Behavior of 5-amino-3-methylisoxazole in multicomponent heterocyclizations with carbonyl compounds under thermal heating and non-classical conditions

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Abstract

Three-component heterocyclizations of 5-amino-3-methylisoxazole, cyclohexanedione derivatives, and aromatic aldehydes, including salicylic aldehydes, are studied under conventional thermal heating, microwave irradiation and ultrasonication. A dependence of the direction of the reaction on the structure of the aldehyde and the reaction conditions was found, which allowed selective synthesis of 6,7,8,9-tetrahydroisoxazolo[5,4-*b*]quinolin-5(4*H*)-ones and 2,3,4,9-tetrahydro-1*H*-xanthen-1-ones. Key stages of the reaction mechanisms are discussed.

Keywords: Multicomponent reaction, heterocycles, 5-amino-3-methylisoxazole, microwave-assisted synthesis, ultrasound-assisted synthesis

Introduction

One of the main challenges of topical chemistry is the efficient design and synthesis of biologically active molecules. The discovery of high-throughput screening has tremendously increased the demand for new testing compounds and, therefore, multicomponent reactions (MCRs) became increasingly useful tools for the synthesis of biologically active compounds. These reactions enable multi-step syntheses to be conducted in a one-pot fashion to obtain a variety of invaluable products. Moreover, MCRs can dramatically reduce the generation of

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chemical waste and reduce the cost of the starting materials. In the past several years various multicomponent reactions that can provide easy and rapid accesses to useful functionalized multiple ring structures have been developed.

Isoxazole is an important heterocyclic unit, which has been widely used as a key building-block. Its derivatives are endowed with many pharmacological properties, such as hypoglycemic, analgesic, anti-inflammatory, antibacterial, anti-HIV, and anticancer activity,[1-3] as well as useful activities in conditions like schizophrenia, hypertension, and Alzheimer's disease.[4-6] Among the isoxazole derivatives, isoxazolopyridines have evoked interest and concern because they showed muscle relaxant, anticonvulsant and CNS depressant activities.[7] To the best of our knowledge, multicomponent reactions involving isoxazole core and carbonyl compounds have been insufficiently studied and there have been only a few publications on the subject. For instance, Shi *et al.*[8] studied the reaction of the aldehydes, mercaptoacetic acid and 5-aminoisoxazole in order to develop diversity-oriented synthesis of novel 1,4-thiazepan-3-ones derivatives embedded with the isoxazole motif. In another publication[9] some new 4-aza-2,3-didehydro-podophyllotoxin congeners were synthesized by applying a multicomponent route involving the condensation of substituted aminoisoxazole, tetronic acid and aromatic aldehydes in refluxing ethanol.

Tu and co-authors[10] studied similar microwave-assisted three-component reaction of 5-amino-3-methylisoxazole and aldehydes with several active methylene compounds, such as tetronic acid, Meldrum's acid, 1,3-indanedione and 1,3-cyclohexanediones. There was shown a superior advantage of water as reaction medium and microwave irradiation to promote these treatments. It is worthy to note that, for some reasons which remained obscure, the reaction involving dimedone gave isoxazolo[5,4-*b*]pyridine while in the case of 1,3-cyclohexanedione the final compound was its dihydro derivative (Scheme 1).

Condensation with Meldrum's acid via ring-opening and release of acetone and carbon dioxide led to the formation of 4.7-dihydroisoxazolo[5,4-*b*]pyridine-6(5*H*)-one.[10] However, in another article[11] the same group reported that the reaction of Meldrum's acid with 5-amino-3-methylisoxazole and aldehydes under analogous conditions yielded spiro[pyrazolo[1,3]-dioxanopyridine]-4,6-diones instead of isoxazolopyridinones (Scheme 1).

In addition, the three-component reaction of 5-amino-3-methylisoxazole with 2-hydroxy-1,4-naphthoquinone and aromatic aldehydes leading to benzo[*h*]isoxazolo[5,4-*b*]quinoline-5,6-diones was studied by Tu *et al.* in a subsequent article.[12]

Thus, it is obvious that published results provide insufficient and sometimes conflicting information on multicomponent heterocyclizations of 5-amino-3-methylisoxazole and, therefore, such processes are challenging objects of detailed study. In the present article we continue developing our concept of tuning the selectivity of MCRs[13-22] (for reviews see refs 13-15). and disclose our recent results in the field of study of MCRs involving 5-amino-3-methylisoxazole, 1,3-cyclohexanediones, and aromatic aldehydes including salicylaldehydes using different reaction conditions (temperature regimes, solvents, catalysts and modes of activation).

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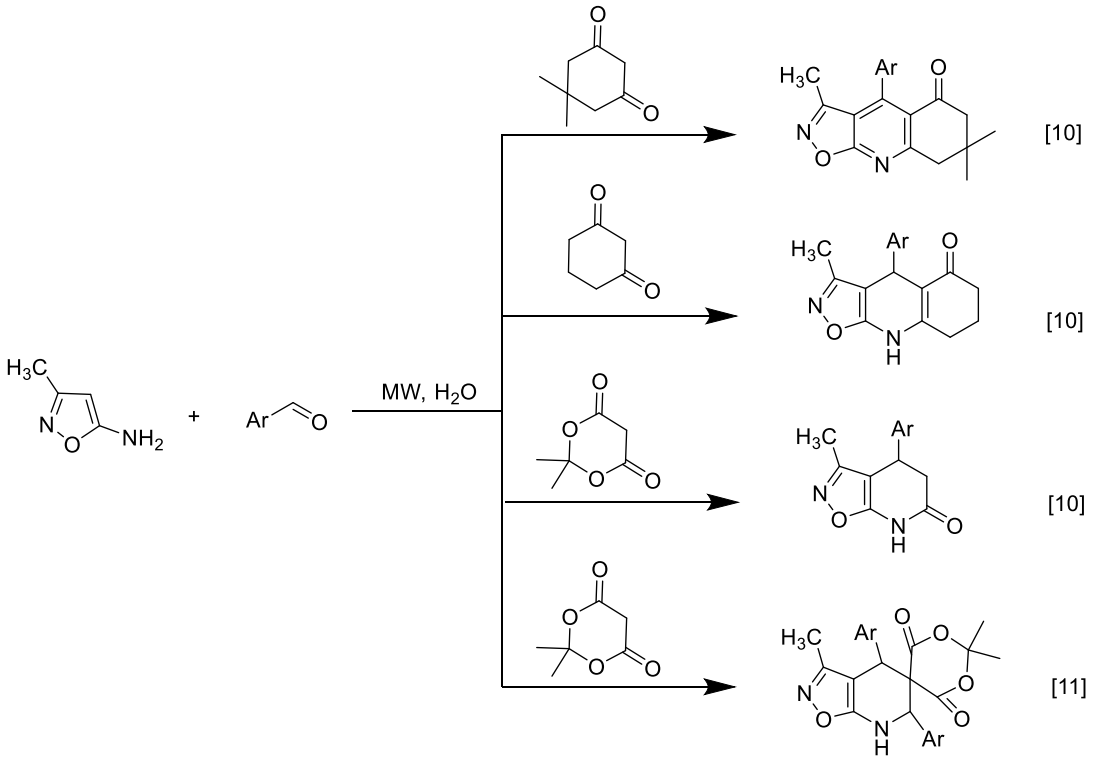

Scheme 1. Some known multicomponent reactions involving 5-amino-3-methylisoxazole

Results and Discussion

The MCR between 5-amino-3-methylisoxazole (**1**), 4-bromobenzaldehyde (**2c**), and dimedone (**3b**) was chosen in order to search for optimal conditions (solvent, activation method, reaction temperature and time). Among the solvents tested (water, different alcohols, DMF, HOAc) water, ethanol and DMF were selected for the model reaction due to better preliminary results.

Ultrasonic-promoted (US) procedures gave the worst results with respect to yields and purity of 4-(4-bromophenyl)-3,7,7-trimethyl-6,7,8,9-tetrahydroisoxazolo[5,4-*b*]quinolin-5(4*H*)-one (**4l**) which was isolated as sole reaction product in the MCR studied (Table 1). The situation was better in the case of conventional heating (Δ) of the starting materials in these solvents - yields of the target heterocycle **4l** lay in the range from 50% for EtOH to 75% for DMF while their purity was about 95% (NMR control). However, irrespective of the solvent type, the best yields of the compound **4l** (~90%) with high purity were observed when the MCR was carried out under microwave irradiation (MW) at 120 °C. At lower temperatures the yields of compound **4l** decreased sufficiently while carrying out the reaction at temperatures higher than 140 °C gave the final heterocycles in unsatisfactory purity or even led to decomposition.

Thus, the above-mentioned results for the model three-component reaction allowed us to choose refluxing the starting materials in DMF or the microwave-assisted reaction in ethanol as procedures for the further study.

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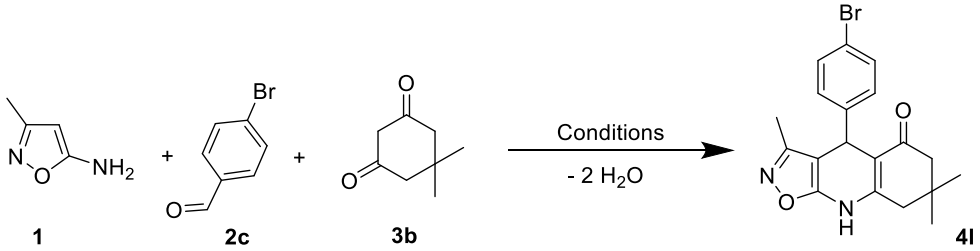
It was found that MCRs between 5-amino-3-methylisoxazole (**1**), aldehydes **2a-i**, and cyclic *β*-diketones **3a-c** in boiling DMF led to the formation of 4-aryl-6,7,8,9-tetrahydroisoxazolo-[5,4-*b*]quinolin-5(4*H*)-ones **4a-z** in 55-91% yields (Scheme 2, Table 2). It should be noted that the microwave-assisted procedure in some cases gave the desired targets in higher yields than conventional heating as it was observed for model reactions (entries 3, 11, 12, 14. 19, 20 and 24), however sometimes the yields were practically the same under both activation methods (entries 1, 2, 4, 6, 7, 13, 15 and 20).

Table 1. Optimization of the conditions of three-component reaction between 5-amino-3-methyl-isoxazole, 4-bromobenzaldehyde and 5,5-dimethylcyclohexane-1.3-dione



Solvent	Method	T (°C)	Time (min)	Yield
	Δ	~100	60	58
H_2O	MW	120	5	91
	US	~25	720	38
	Δ	~78	180	48
EtOH	MW	120	5	89
	US	~25	720	40
	Δ	~153	1	76
DMF	MW	120	5	92
	US	~25	720	41

When 5-(4-chlorophenyl)cyclohexane-1,3-dione (**3c**) was used the final compounds contained two chiral centers and in several cases the formation of mixtures of diastereomers with different ratios were isolated (entries 19, 20, 22-25, Table 2).

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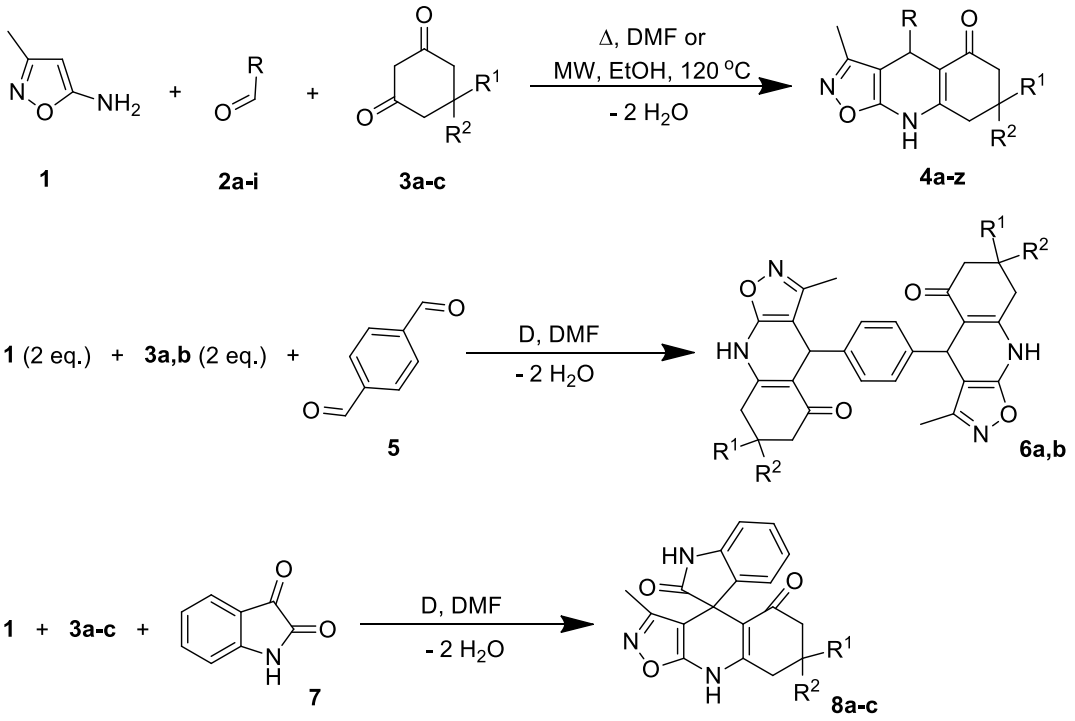

Scheme 2. Multicomponent microwave-assisted synthesis of products **4a-z**, **6a,b** and **8a-c.**

Table 2. Three-component synthesis of compounds **4a-z, 6a-b** and **8a-c**

Entry	Building-blocks: Carbonyl compound		β-Diketone			Reaction product	Yield, %	
		R		R^1	R^2		Δ	MW
1	**2a**	C_6H_5	**3a**	H	H	**4a**	65	68
2	**2b**	4-ClC_6H_4	**3a**	H	H	**4b**	75	74
3	**2c**	4-BrC_6H_4	**3a**	H	H	**4c**	75	90
4	**2d**	4-$CH_3C_6H_4$	**3a**	H	H	**4d**	75	76
5	**2e**	4-$CH_3OC_6H_4$	**3a**	H	H	**4e**	85	-
6	**2f**	4-$O_2NC_6H_4$	**3a**	H	H	**4f**	60	62
7	**2g**	4-$CH_3OCOC_6H_4$	**3a**	H	H	**4g**	60	62
8	**2h**	4-$(CH_3)_2NC_6H_4$	**3a**	H	H	**4h**	65	-
9	**2i**	$(CH_3)_2CH$	**3a**	H	H	**4i**	75	-
10	**2a**	C_6H_5	**3a**	CH_3	CH_3	**4j**	75	-
11	**2b**	4-ClC_6H_4	**3b**	CH_3	CH_3	**4k**	65	80
12	**2c**	4-BrC_6H_4	**3b**	CH_3	CH_3	**4l**	76	92
13	**2d**	4-$CH_3C_6H_4$	**3b**	CH_3	CH_3	**4m**	60	62
14	**2e**	4-$CH_3OC_6H_4$	**3b**	CH_3	CH_3	**4n**	71	90

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Table 2. Continued

Entry	Building-blocks: Carbonyl compound		β-Diketone			Reaction product		
		R		R^1	R^2		Yield, %	
							Δ	MW
15	**2f**	4-$NO_2C_6H_4$	**3b**	CH_3	CH_3	**4o**	55	58
16	**2g**	4-$CH_3OCOC_6H_4$	**3b**	CH_3	CH_3	**4p**	90	-
17	**2h**	4-$(CH_3)_2NC_6H_4$	**3b**	CH_3	CH_3	**4q**	90	-
18	**2i**	$(CH_3)_2CH$	**3b**	CH_3	CH_3	**4r**	85	-
19	**2a**	C_6H_5	**3c**	H	4-ClC_6H_4	**4s**	55 (50/50)[a]	80 (50/50)[a]
20	**2b**	4-ClC_6H_4	**3c**	H	4-ClC_6H_4	**4t**	65 (50/50)[a]	67 (50/50)[a]
21	**2c**	4-BrC_6H_4	**3c**	H	4-ClC_6H_4	**4u**	90 (100/0)[a]	-
22	**2d**	4-$CH_3C_6H_4$	**3c**	H	4-ClC_6H_4	**4v**	90 (95/5)[a]	-
23	**2e**	4-$CH_3OC_6H_4$	**3c**	H	4-ClC_6H_4	**4w**	91 (95/5)[a]	-
24	**2f**	4-$NO_2C_6H_4$	**3c**	H	4-ClC_6H_4	**4x**	58 (50/50)[a]	64 (50/50)[a]
25	**2g**	4-$CH_3OCOC_6H_4$	**3c**	H	4-ClC_6H_4	**4y**	85 (90/10)[a]	-
26	**2h**	4-$(CH_3)_2NC_6H_4$	**3c**	H	4-ClC_6H_4	**4z**	90 (100/0)[a]	-
27	**5**	-	**3a**	H	H	**6a**	56	-
28	**5**	-	**3b**	CH_3	CH_3	**6b**	60	-
29	**7**	-	**3a**	H	H	**8a**	75	-
30	**7**	-	**3b**	CH_3	CH_3	**8b**	72	-
31	**7**	-	**3c**	H	4-ClC_6H_4	**8c**	65	-

[a] ratio (%) of diastereomers according to ^{1}H NMR data.

In the case of terephthalic aldehyde (**5**) in the MCR were involved both its carbonyl groups which allowed to isolate compounds **6a** and **6b** in 56-60% yields (amine **1** and diketones **3a,b** were used in the reaction in 2-fold excess). Isatine was also introduced in this three-component heterocyclization instead of an aldehyde to give spiro-compounds **8a-c** in 65-75% yields (Scheme 2, Table 2). Despite the presence of two chiral centers in the heterocycle **8c** no mixture of diastereomers was obtained in this case.

Application of *o*-salicylic aldehyde in MCRs may complicate their proceeding due to different intramolecular cyclizations involving the OH-group.[23-26] For instance, Gorobets *et al.*[23] described a Biginelli-type three-component reaction between 3-amino-1,2,4-triazole, several carbonyl containing CH-acids and aldehydes. They showed that in the case of salicylic aldehyde depending on conditions applied the treatment yielded either 4,5,6,7-tetrahydro[1,2,4]-

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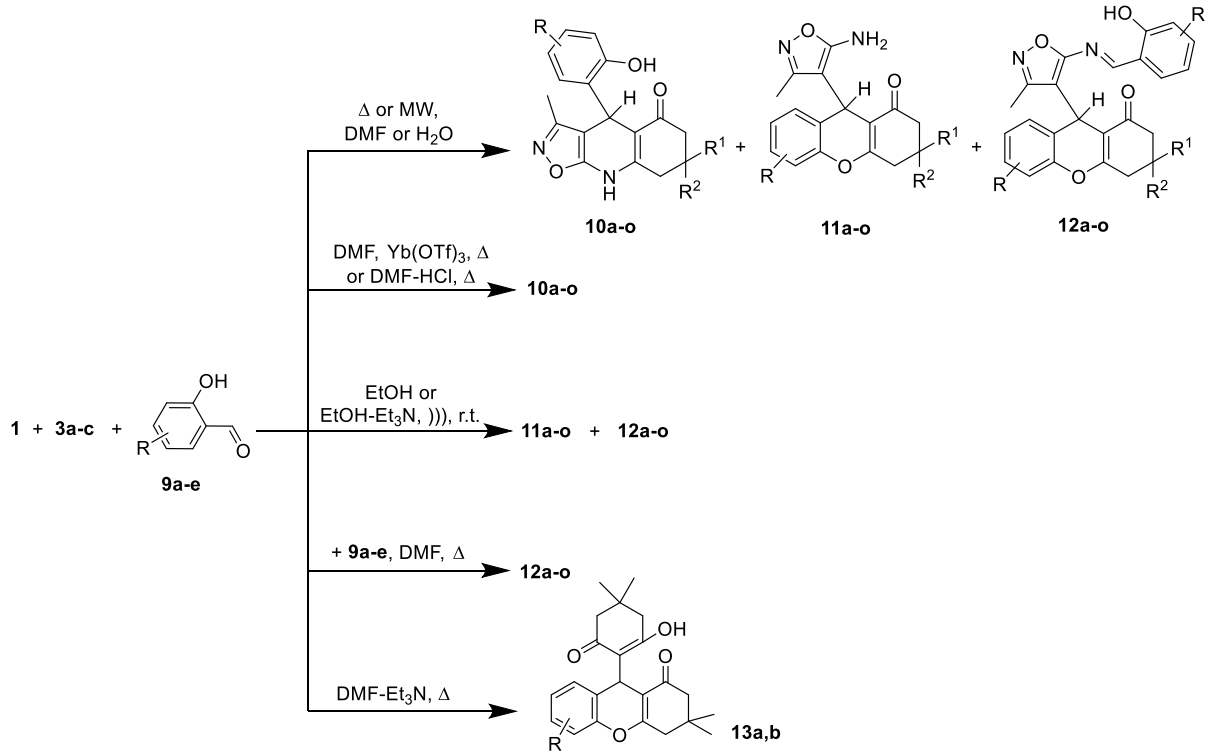
triazolo[1,5-*a*]pyrimidines or 11,12-dihydro-5,11-methano[1,2,4]triazolo[1,5-*c*][1,3,5]benzoxadiazocines. On the other hand, Světlík and Kettmann[24] in a very similar reaction observed the formation of spiro-compounds instead of bridged heterocycles. Another direction for such reaction giving chromeno[4,3-*d*]pyrazolo[3,4-*b*]pyridines was described by Frolova *et al.*[25] and Světlík *et al.*[26]

In our case the three-component reaction of 5-amino-3-methylisoxazole (**1**), cyclic 1,3-diketones **3a-c** and salicylic aldehydes **9a-e** in DMF or H_2O under conventional thermal heating or under microwave irradiation yielded the mixture of 6,7,8,9-tetrahydroisoxazolo[5,4-*b*]-quinolin-5(4*H*)-ones **10a-o**, 2,3,4,9-tetrahydro-1*H*-xanthen-1-ones **11a-o** and **12a-o** in 1:3:1 ratio (Scheme 3, Table 3). Heterocycles obtained were separated by crystallization – compounds **10a-o** were precipitated from acetone while compounds **11a-o** and **12a-o** from ethyl acetate. It should be noted that mode of activation had no influence on the ratio of substances in the mixture.



Scheme 3. Multicomponent reactions of 5-amino-3-methylisoxazole (**1**), cyclic 1,3-diketones **3a-c** and salicylaldehydes **9a-e.**

By using pure ethanol or its mixture with a catalytic amount of Et_3N the formation of quinolinones **10** was avoided and only compounds **11a-o** and **12a-o** were isolated in individual state by crystallization from ethyl acetate. In the case of basic catalysis the mixtures were enriched with compound **11** (75%) while the ratio of **11** and **12** under neutral conditions was 1:1. It can be explained by influence of acidity of the reaction medium on the formation of

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azomethine since basic additives did not promote the reaction leading to such imines in contrast to neutral or acidic conditions.

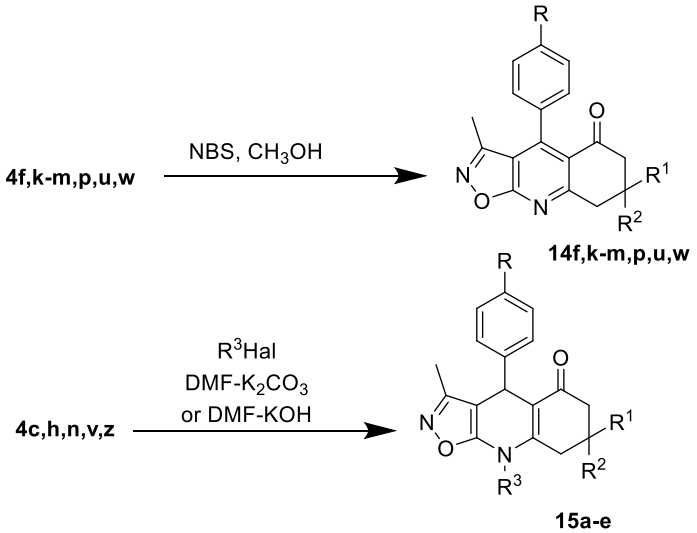
It is noteworthy that the MCR of the starting compounds in boiling in DMF in the presence of catalytic amounts of Et_3N yielded xanthen-1-ones **13a-c** formed without participation of the aminoisoxazole building-block.

Addition to the reaction mixture of a second equivalent of aldehyde allowed directing the MCR in boiling DMF or EtOH towards the exclusive formation of azomethines **12a-o** while the selective procedure for the synthesis of compounds **11a-o** was not elaborated.

Isoxazolo[5,4-*b*]quinolinones **10a-o** were selectively obtained when 5-amino-3-methyl-isoxazole **1**, diketones **3a-c**, and salicylic aldehydes **9a-e** reacted in boiling DMF in the presence of catalytic amounts of HCl or $Yb(OTf)_3$ (5 mol %). The yield of this reaction was moderate [45-50% for $Yb(OTf)_3$], however, this result gives a strong background to be elaborated in a future highly effective and selective procedure for the synthesis of compounds like **10** with application of water-stable Lewis acids.

Additionally it should be noted that oxidation of compounds **4f,k-m,p,u,w** with NBS afforded isoxazolo[5,4-*b*]quinolin-5(4*H*)-ones **14f,k-m,p,u,w** (Scheme 4). Furthermore, the pyridine NH in heterocycles **4** was easily alkylated with alkyl halides in DMF – K_2CO_3 or DMF – KOH to give compounds **15a-e** in 42-65% yields (Scheme 4).

Most likely the three-component reaction of 5-amino-3-methylisoxazole, aldehydes, and derivatives of 1,3-cyclohexanedione pass *via* formation of Michael adduct **I** (Scheme 5) and its further cyclization due to the nucleophilic attack at the carbonyl by NH_2-group giving up isoxazoloquinolinones **4**, **6**, **8** or **10**.



15a-e: a R = 4-BrC_6H_4, R^1 = H, R^2 = H, R^3 = C_2H_5; b R = 4-$N(CH_3)_2C_6H_4$, R^1 = H, R^2 = H, R^3 = $CH_2C_6H_5$; c R = 4-$CH_3OC_6H_4$, R^1 = CH_3, R^2 = CH_3, R^3 = $CH_2C_6H_5$; d R = 4-$CH_3C_6H_4$, R^1 = H, R^2 = 4-ClC_6H_4, R^3 = C_2H_5; e R = 4-$CH_3C_6H_4$, R^1 = H, R^2 = 4-ClC_6H_4, R^3 = $CH_2C_6H_5$; f R = 4-$N(CH_3)_2C_6H_4$, R^1 = H, R^2 = 4-ClC_6H_4, R^3 = $CH_2C_6H_5$

Scheme 4. Oxidation and N-alkylation of heterocycles **4.**

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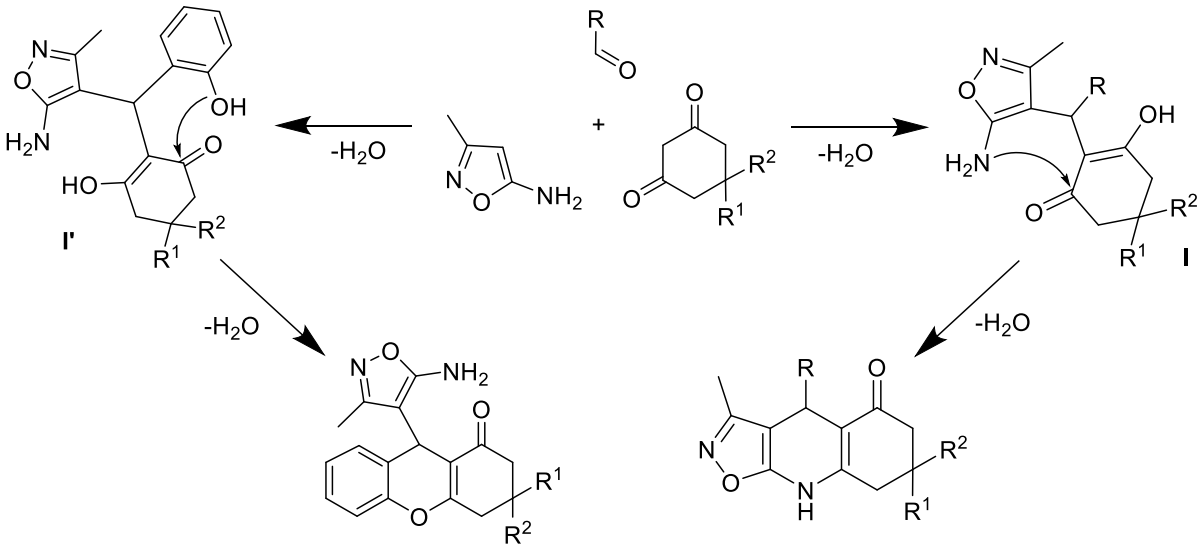
However, in the case of salicylic aldehyde (intermediate **I'**) there is an alternative OH-nucleophilic reaction center which is able to take part in the heterocyclization with formation of the pyran ring (compounds **11** and **12**) instead of the pyridine core. According to experimental data obtained when the salicylic aldehyde is used acidic catalysis with Brønsted or Lewis acids promotes the Hantzsch type of MCR, while a presence in the reaction mixture of Et_3N redirects the reaction towards the formation of xanthenones.



Scheme 5. Possible key-stages of the three-component reaction of 5-amino-3-methylisoxazole, aldehydes, and 1,3-cyclohexanediones.

Identification of all the compounds synthesized was made with help of elemental analysis, MS spectrometry, 1D and 2D NMR spectroscopy.

Thus, ^{1}H NMR spectra of compounds **4a-z**, **6a,b** and **10a-o** showed singlet of methine proton at δ 4.8-5.25 (disappearing in compounds **14**), signals of CH_2-groups of cycloalkenone fragment in the range of δ 2.0–2.9, a singlet of the NH proton near 10.4-11.0 ppm (disappearing in compounds **15**) and signals of aryl group and terminal substituents at appropriate positions. The spectra of the compounds **4s-z** additionally contain singlets of the CH-group of cycloalkenone moiety and in the case of mixtures of diastereomers (see Table 2) – two sets of identical signals. The spectra of the compounds **8a-c** exhibit no signal of methine group in pyridine ring but contain second broad singlet of NH-group of the isatin fragment.

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Table 3. Three-component synthesis of compounds **10a-o, 11a-o** and **12a-o**

Entry	Building-blocks					Reaction product	
	Salicylaldehyde		β-Diketone				
		R		R^1	R^2		Yield, %
1	**9a**	H	**3a**	H	H	**10a**	45[a]
2	**9b**	5-Cl	**3a**	H	H	**10b**	42[a]
3	**9c**	5-Br	**3a**	H	H	**10c**	38[a]
4	**9d**	3-CH_3O	**3a**	H	H	**10d**	40[a]
5	**9e**	5-NO_2	**3a**	H	H	**10e**	57[a]
6	**9a**	H	**3b**	CH_3	CH_3	**10f**	42[a]
7	**9b**	5-Cl	**3b**	CH_3	CH_3	**10g**	54[a]
8	**9c**	5-Br	**3b**	CH_3	CH_3	**10h**	51[a]
9	**9d**	3-CH_3O	**3b**	CH_3	CH_3	**10i**	55[a]
10	**9e**	5-NO_2	**3b**	CH_3	CH_3	**10j**	62[a]
11	**9a**	H	**3c**	H	4-ClC_6H_4	**10k**	38[a] (50/50)[d]
12	**9b**	5-Cl	**3c**	H	4-ClC_6H_4	**10l**	45[a] (50/50)[d]
13	**9c**	5-Br	**3c**	H	4-ClC_6H_4	**10m**	51[a] (50/50)[d]
14	**9d**	3-CH_3O	**3c**	H	4-ClC_6H_4	**10n**	32[a] (50/50)[d]
15	**9e**	5-NO_2	**3c**	H	4-ClC_6H_4	**10o**	38[a] (50/50)[d]
16	**9a**	H	**3a**	H	H	**11a**	36[b]
17	**9b**	5-Cl	**3a**	H	H	**11b**	38[b]
18	**9c**	5-Br	3a	H	H	**11c**	41[b]
19	**9d**	3-CH_3O	**3a**	H	H	**11d**	42[b]
20	**9e**	5-NO_2	**3a**	H	H	**11e**	38[b]
21	**9a**	H	**3b**	CH_3	CH_3	**11f**	45[b]
22	**9b**	5-Cl	**3b**	CH_3	CH_3	**11g**	42[b]
23	**9c**	5-Br	**3b**	CH_3	CH_3	**11h**	40[b]
24	**9d**	3-CH_3O	**3b**	CH_3	CH_3	**11i**	40[b]
25	**9e**	5-NO_2	**3b**	CH_3	CH_3	**11j**	35[b]
26	**9a**	H	**3c**	H	4-ClC_6H_4	**11k**	32[b](50/50)[d]
27	**9b**	5-Cl	**3c**	H	4-ClC_6H_4	**11l**	38[b](50/50)[d]
28	**9c**	5-Br	**3c**	H	4-ClC_6H_4	**11m**	32[b](50/50)[d]
29	**9d**	3-CH_3O	**3c**	H	4-ClC_6H_4	**11n**	34[b](50/50)[d]
30	**9e**	5-NO_2	**3c**	H	4-ClC_6H_4	**11o**	38[b](50/50)[d]
31	**9a**	H	**3a**	H	H	**12a**	53[c]
32	**9b**	5-Cl	**3a**	H	H	**12b**	58[c]
33	**9c**	5-Br	**3a**	H	H	**12c**	62[c]
34	**9d**	3-CH_3O	**3a**	H	H	**12d**	50[c]
35	**9e**	5-NO_2	**3a**	H	H	**12e**	55[c]

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Table 3. Continued

Entry	Building-blocks					Reaction product	
	Salicylaldehyde		*β*-Diketone				
		R		R^1	R^2		Yield, %
36	**9a**	H	**3b**	CH_3	CH_3	**12f**	80[c]
37	**9b**	5-Cl	**3b**	CH_3	CH_3	**12g**	75[c]
38	**9c**	5-Br	**3b**	CH_3	CH_3	**12h**	72[c]
39	**9d**	3-CH_3O	**3b**	CH_3	CH_3	**12i**	68[c]
40	**9e**	5-NO_2	**3b**	CH_3	CH_3	**12j**	65[c]
41	**9a**	H	**3c**	H	4-ClC_6H_4	**12k**	69[c](50/50)[d]
42	**9b**	5-Cl	**3c**	H	4-ClC_6H_4	**12l**	60[c](50/50)[d]
43	**9c**	5-Br	**3c**	H	4-ClC_6H_4	**12m**	62[c](50/50)[d]
44	**9d**	3-CH_3O	**3c**	H	4-ClC_6H_4	**12n**	60[c](50/50)[d]
45	**9e**	5-NO_2	**3c**	H	4-ClC_6H_4	**12o**	57[c](50/50)[d]

[a] DMF-HCl, Δ; [b] DMF, Δ; [c] double excess of the aldehyde, DMF, Δ; [d] ratio (%) of diastereomers according to ^{1}H NMR data.

NOESY spectra of compounds **4**, **6**, **8** and **10** contain cross-peaks of CH-group and *ortho*-protons of R-substituent with CH_3-group in isoxazole fragment but not with pyridine NH (Fig. 1) allowing excluding the formation of position isomeric structures **16.** This fact was additionally proven with COSY and HMBC experiments.

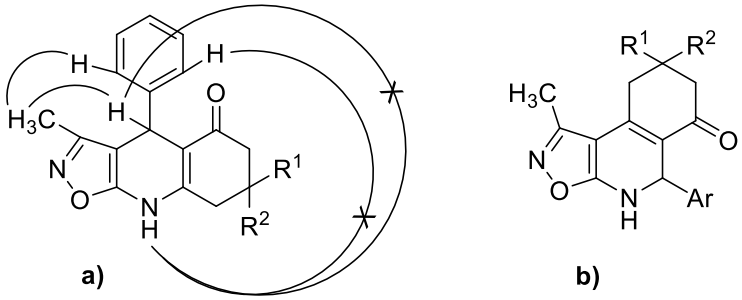

Figure 1. Some data of NOESY experiments (a) and alternative structure (b) for compounds **4**, **6** and **10.**

The ^{1}H NMR spectra of the compounds **11a-o** and **12a-o** contain no signal of NH- and CH-group from the isoxazole moiety but exhibit broad singlets of NH_2 group at 6.35-6.40 ppm (for heterocycles **11a-o**) or sharp singlet of azomethine CH (8.95-9.05 ppm) and signals of protons of second aryl ring (for heterocycles **12a-o**). Additionally, the structure of heterocycles **12** was proven by analysis of correlations in HSQC, HMBC and NOESY spectra.

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Conclusions

In summary, three-component heterocyclizations between 5-amino-3-methylisoxazole, derivatives of cyclohexanedione, and aromatic aldehydes were studied under conventional thermal heating, microwave irradiation, and ultrasonication. These reactions led to the formation of 4-aryl-6,7,8,9-tetrahydroisoxazolo[5,4-*b*]quinolin-5(4*H*)-ones and application of microwave activation in the most cases gave the best results from the viewpoint of yields and purity of the final compounds. Salicylic aldehyde as a substrate complicated the reaction which due to competition of NH_2 and OH reaction centers often gave mixtures of 4-(2-hydroxyaryl)-6,7,8,9-tetrahydroisoxazolo[5,4-*b*]quinolin-5(4*H*)-ones and 2,3,4,9-tetrahydro-1*H*-xanthen-1-ones. However, variation of the catalyst and the reaction conditions allowed tuning the selectivity of the heterocyclization. Thus, in the presence of Brønsted or Lewis acids heating of the starting materials in DMF or H_2O led to the formation of isoxazoloquinolinones while ultrasonication in EtOH-Et_3N gave only tetrahydroxanthenones.

Experimental Section

General. The melting points of all compounds synthesized were determined with a Gallenkamp melting point apparatus (for the mixture of diastereomers melting points were not measured). The NMR spectra were recorded at 400 MHz (100 MHz for ^{13}C) and at 200 MHz (50 MHz for ^{13}C) with a Varian Unity Plus-400 and Varian Mercury VX-200 spectrometers, respectively. The MS spectra were measured on a GC-MS Varian 1200L (ionizing voltage 70 eV, direct input of the sample) instrument. Elemental analysis was realized on EuroVector EA-3000. Analytical samples of the compounds were obtained by their recrystallization from ethanol and further drying in vacuum at room temperature. Sonication was carried out with the help of standard ultrasonic bath producing irradiation at 44.2 kHz. Microwave experiments were performed using the Emrys Creator EXP from Biotage AB (Uppsala, Sweden) possessing a single-mode microwave cavity producing controlled irradiation at 2.45 GHz. Solvents, all reagents were commercially available and used without additional purification.

General procedure for synthesis of 4a-z, 6a,b and 8a-c. Ultrasonic-assisted synthesis. A mixture of 5-amino-3-methylisoxazole **1** (1 mmol), aldehydes **2a-i** (1 mmol), and cyclic *β*-diketones **3a-c** (1 mmol) in ethanol (10 mL) was ultrasonicated at room temperature for 90 min in a round-bottom flask equipped with a condenser. The reaction mixture was allowed to stand up to 12 h at room temperature and then was filtered out to give the solid compounds, which were then washed with acetone and air dried. Reaction products were obtained in high purity and did not require further purification by recrystallization.

Thermal heating. A mixture of 5-amino-3-methylisoxazole 1 (1 mmol), aldehydes 2a-i (1 mmol), and cyclic β-diketones 3a-c (1 mmol) in DMF (0.1 mL) was heated to reflux for 10 min.

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Then after cooling acetone (10 mL) was added and the precipitate formed was filtered out to give the solid compounds, which were washed with acetone and air dried.

Microwave-assisted synthesis. A mixture of 5-amino-3-methylisoxazole **1** (1 mmol), aldehydes **2a-i** (1 mmol), and cyclic β-diketones **3a-c** (1 mmol) in water (0.1 mL) was irradiated in MW reactor at 120 °C for 5 min. Then after cooling acetone (10 mL) was added and the precipitate formed was filtered out to give the solid compounds, which were washed with acetone and air dried.

3-Methyl-4-phenyl-4,7,8,9-tetrahydroisoxazolo[5,4-*b*]quinolin-5(6*H*)-one (4a). Colorless solid, mp 174-175 °C. ^{1}H NMR (200 MHz, DMSO-d_6) δ 10.7 (s, 1NH), 7.29-6.97 (m, 5H), 4.96 (s, 1H), 2.57 (m, 2H), 2.18 (m, 2H), 1.88 (m, 2H), 1.84 (s, 3H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6) δ 194.42, 159.02, 158.31, 152.26, 146.66, 128.02, 127.93, 127.44, 127.08, 125.94, 111.02, 95.68, 36.87, 35.68, 27.11, 20.86, 9.78 ppm. MS (EI, 70 eV): *m/z* (%) 280 (15.1) [M^+], 203 (99.9), 183 (15.5), 154 (10.7), 77 (16.3). Anal. Calcd. for $C_{17}H_{16}N_2O_2$: C 72.84, H 5.75, N 9.99. Found: C 72.65, H 5.63, N 9.87%.

4-(4-Chlorophenyl)-3-methyl-4,7,8,9-tetrahydroisoxazolo[5,4-*b*]quinolin-5(6*H*)-one (4b). Colorless solid, mp 278-279 °C. ^{1}H NMR (200 MHz, DMSO-d_6) δ 10.78 (s, 1NH), 7.29-7.16 (m, 4H), 4.97 (s, 1H), 2.56 (m, 2H), 2.18 (m, 2H), 1.90 (m, 2H), 1.84 (s, 3H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6) δ 194.94, 159.61, 158.80, 152.95, 146.08, 131.01, 129.85, 128.47, 111.23, 107.36, 95.73, 37.34, 35.77, 27.64, 21.35, 10.27 ppm. MS (EI, 70 eV): *m/z* (%) 316 (9.5), 314 (20.8) [M^+], 313 (36.1), 233 (31.3), 203 (78.4), 199 (99.9), 136 (52.8), 101 (29.5), 42 (87.8) Anal. Calcd. for $C_{17}H_{15}ClN_2O_2$: C 64.87, H 4.80, N 8.90. Found: C 64.59, H 4.62, N 8.78%.

4-(4-Bromophenyl)-3-methyl-4,7,8,9-tetrahydroisoxazolo[5,4-*b*]quinolin-5(6*H*)-one (4c). Colorless solid, mp 254-255 °C. ^{1}H NMR (200 MHz, DMSO-d_6) δ 10.77 (s, 1NH), 7.38-7.11 (m, 4H), 4.96 (s, 1H), 2.57 (m, 2H), 2.17 (m, 2H), 1.88 (m, 2H), 1.84 (s, 3H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6) δ 194.94, 159.61, 158.80, 152.98, 146.50, 131.40, 130.26, 119.51, 111.16, 95.66, 37.34, 35.83, 27.64, 21.35, 10.29 ppm. MS (EI, 70 eV): *m/z* (%) 360 (7.3), 358 (7.7) [M^+], 279 (22.5), 203 (99.9), 154 (13.3), 127 (11.9). Anal. Calcd. for $C_{17}H_{15}BrN_2O_2$: C 56.84, H 4.21, N 7.80. Found: C 56.62, H 4.02, N 7.72%.

3-Methyl-4-(4-methylphenyl)-4,7,8,9-tetrahydroisoxazolo[5,4-*b*]quinolin-5(6*H*)-one (4d). Colorless solid, mp 224-225 °C. ^{1}H NMR (200 MHz, DMSO-d_6) δ 10.69 (s, 1NH), 7.02 (m, 4H), 4.90 (s, 1H), 2.55 (m, 2H), 2.19 (s, 3H), 2.17 (m, 2H), 1.88 (m, 2H), 1.84 (s, 3H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6) δ 194.91, 158.90, 152.51, 144.46, 135.53, 129.21, 128.03, 96.44, 37.67, 36.02, 27.90, 21.59, 21.15, 10.35 ppm. MS (EI, 70 eV): *m/z* (%) 294 (22.5) [M^+], 293 (35.5), 203 (84.0), 197 (16.1), 168 (20.1), 154 (17.7), 141 (23.1), 128 (21.6), 115 (51.5), 91 (99.9), 89 (40.1), 65 (95.2). Anal. Calcd. for $C_{18}H_{18}N_2O_2$: C 73.45, H 6.16, N 9.52. Found: C 73.23, H 6.08, N 9.44%.

4-(4-Methoxyphenyl)-3-methyl-4,7,8,9-tetrahydroisoxazolo[5,4-*b*]quinolin-5(6*H*)-one (4e). Colorless solid, mp 219-220 °C. ^{1}H NMR (200 MHz, DMSO-d_6) δ 10.67 (s, 1NH), 7.08-7.64 (m, 4H), 4.90 (s, 1H), 3.66 (s, 3H), 2.52 (m, 2H), 2.17 (m, 2H), 1.88 (m, 2H), 1.84 (s, 3H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6) δ 194.90, 167.92, 159.88, 152.29, 139.73, 129.78, 114.32, 112.37,

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96.52, 55.76, 37.71, 35.60, 34.55, 21.63, 10.29 ppm. MS (EI, 70 eV): *m/z* (%) 310 (47.0) [M^+], 309 (74.8), 295 (60.4), 269 (17.2), 213 (22.9), 203 (99.9), 184 (14.9), 77 (13.1), 62 (11.8). Anal. Calcd. for $C_{18}H_{18}N_2O_3$: C 69.66, H 5.85, N 9.03. Found: C 69.58, H 5.63, N 8.95%.

3-Methyl-4-(4-nitrophenyl)-4,7,8,9-tetrahydroisoxazolo[5,4-*b*]quinolin-5(6*H*)-one (4f). Colorless solid, mp 217-218 °C. ^{1}H NMR (200 MHz, DMSO-d_6) δ 10.90 (s, 1NH), 8.10-7.47 (m, 4H), 5.14 (s, 1H), 2.60 (m, 2H), 2.17 (m, 2H), 1.88 (m, 2H), 1.84 (s, 3H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6) δ 194.96, 159.75, 158.81, 154.42, 153.58, 146.33, 130.28, 123.91, 110.62, 107.36, 95.12, 37.25, 36.54, 27.66, 21.33, 10.30 ppm. MS (EI, 70 eV): *m/z* (%) 325 (9.4) [M^+], 324 (14.3), 228 (26.4), 203 (99.9), 77 (12.5), 42 (16.9). Anal. Calcd. for $C_{17}H_{15}N_3O_4$: C 62.76, H 4.65, N 12.92. Found: C 62.54, H 4.47, N 12.80%

Methyl 4-(3-methyl-5-oxo-4,5,6,7,8,9-hexahydroisoxazolo[5,4-*b*]quinolin-4-yl)benzoate (4g). Colorless solid, mp 292-203 °C. ^{1}H NMR (200 MHz, DMSO-d_6) δ 10.81 (s, 1NH), 7.75-7.30 (m, 4H), 5.05 (s, 1H), 3.79 (s, 3H), 2.60 (m, 2H), 2.17 (m, 2H), 1.88 (m, 2H), 1.84 (s, 3H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6) δ 194.94, 166.60, 159.65, 158.25, 153.24, 152.35, 129.62, 129.24, 128.40, 110.96, 95.53, 52.47, 36.51, 33.30, 27.66, 21.35, 10.15 ppm. MS (EI, 70 eV): *m/z* (%) 338 (4.7) [M^+], 258 (12.7), 257 (17.4), 243 (99.9), 199 (76.3), 157 (23.8), 129 (46.4), 115 (31.9), 101 (56.2), 84 (72.0), 42 (83.8). Anal. Calcd. for $C_{19}H_{18}N_2O_4$: C 67.44, H 5.36, N 8.28. Found: C 67.27, H 5.23, N 8.16%.

4-[4-(Dimethylamino)phenyl]-3-methyl-4,7,8,9-tetrahydroisoxazolo[5,4-*b*]quinolin-5(6*H*)-one (4h). Colorless solid, mp 240-241 °C. ^{1}H NMR (200 MHz, DMSO-d_6) δ 10.60 (s, 1NH), 6.94-6.55 (m, 4H), 4.82 (s, 1H), 2.79 (s, 6H), 2.54 (m, 2H), 2.17 (m, 2H), 1.88 (m, 2H), 1.85 (s, 3H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6) δ 194.42, 158.92, 158.35, 151.99, 148.77, 135.84, 127.93, 112.31, 111.63, 96.06, 40.32, 36.95, 34.34, 27.10, 20.89, 9.76 ppm. MS (EI, 70 eV): *m/z* (%) 323 (34.4) [M^+], 308 (23.6), 282 (99.9), 283 (18.7), 281 (59.4), 205 (17.0), 120 (20.2), 77 (10.7). Anal. Calcd. for $C_{19}H_{21}N_3O_2$: C 70.57, H 6.55, N 12.99. Found: C 70.39, H 6.37, N 12.87%.

4-Isopropyl-3-methyl-4,7,8,9-tetrahydroisoxazolo[5,4-*b*]quinolin-5(6*H*)-one (4i). Colorless solid, mp 190-191 °C. ^{1}H NMR (200 MHz, DMSO-d_6) δ 10.60 (s, 1NH), 3.84 (d, *J* 3.1 Hz, 1H), 2.48 (m, 2H), 2.26 (m, 2H), 2.11 (s, 3H), 1.88 (m, 2H), 1.66 (m, 1H), 0.76 (d, *J* 7.0 Hz, 3H), 0.57 (d, *J* 7.0 Hz, 3H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6) δ 194.40, 160.92, 156.35, 148.87, 106.63, 94.06, 38.32, 36.85, 29.18, 27.80, 23.10, 22.20, 20.80, 12.76 ppm. MS (EI, 70 eV): *m/z* (%) 246 (31.3) [M^+], 203 (56.7), 172 (99.9), 97 (44.5), 77 (14.1). Anal. Calcd. for $C_{14}H_{18}N_2O_2$: C 68.27, H 7.37, N 11.37. Found: C 68.15, H 7.28, N 11.19%.

3,7,7-Trimethyl-4-phenyl-4,7,8,9-tetrahydroisoxazolo[5,4-*b*]quinolin-5(6*H*)-one (4j). Colorless solid, mp 183-184 °C. ^{1}H NMR (200 MHz, DMSO-d_6) δ 10.68 (s, 1NH), 7.26-7.16 (m, 5H), 4.96 (s, 1H), 2.51 (d, *J* 17.1 Hz, 1H), 2.38 (d, *J* 17.1 Hz, 1H), 2.16 (d, *J* 16.1 Hz, 1H), 1.99 (d, *J* 16.1 Hz, 1H), 1.83 (s, 3H), 1.00 (s, 3H), 0.93 (s, 3H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6) δ 194.62, 159.63, 158.84, 150.78, 147.12, 128.52, 127.93, 126.49, 110.35, 96.29, 50.89, 40.89, 36.27, 32.60, 29.06, 27.33, 10.26 ppm. MS (EI, 70 eV): *m/z* (%) 308 (20.8) [M^+], 307 (25.9), 233

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(19.6), 231 (99.9), 183 (16.0), 175 (11.1), 128 (13.1), 77 (7.1). Anal. Calcd. for $C_{19}H_{20}N_2O_2$: C 74.00, H 6.54, N 9.08. Found: C 73.82, H 6.25, N 9.00%.

4-(4-Chlorophenyl)-3,7,7-trimethyl-4,7,8,9-tetrahydroisoxazolo[5,4-*b*]quinolin-5(6*H*)-one (4k). Colorless solid, mp 270-271 °C. ^{1}H NMR (200 MHz, DMSO-d_6) δ 10.74 (s, 1NH), 7.23-7.10 (m, 4H), 4.93 (s, 1H), 2.51 (d, *J* 17.1 Hz, 1H), 2.38 (d, *J* 17.1 Hz, 1H), 2.15(d, *J* 16.1 Hz, 1H), 1.99 (d, *J* 16.1 Hz, 1H), 1.84 (s, 3H), 1.00 (s, 3H), 0.93 (s, 3H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6) δ 194.65, 159.67, 158.94, 151.78, 148.12, 129.52, 128.92, 128.63, 111.35, 97.29, 51.89, 41.09, 36.87, 32.80, 29.66, 28.33, 11.26 ppm. MS (EI, 70 eV): *m/z* (%) 344 (1.5), 342 (4.4) [M^+], 248 (35.8), 231 (99.9), 171 (14.8), 111 (17.4), 77 (12.8). Anal. Calcd. for $C_{19}H_{19}ClN_2O_2$: C 66.57, H 5.59, N 8.17. Found: C 66.35, H 5.40, N 8.05%.

4-(4-Bromophenyl)-3,7,7-trimethyl-4,7,8,9-tetrahydroisoxazolo[5,4-*b*]quinolin-5(6*H*)-one (4l). Colorless solid, mp 224-225 °C. ^{1}H NMR (200 MHz, DMSO-d_6) δ 10.74 (s, 1NH), 7.42-7.10 (m, 4H), 4.94 (s, 1H), 2.51 (d, *J* 17.2 Hz, 1H), 2.38 (d, *J* 17.2 Hz, 1H), 2.15 (d, *J* 16.2 Hz, 1H), 1.99 (d, *J* 16.1 Hz, 1H), 1.84 (s, 3H), 1.00 (s, 3H), 0.93 (s, 3H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6) δ 194.63, 159.70, 158.82, 150.97, 146.44, 131.40, 130.24, 119.52, 109.97, 95.75, 50.82, 40.86, 35.89, 32.59, 29.00, 27.35, 10.26 ppm. MS (EI, 70 eV): *m/z* (%) 388 (5.3), 386 (5.4) [M^+], 307 (17.6), 231 (99.9), 154 (11.3), 62 (12.3). Anal. Calcd. for $C_{19}H_{19}BrN_2O_2$: C 58.93, H 4.95, N 7.23. Found: C 58.75, H 4.76, N 7.11%.

3,7,7-Trimethyl-(4-methylphenyl)-4,7,8,9-tetrahydroisoxazolo[5,4-*b*]quinolin-5(6*H*)-one (4m). Colorless solid, mp 229-230 °C. ^{1}H NMR (200 MHz, DMSO-d_6) δ 10.60 (s, 1NH), 7.02 (m, 4H), 4.89 (s, 1H), 2.51 (d, *J* 17.1 Hz, 1H), 2.38 (d, *J* 17.1 Hz, 1H), 2.19 (s, 3H), 2.15 (d, *J* 16.1 Hz, 1H), 1.99 (d, *J* 16.1 Hz, 1H), 1.84 (s, 3H), 1.00 (s, 3H), 0.93 (s, 3H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6) δ 194.83, 160.70, 152.82, 147.97, 139.44, 137.40, 129.24, 128.52, 106.97, 96.75, 51.82, 40.96, 36.89, 33.59, 29.80, 27.45, 21.82, 10.26 ppm. MS (EI, 70 eV): *m/z* (%) 322 (53.48) [M^+], 265 (28.8), 231 (99.9), 227 (46.5), 179 (56), 97 (14.3). Anal. Calcd. for $C_{20}H_{22}N_2O_2$: C 74.51, H 6.88, N 8.69. Found: C 74.30, H 6.57, N 8.61%.

4-(4-Methoxylphenyl)-3,7,7-trimethyl-4,7,8,9-tetrahydroisoxazolo[5,4-*b*]quinolin-5(6*H*)-one (4n). Colorless solid, mp 226-227 °C. ^{1}H NMR (200 MHz, DMSO-d_6) δ 10.66 (s, 1NH), 7.05-6.75 (m, 4H), 4.90 (s, 1H), 3.66 (s, 3H), 2.51 (d, *J* 17.2 Hz, 1H), 2.38 (d, *J* 17.2 Hz, 1H), 2.15 (d, *J* 16.2 Hz, 1H), 1.99 (d, *J* 16.2 Hz, 1H), 1.84 (s, 3H), 1.00 (s, 3H), 0.93 (s, 3H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6) δ 195.02, 159.84, 158.93, 152.32, 150.39, 139.61, 129.11, 113.97, 112.30, 96.53, 55.72, 52.28, 37.69, 35.66, 32.66, 27.90, 21.58, 10.33 ppm. MS (EI, 70 eV): *m/z* (%) 338 (52.2) [M^+], 337 (47.7), 323 (80.9), 309 (22.6), 233 (99.9), 213 (19.9), 184 (21.9), 170 (18.4), 127 (29.2), 108 (62.9), 92 (62.1), 77 (85.8), 41 (40.9). Anal. Calcd. for $C_{20}H_{22}N_2O_3$: C 70.99, H 6.55, N 8.28. Found: C 70.77, H 6.27, N 8.20%.

3,7,7-Trimethyl-4-(4-nitrophenyl)-4,7,8,9-tetrahydroisoxazolo[5,4-*b*]quinolin-5(6*H*)-one (4o). Colorless solid, mp 232-233 °C. ^{1}H NMR (200 MHz, DMSO-d_6) δ 10.89 (s, 1NH), 8.13-7.44 (m, 4H), 5.13 (s, 1H), 2.57 (d, *J* 17.1 Hz, 1H), 2.38 (d, *J* 17.1 Hz, 1H), 2.18 (d, *J* 16.1 Hz, 1H), 1.99 (d, *J* 16.1 Hz, 1H), 1.84 (s, 3H), 1.00 (s, 3H), 0.93 (s, 3H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6) δ 194.70, 170.85, 154.37, 152.01, 150.44, 149.09, 129.68, 129.02, 95.35, 50.80,

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45.71, 36.94, 32.80, 29.30, 27.75, 11.42 ppm. MS (EI, 70 eV): *m/z* (%) 353 (12.8) [M^+], 233 (50.4), 231 (99.9), 228 (30.8), 175 (17.4), 127 (10.4), 100 (12.1), 98 (14.2), 64 (18.8), 41 (28.2). Anal. Calcd. for $C_{19}H_{19}N_3O_4$: C 64.58, H 5.42, N 11.89. Found: C 64.37, H 5.10, N 11.80%.

Methyl-4-(3,7,7-trimethyl-5-oxo-4,5,6,7,8,9-hexahydroisoxazolo[5,4-*b*]quinolin-4-yl)benzoate (4p). Colorless solid, mp 242-243 °C. ^{1}H NMR (200 MHz, DMSO-d_6) δ 10.78 (s, 1NH), 7.80-7.30 (m, 4H), 5.03 (s, 1H), 3.79 (s, 3H), 2.53 (d, *J* 17.0 Hz, 1H), 2.40 (d, *J* 17.0 Hz, 1H), 2.19 (d, *J* 16.0 Hz, 1H), 1.97 (d, *J* 16.0 Hz, 1H), 1.82 (s, 3H), 1.00 (s, 3H), 0.92 (s, 3H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6) δ 194.12, 166.07, 159.25, 158.33, 151.77, 150.69, 129.10, 127.88, 127.70, 127.47, 109.28, 95.10, 51.94, 50.26, 35.99, 32.10, 30.65, 28.48, 26.77, 9.72 ppm. MS (EI, 70 eV): *m/z* (%) 366 (15.7) [M^+], 231 (99.9), 215 (5.6), 175 (5.2), 154 (5.1), 104 (4.9), 77 (4.2). Anal. Calcd. for $C_{21}H_{22}N_2O_4$: C 68.84, H 6.05, N 7.65. Found: C 68.61, H 5.73, N 7.53%.

4-[4-(Dimethylamino)phenyl]-3,7,7-trimethyl-4,7,8,9-tetrahydroisoxazolo[5,4-*b*]quinolin-5(6*H*)-one (4q). Colorless solid, mp 251-252 °C. ^{1}H NMR (200 MHz, DMSO-d_6) δ 10.54 (s, 1NH), 6.93-6.54 (m, 4H), 4.80 (s, 1H), 2.79 (s, 3H), 2.48 (d, *J* 16.3 Hz, 1H), 2.31 (d, *J* 16.3 Hz, 1H), 2.15 (d, *J* 16.3 Hz, 1H), 1.99 (d, *J* 16.3 Hz, 1H), 1.84 (s, 3H), 1.00 (s, 3H), 0.93 (s, 3H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6) δ 194.62, 159.47, 158.88, 150.03, 149.25, 135.28, 128.41, 112.61, 110.89, 107.36, 96.71, 50.99, 40.72, 39.55, 35.03, 32.56, 29.16, 27.30, 10.26 ppm. MS (EI, 70 eV): *m/z* (%) 351 (37.4) [M^+], 311 (22.4), 310 (99.9), 309 (29.5), 295 (12.2), 231 (20.8), 77 (14.5), 62 (11.8). Anal. Calcd. for $C_{21}H_{25}N_3O_2$: C 71.77, H 7.17, N 11.96. Found: C 71.53, H 6.82, N 11.80%.

4-Isopropyl-3,7,7-trimethyl-4,7,8,9-tetrahydroisoxazolo[5,4-*b*]quinolin-5(6*H*)-one (4r). Colorless solid, mp 225-226 °C. ^{1}H NMR (200 MHz, DMSO-d_6) δ 10.41 (s, 1NH), 3.80 (d, *J* 3.0 Hz, 1H), 2.44 (d, *J* 17.0 Hz, 1H), 2.27 (d, *J* 17.0 Hz, 1H), 2.22 (d, *J* 16.5 Hz, 1H), 2.05 (d, *J* 16.5 Hz, 1H), 2.11 (s, 3H), 1.69 (m, 1H), 1.00 (s, 3H), 0.98 (s, 3H), 0.78 (d, *J* 7.0 Hz, 3H), 0.56 (d, *J* 7.0 Hz, 3H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6) δ 195.01, 162.00, 158.90, 152.19, 109.65, 107.36, 92.67, 51.03, 40.80, 35.57, 34.42, 32.38, 29.48, 27.07, 20.70, 17.66, 11.18 ppm. MS (EI, 70 eV): *m/z* (%) 274 (11.9) [M^+], 170 (99.9), 123 (36.6), 97 (23.3). Anal. Calcd. for $C_{16}H_{22}N_2O_2$: C 70.04, H 8.08, N 10.21. Found: C 70.01, H 7.82, N 10.13%.

7-(4-Chlorophenyl)-3-methyl-4-phenyl-4,7,8,9-tetrahydroisoxazolo[5,4-*b*]quinolin-5(6*H*)-one (4s). Colorless solid; ^{1}H NMR (200 MHz, DMSO-d_6) δ 10.84 (10.31) (s, 1NH), 7.46-7.01 (m,10 H), 5.84 (5.65) (s, 1H), 3.42 (m, 1H), 3.01-2.70 (m, 2H), 2.53-2.34 (m, 2H), 2.16 (1.85) (s, 3H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6) δ 195.05, 160.80, 151.86, 145.08, 141.20, 131.09, 130.39, 127.17, 127.01, 126.08, 124.90, 106.58, 95.05, 40.85, 36.38, 36.09, 31.07, 11.05 ppm. MS (EI, 70 eV): *m/z* (%) 392 (13.1), 390 (39.5) [M^+], 315 (22.8), 280 (99.9), 203 (22.4), 171 (18.8), 77 (45.4). Anal. Calcd. for $C_{23}H_{19}ClN_2O_2$: C 70.68, H 4.90, N 7.17. Found: C 70.43, H 4.55, N 7.02%.

4,7-Bis-(4-chlorophenyl)-3-methyl-4,7,8,9-tetrahydroisoxazolo[5,4-*b*]quinolin-5(6*H*)-one (4t). Colorless solid; ^{1}H NMR (200 MHz, DMSO-d_6) δ 10.99 (10.89) (s, 1NH), 7.47-6.98 (m, 8H), 4.99 (4.98) (s, 1H), 3.42 (m, 1H), 3.01-2.70 (m, 2H), 2.53-2.34 (m, 2H), 2.41 (2.39) (s, 3H)

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ppm; ^{13}C NMR (100 MHz, DMSO-d_6) δ 194.50, 158.9, 151.76, 146.10, 139.04, 131.59, 128.70, 128.07, 125.68, 108.56, 95.23, 44.59, 36.78, 36.09, 30.72, 10.45 ppm. MS (EI, 70 eV): *m/z* (%) 426 (8.5), 424 (12.8) [M^+], 314 (99.9.), 202 (56.5), 96 (11.2), 77 (48.6). Anal. Calcd. for $C_{23}H_{18}Cl_2N_2O_2$: C 64.95, H 4.27, N 6.59. Found: C 64.71, H 4.10, N 6.44%.

4-(4-Bromophenyl)-7-(4-chlorophenyl)-3-methyl-4,7,8,9-tetrahydroisoxazolo[5,4-*b*]quinolin-5(6*H*)-one (4u). Colorless solid, mp 248-249 °C. ^{1}H NMR (200 MHz, DMSO-d_6) δ 10.88 (s, 1NH), 7.39-7.05 (m, 8H), 4.97 (s, 1H), 3.42 (m, 1H), 3.01-2.70 (m, 2H), 2.53-2.34 (m, 2H), 1.85 (s, 3H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6) δ 193.83, 159.53, 158.83, 151.76, 146.14, 142.57, 131.71, 131.26, 130.31, 129.35, 128.86, 119.50, 110.81, 107.36, 95.67, 44.08, 36.07, 34.31, 32.28, 10.34 ppm. MS (EI, 70 eV): *m/z* (%) 472 (14.4), 470 (57.8), 468 (43.2) [M^+], 370 (18.5), 202 (12.2), 172 (99.9), 154 (18.9), 77 (28.9). Anal. Calcd. for $C_{23}H_{18}BrClN_2O_2$: C 58.81, H 3.86, N 5.96. Found: C 58.58, H 3.54, N 5.82%.

7-(4-Chlorophenyl)-3-methyl-4-(4-methylphenyl)-4,7,8,9-tetrahydroisoxazolo[5,4-*b*]quinolin-5(6*H*)-one (4v). Colorless solid; ^{1}H NMR (200 MHz, DMSO-d_6) δ 10.78 (s, 1NH), 7.37-6.97 (m, 8H), 4.92 (s, 1H), 3.46 (m, 1H), 3.01-2.86 (m, 2H), 2.78-2.58 (m, 2H), 2.20 (s, 3H), 1.85 (s, 3H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6) δ 193.79, 159.41, 158.85, 151.29, 143.91, 142.67, 135.37, 131.67, 129.38, 127.94, 111.35, 96.25, 44.16, 38.38, 36.01, 34.38, 21.08, 10.34 ppm. MS (EI, 70 eV): *m/z* (%) 406 (13.8), 404 (41.2) [M^+], 403 (45.7), 389 (23.3), 317 (32.0), 315 (99.9), 313 (94.6), 264 (19.0), 197 (32.3), 125 (26.9), 77 (11.5). Anal. Calcd. for $C_{24}H_{21}ClN_2O_2$: C 71.19, H 5.23, N 6.92. Found: C 71.02, H 5.02, N 6.79%.

7-(4-Chlorophenyl)-4-(4-methoxyphenyl)-3-methyl-4,7,8,9-tetrahydroisoxazolo[5,4-*b*]quinolin-5(6*H*)-one (4w). Colorless solid; ^{1}H NMR (200 MHz, DMSO-d_6) δ 10.78 (s, 1NH), 7.34-6.72 (m, 8H), 4.91 (s, 1H), 3.76 (s, 3H), 3.41 (m, 1H), 3.01-2.86 (m, 2H), 2.78-2.58 (m, 2H), 1.85 (s, 3H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6) δ 193.82, 159.39, 158.86, 157.91, 151.11, 142.66, 139.10, 131.65, 129.38, 128.84, 113.73, 111.49, 96.34, 55.42, 44.18, 38.35, 35.49, 34.34, 10.32 ppm. MS (EI, 70 eV): *m/z* (%) 422 (13.0), 420 (38.6) [M^+], 405 (61.1), 315 (67.4), 313 (99.9), 175 (13.0), 135 (15.3), 101 (15.2) Anal. Calcd. for $C_{24}H_{21}ClN_2O_3$: C 68.49, H 5.03, N 6.66. Found: C 68.32, H 4.70, N 6.51%.

7-(4-Chlorophenyl)-3-methyl-4-(4-nitrophenyl)-4,7,8,9-tetrahydroisoxazolo[5,4-*b*]quinolin-5(6*H*)-one (4x). Colorless solid; ^{1}H NMR (200 MHz, DMSO-d_6) δ 11.15(10.39) (s, 1NH), 8.05-7.30 (m, 8H), 5.66(5.15) (s, 1H), 3.45 (m, 1H), 3.01-2.79 (m, 2H), 2.78-2.31 (m, 2H), 2.15(1.85) (s, 3H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6) δ 195.40, 159.80, 153.86, 148.80, 145.50, 133.10, 130.90, 127.10, 126.48, 123.88, 110.05, 96.53, 40.89, 38.88, 37.80, 31.20, 10.50 ppm. MS (EI, 70 eV): *m/z* (%) 437 (1.9), 435 (5.3) [M^+], 324 (99.9), 203 (18.9), 97 (22.5), 77 (58.9). Anal. Calcd. for $C_{23}H_{18}ClN_3O_4$: C 63.38, H 4.16, N 9.64. Found: C 63.21, H 4.03, N 9.58%.

Methyl-4-[7-(4-chlorophenyl)3-methyl-5-oxo-4,5,6,7,8,9-hexahydroisoxazolo[5,4-*b*]quinolin-4-yl)benzoate (4y). Colorless solid; ^{1}H NMR (200 MHz, DMSO-d_6) δ 10.91 (s, 1NH), 7.81-7.25 (m, 8H), 5.06(5.11) (s, 1H), 3.80(3.89) (s, 3H), 3.42 (m, 1H), 3.03-2.94 (m, 2H), 2.78-2.69 (m, 2H), 1.83(1.76) (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 195.40, 165.90, 159.80, 151.70, 146.87, 144.80, 144.02, 131.12, 129.01, 127.08, 125.02, 110.05, 95.03, 52.05, 41.05, 37.93,

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37.03, 31,01, 11.05 ppm. MS (EI, 70 eV): *m/z* (%) 450 (1.1), 448 (3.5) [M+], 338 (99.9), 244 (23.8), 172 (14.3), 77 (16.5). Anal. Calcd. for $C_{25}H_{21}ClN_2O_4$: C 66.89, H 4.72, N 6.24. Found: C 66.64, H 4.39, N 6.11%.

7-(4-Chlorophenyl)-4-[4-(dimethylamino)phenyl]-3-methyl-4,7,8,9-tetrahydroisoxazolo-[5,4-*b*]quinolin-5(6*H*)-one (4z). Colorless solid, mp 254-255 °C. ^{1}H NMR (200 MHz, DMSO-d_6) δ 10.63 (s, 1NH), 7.30-6.52 (m, 8H), 4.84 (s, 1H), 3.43 (m, 1H), 3.01-2.65 (m, 2H), 2.80 (s, 6H), 2.55-2.42 (m, 2H), 1.86 (s, 3H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6) δ 193.82, 159.34, 158.90, 150.67, 149.25, 142.68, 135.01, 131.62, 129.39, 128.84, 112.55, 11.82, 96.57, 44.23, 38.36, 35.19, 34.35, 10.32 ppm. MS (EI, 70 eV): *m/z* (%) 435 (10.8), 433 (32.1) [M^+], 339 (22.6), 227 (17.8), 203 (99.9), 154 (38.9), 77 (18.9). Anal. Calcd. for $C_{25}H_{24}ClN_3O_2$: C 69.20, H 5.57, N 9.68. Found: C 69.01, H 5.30, N 9.53%.

3-Methyl-4-(4-(3-methyl-4,5,6,7,8,9-hexahydroisoxazolo[5,4-*b*]quinolin-5-one-4-yl)phenyl)-4,5,6,7,8,9-hexahydroisoxazolo[5,4-*b*]quinolin-5-one (6a). Colorless solid, mp 260-261 °C. ^{1}H NMR (200 MHz, DMSO-d_6) δ 10.67 (s, 2NH), 7.02 (m, 4H), 4.89 (s, 2H), 2.60-2.53 (m, 4H), 2.23-2.12 (m, 4H),1.83-1.72 (m, 4H), 1.78 (s, 6H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6) δ 195.01, 159.46, 158.76, 152.79, 144.79, 127.68, 111.46, 96.38, 37.35, 35.74, 27.63, 21.30, 10.26 ppm. MS (EI, 70 eV): *m/z* (%) 480 (2.6) [M^+], 279 (33.0), 205 (59.9), 203 (99.9), 188 (17.0), 112 (13.7), 84 (23.2). Anal. Calcd. for $C_{28}H_{26}N_4O_4$: C 69.70, H 5.43, N 11.61. Found: C 69.37, H 5.00, N 11.49%.

3,7,7-Trimethyl-4-(4-(3,7,7-trimethyl-4,5,6,7,8,9-hexahydroisoxazolo[5,4-*b*]quinolin-5-one-4-yl)phenyl)-4,5,6,7,8,9-hexahydroisoxazolo[5,4-*b*]quinolin-5-one (6b). Colorless solid, mp 266-267 °C. ^{1}H NMR (200 MHz, DMSO-d_6) δ 10.64 (s, 2NH), 7.00 (m, 4H), 4.87 (s, 2H), 2.50 (d, *J* 17.0 Hz, 2H), 2.33 (d, *J* 17.0 Hz, 2H), 2.15 (d, *J* 16.0 Hz, 2H), 1.96 (d, *J* 16.0 Hz, 2H), 1.76 (s, 6H), 0.98 (s, 6H), 0.94 (s, 3H), 0.89 (s, 3H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6) δ 194.63, 159.58, 158.77, 150.63, 144.77, 127.60, 110.35, 96.38, 50.88, 35.76, 32.63, 29.02, 27.72, 21.17, 10.24 ppm MS (EI, 70 eV): *m/z* (%) 536 (36.6) [M^+], 308 (56.6), 232 (99.9), 122 (27.9), 84 (13.6). Anal. Calcd. for $C_{32}H_{34}N_4O_4$: C 71.36, H 6.36, N 10.40. Found: C 71.02, H 6.03, N 10.26%.

Spiro[(3-methyl-7,8-dihydroisoxazolo[5,4-*b*]quinoline)-4,3'-(indole-2'(1'*H*)-one)]-5(4*H*,6*H*,9*H*)-one (8a). Colorless solid, mp 256-257 °C. ^{1}H NMR (200 MHz, DMSO-d_6) δ 11.08 (s, 1NH), 10.40 (s, 1NH), 7.11-6.75 (m, 4H), 2.64-2.57 (m, 2H), 2.19-2.06 (m, 2H), 1.93-1.76 (m, 2H), 1.51 (s, 3H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6) δ 191.03, 162.53, 155.21, 147.08, 135.40, 131.32, 119.08, 118.02, 110.53, 109.09, 98.06, 56.88, 54.26, 35.87, 28.04, 20.52, 11.02 ppm; . MS (EI, 70 eV): *m/z* (%) 320 (23.8) [M^+], 204 (99.9), 125 (15.6), 97 (14.3). Anal. Calcd. for $C_{18}H_{15}N_3O_3$: C 67.28, H 4.71, N 13.08. Found: C 67.08, H 4.43, N 12.99%.

Spiro[(3,7,7-trimethyl-7,8-dihydroisoxazolo[5,4-*b*]quinoline)-4,3'-(indole-2'(1'*H*)-one)]-5(4*H*,6*H*,9*H*)-one (8b). Colorless solid, mp 271-272 °C. 1H NMR (200 MHz, DMSO-d_6) δ ^{1}H NMR (200 MHz, DMSO-d_6) δ 11.09 (s, 1NH), 10.39 (s, 1NH), 7.12-6.75 (m, 4H), 2.56 (d, *J* 17.0 Hz, 1H), 2.44 (d, *J* 17.0 Hz, 1H), 2.11 (d, *J* 16.1 Hz, 1H), 1.96 (d, *J* 16.1 Hz, 1H), 1.52 (s, 3H), 1.01 (s, 3H), 0.98 (s, 3H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6) δ 196.02, 162.08, 154.51,

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147.03, 136.08, 130.02, 119.11, 118.32, 110.86, 109.02, 98.88, 56.89, 53.01, 52.81, 38.78, 31.16, 28.05, 27.14, 11.09 ppm. MS (EI, 70 eV): *m/z* (%) 350 (5.5) [M^+], 267 (99.9), 265 (47.3), 175 (11.3), 77 (21.8). Anal. Calcd. for $C_{20}H_{19}N_3O_3$: C 68.75, H 5.48, N 12.03. Found: C 68.51, H 5.15, N 11.90%.

Spiro[7-(4-chlorophenyl)-(3-methyl-7,8-dihydroisoxazolo[5,4-*b*]quinoline)-4,3'-(indole-2'(1'*H*)-one)]-5(4*H*,6*H*,9*H*)-one (8c). Colorless solid, mp 264-265 °C. ^{1}H NMR (200 MHz, DMSO-d_6) δ 11.23 (s, 1NH), 10.43 (s, 1NH), 7.40-6.79 (m, 8H), 3.43 (m, 1H), 3.06-2.70 (m, 2H), 2.59-2.29 (m, 2H), 1.53 (s, 3H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6) δ 191.86, 161.13, 155.05, 146.89, 144.15, 133.20, 130.05, 127.13, 118.65, 110.03, 109.09, 98.02, 56.32, 54.03, 42.04, 37.04, 31.91, 11.52 ppm. MS (EI, 70 eV): *m/z* (%) 431 (6.8) [M^+], 333 (29.2), 251 (22.2), 183 (14.8), 128 (19.7), 93 (99.9), 77 (11.9). Anal. Calcd. for $C_{24}H_{18}ClN_3O_3$: C 66.75, H 4.20, N 9.73. Found: C 66.51, H 3.87, N 9.59%.

General procedure for synthesis of 10a-o. A mixture of 5-amino-3-methylisoxazole **1** (1 mmol), aldehydes **9a-e** (1 mmol), and cyclic *β*-di-ketones **3a-c** (1 mmol) in DMF (2 mL) in the presence of catalytic amounts of HCl or Yb(OTf)$_3$ (5 mol %) was heated to reflux for 5 min in a roundbottom flask equipped with a condenser. Then after cooling acetone (10 mL) was added and the precipitate formed was filtered out to give the solid compounds, which were washed with acetone and air-dried.

4-(2-Hydroxyphenyl)-3-methyl-4,7,8,9-tetrahydroisoxazolo[5,4-*b*]quinolin-5(6*H*)-one (10a). Colorless solid, mp 243-244 °C. ^{1}H NMR (200 MHz, DMSO-d_6) δ 10.67 (s, 1NH), 9.38 (s, 1H) 7.23-6.70 (m, 4H), 5.21 (s, 1H), 2.57 (m, 2H), 2.18 (m, 2H), 1.88 (m, 2H), 1.86 (s, 3H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6) δ 193.42, 161.42, 159.81, 152.26, 146.13, 128.44, 129.03, 126.03, 119.78, 107.02, 97.99, 37.97, 34.48, 27.97, 21.61, 11.08 ppm. MS (EI, 70 eV): *m/z* (%) 296 (3.5) [M^+], 204 (15.6), 184 (21.5), 172 (99.9), 93 (25.5), 77 (17.7). Anal. Calcd. for $C_{17}H_{16}N_2O_3$: C 68.91, H 5.44, N 9.45. Found: C 68.67, H 5.17, N 9.31%.

4-(5-Chloro-2-hydroxyphenyl)-3-methyl-4,7,8,9-tetrahydroisoxazolo[5,4-*b*]quinolin-5(6*H*)-one (10b). Colorless solid, mp 174-175 °C. ^{1}H NMR (200 MHz, DMSO-d_6) δ 10.72 (s, 1NH), 8.87 (s, 1H), 7.02-6.73 (m, 3H), 5.20 (s, 1H), 2.58 (m, 2H), 2.18 (m, 2H), 1.88 (m, 2H), 1.87 (s, 3H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6) δ 195.17, 163.19, 159.99, 153.74, 147.66, 133.03, 127.93, 127.08, 120.94, 111.02, 97.01, 36.87, 35.68, 27.11, 20.85, 9.79 ppm. MS (EI, 70 eV): *m/z* (%) 330 (2.8) [M^+], 260 (18.8), 236 (19.9), 203 (15.1), 132 (35.6), 127 (99.9), 77 (8.8). Anal. Calcd. for $C_{17}H_{15}ClN_2O_3$: C 61.73, H 4.57, N 8.47. Found: C 61.50, H 4.14, N 8.35%.

4-(5-Bromo-2-hydroxyphenyl)-3-methyl-4,7,8,9-tetrahydroisoxazolo[5,4-*b*]quinolin-5(6*H*)-one (10c). Colorless solid, mp 218-219 °C. ^{1}H NMR (200 MHz, DMSO-d_6) δ 10.72 (s, 1NH), 8.85 (s, 1H), 7.14-6.66 (m, 3H), 5.19 (s, 1H), 2.64 (m, 2H), 2.26 (m, 2H), 1.92 (m, 2H), 1.87 (s, 3H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6) δ 194.09, 160.88, 158.31, 152.26, 145.45, 130.02, 128.17, 125.62, 120.13, 110.18, 95.74, 36.12, 34.98, 27.85, 21.88, 10.78 ppm. MS (EI, 70 eV): *m/z* (%) 375 (15.3) [M^+], 172 (99.9), 280 (14.5), 203 (44.8), 172 (19.5), 77 (8.3). Anal. Calcd. for $C_{17}H_{15}BrN_2O_3$: C 54.42, H 4.03, N 7.47. Found: C 54.20, H 3.75, N 7.34%.

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4-(2-Hydroxy-3-methoxyphenyl)-3-methyl-4,7,8,9-tetrahydroisoxazolo[5,4-*b*]quinolin-5(6*H*)-one (10d). Colorless solid, mp 239-240 °C. ^{1}H NMR (200 MHz, DMSO-d_6) δ 10.68 (s, 1NH), 8.67 (s, 1H), 6.68.-6.44 (m, 3H), 5.24 (s, 1H), 3.73 (s, 3H), 2.55 (m, 2H), 2.18 (m, 2H), 1.88 (m, 2H), 1.85 (s, 3H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6). δ 195.42, 159.02, 153.31, 149.26, 146.66, 128.02, 127.93, 127.44, 127.11, 125.94, 111.02, 95.68, 55.34, 37.55, 34.77, 27.11, 20.89, 10.90 ppm. MS (EI, 70 eV): *m/z* (%) 326 (48.9) [M^+], 230 (22.8), 203 (54.8), 172 (99.9), 123 (14.3). Anal. Calcd. for $C_{18}H_{18}N_2O_4$: C 66.25, H 5.56, N 8.58. Found: C 66.03, H 5.24, N 8.50%.

4-(2-Hydroxy-5-nitrophenyl)-3-methyl-4,7,8,9-tetrahydroisoxazolo[5,4-*b*]quinolin-5(6*H*)-one (10e). Colorless solid, mp 248-249 °C. ^{1}H NMR (200 MHz, DMSO-d_6) δ 11.14 (s, 1OH), 10.82 (s, 1NH), 7.90-6.86 (m, 3H), 5.29 (s, 1H), 2.59 (m, 2H), 2.18 (m, 2H), 1.90 (m, 2H), 1.87 (s, 3H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6) δ 195.11, 162.88, 160.33, 150.79, 146.09, 140.99, 129.03, 127.81, 121.62, 115.91, 110.67, 97.77, 36.93, 35.41, 28.11, 20.99, 11.01 ppm. MS (EI, 70 eV): *m/z* (%) 341 (8.5) [M^+], 285 (15.5), 247 (22.5), 203 (99.9), 172 (15.6), 139 (28.7). Anal. Calcd. for $C_{17}H_{15}N_3O_5$: C 59.82, H 4.43, N 12.31. Found: C 59.60, H 4.15, N 12.19%.

4-(2-Hydroxyphenyl)-3,7,7-trimethyl-4,7,8,9-tetrahydroisoxazolo[5,4-*b*]quinolin-5(6*H*)-one (10f). Colorless solid, mp 248-249 °C. ^{1}H NMR (200 MHz, DMSO-d_6) δ 10.69 (s, 1OH), 9.12 (s, 1NH), 7.28-6.70 (m, 4H), 5.18 (s, 1H), 2.52 (d, *J* 17.1 Hz, 1H), 2.35 (d, *J* 17.1 Hz, 1H), 2.16 (d, *J* 16.1 Hz, 1H), 1.98 (d, *J* 16.1 Hz, 1H), 1.88 (s, 3H), 1.00 (s, 3H), 0.97 (s, 3H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6) δ 195.13, 159.19, 158.11, 155.37, 151.77, 136.04, 131.83, 129.99, 118.00, 110.60, 109.59, 107.36, 96.85, 51.84, 41.91, 31.62, 30.76, 29.64, 27.81, 10.97 ppm. MS (EI, 70 eV): *m/z* (%) 324 (3.2) [M^+], 230 (99.9), 228 (16.8), 202 (48.7), 122 (14.9), 93 (24.2). Anal. Calcd. for $C_{19}H_{20}N_2O_3$: C 70.35, H 6.21, N 8.64. Found: C 70.13, H 6.00, N 8.56%.

4-(5-Chloro-2-hydroxyphenyl)-3,7,7-trimethyl-4,7,8,9-tetrahydroisoxazolo[5,4-*b*]quinolin-5(6*H*)-one (10g). Colorless solid, mp 257-258 °C. ^{1}H NMR (200 MHz, DMSO-d_6) δ 10.68 (s, 1OH), 9.69 (s, 1NH), 6.96-6.70 (m, 3H), 5.17 (s, 1H), 2.50 (d, *J* 16.9 Hz, 1H), 2.39 (d, *J* 16.9 Hz, 1H), 2.19 (d, *J* 16.1 Hz, 1H), 1.97 (d, *J* 16.1 Hz, 1H), 1.88 (s, 3H), 1.00 (s, 3H), 0.97 (s, 3H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6) δ 194.64, 159.95, 158.74, 135.49, 128.93, 127.10, 122.91, 117.44, 109.56, 95.76, 50.85, 40.91, 32.63, 32.11, 29.22, 27.13, 10.22 ppm. MS (EI, 70 eV): *m/z* (%) 358 (23.7) [M^+], 262 (36.5), 231 (14.3), 170 (19.3), 127 (99.9). Anal. Calcd. for $C_{19}H_{19}ClN_2O_3$: C 63.60, H 5.34, N 7.81. Found: C 63.38, H 5.01, N 7.71%.

4-(5-Bromo-2-hydroxyphenyl)-3,7,7-trimethyl-4,7,8,9-tetrahydroisoxazolo[5,4-*b*]quinolin-5(6*H*)-one (10h). Colorless solid, mp 265-266 °C. ^{1}H NMR (200 MHz, DMSO-d_6) δ 10.66 (s, 1OH), 9.72 (s, 1NH), 7.08-6.65 (m, 3H), 5.16 (s, 1H), 2.52 (d, *J* 17.0 Hz, 1H), 2.35 (d, *J* 17.0 Hz, 1H), 2.16 (d, *J* 16.1 Hz, 1H), 1.98 (d, *J* 16.1 Hz, 1H),1.88 (s, 3H), 1.00 (s, 3H), 0.97 (s, 3H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6) δ 194.63, 159.92, 158.75, 153.64, 151.77, 136.04, 131.83, 129.99, 118.00, 110.60, 109.59, 107.36, 95.79, 50.84, 40.90, 32.62, 30.06, 29.31,27.02, 10.23 ppm. MS (EI, 70 eV): *m/z* (%) 404 (22.9) [M^+], 403 (11.1), 387 (26.8), 344 (55.8), 307 (23.1), 279 (22.0), 233 (60.7), 127 (21.6), 63 (43.0) 62 (99.9). Anal. Calcd. for $C_{19}H_{19}BrN_2O_3$: C 56.59, H 4.75, N 6.95. Found: C 56.42, H 4.44, N 6.83%.

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4-(2-Hydroxy-3-methoxyphenyl)-3,7,7-trimethyl-4,7,8,9-tetrahydroisoxazolo[5,4-*b*]quinolin-5(6*H*)-one (10i). Colorless solid, mp 238-239 °C. ^{1}H NMR (200 MHz, DMSO-d_6) δ 10.71 (s, 1OH), 8.61 (s, 1NH), 6.67-6.48 (m, 3H), 5.23 (s, 1H), 3.72 (s, 3H), 2.52 (d, *J* 16.9 Hz, 1H), 2.37 (d, *J* 16.9 Hz, 1H), 2.17 (d, *J* 16.1 Hz, 1H), 1.95 (d, *J* 16.1 Hz, 1H), 1.87 (s, 3H), 1.00 (s, 3H), 0.95 (s, 3H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6) δ 194.95, 159.87, 158.76, 151.68, 147.90, 143.06, 133.90, 121.18, 119.24, 110.24, 109.79, 96.41, 56.15, 50.88, 40.91, 32.55, 29.30, 29.19, 27.27, 10.70 ppm. MS (EI, 70 eV): *m/z* (%) 354 (23.0) [M^+], 258 (15.4), 231 (99.9), 137 (33.5), 151 (43), 96 (45.5). Anal. Calcd. for $C_{20}H_{22}N_2O_4$: C 67.78, H 6.26, N 7.90. Found: C 67.56, H 6.01, N 7.81%.

4-(2-Hydroxy-5-nitrophenyl)-3,7,7-trimethyl-4,7,8,9-tetrahydroisoxazolo[5,4-*b*]quinolin-5(6*H*)-one (10j). Colorless solid, mp 263-264 °C. ^{1}H NMR (200 MHz, DMSO-d_6) δ 11.15 (s, 1OH), 10.78 (s, 1NH), 7.90-6.88 (m, 3H), 5.27 (s, 1H), 2.58 (d, *J* 17.0 Hz, 1H), 2.36 (d, *J* 17.0 Hz, 1H), 2.18(d, *J* 16.1 Hz, 1H), 1.97 (d, *J* 16.1 Hz, 1H), 1.87 (s, 3H), 1.00 (s, 3H), 0.95 (s, 3H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6) δ 194.68, 161.11, 160.38, 158.80, 152.16, 140.59, 134.70, 125.61, 124.13, 116.41, 109.71, 95.56, 51.14, 41.32, 32.73, 30.69, 29.47, 27.21, 10.32 ppm. MS (EI, 70 eV): *m/z* (%) 369 (3.7) [M^+], 352 (22.3), 231 (21.6), 127 (11.1), 106 (13.1), 92 (26.1), 77 (35.8), 63 (49.7), 42 (99.9). Anal. Calcd. for $C_{19}H_{19}N_3O_5$: C 61.78, H 5.18, N 11.38. Found: C 61.55, H 4.89, N 11.27%.

7-(4-Chlorophenyl)-4-(2-hydroxyphenyl)-3-methyl-4,7,8,9-tetrahydroisoxazolo[5,4-*b*]quinolin-5(6*H*)-one (10k). Colorless solid; ^{1}H NMR (200 MHz, DMSO-d_6) δ 10.90 (s, 1NH), 9.04(9.01) (s, 1OH), 6.95-6.42 (m, 8H), 5.03(5.01) (s, 1H), 3.51 (m, 1H), 2.94 (m, 2H), 2.66 (m, 2H), 2.24 (s, 3H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6) δ 195.45, 161.80, 153.76, 147.96, 147.07, 146.03, 131.16, 127.68, 122.25, 118.06, 111.25, 108.04, 95.54, 54.99, 43.48, 38.19, 32.72, 32.10, 11.05 ppm. MS (EI, 70 eV): *m/z* (%) 406 (3) [M^+], 313 (99.9), 294 (15.6), 202 (65.7), 112 (14.3). Anal. Calcd. for $C_{23}H_{19}ClN_2O_3$: C 67.90, H 4.71, N 6.89. Found: C 67.73, H 4.40, N 6.77%.

4-(5-Chloro-2-hydroxyphenyl)-7-(4-chlorophenyl)-3-methyl-4,7,8,9-tetrahydroisoxazolo-[5,4-*b*]quinolin-5(6*H*)-one (10l). Colorless solid; ^{1}H NMR (200 MHz, DMSO-d_6) δ 11.11 (s, 1NH), 8.88(8.75) (s, 1OH), 7.50-7.00 (m, 7H), 4.97(4.91) (s, 1H), 3.51 (m, 1H), 3.08 (m, 2H), 2.66 (m, 2H), 2.40(2.39) (s, 3H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6) δ 195.67, 166.66, 160.33, 157.96, 147.74, 142.19, 137.24, 132.63, 131.09, 129.36, 128.40, 126.29, 123.45, 119.53, 118.79, 95.61, 43.91, 42.57, 37.58, 34.50, 26.21, 11.01 ppm. MS (EI, 70 eV): *m/z* (%) 440 (3.8) [M^+], 329 (99.9), 313 (32.3), 202 (18.9), 127 (16.5). Anal. Calcd. for $C_{23}H_{18}Cl_2N_2O_3$: C 62.60, H 4.11, N 6.35. Found: C 62.38, H 3.83, N 6.27%.

4-(5-Bromo-2-hydroxyphenyl)-7-(4-chlorophenyl)-3-methyl-4,7,8,9-tetrahydroisoxazolo-[5,4-*b*]quinolin-5(6*H*)-one (10m). Colorless solid; ^{1}H NMR (200 MHz, DMSO-d_6) δ 11.02 (s, 1NH), 8.78(8.72) (s, 1OH), 7.52-6.95 (m, 7H), 4.97(4.90) (s, 1H), 3.51 (m, 1H), 2.94 (m, 2H), 2.54 (m, 2H), 2.39 (s, 3H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6) δ 195.69, 165.66, 159.33, 157.96, 148.74, 142.09, 137.24, 132.63, 131.09, 129.36, 128.40, 126.19, 123.45, 119.53, 118.79, 95.61, 43.91, 42.57, 37.58, 34.50, 26.21, 10.97 ppm. MS (EI, 70 eV): *m/z* (%) 484 (3.8) [M^+],

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389 (99.9), 387 (77.5), 251 (16.7), 199 (12.0), 142 (31.2), 114 (10.0). Anal. Calcd. for $C_{23}H_{18}BrClN_2O_3$: C 56.87, H 3.74, N 5.77. Found: C 56.69, H 3.45, N 5.68%.

7-(4-Chlorophenyl)-4-(2-hydroxy-3-methoxyphenyl)-3-methyl-4,7,8,9-tetrahydroisoxazolo-[5,4-*b*]quinolin-5(6*H*)-one (10n). Colorless solid; ^{1}H NMR (200 MHz, DMSO-d_6) δ 10.91 (s, 1NH), 9.04(8.99) (s, 1OH), 6.94-6.42 (m, 7H), 5.00(4.94) (s, 1H), 3.74 (s, 3H), 3.51 (m, 1H), 2.94 (m, 2H), 2.66 (m, 2H), 2.24 (s, 3H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6) δ 195.45, 161.80, 153.76, 147.96, 147.07, 146.03, 131.16, 127.68, 122.25, 118.06, 111.25, 108.04, 95.54, 54.99, 43.48, 38.19, 32.72, 32.10, 11.05 ppm. MS (EI, 70 eV): *m/z* (%) 436 (18.6) [M^+], 438 (5.6), 313 (99.9), 186 (43.5), 123 (15.5). Anal. Calcd. for $C_{24}H_{21}ClN_2O_4$: C 65.98, H 4.84, N 6.41. Found: C 65.77, H 4.55, N 6.30%.

7-(4-Chlorophenyl)-4-(2-hydroxy-5-nitrophenyl)-3-methyl-4,7,8,9-tetrahydroisoxazolo-[5,4-*b*]quinolin-5(6*H*)-one (10o). Colorless solid; ^{1}H NMR (200 MHz, DMSO-d_6) δ 11.12 (s, 1NH), 8.90(8.88) (s, 1OH), 7.54-7.02 (m, 7H), 4.99(4.96) (s, 1H), 3.51 (m, 1H), 3.07 (m, 2H), 2.66 (m, 2H), 2.40(2.39) (s, 3H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6) δ 195.42, 161.76, 152.66, 147.97, 147.17, 146.03, 131.16, 127.68, 122.25, 118.06, 111.25, 108.74, 95.74, 43.48, 38.19, 32.72, 32.10, 11.05 ppm. MS (EI, 70 eV): *m/z* (%) 451 (11.4) [M^+], 340 (18.6), 313 (99.9), 202 (12.2), 139 (18.4). 112 (21.2), 96 (24.5). Anal. Calcd. for $C_{23}H_{18}ClN_3O_5$: C 61.14, H 4.02, N 9.30. Found: C 61.00, H 3.86, N 9.23%.

General procedure for synthesis of 11a-o. A mixture of 5-amino-3-methylisoxazole **1** (1 mmol), aldehydes **9a-e** (1 mmol), and cyclic *β*-di-ketones **3a-c** (1 mmol) with a catalytic amount of Et_3N was ultrasonicated in ethanol (10 mL) at room temperature for 90 min. Compounds **11a-o** were isolated from **12a-o** in individual state by crystallization from ethyl acetate (10 mL).

9-(5-Amino-3-methylisoxazol-4-yl)-2,3,4,9-tetrahydro-1*H*-xanthen-1-one (11a). Colorless solid; mp 196-197 °C. ^{1}H NMR (200 MHz, DMSO-d_6) δ 7.18-6.93 (m, 4H), 6.39 (2, NH_2), 4.78 (s, 1H), 2.63 (m, 2H), 2.27 (m, 2H), 1.93 (m, 2H), 1.62 (s, 3H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6) δ 195.76, 168.82, 159.90, 149.77, 132.45, 131.55, 127.85, 120.87, 117.85, 110.69, 96.02, 35.94, 27.85, 24.48, 18.93, 10.95. MS (EI, 70 eV): *m/z* (%) 296 (31.5) [M^+], 199 (76.5), 183 (16.8), 97 (99.9), 94 (19.9), 78 (22.6). Anal. Calcd. for $C_{17}H_{16}N_2O_3$: C 68.91, H 5.44, N 9.45. Found: C 68.69, H 5.13, N 9.33%.

9-(5-Amino-3-methylisoxazol-4-yl)-7-chloro-2,3,4,9-tetrahydro-1*H*-xanthen-1-one (11b). Colorless solid; mp 209-210 °C. ^{1}H NMR (200 MHz, DMSO-d_6) δ 7.29-7.12 (m, 3H), 6.47 (2, NH_2), 4.83 (s, 1H), 2.65 (m, 2H), 2.29 (m, 2H), 1.93 (m, 2H), 1.68 (s, 3H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6) δ 193.64, 170.72, 159.56, 149.97, 135.45, 131.80, 128.37, 120.03, 118.95, 112.69, 96.12, 36.94, 27.95, 26.18, 21.53, 10.97. MS (EI, 70 eV): *m/z* (%) 330 (3.4) [M^+], 238 (19.9), 217 (99.9), 205 (56.8), 97 (13.0), 77 (16.5). Anal. Calcd. for $C_{17}H_{15}ClN_2O_3$: C 61.73, H 4.57, N 8.47. Found: C 61.54, H 4.25, N 8.39%.

9-(5-Amino-3-methylisoxazol-4-yl)-7-bromo-2,3,4,9-tetrahydro-1*H*-xanthen-1-one (11c). Colorless solid; mp 194-195 °C. ^{1}H NMR (200 MHz, DMSO-d_6) δ 7.38-7.07 (m, 3H), 6.54 (2, NH_2), 4.83 (s, 1H), 2.64 (m, 2H), 2.32 (m, 2H), 1.95 (m, 2H), 1.66 (s, 3H) ppm; ^{13}C NMR (100

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MHz, DMSO-d_6) δ 196.64, 166.72, 159.02, 148.67, 132.45, 131.24, 127.27, 118.87, 116.85, 111.59, 95.02, 36.94, 27.41, 25.18, 20.53, 10.47. MS (EI, 70 eV): *m/z* (%) 375 (3.4) [M^+], 278 (14.8), 207 (22.4),), 182 (99.9), 97 (12.5), 77 (33.1). Anal. Calcd. for $C_{17}H_{15}BrN_2O_3$: C 54.42, H 4.03, N 7.47. Found: C 54.24, H 3.71, N 7.37%.

9-(5-Amino-3-methylisoxazol-4-yl)-5-methoxy-2,3,4,9-tetrahydro-1*H*-xanthen-1-one (11d). Colorless solid; mp 199-200 °C. ^{1}H NMR (200 MHz, DMSO-d_6) δ 6.99-6.52 (m, 3H), 6.39 (2, NH_2), 4.77 (s, 1H), 3.80 (s, 3H), 2.66 (m, 2H), 2.27 (m, 2H), 1.93 (m, 2H), 1.64 (s, 3H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6) δ 193.10, 170.98, 167.95, 159.80, 155.65, 130.92, 128.04, 120.25, 112.44, 111.65, 107.30, 99.89, 55.76, 37.61, 28.65, 25.62, 20.78, 11.01. MS (EI, 70 eV): *m/z* (%) 326 (9.8) [M^+], 257 (33.7), 230 (99.9), 204 (45.6), 123 (18.7), 95 (14.3) Anal. Calcd. for $C_{18}H_{18}N_2O_4$: C 66.25, H 5.56, N 8.58. Found: C 66.03, H 5.24, N 8.50%.

9-(5-Amino-3-methylisoxazol-4-yl)-7-nitro-2,3,4,9-tetrahydro-1*H*-xanthen-1-one (11e). Colorless solid; mp 230-231 °C. ^{1}H NMR (200 MHz, DMSO-d_6) δ 8.10-7.37 (m, 3H), 6.67 (2, NH_2), 4.98 (s, 1H), 2.71 (m, 2H), 2.31 (m, 2H), 1.97 (m, 2H), 1.66 (s, 3H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6) δ 193.30, 171.98, 169.95, 159.80, 158.65, 143.92, 125.90, 122.25, 119.44, 107.30, 99.89, 55.76, 37.61, 28.65, 25.62, 20.78, 11.01. MS (EI, 70 eV): *m/z* (%) 341 (3) [M^+], 245 (99.9), 205 (14.4), 182 (34.4), 138 (18.2), 98 (19.9). Anal. Calcd. for $C_{17}H_{15}N_3O_5$: C 59.82, H 4.43, N 12.31. Found: C 59.64, H 4.11, N 12.20%.

9-(5-Amino-3-methylisoxazol-4-yl)-3,3-dimethyl-2,3,4,9-tetrahydro-1*H*-xanthen-1-one (11f). Colorless solid; mp 126-127 °C. ^{1}H NMR (200 MHz, DMSO-d_6) δ 7.15-7.04 (m, 4H), 6.36 (2, NH_2), 4.79 (s, 1H), 2.56 (d, *J* 17.0 Hz, 1H), 2.52 (d, *J* 17.0 Hz, 1H), 2.22 (s, 2H), 1.61 (s, 3H), 1.03 (s, 3H), 0.99 (s, 3H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6) δ 191.10, 170.18, 167.95, 157.80, 152.85, 130.12, 127.04, 122.11, 119.25, 115.44, 112.65, 107.30, 99.89, 51.84, 33.61, 32.06, 29.65, 27.62, 26.78, 11.08. MS (EI, 70 eV): *m/z* (%) 324 (3.4) [M^+], 234 (15.6), 227 (68.5), 97 (99.9), 93 (13.0). Anal. Calcd. for $C_{19}H_{20}N_2O_3$: C 70.35, H 6.21, N 8.64. Found: C 70.13, H 5.92, N 8.55%.

9-(5-Amino-3-methylisoxazol-4-yl)-7-chloro-3,3-dimethyl-2,3,4,9-tetrahydro-1*H*-xanthen-1-one (11g). Colorless solid; mp 217-218 °C. ^{1}H NMR (200 MHz, DMSO-d_6) δ 7.38-7.08 (m, 3H), 6.40 (2, NH_2), 4.82 (s, 1H), 2.57 (d, *J* 17.0 Hz, 1H), 2.50 (d, *J* 17.0 Hz, 1H), 2.22 (s, 2H), 1.66 (s, 3H), 1.02 (s, 3H), 0.99 (s, 3H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6) δ 194.12, 165.98, 160.95, 152.80, 136.85, 130.12, 128.04, 119.25, 115.04, 112.60, 109.30, 97.89, 51.84, 33.61, 32.06, 29.65, 27.62, 26.91, 10.98. MS (EI, 70 eV): *m/z* (%) 360 (6.7) [M^+], 263 (99.9), 238 (34.8), 228 (24.7), 97 (45.0). Anal. Calcd. for $C_{19}H_{19}ClN_2O_3$: C 63.60, H 5.34, N 7.81. Found: C 63.37, H 5.02, N 7.72%.

9-(5-Amino-3-methylisoxazol-4-yl)-7-bromo-3,3-dimethyl-2,3,4,9-tetrahydro-1*H*-xanthen-1-one (11h). Colorless solid; mp 223-224 °C. ^{1}H NMR (200 MHz, DMSO-d_6) δ 7.40-7.08 (m, 3H), 6.49 (2, NH_2), 4.83 (s, 1H), 2.58 (d, *J* 17.0 Hz, 1H), 2.50 (d, *J* 17.0 Hz, 1H), 2.22 (s, 2H), 1.66 (s, 3H), 1.02 (s, 3H), 0.99 (s, 3H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6) δ 196.11, 164.93, 159.91, 151.75, 136.04, 129.99, 128.44, 118.21, 115.94, 110.60, 109.30, 95.79, 50.84, 32.61, 32.09, 29.63, 29.32, 26.62, 10.23. MS (EI, 70 eV): *m/z* (%) 404 (8.5) [M^+], 306 (44.5), 227 (99.9), 175

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(22.3), 142 (24.5), 128 (55.3), 98 (18.5). Anal. Calcd. for $C_{19}H_{19}BrN_2O_3$: C 56.59, H 4.75, N 6.95. Found: C 56.36, H 4.44, N 6.83%.

9-(5-Amino-3-methylisoxazol-4-yl)-5-methoxy-3,3-dimethyl-2,3,4,9-tetrahydro-1*H*-xanthen-1-one (11i). Colorless solid; mp 210-211 °C. ^{1}H NMR (200 MHz, DMSO-d_6) δ 7.03-6.60 (m, 3H), 6.37 (2, NH_2), 4.76 (s, 1H), 3.80 (s, 3H), 2.59 (d, *J* 16.9 Hz, 1H), 2.52 (d, *J* 16.9 Hz, 1H), 2.21 (s, 2H), 1.62 (s, 3H), 1.03 (s, 3H), 0.99 (s, 3H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6) δ 197.00, 166.87, 164.69, 159.18, 147.93, 125.42, 124.58, 121.22, 111.67, 110.85, 96.02, 56.71, 51.07, 32.30, 28.92, 27.57, 25.75, 25.06, 10.42. MS (EI, 70 eV): *m/z* (%) 355 (2.6) [M^+], 259 (99.9), 233 (61.3), 180 (57.7), 159 (28.5), 123 (44.5), 98 (17.7). Anal. Calcd. for $C_{20}H_{22}N_2O_4$: C 67.78, H 6.26, N 7.90. Found: C 67.55, H 6.01, N 7.81%.

9-(5-Amino-3-methylisoxazol-4-yl)-3,3-dimethyl-7-nitro-2,3,4,9-tetrahydro-1*H*-xanthen-1-one (11j). Colorless solid; mp 241-242 °C. ^{1}H NMR (200 MHz, DMSO-d_6) δ 7.91-7.33 (m, 3H), 6.68 (2, NH_2), 4.97 (s, 1H), 2.58 (d, *J* 16.9 Hz, 1H), 2.50 (d, *J* 16.9 Hz, 1H), 2.22 (s, 2H), 1.66 (s, 3H), 1.02 (s, 3H), 0.99 (s, 3H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6) δ 189.90, 170.87, 165.69, 159.18, 157.93, 143.42, 126.58, 122.22, 119.67, 109.85, 96.02, 51.71, 32.30, 30.92, 27.57, 26.75, 25.06, 10.92. MS (EI, 70 eV): *m/z* (%) 369 (21.5) [M^+], 273 (99.9), 248 (30.1), 174 (63.5), 98 (85.7). Anal. Calcd. for $C_{19}H_{19}N_3O_5$: C 61.78, H 5.18, N 11.38. Found: C 61.60, H 4.86, N 11.30%.

9-(5-Amino-3-methylisoxazol-4-yl)-3-(4-chlorophenyl)-2,3,4,9-tetrahydro-1*H*-xanthen-1-one (11k). Colorless solid; ^{1}H NMR (200 MHz, DMSO-d_6) δ 7.48-7.09 (m, 8H), 6.40 (2, NH_2), 4.80(4.79) (s, 1H), 3.46 (m, 1H), 2.98(2.94) (m, 2H), 2.75(2.68) (m, 2H), 2.28(2.21) (s, 3H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6) δ 194.76, 170.82, 169.90, 150.77, 142.10, 132.87, 132.45, 131.55, 130.52, 128.86, 127.85, 120.87, 117.85, 110.69, 98.02, 45.88, 38.59, 35.55, 26.53, 10.98. MS (EI, 70 eV): *m/z* (%) 406 (15.5) [M^+], 310 (34.4), 227 (18.5), 205 (27.3), 198 (99.9), 97 (25.3), 77 (16.1). Anal. Calcd. for $C_{23}H_{19}ClN_2O_3$: C 67.90, H 4.71, N 6.89. Found: C 67.72, H 4.39, N 6.81%.

9-(5-Amino-3-methylisoxazol-4-yl)-7-chloro-3-(4-chlorophenyl)-2,3,4,9-tetrahydro-1*H*-xanthen-1-one (11l). Colorless solid; ^{1}H NMR (200 MHz, DMSO-d_6) δ 7.47-6.79 (m, 7H), 6.47 (2, NH_2), 4.83(4.82) (s, 1H), 3.52 (m, 1H), 3.08(3.04) (m, 2H), 2.66(2.63) (m, 2H), 2.20(2.19) (s, 3H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6) δ 194.76, 171.82, 169.90, 151.77, 142.10, 133.87, 132.45, 131.55, 130.52, 128.86, 127.75, 121.87, 116.85, 110.89, 98.12, 45.98, 38.69, 34.55, 27.85, 11.08. MS (EI, 70 eV): *m/z* (%) 440 (4.3) [M^+], 345 (33.5), 262 (18.9), 245 (99.9), 205 (17.7), 97 (57.3), 77 (39.1). Anal. Calcd. for $C_{23}H_{18}Cl_2N_2O_3$: C 62.60, H 4.11, N 6.35. Found: C 62.37, H 3.79, N 6.25%.

9-(5-Amino-3-methylisoxazol-4-yl)-7-bromo-3-(4-chlorophenyl)-2,3,4,9-tetrahydro-1*H*-xanthen-1-one (11m). Colorless solid; ^{1}H NMR (200 MHz, DMSO-d_6) δ 7.57-7.09 (m, 7H), 6.48 (2, NH_2), 4.80(4.79) (s, 1H), 3.50 (m, 1H), 3.08(3.04) (m, 2H), 2.66(2.63) (m, 2H), 2.20(2.19) (s, 3H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6) δ 195.86, 171.82, 169.10, 152.16, 143.29, 134.85, 132.15, 131.05, 130.52, 128.84, 127.15, 121.07, 116.15, 111.89, 97.10, 45.98, 36.69, 33.55, 28.85, 10.98. MS (EI, 70 eV): *m/z* (%) 486 (7.5) [M^+], 389 (73.4), 304 (19.5), 277

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(67.4), 197 (99.9), 111 (23.1), 92 (16.3), 77 (39.1). Anal. Calcd. for $C_{23}H_{18}BrClN_2O_3$: C 56.87, H 3.74, N 5.77. Found: C 56.69, H 3.43, N 5.67%.

9-(5-Amino-3-methylisoxazol-4-yl)-3-(4-chlorophenyl)-5-methoxy-2,3,4,9-tetrahydro-1*H*-xanthen-1-one (11n). Colorless solid; ^{1}H NMR (200 MHz, DMSO-d_6) δ 7.57-7.09 (m, 7H), 6.48 (2, NH_2), 4.80(4.79) (s, 1H), 3.80(3.78) (s, 3H), 3.46 (m, 1H), 2.99(2.94) (m, 2H), 2.66(2.60) (m, 2H), 2.24(2.22) (s, 3H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6) δ 194.86, 172.89, 169.95, 153.16, 144.29, 136.85, 134.15, 132.05, 131.52, 128.90, 126.15, 121.97, 115.15, 111.09, 98.10, 54.34, 45.98, 36.69, 33.55, 28.85, 11.08. MS (EI, 70 eV): *m/z* (%) 437 (3.8) [M^+], 341 (63.5), 233 (12.5), 229 (17.2), 228 (99.9), 93 (18.3), 77 (12.3). Anal. Calcd. for $C_{24}H_{21}ClN_2O_4$: C 65.98, H 4.84, N 6.41. Found: C 65.77, H 4.55, N 6.32%.

9-(5-Amino-3-methylisoxazol-4-yl)-3-(4-chlorophenyl)-7-nitro-2,3,4,9-tetrahydro-1*H*-xanthen-1-one (11o). Colorless solid; ^{1}H NMR (200 MHz, DMSO-d_6) δ 7.88-7.09 (m, 7H), 6.65 (2, NH_2), 4.98(4.97) (s, 1H), 3.51 (m, 1H), 3.05(2.95) (m, 2H), 2.68(2.63) (m, 2H), 2.32(2.30) (s, 3H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6) δ 195.86, 171.80, 165.12, 151.22, 141.10, 134.17, 132.16, 131.22, 130.10, 128.17, 126.15, 122.07, 119.15, 111.89, 97.10, 45.98, 36.69, 33.55, 28.85, 10.97. MS (EI, 70 eV): *m/z* (%) 451 (5.8) [M^+], 356 (99.9), 259 (17.8), 244 (32.1), 228 (16.5), 97 (14.5). Anal. Calcd. For $C_{23}H_{18}ClN_3O_5$: C 61.14, H 4.02, N 9.30. Found: C 60.91, H 3.75, N 9.17%.

General procedure for synthesis of 12a-o. A mixture of 5-amino-3-methylisoxazole **1** (1 mmol), aldehydes **9a-e** (2 mmol) and cyclic *β*-di-ketones **3a-c** (1 mmol) in DMF (2 mL) was heated to reflux for 5 min in a roundbottom flask equipped with a condenser. Then after cooling ethanol (10 mL) was added and the precipitate formed was filtered out to give the solid compounds, which were washed with ethanol and air dried.

9-(5-{[(2-Hydroxyphenyl)methylene]amino}-3-methylisoxazol-4-yl)-2,3,4,9-tetrahydro-1*H*-xanthen-1-one (12a). Colorless solid; mp 263-264 °C. ^{1}H NMR (200 MHz, DMSO-d_6) δ 11.28 (s, 1OH), 9.00 (s, 1H), 7.80-6.97 (m, 8H), 4.97 (s, 1H), 3.48 (m, 1H), 2.29 (m, 2H), 2.24 (s, 3H), 1.94 (m, 2H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6) δ 194.45, 163.08, 160.23, 159.20, 149.65, 135.43, 131.82, 130.40, 128.61, 125.76, 123.46, 120.79, 120.26, 117.52, 116.94, 114.93, 110.76, 50.84, 39.68, 32.31, 29.12, 27.41, 26.49, 10.95. MS (EI, 70 eV): *m/z* (%) 400 (63.2) [M^+], 239 (55.4), 199 (87.1), 181 (32.3), 152 (20.3), 127 (47.9), 115 (71.6), 102 (59.6), 93 (26.2), 77 (99.9), 65 (96.1), 42 (27.5). Anal. Calcd. for $C_{24}H_{20}N_2O_4$: C 71.99, H 5.03, N 7.00. Found: C 71.81, H 4.75, N 6.93%.

7-Chloro-9-(5-{[(5-chloro-2-hydroxyphenyl)methylene]amino}-3-methylisoxazol-4-yl)-2,3,4,9-tetrahydro-1*H*-xanthen-1-one (12b). Colorless solid; mp 232-233 °C. ^{1}H NMR (200 MHz, DMSO-d_6) δ 11.16 (s, 1OH), 8.86 (s, 1H), 7.83-7.00 (m, 6H), 4.91 (s, 1H), 2.68 (m, 2H), 2.38 (s, 3H), 2.28 (m, 2H), 1.94 (m, 2H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6) δ 196.05, 164.78, 161.33, 160.20, 149.05, 138.43, 135.82, 133.40, 128.61, 125.76, 123.46, 120.79, 120.26, 117.52, 116.94, 114.93, 108.76, 51.84, 39.08, 32.30, 29.12, 28.41, 23.49, 11.95. MS (EI, 70 eV):

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m/z (%) 468 (3.2) [M^+], 327 (23.3), 237 (28.5), 233 (99.9), 139 (17.7), 96 (17.4). Anal. Calcd. for $C_{24}H_{18}Cl_2N_2O_4$: C 61.42, H 3.87, N 5.97. Found: C 61.20, H 3.55, N 5.89%.

7-Bromo-9-(5-{[(5-bromo-2-hydroxyphenyl)methylene]amino}-3-methylisoxazol-4-yl)-2,3,4,9-tetrahydro-1*H*-xanthen-1-one (12c). Colorless solid; mp 248-249 °C. ^{1}H NMR (200 MHz, DMSO-d_6) δ 11.10 (s, 1OH), 8.82 (s, 1H), 7.75-6.98 (m, 6H), 4.90 (s, 1H), 2.68 (m, 2H), 2.38 (s, 3H), 2.28 (m, 2H), 1.94 (m, 2H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6) δ 195.65, 165.18, 161.03, 160.25, 150.65, 133.43, 131.82, 130.60, 128.61, 125.96, 123.86, 120.09, 119.26, 117.52, 116.95, 114.03, 110.16, 51.84, 40.68, 33.31, 29.22, 27.81, 26.09, 10.55. MS (EI, 70 eV): *m/z* (%) 557 (4.5) [M^+], 372 (51.1), 278 (99.9), 185 (41.2), 170 (14.2), 78 (14.5). Anal. Calcd. for $C_{24}H_{18}Br_2N_2O_4$: C 51.64, H 3.25, N 5.02. Found: C 51.41, H 3.01, N 4.91%.

9-(5-{[(2-Hydroxy-3-methoxyphenyl)methylene]amino}-3-methylisoxazol-4-yl)-5-methoxy-2,3,4,9-tetrahydro-1*H*-xanthen-1-one (12d). Colorless solid; mp 211-212 °C. ^{1}H NMR (200 MHz, DMSO-d_6) δ 11.04 (s, 1OH), 8.67 (s, 1H), 7.38-6.49 (m, 6H), 4.95 (s, 1H), 3.73 (s, 3H), 2.68 (m, 2H), 2.20 (s, 3H), 2.28 (m, 2H), 1.94 (m, 2H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6) δ 194.65, 167.18, 165.23, 160.20, 149.65, 135.43, 131.82, 130.40, 128.61, 125.76, 123.46, 120.79, 120.26, 117.52, 116.94, 114.93, 110.76, 56.35, 55.86, 50.84, 39.68, 32.31, 29.92, 28.41, 26.89, 10.90. MS (EI, 70 eV): *m/z* (%) 460 (11.5) [M^+], 232 (24.3), 230 (99.9), 182 (37.1), 123 (14.1). Anal. Calcd. for $C_{26}H_{24}N_2O_6$: C 67.82, H 5.25, N 6.08. Found: C 67.64, H 5.00, N 5.95%.

9-(5-{[(2-Hydroxy-5-nitrophenyl)methylene]amino}-3-methylisoxazol-4-yl)-7-nitro-2,3,4,9-tetrahydro-1*H*-xanthen-1-one (12e). Colorless solid; mp 195-196 °C. ^{1}H NMR (200 MHz, DMSO-d_6) δ 11.10 (s, 1OH), 8.97 (s, 1H), 8.38-6.89 (m, 6H), 4.98 (s, 1H), 2.68 (m, 2H), 2.20 (s, 3H), 2.28 (m, 2H), 2.04 (m, 2H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6) δ 195.15, 170.28, 168.23, 164.20, 155.65, 145.43, 135.82, 130.40, 129.61, 125.96, 123.46, 120.79, 120.26, 117.52, 116.94, 114.93, 109.76, 48.94, 38.68, 32.31, 30.92, 29.41, 27.89, 11.10. MS (EI, 70 eV): *m/z* (%) 490 (7.4) [M^+], 245 (99.9), 182 (36.6), 175 (14.3), 139 (24.2), 95 (18.9), 77 (44.2). Anal. Calcd. for $C_{24}H_{18}N_4O_8$: C 58.78, H 3.70, N 11.42. Found: C 58.60, H 3.41, N 11.33%.

9-(5-{[(2-Hydroxyphenyl)methylene]amino}-3-methylisoxazol-4-yl)-3,3-dimethyl-2,3,4,9-tetrahydro-1*H*-xanthen-1-one (12f). Colorless solid; mp 180-181 °C. ^{1}H NMR (200 MHz, DMSO-d_6) δ 11.10 (s, 1OH), 8.96 (s, 1H), 7.80-6.96 (m, 8H), 4.90 (s, 1H), 2.64 (d, *J* 16.9 Hz, 1H), 2.40 (d, *J* 16.9 Hz, 1H), 2.30 (d, *J* 16.1 Hz, 1H), 2.10 (d, *J* 17.0 Hz, 1H), 2.25 (s, 3H), 1.02 (s, 3H), 0.83 (s, 3H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6) δ 196.65, 165.18, 161.23, 160.20, 149.65, 135.43, 131.82, 130.40, 128.61, 125.76, 123.46, 120.79, 120.26, 117.52, 116.94, 114.93, 110.76, 50.84, 39.68, 32.31, 29.12, 27.41, 26.49, 10.95. MS (EI, 70 eV): *m/z* (%) 428 (3.5) [M^+], 322 (19.6), 228 (99.9), 202 (37.5), 123 (45.6), 95 (18.5). Anal. Calcd. for $C_{26}H_{24}N_2O_4$: C 72.88, H 5.65, N 6.54. Found: C 72.70, H 5.36, N 6.44%.

7-Chloro-9-(5-{[(5-chloro-2-hydroxyphenyl)methylene]amino}-3-methylisoxazol-4-yl)-3,3-dimethyl-2,3,4,9-tetrahydro-1*H*-xanthen-1-one (12g). Colorless solid; mp 241-242 °C. ^{1}H NMR (200 MHz, DMSO-d_6) δ 10.68 (s, 1OH), 8.80 (s, 1H), 7.34-6.69 (m, 6H), 5.01 (s, 1H), 2.64 (d, *J* 17.0 Hz, 1H), 2.40 (d, *J* 17.0 Hz, 1H), 2.30 (d, *J* 16.1 Hz, 1H), 2.10 (d, *J* 16.1 Hz, 1H), 2.21 (s, 3H), 1.02 (s, 3H), 0.83 (s, 3H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6) δ 193.45, 170.18,

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168.45, 156.21, 150.65, 135.58, 131.95, 130.10, 128.56, 124.96, 123.90, 122.15, 120.28, 118.14, 117.84, 115.25, 106.12, 50.04, 39.85, 32.49, 30.92, 28.08, 27.10, 11.02. MS (EI, 70 eV): *m/z* (%) 496 (11.2) [M^+], 263 (99.9), 235 (30.1), 165 (28.3), 129 (43.5), 122(16.7). Anal. Calcd. for $C_{26}H_{22}Cl_2N_2O_4$: C 62.79, H 4.46, N 5.63. Found: C 62.61, H 4.18, N 5.55%.

7-Bromo-9-(5-[[(5-bromo-2-hydroxyphenyl)methylene]amino]-3-methylisoxazol-4-yl)-3,3-dimethyl-2,3,4,9-tetrahydro-1*H*-xanthen-1-one (12h). Colorless solid; mp 256-257 °C. ^{1}H NMR (200 MHz, DMSO-d_6) δ 11.07 (s, 1OH), 8.82 (s, 1H), 7.80-7.01 (m, 6H), 4.92 (s, 1H), 2.58 (d, *J* 17.0 Hz, 1H), 2.39 (d, *J* 17.0 Hz, 1H), 2.32 (d, *J* 16.1 Hz, 1H), 2.11 (d, *J* 16.1 Hz, 1H), 2.30 (s, 3H), 1.02 (s, 3H), 0.88 (s, 3H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6) δ 190.45, 173.08, 168.25, 155.21, 150.65, 135.48, 130.95, 130.01, 127.56, 125.86, 123.40, 122.10, 120.23, 118.14, 117.84, 111.55, 108.01, 50.84, 39.90, 32.39, 30.82, 27.08, 26.09, 11.08. MS (EI, 70 eV): *m/z* (%) 586 (13.4) [M^+], 402 (34.4), 307 (99.9), 281 (54.1), 171 (17.8), 123 (34.1). Anal. Calcd. for $C_{26}H_{22}Br_2N_2O_4$: C 53.27, H 3.78, N 4.78. Found: C 53.10, H 3.49, N 4.67%.

9-(5-{[(2-Hydroxy-3-methoxyphenyl)methylene]amino}-3-methylisoxazol-4-yl)-5-methoxy-3,3-dimethyl-2,3,4,9-tetrahydro-1*H*-xanthen-1-one (12i). Colorless solid; mp 211-212 °C. ^{1}H NMR (200 MHz, DMSO-d_6) δ 10.77 (s, 1OH), 8.98 (s, 1H), 7.42-6.62 (m, 6H), 4.90 (s, 1H), 3.81 (s, 6H), 2.64 (d, *J* 16.9 Hz, 1H), 2.40 (d, *J* 16.9 Hz, 1H), 2.30 (d, *J* 16.0 Hz, 1H), 2.10 (d, *J* 16.0 Hz, 1H), 2.26 (s, 3H), 1.02 (s, 3H), 0.84 (s, 3H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6) δ 194.65, 164.90, 160.25, 158.21, 150.65, 145.48, 130.81, 130.08, 128.69, 125.06, 124.41, 122.80, 120.86, 118.40, 117.04, 115.93, 110.01, 55.64, 54.35, 50.04, 39.88, 32.35, 30.12, 28.48, 27.49, 11.05. MS (EI, 70 eV): *m/z* (%) 489 (4.8) [M^+], 353 (48.1), 232 (33.8), 231 (99.9), 258 (25.5), 124 (48.9), 77 (16.9). Anal. Calcd. for $C_{28}H_{28}N_2O_6$: C 68.84, H 5.78, N 5.73. Found: C 68.67, H 5.50, N 5.64%.

9-(5-{[(2-Hydroxy-5-nitrophenyl)methylene]amino}-3-methylisoxazol-4-yl)-3,3-dimethyl-7-nitro-2,3,4,9-tetrahydro-1*H*-xanthen-1-one (12j). Colorless solid; mp 214-215 °C. ^{1}H NMR (200 MHz, DMSO-d_6) δ 10.98 (s, 1OH), 8.82 (s, 1H), 7.84-7.05 (m, 6H), 4.99 (s, 1H), 2.62 (d, *J* 17.0 Hz, 1H), 2.40 (d, *J* 17.0 Hz, 1H), 2.28 (d, *J* 16.1 Hz, 1H), 2.10 (d, *J* 17.0 Hz, 1H), 2.22 (s, 3H), 1.01 (s, 3H), 0.89 (s, 3H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6) δ 188.45, 170.18, 168.45, 158.21, 152.65, 145.58, 135.95, 128.10, 126.56, 124.96, 122.90, 122.15, 120.28, 118.14, 117.84, 111.25, 104.12, 51.04, 40.05, 37.49, 34.92, 28.08, 27.10, 11.01. MS (EI, 70 eV): *m/z* (%) 518 (4.5) [M^+], 368 (99.9), 272 (28.3), 247 (43.5), 139 (56.8), 122 (16.6), 95 (9.8). Anal. Calcd. for $C_{26}H_{22}N_4O_8$: C 60.23, H 4.28, N 10.81. Found: C 60.01, H 4.00, N 10.70%.

3-(4-Chlorophenyl)-9-(5-{[(2-hydroxyphenyl)methylene]amino}-3-methylisoxazol-4-yl)-2,3,4,9-tetrahydro-1*H*-xanthen-1-one (12k). Colorless solid; ^{1}H NMR (200 MHz, DMSO-d_6) δ 11.35(11.18) (s, 1OH), 9.03(8.95), (s, 1H), 7.80-6.97 (m, 12H), 5.02(4.97) (s, 1H), 3.52 (m, 1H), 2.98(2.94) (m, 2H), 2.75(2.68) (m, 2H), 2.28(2.21) (s, 3H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6) δ 195.84, 166.29, 165.32, 164.40, 162.14, 160.48, 149.31, 142.19, 135.35, 131.30, 130.70, 129.33, 125.82, 123.15, 120.60, 117.36, 116.82, 111.07, 43.88, 37.59, 34.55, 26.33, 10.98. MS (EI, 70 eV): *m/z* (%) 510 (14.8) [M^+], 400 (10.1), 294 (29.5), 205 (19.8), 199 (99.9), 113 (14.9),

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93 (27.5). Anal. Calcd. for $C_{30}H_{23}ClN_2O_4$: C 70.52, H 4.54, N 5.48. Found: C 70.34, H 4.23, N 5.40%.

7-Chloro-9-(5-{[(5-chloro-2-hydroxyphenyl)methylene]amino}-3-methylisoxazol-4-yl)-3-(4-chlorophenyl)-2,3,4,9-tetrahydro-1*H*-xanthen-1-one (12l). Colorless solid; ^{1}H NMR (200 MHz, DMSO-d_6) δ 11.09 (s, 1OH), 8.89(8.75) (s, 1H), 7.83-6.93 (m, 10H), 4.98(4.91) (s, 1H), 3.53 (m, 1H), 3.08(3.04) (m, 2H), 2.66(2.63) (m, 2H), 2.40(2.39) (s, 3H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6) δ 195.67, 165.72, 161.10, 158.29, 148.27, 142.08, 134.49, 131.68, 129.74, 128.91, 125.69, 123.89, 122.82, 119.34, 118.47, 115.55, 111.34, 43.90, 37.56, 34.50, 26.32, 10.96. MS (EI, 70 eV): *m/z* (%) 578 (14.5), 580 (18.9) [M^+], 469 (19.5), 438 (69.7), 329 (35.4), 237 (16.6), 234 (99.9), 204 (17.2), 129 (34.5), 95 (14.2). Anal. Calcd. for $C_{30}H_{21}Cl_3N_2O_4$: C 62.14, H 3.65, N 4.83. Found: C 61.91, H 3.33, N 4.71%.

7-Bromo-9-(5-{[(5-bromo-2-hydroxyphenyl)methylene]amino}-3-methylisoxazol-4-yl)-3-(4-chlorophenyl)-2,3,4,9-tetrahydro-1*H*-xanthen-1-one (12m). Colorless solid; ^{1}H NMR (200 MHz, DMSO-d_6) δ 11.09 (s, 1OH), 8.87(8.72) (s, 1H), 7.95-6.91 (m, 10H), 4.97(4.89) (s, 1H), 3.52 (m, 1H), 3.07(3.00) (m, 2H), 2.67(2.60) (m, 2H), 2.41(2.40) (s, 3H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6) δ 194.59, 165.66, 164.72, 160.40, 159.14, 148.48, 142.09, 137.09, 132.35, 129.30, 128.70, 126.13, 123.34, 119.15, 118.60, 117.06, 111.39, 43.91, 42.57, 37.59, 36.61, 34.50, 26.21, 10.97. MS (EI, 70 eV): *m/z* (%) 668 (2.8) [M^+], 556 (14.1), 485 (17.7), 373 (29.3), 279 (29.1), 198 (99.9), 172 (19.5), 113 (14.5). Anal. Calcd. for $C_{30}H_{21}Br_2ClN_2O_4$: C 53.88, H 3.17, N 4.19. Found: C 53.70, H 2.85, N 4.10%.

3-(4-Chlorophenyl)-9-(5-{[(2-hydroxy-3-methoxyphenyl)methylene]amino}-3-methylisoxazol-4-yl)-5-methoxy-2,3,4,9-tetrahydro-1*H*-xanthen-1-one (12n). Colorless solid; ^{1}H NMR (200 MHz, DMSO-d_6) δ 10.91 (s, 1OH), 9.04(8.99) (s, 1H), 7.35-6.40 (m, 10H), 5.00(4.94) (s, 1H), 3.81(3.74) (s, 6H), 3.46 (m, 1H), 2.96(2.88) (m, 2H), 2.71(2.61) (m, 2H), 2.24(2.13) (s, 3H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6) δ 194.67, 163.72, 162.10, 156.29, 149.27, 141.08, 135.49, 131.68, 129.84, 128.91, 124.69, 123.89, 122.80, 118.34, 116.47, 115.55, 109.34, 55.47, 53.98, 43.90, 37.56, 34.50, 26.32, 10.96. MS (EI, 70 eV): *m/z* (%) 570 (6.8) [M^+], 434 (49.8), 323 (17.4), 231 (14.3), 228 (99.9), 123 (74.1), 111 (19.4), 95 (32.1). Anal. Calcd. for $C_{32}H_{27}ClN_2O_6$: C 67.31, H 4.77, N 4.91. Found: C 67.13, H 4.45, N 4.83%.

3-(4-Chlorophenyl)-9-(5-{[(2-hydroxy-5-nitrophenyl)methylene]amino}-3-methylisoxazol-4-yl)-7-nitro-2,3,4,9-tetrahydro-1*H*-xanthen-1-one (12o). Colorless solid; ^{1}H NMR (200 MHz, DMSO-d_6) δ 11.01 (s, 1OH), 9.03(8.99) (s, 1H), 7.48-6.40 (m, 10H), 5.01(4.95) (s, 1H), 3.49 (m, 1H), 2.99(2.90) (m, 2H), 2.79(2.68) (m, 2H), 2.34(2.23) (s, 3H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6) δ 191.67, 165.72, 162.30, 155.29, 150.27, 141.08, 132.49, 131.68, 129.84, 127.91, 124.69, 123.89, 122.80, 115.34, 111.47, 110.55, 105.34, 42.90, 37.56, 34.50, 25.32, 11.06. MS (EI, 70 eV): *m/z* (%) 600 (4.5) [M^+], 490 (18.5), 451 (34.1), 339 (74.1), 247 (17.1), 244 (99.9), 139 (71.1), 113 (14.4), 95 (21.7). Anal. Calcd. for $C_{30}H_{21}ClN_4O_8$: C 59.96, H 3.52, N 9.32. Found: C 59.77, H 3.20, N 9.23%.

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General procedure for synthesis of 14f,k-m,p,u,w. Compounds **4f**,**k**,**l**,**m**,**o**,**p**,**u**,**w** (1mmol) were dissolved in methanol at reflux, and then NBS (1 mmol) was added. The mixture was heated for an 1 h, then cooled to room temperature and the precipitate formed was filtered off.

3-Methyl-4-(4-nitrophenyl)-7,8-dihydroisoxazolo[5,4-*b*]quinolin-5(6*H*)-one (14f). Colorless solid, mp 179-180 °C. ^{1}H NMR (200 MHz, DMSO-d_6) δ 8.30-7.58 (m, 4H), 3.23 (m, 2H), 2.62 (m, 2H), 2.09 (m, 2H), 1.80 (s, 3H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6) δ 200.02, 167.78, 164.01, 160.45, 150.60, 148.35, 139.85, 135.44, 130.28, 122.95, 116.97, 36.87, 27.89, 22.33, 10.45 ppm. MS (EI, 70 eV): *m/z* (%) 323 (56.5) [M$^+$], 267 (43.1), 201 (99.9), 123 (17.6), 95 (12.3). Anal. Calcd. for $C_{17}H_{13}N_3O_4$: C 63.16, H 4.05, N 13.00. Found: C 62.94, H 3.76, N 12.91%.

4-(4-Chlorophenyl)-3,7,7-trimethyl-7,8-dihydroisoxazolo[5,4-*b*]quinolin-5(6*H*)-one (14k). Colorless solid, mp 240-241 °C. ^{1}H NMR (200 MHz, DMSO-d_6) δ 7.50-7.30 (m, 4H), 3.17 (s, 2H), 2.52 (s, 2H), 1.80 (s, 3H), 1.04 (s, 6H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6) δ 199.65, 165.67, 163.80, 158.94, 151.78, 148.12, 138.90, 129.52, 128.92, 128.63, 119.28, 52.95, 45.14, 32.91, 29.88, 28.45, 11.60 ppm. MS (EI, 70 eV): *m/z* (%) 340 (49.5) [M$^+$], 230 (99.9), 169 (52.3), 113 (77.4), 96 (17.8). Anal. Calcd. for $C_{19}H_{17}ClN_2O_2$: C 66.96, H 5.03, N 8.22. Found: C 66.74, H 4.73, N 8.10%.

4-(4-Bromophenyl)-3,7,7-trimethyl-7,8-tetrahydroisoxazolo[5,4-*b*]quinolin-5(6*H*)-one (14l). Colorless solid, mp 256-257 °C. ^{1}H NMR (200 MHz, DMSO-d_6) δ 7.63-7.26 (m, 4H), 3.17 (s, 2H), 2.51 (s, 2H), 1.81 (s, 3H), 1.05 (s, 6H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6) δ 199.56, 166.80, 163.88, 160.95, 146.44, 140.87, 131.40, 130.24, 127.88, 125.76, 119.52, 50.98, 41.88, 32.99, 30.02, 27.85, 11.06 ppm. MS (EI, 70 eV): *m/z* (%) 384 (47.3) [M$^+$], 275 (31.1), 230 (99.9), 156 (27.1), 123 (18.5). Anal. Calcd. for $C_{19}H_{17}BrN_2O_2$: C 59.24, H 4.45, N 7.27. Found: C 59.05, H 4.14, N 7.18%.

3,7,7-Trimethyl-(4-methylphenyl)-7,8-tetrahydroisoxazolo[5,4-*b*]quinolin-5(6*H*)-one (14m). Colorless solid, mp 218-219 °C. ^{1}H NMR (200 MHz, DMSO-d_6) 7.25-7.13 (m, 4H), 3.16 (s, 2H), 2.50 (s, 2H), 2.38 (s, 3H), 1.78 (s, 3H), 1.04 (s, 3H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6) δ 199.89, 166.78, 164.02, 160.78, 148.19, 140.45, 139.00, 133.73, 131.22, 125.52, 119.01, 51.89, 41.06, 33.67, 30.08, 27.88, 21.89, 10.86 ppm. MS (EI, 70 eV): *m/z* (%) 320 (41.7) [M$^+$], 230 (99.9), 223 (19.9), 123 (19.3), 92(24.1). Anal. Calcd. for $C_{20}H_{20}N_2O_2$: C 74.98, H 6.29, N 8.74. Found: C 74.77, H 6.01, N 8.64%.

Methyl-4-(3,7,7-trimethyl-5-oxo-5,6,7,8-tetrahydroisoxazolo[5,4-*b*]quinolin-4-yl)benzoate (14p). Colorless solid, mp 164-165 °C. ^{1}H NMR (200 MHz, DMSO-d_6) δ 8.04-7.42 (m, 4H), 3.89 (s, 3H), 3.18 (s, 2H), 2.52 (s, 2H), 1.74 (s, 3H), 1.05 (s, 6H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6) δ 198.99, 167.07, 165.25, 163.56, 160.07, 142.89, 140.22, 138.76, 132.10, 121.65, 118.12, 51.95, 50.88, 41.87, 30.93, 28.72, 26.99, 10.14 ppm. MS (EI, 70 eV): *m/z* (%) 364 (17.9) [M$^+$], 230 (99.9), 169 (51.1), 135 (68.5). Anal. Calcd. for $C_{21}H_{20}N_2O_4$: C 69.22, H 5.53, N 7.69. Found: C 69.03, H 5.22, N 7.60%.

4-(4-Bromophenyl)-7-(4-chlorophenyl)-3-methyl-7,8-dihydroisoxazolo[5,4-*b*]quinolin-5(6*H*)-one (14u). Colorless solid, mp 188-189 °C. ^{1}H NMR (200 MHz, DMSO-d_6) δ 7.68-7.28

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(m, 8H), 3.60 (m, 2H), 3.27 (m, 1H), 3.01 (m, 1H), 2.71 (m, 1H), 1.83 (s, 3H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6) δ 198.11, 166.95, 164.12, 160.76, 146.54, 142.56, 138.89, 136.26, 133.45, 132.11, 129.86, 127.44, 124.25, 122.19, 119.50, 47.01, 40.14, 37.31, 11.34 ppm. MS (EI, 70 eV): *m/z* (%) 468 (9.8) [M^+], 357 (81.2), 311 (99.9), 201 (41.2), 156 (17.8), 113 (14.3). Anal. Calcd. for $C_{23}H_{16}BrClN_2O_2$: C 59.06, H 3.45, N 5.99. Found: C 58.84, H 3.17, N 5.88%.

7-(4-Chlorophenyl)-4-(4-methoxylphenyl)-3-methyl-7,8-dihydroisoxazolo[5,4-*b*]quinolin-5(6*H*)-one (14w). Colorless solid; mp 168-169 °C. ^{1}H NMR (200 MHz, DMSO-d_6) δ 7.75-7.04 (m, 8H), 3.65 (s, 3H), 3.60 (m, 2H), 3.27 (m, 1H), 3.01 (m, 1H), 2.71 (m, 1H), 1.83 (s, 3H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6) δ 199.89, 167.99, 164.59, 160.05, 158.98, 151.19, 144.45, 141.22, 138.30, 131.98, 130.31, 128.78, 126.84, 123.87, 119.58, 56.32, 46.18, 42.35, 37.16, 10.92 ppm. MS (EI, 70 eV): *m/z* (%) 418 (49.8) [M^+], 360 (20.9), 280 (99.9), 279 (30.9), 140 (18.6), 125 (18.6), 102 (14.6). Anal. Calcd. for $C_{24}H_{19}ClN_2O_3$: C 68.82, H 4.57, N 6.69. Found: C 68.64, H 4.25, N 6.61%.

General procedure for synthesis of 15a-f. A mixture of **4c,h,n,v,z** (1 mmol), ethyl or benzyl bromide (1 mmol) and K_2CO_3 (3 mmol) was heated in DMF (0.3 mL) for 2 h. The reaction mixture was poured into water and the precipitate formed was filtered off, recrystallized from ethanol and dried in air.

4-(4-Bromophenyl)-9-ethyl-3-methyl-4,7,8,9-tetrahydroisoxazolo[5,4-*b*]quinolin-5(6*H*)-one (15a). Colorless solid, mp 235-236 °C. ^{1}H NMR (200 MHz, DMSO-d_6) δ 7.42-7.10 (m, 4H), 5.01 (s, 1H), 3.85 (q, *J* 7.0 Hz, 2H), 2.74 (m, 2H), 2.18 (m, 2H), 1.87 (s, 3H), 1.83 (m, 2H), 1.24 (t, *J* 7.0 Hz, 3H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6) δ 195.04, 158.60, 156.80, 151.13, 145.88, 130.11, 128.19, 119.51, 111.12, 95.75, 42.15, 37.34, 35.83, 27.64, 21.35, 14.29, 10.29 ppm. MS (EI, 70 eV): *m/z* (%) 386 (14.5) [M^+], 359 (16.9), 232 (49.7), 203 (99.9), 156 (17.4), 95 (37.8). Anal. Calcd. for $C_{19}H_{19}BrN_2O_2$: C 58.93, H 4.95, N 7.23. Found: C 58.71, H 4.66, N 7.09%.

9-Benzyl-4-[4-(dimethylamino)phenyl]-3-methyl-4,7,8,9-tetrahydroisoxazolo[5,4-*b*]quinolin-5(6*H*)-one (15b). Colorless solid, mp 228-229 °C. ^{1}H NMR (200 MHz, DMSO-d_6) δ 7.34-6.60 (m, 9H), 5.11 (s, 2H), 4.94 (s, 1H), 2.83 (m, 2H), 2.80 (s, 6H), 2.15 (m, 2H), 1.89 (s, 3H), 1.81 (m, 2H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6) δ 194.42, 158.92, 158.35, 151.99, 148.77, 137.13, 135.84, 128.76, 127.93, 127.09, 112.31, 111.63, 96.06, 48.76, 40.34, 36.98, 34.33, 27.54, 20.12, 9.89 ppm. MS (EI, 70 eV): *m/z* (%) 413 (9.2) [M^+], 391 (19.8), 343 (46.9), 341 (99.9), 153 (10.3), 138 (11.6), 125 (15.8), 103 (17.7), 91 (19.3), 77 (18.1). Anal. Calcd. for $C_{26}H_{27}N_3O_2$: C 75.52, H 6.58, N 10.16. Found: C 75.34, H 6.26, N 10.03%.

9-Benzyl-4-(4-methoxyphenyl)-3,7,7-trimethyl-4,7,8,9-tetrahydroisoxazolo[5,4-*b*]quinolin-5(6*H*)-one (15c). Colorless solid, mp 243-244 °C. ^{1}H NMR (200 MHz, DMSO-d_6) δ 7.42-6.75 (m, 9H), 5.12 (s, 2H), 4.99 (s, 1H), 3.68 (s, 3H), 2.65-2.45 (dd, 2H), 2.16-1.99 (dd, 2H), 1.87 (s, 3H), 0.93 (s, 3H), 0.83 (s, 3H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6) δ 195.16, 159.76, 158.93, 153.32, 150.44, 139.60, 137.23, 129.10, 128.19, 127.65, 113.98, 112.13, 96.53, 55.76, 52.31, 49.37, 37.81, 35.23, 32.56, 27.91, 21.59, 10.85 ppm. MS (EI, 70 eV): *m/z* (%) 429 (12.3) [M^+],

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339 (99.9), 323 (14.5), 231 (19.6), 170 (38.4), 108 (41.3). Anal. Calcd. for $C_{27}H_{28}N_2O_3$: C 75.68, H 6.59, N 6.54. Found: C 75.50, H 6.27, N 6.42%.

7-(4-Chlorophenyl)-9-ethyl-3-methyl-4-(4-methylphenyl)-4,7,8,9-tetrahydroisoxazolo-[5,4-*b*]quinolin-5(6*H*)-one (15d). Colorless solid, mp 139-140 °C. ^{1}H NMR (200 MHz, DMSO-d_6) δ 7.33-6.97 (m, 8H), 4.95 (s, 1H), 3.88 (m, 2H), 3.46 (m, 1H), 3.00 (m, 2H), 2.40 (m, 2H), 2.20 (s, 3H), 1.87 (s, 3H), 1.22 (m, 3H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6) δ 193.12, 159.40, 158.15, 155.25, 151.30, 147.20, 143.95, 142.67, 135.37, 131.67, 129.38, 127.94, 111.25, 96.55, 44.16, 41.25, 38.38, 36.01, 34.38, 21.08, 14.29, 10.34 ppm. MS (EI, 70 eV): *m/z* (%) 432 (33.1) [M^+], 431 (40.9), 343 (50.8), 341 (99.9), 225 (13.1), 174 (16.3), 153 (13.7), 127 (15.8), 102 (18.0). Anal. Calcd. for $C_{26}H_{25}N_2O_2$: C 72.13, H 5.82, N 6.47. Found: C 71.91, H 5.53, N 6.35%.

9-Benzyl-7-(4-chlorophenyl)-3-methyl-4-(4-methylphenyl)-4,7,8,9-tetrahydroisoxazolo-[5,4-*b*]quinolin-5(6*H*)-one (15e). Colorless solid, mp 225-226 °C. ^{1}H NMR (200 MHz, DMSO-d_6) δ 7.38-6.95 (m, 13H), 5.13 (s, 2H), 5.00 (s, 1H), 3.46 (m, 1H), 2.98 (m, 2H), 2.54 (m, 2H), 2.20 (s, 3H), 1.88 (s, 3H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6) δ 193.72, 159.42, 158.90, 155.35, 147.18, 143.90, 142.54, 138.18, 135.17, 132.23, 129.18, 127.04, 126.93, 125.16, 124.88, 110.18, 96.17, 47.65, 44.18, 38.42, 36.16, 34.25, 21.38, 10.85 ppm. MS (EI, 70 eV): *m/z* (%) 494 (10.7) [M^+], 453 (22.3), 405 (46.6), 403 (97.3), 127 (11.2), 115 (14.8), 92 (44.3), 91 (99.9), 77 (12.1). Anal. Calcd. for $C_{31}H_{27}ClN_2O_2$: C 75.22, H 5.50, N 5.66. Found: C 75.01, H 5.19, N 5.56%.

9-Benzyl-7-(4-chlorophenyl)-4-[4-(dimethylamino)phenyl]-3-methyl-4,7,8,9-tetrahydroisox-azolo[5,4-*b*]quinolin-5(6*H*)-one (15f). Colorless solid, mp 152-153 °C. ^{1}H NMR (200 MHz, DMSO-d_6) δ 7.38-6.49 (m, 13H), 5.13 (s, 2H), 4.92 (s, 1H), 3.54 (m, 1H), 2.97 (m, 2H), 2.81 (s, 6H), 2.51 (m, 2H), 1.89 (s, 3H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6) δ 194.87, 161.12, 155.90, 150.35, 147.18, 143.90, 138.18, 135.17, 130.23, 129.18, 127.04, 126.93, 125.66, 114.98, 109.18, 95.88, 47.15, 44.20, 41.95, 38.28, 36.22, 33.28, 10.85 ppm. MS (EI, 70 eV): *m/z* (%) 523 (17.4) [M^+], 482 (33.8), 391 (15.7), 91 (99.9), 65 (18.0). Anal. Calcd. for $C_{32}H_{30}ClN_3O_2$: C 73.34, H 5.77, N 8.02. Found: C 73.12, H 5.48, N 7.91%.

General procedure for synthesis of 13a,b. A mixture of 5-amino-3-methylisoxazole **1** (1 mmol), aldehydes **9a,d** (1 mmol), cyclic β-di-ketones **3b** (1 mmol) and Et_3N (0.1 mmol) in DMF (2 mL) was heated to reflux for 10 min in a roundbottom flask equipped with a condenser. Then after cooling ethanol (10 mL) was added and the precipitate formed was filtered off to give the solid compounds.

9-(2-Hydroxy-4,4-dimethyl-6-oxocyclohex-1-enyl)-3,3-dimethyl-3,4-dihydro-2*H*-xanthen-1(9*H*)-one (13a). Colorless solid, mp 209-210 °C. ^{1}H NMR (200 MHz, DMSO-d_6) δ 10.29 (s, 1OH), 7.00-6.82 (m, 4H), 5.02 (s, 1H), 2.50-2.20 (m, 4H), 2.09-1.94 (m, 4H), 1.02 (s, 3H), 0.96 (s, 3H), 0.87 (s, 6H) ppm; Anal. Calcd. for $C_{23}H_{26}O_4$: C 75.38, H 7.15. Found: C 75.12, H 6.86%.

9-(2-Hydroxy-4,4-dimethyl-6-oxocyclohex-1-enyl)-5-methoxy-3,3-dimethyl-3,4-dihydro-2*H*-xanthen-1(9*H*)-one (13b). Colorless solid, mp 235-236 °C. ^{1}H NMR (200 MHz, DMSO-d_6) δ

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10.29 (s, 1OH), 6.92-6.49 (m, 3H), 5.01 (s, 1H), 3.76 (s, 3H), 2.54-2.27 (m, 4H), 2.14-1.99 (m, 2H), 1.02 (s, 3H), 0.96 (s, 3H), 0.86 (s, 6H) ppm; Anal. Calcd. for $C_{24}H_{28}O_5$: C 72.70, H 7.12. Found: C 72.46, H 6.84%.

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