


Cite this: *RSC Adv.*, 2023, 13, 28362

# Microwave assisted one-pot access to pyrazolo quinolinone and tetrahydroisoxazolo quinolinone derivatives via T3P®-DMSO catalysed tandem oxidative–condensation reaction†

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A new approach for the synthesis of two important annulated pyrazolo quinolinone and tetrahydroisoxazolo quinolinone derivatives from multicomponent reactions was achieved by using T3P®-DMSO-catalysed reactions of stable alcohols, cyclic 1,3-dicarbonyl compounds and amino derivatives of phenyl pyrazoles and isoxazole and has been reported for the first time. This reaction occurred via a tandem oxidative–condensation reaction under microwave irradiation and notable characteristics of this protocol are MCR reactions, shorter reaction time, less waste creation, ease of workup, stable precursors, broad substrate scope and functional group tolerance.

Received 2nd August 2023  
Accepted 18th September 2023

DOI: 10.1039/d3ra05235d

rsc.li/rsc-advances

## Introduction

The construction of annulated bioactive heterocyclic small molecules using MW irradiation from MCR is of great importance in the field of synthetic organic chemistry. These MCRs are frequently employed in synthetic organic chemistry as instruments for producing simple C–C bonds<sup>1a</sup> because they provide a simple workup technique, increased selectivity, and improved yields by simultaneously producing C–C and C–heteroatom bonds.<sup>1b</sup> Due to its capacity to produce higher yields in shorter reaction times, microwave (MW) irradiation has emerged as a crucial tool in the generation of heterocyclic compounds and drug discovery processes in organic synthesis.<sup>2a–d</sup> In particular, two important biological structures with a wide range of applications in the pharmaceutical and medical industries are pyrazoloquinolines and tetrahydroisoxazolo quinolinone derivatives. Out of these two, fused pyrazole derivatives exhibit a wide range of biological applications, such as anticancer,<sup>3a</sup> antimicrobial,<sup>3b</sup> antimalarial,<sup>3c</sup> antiviral,<sup>3d</sup> anti-inflammatory,<sup>3e</sup> antiplatelet,<sup>3f</sup> pulmonary hypertension,<sup>3g</sup> cytotoxicity,<sup>3h</sup> and translocator protein ligands.<sup>3i</sup> Furthermore, utilisation of these compounds as therapeutic agents

for the treatment of Alzheimer's disease<sup>4a</sup> and influenza virus<sup>4b</sup> has been reported. Pyrazolo quinolines, which are also used in advanced dye chemistry, second-order nonlinear optical materials,<sup>5</sup> electroluminescent materials,<sup>6a,b</sup> and fluorescence sensors,<sup>7a,b</sup> occasionally reach unity and are extremely fluorescent in the blue or greenish-blue portion of the spectrum.<sup>8a,b</sup> Numerous synthetic techniques have been devised for the synthesis of different substituted pyrazoloquinolines due to their broad variety of biological applications and technical interest. One of the main synthetic techniques for creating bioactive pyrazoloquinoline nuclei from commonly available precursors like *o*-amino benzaldehydes, *o*-amino acetophenones, and *o*-aminobenzophenones via condensation reactions<sup>9a–f</sup> has been reported, and the same annulated derivatives are synthesised from commonly available precursors such as 5-aminopyrazoles, less stable aldehydes, and suitable cyclic ketones.<sup>10a–d</sup> Similarly, isoxazolo quinolinones are important heterocyclic compounds with a wide range of pharmacological properties. These properties include hypoglycemic, analgesic, anti-inflammatory, antibacterial, anti-HIV, and anticancer activity.<sup>11a–c</sup> They also have positive effects on conditions like schizophrenia, hypertension, and Alzheimer's disease.<sup>12a–c</sup> Isoxazolopyridines are isoxazole derivatives that have raised attention and concern due to their CNS depressive, anticonvulsant, and muscle relaxant properties.<sup>12d</sup> Because of this wide range of biological applications, a lot of synthetic strategies have been documented for the synthesis of fused isoxazole derivatives from aminoisoxazole, aldehydes, and ketones.<sup>13a–d</sup> The significant disadvantages of the reported protocols for the synthesis of both the heterocycles are the use of less stable aldehydes as precursors. In addition to that, reported methods exhibit a few more disadvantages, such as poor substrate scope, longer reaction time, less functional group tolerance, costly

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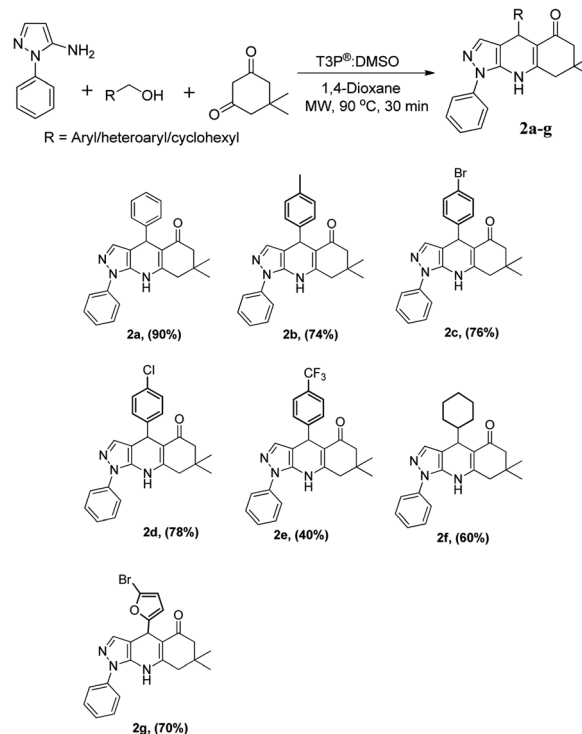
† Electronic supplementary information (ESI) available. CCDC 2267726. For ESI and crystallographic data in CIF or other electronic format see DOI: <https://doi.org/10.1039/d3ra05235d>

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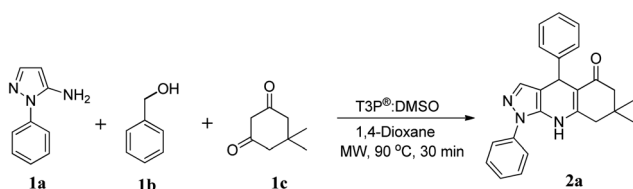


synthesis, tedious work-up procedures, and undesirable side products. In continuation of our research interest from the past few years, the synthetic utility of T3P® in the presence of DMSO towards the development of various synthetic strategies for the synthesis of very important bioactive heterocycles *via* the oxidation-condensation reaction has been reported.<sup>14a-e</sup> We report herein a new strategic approach for the synthesis of both pyrazolo quinolinones and tetrahydroisoxazolo quinolinone from stable electronically diversified alcohols, cyclic 1,3 diketones and amino derivative of both phenyl pyrazole and isoxazole using T3P®-DMSO as a catalyst under microwave irradiation.

To optimise the reaction conditions, initially we conducted the experiments by choosing amino phenyl pyrazole **1a** and dimedone **1c** with benzyl alcohol **1b** in a mixed solvent of 1,4-dioxane:DMSO in the ratio 2 : 1, followed by the addition of 1 equivalent T3P® (50% in EtOAc) at RT to afford the desired pyrazoloquinoline in a 4% yield (Scheme 1). The same reaction was transferred from RT to MW irradiation at 90 °C for 30 min, yielding the desired pyrazoloquinoline in 24% yield. Further, varying different equivalents of T3P® could affect the course of the reaction; the best result was obtained by choosing 2.5 equivalents of T3P® and keeping the temperature at 90 °C for 30 min, which afforded the desired compound at around 90% yield. To determine the precise experimental parameter, the same reaction was carried out by varying the time and temperature while keeping the equivalent of T3P® (2.5



Scheme 2 Synthesis of pyrazolo quinolinone derivatives from 1-phenyl-1H-pyrazol-5-amine and dimedone.

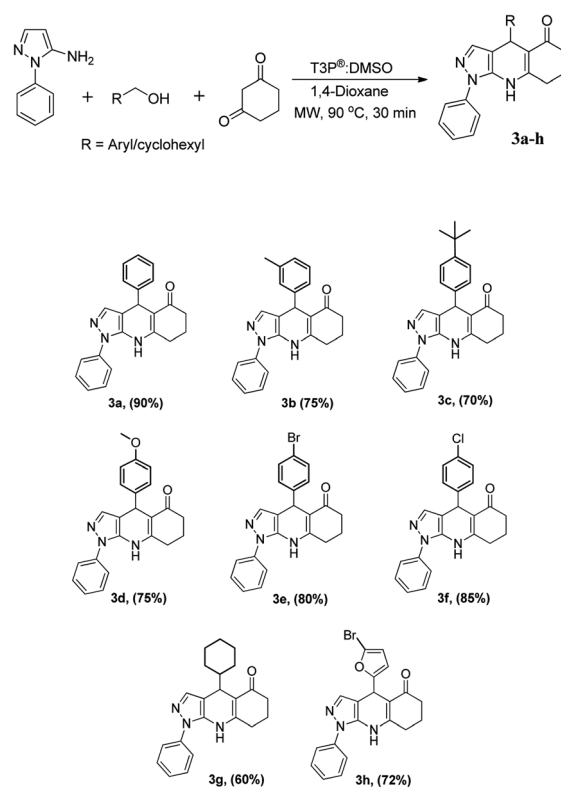


Scheme 1 The T3P®-DMSO mediated synthesis of **2a** under different reaction conditions and solvents.

Table 1 Optimization of reaction conditions

Entry	Solvent <sup>a</sup>	T3P® <sup>b</sup>	Time (min)	T [°C]	Yield <sup>c</sup> [%] of <b>2a</b>
1	Dioxane	1.0	30	RT	4
1	Dioxane	1.0	30	90	24
2	Dioxane	1.5	30	90	41
3	Dioxane	2.0	30	90	76
4	Dioxane	2.5	30	90	90
5	Dioxane	3.0	30	100	88
7	Dioxane	2.5	35	90	90
8	Dioxane	2.5	40	90	86
9	Dioxane	2.5	45	90	80
10	Toluene	2.5	30	100	60
11	EtOAc	2.5	30	75	40
12	MeCN	2.5	30	80	18
13	Benzene	2.5	30	80	21
14	DMF	2.5	30	140	27

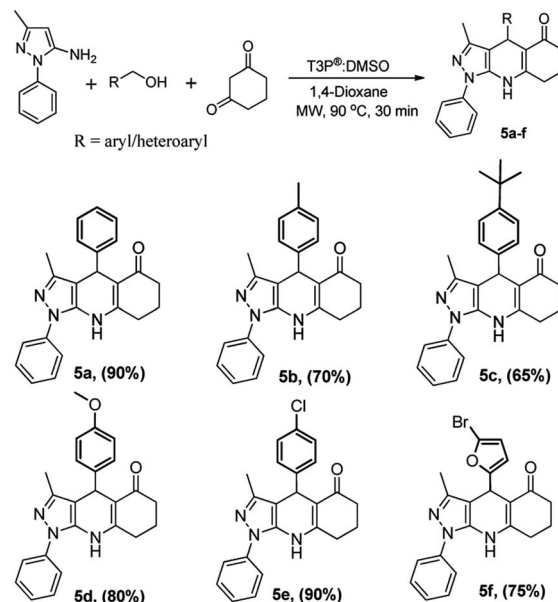
<sup>a</sup> Reactions were performed with solvent and DMSO were taken in 2 : 1 (1,4-dioxane : DMSO) volume ratio, 1mmol of **1a**, 1mmol of **1c** and 1.2 mmol of alcohol in case of **2a**. <sup>b</sup> T3P® (50% solution in EtOAc) was used to carry out the reactions. <sup>c</sup> Isolated yield after purified by column chromatography.



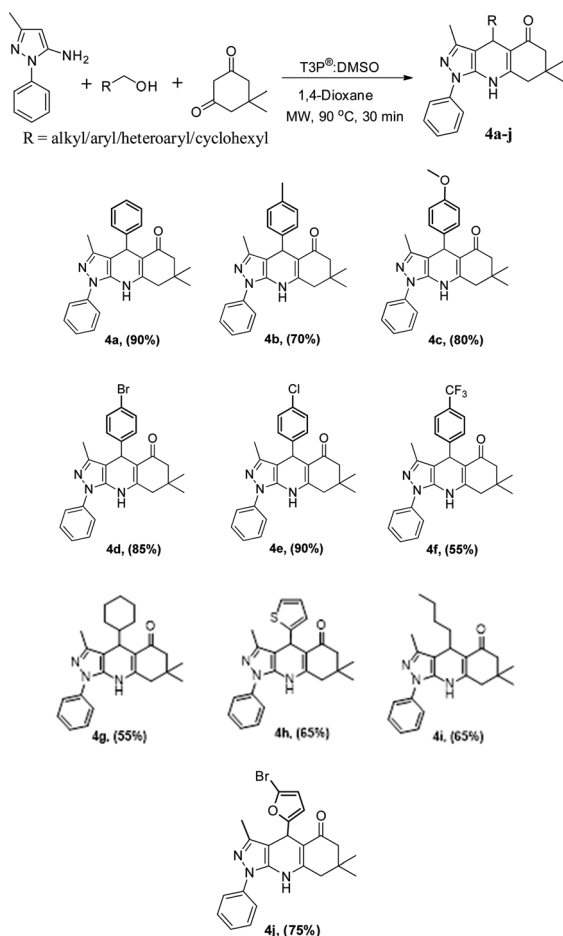
Scheme 3 Synthesis of pyrazolo quinolinone derivatives from 1-phenyl-1H-pyrazol-5-amine and 1,3-cyclohexanedione.



eq.) constant. Notably, the product yield was not adversely affected. And also, by changing the solvent conditions, we could not find any further improvement in the desired product yield. The overall optimisation results are summarised in Table 1. Thus, a clear optimisation reaction condition to obtain desired pyrazolo quinolinone from dimedone and benzyl alcohol was revealed from our studies, which entailed employing 2.5 eq. of T3P® at 90 °C and a duration of 30 min in the presence of 1,4-dioxane as a solvent under MW irradiation. The product was isolated by initially washing the reaction mixture with water followed by brine, then purified by column chromatography using 60–120 silica gel. With the clear optimisation condition in our hands, we carried out a series of reactions with amino phenyl pyrazole with 1,3-dicarbonyl compounds and various electronically diversified alcohols in the presence of an optimised reaction condition to afford the desired pyrazolo quinolinone derivatives. **2a–g** are summarised in Scheme 2. To increase the substrate scope, the titled reactions are carried out by changing substituents in the 1,3-dicarbonyl compound to afford the desired compounds. **3a–g** are summarised under Scheme 3. Similarly, by choosing the methyl group on pyrazolo quinolinone, it reacts with methyl substituted 1,3-dicarbonyl compounds and various alcohols to afford the desired pyrazolo quinolinone derivatives (**4a–i**), and the results are summarised



Scheme 5 Synthesis of pyrazolo quinolinone derivatives from 3-methyl-1-phenyl-1H-pyrazol-5-amine and 1,3-cyclohexanedione.



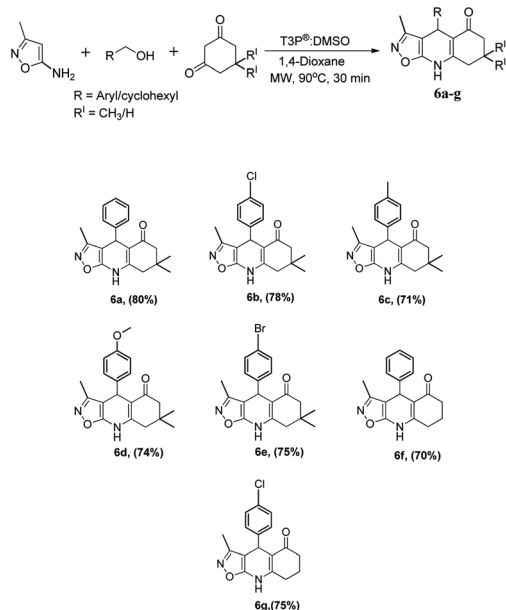
Scheme 4 Synthesis of pyrazolo quinolinone derivatives from 3-methyl-1-phenyl-1H-pyrazol-5-amine and dimedone.

under Scheme 4. Further, to broaden the substrate scope even more, the same methyl substituted phenyl pyrazole amine reacts with various alcohols and 1,3-dicarbonyl compounds containing without substitution the desired pyrazolo quinolinone derivatives (**5a–f**), and the results are summarised in Scheme 5. The overall product yields of the pyrazolo quinolinone derivatives were moderate to good. In all circumstances, the substitution that is present in the alcohols has a significant impact on the overall product yield. In Schemes 2 and 3, alcohols without substitution and alcohols containing halogens are the substituents, which comparatively give higher yields than alcohols containing electron-donating groups, followed by heterocyclic and cyclohexyl alcohols. Similarly, in Schemes 4 and 5, alcohols containing without substitution and alcohols containing halogens, particularly chloro substitution, comparatively gives equal and higher yield than the other categories of alcohols. But electron withdrawing groups other than halogens like  $-\text{CF}_3$  affords poor yield compared to other substituents present on the alcohols as mentioned in the case of **2e** and **4f**.

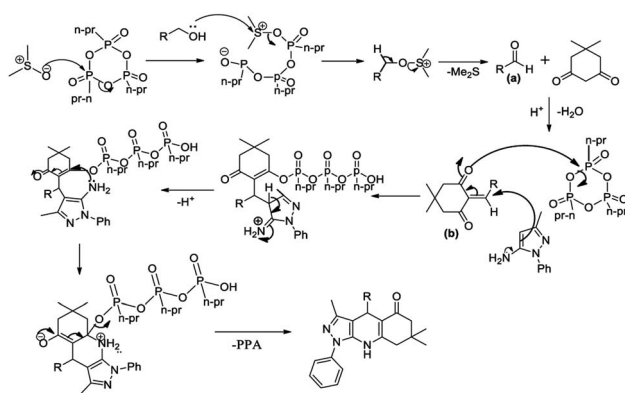
We succeeded in extending the scope of this synthetic methodology for the synthesis of biologically most important tetrahydroisoxazolo quinolinone derivatives by using methyl substituted amino isoxazole with same optimised reaction parameters, which afforded the desired tetrahydroisoxazolo quinolinones (**6a–g**) in moderate to good yield. The results are summarized in Scheme 6. In this instance also, alcohol without substitution gives a higher yield, and in the remaining cases, yields are mostly influenced by the substitutions that are present in the alcohols. Alcohols with halogens have a higher yield than alcohols without substitution, followed by alcohols with electron-donating groups.

The possible mechanism involves the reaction of DMSO with T3P® followed by the substitution reaction of alcohol, which results in the cleavage of the phosphoester bond and the





**Scheme 6** Synthesis of tetrahydroisoxazolo quinolinone derivative from 3-methylisoxazol-5-amine, 1,3-cyclohexanedione with alcohols.

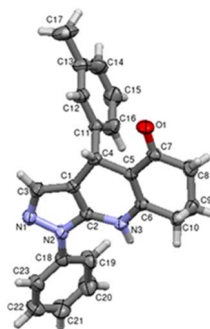


**Scheme 7** Possible mechanism for the synthesis of 1-phenyl-1H-pyrazolo-5-amine **2a** from the Scheme 2.

subsequent elimination of dimethyl sulphide, affords respective carbonyl compound (a). The formed carbonyl compound undergoes condensation reaction with the active methylene group of the 1,3-dicarbonyl compound to form intermediate (b); this intermediate undergoes 1,4 addition reaction with amino phenyl pyrazole in the presence of another equivalence of  $\text{T3P}^\circ$  to form the desired pyrazolo quinolinone derivative with the elimination of propylphosphonic acid (PPA) (Scheme 7).

### X-ray crystallography analysis

The compound **3b** crystallizes in the monoclinic space group  $P21/n$ . The unit cell parameters are  $a = 10.7713(16) \text{ \AA}$ ,  $b = 13.2410(18) \text{ \AA}$ ,  $c = 13.3621(18) \text{ \AA}$ ,  $\beta = 108.828(5)^\circ$  and  $Z = 4$ . The ORTEP of compound **3b** with 50% probability ellipsoids is shown in Fig. 1. The various hydrogen bond interactions, along with the geometry, are listed in Table 2. The packing of the molecules viewed down the  $b$  axis is shown in Fig. 2.

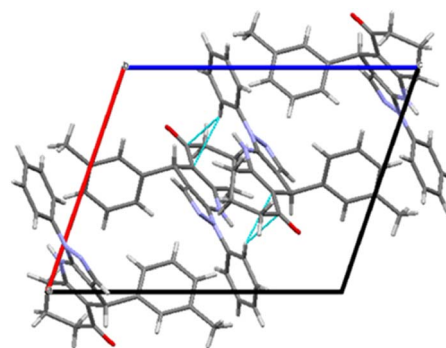


**Fig. 1** The ORTEP of **3b** with 50% probability (CCDC: 2267726).

**Table 2** The calculated hydrogen bond geometry details of the compound **3b**<sup>a</sup>

Sl. no	Atoms	D–H (Å)	H···A (Å)	D···A (Å)	D–H···A (°)
1	N3–H3···O1a	0.86	2.19	2.9418(16)	146
2	C10–H10B···O1a	0.97	2.54	3.3484(19)	140

<sup>a</sup>  $a: 1/2 + x, 3/2 - y, 1/2 + z$ .



**Fig. 2** Packing diagram of compound **3b** along  $b$  axis.

The plane of the quinolin ring is oriented at  $-169.8(1)^\circ$  from the pyrazole ring. The ring C18–C23 has trigonal geometry as it is indicated by the bond angle values of  $\text{C18–C19–C20} = 119.2(2)^\circ$ ,  $\text{C19–C20–C21} = 120.5(2)^\circ$ ,  $\text{C20–C21–C22} = 119.7(2)^\circ$ ,  $\text{C21–C22–C23} = 119.8(2)^\circ$ ,  $\text{C22–C23–C18} = 119.8(2)^\circ$ ,  $\text{C23–C18–C19} = 120.3(5)^\circ$ .

## Conclusion

In summary, we have described three component annulation reaction for the synthesis of two crucial heterocycles exhibiting broad biological spectrum, such as pyrazolo quinolinone and tetrahydroisoxazolo quinolinone derivatives, from stable alcohols using  $\text{T3P}^\circ$ -DMSO as a catalyst under microwave irradiation. This method requires less reaction time and energy usage, less waste creation, and an atom economy under MW irradiation. And also, this gives insight into the synthesis of libraries of bioactive pyrazolo quinolinone and tetrahydroisoxazolo quinolinone derivatives. Further studies on this and related reactions are ongoing.





## Experimental section

### Materials and instruments

Using Sorbent Technologies standard-grade silica gel, reaction products were purified using standard column chromatography (60–120 mesh). On Merck silica gel 60 F254 plates, analytical thin-layer chromatography was carried out. Visualization was accomplished with UV light. Melting points were recorded on a Thomas Hoover capillary melting point apparatus and are uncorrected. Infrared spectra were recorded on an ATI Mattson Genesis Series FT-Infrared spectrophotometer. Proton nuclear magnetic resonance spectra ( $^1\text{H}$  NMR) were recorded on Agilent-400 MHz and are reported in ppm using  $\text{CDCl}_3$  (7.24 ppm) and  $\text{DMSO-d}_6$  (2.47 ppm) as the internal standards. Proton-decoupled carbon nuclear magnetic resonance spectra ( $^{13}\text{C}$ -NMR) were recorded on an Agilent-100 MHz and reported in ppm using  $\text{CDCl}_3$  as the internal standard (77.0 ppm). Mass spectra were recorded on Waters' mass spectrum.

### General procedure for the synthesis of pyrazolo quinolinone and tetrahydroisoxazolo quinolinone derivative

The stirred suspension of alcohol (1.2 mmol) was added to the mixture of amino phenyl pyrazole or amino isoxazole (1 mmol) and cyclic 1,3 cyclic diketone in 1,4-dioxane as a solvent. It was followed by the addition of T3P® (2.0 mmol), and then the reaction mixture was kept under microwave irradiation at 90 °C for 30 minutes. The progress of the reaction was monitored by TLC. The reaction mixture was quenched by  $\text{NaHCO}_3$  solution under an ice bath, and the reaction mixture was extracted with EtOAc (2). The collected organic layer was washed with brine solution and dried over anhydrous sodium sulphate. The organic layer was removed under reduced pressure using a rotoevaporator to afford the desired compounds, which were purified by column chromatography using hexane and ethyl acetate as an eluent.

**7,7-Dimethyl-1,4-diphenyl-6,7,8,9-tetrahydro-1H-pyrazolo[3,4-*b*]quinolin-5(4H)-one (2a).** White solid; 90% yield ( $R_f = 0.45$  in hexane/EtOAc 60 : 40 v/v); MP: 138–142 °C; IR (KBr): 3236, 3055, 2956, 1578, 1549, 1247, 767  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 400 MHz): 7.49 (d,  $J = 4.4$  Hz, 4H), 7.39–7.36 (m, 1H), 7.27–7.21 (m, 5H), 7.13–7.11 (m, 1H), 6.53 (s, 1H), 5.22 (s, 1H), 2.36 (s, 2H), 2.19 (d,  $J = 1.6$  Hz, 2H), 1.06 (s, 3H), 1.03 (s, 3H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 100 MHz): 195.2, 149.0, 147.2, 138.7, 138.0, 135.0, 129.9, 128.2, 127.3, 127.3, 126.0, 122.9, 111.5, 106.5, 50.8, 42.5, 36.2, 32.5, 28.9, 27.4; HRMS (ESI)  $[\text{M} + \text{H}]^+$  calculated  $\text{C}_{24}\text{H}_{23}\text{N}_3\text{O}$  370.1919 found 370.1923.

**7,7-Dimethyl-1-phenyl-4-(*p*-tolyl)-6,7,8,9-tetrahydro-1H-pyrazolo[3,4-*b*]quinolin-5(4H)-one (2b).** White solid; 75% yield ( $R_f = 0.40$  in hexane/EtOAc 60 : 40 v/v); MP: 142–146 °C; IR (KBr): 3225, 3028, 2963, 1569, 1541, 1253, 775  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 400 MHz): 7.48–7.45 (m, 4H), 7.37–7.34 (m, 1H), 7.27 (d,  $J = 6.0$  Hz, 1H), 7.12 (t,  $J = 7.6$  Hz, 1H), 7.04 (t,  $J = 7.4$  Hz, 2H), 6.93 (d,  $J = 7.6$  Hz, 1H), 6.70 (s, 1H), 5.14 (s, 1H), 2.34 (d,  $J = 6.8$  Hz, 2H), 2.28 (s, 3H), 2.18 (s, 2H), 1.048 (s, 6H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 100 MHz): 195.2, 149.3, 147.2, 138.7, 138.0, 137.6, 135.1, 129.9,

128.1, 128.0, 127.6, 126.8, 124.3, 123.0, 111.4, 106.6, 50.8, 42.4, 36.1, 32.5, 29.0, 27.5, 21.5; HRMS (ESI)  $[\text{M} + \text{H}]^+$  calculated  $\text{C}_{25}\text{H}_{25}\text{N}_3\text{O}$  384.2076 found 384.2079.

**4-(4-Bromophenyl)-7,7-dimethyl-1-phenyl-6,7,8,9-tetrahydro-1H-pyrazolo[3,4-*b*]quinolin-5(4H)-one (2c).** Brown solid; 80% yield ( $R_f = 0.36$  in hexane/EtOAc 60 : 40 v/v); MP: 197–201 °C; IR (KBr): 3231, 3120, 2958, 1575, 1541, 1256, 791  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 400 MHz): 7.49 (s, 4H), 7.35 (d,  $J = 7.6$  Hz, 3H), 7.25 (d,  $J = 4.4$  Hz, 1H), 7.14 (d,  $J = 7.6$  Hz, 2H), 6.63 (s, 1H), 5.18 (s, 1H), 2.36 (s, 2H), 2.19 (d,  $J = 2.0$  Hz, 2H), 1.05 (s, 3H), 1.01 (s, 3H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 100 MHz): 195.2, 149.2, 146.2, 138.6, 137.9, 135.1, 131.2, 129.9, 129.2, 127.8, 123.0, 119.8, 111.1, 105.9, 50.8, 42.5, 35.8, 32.5, 28.9, 27.4; HRMS (ESI)  $[\text{M} + \text{H}]^+$  calculated  $\text{C}_{24}\text{H}_{22}\text{BrN}_3\text{O}$  448.1024 found 448.1021.

**4-(4-Chlorophenyl)-7,7-dimethyl-1-phenyl-6,7,8,9-tetrahydro-1H-pyrazolo[3,4-*b*]quinolin-5(4H)-one (2d).** White solid; 85% yield ( $R_f = 0.38$  in hexane/EtOAc 60 : 40 v/v); MP: 194–198 °C; IR (KBr): 3254, 3070, 2954, 1572, 1545, 1251, 771  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 400 MHz): 7.57–7.53 (m, 6H), 7.44–7.37 (m, 2H), 7.17 (d,  $J = 8.0$  Hz, 2H), 6.53 (s, 1H), 5.22 (s, 1H), 2.41 (s, 2H), 2.24 (d,  $J = 3.2$  Hz, 2H), 1.09 (s, 3H), 1.05 (s, 3H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 100 MHz): 195.8, 150.8, 139.6, 137.9, 136.7, 129.9, 129.6, 123.0, 122.6, 121.2, 110.6, 102.9, 50.9, 42.3, 35.5, 32.3, 29.2, 27.3; HRMS (ESI)  $[\text{M} + \text{H}]^+$  calculated  $\text{C}_{24}\text{H}_{22}\text{ClN}_3\text{O}$  404.1530 found 404.1525.

**4-Cyclohexyl-7,7-dimethyl-1-phenyl-6,7,8,9-tetrahydro-1H-pyrazolo[3,4-*b*]quinolin-5(4H)-one (2e).** Light brown solid; 60% yield ( $R_f = 0.42$  in hexane/EtOAc 60 : 40 v/v); MP: 136–140 °C; IR (KBr): 3436, 2868, 1653, 1589, 1375, 832, 695  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 400 MHz): 7.48–7.35 (m, 6H), 6.41 (s, 1H), 4.01 (s, 1H), 2.30–2.14 (m, 2H), 1.74–1.44 (m, 5H), 1.24–0.87 (m, 14H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 100 MHz): 195.8, 150.6, 139.3, 138.0, 136.7, 129.9, 127.6, 122.9, 110.8, 103.0, 51.0, 43.1, 42.4, 35.7, 32.4, 30.9, 29.3, 27.4, 27.3, 26.5, 26.4, 26.2; HRMS (ESI)  $[\text{M} + \text{H}]^+$  calculated  $\text{C}_{24}\text{H}_{29}\text{N}_3\text{O}$  376.2389 found 376.2394.

**4-(5-Bromofuran-2-yl)-7,7-dimethyl-1-phenyl-6,7,8,9-tetrahydro-1H-pyrazolo[3,4-*b*]quinolin-5(4H)-one (2f).** Pale yellow solid; 70% yield ( $R_f = 0.34$  in hexane/EtOAc 60 : 40 v/v); MP: 162–166 °C; IR (KBr): 3430, 2935, 1663, 1557, 1392, 1327, 695  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 400 MHz): 7.49–7.43 (m, 6H), 7.24 (s, 1H), 6.12 (d,  $J = 3.6$  Hz, 1H), 5.98 (d,  $J = 3.2$  Hz, 1H), 5.32 (s, 1H), 2.37 (s, 2H), 2.25 (d,  $J = 3.2$  Hz, 2H), 1.09 (s, 3H), 1.06 (s, 3H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 100 MHz): 195.2, 159.6, 150.2, 138.7, 137.8, 135.2, 129.9, 123.1, 119.2, 111.9, 107.5, 103.1, 50.7, 45.4, 42.5, 32.5, 30.2, 30.1, 27.2; HRMS (ESI)  $[\text{M} + \text{H}]^+$  calculated  $\text{C}_{22}\text{H}_{20}\text{BrN}_3\text{O}_2$  438.0817 found 438.0820.

**1,4-Diphenyl-6,7,8,9-tetrahydro-1H-pyrazolo[3,4-*b*]quinolin-5(4H)-one (3a).** White solid; 90% yield ( $R_f = 0.36$  in hexane/EtOAc 60 : 40 v/v); MP: 128–132 °C; IR (KBr): 3243, 3058, 2963, 1563, 1549, 1248, 768  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 400 MHz): 7.47–7.42 (m, 5H), 7.37–7.33 (m, 1H), 7.28–7.24 (m, 4H), 7.16–7.12 (m, 1H), 7.11 (s, 1H), 5.24 (s, 1H), 2.49–2.43 (m, 2H), 2.29–2.22 (m, 2H), 1.99–1.92 (m, 2H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 100 MHz): 195.6, 151.5, 147.3, 138.6, 137.9, 135.1, 129.8, 128.2, 127.6, 127.3, 126.0, 123.1, 112.3, 106.5, 37.1, 36.1, 28.7, 21.2; HRMS (ESI)  $[\text{M} + \text{H}]^+$  calculated  $\text{C}_{22}\text{H}_{19}\text{N}_3\text{O}$  342.1606 found 342.1612.



**1-Phenyl-4-(*m*-tolyl)-6,7,8,9-tetrahydro-1*H*-pyrazolo[3,4-*b*]quinolin-5(4*H*)-one (3b).** White solid; 75% yield ( $R_f = 0.37$  in hexane/EtoAc 60 : 40 v/v); MP: 158–162 °C; IR (KBr): 3238, 3016, 2964, 1568, 1556, 1239, 772  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 400 MHz): 7.48–7.47 (m, 5H), 7.37–7.25 (m, 2H), 7.13–7.07 (m, 3H), 6.71 (s, 1H), 5.22 (s, 1H), 2.34–2.29 (m, 6H), 1.99–1.98 (m, 3H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 100 MHz): 195.6, 147.2, 138.7, 138.1, 138.0, 137.6, 135.0, 129.9, 128.9, 128.5, 128.3, 128.1, 128.0, 127.7, 126.9, 124.8, 124.4, 123.0, 121.9, 112.6, 106.6, 87.4, 37.1, 35.9, 28.9, 21.5; HRMS (ESI)  $[\text{M} + \text{H}]^+$  calculated  $\text{C}_{23}\text{H}_{21}\text{N}_3\text{O}$  356.1763 found 356.1758.

**4-(4-(*tert*-Butyl)phenyl)-1-phenyl-6,7,8,9-tetrahydro-1*H*-pyrazolo[3,4-*b*]quinolin-5(4*H*)-one (3c).** White solid; 70% yield ( $R_f = 0.38$  in hexane/EtoAc 60 : 40 v/v); MP: 144–148 °C; IR (KBr): 3228, 3051, 2965, 1569, 1548, 1245, 771  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 400 MHz): 7.42–7.24 (m, 9H), 7.20–7.16 (m, 2H), 5.21 (s, 1H), 2.53–2.24 (m, 2H), 2.25–2.19 (m, 2H), 1.94–1.87 (m, 2H), 1.25 (s, 9H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 100 MHz): 195.8, 151.7, 148.5, 144.2, 138.6, 138.0, 135.2, 129.7, 127.6, 127.3, 126.8, 125.5, 125.1, 123.1, 121.9, 112.3, 106.6, 37.1, 35.3, 34.2, 31.3, 28.6, 21.1; HRMS (ESI)  $[\text{M} + \text{H}]^+$  calculated  $\text{C}_{26}\text{H}_{27}\text{N}_3\text{O}$  398.2232 found 398.2238.

**4-(4-Methoxyphenyl)-1-phenyl-6,7,8,9-tetrahydro-1*H*-pyrazolo[3,4-*b*]quinolin-5(4*H*)-one (3d).** Light brown solid; 75% yield ( $R_f = 0.40$  in hexane/EtoAc 60 : 40 v/v); MP: 163–167 °C; IR (KBr): 3248, 3076, 2973, 1580, 1556, 1254, 765  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 400 MHz): 7.44–7.38 (m, 4H), 7.33–7.24 (m, 3H), 7.17 (d,  $J = 8.4$  Hz, 2H), 6.77 (d,  $J = 8.4$  Hz, 2H), 5.16 (s, 1H), 3.72 (s, 3H), 2.53–2.40 (m, 2H), 2.25–2.18 (m, 2H), 1.90 (t,  $J = 6.0$  Hz, 2H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 100 MHz): 195.8, 157.7, 151.5, 139.8, 138.6, 138.0, 135.2, 129.7, 128.3, 127.6, 123.1, 113.5, 112.5, 106.6, 55.1, 37.1, 35.1, 28.6, 21.1; HRMS (ESI)  $[\text{M} + \text{H}]^+$  calculated  $\text{C}_{23}\text{H}_{21}\text{N}_3\text{O}_2$  372.1712 found 372.1715.

**4-(4-Bromophenyl)-1-phenyl-6,7,8,9-tetrahydro-1*H*-pyrazolo[3,4-*b*]quinolin-5(4*H*)-one (3e).** White solid; 80% yield ( $R_f = 0.33$  in hexane/EtoAc 60 : 40 v/v); MP: 212–216 °C; IR (KBr): 3239, 3115, 2948, 1568, 1575, 1256, 776  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 400 MHz): 7.53–7.43 (m, 5H), 7.37 (d,  $J = 8$  Hz, 3H), 7.16 (d,  $J = 8.0$  Hz, 2H), 6.76 (s, 1H), 5.23 (s, 1H), 2.55–2.50 (m, 2H), 2.40–2.29 (m, 2H), 2.02–1.98 (m, 2H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 100 MHz): 195.5, 151.1, 146.2, 138.6, 137.9, 135.0, 131.2, 129.5, 128.3, 123.0, 119.8, 116.0, 112.2, 105.8, 105.8, 37.1, 35.7, 28.8, 21.1; HRMS (ESI)  $[\text{M} + \text{H}]^+$  calculated  $\text{C}_{22}\text{H}_{18}\text{BrN}_3\text{O}$  421.3098 found 421.3091.

**4-(4-Chlorophenyl)-1-phenyl-6,7,8,9-tetrahydro-1*H*-pyrazolo[3,4-*b*]quinolin-5(4*H*)-one (3f).** White solid; 85% yield ( $R_f = 0.35$  in hexane/EtoAc 60 : 40 v/v); MP: 200–204 °C; IR (KBr): 3254, 3071, 2953, 1572, 1546, 1256, 770  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 400 MHz): 7.54–7.48 (m, 5H), 7.42–7.25 (m, 6H), 6.58 (s, 1H), 5.25 (s, 1H), 2.54–2.52 (m, 2H), 2.38–2.31 (m, 2H), 2.03–1.98 (m, 2H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 100 MHz): 195.5, 150.8, 145.6, 138.6, 137.9, 130.0, 128.8, 128.3, 127.9, 123.0, 112.4, 105.9, 37.1, 35.6, 28.9, 21.183; HRMS (ESI)  $[\text{M} + \text{H}]^+$  calculated  $\text{C}_{22}\text{H}_{18}\text{ClN}_3\text{O}$  376.1217 found 376.1224.

**4-Cyclohexyl-1-phenyl-6,7,8,9-tetrahydro-1*H*-pyrazolo[3,4-*b*]quinolin-5(4*H*)-one (3g).** Pale yellow solid; 60% yield ( $R_f = 0.41$

in hexane/EtoAc 60 : 40 v/v); MP: 132–136 °C; IR (KBr): 3238, 3048, 2964, 1575, 1543, 1249, 773  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 400 MHz): 7.40–7.27 (m, 6H), 6.64 (s, 1H), 3.95 (s, 1H), 2.39–2.38 (m, 4H), 1.92 (s, 2H), 1.66–1.49 (m, 7H), 1.14–1.12 (m, 4H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 100 MHz): 196.2, 152.6, 139.2, 137.9, 136.6, 129.8, 127.9, 122.9, 111.7, 103.0, 42.9, 37.3, 35.6, 35.4, 30.7, 28.7, 27.0, 26.4, 26.4, 26.2, 21.2; HRMS (ESI)  $[\text{M} + \text{H}]^+$  calculated  $\text{C}_{22}\text{H}_{25}\text{N}_3\text{O}$  348.2076 found 348.2069.

**3,7,7-Trimethyl-1,4-diphenyl-6,7,8,9-tetrahydro-1*H*-pyrazolo[3,4-*b*]quinolin-5(4*H*)-one (4a).** White solid; 90% yield ( $R_f = 0.40$  in hexane/EtoAc 60 : 40 v/v); MP: 126–130 °C (lit. 128–132 °C);<sup>15</sup> IR (KBr): 3231, 3062, 2958, 1585, 1543, 1256, 765  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 400 MHz): 7.49 (d,  $J = 4.0$  Hz, 4H), 7.36 (d,  $J = 4.4$  Hz, 1H), 7.31–7.22 (m, 4H), 7.14 (d,  $J = 7.2$  Hz, 1H), 6.58 (s, 1H), 5.15 (s, 1H), 2.37 (s, 2H), 2.192 (d,  $J = 6.8$  Hz, 2H), 2.03 (s, 3H), 1.07 (s, 3H), 1.02 (s, 3H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 100 MHz): 195.2, 148.6, 147.6, 146.4, 138.0, 135.5, 129.8, 128.0, 127.9, 127.3, 125.9, 122.7, 112.1, 104.7, 65.8, 50.8, 42.5, 36.1, 32.5, 29.0, 27.3, 12.1; HRMS (ESI)  $[\text{M} + \text{H}]^+$  calculated  $\text{C}_{25}\text{H}_{25}\text{N}_3\text{O}$  384.2076 found 384.2079.

**3,7,7-Trimethyl-1-phenyl-4-(*p*-tolyl)-6,7,8,9-tetrahydro-1*H*-pyrazolo[3,4-*b*]quinolin-5(4*H*)-one (4b).** White solid; 70% yield ( $R_f = 0.42$  in hexane/EtoAc 60 : 40 v/v); MP: 196–200 °C (lit. 200–201 °C);<sup>15</sup> IR (KBr): 3236, 3025, 2957, 1578, 1545, 1249, 770  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 400 MHz): 7.47–7.41 (m, 4H), 7.32 (d,  $J = 6.4$  Hz, 1H), 7.10–7.04 (m, 3H), 6.92 (d,  $J = 7.2$  Hz, 1H), 6.82 (s, 1H), 5.05 (s, 1H), 2.32 (d,  $J = 3.2$  Hz, 2H), 2.28 (s, 3H), 2.15 (d,  $J = 5.6$  Hz, 2H), 2.02 (s, 3H), 1.03 (s, 3H), 1.00 (s, 3H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 100 MHz): 195.3, 149.1, 147.5, 146.4, 138.0, 137.4, 135.5, 129.8, 128.5, 127.9, 127.2, 126.8, 124.9, 122.8, 111.9, 104.8, 50.8, 42.3, 36.1, 32.5, 29.0, 27.3, 21.5, 12.2; HRMS (ESI)  $[\text{M} + \text{H}]^+$  calculated  $\text{C}_{26}\text{H}_{27}\text{N}_3\text{O}$  398.2232 found 398.2228.

**4-(4-Methoxyphenyl)-3,7,7-trimethyl-1-phenyl-6,7,8,9-tetrahydro-1*H*-pyrazolo[3,4-*b*]quinolin-5(4*H*)-one (4c).** White solid; 80% yield ( $R_f = 0.43$  in hexane/EtoAc 60 : 40 v/v); MP: 170–174 °C (lit. 166–170 °C);<sup>15</sup> IR (KBr): 3237, 3060, 2958, 1596, 1541, 1248, 761  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 400 MHz): 7.47 (d,  $J = 4.4$  Hz, 4H), 7.34 (t,  $J = 4.4$  Hz, 1H), 7.19 (d,  $J = 8.4$  Hz, 2H), 6.77 (d,  $J = 8.4$  Hz, 2H), 6.53 (s, 1H), 5.08 (s, 1H), 3.74 (s, 3H), 2.34 (s, 2H), 2.17 (d,  $J = 5.2$  Hz, 2H), 2.01 (s, 3H), 1.04 (s, 3H), 0.94 (s, 3H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 100 MHz): 195.3, 157.7, 148.4, 147.6, 138.9, 138.0, 135.5, 129.8, 128.8, 127.3, 122.7, 113.4, 112.3, 104.8, 55.1, 50.8, 42.5, 35.2, 32.5, 28.9, 27.3, 12.1; HRMS (ESI)  $[\text{M} + \text{H}]^+$  calculated  $\text{C}_{26}\text{H}_{27}\text{N}_3\text{O}_2$  414.2182 found 414.2185.

**4-(4-Bromophenyl)-3,7,7-trimethyl-1-phenyl-6,7,8,9-tetrahydro-1*H*-pyrazolo[3,4-*b*]quinolin-5(4*H*)-one (4d).** White solid; 85% yield ( $R_f = 0.36$  in hexane/EtoAc 60 : 40 v/v); MP: 208–212 °C (lit. 206–210 °C);<sup>15</sup> IR (KBr): 3228, 3121, 2950, 1571, 1543, 1251, 786  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 400 MHz): 7.51–7.46 (m, 5H), 7.35 (t,  $J = 7.0$  Hz, 2H), 7.16–7.10 (m, 2H), 6.65 (s, 1H), 5.09 (s, 1H), 2.34 (s, 2H), 2.22–2.11 (m, 2H), 1.98 (s, 3H), 1.04 (s, 3H), 0.98 (s, 3H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 100 MHz): 195.3, 148.9, 147.5, 145.5, 137.9, 135.5, 131.1, 129.9, 129.7, 129.0, 128.9, 127.7, 126.0, 121.1, 119.7, 50.7, 42.4, 35.7, 32.5, 29.0, 27.3, 12.1; HRMS (ESI)  $[\text{M} + \text{H}]^+$  calculated  $\text{C}_{25}\text{H}_{24}\text{BrN}_3\text{O}$  462.1181 found 462.1175.

**4-(4-Chlorophenyl)-3,7,7-trimethyl-1-phenyl-6,7,8,9-tetrahydro-1*H*-pyrazolo[3,4-*b*]quinolin-5(4*H*)-one (4e).** White solid;



90% yield ( $R_f = 0.37$  in hexane/EtoAc 60 : 40 v/v); MP: 210–214 °C (lit. 212–216 °C);<sup>15</sup> IR (KBr): 3258, 3073, 2952, 1573, 1547, 1255, 770  $\text{cm}^{-1}$ ; <sup>1</sup>H NMR ( $\text{CDCl}_3$ , 400 MHz): 7.51–7.45 (m, 4H), 7.36 (t,  $J = 3.2$  Hz, 1H), 7.25–7.17 (m, 4H), 6.48 (s, 1H), 5.11 (s, 1H), 2.35 (d,  $J = 2.4$  Hz, 2H), 2.17 (d,  $J = 8.4$  Hz, 2H), 1.98 (s, 3H), 1.05 (s, 3H), 0.98 (s, 3H); <sup>13</sup>C NMR ( $\text{CDCl}_3$ , 100 MHz): 195.3, 149.3, 147.4, 145.0, 137.9, 135.6, 131.5, 129.8, 129.3, 128.2, 127.4, 122.9, 111.4, 104.2, 50.7, 42.2, 35.7, 35.6, 32.4, 29.0, 27.2, 12.1; HRMS (ESI)  $[M + H]^+$  calculated  $\text{C}_{25}\text{H}_{24}\text{ClN}_3\text{O}$  418.1686 found 418.1682.

**4-Cyclohexyl-3,7,7-trimethyl-1-phenyl-6,7,8,9-tetrahydro-1H-pyrazolo[3,4-*b*]quinolin-5(4H)-one (4f).** White solid; 55% yield ( $R_f = 0.44$  in hexane/EtoAc 60 : 40 v/v); MP: 168–172 °C; IR (KBr): 3435, 2928, 1643, 1504, 1385, 1065, 694  $\text{cm}^{-1}$ ; <sup>1</sup>H NMR ( $\text{CDCl}_3$ , 400 MHz): 9.17 (broad s, 1H), 7.53–7.35 (m, 5H), 3.87 (s, 1H), 2.44 (s, 2H), 2.20–2.09 (m, 5H), 1.67–1.53 (m, 5H), 1.34–1.11 (m, 1H), 1.10–0.96 (m, 10H), 0.84–0.74 (m, 1H); <sup>13</sup>C NMR ( $\text{CDCl}_3$ , 100 MHz): 197.5, 162.6, 147.3, 137.4, 130.0, 129.1, 198.9, 122.0, 120.9, 116.5, 102.5, 52.2, 47.3, 32.9, 32.4, 28.2, 28.1, 27.4, 27.3, 26.5, 26.4, 12.2; HRMS (ESI)  $[M + H]^+$  calculated  $\text{C}_{25}\text{H}_{31}\text{N}_3\text{O}$  390.2545 found 390.2543.

**3,7,7-Trimethyl-1-phenyl-4-(thiophen-2-yl)-6,7,8,9-tetrahydro-1H-pyrazolo[3,4-*b*]quinolin-5(4H)-one (4g).** Off white solid; 65% yield ( $R_f = 0.40$  in hexane/EtoAc 60 : 40 v/v); MP: 223–227 °C (lit. 226–229 °C);<sup>16</sup> IR (KBr): 3439, 2846, 1648, 1514, 1373, 971, 695  $\text{cm}^{-1}$ ; <sup>1</sup>H NMR ( $\text{DMSO}-d_6$ , 400 MHz): 9.54 (broad s, 1H), 7.55–7.41 (m, 4H), 7.39–7.38 (m, 1H), 7.21 (d,  $J = 4.4$  Hz, 1H), 6.87–6.81 (m, 2H), 5.37 (s, 1H), 2.54–2.50 (m, 2H), 2.23–2.19 (m, 1H), 2.10–1.97 (m, 4H), 1.01 (s, 3H), 0.98 (s, 3H); <sup>13</sup>C NMR ( $\text{CDCl}_3$ , 100 MHz): 199.9, 155.5, 153.7, 151.8, 142.2, 140.0, 134.1, 130.8, 130.7, 127.8, 127.3, 108.4, 55.0, 46.5, 36.8, 34.9, 29.7, 27.8, 12.2; HRMS (ESI)  $[M + H]^+$  calculated  $\text{C}_{23}\text{H}_{23}\text{N}_3\text{OS}$  390.1640 found 390.1649.

**4-Butyl-3,7,7-trimethyl-1-phenyl-6,7,8,9-tetrahydro-1H-pyrazolo[3,4-*b*]quinolin-5(4H)-one (4h).** White solid; 65% yield ( $R_f = 0.44$  in hexane/EtoAc 60 : 40 v/v); MP: 154–158 °C; IR (KBr): 3463, 2945, 2868, 1645, 1524, 1375, 698  $\text{cm}^{-1}$ ; <sup>1</sup>H NMR ( $\text{CDCl}_3$ , 400 MHz): 7.42 (d,  $J = 4.0$  Hz, 5H), 7.30–7.25 (m, 1H), 6.81 (s, 1H), 4.12–4.10 (m, 1H), 2.28 (s, 2H), 2.21 (s, 3H), 2.16 (d,  $J = 5.6$  Hz, 2H), 2.15–1.62 (m, 1H), 1.48 (t,  $J = 6.8$  Hz, 1H), 1.35–1.12 (m, 2H), 1.11–1.08 (m, 2H), 1.06 (s, 3H), 1.01 (s, 3H), 0.80 (t,  $J = 7.2$  Hz, 3H); <sup>13</sup>C NMR ( $\text{CDCl}_3$ , 100 MHz): 195.9, 150.8, 147.0, 138.0, 136.6, 129.7, 128.9, 127.1, 122.7, 111.1, 103.9, 50.9, 42.2, 35.6, 32.3, 29.4, 29.3, 27.4, 27.1, 22.8, 14.1, 12.4; HRMS (ESI)  $[M + H]^+$  calculated  $\text{C}_{23}\text{H}_{29}\text{N}_3\text{O}$  364.2389 found 364.2387.

**4-(5-Bromofuran-2-yl)-3,7,7-trimethyl-1-phenyl-6,7,8,9-tetrahydro-1H-pyrazolo[3,4-*b*]quinolin-5(4H)-one (4i).** Light yellow solid; 75% yield ( $R_f = 0.38$  in hexane/EtoAc 60 : 40 v/v); MP: 172–176 °C; IR (KBr): 3433, 2861, 1651, 1575, 1378, 1056, 699  $\text{cm}^{-1}$ ; <sup>1</sup>H NMR ( $\text{CDCl}_3$ , 400 MHz): 7.43–7.23 (m, 5H), 6.89 (s, 1H), 6.12 (d,  $J = 3.2$  Hz, 1H), 6.01 (d,  $J = 2.8$  Hz, 1H), 5.24 (s, 1H), 2.35 (s, 2H), 2.27–2.18 (m, 4H), 1.22 (s, 1H), 1.076 (s, 3H), 1.05 (s, 3H); <sup>13</sup>C NMR ( $\text{CDCl}_3$ , 100 MHz): 195.4, 163.3, 159.1, 150.6, 147.4, 138.8, 137.8, 135.8, 121.2, 120.9, 111.9, 107.6, 101.3, 53.8, 50.6, 48.3, 32.5, 28.2, 28.1, 12.3; HRMS (ESI)  $[M + H]^+$  calculated  $\text{C}_{23}\text{H}_{22}\text{BrN}_3\text{O}_2$  452.0974 found 452.0979.

**3-Methyl-1,4-diphenyl-6,7,8,9-tetrahydro-1H-pyrazolo[3,4-*b*]quinolin-5(4H)-one (5a).** White solid; 90% yield ( $R_f = 0.38$  in hexane/EtoAc 60 : 40 v/v); MP: 125–129 °C (lit. 122–126 °C);<sup>15</sup> IR (KBr): 3239, 3053, 2946, 1575, 1543, 1248, 762  $\text{cm}^{-1}$ ; <sup>1</sup>H NMR ( $\text{CDCl}_3$ , 400 MHz): 7.43 (t,  $J = 5.2$  Hz, 4H), 7.33–7.31 (m, 3H), 7.29–7.23 (m, 2H), 7.12 (t, 1H, 7 Hz), 6.90 (s, 1H), 5.14 (s, 1H), 2.50–2.44 (m, 2H), 2.28–2.22 (m, 2H), 2.00 (s, 3H), 1.93 (t,  $J = 4.8$  Hz, 2H); <sup>13</sup>C NMR ( $\text{CDCl}_3$ , 100 MHz): 195.6, 150.8, 147.5, 146.6, 138.0, 135.5, 129.8, 128.1, 128.0, 127.2, 126.0, 122.8, 113.2, 104.6, 37.1, 36.0, 28.7, 21.1, 12.2; HRMS (ESI)  $[M + H]^+$  calculated  $\text{C}_{23}\text{H}_{21}\text{N}_3\text{O}$  356.1763 found 356.1759.

**3-Methyl-1-phenyl-4-(*p*-tolyl)-6,7,8,9-tetrahydro-1H-pyrazolo[3,4-*b*]quinolin-5(4H)-one (5b).** White solid; 70% yield ( $R_f = 0.39$  in hexane/EtoAc 60 : 40 v/v); MP: 188–192 °C; IR (KBr): 3234, 3018, 2963, 1565, 1529, 1236, 765  $\text{cm}^{-1}$ ; <sup>1</sup>H NMR ( $\text{CDCl}_3$ , 400 MHz): 7.42–7.34 (m, 5H), 7.27 (d,  $J = 7.2$  Hz, 1H), 7.11–7.04 (m, 3H), 6.92 (d,  $J = 6.8$  Hz, 1H), 5.06 (s, 1H), 2.47 (s, 1H), 2.39 (d,  $J = 6.8$  Hz, 1H), 2.28 (s, 3H), 2.22–2.16 (m, 2H), 2.00 (s, 3H), 1.89 (d,  $J = 5.6$  Hz, 2H); <sup>13</sup>C NMR ( $\text{CDCl}_3$ , 100 MHz): 195.8, 151.6, 147.4, 146.6, 138.0, 137.4, 135.6, 129.6, 128.6, 127.1, 126.8, 125.0, 123.0, 112.9, 104.7, 37.1, 36.0, 28.5, 21.5, 21.1, 12.2; HRMS (ESI)  $[M + H]^+$  calculated  $\text{C}_{24}\text{H}_{23}\text{N}_3\text{O}$  370.1919 found 370.1922.

**4-(4-*tert*-Butylphenyl)-3-methyl-1-phenyl-6,7,8,9-tetrahydro-1H-pyrazolo[3,4-*b*]quinolin-5(4H)-one (5c).** Pale yellow solid; 65% yield ( $R_f = 0.40$  in hexane/EtoAc 60 : 40 v/v); MP: 155–159 °C; IR (KBr): 3239, 3056, 2943, 1565, 1573, 1242, 769  $\text{cm}^{-1}$ ; <sup>1</sup>H NMR ( $\text{CDCl}_3$ , 400 MHz): 7.42–7.35 (m, 4H), 7.29–7.23 (m, 4H), 7.197 (d,  $J = 8.8$  Hz, 2H), 5.11 (s, 1H), 2.55–2.51 (m, 2H), 2.24–2.19 (m, 2H), 2.03 (s, 3H), 1.92 (t,  $J = 5.6$  Hz, 2H), 1.27 (s, 9H); <sup>13</sup>C NMR ( $\text{CDCl}_3$ , 100 MHz): 195.8, 151.3, 148.4, 147.4, 143.6, 138.0, 135.6, 129.6, 127.3, 127.1, 124.9, 122.9, 113.1, 104.9, 37.1, 35.4, 34.2, 31.3, 28.6, 21.1, 12.2; HRMS (ESI)  $[M + H]^+$  calculated  $\text{C}_{27}\text{H}_{29}\text{N}_3\text{O}$  412.2389 found 412.2381.

**4-(4-Methoxyphenyl)-3-methyl-1-phenyl-6,7,8,9-tetrahydro-1H-pyrazolo[3,4-*b*]quinolin-5(4H)-one (5d).** White solid; 80% yield ( $R_f = 0.41$  in hexane/EtoAc 60 : 40 v/v); MP: 122–126 °C (lit. 124–128 °C);<sup>15</sup> IR (KBr): 3234, 3055, 2952, 1580, 1541, 1253, 755  $\text{cm}^{-1}$ ; <sup>1</sup>H NMR ( $\text{CDCl}_3$ , 400 MHz): 7.53–7.48 (m, 4H), 7.39–7.35 (m, 1H), 7.22 (t,  $J = 5.8$  Hz, 2H), 6.78 (d,  $J = 8.8$  Hz, 2H), 6.47 (s, 1H), 5.16 (s, 1H), 3.76 (s, 3H), 2.51 (t,  $J = 5.6$  Hz, 2H), 2.40–2.31 (m, 2H), 2.02 (s, 3H), 1.98 (s, 2H); <sup>13</sup>C NMR ( $\text{CDCl}_3$ , 100 MHz): 190.9, 145.3, 142.9, 134.2, 133.3, 130.6, 125.1, 123.9, 123.7, 122.5, 118.0, 109.3, 109.3, 109.0, 108.6, 50.4, 32.4, 30.4, 24.1, 16.4, 7.4; HRMS (ESI)  $[M + H]^+$  calculated  $\text{C}_{24}\text{H}_{23}\text{N}_3\text{O}_2$  386.1869 found 386.1864.

**4-(4-Chlorophenyl)-3-methyl-1-phenyl-6,7,8,9-tetrahydro-1H-pyrazolo[3,4-*b*]quinolin-5(4H)-one (5e).** White solid; 90% yield ( $R_f = 0.35$  in hexane/EtoAc 60 : 40 v/v); MP: 202–206 °C (lit. 202–204 °C);<sup>15</sup> IR (KBr): 3257, 3066, 2958, 1577, 1546, 1255, 745  $\text{cm}^{-1}$ ; <sup>1</sup>H NMR ( $\text{CDCl}_3$ , 400 MHz): 7.47–7.44 (m, 4H), 7.37–7.33 (m, 1H), 7.25–7.18 (m, 4H), 6.71 (s, 1H), 5.13 (s, 1H), 2.50–2.46 (m, 2H), 2.31–2.26 (m, 2H), 1.98–1.91 (m, 5H); <sup>13</sup>C NMR ( $\text{CDCl}_3$ , 100 MHz): 195.5, 150.6, 147.4, 145.0, 137.8, 135.4, 131.6, 129.4, 128.1, 127.4, 122.8, 113.0, 104.1, 37.1, 35.6, 28.8, 21.1, 12.1; HRMS (ESI)  $[M + H]^+$  calculated  $\text{C}_{23}\text{H}_{20}\text{ClN}_3\text{O}$  390.1373 found 390.1378.





**4-(5-Bromofuran-2-yl)-3-methyl-1-phenyl-6,7,8,9-tetrahydro-1H-pyrazolo[3,4-*b*]quinolin-5(4H)-one (5f).** Pale yellow solid; 75% yield ( $R_f = 0.35$  in hexane/EtoAc 60 : 40 v/v); MP: 166–170 °C; IR (KBr): 3228, 3045, 2952, 1573, 1541, 1239, 772  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 400 MHz): 7.41–7.38 (m, 5H), 7.31–7.30 (m, 1H), 6.12 (t,  $J = 3.2$  Hz, 1H), 5.97 (d,  $J = 2.8$  Hz, 1H), 5.25 (s, 1H), 2.48–2.28 (m, 3H), 2.17–2.15 (m, 4H), 1.97–1.95 (m, 2H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 100 MHz): 195.6, 164.5, 159.1, 152.1, 150.3, 135.7, 134.5, 122.0, 121.3, 121.2, 113.8, 112.7, 108.9, 101.3, 40.0, 34.6, 28.8, 21.6, 12.2; HRMS (ESI)  $[\text{M} + \text{H}]^+$  calculated  $\text{C}_{21}\text{H}_{18}\text{BrN}_3\text{O}_2$  424.0661 found 424.0669.

**3,7,7-Trimethyl-4-phenyl-6,7,8,9-tetrahydroisoxazolo[5,4-*b*]quinolin-5(4H)-one (6a).** White solid; 75% yield ( $R_f = 0.40$  in hexane/EtoAc 60 : 40 v/v); MP: 182–186 °C (lit. 183–184 °C);<sup>17</sup> IR (KBr): 3436, 2927, 1645, 1563, 1504, 1452, 1257;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 400 MHz): 9.40 (broad s, 1H), 7.49–7.27 (m, 5H), 5.28–5.27 (m, 1H), 2.63 (s, 2H), 2.45–2.42 (m, 2H), 2.15 (s, 3H), 1.36–1.22 (m, 6H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 100 MHz): 196.1, 165.4, 161.1, 149.6, 138.8, 129.4, 128.7, 128.5, 128.1, 126.5, 117.1, 113.0, 96.9, 51.1, 43.2, 37.2, 33.2, 28.2, 28.0, 11.1 HRMS (ESI)  $[\text{M} + \text{H}]^+$  calculated  $\text{C}_{19}\text{H}_{20}\text{N}_2\text{O}_2$  309.1603 found 309.1606.

**4-(4-Chlorophenyl)-3,7,7-trimethyl-6,7,8,9-tetrahydroisoxazolo[5,4-*b*]quinolin-5(4H)-one (6b).** White solid; 78% yield ( $R_f = 0.37$  in hexane/EtoAc 60 : 40 v/v); MP: 269–273 °C (lit. 270–271 °C);<sup>17</sup> IR (KBr): 3430, 2925, 1645, 1562, 1505, 1454, 1251;  $^1\text{H}$  NMR ( $\text{DMSO}-d_6$ , 400 MHz): 10.77 (broad s, 1H), 7.30 (d,  $J = 8.4$  Hz, 2H), 7.20 (d,  $J = 8.4$  Hz, 2H), 4.98 (s, 1H), 3.34–2.53 (m, 1H), 2.51–2.40 (m, 1H), 2.19–1.91 (m, 2H), 1.86 (s, 3H), 1.05 (s, 3H), 0.85 (s, 3H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 100 MHz): 191.2, 154.6, 153.7, 146.0, 139.2, 127.4, 124.6, 123.5, 108.2, 91.5, 53.3, 48.7, 32.3, 31.0, 26.8, 26.4, 10.4; HRMS (ESI)  $[\text{M} + \text{H}]^+$  calculated  $\text{C}_{19}\text{H}_{19}\text{ClN}_2\text{O}_2$  343.1213 found 343.1209.

**3,7,7-Trimethyl-4-(*p*-tolyl)-6,7,8,9-tetrahydroisoxazolo[5,4-*b*]quinolin-5(4H)-one (6c).** White solid; 71% yield ( $R_f = 0.38$  in hexane/EtoAc 60 : 40 v/v); MP: 288–232 °C (lit. 289–230 °C);<sup>17</sup> IR (KBr): 3437, 2920, 1645, 1570, 1501, 1459, 1249;  $^1\text{H}$  NMR ( $\text{DMSO}-d_6$ , 400 MHz): 10.71 (broad s, 1H), 7.24–7.10 (m, 4H), 4.95 (s, 1H), 2.54–2.41 (m, 2H), 2.18 (d,  $J = 16$  Hz, 1H), 2.01 (t,  $J = 3.6$  Hz, 1H), 1.86 (s, 3H), 1.34 (s, 3H), 1.02 (s, 3H), 0.96 (s, 3H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 100 MHz): 195.9, 160.1, 159.5, 151.1, 145.5, 132.1, 129.6, 128.9, 128.4, 111.9, 96.3, 51.4, 41.7, 40.1, 33.0, 29.5, 29.1, 21.7, 11.1; HRMS (ESI)  $[\text{M} + \text{H}]^+$  calculated 323.1760 found 323.1767.

**4-(4-Methoxyphenyl)-3,7,7-trimethyl-6,7,8,9-tetrahydroisoxazolo[5,4-*b*]quinolin-5(4H)-one (6d).** Pale yellow solid; 76% yield ( $R_f = 0.36$  in hexane/EtoAc 60 : 40 v/v); MP: 226–230 °C (lit. 226–227 °C);<sup>17</sup> IR (KBr): 3435, 2922, 1641, 1567, 1509, 1452, 1251;  $^1\text{H}$  NMR ( $\text{DMSO}-d_6$ , 400 MHz): 8.02–8.01 (m, 1H), 7.87–7.80 (m, 2H), 7.57–7.46 (m, 2H), 3.97 (s, 1H), 3.32–3.30 (m, 3H), 2.28 (s, 3H), 1.86–1.69 (m, 10H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 100 MHz): 196.1, 166.3, 162.1, 149.2, 139.1, 135.2, 131.1, 130.2, 118.1, 113.0, 100.0, 55.4, 51.1, 43.2, 38.2, 33.2, 28.2, 11.2; HRMS (ESI)  $[\text{M} + \text{H}]^+$  calculated 339.1709 found 339.1701.

**4-(4-Bromophenyl)-3,7,7-trimethyl-6,7,8,9-tetrahydroisoxazolo[5,4-*b*]quinolin-5(4H)-one (6e).** White solid; 75% yield ( $R_f = 0.33$  in hexane/EtoAc 60 : 40 v/v); MP: 224–226 °C (lit. 224–225 °C);<sup>17</sup> IR (KBr): 3430, 2926, 1642, 1568, 1503, 1453, 1254;  $^1\text{H}$

NMR ( $\text{DMSO}-d_6$ , 400 MHz): 10.61 (broad s, 1H), 7.08 (d,  $J = 8.0$  Hz, 2H), 6.79 (d,  $J = 8.0$  Hz, 2H), 4.90 (s, 1H), 2.51–2.39 (m, 2H), 2.19–2.15 (m, 1H), 2.03–1.99 (m, 1H), 1.861 (s, 3H), 1.18 (m, 6H), 1.09 (m, 3H);  $^{13}\text{C}$  NMR ( $\text{DMSO}-d_6$ , 100 MHz): 194.6, 159.5, 158.8, 157.8, 150.3, 139.3, 128.8, 113.8, 110.5, 96.4, 55.3, 50.8, 35.2, 32.5, 29.0, 27.2, 10.2; HRMS (ESI)  $[\text{M} + \text{H}]^+$  calculated 345.1415 found 345.1418.

**3-Methyl-4-phenyl-6,7,8,9-tetrahydroisoxazolo[5,4-*b*]quinolin-5(4H)-one (6f).** White solid; 70% yield ( $R_f = 0.35$  in hexane/EtoAc60 : 40 v/v); MP: 172–176 °C (lit. 174–175 °C);<sup>17</sup> IR (KBr): 3433, 2926, 1642, 1568, 1503, 1453, 1254;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 400 MHz): 8.94 (broad s, 1H), 7.55–7.40 (m, 5H), 4.17 (s, 1H), 2.81–74 (m, 2H), 2.53–2.39 (m, 2H), 2.22–2.16 (m, 3H), 2.09 (s, 1H), 1.48–1.42 (m, 1H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 100 MHz): 195.9, 168.8, 165.7, 155.8, 150.4, 148.1, 147.0, 132.1, 123.0, 121.7, 111.9, 52.9, 47.3, 31.7, 29.0, 27.4, 11.4; HRMS (ESI)  $[\text{M} + \text{H}]^+$  calculated  $\text{C}_{17}\text{H}_{16}\text{N}_2\text{O}_2$  281.1290 found 281.1295.

**4-(4-Chlorophenyl)-3-methyl-6,7,8,9-tetrahydroisoxazolo[5,4-*b*]quinolin-5(4H)-one (6g).** White solid; 73% yield ( $R_f = 0.32$  in hexane/EtoAc60 : 40 v/v); MP: 278–282 °C (lit. 278–279 °C);<sup>17</sup> IR (KBr): 3435, 2924, 1640, 1569, 1501, 1452, 1256;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 400 MHz): 8.08 (broad s, 1H), 7.27–7.18 (m, 4H), 5.08 (s, 1H), 2.55 (t,  $J = 5.6$  Hz, 2H), 2.38 (t,  $J = 5.6$  Hz, 2H), 2.09–1.96 (m, 2H), 1.94 (s, 3H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 100 MHz): 196.5, 162.8, 157.1, 145.0, 137.8, 131.6, 129.9, 129.4, 122.8, 113.0, 104.2, 37.1, 35.6, 28.8, 22.1, 11.2; HRMS (ESI)  $[\text{M} + \text{H}]^+$  calculated  $\text{C}_{17}\text{H}_{15}\text{ClN}_2\text{O}$  315.0900 found 315.0908.

## Conflicts of interest

The authors declare that they have no known conflict or competing financial interests that could have appeared to influence the work which is reported.

## Note added after first publication

This article replaces the version published on the 3<sup>rd</sup> of October 2023, which contained errors in the scheme layout.

## Acknowledgements

DG thanks to CSIR for providing JRF fellowship (Grant No. 09/119(0217)2019EMR-I), KSR thanks to Indian Science congress for providing Asutosh Mookerjee fellowship (Grant No. 595/73/2020-21) and CSIR for Emeritus fellowship (Grant No. 21(1117)/20/EMR-II). We are also thankful to the Institution of Excellence (IOE), University of Mysore, Manasagangotri, Mysuru-570006, India, for the spectral data and Indian Institute of chemical technology (IICT), Hyderabad-500007, India for X-ray crystallographic data.

## References

- (a) S. Maddila, S. B. Jonnalagadda, K. K. Gangu and S. N. Maddila, *Curr. Org. Synth.*, 2017, **14**, 634–653; (b) S. Maddila, K. K. Gangu, S. N. Maddila and S. B. Jonnalagadda, *Mol. Diversity*, 2017, **21**, 247–255.





- 2 (a) H. Cho, F. Török and B. Török, *Green Chem.*, 2014, **16**, 3623–3634; (b) E. Petruzzella, C. V. Chiroasca, C. S. Heidenga and J. D. Hoeschele, *Dalton Trans.*, 2015, **44**, 3384–3392; (c) A. Kokel, C. Schäfer and B. Török, *Green Chem.*, 2017, **19**, 3729–3751; (d) A. Kulkarni and B. Török, *Green Chem.*, 2010, **12**, 875–878.
- 3 (a) C. Karthikeyan, R. Malla, C. R. Ashby Jr, H. Amawi, K. L. Abbott, J. Moore, J. Chen, C. Balch, C. Lee and P. C. Flannery, *Cancer Lett.*, 2016, **376**, 118–126; (b) S. T. Selvi, V. Nadaraj, S. Mohan, R. Sasi and M. Hema, *Bioorg. Med. Chem.*, 2006, **14**, 3896–3903; (c) A. M. Hussein, F. A. Abu-Shanab and E. A. Ishak, *Phosphorus, Sulfur Silicon Relat. Elem.*, 2000, **159**, 55–68; (d) A. R. Azevedo, V. F. Ferreira, H. de Mello, L. R. Leão-Ferreira, A. V. Jabor, I. C. Frugulhetti, H. S. Pereira, N. Moussatche and A. M. R. Bernardino, *Heterocycl. Commun.*, 2002, **8**, 427–432; (e) L. W. Mohamed, M. A. Shaaban, A. F. Zaher, S. M. Alhamaky and A. M. Elshahar, *Bioorg. Chem.*, 2019, **83**, 47–54; (f) A. L. Lourenço, R. R. Salvador, L. A. Silva, M. S. Saito, J. F. Mello, L. M. Cabral, C. R. Rodrigues, M. A. Vera, E. M. Muri and A. M. de Souza, *Eur. J. Med. Chem.*, 2017, **135**, 213–229; (g) L. Li, W. Zhang, F. Lin, X. Lu, W. Chen, X. Li, X. Zhou, R. Su, L. Wang and Z. Zheng, *Eur. J. Med. Chem.*, 2019, **173**, 107–116; (h) C. Kurumurthy, B. Veeraswamy, P. S. Rao, G. S. Kumar, P. S. Rao, V. L. Reddy, J. V. Rao and B. Narsaiah, *Bioorg. Med. Chem. Lett.*, 2014, **24**, 746–749; (i) A. Cappelli, G. Bini, S. Valenti, G. Giuliani, M. Paolino, M. Anzini, S. Vomero, G. Giorgi, A. Giordani and L. P. Stasi, *J. Med. Chem.*, 2011, **54**, 7165–7175.
- 4 (a) T. Umar, S. Shalini, M. K. Raza, S. Gusain, J. Kumar, P. Seth, M. Tiwari and N. Hoda, *Eur. J. Med. Chem.*, 2019, **175**, 2–19; (b) L.-Y. Zeng, T. Liu, J. Yang, Y. Yang, C. Cai and S. Liu, *ACS Comb. Sci.*, 2017, **19**, 437–446.
- 5 I. Kanwal, N. Rasool, S. H. M. Zaidi, Z. A. Zakaria, M. Bilal, M. A. Hashmi, A. Mubarik, G. Ahmad and S. A. A. Shah, *Molecules*, 2022, **27**, 360.
- 6 (a) I. V. Taydakov, A. A. Akkuzina, R. I. Avetisov, A. V. Khomyakov, R. R. Saifutiyarov and I. C. Avetissov, *J. Lumin.*, 2016, **177**, 31–39; (b) G. Lewińska, K. Khachatryan, K. S. Danel, Z. Danel, J. Sanetra and K. W. Marszałek, *Polymers*, 2020, **12**, 2707.
- 7 (a) M. García, I. Romero and J. Portilla, *ACS Omega*, 2019, **4**, 6757–6768; (b) J. Orrego-Hernández, C. Lizarazo, J. Cobo and J. Portilla, *RSC Adv.*, 2019, **9**, 27318–27323.
- 8 (a) J. Nizioł, A. Danel, G. Boiteux, J. Davenas, B. Jarosz, A. Wisla and G. Seytre, *Synth. Met.*, 2002, **127**, 175–180; (b) E. Gondek, A. Danel, J. Nizioł, P. Armatys, I. V. Kityk, P. Szlachcic, M. Karelus, T. Uchacz, J. Chwast and G. Lakshminarayana, *J. Lumin.*, 2010, **130**, 2093–2099.
- 9 (a) P. Friedlaender, *Berichte Dtsch. Chem. Ges.*, 1882, **15**, 2572–2575; (b) J. Marco-Contelles, E. Pérez-Mayoral and A. Samadi, *Chem. Rev.*, 2009, **109**, 2652–2671; (c) C.-C. Cheng and S.-J. Yan, *Org. React.*, 2004, **28**, 37–201; (d) M. Fallah-Mehrjardi, *Mini-Rev. Org. Chem.*, 2017, **14**, 187–196; (e) G. A. Ramann and B. J. Cowen, *Molecules*, 2016, **21**, 986; (f) L. M. Nainwal, S. Tasneem, W. Akhtar, G. Verma, M. F. Khan, S. Parvez, M. Shaquiquzzaman, M. Akhter and M. M. Alam, *Eur. J. Med. Chem.*, 2019, **164**, 121–170.
- 10 (a) S. L. Wang, Y. P. Liu, B. H. Xu, X. H. Wang, B. Jiang and S. J. Tu, *Tetrahedron*, 2011, **67**, 9417–9425; (b) J. Quiroga, A. Hormaza, B. Insuasty and M. Marquez, *J. Heterocycl. Chem.*, 1998, **35**, 409–412; (c) I. Drizin, R. J. Altenbach, S. A. Buckner, K. L. Whiteaker, V. E. Scott, J. F. Darbyshire, V. Jayanti, R. F. Henry, M. J. Coghlan and M. Gopalakrishnan, *Bioorg. Med. Chem.*, 2004, **12**, 1895–1904; (d) J. Quiroga, J. Portilla, H. Serrano, R. Abonia, B. Insuasty, M. Noguera and J. Cobo, *Tetrahedron Lett.*, 2007, **48**, 1987–1990.
- 11 (a) K. D. Shin, M.-Y. Lee, D.-S. Shin, S. Lee, K.-H. Son, S. Koh, Y.-K. Paik, B.-M. Kwon and D. C. Han, *J. Biol. Chem.*, 2005, **280**, 41439–41448; (b) J. P. Demers, W. E. Hageman, S. G. Johnson, D. H. Klaubert, R. A. Look and J. B. Moore, *Bioorg. Med. Chem. Lett.*, 1994, **4**, 2451–2456; (c) D. Simoni, M. Roberti, F. P. Invidiata, R. Rondanin, R. Baruchello, C. Malagutti, A. Mazzali, M. Rossi, S. Grimaudo and F. Capone, *J. Med. Chem.*, 2001, **44**, 2308–2318.
- 12 (a) M. Rowley, H. B. Broughton, I. Collins, R. Baker, F. Emms, R. Marwood, S. Patel, S. Patel, C. I. Ragan and S. B. Freedman, *J. Med. Chem.*, 1996, **39**, 1943–1945; (b) S. J. Wittenberger, *J. Org. Chem.*, 1996, **61**, 356–358; (c) G. Dannhardt, P. Dominiak and S. Laufer, *Arzneimittelforschung*, 1993, **43**, 441–444; (d) T. Tatee, K. Narita, S. Kurashige, S. I. H. Miyazaki, H. Yamanaka, M. Mizugaki and T. S. H. Fukuda, *Chem. Pharm. Bull.*, 1987, **35**, 3676–3690.
- 13 (a) M. Suzuki, H. Iwasaki, Y. Fujikawa, M. Sakashita, M. Kitahara and R. Sakoda, *Bioorg. Med. Chem. Lett.*, 2001, **11**, 1285–1288; (b) P. Pevarello, R. Amici, M. G. Brasca, M. Villa and M. Varasi, *Syst.*, 1999, **3**, 301–339; (c) M. S. Chande, R. S. Verma, P. A. Barve, R. R. Khanwelkar, R. B. Vaidya and K. B. Ajaikumar, *Eur. J. Med. Chem.*, 2005, **40**, 1143–1148; (d) V. K. DC, B. S. Chethan, D. Gowda, K. S. Rangappa and N. K. Lokanath, *J. Mol. Struct.*, 2023, 135770.
- 14 (a) K. S. S. Kumar, T. R. Swaroop, K. B. Harsha, K. H. Narasimhamurthy and K. S. Rangappa, *Tetrahedron Lett.*, 2012, **53**, 5619–5623; (b) K. B. Harsha and K. S. Rangappa, *J. Chem. Sci.*, 2017, **129**, 141; (c) A. B. Ramesha, G. M. Raghavendra, K. N. Nandeesh, K. S. Rangappa and K. Mantelingu, *Tetrahedron Lett.*, 2013, **54**, 95–100; (d) G. M. Raghavendra, A. B. Ramesha, C. N. Revanna, K. N. Nandeesh, K. Mantelingu and K. S. Rangappa, *Tetrahedron Lett.*, 2011, **52**, 5571–5574; (e) K. Vinaya, P. D. Shivaramu, G. K. Chandrashekhara, S. Chandrappa and K. S. Rangappa, *Lett. Org. Chem.*, 2018, **15**, 241–245.
- 15 M. G. Sharma, R. M. Vala and H. M. Patel, *RSC Adv.*, 2020, **10**, 35499–35504.
- 16 D. M. Patel, M. G. Sharma, R. M. Vala, I. Lagunes, A. Puerta, J. M. Padrón, D. P. Rajani and H. M. Patel, *Bioorg. Chem.*, 2019, **86**, 137–150.
- 17 E. A. Muravyova, V. V. Tkachenko, S. M. Desenko, Y. V. Sen'ko, T. J. Müller, E. V. Vashchenko and V. A. Chebanov, *Arkivoc*, 2013, **2013**, 338–371.

