 495 cm^{-1}; anal. calcd for $[C_{26}H_{24}BrN_3O_4]$: C 59.78; H 4.63; Br 15.30; N 8.04; O 12.25. Found: C 59.79; H 4.61; Br 15.31; N 8.05; O 12.24.

1-(4-(*tert*-Butyl)benzoyl)-2-(4-fluorophenyl)-5,7-dimethyl-4,6,8-trioxo-5,7-diazaspiro[2.5]octane-1-carbonitrile (5e). Yellow (406.1 mg, 88%); mp: 210–212 °C; ^1H NMR (300 MHz; $CDCl_3$; Me_4Si): δ 7.91 (d, J = 8.6 Hz, 2H), 7.58–7.47 (m, 4H), 7.13 (t, J = 8.6 Hz, 2H), 4.31 (s, 1H), 3.38 (s, 3H), 3.19 (s, 3H), 1.36 (s, 9H); $^{13}C\{^1H\}$NMR (75 MHz; $CDCl_3$; Me_4Si): δ 183.3, 164.3, 163.4, 160.3, 159.1, 150.2, 130.8, 130.7, 130.4, 128.6, 126.2, 124.4, 116.08, 115.7, 112.7, 43.2, 42.0, 40.8, 35.3, 30.7, 29.1; IR (KBr): 3427, 2940, 2230, 1671, 1425, 1252, 1113, 1012, 835, 743, 487 cm^{-1}; anal. calcd for $[C_{26}H_{24}FN_3O_4]$: C 67.67; H 5.24; F 4.12; N 9.11; O 13.87. Found: C 67.69; H 5.22; F 4.12; N 9.10; O 13.88.

1-(4-(*tert*-Butyl)benzoyl)-5,7-dimethyl-2-(4-nitrophenyl)-4,6,8-trioxo-5,7-diazaspiro[2.5]octane-1-carbonitrile (5f). Yellow (400.5 mg, 82%); mp: 216 °C; ^1H NMR (300 MHz; $CDCl_3$; Me_4Si): δ 8.32–8.26 (m, 2H), 7.90–7.83 (m, 2H), 7.66 (d, J = 8.3 Hz, 2H), 7.56–7.51 (m, 2H), 4.40 (s, 1H), 3.38 (s, 3H), 3.14 (s, 3H), 1.34 (s, 9H); $^{13}C\{^1H\}$NMR (75 MHz; $CDCl_3$; Me_4Si): δ 182.7, 162.9, 160.3, 159.6, 150.1, 147.9, 136.2, 130.2, 130.0, 128.7, 126.4, 123.9, 112.3, 94.1, 41.9, 41.6, 40.8, 35.4, 30.8, 29.3; IR (KBr): 3412, 2941, 2237, 1671, 1535, 1419, 1346, 1251, 1112, 831, 739, 492 cm^{-1}; anal. calcd for $[C_{26}H_{24}N_4O_6]$: C 63.93; H 4.95; N 11.47; O 19.65. Found: C 63.91; H 4.94; N 11.48; O 19.67.

2-([1,1′-Biphenyl]-4-yl)-1-(4-(*tert*-butyl)benzoyl)-5,7-dimethyl-4,6,8-trioxo-5,7-diazaspiro[2.5]octane-1-carbonitrile (5g). Yellow (498.8 mg, 96%); mp: 194–196 °C; ^1H NMR (300 MHz; $CDCl_3$; Me_4Si): δ 7.94 (d, J = 8.5 Hz, 2H), 7.60 (ddd, J = 30.2, 13.2, 8.5 Hz, 9H), 7.46 (t, J = 7.3 Hz, 2H), 4.38 (s, 1H), 3.38 (s, 3H), 3.22 (s, 3H), 1.34 (s, 9H); $^{13}C\{^1H\}$NMR (75 MHz; $CDCl_3$; Me_4Si): δ 183.7, 163.7, 160.5, 159.0, 150.3, 141.7, 140.0, 130.6, 129.3, 128.7, 127.6, 127.4, 127.1, 126.2, 112.9, 44.1, 42.1, 40.9, 35.3, 30.8, 29.28, 29.2; IR (KBr): 3421, 2951, 2235, 1689, 1433, 1268, 1123, 848, 749, 491 cm^{-1}; anal. calcd for $[C_{32}H_{29}N_3O_4]$: C 73.97; H 5.63; N 8.09; O 12.32. Found: C 73.99; H 5.64; N 8.08; O 12.31.

1-(4-(*tert*-Butyl)benzoyl)-5,7-dimethyl-2-(3-nitrophenyl)-4,6,8-trioxo-5,7-diazaspiro[2.5]octane-1-carbonitrile (5h). Yellow (420.1 mg, 86%); mp: 200–202 °C; ^1H NMR (300 MHz; $CDCl_3$; Me_4Si): δ 8.17–8.12 (m, 2H), 7.88 (d, J = 7.5 Hz, 1H), 7.79 (d, J = 8.4 Hz, 2H), 7.57 (t, J = 7.8 Hz, 1H), 7.44 (d, J = 8.7 Hz, 2H), 4.31 (s, 1H), 3.26 (s, 3H), 3.05 (s, 3H), 1.25 (s, 9H); $^{13}C\{^1H\}$ NMR (75 MHz; $CDCl_3$; Me_4Si): δ 182.7, 162.9, 160.4, 159.5, 150.1, 148.1, 134.7, 131.2, 130.2, 129.9, 128.6, 126.3, 124.3, 123.6, 112.3, 41.8, 41.3, 40.7, 35.3, 30.7, 29.2; IR (KBr): 3410, 2940, 2238, 1675, 1540, 1422, 1344, 1249, 1132, 836, 732, 484 cm^{-1}; anal. calcd for $[C_{26}H_{24}N_4O_6]$: C 63.93; H 4.95; N 11.47; O 19.65. Found: C 63.91; H 4.94; N 11.48; O 19.67.

1-(4-Ethylbenzoyl)-5,7-dimethyl-4,6,8-trioxo-2-phenyl-5,7-diazaspiro[2.5]octane-1-carbonitrile (5i). White solid (398.7 mg, 96%); mp: 189–190 °C; 1H NMR (300 MHz; $CDCl_3$; Me_4Si): δ 7.90 (d, J = 8.3 Hz, 2H), 7.51–7.40 (m, 5H), 7.34 (d, J = 8.3 Hz,

2H), 4.34 (s, 1H), 3.36 (s, 3H), 3.19 (s, 3H), 2.73 (q, J = 7.6 Hz, 2H), 1.26 (t, J = 7.6 Hz, 3H); $^{13}C\{^1H\}$NMR (75 MHz; $CDCl_3$; Me_4Si): δ 183.73, 163.81, 160.55, 152.45, 150.48, 131.02, 129.10, 129.06, 128.97, 128.88, 128.79, 112.91, 77.49, 77.07, 76.64, 44.39, 42.16, 40.97, 29.41, 29.34, 29.14, 15.01; IR (KBr): 3427, 2971, 2235, 1689, 1439, 1379, 1268, 1127, 851, 761, 495 cm^{-1}; anal. calcd for $[C_{24}H_{21}N_3O_4]$: C 69.39; H 5.10; N 10.11; O 15.40. Found: C 69.41; H 5.11; N 10.09; O 15.41.

Characterization data for the products 4x, 7, 9, 11, 14 and 15

1-Benzoyl-2-(4-benzoylphenyl)-4-methyl-7-oxo-6-phenyl-5,6-diazaspiro[2.4]hept-4-ene-1-carbonitrile (4x). Off-white solid (458.6 mg, 90%); mp: 196–198 °C; ^1H NMR (300 MHz; $CDCl_3$; Me_4Si): δ 7.88–7.72 (m, 6H), 7.58 (ddt, J = 11.2, 7.4, 2.3 Hz, 6H), 7.49–7.37 (m, 4H), 7.31–7.23 (m, 2H), 7.11 (ddd, J = 8.5, 2.2, 1.1 Hz, 1H), 4.20 (s, 1H), 1.96 (s, 3H); $^{13}C\{^1H\}$NMR (75 MHz; $CDCl_3$; Me_4Si): δ 195.7, 183.2, 165.4, 152.9, 138.4, 137.3, 136.9, 135.2, 133.2, 132.98, 132.9, 130.8, 130.0, 129.6, 129.4, 129.0, 128.9, 128.5, 125.9, 118.8, 113.8, 46.4, 39.7, 36.7, 16.9; IR (KBr): 2972, 2244, 1731, 1708, 1581, 1489, 1306, 1240, 1147, 1117, 1021, 835 cm^{-1}; anal. calcd for $[C_{33}H_{23}N_3O_3]$: C 77.78; H 4.55; N 8.25; O 9.42. Found: C 77.79; H 4.54; N 8.24; O 9.44.

1,7-Diphenylheptane-1,7-dione (7). White (263.5 mg, 94%); mp: 94–96 °C; 1H NMR (400 MHz; $CDCl_3$; Me_4Si): δ 7.96–7.93 (m, 4H), 7.56–7.52 (m, 2H), 7.46–7.42 (m, 4H), 2.98 (t, J = 7.6 Hz, 4H), 1.80 (p, J = 7.6 Hz, 4H), 1.52–1.46 (m, 2H); $^{13}C\{^1H\}$ NMR (100 MHz; $CDCl_3$; Me_4Si): δ 200.3, 137.1, 133.0, 128.6, 128.1, 38.4, 29.0, 24.1; IR (KBr): 3050, 1790, 1785, 1580, 1447, 986, 835 cm^{-1}; anal. calcd for $[C_{17}H_{16}O_2]$: C 80.94; H 6.37; O 12.70. Found: C 80.93; H 6.39; O 12.69.

1,2-Diphenylethan-1-one (9). White (188.4 mg, 96%); mp: 58–60 °C; ^1H NMR (300 MHz; $CDCl_3$; Me_4Si): δ 8.10–8.03 (m, 2H), 7.63–7.56 (m, 1H), 7.54–7.46 (m, 2H), 7.43–7.25 (m, 5H), 4.33 (s, 2H); $^{13}C\{^1H\}$NMR (75 MHz; $CDCl_3$; Me_4Si): δ 197.2, 136.2, 134.2, 132.8, 129.2, 129.17, 129.1, 128.7, 128.4, 128.3, 128.2, 128.1, 127.6, 127.5, 126.5, 45.1; IR (KBr): 3090, 1792, 1496, 992, 842 cm^{-1}; anal. calcd for $[C_{14}H_{12}O]$: C 85.68; H 6.16; O 8.15. Found: C 85.69; H 6.14; O 8.16.

1,3-Diphenylpropane-1,3-dione (or 3-hydroxy-1,3-diphenyl-prop-2-en-1-one) (11). White (197.2 mg, 88%); mp: 76–77 °C; ^1H NMR (300 MHz; $CDCl_3$; Me_4Si): δ 8.07–7.99 (m, 4H), 7.63–7.48 (m, 6H), 6.90 (s, 1H); $^{13}C\{^1H\}$NMR (75 MHz; $CDCl_3$; Me_4Si): δ 185.80, 135.56, 132.51, 128.73, 127.21, 93.19, 77.52, 77.10, 76.68; IR (KBr): 3065, 1602, 1296, 1004 cm^{-1}; anal. calcd for $[C_{15}H_{12}O_2]$: C 80.34; H 5.39; O 14.27. Found: C 80.33; H 5.38; O 14.27.

(2-Phenylcyclopropane-1,1-diyl)bis(phenylmethanone) (14). White (297.0 mg, 91%); mp: 96–97 °C; ^1H NMR (300 MHz; $CDCl_3$; Me_4Si): δ 7.83–7.76 (m, 2H), 7.66–7.58 (m, 2H), 7.34 (dddd, J = 10.9, 6.0, 2.9, 1.3 Hz, 5H), 7.25–7.05 (m, 6H), 4.03 (t, J = 8.5 Hz, 1H), 2.88 (dd, J = 8.0, 4.7 Hz, 1H), 1.76 (dd, J = 9.0, 4.7 Hz, 1H); $^{13}C\{^1H\}$NMR (75 MHz; $CDCl_3$; Me_4Si): δ 197.00, 194.45, 137.88, 137.69, 134.10, 132.95, 132.74, 128.58, 128.56, 128.49, 128.26, 128.10, 127.11, 49.90, 32.40, 19.74; anal. calcd for $[C_{23}H_{18}O_2]$: C 84.64; H 5.56; O 9.80. Found: C 84.65; H 5.57; O 9.79.

Cyclopropane-1,1-diylbis(phenylmethanone) (15). White (220.3 mg, 88%); mp: 69–70 °C; ^1H NMR (300 MHz; $CDCl_3$; Me_4Si): δ 7.79–7.72 (m, 4H), 7.36 (dd, J = 5.0, 3.7 Hz, 2H), 7.27 (ddd, J = 8.1, 3.4, 1.1 Hz, 4H), 1.79 (s, 4H); $^{13}C\{^1H\}$NMR (75 MHz; $CDCl_3$; Me_4Si): δ 197.49, 137.64, 132.88, 128.53, 128.45, 40.71, 16.63; anal. calcd for $[C_{17}H_{14}O_2]$: C 81.58; H 5.64; O 12.78. Found: C 81.56; H 5.65; O 12.79.

Conflicts of interest

There are no conflicts to declare.

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Notes and references

1 (*a*) P. Arenas, A. Peña, D. Ríos, J. Benites, G. G. Muccioli, P. B. Calderon and J. A. Valderrama, *Molecules*, 2013, **18**, 9818; (*b*) B. Reux, T. Nevalainen, K. H. Raitio and A. M. P. Koskinen, *Bioorg. Med. Chem.*, 2009, **17**, 4441; (*c*) D. G. Batt, R. Goodman, D. G. Jones, J. S. Kerr, L. R. Mantegna, C. McAllister, R. C. Newton, S. Nurnberg, P. K. Welch and M. B. Covington, *J. Med. Chem*, 1993, **36**, 1434.

2 (*a*) Y. M. Chang, W. F. Yin, C. Y. Ho, M. R. Mustafa, A. H. A. Hadi, K. Awang, P. Narrima, C. Koh, D. R. Appleton and K. G. Chan, *J. Nat. Prod.*, 2011, **74**, 2261; (*b*) U. Battaglia and C. J. Moody, *J. Nat. Prod.*, 2010, **73**, 1938; (*c*) W. Wang, Y. H. Zeng, K. Osman, K. Shinde, M. Rahman, S. Gibbons and Q. Mu, *J. Nat. Prod.*, 2010, **73**, 1815; (*d*) J. Veda, M. Takagi and K. Shin-Ya, *J. Nat. Prod.*, 2009, **72**, 2181.

3 (*a*) A. Świzdor, *Molecules*, 2013, **18**, 13812; (*b*) R. Robinson, *J. Chem. Soc., Trans.*, 1909, **95**, 2167; (*c*) M. Pulici, F. Quartieri and E. R. Felder, *J. Comb. Chem.*, 2005, **7**, 463; (*d*) M. Keni and J. J. Tepe, *J. Org. Chem.*, 2005, **70**, 4211; (*e*) D. F. DeTar and M. Carmack, *J. Am. Chem. Soc.*, 1946, **68**, 2025; (*f*) H. Renata, Q. Zhou and P. S. Baran, *Science*, 2013, **339**, 53; (*g*) K. L. McGilvray, M. R. Decan, D. Wang

and J. C. Scaiano, *J. Am. Chem. Soc.*, 2006, **128**, 15980; (*h*) G. Wittig and U. Schöllkopf, *Chem. Ber.*, 1954, **87**, 1318.

4 (*a*) M. H. Sarvari and H. Sharghi, *J. Org. Chem.*, 2004, **69**, 6953; (*b*) C. O. Kangani and B. W. Day, *Org. Lett.*, 2008, **10**, 2645; (*c*) L. J. Gooβen and K. Ghosh, *Angew. Chem., Int. Ed.*, 2001, **40**, 3458; (*d*) C. E. Song, W. H. Shim, E. J. Roh and J. H. Choi, *Chem. Commun.*, 2000, 1695; (*e*) M. C. Wilkinson, *Org. Lett.*, 2011, **13**, 2232; (*f*) M. H. Sarvari and H. Sharghi, *Synthesis*, 2004, 2165; (*g*) R. H. Vekariya and J. Aubé, *Org. Lett.*, 2016, **18**, 3534; (*h*) S. A. Babu, M. Yasuda and A. Baba, *Org. Lett.*, 2007, **9**, 405; (*i*) J. Ross and J. Xiao, *Green Chem.*, 2002, **4**, 129.

5 (*a*) D. B. Dess and J. C. Martin, *J. Am. Chem. Soc.*, 1991, **113**, 7277; (*b*) M. A. Lapitskaya, L. L. Vasiljeva and K. K. Pivnitsky, *Mendeleev Commun.*, 2008, **18**, 309; (*c*) A. G. M. Barrett, D. Hamprecht and M. Ohkubo, *J. Org. Chem.*, 1997, **62**, 9376; (*d*) T. Nishimura, T. Onoue, K. Ohe and S. Uemura, *J. Org. Chem.*, 1999, **64**, 6750; (*e*) T. Miyazawa, T. Endo, S. Shiihashi and M. Okawara, *J. Org. Chem.*, 1985, **50**, 1332; (*f*) T. Hirao, D. Misu and T. Agawa, *J. Am. Chem. Soc.*, 1985, **107**, 7179; (*g*) J. S. Yadav, B. V. S. Reddy, A. K. Basak and A. V. Narsaiah, *Tetrahedron*, 2004, **60**, 2131.

6 (*a*) M. J. Zacuto, R. F. Dunn and M. Figus, *J. Org. Chem.*, 2014, **79**, 8917; (*b*) W. J. Kerr, A. J. Morrison, M. Pazicky and T. Weber, *Org. Lett.*, 2012, **14**, 2250; (*c*) L. De Luca, G. Giacomelli and M. Taddei, *J. Org. Chem.*, 2001, **66**, 2534–2537; (*d*) V. Pace, L. Castoldi and W. Holzer, *J. Org. Chem.*, 2013, **78**, 7764.

7 (*a*) M. S. Malamas, J. Erdei, I. Gunawan, K. Barnes, M. Jhonson, Y. Hui, J. Turner, Y. Hu, E. Wagner, K. Fan, A. Oll, J. Bard and A. J. Robichaud, *J. Med. Chem.*, 2009, **52**, 6314; (*b*) M. S. Kharasch and O. Reimuth, *Grignard Reactions of Non-metallic Substances*, Prentice-Hall, Englewood Cliffs, NJ, 1954, p. 138; (*c*) S. Jie, S. Zhang and W. Sun, *Eur. J. Inorg. Chem.*, 2007, 5584–5598; (*d*) S. C. Ball, R. P. Davies, P. R. Raithby, G. P. Shields and R. Snaith, *J. Organomet. Chem.*, 1998, **550**, 457.

8 (*a*) C. Zhou and R. C. Larock, *J. Am. Chem. Soc.*, 2004, **126**, 2302; (*b*) C. Zhou and R. C. Larock, *J. Org. Chem.*, 2006, **71**, 3551; (*c*) B. Zhao and X. Lu, *Tetrahedron Lett.*, 2006, **47**, 6765; (*d*) T. Das, A. Chakraborty and A. Sarkar, *Tetrahedron Lett.*, 2014, **55**, 7198; (*e*) H. Shimizu and M. Murakami, *Chem. Commun.*, 2007, 2855; (*f*) K. Ueura, S. Miyamura, T. Satoh and M. Miura, *J. Organomet. Chem.*, 2006, **691**, 2821; (*g*) Y. C. Wong, K. Parthasarathy and C. H. Cheng, *Org. Lett.*, 2010, **12**, 1736; (*h*) Y. Weng, T. Yang, H. Chen, Z. Chen, M. Zhu and X. Zhan, *ChemistrySelect*, 2019, **4**, 14233; (*i*) C. A. Malapit, J. T. Reeves, C. A. Busacca, A. R. Howell and C. H. Senanayake, *Angew. Chem., Int. Ed.*, 2016, **55**, 326; (*j*) C. A. Malapit, D. R. Caldwell, I. K. Luvaga, J. T. Reeves, I. Volchkov, N. C. Gonnella, Z. S. Han, C. A. Busacca, A. R. Howell and C. H. Senanayake, *Angew. Chem., Int. Ed.*, 2017, **56**, 6999.

9 (*a*) B. Zhao and X. Lu, *Org. Lett.*, 2006, **8**, 5987; (*b*) K. Hu, Q. Zhen, J. Gong, T. Cheng, L. Qi, Y. Shao and J. Chen, *Org. Lett.*, 2018, **20**, 3083; (*c*) K. Hu, L. Qi, S. Yu, T. Cheng, X. Wang, Z. Li, Y. Xia, J. Chen and H. Wu, *Green Chem.*, 2017, **19**, 1740; (*d*) L. Qi, K. Hu, S. Yu, J. Zhu, T. Cheng, X. Wang, J. Chen and H. Wu, *Org. Lett.*, 2017, **19**, 218; (*e*) H. Yu, L. Xiao, X. Yang and L. Shao, *Chem. Commun.*, 2017, **53**, 9745; (*f*) Y. Zhang, Y. Shao, J. Gong, K. Hu, T. Cheng and J. Chen, *Adv. Synth. Catal.*, 2018, **360**, 3260; (*g*) J. Zhu, Y. Shao, K. Hu, L. Qi, T. Cheng and J. Chen, *Org. Biomol. Chem.*, 2018, **16**, 8596; (*h*) T. Xu, Y. Shao, L. Dai, S. Yu, T. Cheng and J. Chen, *J. Org. Chem.*, 2019, **84**, 13604; (*i*) X. Yao, Y. Shao, M. Hu, Y. Xia, T. Cheng and J. Chen, *Org. Lett.*, 2019, **21**, 7697; (*j*) X. Yao, Y. Shao, M. Hu, M. Zhang, S. Li, Y. Xia, T. Cheng and J. Chen, *Adv. Synth. Catal.*, 2019, **361**, 4707; (*k*) L. Qi, R. Li, X. Yao, Q. Zhen, P. Ye, Y. Shao and J. Chen, *J. Org. Chem.*, 2020, **85**, 1097; (*l*) W. Xiong, K. Hu, Y. Lei, Q. Zhen, Z. Zhao, Y. Shao, R. Li, Y. Zhang and J. Chen, *Org. Lett.*, 2020, **22**, 1239; (*m*) J. Gong, K. Hu, Y. Shao, R. Li, Y. Zhang, M. Hu and J. Chen, *Org. Biomol. Chem.*, 2020, **18**, 488; (*n*) X. Yao, L. Qi, R. Li, Q. Zhen, J. Liu, Z. Zhao, Y. Shao, M. Hu and J. Chen, *ACS Comb. Sci.*, 2020, **22**, 114; (*o*) Q. Zhen, L. Chen, L. Qi, K. Hu, Y. Shao, R. Li and J. Chen, *Chem. – Asian J.*, 2020, **15**, 106.

10 (*a*) P. Mukherjee and A. R. Das, *J. Org. Chem.*, 2016, **81**, 5513; (*b*) A. Pinna, A. Basso, C. Lambruschini, L. Moni, R. Riva, V. Rocca and L. Banfi, *RSC Adv.*, 2020, **10**, 965; (*c*) A. I. Said and T. I. El-Emarya, *RSC Adv.*, 2020, **10**, 845; (*d*) A. P. Gomez, O. R. Bejarano, V. V. Kouznetsov and C. O. Puentes, *ACS Sustainable Chem. Eng.*, 2019, **7**, 18630; (*e*) L. Y. Zeng, B. Xi, K. Huang, J. Bi, L. Wei, C. Cai and S. Liu, *ACS Comb. Sci.*, 2019, **21**, 656; (*f*) R. Zeng, J. L. Li, X. Zhang, Y. Q. Liu, Z. Q. Jia, H. J. Leng, Q. W. Huang, Y. Liu and Q. Z. Li, *ACS Catal.*, 2019, **9**, 8256; (*g*) T. Aubineau and J. Cossy, *Org. Lett.*, 2018, **20**, 7419.

11 (*a*) G. Pal, S. Paul, P. P. Ghosh and A. R. Das, *RSC Adv.*, 2014, **4**, 8300; (*b*) P. P. Ghosh, P. Mukherjee and A. R. Das, *RSC Adv.*, 2013, **3**, 8220; (*c*) V. I. Petrenko, M. V. Avdeev, V. M. Garamus, L. A. Bulavin, V. L. Aksenov and L. Rosta, *Colloids Surf., A*, 2010, **369**, 160; (*d*) N. Zhao, X. Yang, J. Zhang, L. Zhu and Y. Lv, *Materials*, 2017, **10**, 1119.

12 (*a*) P. Mukherjee, S. Paul and A. R. Das, *New J. Chem.*, 2015, **39**, 9480; (*b*) M. Esmaeilpour and A. Z. Sardarian, *IJST*, 2013, **37A3**, 277; (*c*) D. Prasad, A. Preetam and M. Nath, *RSC Adv.*, 2012, **2**, 3133; (*d*) F. Qi, H. F. Yu, Y. N. Wang, Y. Lv, Y. X. Li, L. Han, R. Wang and X. N. Feng, *Synth. Commun.*, 2017, **47**, 2220.

13 P. Mukherjee and A. R. Das, *J. Org. Chem.*, 2017, **82**, 2794.

14 K. Manabe, X. M. Sun and S. Kobayashi, *J. Am. Chem. Soc.*, 2001, **123**, 10101.

15 T. Nishikata, Y. Yamamoto and N. Miyaura, *Organometallics*, 2004, **23**, 4317.

16 P. Mukherjee and A. R. Das, *Org. Biomol. Chem.*, 2017, **15**, 7267.

17 S. Lin, M. Li, Z. Dong, F. Liang and J. Zhang, *Org. Biomol. Chem.*, 2014, **12**, 1341.

18 T. Lavoisier and J. Rodriguez, *Synth. Commun.*, 1996, **26**, 525.