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Phosphotungstic Acid Mediated, Microwave Assisted Solvent-Free Green Synthesis of Highly Functionalized 2'-Spiro and 2, 3-dihydro Quinazolinone and 2-Methylamino benzamide Derivatives from Aryl and Heteroaryl 2-Amino amides

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ABSTRACT

Abstract: Phosphotungstic acid has been found as green catalyst for the synthesis of spiro- and cyclized quinazolinones and 2-amino substituted carboxamide under microwave irradiation and solvent-free condition has been developed. The scope of the reaction has been demonstrated for a variety of aldehydes and ketones with *O*-amino amides such as 2-amino-benzamide, 2-amino-5-iodo benzamide, 3-aminothiophene-2-carboxamide, 3-aminobenzofuran-2-carboxamide and 2-aminopyridine-3-carboxamides. The reaction afforded spiro-, cyclized quinazolinones and 2-amino substituted carboxamide derivatives within few minutes of irradiation in excellent yield. Plausible mechanism for the formation of products is provided. Synthetic utility of 1'H-spiro[fluorene-9,2'-quinazolin]-4'(3'H)-one **3a** has been demonstrated by synthesis of 1,4-di(1'H-spiro[fluorene-9,2'-quinazolin]-4'(3'H)-one) buta-1,3-diyne **12**, 1'-((1-benzyl-1H-1,2,3-triazol-4-yl) methyl)-1'H-spiro[fluorene-9,2'-quinazolin]-4'(3'H)-one **13** and 1'-phenyl-1'H-spiro[fluorene-9,2'-quinazolin]-4'(3'H)-one **14** under standard protocols.

1. Introduction

Heteropoly acids (HPAs) are heterogeneous green solid acid catalyst extensively used in organic synthesis.[1] The advantages of HPAs catalysts are eco-friendly, easy to handle, low toxicity and economical. Among the HPAs, phosphotungstic acid ($H_3PW_{12}O_{40}$) (HPW) with Keggin-type structure stands out as an efficient catalyst due to its high acidic strength[2] and thermal stability.[3] HPW has also been proved as effective and versatile catalyst in many organic reactions[4] include Aldol reaction, aza-Diels-Alder reaction, Beckman rearrangement, Claisen-Schmidt reaction, Friedel-Crafts acylation, Fries rearrangement, Mannich reaction and alcoholysis, oxidation and azidation of alcohols, dehydration of carbohydrates, esterification and trans esterification reactions. Particularly, the HPW has been employed as catalyst in the synthesis of coumarins,[5] naphthyridinones,[6] pyridones[7] and quinolones.[8]

Non-conventional chemical synthesis using microwave[9] irradiation has been developed as a tool for one of the green chemistry techniques. Microwave assisted organic reactions have an advantage of exposure to specific thermal effects that leads to the selective absorption of microwave energy and hence speed up the reaction and higher yields. Microwave method simplifies conventionally tedious research areas such as drug discovery, chemo-, regio- and stereo selective synthesis and multistep reactions. Development of solvent free/solid-state[10] green chemistry synthesis is current interest of chemists due to environmental concerns.

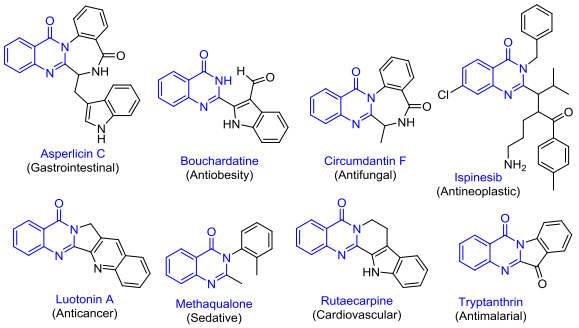


Figure 1 Quinazolinone cores in natural products and pharmaceuticals

Quinazolinones[11] have been extensively used as antitumor, antihypertensive, anticonvulsants, antiviral, antimicrobial, antifungal, anti-inflammatory activity and a number of natural products with quinazolinone backbone prone to exhibit prominent bioactivities (Figure 1).[12] Hence a number of methods have been developed to synthesize quinazolinones using transition metals such as copper,[13] iridium,[14] manganese,[15] silver,[16] vanadium[17] and cyanuric chloride,[18]

cationic amberlyst-15 resin,[19] clays,[20] PTSA,[21] starch sulfate,[22] and TFA[23] were employed as catalysts. Recently, a metal free synthesis of quinazolinone has been also reported.[24] Despite having various methods to synthesize quinazolinones, it is limitedly explored using green chemistry protocol and thus prompted us to explore the prospect of HPW as a green catalyst. Hence herein we report the HPW catalysed synthesis of highly functionalized title compounds from various aryl and heteroaryl amino amides under solvent-free microwave irradiation.

Initially, a mixture of 1 equivalent of 2-amino benzamide (**1a**) and 1 equivalent of 9H-fluoren-9-one (**2a**) and 50 w/w HPW was microwave irradiated (100 Watts) for 2 minutes afforded 1'H-spiro[fluorene-9,2'-quinazolin]-4'(3'H)-one (**3a**) in 30% yield (table 1, entry1). Compound **3a** was thoroughly characterised by spectroscopic and XRD method (Figure 2).[25]

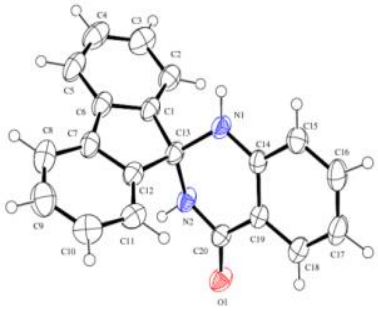


Figure 2 ORTEP diagram of compound **3a** (CCDC 1582823)[25]

In order to optimize the reaction condition for the synthesis of **3a**, parameters such as microwave power and irradiation time, mole ratio of reactants and percentage load of catalyst were considered. Thus, a reaction of 1:1 ratio of compounds **1a** and **2a** and 50 W/W of HPA without any solvent was microwave irradiated at 100 W for 4 min. afforded product **3a** only in 30% yield (Table 1, entry 2). Hence, repeating the reaction with increased power level 200 W for one minute afforded increased yield of (50%) **3a** (Table 1, entry 3). The reaction with 200 W PL for 3 minutes improved the yield substantially to 90%(Table 1, entry 4). To optimise the catalyst load, reactions with 20 w/w and 100 w/w percent catalyst afforded 80% and 90% yield of **3a** indicates lower load of catalyst decreased the yield while higher load did not alter the yield and hence 50 W/W catalyst load is optimum (Table 1, entries 5 and 6). Increasing the microwave power level and change of mole ratio of starting materials afforded the desired product **3a** in decreased or no improvement in the yield (Table 1, entries 7-10).

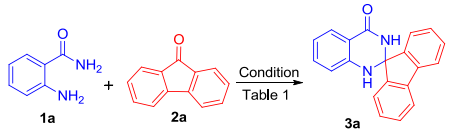


Table 1 Optimization of synthesis of spiro compound **3a**[a, b]

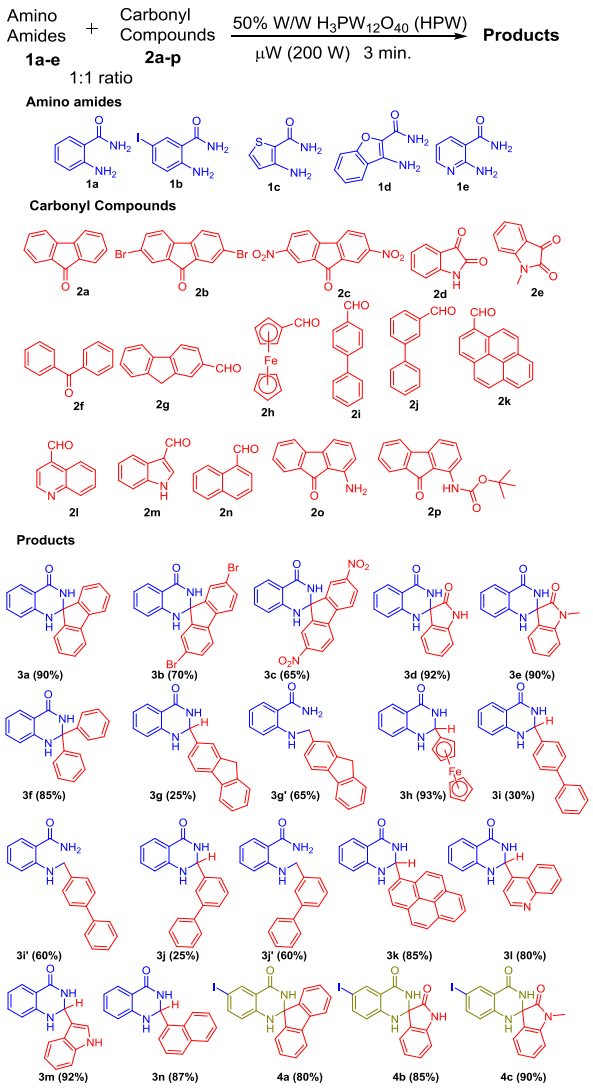
Entry	Substrate ratio **1a:2a**	Catalyst (% W/W)	MW power (Watt)	Irradiation Time (min.)	% Yield **3a**[c]
1	1:1	HPW (50)	100W	2	30
2	1:1	HPW (50)	100W	4	30
3	1:1	HPW (50)	200W	1	50
4	1:1	HPW (50)	200W	3	90[d]
5	1:1	HPW (20)	200W	3	80
6	1:1	HPW (100)	200W	3	90
7	1:1.2	HPW (50)	200W	3	90
8	1.2:1	HPW (50)	200W	3	90
9	1:1	HPW (50)	300W	3	90
10	1:1	HPW (50)	300W	5	75
11	1:1	H_3BO_3(50)	200W	3	50
12	1:1	MK-10(50)	200W	3	80
13	1:1	CeraliteIR120 (50)	200W	3	75
14	1:1		200W	3	20

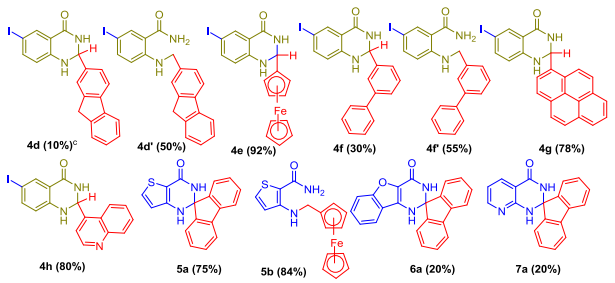
[a]All the reactions were carried out on a CEM Discover 300 microwave synthesiser under neat condition; [b]Standard mode, 50 psi, at 100 °C; [c]Isolated yield; [d]Optimised condition.

In order to compare the efficiency of other green acid catalysts, experiments with boric acid, montmorillonite K10 clay and Ceralite IR 120 were carried out (Table 1, entries 11-13). However, no comparable yields were obtained. The reaction without any catalyst afforded only 20% of the product indicated the necessity of the catalyst in the reaction. Hence, conditions shown in entry 4 of table 1 were found to be optimum.

Encouraged by the preliminary results and in order to demonstrate the scope of the method, the reaction was elaborated to a variety of aryl and heteroaryl amino amides **1a-e**[17] and ketones/aldehydes **2a-p** (Table 2). The reaction afforded title compounds **3a-n**, **4a-h**, **5a**, **5b**, **6a** and **7a** in very good to excellent yields. The results are summarised in Table 2.

Table 2 Scope of the reaction[a, b]

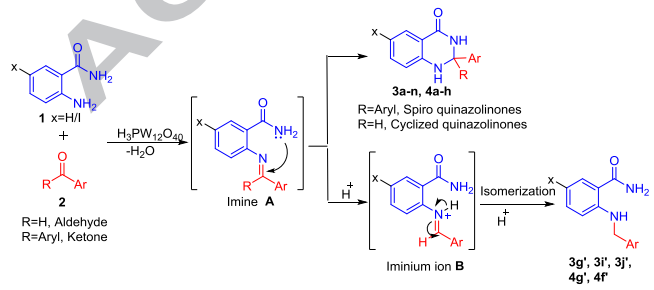




[a]All the reactions were carried out on a CEM Discover 300 microwave synthesiser under neat condition; [b]Standard mode, 200 W, 50 psi, 100 °C for 3 min; [c]Compound **4d** was isolated as trace along with starting amino amide impurity; [e]Increased power (300 W) and extended irradiation time (15 min.) resulted charred material.

It should be noted that in the case of reactions of biphenyl and flourene aldehydes **2g**, **2i**, **2j** with amino amides **1a** and **1b,** along with minor cyclised derivatives, an open chain major products **3g'**, **3i'**, **3j'**, **4d'** and **4f'** were observed as main products. It has been observed that amine substituted products formed rather than amide substituted products as evidenced from ^{13}C NMR chemical shift value of amide carbonyl at δ 171.7. Accordingly, no change of chemical shift was observed for amide carbonyl in the isolated product and hence confirmed amine substituted products. Under optimised condition, 2-amino-9-flourenone **2o** and deactivated Boc protected 2-amino-9-flourenone **2p** was found to be unsuccessful with amides **1a-d**. In order to show reactivity and diversity of the reactions, amino amides such as 3-aminobenzofuran-2-carboxamide **1d** (position of amine and amide reverted) and 2-amino pyridine-3-carboxamide **1e** with ketone **2a** was examined and the reaction afforded 1H-spiro[benzofuro[3,2-d] pyrimidine-2,9'-fluoren]-4(3H)-one **6a** and 1'H-spiro[fluorene-9,2'-pyrido[2,3-d]pyrimidin]-4'(3'H)-one **7a.** However, the reaction afforded lower yield of products upon irradiating with higher power level (250 W) and duration (10 min.). Further, reaction of **1c** with ketone **2a** afforded 1'H-spiro[fluorene-9,2'-thieno[3,2-d]pyrimidin]-4'(3'H)-one **5a** and with ferrocene carboxaldehydes **2h** an open chain product **5b** was observed as a single product**.**

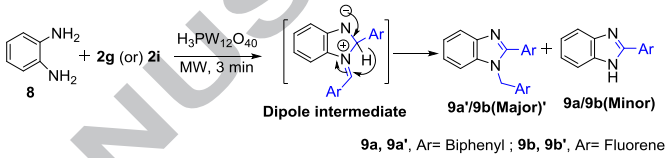
To explain the diverse product formation, a plausible mechanism for the formation of spiro-, cyclised and open chain products are discussed in Scheme 1.



Scheme 1 Plausible mechanism for the formation of spiro- and cyclized quinazolinones and 2-methyl amino benzamide

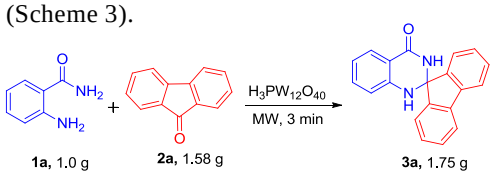
The spiro and cyclised quinazolinone formation may be explained as under the influence of HPW, initial formation an imine intermediate from anthranilamide **1** with ketone/aldehyde **2** subsequently undergoes nucleophilic attack by the amide nitrogen to yield corresponding spiro or cyclised quinazolinones **3**. The formation of *N*-substituted amino amides can be explained based on analogy of imine-iminium ion isomerization mechanism[26] from the imine intermediate **A** and iminium ion **B** under the influence of HPW-microwave irradiation condition. The formation of iminium ion under acidic condition is evident[26] that subsequently undergoes isomerization leads to the observed product. However, no conclusive evidence is available for the mechanism of reduced product formation and the mechanism discussed is tentative.

To substantiate the mechanistic proposal shown in scheme 1, under optimised conditions, reactions using *o*-phenylenediamine **8** and aldehydes **2g** and **2i** afforded corresponding reduced products **9a'**and **9b'**. Herein, the mechanism for the reduced product formation is explained invoking a dipole intermediate[27d] followed by hydride shift. (Scheme 2).[27] However, mono amino compound such as aniline failed to provide reduced product and imine only isolated.



Scheme 2 Reaction of **2g** and **2i** with *o*-phenylenediamine **8**

The effectiveness of this methodology was further scrutinized by a gram scale synthesis of **3a** under optimized reaction condition without notable decrease in the yield (80 %) (Scheme 3).



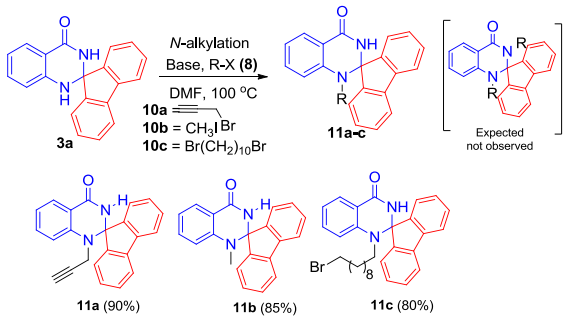
Scheme 3 Gram scale synthesis of **3a**

The nature of structural and diversity of the products obtained prompted us to examine the synthetic utility of the synthesised quinazolinones, firstly *N*-alkylation was considered. Thus, reaction between **3a** and propargyl bromide **10a** in ACN under the influence of K_2CO_3 afforded mono alkylated product **11a** in only 10% yield. However, change of base to NaH and solvent DMF afforded an optimum yield of **11a** in 90% yield (Table 3. Entry 4). To our dismay, di alkylation of **3a** was not observed with excess of alkylating agent, base and prolonged reaction times. Similarly, synthesis of compounds **11b-c** were achieved from the reaction between **3a** and alkyl halides **10b** and **10c**, respectively (Scheme 4).

Table 3 Optimization of synthesis of **11a**

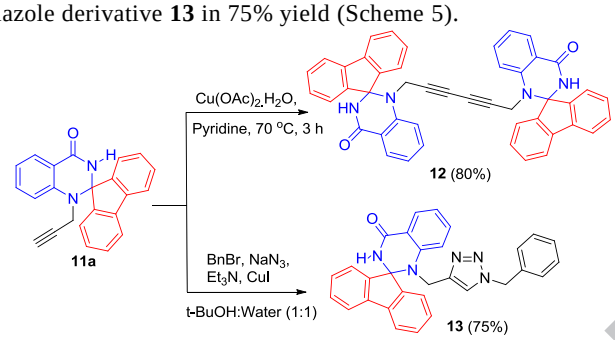
Entry	Solvent	Base[a]	Time (h)	% Yield of **9a**[b]
1	CH_3CN	K_2CO_3	24	10
2	CH_3CN	Et_3N	24	25
3	DMF	CaH_2	24	50
4	**DMF**	**NaH**	**1**	**90**
5	THF	NaH	1	65

[a]2.5 equiv. of base was used in all the reactions, change of equivalents did not alter the observed product formation and yield; [b]Isolated yield



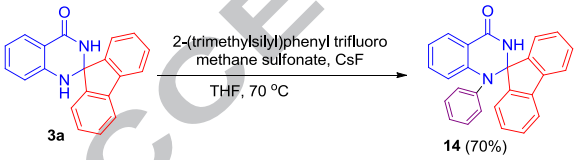
Scheme 4 *N*-alkylation of **3a** by propargyl bromide **10a**, methyl iodide **10b** and 1, 10-dibromodecane **10c**

Further, the spiro derivative **11a** was explored synthetically through Eglinton[28]coupling afforded structurally unique 1,3-diyne derivative **12** in 80% yield and Click[29] reaction afforded triazole derivative **13** in 75% yield (Scheme 5).

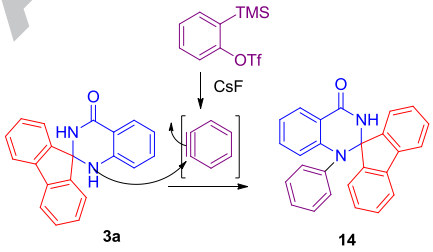


Scheme 5 Synthetic transformation of **11a** to 1,3-diyne derivative **12** and 1,2,3-triazol-4-yl derivative **13**

To further demonstrate the synthetic utility, *N*-arylation of **3a** through benzyne addition[30] yielded 1'-phenyl-1'H-spiro [fluorene-9, 2'-quinazolin]-4'(3'H)-one **14** in 70% yield (Scheme 6) and a plausible aryne insertion mechanism for the formation of compound **14** is depicted in Scheme 7. Attempts to derivatise diarylated product of **3a** was failed using higher equivalents of benzyne, solvent and temperature.



Scheme 6 Synthesis of 1'-phenyl-1'H-spiro [fluorene-9, 2'-quinazolin]-4'(3'H)-one **14**



Scheme 7 Mechanism for the formation of compound **14**

In conclusion, we have demonstrated HPW has been found as a green catalyst for the synthesis of spiro- and fused quinazolinones under microwave irradiation and solvent-free condition. The catalyst utility was tested by reacting a variety of aldehydes and ketones with *O*-amino amides. Plausible mechanism for the formation of products is provided. Synthetic utility of 1'H-spiro[fluorene-9,2'-quinazolin]-4'(3'H)-one 3a has been demonstrated by synthesis of highly functionalized heterocycles such as 1,4-di(1'H-spiro[fluorene-9,2'-quinazolin]-4'(3'H)-one) buta-1,3-diyne **12**, 1'-((1-benzyl-1H-1,2,3-triazol-4-yl) methyl)-1'H-spiro[fluorene-9,2'-quinazolin]-4' (3'H)-one **13** and 1'-phenyl-1'H-spiro[fluorene-9,2'-quinazolin]-4'(3'H)-one **14** under standard reaction protocols.

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Supplementary Material

Supplementary data (detailed experimental procedure, characterization of the products and copies of spectra are provided) associated with this article can be found, in the online version.

References and Notes

1 Wang, S. S.; Yang, G. Y. *Chem. Rev.* **2015**, *115*, 4893-4962.
2 Yang, J.; Janik, M. J.; Ma, D.; Zheng, A.; Zhang, M.; Neurock, M.; Davis, R. J.; Ye, C.; Deng, F. *J. Am. Chem. Soc.* **2005**, *127*, 18274-18280.
3 Kozhevnikov, I. V. *J. Mol. Catal. A: Chem.* **2009,** *305*, 104-111.
4 (a) Kozhevnikov, I. V. *Chem. Rev.* **1998**, *98*, 171-198. (b) Kozhevnikov, I. V. *Catal. Rev.* **1995,** *37*, 311-352. (c) Azizi, N.; Torkiyan, L.; Saidi, M. R. *Org. Lett.* **2006**, *8*, 2079-2082. (d) Lan, L.; Xie, G.; Wu, T.; Feng D.; Ma, X. *RSC Adv.* **2016**, *6*, 55894-55902. (e) He, W.; Fang, Z.; Yang, Z.; Ji D.; Guo, K. *RSC Advances* **2015**, *5*, 58798-58803. (f) Siddiqui, S.; Khan M. U.; Siddiqui, Z. N. *ACS Sustainable Chem. Eng.* **2017**, *5*, 7932-7941. (g) Kozhevnikova, E. F.; Quartararo, J.; Kozhevnikov, I. V. *Appl. Catal. A.* **2003**, *245*, 69-78. (h) Wee, L. H.; Bonino, F.; Lamberti, C.; Bordiga S.; Martens, J. A. *Green Chem.* **2014**, *16*, 1351-1357. (i) Gomes, F. N.; Mendes F. M.; Souza, M. M. *Catal. Today* **2017**, *279*, 296-304.
5 Li, S.; Qi, X.; Huang, B. *Catal. Today* **2016**, *276*, 139-144.
6 Makhanya, T. R.; Gengan, R. M.; Pandian, P.; Chuturgoon, A. A.; Tiloke C.; Atar, A. *J. Heterocycl. Chem.* **2018**, *55*, 1193-1204.
7 Samzadeh-Kermani, A. *Synlett* **2016**, *27*, 461-464.
8 (a) Achar, K. C.; Hosamani K. M.; Seetharamareddy, H. R. *Synth. Commun.* **2010**, *41*, 33-40. (b) Dabiri M.; Bashiribod, S. *Molecules* **2009**, *14*, 1126-1133.
9 (a) de la Hoz, A.; Diaz-Ortiz, A.; Moreno, A. *Chem. Soc. Rev.* **2005**, *34*, 164-178. (b) Varma, R. S. Microwave Technology-Chemical Synthesis Applications, in *Kirk-Othmer Encyclopedia of Chemical Technology*, J. Wiley & Sons, Inc., 2003.

(c) Mingos D. M. P.; Whittaker, A. G. *Microwave Dielectric Heating Effects in Chemical Synthesis, in Chemistry under Extreme or non-Classical Conditions*, ed. R. van Eldik and C. D. Hubbard, John Wiley & Sons, New York, 1997, pp. 479–545. (d) Kappe, C. O. *Angew. Chem. Int. Ed.* **2004**, *43*, 6250-6284.

10 (a) Tanaka K.; Toda, F. *Chem. Rev.* **2000**, *100*, 1025-1074. (b) Sarkar, A.; Santra, S.; Kundu, K.; Hajra, A.; Zyryanov, G. V.; Chupakhin, O. N.; Charushin V. N.; Majee, A. *Green Chem.* ***2016***, *18*, 4475-4525. (c) Varma, R. S. *Green chem.* **1999**, *1*, 43-55.

11 (a) Khan, I.; Zaib, S.; Batool, S.; Abbas, N.; Ashraf, Z.; Iqbal J.; Saeed, A. *Bioorg. Med. Chem.* **2016**, *24*, 2361-2381. (b) He, D.; Wang, M.; Zhao, S.; Shu, Y.; Zeng, H.; Xiao, C.; Lu C.; Liu, Y. *Fitoterapia* **2017**, *119*, 136-149.

12 Kshirsagar, U. A. *Org. Biomol. Chem.* **2015**, *13*, 9336-9352.

13 (a) Liu, X.; Fu, H.; Jiang Y.; Zhao, Y. *Angew. Chem.* **2009**, *121*, 354-357. (b) Xu, W.; Jin, Y.; Liu, H.; Jiang Y.; Fu, H. *Org. Lett.* **2011**, *13*, 1274-1277. (c) Yamaguchi, K.; Kawaguchi, S. I.; Sonoda, M.; Tanimori S.; Ogawa, A. *Tetrahedron Lett.* **2017**, *58*, 4043-4047. (d) Xu, L.; Jiang Y.; Ma, D. *Org. Lett.* **2012**, *14*, 1150-1153.

14 Zhou J.; Fang, J. *J. Org. Chem.* **2011**, *76*, 7730-7736.

15 Zhang, Z.; Wang, M.; Zhang, C.; Zhang, Z.; Lu J.; Wang, F. *Chem. Commun.* **2015**, *51*, 9205-9207.

16 Zheng, J.; Zhang, Y.; Wang D.; Cui, S.; *Org. Lett.* ***2016***, *18*, 1768-1771.

17 Bie, Z.; Li, G.; Wang, L.; Lv, Y.; Niu J.; Gao, S. *Tetrahedron Lett.* **2016**, *57*, 4935-4938.

18 Sharma, M.; Pandey, S.; Chauhan, K.; Sharma, D.; Kumar B.; Chauhan, P. M. *J. Org. Chem.* **2012**, *77*, 929-937.

19 Compound **1b** was synthesized from: Rambabu, D.; Kumar, S. K.; Sreenivas, B. Y.; Sandra, S.; Kandale, A.; Misra, P.; Rao M. B.; Pal, M. *Tetrahedron Lett.* **2013**, *54*, 495-501.

20 Salehi, P.; Dabiri, M.; Baghbanzadeh M.; Bahramnejad, M. *Synth. Commun.* **2006**, *36*, 2287-2292.

21 Revathy K.; Lalitha, A. *J. Iran. Chem. Soc.* **2015**, *12*, 2045-2049.

22 Shaterian H. R.; Rigi, F. *Res. Chem. Intermed.* **2015**, *41*, 721-738.

23 Yang, X.; Cheng, G.; Shen, J.; Kuai C.; Cui, X. *Org. Chem. Front.* **2015**, *2*, 366-368.

24 (a) Sun, J.; Tao, T.; Xu, D.; Cao, H.; Kong, Q.; Wang, X.; Liu, Y.; Zhao, J.; Wang Y.; Pan, Y. *Tetrahedron Lett.* **2018**, *59*, 2099-2012. (b) Yu, Z. Y.; Chen, M. Y.; He, J. X.; Tao, D. J.; Yuan, J. J.; Peng Y. Y.; Song, Z. B. *Mol. Catal.* **2017**, *434*, 134-139. (c) Mirza, B. *Tetrahedron Lett.* **2016**, *57*, 146-147. (d) Qi, X. X.; Song, Z. Z.; Gong, J. L.; Fang Z. Y.; Wu, X. F. *Chin. Chem. Lett*. **2016**, *27*, 21-24.

25 CCDC-1582823 (**3a**) contains the supplementary crystallographic data for this paper. This data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data request/cif.

26 Zheng, L.; Yang, F.; Dang Q.; Bai, X. *Org. Lett.* **2008**, *10*, 889-892.

27 (a) Liang, Y.; Wang, J.; Cheng, C.; Jing, H. *RSC Adv.* **2016**, *6*, 93546-93550. (b) Cano, N. H.; Uranga, J. G.; Nardi, M.; Procopio, A.; Wunderlin, D. A.; Santiago, A. N. *Beilstein J. Org. Chem*. **2016**, *12*, 2410-2419. (c) Fekri, L. Z.; Maleki, R. *J. Heterocycl. Chem.* **2017**, *54*, 1167-1171. (d) Madddiguda, P. R.; Angapalley, S.; Sawner, S.; Mohammed, A. *Heterocylic Lett.* **2017**, *7*,65-73.

28 (a) Balaraman K.; Kesavan, V. *Synthesis* **2010**, *20*, 3461-3466. (b) Shi W.; Lei, A. *Tetrahedron Lett.* ***2014***, *55*, 2763-2772. (c) Shi, W.; Luo, L.; Luo, X.; Chao, L.; Zhang, H.; Wang J.; Lei, A. *J. Am. Chem. Soc*., **2008**, *130*, 14713-14720.

29 Ackermann, L.; Potukuchi, H. K.; Landsberg D.; Vicente, R. *Org. Lett.* **2008**, *10*, 3081-3084.

30 Bhojgude, S. S.; Bhunia A.; Biju, A. T. *Acc. Chem. Res.* **2016**, *49*, 1658-1670.

Highlights

- Spiro-quinazolinones were synthesized using phosphotungstic acid (HPW) as catalyst.
- The method is optimized under HPW catalyst, neat and microwave irradiation.
- The catalytic efficiency of HPW was compared with Mont. K10 clay and boric acid.
- The scope of the reaction is demonstrated.
- Tentative mechanism and synthetic utility has been demonstrated.

Graphical Abstract

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Phosphotungstic Acid Mediated, Microwave Assisted Solvent-Free Green Synthesis of Highly Functionalized 2'-Spiro and 2, 3-dihydro Quinazolinone and 2-Methylamino benzamide Derivatives from Aryl and Heteroaryl 2-Amino amides

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