JOC The Journal of Organic Chemistry

Anatolian University Libraries Consortium a·n·k·o·s

Subscriber access provided by HACETTEPE UNIVERSITESI KUTUPHANESI

Article

Unexpected O-H insertion of Rhodium-Azavinylcarbenes with N-acylhydrazones: Divergent Synthesis of 3,6-disubstituted- and 3,5,6-trisubstituted-1,2,4-Triazines

Jiang Meng, Min Wen, Shiwei Zhang, Peiwen Pan, Xingxin Yu, and Wei-Ping Deng

J. Org. Chem., **Just Accepted Manuscript** • DOI: 10.1021/acs.joc.6b02846 • Publication Date (Web): 17 Jan 2017

Downloaded from http://pubs.acs.org on January 18, 2017

Just Accepted

"Just Accepted" manuscripts have been peer-reviewed and accepted for publication. They are posted online prior to technical editing, formatting for publication and author proofing. The American Chemical Society provides "Just Accepted" as a free service to the research community to expedite the dissemination of scientific material as soon as possible after acceptance. "Just Accepted" manuscripts appear in full in PDF format accompanied by an HTML abstract. "Just Accepted" manuscripts have been fully peer reviewed, but should not be considered the official version of record. They are accessible to all readers and citable by the Digital Object Identifier (DOI®). "Just Accepted" is an optional service offered to authors. Therefore, the "Just Accepted" Web site may not include all articles that will be published in the journal. After a manuscript is technically edited and formatted, it will be removed from the "Just Accepted" Web site and published as an ASAP article. Note that technical editing may introduce minor changes to the manuscript text and/or graphics which could affect content, and all legal disclaimers and ethical guidelines that apply to the journal pertain. ACS cannot be held responsible for errors or consequences arising from the use of information contained in these "Just Accepted" manuscripts.

ACS Publications

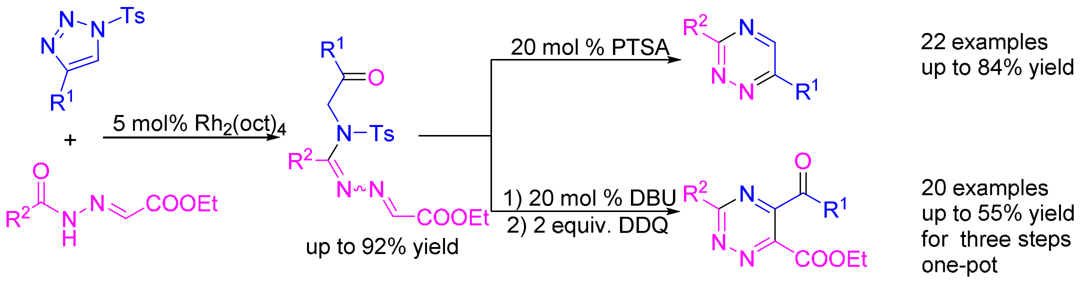
The Journal of Organic Chemistry is published by the American Chemical Society.
1155 Sixteenth Street N.W., Washington, DC 20036

Published by American Chemical Society. Copyright © American Chemical Society.
However, no copyright claim is made to original U.S. Government works, or works produced by employees of any Commonwealth realm Crown government in the course of their duties.

Unexpected O-H insertion of Rhodium-Azavinylcarbenes with *N*-acylhydrazones: Divergent Synthesis of 3,6-disubstituted- and 3,5,6-trisubstituted-1,2,4-Triazines

Jiang Meng, Min Wen, Shiwei Zhang, Peiwen Pan, Xingxin Yu* and Wei-Ping Deng*

Shanghai Key Laboratory of New Drug Design & School of Pharmacy, East China University of Science and Technology, 130 Meilong Road, Shanghai, 200237, China



ABSTRACT: A practical and efficient method for divergent synthesis of 3,6-disubstituted- and 3,5,6-trisubstituted-1,2,4-triazines *via* unexpected rhodium-catalyzed O-H insertion/rearrangement/conditions-controlled intramolecular cyclization and oxidation reaction under mild conditions has been developed. Notably, it is the first example for the synthesis of 1,2,4-triazines with different substituted-patterns *via* a common intermediate with excellent chemoselectivities by the reaction of *N*-acylhydrazones as aze-[3C] or [4C] synthons with *N*-sulfonyl-1,2,3-triazoles as aze-[2C] synthons. Furthermore, this method allows direct access to di-(het)aryl ketone frameworks containing 1,2,4-triazine moiety for the first time, serving as versatile building block for the synthesis of other useful heterocyclic skeletons, such as pyridine or pyridazinone-fused triazine in excellent yields.

INTRODUCTION

Aromatic heterocycles are highly important structural units found in a large number of biologically active natural products, pharmaceutical compounds and functional materials.[1] Among them, those nitrogen-containing heterocycles are the most indispensable structural motifs with great value in organic syntheses. 1,2,4-Triazines and its derivatives are a well-known class of azaheterocycles for their broad spectrum of biological activities and natural occurrences (Figure 1).[2] Taking Lamictal for example, as a member of the sodium channel blocking class of antiepileptic drugs, it has been used in the treatment of epilepsy, bipolar disorder and so on for a long time. Apart from these impressive biological properties, 1,2,4-triazines have been widely used as 2-azadienes in the inverse electron demanded Diels-Alder reactions to build important heterocyclic skeletons.[3] Moreover, 1,2,4-triazines are also used as key metal coordinating ligands and fluorescent sensor.[4]

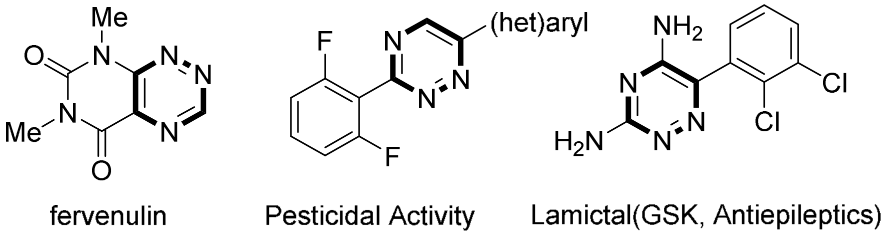


Figure 1. Selected natural products and pharmaceutical compounds.

Given the wide usefulness of 1,2,4-triazines and its derivatives, considerable efforts have been devoted to the development of improved methods for their synthesis (Figure 2).[5] To date, several efficient methods are available for their construction. The mainstay for the synthesis of substituted 1,2,4-triazine is the condensation of a 1,2-dicarbonyl equivalent or its precursor with an amidrazone.[5] However, many of these reported methods have drawbacks such as tedious substrate preparation procedure, harsh reaction conditions, limited substrates scope and especially low regioselectivity.[5] Therefore, the development of a more convenient and regiospecific methodology is highly desired.

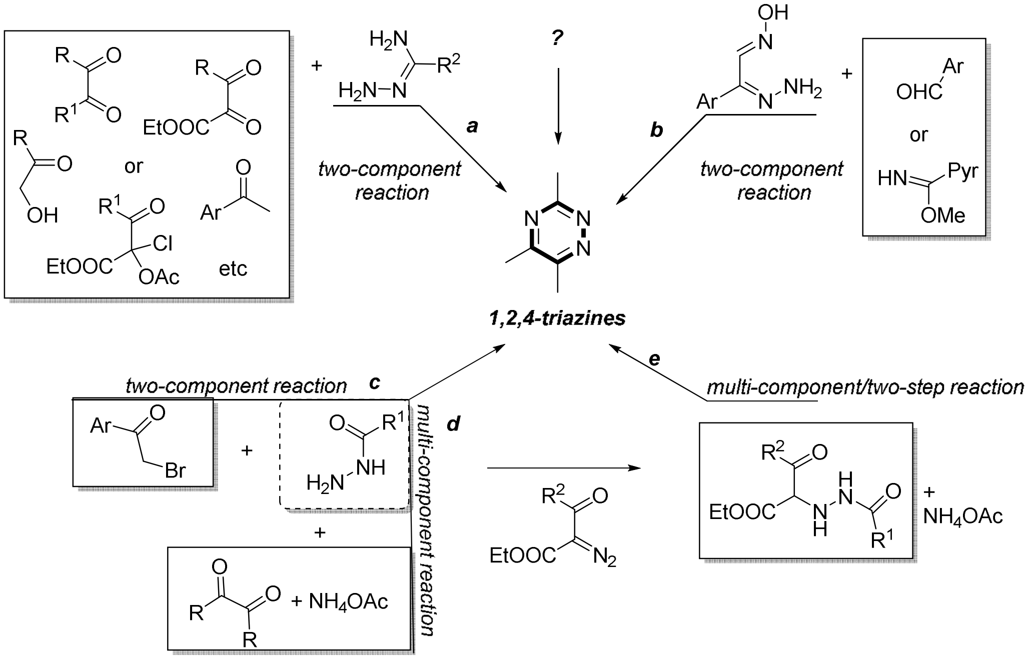
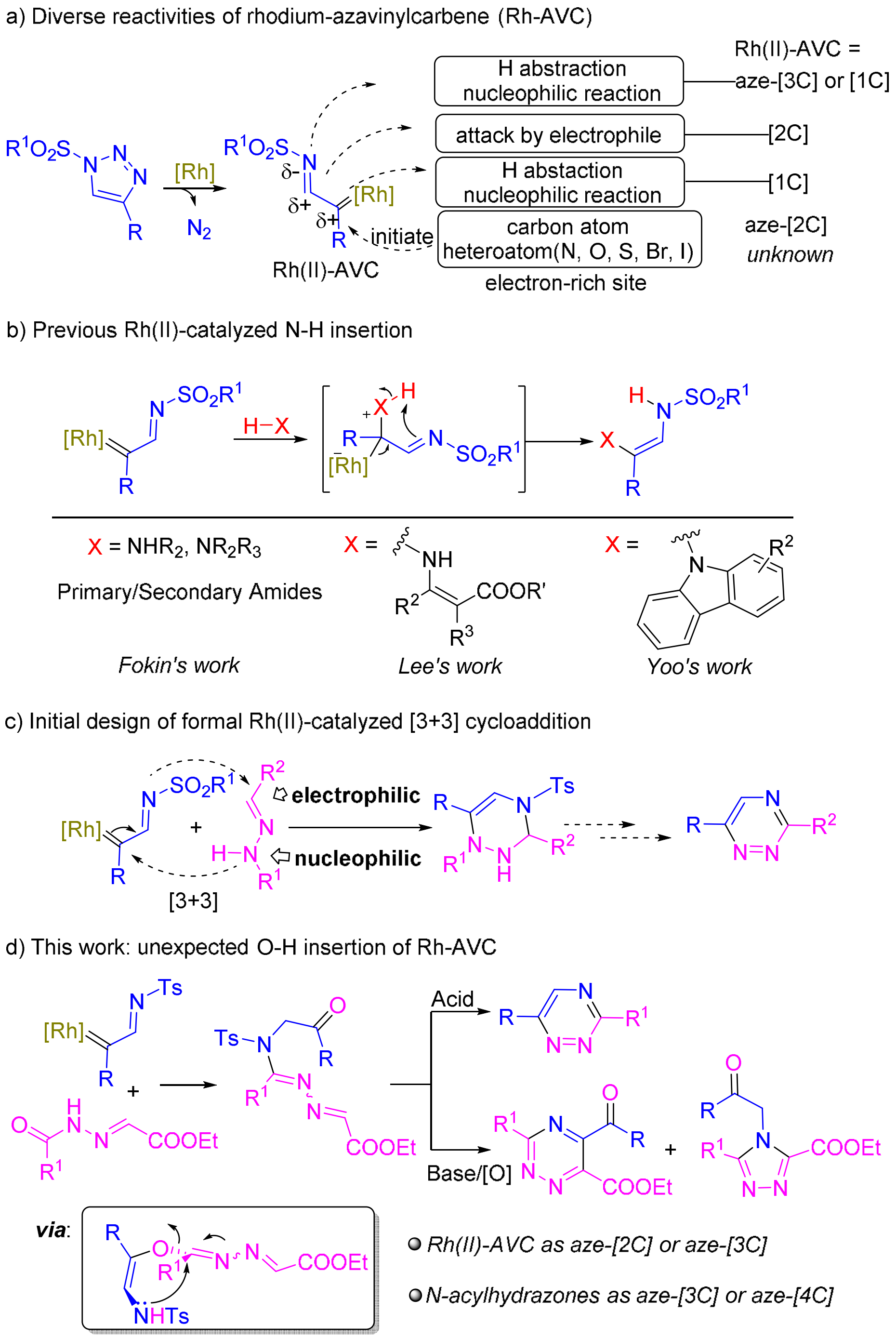


Figure 2. Previous methods for the construction of 1,2,4-triazines.

Multi-heteroatom heterocycles are of very considerable significance particularly in medicinal chemistry, for example analogues of the pyrimidine and purine nucleosides have been extensively studied.[1] In recent years, the rhodium-catalyzed denitrogenative transformations of readily accessible *N*-sulfonyl-1,2,3-triazoles have led to a new family of synthetic methods toward a variety of valuable organic molecules.[6-11] As shown, the *in situ* generated rhodium-azavinylcarbene (Rh-AVC) displays diverse reactivities, which could be used as [1C]-/[2C]-/aze-[3C]-synthon (Figure 3a), especially for the synthesis of nitrogen-containing heterocycles. But up to now, its potential as a aze-[2C]-synthon remains untouched.[9b] And also, there was, to the best of our knowledge, rare method developed for synthesis of important heterocycles containing more than two heteroatoms in rhodium-azavinylcarbene chemistry owing to the challenge of choosing an appropriate substrate.[6-11] With our research interests in azaheterocycle synthesis and *N*-sulfonyl-1,2,3-triazoles chemistry,[12] we have reported a novel and efficient route for the construction of oxa-bridged 2,5-epoxy-1,4-benzoxazepines *via* Rh(II)-catalyzed reaction of *N*-sulfonyl-1,2,3-triazoles and salicylaldehydes.[12b] We envisaged that the triazoles could be used to construct multi-heteroatom heterocycles according to the high nucleophilicity feature of nitrogen atom in Rh-AVC (Figure 3a).

Formal 1,3-insertions of the Rh-AVC into N-H bonds of amides, ambiphilic *β*-enamino esters, 9*H*-carbazoles have been achieved (Figure 3b).[13a-c] Meanwhile, hydrazones have been widely used to react with olefins *via* [3+2] cycloaddition to form pyrazolidines. Inspiringly, hydrazone may be the possible substrate for the construction of 1,2,4-triazine *via* a formal [3+3] cycloaddition owing to its feature containing two nitrogen atoms (Figure 3c). Herein, we describe a novel method for the divergent synthesis of 3,6-disubstituted- and 3,5,6-trisubstituted-1,2,4-triazines *via* an unexpected O-H insertion of Rh-AVC with *N*-acylhydrazones rather than the initial hypothesis (Figure 3d).



a) Diverse reactivities of rhodium-azavinylcarbene (Rh-AVC)

b) Previous Rh(II)-catalyzed N-H insertion

c) Initial design of formal Rh(II)-catalyzed [3+3] cycloaddition

d) This work: unexpected O-H insertion of Rh-AVC

- Rh(II)-AVC as aze-[2C] or aze-[3C]
- N-acylhydrazones as aze-[3C] or aze-[4C]

Figure 3. Rhodium-catalyzed reactions of *N*-sulfonyl 1,2,3-triazoles.

RESULTS AND DISCUSSION

We initiated our studies by testing the reactions of different types of hydrazones with triazole **1a** (Scheme 1). Disappointingly, the desired cycloaddition product was not detected, and there were even no reactions taking place in most cases. Surprisingly, when hydrazone **2a** was used, an unexpected product **3aa** was obtained in 57% yield. We reasoned that the hydroxy tautomer of benzoylhydrazone is easily formed under the reaction conditions and then could been captured by Rh-AVC through O-H insertion rather than the assumed N-H insertion.[13c] Interestingly, **3aa** would degenerate after a long time exposing to air or remaining in NMR tube to form the expected 3,6-disubstituted-1,2,4-triazine **4aa**. The encouraging results promoted us to do a further study of this transformation.

Scheme 1. Initial findings.

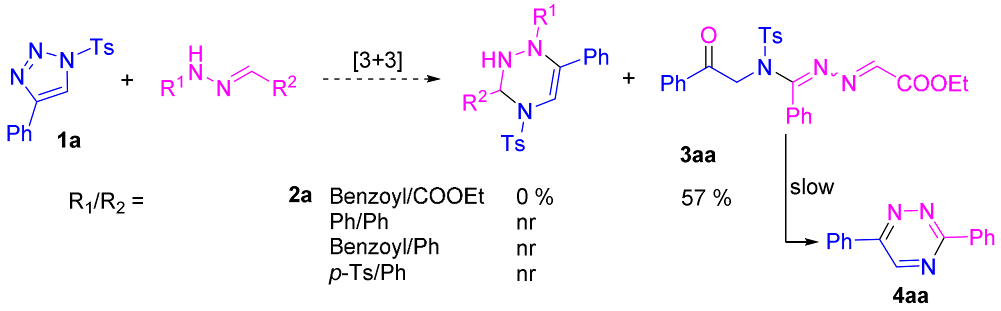
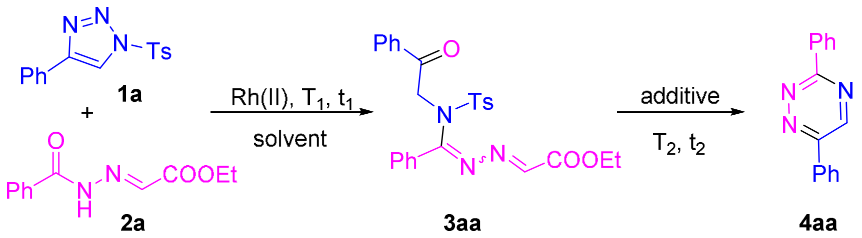


Table 1. Optimization of reaction conditions for the synthesis of 3,6-disubstituted-1,2,4-triazine 4aa.[a]

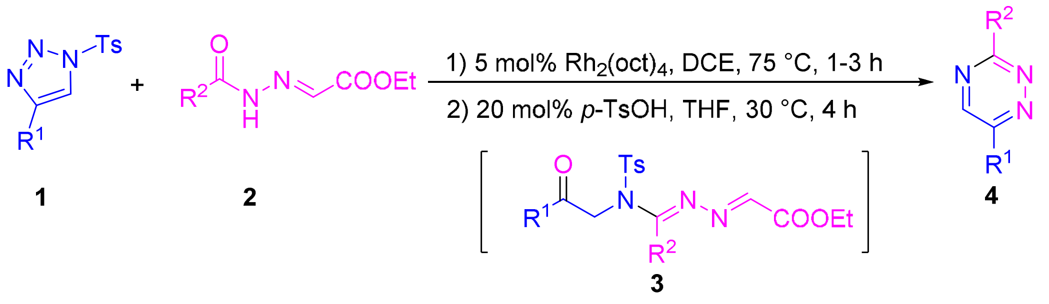


entry	solvent	Rh (II)	T$_1$(°C)/t$_1$(h)	**3aa**(%)[b]	**4aa**(%)[c]
1[d]	$CHCl_3$	$Rh_2(oct)_4$	75/3.5	57	--
2	$CHCl_3$	$Rh_2(oct)_4$	75/3.5	66	--
3	DCE	$Rh_2(oct)_4$	75/3.5	69	--
4	DCE	$Rh_2(oct)_4$	100/3.5	47	--
5	DCE	$Rh_2(oct)_4$	65/3.5	68	--
6	DCE	$Rh_2(oct)_4$	75/4	67	--
7	DCE	$Rh_2(oct)_4$	75/3	69	--
8	DCE	$Rh_2(piv)_4$	75/3	53	--
9	DCE	$Rh_2(oAc)_4$	75/3	NP	--
10	Toluene	$Rh_2(oct)_4$	75/3	56	--
11[e]	DCE	$Rh_2(oct)_4$	75/1	69	--
12[e]	DCE	$Rh_2(oct)_4$	75/4	70	--
13[e,f]	DCE	$Rh_2(oct)_4$	75/1	75	--
14[e,g]	DCE	$Rh_2(oct)_4$	75/1	75	--
15[e,f,h]	DCE	$Rh_2(oct)_4$	75/1	75	68
16[e,f,i]	DCE	$Rh_2(oct)_4$	75/1	75	68
17[e,f,j]	DCE	$Rh_2(oct)_4$	75/1	75	< 10
18[e,f,k]	DCE	$Rh_2(oct)_4$	75/1	75	trace
19[e,f,l]	DCE	$Rh_2(oct)_4$	75/1	75	67

[a] Conditions: Under N_2, **1a** (0.24 mmol), **2a** (0.2 mmol), Rh(II) (2 mol%), and solvent (1.0 mL) were heated at 75°C until **2a** was consumed, then the next step was conducted. [b] Isolated yields. [c] Isolated yields based on intermediate **3**. [d] 1 equiv. **1a** was used. [e] 5 mol% Rh(II) was used. [f] 1.4 equiv. **1a** was used. [g] 1.5 equiv. **1a** was used. [h] 20 mol% *p*-TsOH was added, 2 mL THF was used as the solvent, T_2 = 30°C, t_2 = 4 h. [i] The intermediate **3aa** was directly exposed to air, T_2 = 30°C, t_2 > 72 h. [j] 20 mol% CF_3COOH was used instead of *p*-TsOH. [k] 20 mol% PhCOOH was used instead of *p*-TsOH. [l] 50 mol% $FeCl_3$ was used instead of *p*-TsOH. NP = No Product.

With the initial results in hand, we first focused on the improvement of rhodium-catalyzed reaction of triazole **1a** with hydrazone **2a**. Slightly increasing the amount of triazole **1a**, the yield of **3aa** was improved to 66% (Table 1, entry 2). Using 1,2-dichloroethane (DCE) as the solvent instead of CHCl$_3$ provided **3aa** in 69% yield (Table 1, entry 3). An attempt to increase the temperature to 100 °C resulted in a lower yield, while decreasing the temperature to 65 °C or prolonging the reaction time did not give a better result (Table 1, entries 4-6). Shorting the reaction time to 3 h did not deteriorate the result and based on this, different Rh(II)-catalysts were examined (Table 1, entries 7-9). It was found that Rh$_2$(oct)$_4$ was still the optimal choice, while Rh$_2$(piv)$_4$ gave a lower yield and Rh$_2$(oAc)$_4$ afforded a mixture. The optimal reaction conditions for **3aa** were finally obtained by increasing the catalyst loading to 5 mol% and using 1.4 equiv. triazole **1a** (Table 1, entries 10-14). Key step for the formation of 3,6-disubstituted-1,2,4-triazine **4aa**, we think, is the hydrolysis of **3aa**. So, 20 mol% *p*-TsOH as additive promoting hydrolysis was added after the rhodium-catalyzed reaction in the one-pot process. The desired product could be obtained but with an impurity difficult to separate. With these information in mind, a novel two-step method to form 3,6-disubstituted-1,2,4-triazine **4aa** was set up after optimization (Table 1, entries 15-19).

Table 2. Synthesis of 3,6-disubstituted-1,2,4-triazines 4.[a]



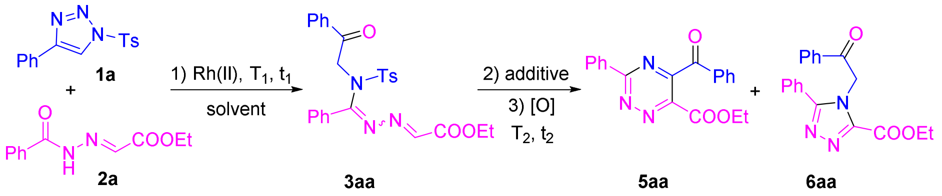
entry	substrate **1**/ **2** (R^1/R^2)	t(h)[b]	**3**(%)[c]	**4**(%)[d]
1	**1a**/ **2a** (Ph/ Ph)	1	**3aa**/ 75	**4aa**/ 68
2	**1a**/ **2b** (Ph/ 2-Me-Ph)	1	**3ab**/ 91	**4ab**/ 77
3	**1a**/ **2c** (Ph/ 2-F-Ph)	1	**3ac**/ 77	**4ac**/ 81
4	**1a**/ **2d** (Ph/ 3-Me-Ph)	2	**3ad**/ 60	**4ad**/ 68

5	**1a**/ **2e** (Ph/ 3-CF_3-Ph)	1	**3ae**/ 42	**4ae**/ 38
6	**1a**/ **2f** (Ph/ 4-Me-Ph)	2	**3af**/ 69	**4af**/ 84
7	**1a**/ **2g** (Ph/ 4-F-Ph)	1.5	**3ag**/ 67	**4ag**/ 60
8	**1a**/ **2h** (Ph/ 4-Pyridinyl)	30	**3ah**/ 0	**4ah**/ --[e]
9	**1a**/ **2i** (Ph/ Me)	1	**3ai**/ 78	**4ai**/ --[f,g]
10	**1a**/ **2j** (Ph/ Benzyl)	2	**3aj**/ 70	**4aj**/ 43
11	**1b**/ **2a** (4-Br-Ph / Ph)	1	**3ba**/ 76	**4ba**/ 67
12	**1c**/ **2a** (4-Cl-Ph / Ph)	1.5	**3ca**/ 81	**4ca**/ 58
13	**1d**/ **2a** (4-F-Ph / Ph)	1	**3da**/ 80	**4da**/ 52
14	**1e**/ **2a** (4-Me-Ph / Ph)	1.5	**3ea**/ 76	**4ea**/ 68
15	**1f**/ **2a** (4-MeO-Ph / Ph)	1	**3fa**/ 83	**4fa**/ 57
16	**1g**/ **2a** (3-MeO-Ph/ Ph)	1	**3ga**/ 69	**4ga**/ 66
17	**1h**/ **2a** (3-Br-Ph/ Ph)	1.5	**3ha**/ 68	**4ha**/ 56
18	**1i**/ **2a** (2-MeO-Ph/ Ph)	1	**3ia**/ 72	**4ia**/ 68
19	**1j**/ **2a** (2-Cl-Ph/ Ph)	3	**3ja**/ 73	**4ja**/ 61
20	**1k**/ **2a** (3,4,5-$(MeO)_3$-Ph/ Ph)	1.5	**3ka**/ 61	**4ka**/ 73
21	**1l**/ **2a** (3-Thienyl / Ph)	1	**3la**/ 55	**4la**/ 56
22	**1m**/ **2a** (*N*-$PhSO_2$-3-indolyl/ Ph)	1	**3ma**/ 92	**4ma**/ 57

[a]Standard conditions without changes. [b]Reaction time of step one. [c]Isolated yields based on substrates **2**. [d]Isolated yields based on intermediates **3**. [e]No product, substrate **1a** degraded. [f]Intermediate **3ai** was stable under standard conditions. [g]A mixture was obtained when raising the temperature to 75°C or 50 mol% $FeCl_3$ was used as additive at 50°C.

After that, our next step was to explore the generality of this approach to assemble a range of 3,6-disubstituted-1,2,4-triazines under the established optimal reaction conditions. As indicated in Table 2, various substituted *N*-benzoylhydrazones **2a-2g** reacted smoothly with the triazole **1a** in moderate to excellent yields to afford **3aa-3ag**, while 4-pyridinyl substituted hydrazone **2h** did not give the target **3ah** (Table 2, entries 1-8). It should be noted that *N*-benzoylhydrazones **2b-2c** with substituents at the *ortho*-position gave better results (Table 2, entries 2-3). Further transformations of **3** to 3,6-disubstituted-1,2,4-triazines **4** were completed very well under the standard conditions, except for that one with strong electron-withdrawing group (Table 2, entry 5). Reactions with methyl- and benzyl- substituted *N*-acylhydrazones **2i-2j** also successfully provided the intermediates **3ai-3aj**, but the methyl-substituted one was rather stable to be hydrolyzed (Table 2, entries 9-10). After testing the limitation of *N*-acylhydrazones **2**, we moved forward to examine varying substitution patterns for various triazoles **1**. As shown, the results revealed that C4 arylsubstituted triazoles **1b-1k** afforded corresponding products in both rhodium-catalyzed and hydrolysis steps in good yields, which were insignificantly affected by positions or electronic properties of the substituents (Table 2, entries 11-20).[14] The reactions still proceeded smoothly affording products **4la** and **4ma** in good yields when C4 heteroaryl-substituted triazoles **1l** and **1m** were used (Table 2, entries 21-22).

Table 3. Optimization of reaction conditions for the synthesis of 3,5,6-trisubstituted-1,2,4-triazines 5.[a]



entry	solvent	base	T$_2$(°C) /t$_2$(h)	**5aa/6aa**(%)^b
1	CHCl$_3$	DBU/ 1eq	75/ 0.2	24/10
2	CHCl$_3$	DBU/ 1eq	rt/ 16	25/11
3	CHCl$_3$	DBU/ 2eq	rt/ 22	--/10
4^c	CHCl$_3$	Et$_3$N/ 3eq	rt/ 144	46/ <5
5^d	CHCl$_3$	DBU/ 0.2 eq	30/ 36	45/ <5
6^{d,e}	CHCl$_3$	DBU/ 0.2 eq	30/ 36	43/ <5
7^{d,f,g}	DCE	DBU/ 0.2 eq	30/ 36	48/ <5

[a]Conditions: Under N$_2$, **1a** (0.24 mmol), **2a** (0.2 mmol), Rh$_2$(oct)$_4$ (2 mol%), and solvent (1.0 mL) were heated at 75 °C until **2a** was consumed, then the next step was conducted. [b]Isolated yields. [c]1 eq Et$_3$N was added every 48 h for three times. No additional oxidant was added. [d]After **2a** consumed, the solution was cooled to 30 °C, then 0.2 equiv. DBU was added. After stirring 12 h for cyclization, 2 equiv. DDQ was added for oxidation, 24 h. [e]1 equiv. PIDA was used instead of DDQ. [f]5 mol% Rh$_2$(oct)$_4$ was used. [g]1.4 equiv. **1a** was used.

Meanwhile, we wondered that base would promote the intramolecular cyclization reaction by deprotonation of **3**. To test our hypothesis, 1 equivalent DBU was added after the rhodium-catalyzed reaction. As expected, 3,5,6-trisubstituted-1,2,4-triazines **5aa** (X-ray) was obtained in 24% yield along with unexpected **6aa** in 10% yield after silic gel column chromatographic separation.[15] Decreasing the reaction temperature to ambient temperature, the reaction provided nearly the same result but with a longer reaction time (Table 3, entries 1-2). 2 equivalent DBU would obviously deteriorate the reaction and made **5aa** degraded (Table 3, entry 3). After screening of different bases, we found that inorganic bases could not catalyze the cyclization reaction since the blocking of byproduct formed in rhodium-catalyzed step in one-pot manner. Moreover, bases like Cs_2CO_3, KOH, NaOH and LDA were also not compatible with **5aa** and made it degraded, while K_2CO_3 catalyzed the cyclization reaction smoothly in two-step process affording 1,4,5,6-tetrahydro-1,2,4-triazines **7** in good yields and diastereoselectivities with trace amounts of **5** (Scheme 2). Also, we found that catalytic amount of DBU was enough to catalyze the cyclization step and stoichiometric Et_3N were equally effective, albeit with a longer reaction time. It is noteworthy that the oxidation process of amine in **7** to imine is key step for producing **5**.[16] So, additional oxidants were screened for the improvement of synthesis of 3,5,6-trisubstituted-1,2,4-triazines **5aa**, and 2 equivalent DDQ was optimal for the oxidation process (Table 1, entry 5).

Scheme 2. Synthesis of 1,4,5,6-tetrahydro-1,2,4-triazines 7.

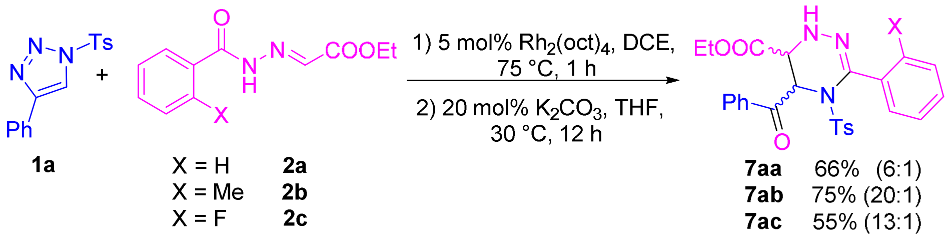
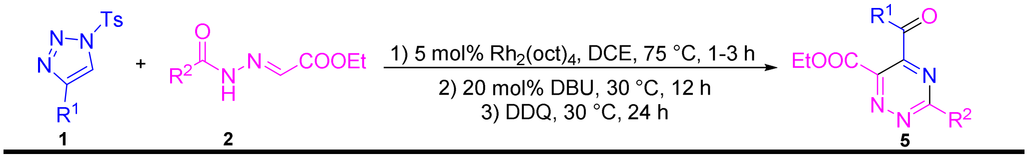
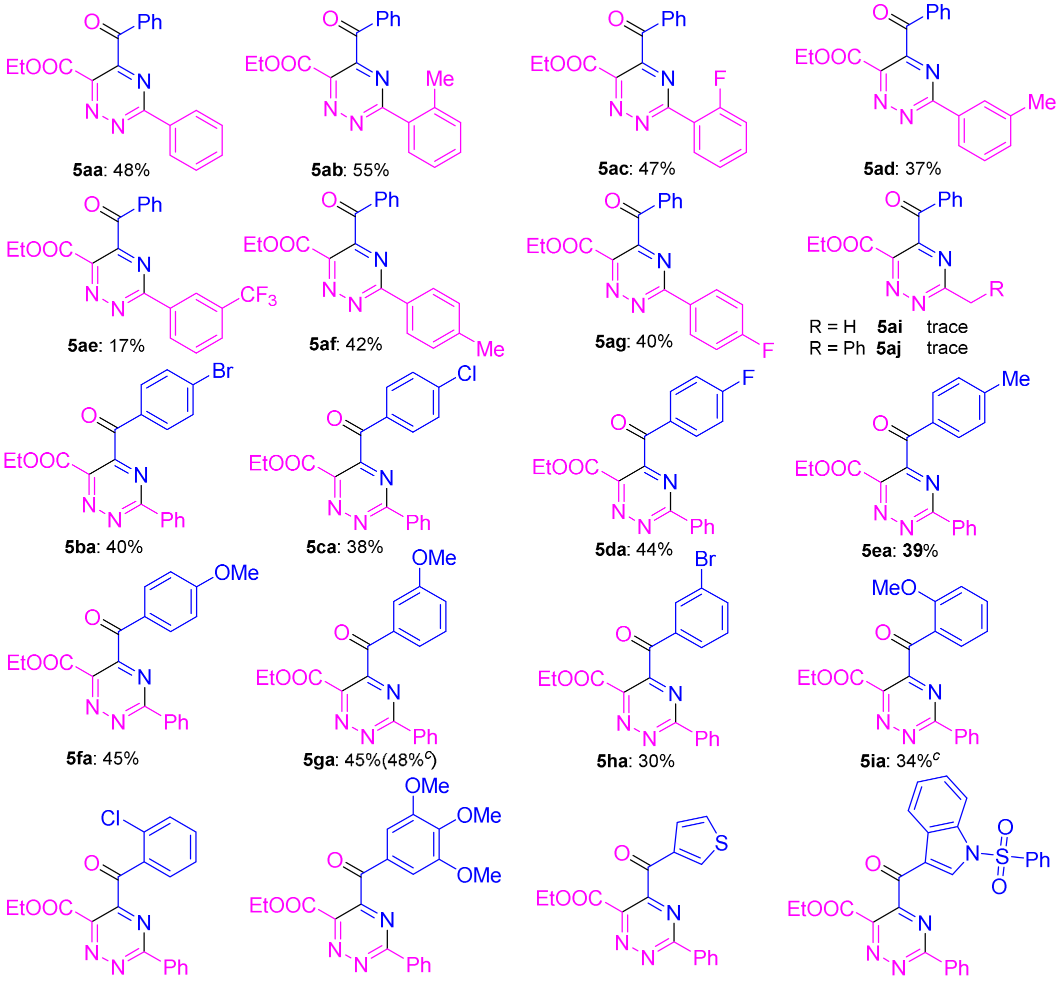


Table 4. Synthesis of 3,5,6-trisubstituted-1,2,4-triazines 5.[a]



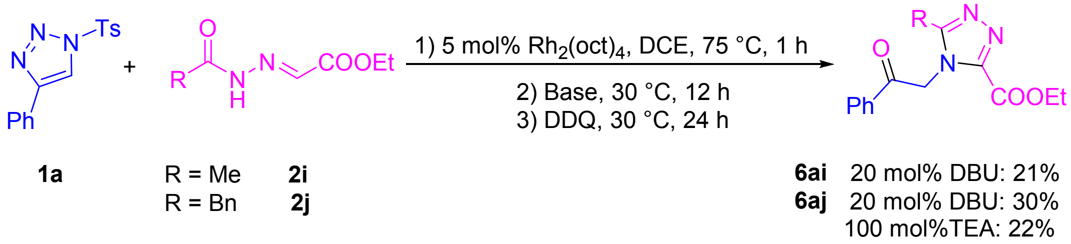


5aa: 48%
5ab: 55%
5ac: 47%
5ad: 37%
5ae: 17%
5af: 42%
5ag: 40%
R = H **5ai** trace
R = Ph **5aj** trace
5ba: 40%
5ca: 38%
5da: 44%
5ea: 39%
5fa: 45%
5ga: 45%(48%[c])
5ha: 30%
5ia: 34%[c]
5ja: 37%
5ka: 39%[b](46%[c])
5la: 36%[c]
5ma: 30%(51%[c])

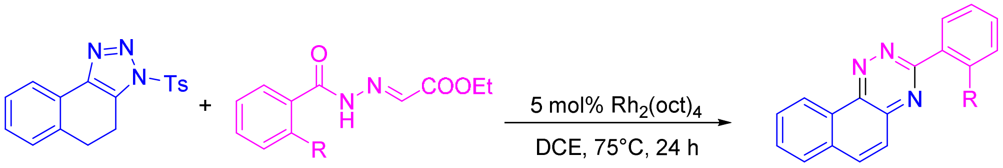
[a] Standard conditions without changes. [b] 0.3 equiv. DBU was used as the base.
[c] 1 equiv. Et_3N was used as the base.

Next, attention was paid to test the scope of this protocol with various triazoles **1** and hydrazones **2**, and the results are presented in Table 4. All examined substrates were effectively transformed to the desired products **5** in moderate to good yields. But, methyl-substituted *N*-acylhydrazone **2i** and benzyl- substituted *N*-acylhydrazone **2j** were not suitable substrates for this transformation, as only trace amounts of the desired products were observed. However, full-substituted 1,2,4-triazoles **6ai** and **6aj** were successfully obtained in acceptable yields (Scheme 3). Notably, when C4 arylsubstituted triazoles with electron-donating groups or heteroaryl-substituted triazoles were used, stoichiometric Et_3N was a better choice to promote cyclization step for preparation of **5ga**, **5ia**, **5ka**, **5la** and **5ma**. And also, no additive was needed in the reaction of tricyclic-triazole **1n** with hydrazones **2a** and **2b**, and 3-substituted-naphtho[2,1-*e*][1,2,4]triazines **8na** and **8nb** were obtained in good yields (Scheme 4). This method is, in our knowledge, the first case to access the 5-acyl-substituted-1,2,4-triazines directly. It should be mentioned that diaryl or hetaryl ketone frameworks are of great important that can be found in several currently marketed drugs or compounds under clinical evaluation.[17]

Scheme 3. Synthesis of 1,2,4-triazoles 6ai and 6aj.



Scheme 4. Synthesis of 3-substituted-naphtho[2,1-*e*][1,2,4]triazines 8na and 8nb.



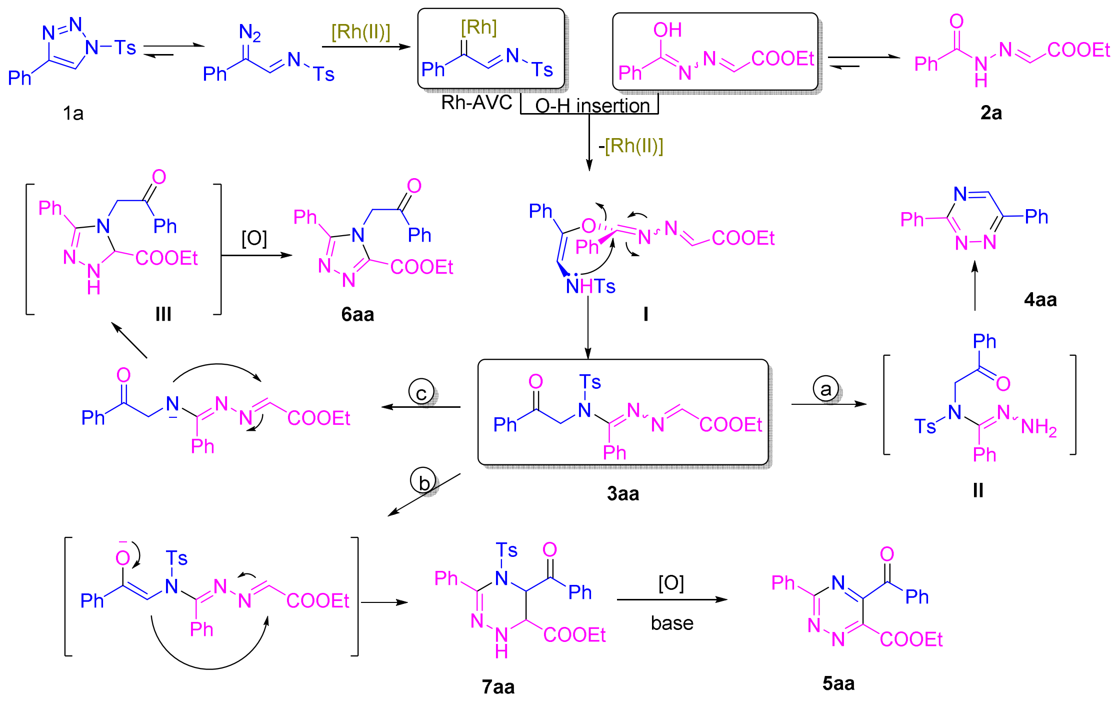
1n

R = H **2a**
R = Me **2b**

8na 41%
8nb 46%

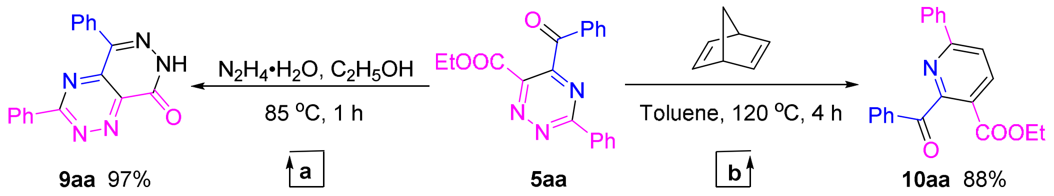
On the basis of the known *N*-sulfonyl-1,2,3-triazole chemistry and the above outcomes, a plausible mechanism for this divergent transformation is delineated in Scheme 5. The azavinyl carbene first reacts with the hydroxy tautomer of *N*-acylhydrazone **2a** *via* an initial O-H insertion to form the putative intermediate **I** and releases the Rh(II)-catalyst, which will enter the next catalytic cycle to initiate the reaction. Then, intermediate **I** undergoes intramolecular rearrangement to afford intermediate **3aa**. **3aa** as the key intermediate can undergo different routes to yield diversified products: a) after a hydrolysis process, **3aa** can transform into intermediate **II**. Then intramolecular condensation/ aromatization processes take place successively to yield 3,6-disubstituted-1,2,4-triazine **4aa**; b) under basic conditions, 1,4,5,6-tetrahydro-1,2,4-triazine **7aa** is first obtained through the intramolecular cyclization reaction, then with the help of additional oxidant or air, the desired 3,5,6-trisubstituted-1,2,4-triazine **5aa** is afforded through oxydehydrogenation/aromatization steps; c) intermediate **3aa** partly degrades in the presence of base followed by intramolecular cyclization reaction to give intermediate **III**, which gives rise to 1,2,4-triazole **6aa** after oxidation.

Scheme 5. Proposed reaction pathway.



Finally, to demonstrate the further applications of the 1,2,4-triazines for preparing useful heterocyclic skeletons, condensation reaction and inverse electron demand Diels-Alder reaction of **5aa** were examined respectively (Scheme 6). As a result, reaction of 1,2,4-triazines **5aa** with hydrazine hydrate at 85 °C in ethanol was performed smoothly to afford desired product **9aa** in nearly quantitative yield, while the reaction with 2,5-norbornadiene in toluene gave ethyl 2-benzoyl-6-phenylnicotinate **10aa** with *α*-aryl pyridyl ketone moiety in 88% yield at 120 °C for 4 h. Notably, *α*-aryl pyridyl ketone derivatives are useful intermediates in the syntheses of various natural products and drugs, which have drawn wide attention.[18] This method here provides a new perspective for their preparation.

Scheme 6. Further transformation of **5aa**.



CONCLUSION

In summary, we have described an unexpected O-H insertion of α-imino carbenes derived from readily accessible *N*-sulfonyl-1,2,3-triazoles with *N*-acylhydrazones. Followed by intramolecular rearrangement/acid or basic-catalyzed intramolecular cyclization and oxidation reaction, it provides a facile protocol for the divergent synthesis of 3,6-disubstituted- and 3,5,6-trisubstituted-1,2,4-triazines with excellent chemoselectivities in moderate to good yields under mild conditions. To the best of our knowledge, it constitutes the first example for the synthesis of 1,2,4-triazines with different substituted-patterns from a common intermediate, which greatly enriches compound libraries of 1,2,4-triazine scaffolds with potential medicinal utilities, and the first example for the construction of multi-heteroatom heteroaromatic rings using *N*-sulfonyl-1,2,3-triazoles as aze-[2C] synthons. Importantly, this research describes an unprecedented application of *N*-acylhydrazones as aze-[3C] or [4C] synthons differing from the traditional to construct azaheterocycles, which might be of potential use for the synthesis of other useful skeletons. Moreover, transformations of the 3,5,6-trisubstituted-1,2,4-triazine products was demonstrated by hydrazine condensation reaction and inverse electron demand Diels-Alder reaction, providing structurally important azaheterocycles such as pyridine or pyridazinone-fused triazine in excellent yields. Further studies on the construction of other pharmaceutically important heterocycles and biological assessment are in progress.

EXPERIMENTAL SECTION

General Information

All reactions were carried out using standard Schlenk techniques under nitrogen atmosphere unless otherwise stated. $CHCl_3$, 1,2-dichloroethane(DCE) were dried with CaH_2. THF and Toluene were dried with sodium (Na). Reactions were monitored by thin layer chromatography (TLC) carried out on 0.20-0.3 mm silica gel plates (GF254) using UV light as the visualizing agent. Silica gel (200-300 mesh) was used for column chromatography. NMR spectra were recorded on 400M instrument and calibrated using residual undeuterated solvent as an internal reference ($CHCl_3$ @ 7.26 ppm ^1H NMR, 77.16 ppm ^{13}C NMR). The following abbreviations (or combinations thereof) were used to explain the multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet. High-resolution mass spectra (HRMS) were recorded on Q-TOF LC/MS system. Melting points were obtained in open capillary tubes using a micro melting point apparatus which were uncorrected. Rh(II) acetate, Rh(II) octanoate were purchased from Adamas-beta. $Rh_2(piv)_4$ were prepared using literature procedures.[19] *N*-sulfonyl-1,2,3-triazoles[20-22] and *N*-acylhydrazones were prepared according to the literature procedures.[23-25]

General procedure for synthesis of 3,6-disubstituted-1,2,4-triazines 4

To an oven-dried Schlenk tube was added 0.28 mmol (1.4 equiv.) *N*-sulfonyl-1,2,3-triazoles, 0.20 mmol (1.0 equiv.) *N*-acylhydrazones and 0.01 mmol (5 mol%) Rh(II), successively. The Schlenk tube was sealed with a Rubber plug and the atmosphere was replaced using standard Schlenk techniques under nitrogen atmosphere. Then 1 mL dried solvent was added and the reaction mixture was heated at 75 °C, with vigorous stirring, for 1-3 h. Once hydrazones consumed, the reaction mixture was cooled to ambient temperature. Then reaction mixture was purified by flash chromatography (petroleum ether/ethyl acetate= 5:1~3:1) to provide the intermediate. The intermediate was then dissolved in 2 mL dried THF and 20 mol % *p*-TsOH was added. The resulting solution was stirred at 30 °C for 4 h. After reaction, solvent was evaporated and the residue was purified by flash chromatography (petroleum ether/ ethyl acetate = 10:1~5:1) to afford the desired product.

3,6-diphenyl-1,2,4-triazine (4aa): yellow solid, 24 mg, 51% yield, mp: 148-150 °C (literature: 158-160 °C)[26]; **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 9.06 (s, 1H), 8.65-8.53 (m, 2H), 8.17-8.15 (m, 2H), 7.63-7.51 (m, 6H). **^{13}C NMR** (100 MHz, Chloroform-*d*) δ 162.5, 155.2 146.6, 134.7, 133.4, 131.8, 131.0, 129.5, 129.1, 128.3, 126.8; **IR**(KBr): $\tilde{\nu}$ = 3049, 2957, 2923, 2853, 1964, 1905, 1655, 1636, 1599, 1452, 1405, 1320, 1178, 1087, 1025, 764, 583 cm^{-1}; **HRMS** (EI-TOF): calcd for, $C_{15}H_{11}N_3$ $[M]^+$, 233.0953; found, 233.0950.

6-phenyl-3-(o-tolyl)-1,2,4-triazine (4ab): yellow solid, 35 mg, 70% yield, mp: 125-127 °C (literature: 118-120 °C)[27]; **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 9.11 (s, 1H), 8.20-8.18 (m, 2H), 8.03 (d, *J* = 7.5 Hz, 1H), 7.62-7.58 (m, 3H), 7.46-7.42 (m, 1H), 7.38 (t, *J* = 7.2 Hz, 2H), 2.68 (s, 3H); **^{13}C NMR** (100 MHz, Chloroform-*d*) δ 165.4, 154.4, 146.1, 138.3, 134.8, 133.3, 131.8, 131.0, 130.9, 130.5, 129.5, 126.9, 126.3, 21.7; **IR**(KBr): $\tilde{\nu}$ = 3053, 2959, 2923, 2853, 1968, 1915, 1600, 1578, 1495, 1439, 1401, 1329, 1127, 1080, 988, 932, 821, 767, 725, 694, 590 cm^{-1}; **HRMS** (EI-TOF): calcd for, $C_{16}H_{13}N_3$ $[M]^+$, 247.1109; found, 247.1110.

3-(2-fluorophenyl)-6-phenyl-1,2,4-triazine (4ac): yellow solid, 31 mg, 62% yield, mp: 118-120 °C; **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 9.13 (s, 1H), 8.28-8.23 (m, 1H), 8.20-8.17 (m, 2H), 7.62-7.52 (m, 4H), 7.35 (t, *J* = 7.6 Hz, 1H), 7.30-7.26 (m, 1H); **^{13}C NMR** (100 MHz, Chloroform-*d*) δ 161.9 (d, *J* = 5.4 Hz), 161.6 (d, *J* = 257.3 Hz), 154.9, 146.3, 133.1 (d, *J* = 23.3 Hz), 133.0, 131.8, 131.2, 129.5, 126.9, 124.6 (d, *J* = 3.9 Hz), 123.6 (d, *J* = 9.6 Hz), 117.2 (d, *J* = 22.1 Hz); **IR**(KBr): $\tilde{\nu}$ = 3059, 2924, 2853, 1974, 1914, 1611, 1580, 1495, 1452, 1407, 1322, 1233, 1115, 1081, 1040, 831, 769, 696 cm^{-1}; **HRMS** (EI-TOF): calcd for, $C_{15}H_{10}N_3F$ [M]$^+$, 251.0859; found, 251.0860.

6-phenyl-3-(m-tolyl)-1,2,4-triazine (4ad): yellow solid, 20mg, 41% yield, mp: 108-110°C; **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 9.05 (s, 1H), 8.42 (s, 1H), 8.38 (d, *J* = 7.8 Hz, 1H), 8.18-8.16 (m, 2H), 7.60-7.57 (m, 3H), 7.45 (t, *J* = 7.6 Hz, 1H), 7.38 (d, *J* = 7.5 Hz, 1H), 2.49 (s, 3H); **^{13}C NMR** (100 MHz, Chloroform-*d*) δ 162.6, 155.1, 146.5, 138.8, 134.7, 133.4, 132.6, 130.9, 129.5, 128.9, 128.8, 126.8, 125.5, 21.7; **IR**(KBr): $\tilde{\nu}$ = 3046, 2922, 2852, 1961, 1898, 1816, 1598, 1493, 1431, 1395, 1331, 1090, 1039, 922, 781, 693 cm^{-1}; **HRMS** (EI-TOF): calcd for, $C_{16}H_{13}N_3$ [M]$^+$, 247.1109; found, 247.1108.

6-phenyl-3-(3-(trifluoromethyl)phenyl)-1,2,4-triazine (4ae): yellow solid, 10 mg, 16% yield, mp: 156-158 °C; **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 9.11 (s, 1H), 8.89 (s, 1H), 8.80 (d, *J* = 7.9 Hz, 1H), 8.19-8.17 (m, 2H), 7.82 (d, *J* = 7.7 Hz, 1H), 7.70 (t, *J* = 7.8 Hz, 1H), 7.63-7.60 (m, 3H); **^{13}C NMR** (100 MHz, Chloroform-*d*) δ 161.4, 155.8, 146.7, 135.6, 133.1, 131.6 (q, *J* = 32.6 Hz), 131.4, 131.4, 129.6, 129.6, 128.2 (q, *J* = 3.7 Hz), 126.9, 125.2 (q, *J* = 3.8 Hz), 124.1 (q, *J* = 272.3 Hz); **IR**(KBr): $\tilde{\nu}$ = 3059, 2924, 2853, 1654, 1613, 1579, 1441, 1396, 1346, 1315, 1271, 1168, 1112, 1068, 923, 803, 693 cm^{-1}; **HRMS** (EI-TOF): calcd for, $C_{16}H_{10}N_3F_3$ [M]$^+$, 301.0827; found, 301.0828.

6-phenyl-3-(p-tolyl)-1,2,4-triazine (4af): yellow solid, 29 mg, 58% yield, mp: 161-163 °C; **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 9.04 (s, 1H), 8.48 (d, *J* = 8.1 Hz, 2H), 8.17-8.15 (m, 2H), 7.60 -7.57 (m, 3H), 7.37 (d, *J* = 8.0 Hz, 2H), 2.46 (s, 3H).[28] **^{13}C NMR** (100 MHz, Chloroform-*d*) δ 162.6, 154.9, 146.5, 142.3, 133.5, 132.1, 130.9, 129.8, 129.5, 128.3, 126.7, 21.7; **IR**(KBr): $\tilde{\nu}$ = 3031, 2920, 2853, 1926, 1739, 1654, 1607, 1507, 1442, 1404, 1331, 1181, 1086, 1033, 795, 687, 581 cm^{-1}; **HRMS** (EI-TOF): calcd for, $C_{16}H_{13}N_3$ [M]$^+$, 247.1109; found, 247.1108.

3-(4-fluorophenyl)-6-phenyl-1,2,4-triazine (4ag): yellow solid, 21 mg, 40% yield, mp: 176-178 °C; **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 9.05 (s, 1H), 8.62-8.59 (m, 2H), 8.17-8.15 (m, 2H), 7.62-7.58 (m, 3H), 7.27-7.22 (m, 2H). **^{13}C NMR** (100 MHz, Chloroform-*d*) δ 165.4 (d, *J* = 252.3 Hz), 161.7, 155.1, 146.6, 133.3, 131.1, 130.9 (d, *J* = 3.1 Hz), 130.5 (d, *J* = 8.8 Hz), 129.5, 126.8, 116.2 (d, *J* = 21.9 Hz); **IR**(KBr): $\tilde{\nu}$ = 3054, 2923, 2853, 1972, 1912, 1600, 1509, 1442, 1407, 1227, 1155, 1084, 1040, 846, 806, 762, 701, 586 cm^{-1}; **HRMS** (EI-TOF): calcd for, $C_{15}H_{10}N_3F$ [M]$^+$, 251.0859; found, 251.0858.

3-benzyl-6-phenyl-1,2,4-triazine (4aj): yellow solid, 15 mg, 30% yield, mp: 143-145 °C; **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 8.93 (s, 1H), 8.10-7.98 (m, 2H), 7.59-7.50 (m, 3H), 7.43 (d, *J* = 7.4 Hz, 2H), 7.33 (t, *J* = 7.5 Hz, 2H), 7.25 (t, *J* = 7.3 Hz, 1H), 4.51 (s, 2H); **^{13}C NMR** (100 MHz, Chloroform-*d*) δ 167.5, 155.4, 147.0, 137.3, 133.3, 130.9, 129.5, 129.4, 128.9, 127.1, 126.9, 43.5; **IR**(KBr): $\tilde{\nu}$ = 3058, 2925, 2853, 1720, 1636, 1562, 1495, 1437, 1406, 1318, 1080, 1047, 1004, 919, 758, 694 cm^{-1}; **HRMS** (EI-TOF): calcd for, $C_{16}H_{13}N_3$ [M]$^+$, 247.1109; found, 247.1110.

6-(4-bromophenyl)-3-phenyl-1,2,4-triazine (4ba): yellow solid, 32 mg, 51% yield, mp: 144-146 °C (literature: 201 °C)[28]; **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 9.05 (s, 1H), 8.59-8.57 (m, 2H), 8.05 (d, *J* = 8.5 Hz, 2H), 7.73 (d, *J* = 8.4 Hz, 2H), 7.58-7.56 (m, 3H); **^{13}C NMR** (100 MHz, Chloroform-*d*) δ 162.7, 154.3, 146.3, 134.6, 132.8, 132.3, 131.9, 129.1, 128.4, 128.2, 125.9; **IR**(KBr): $\tilde{\nu}$ = 3050, 2924, 2853, 1737, 1654, 1636, 1561, 1459, 1404, 1380, 1309, 1165, 1091, 617 cm^{-1}; **HRMS** (EI-TOF): calcd for, $C_{15}H_{10}N_3Br^{79}$ $[M]^+$, 311.0058; found, 311.0060.

6-(4-chlorophenyl)-3-phenyl-1,2,4-triazine (4ca): yellow solid, 25 mg, 47% yield, mp: 148-151 °C (literature: 197-198 °C)[26]; **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 9.04 (s, 1H), 8.59-8.57 (m, 2H), 8.13 – 8.10 (m, 2H), 7.58-7.55 (m, 5H); **^{13}C NMR** (100 MHz, Chloroform-*d*) δ 162.7, 154.2, 146.3, 137.5, 134.6, 131.9, 131.8, 129.8, 129.1, 128.3, 127.9; **IR**(KBr): $\tilde{\nu}$ = 3056, 2922, 1920, 1673, 1596, 1489, 1448, 1412, 1326, 1236, 1089, 1009, 841, 749, 692, 581 cm^{-1}; **HRMS** (EI-TOF): calcd for, $C_{15}H_{10}N_3Cl^{35}$ $[M]^+$, 267.0563; found, 267.0565.

6-(4-fluorophenyl)-3-phenyl-1,2,4-triazine (4da): yellow solid, 21 mg, 42% yield, mp: 137-139 °C; **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 9.04 (s, 1H), 8.59-8.57 (m, 2H), 8.19-8.16 (m, 2H), 7.58-7.56 (m, 3H), 7.30-7.26 (m, 2H); **^{13}C NMR** (100 MHz, Chloroform-*d*) δ 164.8 (d, *J* = 251.8 Hz), 162.5, 154.3, 146.3, 134.7, 131.9, 129.6 (d, *J* = 3.3 Hz), 129.1, 128.8 (d, *J* = 8.6 Hz), 128.3, 116.7 (d, *J* = 22.0 Hz); **IR**(KBr): $\tilde{\nu}$ = 3066, 2922, 2852, 1738, 1703, 1601, 1512, 1451, 1414, 1327, 1239, 1161, 1106, 1033, 842, 753, 689 cm^{-1}; **HRMS** (EI-TOF): calcd for, $C_{15}H_{10}N_3F$ $[M]^+$, 251.0859; found, 251.0858.

3-phenyl-6-(p-tolyl)-1,2,4-triazine (4ea): yellow solid, 26 mg, 52% yield, mp: 158-160 °C (literature: 156-157 °C)[26]; **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 9.04 (s, 1H), 8.60-8.57 (m, 2H), 8.08-8.06 (m, 2H), 7.58-7.55 (m, 3H), 7.40-7.38 (m, 2H), 2.46 (s, 3H); **^{13}C NMR** (100 MHz, Chloroform-*d*) δ 162.3 , 155.1 , 146.4, 141.5, 134.9, 131.7, 130.6, 130.2, 129.0, 128.2, 126.7, 21.6; **IR**(KBr): $\tilde{\nu}$ = 3056, 2922, 2853, 1917, 1776, 1614, 1601, 1563, 1447, 1408, 1329, 1189, 1085, 1036, 988, 830, 750, 690 cm^{-1}; **HRMS** (EI-TOF): calcd for, $C_{16}H_{13}N_3$ $[M]^+$, 247.1109; found, 247.1110.

6-(4-methoxyphenyl)-3-phenyl-1,2,4-triazine (4fa): yellow solid, 25 mg, 47% yield, mp: 165-167 °C (literature: 161-164 °C)[27]; **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 9.02 (s, 1H), 8.58-8.55 (m, 2H), 8.13 (d, *J* = 8.7 Hz, 2H), 7.56-7.55 (m, 3H), 7.09 (d, *J* = 8.7 Hz, 2H), 3.90 (s, 3H); **^{13}C NMR** (100 MHz, Chloroform-*d*) δ 162.1, 161.9, 154.7, 146.0, 134.9, 131.6, 129.0, 128.2, 128.1, 125.7, 114.9, 55.6; **IR**(KBr): $\tilde{\nu}$ = 3043, 2923, 2852, 1971, 1923, 1655, 1605, 1512, 1407, 1296, 1255, 1179, 1040, 988, 840, 755, 692 cm^{-1}; **HRMS** (EI-TOF): calcd for, $C_{16}H_{13}N_3O$ $[M]^+$, 263.1059; found, 263.1061.

6-(3-methoxyphenyl)-3-phenyl-1,2,4-triazine (4ga): yellow solid, 24 mg, 46% yield, mp: 128-130 °C; **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 9.06 (s, 1H), 8.60-8.58 (m, 2H), 7.82-7.81 (m, 1H), 7.68-7.65 (m, 1H), 7.59-7.55 (m, 3H), 7.49 (t, *J* = 8.0 Hz, 1H), 7.11 (ddd, *J* = 8.3, 2.6, 0.8 Hz, 1H), 3.93 (s, 3H); **^{13}C NMR** (100 MHz, Chloroform-*d*) δ 162.6, 160.6, 154.9, 146.7, 134.7 , 134.7, 131.8, 130.5, 129.1, 128.3, 118.9, 117.4, 111.6, 55.6; **IR**(KBr): $\tilde{\nu}$ = 3065, 2923, 2852, 1604, 1582, 1494, 1457, 1405, 1328, 1253, 1205,1085, 1047, 891, 780, 687 cm^{-1}; **HRMS** (EI-TOF): calcd for, $C_{16}H_{13}N_3O$ $[M]^+$, 263.1059; found, 263.1058.

6-(3-bromophenyl)-3-phenyl-1,2,4-triazine (4ha): yellow solid, 24 mg, 38% yield, mp: 123-125 °C; **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 9.04 (s, 1H), 8.60-8.58 (m, 2H), 8.35 (s, 1H), 8.09 (d, *J* = 7.8 Hz, 1H), 7.70 (d, *J* = 8.0 Hz, 1H), 7.58-7.55 (m, 3H), 7.47 (t, *J* = 7.9 Hz, 1H); **^{13}C NMR** (100 MHz, Chloroform-*d*) δ 162.9, 153.9, 146.5, 135.4, 134.5, 133.9, 132.0, 130.9, 129.8, 129.1, 128.4, 125.2, 123.7; **IR**(KBr): $\tilde{\nu}$ = 3064, 2954, 2923, 2852, 1949, 1634, 1564, 1446, 1407, 1319, 1089, 904, 788, 687 cm^{-1}; **HRMS** (EI-TOF): calcd for, $C_{15}H_{10}N_3Br^{79}$ $[M]^+$, 311.0058; found, 311.0060.

6-(2-methoxyphenyl)-3-phenyl-1,2,4-triazine (4ia): yellow solid, 26 mg, 49% yield, mp: 159-161 °C; **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 9.26 (s, 1H), 8.60-8.57 (m, 2H), 8.13 (dd, *J* = 7.7, 1.7 Hz, 1H), 7.58-7.55 (m, 3H), 7.51 (ddd, *J* = 8.4, 7.5, 1.8 Hz, 1H), 7.18 (td, *J* = 7.6, 0.9 Hz, 1H), 7.07 (d, *J* = 8.3 Hz, 1H), 3.93 (s, 3H); **^{13}C NMR** (100 MHz, Chloroform-*d*) δ 161.6, 157.5, 155.1, 150.5, 135.1, 132.3, 131.6, 130.9, 128.9, 128.2, 122.8, 121.7, 111.5, 55.8; **IR**(KBr): $\tilde{\nu}$ = 3057, 3004, 2924, 2853, 1753, 1658, 1601, 1494, 1457, 1406, 1270, 1179, 1088, 1020, 743, 685 cm^{-1}; **HRMS** (EI-TOF): calcd for, $C_{16}H_{13}N_3O$ $[M]^+$, 263.1059; found, 263.1060.

6-(2-chlorophenyl)-3-phenyl-1,2,4-triazine (4ja): yellow solid, 24 mg, 45% yield, mp: 140-142 °C (literature: 89-90 °C)[26]; **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 9.10 (s, 1H), 8.63-8.60 (m, 2H), 7.88-7.86 (m, 1H), 7.59-7.55 (m, 4H), 7.52-7.48 (m, 2H); **^{13}C NMR** (100 MHz, Chloroform-*d*) δ 162.3, 155.9, 150.0, 134.6, 133.2, 132.6, 132.0, 131.9, 131.6, 130.5, 129.1, 128.5, 127.8; **IR**(KBr): $\tilde{\nu}$ = 3095, 3059, 2923, 2853, 1739, 1654, 1560, 1452, 1402, 1164, 1085, 1057, 1031, 765, 687 cm^{-1}; **HRMS** (EI-TOF): calcd for, $C_{15}H_{10}N_3Cl^{35}$ $[M]^+$, 267.0563; found, 267.0568.

3-phenyl-6-(3,4,5-trimethoxyphenyl)-1,2,4-triazine (4ka): yellow solid, 29 mg, 45% yield, mp: 129-131 °C; **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 9.03 (s, 1H), 8.59-8.57 (m, 2H), 7.57-7.54 (m, 3H), 7.41 (s, 2H), 3.99 (s, 6H), 3.95 (s, 3H); **^{13}C NMR** (100 MHz, Chloroform-*d*) δ 162.3, 154.6, 154.1, 146.3, 140.8, 134.6, 131.8, 129.0, 128.5, 128.2, 103.9, 61.1, 56.5; **IR**(KBr): $\tilde{\nu}$ = 3051, 2992, 2926, 2852, 1654, 1589, 1507, 1458, 1399, 1350, 1132, 995, 882, 751, 690 cm^{-1}; **HRMS** (EI-TOF): calcd for, $C_{18}H_{17}N_3O_3$ $[M]^+$, 323.1270; found, 323.1271.

3-phenyl-6-(thiophen-3-yl)-1,2,4-triazine (4la): yellow solid, 15 mg, 31% yield, mp: 150-152 °C; **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 8.98 (s, 1H), 8.57-8.55 (m, 2H), 8.18-8.17 (m, 1H), 7.88 (d, *J* = 4.9 Hz, 1H), 7.57-7.55 (m, 4H); **^{13}C NMR** (100 MHz, Chloroform-*d*) δ 162.1, 151.8, 146.4, 135.7, 134.8, 131.7, 129.1, 128.2, 127.8, 125.8, 125.6; **IR**(KBr): $\tilde{\nu}$ = 3082, 2957, 2922, 2852, 1965, 1908, 1654, 1600, 1528, 1427, 1385, 1310, 1087, 1040, 960, 868, 799, 751, 690, 646 cm^{-1}; **HRMS** (EI-TOF): calcd for, $C_{13}H_9N_3S$ $[M]^+$, 239.0517; found, 239.0518.

3-(3-phenyl-1,2,4-triazin-6-yl)-1-(phenylsulfonyl)-1*H*-indole (4ma): yellow solid, 43 mg, 52% yield, mp: 241-243 °C; **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 9.04 (s, 1H), 8.58-8.53 (m, 3H), 8.30 (s, 1H), 8.07 (d, *J* = 8.1 Hz, 1H), 7.98 (d, *J* = 7.7 Hz, 2H), 7.60-7.55 (m, 4H), 7.51-7.39 (m, 4H); **^{13}C NMR** (100 MHz, Chloroform-*d*) δ 161.8, 152.2, 146.9, 137.8, 135.6, 134.8, 134.6, 131.8, 129.7, 129.0, 128.2, 127.7, 127.1, 126.1, 125.9, 124.7, 123.2, 116.8, 113.6; **IR**(KBr): $\tilde{\nu}$ = 3143, 3055, 2923, 2853, 1602, 1566, 1546, 1444, 1411, 1370, 1334, 1285, 1173, 1140, 1107, 1088, 1024, 999, 750, 686, 593 cm^{-1}; **HRMS** (EI-TOF): calcd for, $C_{23}H_{16}N_4O_2S$ $[M]^+$, 412.0994; found, 412.0996.

General procedure for synthesis of 3,5,6-trisubstituted-1,2,4-triazines 5

To an oven-dried Schlenk tube was added 0.28 mmol (1.4 equiv.) *N*-sulfonyl-1,2,3-triazoles, 0.20 mmol (1.0 equiv.) *N*-acylhydrazones and 0.01 mmol (5 mol%) Rh(II), successively. The Schlenk tube was sealed with a Rubber plug and the atmosphere was replaced using standard Schlenk techniques under nitrogen atmosphere. Then 1 mL dried solvent was added and the reaction mixture was heated at 75 °C, with vigorous stirring, for 1-3 h. Once hydrazones consumed, the reaction mixture was cooled to 30 °C and 20 mol % DBU or 100 mol% TEA was added. About 12 h later, the intermediate was consumed, then DDQ 0.4 mmol (2.0 equiv.) was added. The resulting solution was stirred for further 24 h. After reaction, solvent was evaporated and the residue was purified by flash chromatography (petroleum ether/ ethyl acetate = 10:1~5:1) to afford the desired product.

Ethyl 5-benzoyl-3-phenyl-1,2,4-triazine-6-carboxylate (5aa): yellow solid, 31 mg, 46% yield, mp: 119-121 °C; ^{1}**H NMR** (400 MHz, Chloroform-*d*) δ 8.63 (d, *J* = 7.5 Hz, 2H), 7.89 (d, *J* = 7.8 Hz, 2H), 7.69 (t, *J* = 7.4 Hz, 1H), 7.63 (t, *J* = 7.2 Hz, 1H), 7.55 (q, *J* = 7.6 Hz, 4H), 4.43 (q, *J* = 7.1 Hz, 2H), 1.31 (t, *J* = 7.1 Hz, 3H); ^{13}**C NMR** (100 MHz, Chloroform-*d*) δ 190.3, 163.6, 162.6, 157.1, 146.4, 134.8, 134.2, 133.4, 133.4, 130.1, 129.6, 129.3, 129.1, 63.4, 13.9; **IR**(KBr): $\tilde{\nu}$ = 3061, 2986, 2925, 2853, 1973, 1749, 1720, 1685, 1596, 1450, 1388, 1307, 1279, 1201, 1046, 968, 861, 779, 692 cm^{-1}; **HRMS** (EI-TOF): calcd for, $C_{19}H_{15}N_3O_3$ $[M]^+$, 333.1113; found, 333.1112.

Ethyl 5-benzoyl-3-(o-tolyl)-1,2,4-triazine-6-carboxylate (5ab): yellow solid, 38 mg, 55% yield, mp: 80-82 °C; ^{1}**H NMR** (400 MHz, Chloroform-*d*) δ 8.16 (d, *J* = 7.4 Hz, 1H), 7.89 (d, *J* = 7.5 Hz, 2H), 7.68 (t, *J* = 7.4 Hz, 1H), 7.53 (t, *J* = 7.7 Hz, 2H), 7.47 (t, *J* = 7.1 Hz, 1H), 7.37 (t, *J* = 6.9 Hz, 2H), 4.44 (q, *J* = 7.1 Hz, 2H), 2.68 (s, 3H), 1.32 (t, *J* = 7.1 Hz, 3H); ^{13}**C NMR** (100 MHz, Chloroform-*d*) δ 190.2, 166.4, 162.6, 156.5, 145.6, 139.7, 134.8, 134.2, 133.2, 132.3, 131.9, 131.9, 130.1, 129.1, 126.5, 63.4, 22.2, 13.9; **IR**(KBr): $\tilde{\nu}$ = 3066, 2964, 2925, 2853, 1988, 1723, 1684, 1597, 1507, 1369,, 1289, 1211, 1109, 966, 877, 776, 710, 657 cm^{-1}; **HRMS** (EI-TOF): calcd for, $C_{20}H_{17}N_3O_3$ $[M]^+$, 347.1270; found, 347.1271.

Ethyl 5-benzoyl-3-(2-fluorophenyl)-1,2,4-triazine-6-carboxylate (5ac): yellow solid, 33 mg, 47% yield, mp: 106-108 °C; ^{1}**H NMR** (400 MHz, Chloroform-*d*) δ 8.28 (td, *J* = 7.7, 1.5 Hz, 1H), 7.93 (d, *J* = 7.4 Hz, 2H), 7.69 (t, *J* = 7.5 Hz, 1H), 7.62-7.52 (m, 3H), 7.34 (t, *J* = 7.6 Hz, 1H), 7.29-7.24 (m, 1H), 4.44 (q, *J* = 7.1 Hz, 2H), 1.32 (t, *J* = 7.1 Hz, 3H); ^{13}**C NMR** (100 MHz, Chloroform-*d*) δ 189.9, 162.9 (d, *J* = 5.7 Hz), 162.5, 162.0 (d, *J* = 260.7 Hz), 156.5, 146.4, 134.9, 134.4 (d, *J* = 8.8 Hz), 134.1, 132.4, 130.7, 130.2, 129.1, 129.0, 124.7 (d, *J* = 3.9 Hz), 122.4 (d, *J* = 9.1 Hz), 117.5 (d, *J* = 21.8 Hz), 63.4, 13.9; **IR**(KBr): $\tilde{\nu}$ = 3068, 2980, 2924, 2853, 1986, 1725, 1679, 1611, 1498, 1452, 1385, 1286, 1208, 1110, 1065, 967, 772, 713, 652 cm^{-1}; **HRMS** (EI-TOF): calcd for, $C_{19}H_{14}N_3O_3F$ $[M]^+$, 351.1019; found, 351.1018.

Ethyl 5-benzoyl-3-(m-tolyl)-1,2,4-triazine-6-carboxylate (5ad): yellow solid, 26 mg, 37% yield, mp: 95-97 °C; **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 8.43-8.41 (m, 2H), 7.89 (d, *J* = 7.6 Hz, 2H), 7.69 (t, *J* = 7.4 Hz, 1H), 7.54 (t, *J* = 7.7 Hz, 2H), 7.47-7.43 (m, 2H), 4.42 (q, *J* = 7.1 Hz, 2H), 2.45 (s, 3H), 1.30 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (100 MHz, Chloroform-*d*) δ 190.3, 163.7, 162.6, 157.1, 146.2, 139.1, 134.8, 134.3, 134.2, 133.3, 130.1, 130.0, 129.2, 129.1, 126.8, 63.3, 21.6, 13.9; **IR**(KBr): $\tilde{\nu}$ = 3066, 2995, 2924, 2854, 1713, 1682, 1598, 1511, 1450, 1378, 1287, 1218, 1122, 1035, 971, 798, 709, 645 cm^{-1}; **HRMS** (EI-TOF): calcd for, $C_{20}H_{17}N_3O_3$ $[M]^+$, 347.1270; found, 347.1271.

Ethyl 5-benzoyl-3-(3-(trifluoromethyl)phenyl)-1,2,4-triazine-6-carboxylate (5ae): yellow solid, 13 mg, 17% yield, mp: 104-106 °C; **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 8.88 (s, 1H), 8.83 (d, *J* = 7.9 Hz, 1H), 7.88 (d, *J* = 7.8 Hz, 3H), 7.71 (t, *J* = 7.9 Hz, 2H), 7.55 (t, *J* = 7.8 Hz, 2H), 4.44 (q, *J* = 7.1 Hz, 2H), 1.31 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (100 MHz, Chloroform-*d*) δ 190.0, 162.5, 162.4, 157.3, 146.9, 134.9, 134.2, 134.1, 132.6, 131.9 (q, *J* = 33.0 Hz), 130.1, 129.9, 129.7 (q, *J* = 3.5 Hz), 129.2, 126.3 (q, *J* = 3.9 Hz), 123.8 (d, *J* = 272.7 Hz), 63.5, 13.9; **IR**(KBr): $\tilde{\nu}$ = 3085, 2982, 2920, 2850, 1723, 1686, 1597, 1511, 1450, 1394, 1272, 1173, 1123, 971, 818, 697, 645 cm^{-1}; **HRMS** (EI-TOF): calcd for, $C_{20}H_{14}N_3O_3F_3$ $[M]^+$, 401.0987; found, 401.0984.

Ethyl 5-benzoyl-3-(p-tolyl)-1,2,4-triazine-6-carboxylate (5af): yellow solid, 29 mg, 42% yield, mp: 130-132 °C; **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 8.51 (d, *J* = 8.1 Hz, 2H), 7.88 (d, *J* = 7.9 Hz,2H), 7.68 (t, *J* = 7.4 Hz, 1H), 7.53 (t, *J* = 7.7 Hz, 2H), 7.35 (d, *J* = 8.1 Hz, 2H), 4.42 (q, *J* = 7.1 Hz, 2H), 2.46 (s, 3H), 1.30 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (100 MHz, Chloroform-*d*) δ 190.4, 163.6, 162.7, 157.1, 146.1, 144.3, 134.7, 134.3, 130.7, 130.1, 130.1, 129.6, 129.9, 63.2, 21.9, 13.9; **IR**(KBr): ṽ = 3067. 2992, 2924, 2855, 1981, 1720, 1677, 1608, 1502, 1449, 1371, 1288, 1208, 1178, 1045, 963, 814, 725, 653 cm^{-1}; **HRMS** (EI-TOF): calcd for, $C_{20}H_{17}N_3O_3$ $[M]^+$, 347.1270; found, 347.1272.

Ethyl 5-benzoyl-3-(4-fluorophenyl)-1,2,4-triazine-6-carboxylate (5ag): yellow solid, 28 mg, 40% yield, mp: 170-172 °C; **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 8.67-8.63 (m, 2H), 7.88 (d, *J* = 7.5 Hz, 2H), 7.69 (t, *J* = 7.4 Hz, 1H), 7.54 (t, *J* = 7.7 Hz, 2H), 7.27-7.21 (m, 2H), 4.42 (q, *J* = 7.1 Hz, 2H), 1.31 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (100 MHz, Chloroform-*d*) δ 190.2, 166.2 (d, *J* = 255.3 Hz), 162.7, 162.5, 157.2, 146.2, 134.8, 134.2, 131.9 (d, *J* = 9.2 Hz), 130.1, 129.6 (d, *J* = 3.0 Hz), 129.1, 116.5 (d, *J* = 22.0 Hz), 63.4, 13.9; **IR**(KBr): ṽ = 3069, 2924, 2853, 1721, 1675, 1598, 1509, 1375, 1285, 1208, 1154, 1110, 1046, 965, 877, 788, 652 cm^{-1}; **HRMS** (EI-TOF): calcd for, $C_{19}H_{14}N_3O_3F$ $[M]^+$, 351.1019; found, 351.1020.

Ethyl 5-(4-bromobenzoyl)-3-phenyl-1,2,4-triazine-6-carboxylate (5ba): yellow solid, 33 mg, 40% yield, mp: 144-146 °C; **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 8.62-8.59 (m, 2H), 7.76 (d, *J* = 8.5 Hz, 2H), 7.68 (d, *J* = 8.5 Hz, 2H), 7.63 (t, *J* = 7.3 Hz, 1H), 7.56 (t, *J* = 7.5 Hz, 2H), 4.45 (q, *J* = 7.1 Hz, 2H), 1.35 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (100 MHz, Chloroform-*d*) δ 189.3, 163.5, 162.6, 156.5, 146.4, 133.4, 133.2, 133.0, 132.5, 131.4, 130.4, 129.5, 129.3, 63.4, 14.0; **IR**(KBr): ṽ = 3096, 2989, 2936, 2867, 1720, 1682, 1584, 1507, 1375, 1285, 1211, 1126, 1070, 967, 879, 779, 703, 672 cm^{-1}; **HRMS** (EI-TOF): calcd for, $C_{19}H_{14}N_3O_3Br^{79}$ $[M]^+$, 411.0219; found, 411.0218.

Ethyl 5-(4-chlorobenzoyl)-3-phenyl-1,2,4-triazine-6-carboxylate (5ca): yellow solid, 28 mg, 38% yield, mp: 148-151 °C; **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 8.61 (d, *J* = 7.5 Hz, 1H), 7.84 (d, *J* = 8.5 Hz, 1H), 7.63 (t, *J* = 7.3 Hz, 1H), 7.56 (t, *J* = 7.6 Hz, 1H), 7.52 (d, *J* = 8.5 Hz, 1H), 4.45 (q, *J* = 7.1 Hz, 1H), 1.35 (t, *J* = 7.1 Hz, 1H); **^{13}C NMR** (100 MHz, Chloroform-*d*) δ 189.1, 163.6, 162.7, 156.6, 146.5, 141.5, 133.4, 133.3, 132.6, 131.4, 129.5, 129.5, 129.3, 63.4, 14.0; **IR**(KBr): $\tilde{\nu}$ = 3096, 2968, 2923, 2852, 1720, 1683, 1586, 1508, 1377, 1284, 1211, 1115, 1089, 1044, 967, 779, 703, 672 cm^{-1}; **HRMS** (EI-TOF): calcd for, $C_{19}H_{14}N_3O_3Cl^{35}$ $[M]^+$, 367.0724; found, 367.0726.

Ethyl 5-(4-fluorobenzoyl)-3-phenyl-1,2,4-triazine-6-carboxylate (5da): yellow solid, 31 mg, 44% yield, mp: 137-139 °C; **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 8.63-8.60 (m, 2H), 7.96-7.92 (m, 2H), 7.65-7.61 (m, 1H), 7.56 (t, *J* = 7.4 Hz, 2H), 7.22 (t, *J* = 8.6 Hz, 2H), 4.45 (q, *J* = 7.1 Hz, 2H), 1.34 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (100 MHz, Chloroform-*d*) δ 188.8, 166.8 (d, *J* = 258.4 Hz), 163.5, 162.7, 156.7, 146.5, 133.4, 133.3, 132.9 (d, *J* = 9.7 Hz), 130.8 (d, *J* = 2.9 Hz), 129.5, 129.3, 116.5 (d, *J* = 22.3 Hz), 63.4, 14.0; **IR**(KBr): $\tilde{\nu}$ = 3074, 2985, 2929, 1921, 1721, 1680, 1596, 1507, 1373, 1285, 1242, 1211, 1160, 971, 837, 691, 608 cm^{-1}; **HRMS** (EI-TOF): calcd for, $C_{19}H_{14}N_3O_3F$ $[M]^+$, 351.1019; found, 351.1021.

Ethyl 5-(4-methylbenzoyl)-3-phenyl-1,2,4-triazine-6-carboxylate (5ea): yellow solid, 28 mg, 39% yield, mp: 158-160 °C; **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 8.62-8.61 (m, 1H), 7.78 (d, *J* = 7.2 Hz, 1H), 7.61-7.60 (m, 1H), 7.56-7.55 (m, 1H), 7.33 (d, *J* = 7.0 Hz, 1H), 4.46-4.39 (m, 1H), 2.46 (s, 1H), 1.33-1.29 (m, 1H); **^{13}C NMR** (100 MHz, Chloroform-*d*) δ 189.9, 163.5, 162.6, 157.2, 146.5, 146.1, 133.4, 133.3, 131.8, 130.2, 129.8, 129.5, 129.2, 63.3, 22.1, 13.9; **IR**(KBr): $\tilde{\nu}$ = 3064, 2973, 2924, 1723, 1677, 1603, 1505, 1376, 1286, 1211, 1123, 1045, 966, 879, 773, 692 cm^{-1}; **HRMS** (EI-TOF): calcd for, $C_{20}H_{17}N_3O_3$ $[M]^+$, 347.1270; found, 347.1271.

Ethyl 5-(4-methoxybenzoyl)-3-phenyl-1,2,4-triazine-6-carboxylate (5fa): yellow solid, 33 mg, 45% yield, mp: 165-167 °C; **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 8.63-8.61 (m, 2H), 7.89-7.86 (m, 2H), 7.64-7.60 (m, 1H), 7.57-7.53 (m, 2H), 7.02-6.98 (m, 2H), 4.43 (q, *J* = 7.1 Hz, 2H), 3.90 (s, 3H), 1.32 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (100 MHz, Chloroform-*d*) δ 188.9, 164.9, 163.5, 162.7, 157.2, 146.7, 133.5, 133.2, 132.6, 129.5, 129.3, 127.4, 114.5, 63.2, 55.8, 13.9; **IR**(KBr): $\tilde{\nu}$ = 3082, 2987, 2932, 2836, 1724, 1671, 1598, 1511, 1454, 1387, 1323, 1269, 1173, 1125, 1023, 968, 856, 777, 694, 610 cm^{-1}; **HRMS** (EI-TOF): calcd for, $C_{20}H_{17}N_3O_4$ $[M]^+$, 363.1219; found, 363.1218.

Ethyl 5-(3-methoxybenzoyl)-3-phenyl-1,2,4-triazine-6-carboxylate (5ga): yellow solid, 35 mg, 48% yield, mp: 128-130 °C; ^{1}**H NMR** (400 MHz, Chloroform-*d*) δ 8.63-8.61 (m, 2H), 7.62 (t, *J* = 7.3 Hz, 1H), 7.57-7.54 (m, 3H), 7.40 (t, *J* = 7.9 Hz, 1H), 7.29 (d, *J* = 7.7 Hz, 1H), 7.22 (dd, *J* = 8.2, 2.0 Hz, 1H), 4.44 (q, *J* = 7.1 Hz, 2H), 3.88 (s, 3H), 1.33 (t, *J* = 7.1 Hz, 3H); ^{13}**C NMR** (100 MHz, Chloroform-*d*) δ 190.1, 163.6, 162.6, 160.2, 157.1, 146.3, 135.5, 133.4, 133.3, 130.1, 129.5, 129.3, 123.4, 121.6, 113.3, 63.3, 55.7, 13.9; **IR**(KBr): $\tilde{\nu}$ = 3070, 2989, 2958, 2922, 1720, 1683, 1596, 1512, 1466, 1385, 1285, 1194, 1109, 998, 767, 692 cm^{-1}; **HRMS** (EI-TOF): calcd for, $C_{20}H_{17}N_3O_4$ $[M]^+$, 363.1219; found, 363.1221.

Ethyl 5-(3-bromobenzoyl)-3-phenyl-1,2,4-triazine-6-carboxylate (5ha): yellow solid, 25 mg, 30% yield, mp: 123-125 °C; ^{1}**H NMR** (400 MHz, Chloroform-*d*) δ 8.62 (d, *J* = 7.4 Hz, 2H), 8.06 (s, 1H), 7.81 (d, *J* = 7.9 Hz, 1H), 7.77 (d, *J* = 7.8 Hz, 1H), 7.64 (t, *J* = 7.3 Hz, 1H), 7.57 (t, *J* = 7.5 Hz, 2H), 7.41 (t, *J* = 7.9 Hz, 1H), 4.46 (q, *J* = 7.1 Hz, 2H), 1.36 (t, *J* = 7.1 Hz, 3H); ^{13}**C NMR** (100 MHz, Chloroform-*d*) δ 188.9, 163.6, 162.6, 156.5, 146.3, 137.6, 135.9, 133.5, 133.2, 132.7, 130.6, 129.6, 129.3, 128.7, 123.5, 63.5, 14.0; **IR**(KBr): $\tilde{\nu}$ = 3068, 2924, 2853, 1970, 1716, 1684, 1567, 1509, 1425, 1373, 1309, 1286, 1207, 1123, 1045, 782, 723, 670 cm^{-1}; **HRMS** (EI-TOF): calcd for, $C_{19}H_{14}N_3O_3Br^{79}$ $[M]^+$, 411.0219; found, 411.0214.

Ethyl 5-(2-methoxybenzoyl)-3-phenyl-1,2,4-triazine-6-carboxylate (5ia): yellow solid, 25 mg, 34% yield, mp: 159-161 °C; ^{1}**H NMR** (400 MHz, Chloroform-*d*) δ 8.62-8.60 (m, 2H), 8.23 (dd, *J* = 7.8, 1.7 Hz, 1H), 7.65-7.57 (m, 2H), 7.55-7.51 (m, 2H), 7.19 (t, *J* = 8.0 Hz, 1H), 6.91 (d, *J* = 8.3 Hz, 1H), 4.42 (q, *J* = 7.1 Hz, 1H), 3.45 (s, 2H), 1.30 (t, *J* = 7.1 Hz, 3H); ^{13}**C NMR** (100 MHz, Chloroform-*d*) δ 188.8, 163.7, 162.8, 160.4, 159.9, 144.9, 136.7, 133.8, 132.9, 131.2, 129.4, 129.1, 123.7, 121.7, 112.3, 63.0, 55.8, 14.0; **IR**(KBr): $\tilde{\nu}$ = 3073, 2924, 2852, 1725, 1672, 1596, 1510, 1376, 1298, 1201, 1017, 967, 875, 760, 666, 646 cm^{-1}; **HRMS** (EI-TOF): calcd for, $C_{20}H_{17}N_3O_4$ $[M]^+$, 363.1219; found, 363.1220.

Ethyl 5-(2-chlorobenzoyl)-3-phenyl-1,2,4-triazine-6-carboxylate (5ja): yellow solid, 27 mg, 37% yield, mp: 140-142 °C; ^{1}**H NMR** (400 MHz, Chloroform-*d*) δ 8.56 (d, *J* = 7.9 Hz, 2H), 8.06 (d, *J* = 8.6 Hz, 1H), 7.61-7.50 (m, 4H), 7.49-7.45 (m, 2H), 4.48 (q, *J* = 7.1 Hz, 2H), 1.38 (t, *J* = 7.1 Hz, 3H); ^{13}**C NMR** (100 MHz, Chloroform-*d*) δ 189.6, 163.7, 162.8, 157.7, 146.1, 135.0, 134.7, 133.4, 133.2, 133.1, 132.7, 131.4, 129.4, 129.2, 127.5, 63.4, 14.0; **IR**(KBr): $\tilde{\nu}$ = 3066, 2921, 2851, 1992, 1721, 1672, 1584, 1508, 1376, 1293, 1202, 1061, 963, 872, 781, 746, 701, 634 cm^{-1}; **HRMS** (EI-TOF): calcd for, $C_{19}H_{14}N_3O_3Cl^{35}$ $[M]^+$, 367.0724; found, 367.0722.

Ethyl 3-phenyl-5-(3,4,5-trimethoxybenzoyl)-1,2,4-triazine-6-carboxylate (5ka): yellow solid, 39 mg, 46% yield, mp: 129-131 °C; ^{1}**H NMR** (400 MHz, Chloroform-*d*) δ 8.65-8.62 (m, 2H), 7.63 (t, *J* = 7.3 Hz, 1H), 7.57 (t, *J* = 7.4 Hz, 2H), 7.15 (s, 2H), 4.47 (q, *J* = 7.1 Hz, 2H), 3.97 (s, 3H), 3.85 (s, 6H), 1.37 (t, *J* = 7.1 Hz, 3H); ^{13}**C NMR** (100 MHz, Chloroform-*d*) δ 189.1, 163.4, 162.8, 156.8, 153.5, 146.8, 144.3, 133.4, 133.4, 129.4, 129.3, 129.1, 107.7, 63.3, 61.2, 56.5, 14.0; **IR**(KBr): $\tilde{\nu}$ = 3093, 2985, 2940, 2848, 1731, 1674, 1581, 1504, 1463, 1415, 1333, 1271, 1125, 1000, 769, 705, 687 cm^{-1}; **HRMS** (EI-TOF): calcd for, $C_{22}H_{21}N_3O_6$ $[M]^+$, 423.1430; found, 423.1431.

Ethyl 3-phenyl-5-(thiophene-3-carbonyl)-1,2,4-triazine-6-carboxylate (5la): yellow solid, 24 mg, 36% yield, mp: 150-152 °C; ^{1}**H NMR** (400 MHz, Chloroform-*d*) δ 8.62 (dt, *J* = 7.1, 1.3 Hz, 2H), 8.18 (dd, *J* = 2.8, 1.2 Hz, 1H), 7.70 (dd, *J* = 5.1, 1.2 Hz, 1H), 7.66-7.61 (m, 1H), 7.59-7.55 (m, 2H), 7.46 (dd, *J* = 5.1, 2.9 Hz, 1H), 4.47 (q, *J* = 7.1 Hz, 2H), 1.37 (t, *J* = 7.1 Hz, 3H); ^{13}**C NMR** (100 MHz, Chloroform-*d*) δ 183.7, 163.5, 162.9, 155.5, 147.2, 139.1, 136.9, 133.4, 133.3, 129.4, 129.3, 127.7, 127.4, 63.3, 14.0; **IR**(KBr): $\tilde{\nu}$ = 3080, 2981, 2931, 2871, 1744, 1674, 1506, 1402, 1305, 1199, 1048, 833, 768, 702, 669 cm^{-1}; **HRMS** (EI-TOF): calcd for, $C_{17}H_{13}N_3O_3S$ $[M]^+$, 339.0678; found, 339.0679.

Ethyl 3-phenyl-5-(1-(phenylsulfonyl)-1H-indole-3-carbonyl)-1,2,4-triazine-6-carboxylate (5ma): yellow solid, 52 mg, 51% yield, mp: 241-243 °C; **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 8.65 (d, *J* = 8.5 Hz, 2H), 8.48 (s, 1H), 8.43-8.41 (m, 1H), 8.03-8.01 (m, 1H), 7.97 (d, *J* = 7.9 Hz, 2H), 7.69-7.61 (m, 4H), 7.53 (t, *J* = 7.8 Hz, 2H), 7.49-7.42 (m, 2H), 4.48 (q, *J* = 7.1 Hz, 2H), 1.34 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (100 MHz, Chloroform-*d*) δ 184.7, 163.5, 163.4, 153.6, 148.1, 137.4, 136.2, 135.0, 134.9, 133.5, 133.3, 129.9, 129.4, 129.3, 127.8, 127.4, 126.7, 125.7, 123.3, 118.4, 113.4, 63.3, 14.0; **IR**(KBr): $\tilde{\nu}$ = 3127, 3065, 2959, 2924, 2854, 1974, 1723, 1660, 1540, 1446, 1394, 1369, 1300, 1265, 1176, 1083, 982, 755, 683, 593 cm^{-1}; **HRMS** (EI-TOF): calcd for, $C_{27}H_{20}N_4O_5S$ $[M]^+$, 512.1154; found, 512.1161.

Ethyl 4-(2-oxo-2-phenylethyl)-5-phenyl-4*H*-1,2,4-triazole-3-carboxylate (6aa): yellow oil, 14 mg, 20% yield (2 equiv. NaOH as base in two-step way); **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 8.52 (d, *J* = 7.7 Hz, 2H), 8.18 (d, *J* = 7.2 Hz, 2H), 7.68 (t, *J* = 7.3 Hz, 1H), 7.55 (t, *J* = 7.5 Hz, 2H), 7.52-7.39 (m, 3H), 5.45 (s, 2H), 4.25 (q, *J* = 7.1 Hz, 2H), 1.26 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (100 MHz, Chloroform-*d*) δ 183.3, 166.9, 161.1, 150.3, 135.6, 134.4, 131.4, 130.2, 129.9, 128.8, 128.6, 126.7, 62.3, 53.1, 14.2; **IR**(KBr): $\tilde{\nu}$ = 3050, 2924, 2853, 1752, 1654, 1561, 1459, 1404, 1282, 1209, 1092, 918, 686 cm^{-1}; **HRMS** (EI-TOF): calcd for, $C_{19}H_{17}N_3O_3$ $[M]^+$, 335.1270; found, 335.1271.

Ethyl 5-methyl-4-(2-oxo-2-phenylethyl)-4*H*-1,2,4-triazole-3-carboxylate (6ai): yellow oill, 11 mg, 21% yield; **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 8.36 (d, *J* = 8.0 Hz, 2H), 7.64 (t, *J* = 7.4 Hz, 1H), 7.52 (t, *J* = 7.7 Hz, 2H), 5.33 (s, 2H), 4.23 (q, *J* = 7.1 Hz, 2H), 2.50 (s, 3H), 1.26 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (100

MHz, Chloroform-*d*) δ 183.5, 167.0, 160.0, 149.9, 135.7, 134.3, 131.1, 128.6, 62.3, 52.5, 14.2, 14.1; **IR**(KBr): $\tilde{\nu}$ = 3068, 2960, 2927, 2854, 1754, 1658, 1597, 1478, 1434, 1375, 1280, 1214, 1127, 1025, 922, 736, 692 cm^{-1}; **HRMS** (EI-TOF): calcd for, $C_{14}H_{15}N_3O_3$ $[M]^+$, 273.1113; found, 273.1111.

Ethyl 5-benzyl-4-(2-oxo-2-phenylethyl)-4*H*-1,2,4-triazole-3-carboxylate (6aj): yellow oill, 21 mg, 30% yield; ^{1}**H NMR** (400 MHz, Chloroform-*d*) δ 8.37 (d, *J* = 7.6 Hz, 2H), 7.64 (t, *J* = 7.4 Hz, 1H), 7.51 (t, *J* = 7.7 Hz, 2H), 7.37-7.30 (m, 4H), 7.23 (d, *J* = 7.1 Hz, 1H), 5.34 (s, 2H), 4.22 (q, *J* = 7.2 Hz, 2H), 4.18 (s, 2H), 1.25 (t, *J* = 7.1 Hz, 3H); ^{13}**C NMR** (100 MHz, Chloroform-*d*) δ 183.4, 166.9, 162.3, 150.1, 137.7, 135.6, 134.3, 131.2, 128.9, 128.7, 128.6, 126.8, 62.3, 52.6, 34.8, 14.2; **IR**(KBr): $\tilde{\nu}$ = 3063, 2958, 2928, 2855, 1753, 1702, 1658, 1597, 1475, 1354, 1281, 1215, 1127, 1025, 922, 875, 732, 691, 576 cm^{-1}; **HRMS** (EI-TOF): calcd for, $C_{20}H_{19}N_3O_3$ $[M]^+$, 349.1426; found, 349.1421.

General procedure for synthesis of 1,4,5,6-tetrahydro-1,2,4-triazines 7

To an oven-dried Schlenk tube was added 0.28 mmol (1.4 equiv.) *N*-sulfonyl-1,2,3-triazoles, 0.20 mmol (1.0 equiv.) *N*-acylhydrazones and 0.01 mmol (5 mol%) Rh(II), successively. The Schlenk tube was sealed with a Rubber plug and the atmosphere was replaced using standard Schlenk techniques under nitrogen atmosphere. Then 1 mL dried solvent was added and the reaction mixture was heated at 75 °C, with vigorous stirring, for 1-3 h. Once hydrazones consumed, the reaction mixture was cooled to ambient temperature. Then reaction mixture was purified by flash chromatography (petroleum ether/ ethyl acetate = 5:1~3:1) to provide the intermediate. The intermediate was then dissolved in 2 mL dried THF and 20 mol % K_2CO_3 was added. The resulting solution was stirred at 30 °C for 12 h. After reaction, solvent was evaporated and the residue was purified by flash chromatography (petroleum ether/ ethyl acetate = 10:1~5:1) to afford the desired product.

3-(3-phenyl-1,2,4-triazin-6-yl)-1-(phenylsulfonyl)-1*H*-indole (7aa): yellow solid, 60 mg, 66% yield, mp: 151-153 °C; **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 8.08 (d, *J* = 7.6 Hz, 2H), 7.67 (t, *J* = 7.4 Hz, 1H), 7.60 (d, *J* = 8.2 Hz, 2H), 7.52 (t, *J* = 7.7 Hz, 2H), 7.31 (d, *J* = 8.1 Hz, 2H), 7.17 (t, *J* = 7.2 Hz, 1H), 7.08 (t, *J* = 7.6 Hz, 2H), 6.99 (d, *J* = 7.5 Hz, 2H), 6.41 (d, *J* = 3.9 Hz, 1H), 6.03 (d, *J* = 5.2 Hz, 1H), 4.28-4.18 (m, 2H), 3.63 (t, *J* = 4.7 Hz, 1H), 2.45 (s, 3H), 1.23 (t, *J* = 7.2 Hz, 3H); **^{13}C NMR** (100 MHz, Chloroform-*d*) δ 192. , 168.4, 145.6, 135.2, 134.7, 134.1, 134.0, 130.7, 130.4, 129.6, 128.9, 128.5, 127.8, 127.7, 126.9, 62.2, 54.7, 54.5, 21.9, 14.1; **IR**(KBr): $\tilde{\nu}$ = 3372, 3061, 2961, 2924, 2854, 1732, 1690, 1596, 1446, 1366, 1307, 1229, 1166, 1091, 993, 767, 743, 699,666, 612 cm^{-1}; **HRMS** (EI-TOF): calcd for, $C_{26}H_{25}N_3O_5S$ $[M]^+$, 491.1515; found, 491.1513.

Ethyl 5-benzoyl-3-(o-tolyl)-4-tosyl-1,4,5,6-tetrahydro-1,2,4-triazine-6-carboxylate (7ab): yellow solid, 76 mg, 75% yield, mp: 166-168 °C; **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 8.06 (d, *J* = 7.5 Hz, 2H), 7.67 (t, *J* = 7.4 Hz, 1H), 7.51 (t, *J* = 7.7 Hz, 2H), 7.47 (d, *J* = 8.2 Hz, 2H), 7.21 (d, *J* = 8.1 Hz, 2H), 7.04 (d, *J* = 3.7 Hz, 2H), 6.68 (dt, *J* = 8.3, 4.1 Hz, 1H), 6.36 (d, *J* = 4.0 Hz, 1H), 6.22 (d, *J* = 7.7 Hz, 1H), 6.18 (d, *J* = 4.8 Hz, 1H), 4.22 (q, *J* = 6.9 Hz, 2H), 3.88 (t, *J* = 4.6 Hz, 1H), 2.41 (s, 3H), 2.28 (s, 3H), 1.22 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (100 MHz, Chloroform-*d*) δ 192.8, 168.2, 145.2, 137.2, 134.9, 134.8, 134.0, 133.7, 130.8, 130.0, 129.6, 129.5, 129.4, 128.9, 128.2, 127.9, 124.9, 62.2, 55.4, 53.5, 21.8, 20.6, 14.1; **IR**(KBr): $\tilde{\nu}$ = 3388, 2962, 2922, 2852, 1741, 1688, 1595, 1453, 1332, 1301, 1231, 1158, 1086, 1036, 973, 751, 679, 616 cm^{-1}; **HRMS** (EI-TOF): calcd for, $C_{27}H_{27}N_3O_5S$ $[M]^+$, 505.1671; found, 505.1670.

Ethyl 5-benzoyl-3-(2-fluorophenyl)-4-tosyl-1,4,5,6-tetrahydro-1,2,4-triazine-6-carboxylate (7ac): yellow solid, 56 mg, 55% yield, mp: 174-176 °C; **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 8.16 (d, *J* = 7.8 Hz, 2H), 7.68 (t, *J* = 7.3 Hz, 1H), 7.63 (d, *J* = 8.1 Hz, 2H), 7.55 (t, *J* = 7.5 Hz, 2H), 7.32 (d, *J* = 8.0 Hz, 2H), 7.20-7.13 (m, 1H), 6.92-6.84 (m, 2H), 6.70 (t, *J* = 7.6 Hz, 1H), 6.47 (d, *J* = 3.3 Hz, 1H), 6.05 (d, *J* = 5.0 Hz, 1H), 4.28-4.13 (m, 2H), 3.51 (t, *J* = 4.5 Hz, 1H), 2.44 (s, 3H), 1.20 (t, *J* = 7.0 Hz, 2H); **^{13}C NMR** (100 MHz, Chloroform-*d*) δ 192.2, 168.1, 160.1 (d, *J* = 252.1 Hz), 145.6, 134.5, 134.4, 134.1, 130.5, 130.3, 130.1 (d, *J* = 8.2 Hz), 129.7, 128.9, 127.8, 125.2 (d, *J* = 2.6 Hz), 123.7 (d, *J* = 10.8 Hz), 123.5 (d, *J* = 3.7 Hz), 115.9 (d, *J* = 21.7 Hz), 62.2, 54.5, 53.4, 21.9, 14.1; **IR**(KBr): $\tilde{\nu}$ = 3378, 3053, 2962, 2922, 2852, 1731, 1689, 1596, 1494, 1451, 1365, 1309, 1227, 1163, 1090, 1040, 767, 666, 554 cm^{-1}; **HRMS** (EI-TOF): calcd for, $C_{26}H_{24}N_3O_5SF$ [M]$^+$, 509.1421; found, 509.1420.

3-phenylnaphtho[2,1-*e*][1,2,4]triazine (8na): yellow solid, 20 mg, 41% yield, mp: 142-144 °C (literature: 117-118 °C)[29]; **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 9.53 (d, *J* = 8.0 Hz, 1H), 8.80-8.78 (m, 2H), 8.23 (d, *J* = 9.1 Hz, 1H), 7.98 (d, *J* = 7.7 Hz, 1H), 7.92-7.82 (m, 3H), 7.64-7.60 (m, 3H); **^{13}C NMR** (100 MHz, Chloroform-*d*) δ 161.4, 144.9, 143.2, 138.3, 135.8, 132.8, 131.5, 130.3, 129.5, 129.4, 129.1, 128.7, 128.6, 125.9, 124.1; **IR**(KBr): $\tilde{\nu}$ = 3054, 2923, 2853, 1598, 1517, 1467, 1433, 1383, 1276, 1138, 1047, 848, 737, 690 cm^{-1}; **HRMS** (EI-TOF): calcd for, $C_{17}H_{11}N_3$ [M]$^+$, 257.0953; found, 257.0952.

3-(o-tolyl)naphtho[2,1-*e*][1,2,4]triazine (8nb): yellow solid, 25 mg, 46% yield, mp: 132-134 °C; **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 9.58 (d, *J* = 7.9 Hz, 1H), 8.26 (d, *J* = 9.1 Hz, 1H), 8.13-8.11 (m, 1H), 8.01 (d, *J* = 7.8 Hz, 1H), 7.94-7.85 (m, 3H), 7.48-7.41 (m, 3H), 2.72 (s, 3H); **^{13}C NMR** (100 MHz, Chloroform-*d*) δ 164.6, 144.2, 142.8, 138.4, 138.3, 135.9, 132.9, 131.7, 131.4, 130.4, 130.3, 129.5, 129.3, 128.7, 126.4, 125.8, 124.2, 21.6; **IR**(KBr): $\tilde{\nu}$ = 3058, 2921, 2853, 1968, 1597, 1516, 1438, 1383, 1330, 1142, 1033, 851, 813, 745, 652 cm^{-1}; **HRMS** (EI-TOF): calcd for, $C_{18}H_{13}N_3$ $[M]^+$, 271.1109; found, 271.1110.

General procedure for further transformation of 3,5,6-trisubstituted-1,2,4-triazine 5aa

Reaction a: with hydrazine hydrate. The 0.1 mmol (1.0 equiv.) was dissolved in 2 mL absolute ethanol. To this solution was added hydrazine hydrate 0.15 mmol (80%, 1.5 equiv.). The resulting solution was heated at 85 °C for 1 h. After reaction, solvent was evaporated and the residue was recrystallized from hexane containing a small amount of DCM to afford the desired product **9aa** 29 mg (97% yield).

3,5-diphenylpyridazino[4,5-*e*][1,2,4]triazin-8(7*H*)-one (9aa): yellow solid, 29 mg, 97% yield, mp: > 250 °C; **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 10.62 (s, 1H), 8.69 (d, *J* = 7.3 Hz, 2H), 8.05-8.02 (m, 2H), 7.68-7.65 (m, 1H), 7.62-7.59 (m, 5H); **^{13}C NMR** (125 MHz, Chloroform-*d*) δ 165.3, 146.9, 142.8, 142.5, 133.8, 133.7, 132.1, 130.4, 129.9, 129.8, 129.8, 129.5, 128.7; **IR**(KBr): $\tilde{\nu}$ = 3450, 3064, 2955, 2923, 2854, 1689, 1508, 1460, 1354, 1215, 1086, 881, 698 cm^{-1}; **HRMS** (EI-TOF): calcd for, $C_{17}H_{11}N_5O$ $[M]^+$, 301.0964; found, 301.0962.

Reaction b: with 2,5-norbornadiene. The 0.2 mmol (1.0 equiv.) was dissolved in 2 mL dried Toluene. To this solution was added 2,5-norbornadiene 0.2 mL (10 equiv., 2 mmol). The resulting solution was heated at 120 °C for 4 h. After reaction, the reaction mixture was purified by flash chromatography (petroleum ether/ ethyl acetate = 5:1~3:1) to provide the desired product **10aa** 58 mg (88% yield).

Ethyl 2-benzoyl-6-phenylnicotinate (10aa): yellow solid, 58 mg, 88% yield, mp: 112-114 °C; **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 8.44 (d, *J* = 8.4 Hz, 1H), 8.10-8.07 (m, 2H), 7.94 (d, *J* = 8.4 Hz, 1H), 7.88 (d, *J* = 7.4 Hz, 2H), 7.59 (t, *J* = 7.4 Hz, 1H), 7.48-7.44 (m, 5H), 4.21 (q, *J* = 7.1 Hz, 2H), 1.11 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (100 MHz, Chloroform-*d*) δ 194.2, 164.9, 159.7, 158.7, 139.3, 137.5, 135.9, 133.5, 130.4, 130.0, 129.0, 128.6, 127.7, 123.2, 120.1, 61.9, 13.7; **IR**(KBr): $\tilde{\nu}$ = 3059, 2959, 2923, 2852, 1717, 1675, 1582, 1451, 1294, 1168, 1095, 955, 760, 707, 641 cm^{-1}; **HRMS** (EI-TOF): calcd for, $C_{21}H_{17}NO_3$ $[M]^+$, 331.1208; found, 331.1207.

ASSOCIATED CONTENT

Supporting Information

Crystallographic data and NMR. This material is available free of charge via the Internet at http://pubs.acs.org.

AUTHOR INFORMATION

Corresponding Author

xxyu@ecust.edu.cn; weiping_deng@ecust.edu.cn

Notes

The authors declare no competing financial interest.

ACKNOWLEDGMENT

This work is supported by The National Natural Science Foundation of China (No. 21402049) and the Shanghai Comittee of Science and Technology (No. 14431902500).

REFERENCES

(1) Joule, J. A.; Mills K. in *Heterocyclic Chemistry*, 5th edition, Wiley-Blackwell, New York, **2010**, pp. 1-689

(2) (a) Tyndall, E. M.; Draffan, A. G.; Frey, B. *et al Bioorg. Med. Chem. Lett.* **2015**, *25*, 869-873; (b) Gianella-Borradori, M.; Christou, I.; Bataille, C. J. R.; Cross, R. L.; Wynne, G. M.; Greaves, D. R.; Russell, A. J. *Bioorg. Med. Chem.* **2015**, *23*, 241-263; (c) Mojzych, M.; Šubertová, V.; Bielawska, A.; Bielawski, K.; Bazgier, V.; Berka, K.; Gucky, T.; Fornal, E.; Krystof, V. *Eur. J. Med. Chem.* **2014**, *78*, 217-224; (d) Kelly, T. R.; Elliott, E. L.; Lebedev, R.; Pagalday, J. *J. Am. Chem. Soc.* **2006**, *128*, 5646-5647; (e) O'Rourke, M.; Lang, S. A.; Cohen, E. *J. Med. Chem.* **1977**, *20*, 723-726; (f) Steiger, A. *et al US Pat*. 2003036544 (A1).

(3) For selected examples, see: (a) Kamber, D. N.; Liang, Y.; Blizzard, R. J.; Liu, F.; Mehl, R. A.; Houk, K. N.; Prescher, J. A. *J. Am. Chem. Soc.* **2015**, *137*, 8388-8391; (b) Lipińska, T. M. *Tetrahedron* **2006**, *62*, 5736-5747; (c) Raw, S. A.; Taylor, R. J. K. *J. Am. Chem. Soc.* **2004**, *126*, 12260-12261.

(4) (a) Lewis, F. W.; Harwood, L. M.; Hudson, M. J.; Geist, A.; Kozhevnikov, V. N.; Distler, P.; John, J. *Chem. Sci.* **2015**, *6*, 4812-4821 and references cited therein; (b) Wolińska, E. *Tetrahedron* **2013**, *69*, 7269-7278.

(5) For examples of previous reviews, see: (a) Abdel-Rahman, R. M.; Makki, M. S. T.; Ali, T. E.; Ibrahim, M. A. *Curr. Org. Synth*. **2013**, *10*, 136-160; (b) Kozhevnikov, D. N.; Prokhorov, A. M. *Prog. Heterocycl. Chem.* **2011**, *22*, 427-447; (c) Raw, S. A.; Taylor, R. J. K. *Adv. Heterocycl. Chem.* **2010**, *100*, 75-100; for examples, see: (d) Tang, D.; Wang, J.; Wu, P.; Guo, X.; Li, J. H.; Yang, S.; Chen, B.-H. *RSC. Adv.* **2016**, *6*, 12514-12518 and

references cited therein; (e) Shi, B.; William, L.; Campbell, I. B.; Moody, C. J. *Org. Lett.* **2009**, *11*, 3686-3688.

(6) For reviews, see: (a) Jiang, Y.; Sun, R.; Tang, X.-Y.; Shi, M. *Chem. Eur. J.* **2016**, *22*, 17910-17924; (b) Hockey, S. C.; Henderson, L. C. *Aust. J. Chem.* **2015**, *68*, 1796-1800; (c) Wang, Y.; Lei, X.; Tang, Y. *Synlett* **2015**, *26*, 2051-2059; (d) Anbarasan, P.; Yadagiri, D.; Rajasekar, S. *Synthesis* **2014**, *46*, 3004-3023; (e) Davies, H. M. L.; Alford, J. S. *Chem. Soc. Rev.* **2014**, *43*, 5151-5162; (f) Gulevich, A. V.; Gevorgyan, V. *Angew. Chem. Int. Ed.* **2013**, *52*, 1371-1373; (g) Chattopadhyay, B.; Gevorgyan, V. *Angew. Chem. Int. Ed.* **2012**, *51*, 862-872.

(7) Recent examples for synthesis of dihydroisoquinolines, see: (a) He, J.; Shi, Y.; Cheng, W.; Man, Z.; Yang, D.; Li, C.-Y. *Angew. Chem. Int. Ed.* **2016**, *55*, 4557-5561; (b) Sun, R.; Jiang, Y.; Tang, X.-Y.; Shi, M. *Chem. Eur. J.* **2016**, *22*, 5727-5733; (c) Yu, Y.; Zhu, L.; Liao, Y.; Mao, Z.; Huang, X. *Adv. Synth. Catal.* **2016**, *358*, 1059-1064.

(8) Recent examples for synthesis of indolines, see: (a) Yadagiri, D.; Reddy, A. C. S.; Anbarasan, P. *Chem. Sci*. **2016**, *7*, 5934-5938; (b) Li, Y.; Zhang, Q.; Du, Q.; Zhai, H. *Org. Lett*. **2016**, *18*, 4076-4079.

(9) Recent examples for synthesis of other azaheterocycles. For tetrahydropyridines, see: (a) Man, Z.; Dai, H.; Shi, Y.; Yang, D.; Li, C.-Y.; *Org. Lett.* **2016**, *18*, 4962-4965; for quinazoline, see: (b) when we were ready to submit this article, Tang's work using Rh-AVC as aze-[2C] synthon was published online. Lei, X.; Gao, M.; Tang, Y. *Org. Lett.* **2016**, *18*, 4990-4993; for 1,4-Diazepines, see: (c) Lee, D.; Han, H.; Shin, J.; Yoo, E. *J. Am. Chem. Soc.* **2014**, *136*, 11606-11609.(10) Recent examples for synthesis of

O/S-heterocycles, see: (a) Lu, X.-L.; Liu, Y.-T.; Wang, Q.-X.; Shen, M.-H.; Xu, H.-D. *Org. Chem. Front.* **2016**, *3*, 725-729; (b) Cheng, X.; Yu, Y.; Mao, Z.; Chen, J.; Huang, X. *Org. Biomol. Chem.* **2016**, *14*, 3878-3882.

(11) Recent examples for synthesis acyclic compounds, see: (a) Miura, T.; Nakamuro, T.; Miyakawa, S.; Murakami, M. *Angew. Chem. Int. Ed.* **2016**, *55*, 8732-8735; (b) KubiakII, R. W.; Mighion, J. D.; Wilkerson-Hill, S. M.; Alford, J. S.; Yoshidomi, T.; Davies, H. M. L. *Org. Lett.* **2016**, *18*, 3118-3121.

(12) (a) Meng, J.; Wu, D.; Shi, Y.; Yu, X.; Deng, W.-P. *Tetrahedron* **2015**, *71*, 1074-1079; (b) Meng, J.; Ding, X.; Yu, X.; Deng, W.-P. *Tetrahedron* **2016**, *72*, 176-183.

(13) In Fokin's work, when cyclic secondary amides with relative steric hindrance was used, a competing O-H insertion was observed. For N-H insertions, see: (a) Lee, D. J.; Yoo, E. J. *Org. Lett.* **2015**, *17*, 1830-1833; (b) Jeon, H. J.; Jung, D. J.; Kim, J. H.; Kim, Y.; Bouffard, J.; Lee, S.-g. *J. Org. Chem.* **2014**, *79*, 9865-9871; (c) Chuprakov, S.; Worrell, B. T.; Selander, N.; Sit, R. K.; Fokin, V. V. *J. Am. Chem. Soc.* **2014**, *136*, 195-202; for selected O-H insertions, see: (d) Mi, P.; Kumar, R.- K.; Liao, P.; Bi, X. *Org. Lett.* **2016**, *18*, 4998-5001; (e) Seo, B.; Jeon, W. H.; Kim, C. E.; Kim, S.; Kim, S. H.; Lee, P. H. *Adv. Synth. Catal.* **2015**, *358*, 341-347.

(14) C4-Alkyl substituted triazoles were not suitable for rhodium-catalyzed step with rather low conversion.

(15) Detailed X-ray crystallographic data for **5aa** (CCDC 1494303) can be obtained free of charge from the Cambridge Crystallographic Data Centre.

(16) (a) Vicente-García, E.; Catti, F.; Ramón, R.; Lavilla, R. *Org. Lett.* **2010**, *12*, 860-863; (b) Xie, J.; Huang, Z.-Z. *Angew. Chem. Int. Ed.* **2010**, *49*, 10181-10185; (c) Zhang, G.; Zhang, Y.; Wang, R. *Angew. Chem. Int. Ed*. **2011**, *50*, 10429-10432; (d) Qiu, L.; Guo, X.; Qian, Y.; Jing, C.; Ma, C.; Liu, S.; Hu. W. *Chem. Commun*. **2016**, *52*, 11831-11833.

(17) For examples of recent works for synthesis of diaryl ketones, see: (a) Weires, N. A.; Baker, E. L.; Garg, N. K. *Nat. Chem.* **2016**, *8*, 75-79; (b) Shi, S.; Szostak, M. *Chem. Eur. J.* **2016**, *22*, 10420-10425 and references cited therein.(18) For selected examples, see: (a) Li, B.; Darcel, C.; Dixneuf, P. H.; *ChemCatChem*. **2014**, *6*, 127-130; (b) Tao, X.; Li, W.; Ma, X.; Li, X.; Fan, W.; Xie, X.; Ayad, T.; Ratovelomanana-Vidal, V.; Zhang, Z. *J. Org. Chem*. **2012**, *77*, 612-616; (c) Choshi, T.; Yamada, S.; Sugino, E.; Kuwada, T.; Hibino, S. *J. Org. Chem.* **1995**, *60*, 5899-5904.

(19) DeAngelis, A.; Dmitrenko, O.; Fox, J. M. *J. Am. Chem. Soc.* **2012**, *134*, 11035-11043.

(20) Yoo, E. J.; Ahlquist, M.; Kim, S. H.; Bae, I.; Fokin, V. V.; Sharpless, K. B.; Chang, S. *Angew. Chem. Int. Ed*. **2007**, *46*, 1730-1733.

(21) Raushel, J.; Fokin, V. V. *Org. Lett.* **2010**, *12*, 4952-4955.

(22) Wang, K.; Bi, X. H.; Xing, S. X.; Liao, P. Q.; Fang, Z. X.; Meng, X. Y.; Zhang, Q.; Liu, Q.; Ji, Y. *Green Chem.* **2011**, *13*, 562-565.

(23) Hamada, T.; Manabe, K.; Kobayashi, S. *Chem. Eur. J.* **2006**, *12*, 1205-1215.

(24) Rueping, M.; Maji, M. S. *et al Angew. Chem. Int. Ed.* **2012**, *51*, 12864-12868.

(25) Yu, B.; Chen, Y.; Hong, M.; Duan, P.; Gan, S.; Chao, H.; Zhao, Z.; Zhao, J. *Chem. Commun.* **2015**, *51*, 14365-14368.

(26) Konno, S.; Osawa, N.; Yamanaka, Y. *J. Agric. Food Chem*. **1995**, *43*, 838-842.

(27) Ernd, M.; Heuschmann, M.; Zipse, H. *Helv. Chim. Acta* **2005**, *88*, 1491-1518.

(28) Saraswathi, T. V.; Sriniwasan, V. R. *Tetrahedron* **1977**, *33*, 1043-1051.

(29) Bennett, G. B.; Mason, R. B.; Alden, L. J.; Roach, J. B. *J. Med. Chem.* **1978**, *21*, 623-628.