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Bismuth triflate catalyzed solvent-free synthesis of 2,4,6-triaryl pyridines and an unexpected selective acetalization of tetrazolo[1,5-*a*]-quinoline-4-carbaldehydes

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ABSTRACT

Bismuth triflate has been found as a potential catalyst for an efficient and solvent-free synthesis of symmetrical 2,4,6-triarylpyridines in 86–93% yields. Moreover, catalytic reactivity of bismuth triflate toward tetrazolo[1,5-*a*]quinoline-4-carbaldehydes for the unexpected formation of their corresponding acetals has been exploited.

Being environment friendly, bismuth compounds have been used in catalysis and organic synthesis in the past two decades. However, till now there are only a few reports on the use of bismuth compounds, for example, Bismuth chloride ($BiCl_3$), Bismuth nitrate ($Bi(NO_3)_3$), Bismuth bromide ($BiBr_3$), Bismuth triflate ($Bi(OTf)_3$), etc., as catalysts in organic synthesis[1] possibly due to the unstable nature of Bi–C bonds. In view of the ever increasing importance of green/sustainable chemistry and significance of bismuth compounds as catalysts, it was aimed to develop bismuth catalyzed ecofriendly organic transformations.

Pyridine ring system, particularly 2,4,6-triarylpyridine is of immense interest because of its unique position in medicinal chemistry.[2,3] Moreover, they are prominent synthons in supramolecular chemistry, with their Π-stacking ability along with directional H-bonding capacity.[4] In addition, the excellent thermal stabilities of these pyridines have instigated a growing interest for their use as monomeric building blocks in thin films and organometallic polymers.[5] Recent studies have highlighted the biological activity of triarylpyridines, providing impetus for further studies in utilizing this scaffold in new therapeutic drug classes.[6] These molecules have been found to be useful for the synthesis of DNA binding ligands, in particular targeting G-quadruplex DNA which has recently received much attention as a possible target in cancer therapy.[7,8]

Since, Krohnke's original report on the synthesis of 2,4,6-triarylpyridines,[9] there has been a plethora of research targeting their syntheses.[10] Pyridines with 2,4,6-triaryl substitution pattern (Krohnke pyridines) have been synthesized using various methods and procedures.[11] Traditionally, these compounds have been synthesized through the reaction of *N*-phenacyl pyridinium salts with α,β-unsaturated ketones in the presence of ammonium acetate (NH_4OAc).[10,12] Recently, several new improved methods have been developed for the synthesis of these 2,4,6-triaryl pyridines.[13–17] Among all these methods, one pot reaction between acetophenones, aryl aldehydes, and NH_4OAc is the well established protocol for the synthesis of triaryl pyridines using NaOH in PEG-400,[18] PEG-300 along with NaOH,[19] catalytic amount of acetic acid,[20] $HClO_4$–SiO_2,[21] preyssler type heteropolyacid $H_{14}[NaP_5W_{30}O_{110}]$,[22] wet 2,4,6-trichloro-1,3,5-triazine (TCT),[23] 3-methyl-1-(4-sulfonylbutyl) imidazolium hydrogen sulfate $[HO_3S(CH_2)_4MIM][HSO_4]$ and a Bronsted acidic ionic liquid.[24] But, most of these protocols are having one or more drawbacks, thus leaving room for further improvements.

Owing to the aforementioned chemical and pharmacological significance of the Krohnke pyridines, synthesis of such type of molecules is becoming interesting area of research and hence, chemists are diverting their attention to search simple routes for their syntheses exploring the applications of efficient catalysts by utilizing the concepts of greener chemistry.

In the pharmaceutical,[25] phyto pharmaceutical, fragrance,[26] and lacquer industries,[27] acetals are used both as intermediates and as end products. Different types of acetals are also applied as plasticizers and vulcanizers, as physiologically active substances, and

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as potential protective groups for aldehydes and ketones. Acetalization is probably the most important protection strategy for carbonyl groups and it plays an important role in organic synthesis.[28]

In general, this aim of formation of acetals and ketals is generally achieved in the presence of mineral liquid acids or Lewis acids as catalysts.[28,29] Acetal formation is achieved by treating aldehydes or ketones with an excess (10 equiv or more) of an alcohol or diol in the presence of a drying reagent and a Lewis or Bronsted acid,[30] or by removing water through the formation of an azeotrope with the solvent and the use of a Dean–Stark trap.[28]

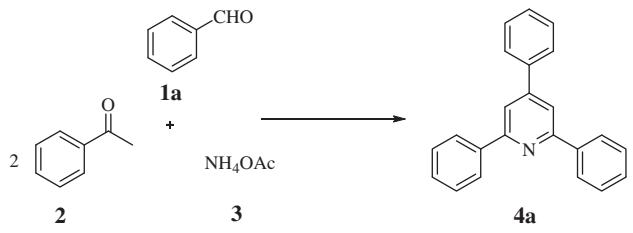
It is worthy to point out here that, most of the catalysts are not selective toward the substrates, that is, aldehydes and ketones. Consequently, there is a demand for selective acetalization methods, which can selectively carry out acetalization of aldehyde in the presence of ketone and vice-versa. But, this could be rarely achieved, since requirement of acetalizing reagent, for example, ethanol for the reaction is 10 equiv, which leaves room for both the substrates, that is, aldehyde and ketone to form their corresponding acetals and ketals, respectively.

Traditionally acetals and ketals are synthesized by the reaction of aldehyde and ketones with alcohol in the presence of acid catalysts.[31] Magnesium perchlorate, *p*-toluene sulfonic acid, and different metal complexes of Pt(II), Pd(II), Rh(II) are also reported to accomplish this organic transformation.[32–34] Progress has also been made in the alternative catalysts for the acetalization of carbonyl compounds, such as organometallic reagents,[35] silyl reagents,[36] inorganic compounds,[37] etc.

Copper(II) tetrafluoroborate is an effective catalyst for the formation of acetals,[38] but the BF_4^- counter ion is harmful to the environment. Metal triflates have previously been reported to catalyze acetalization reactions.[39,40] In particular, $Bi(OTf)_3$ and $In(OTf)_3$ effectively catalyze this process. But, literature reveals that, these triflates, while being efficient, are associated with some drawbacks. For example, when reactions are carried out using $In(OTf)_3$ an aqueous work-up cannot be used as the acetal undergoes rapid hydrolysis back to the corresponding carbonyl,[39] making recycling of the catalyst difficult, whereas, previous protocol involving the use of $Bi(OTf)_3$ reveals that there is a need of reagent trialkyl orthoformate for acetalization of carbonyl compounds. Moreover, the reactions require to be carried out under reflux condition and suffer from relatively longer reaction times.[40]

However, all these methods have not been entirely satisfactory, owing to various side-effects associated with them. Notably, almost all of the reported procedures do not selectively form corresponding acetal of only one carbonyl compound either aldehyde or ketone.

In search of the best experimental reaction conditions for the preparation of 2,4,6-triaryl pyridines, reaction of benzaldehyde **1a**, two molecules of acetophenone **2**, and ammonium acetate **3** was selected as a model reaction (Scheme 1). For this study, we have screened various acid catalysts bearing sulphonated functionalities owing to their wide spread catalytic applications in organic synthesis. For this purpose, sulfamic acid, sulfanilic acid, *p*-TSA, (±) CSA, and $Bi(OTf)_3$ were screened as catalysts in aq. ethanol.



Scheme 1. Standard model reaction.

We observed that sulfamic acid and sulfanilic acid cannot afford more than 32 and 43% yields (Table 1, entries 1–2). In comparison, (±) CSA is able to deliver only 59% product yield after 4 h (Table 1, entry 3). As a matter of fact *p*-TSA and $Bi(OTf)_3$ furnished the desired product in good, 77, and 83% yields, respectively, within 2 h (Table 1, entries 4–5). In view of the good catalytic activity of $Bi(OTf)_3$ it was finalized for subsequent optimization studies.

To evaluate the effect of solvent, model reaction was further performed using $Bi(OTf)_3$ in ethanol and water as solvent. Water did not bring the reaction to completion (Table 1, entry 7), but in contrast ethanol found to furnish the product in a good yield (Table 1, entry 6). Considering the increasing importance of solvent-free reactions in organic synthesis, our next attempt was to examine the catalytic efficiency of $Bi(OTf)_3$ in the absence of solvent. Predictably, it was observed that in the absence of solvent, reaction rate increased enormously and desired product was obtained in higher yields (Table 1, entry 8).

To determine the appropriate concentration of the catalyst, that is, $Bi(OTf)_3$, model reaction was investigated at different concentrations of $Bi(OTf)_3$ such as 1, 2, 5, and 10 mol %. This study revealed that the product was formed in 56%, 69%, 89%, and 90% yields, respectively. This indicates that 5 mol % of $Bi(OTf)_3$ is enough to carry out the reaction efficiently.

A mechanism for the formation of triaryl pyridines has been proposed with the help of Figure 1.

Initially, acetophenone **A** in the presence of $Bi(OTf)_3$ is converted into its enol form, which gives nucleophilic addition on the aldehyde molecule **B** to afford aldol condensation product **C**. Then second molecule of acetophenone undergoes Michael addition reaction with **C** to form the 1,5-diketone intermediate **D**. This 1,5-diketone on reaction with ammonium acetate followed by cyclization and dehydration gives compounds **E**. Finally, air oxidation of E leads to the formation of corresponding triaryl pyridine **F**.

To establish generality of the optimized reaction conditions, various aldehydes were allowed to undergo this cyclocondensation reaction.[41] Almost all the aromatic aldehydes proved to be amenable to these reaction conditions. However, no significant substituent effect was found in case of all aryl aldehydes (Table 2).

To sum up, we have investigated a new approach for the synthesis of 2,4,6-triaryl pyridines in the presence of $Bi(OTf)_3$ as an efficient catalyst. The remarkable advantages offered by this method are- (i) solvent-free reaction conditions which do not need any solvent or reaction medium to achieve the targeted compounds, (ii) short reaction times as compared to other protocols, (iii) ease of product isolation, purification and avoids the need of column chromatography technique, and (iv) high yields of the desired products. We believe that this method is a useful alternative to the existing methodologies for the synthesis of 2,4,6-triaryl pyridine derivatives.

Table 1
Screening of catalysts and solvents[a]

Entry	Catalyst	Solvent	Time (h)	Yield[b] (%)
1	Sulfamic acid	Aq. Ethanol	4	32
2	Sulphanilic acid	Aq. ethanol	2	43
3	(±) CSA	Aq. ethanol	4	59
4	*p*-TSA	Aq. ethanol	2	77
5	$Bi(OTf)_3$	Aq. ethanol	2	83
6	$Bi(OTf)_3$	Ethanol	3	78
7	$Bi(OTf)_3$	Water	4	Trace
8	$Bi(OTf)_3$	Neat	2	89

Note: Aq. Ethanol used was 30% aqueous.
[a] Reaction and conditions: **1a** (0.001 mol), **2** (0.002 mol), **3** (0.0015 mol) and catalyst (5 mol %).
[b] Isolated Yields.

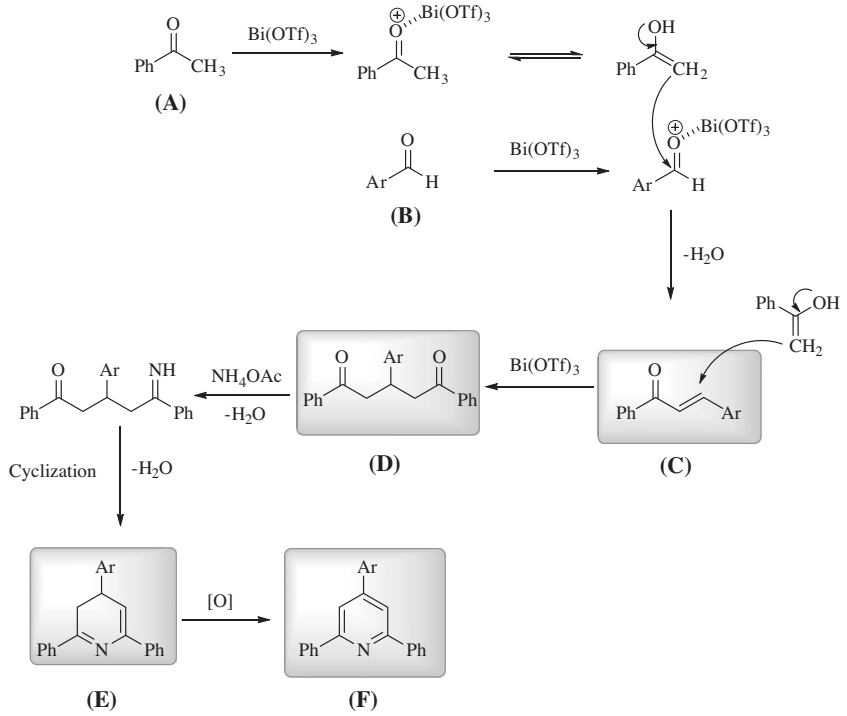
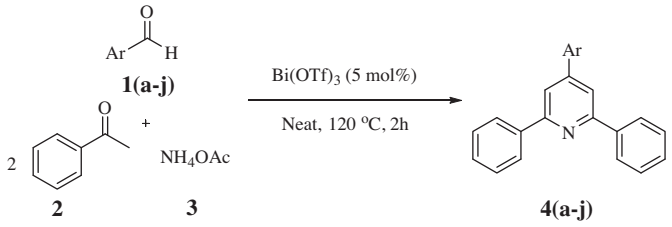


Figure 1. A plausible mechanism involved in the synthesis of 2,4,6-triaryl pyridines.

Table 2
Synthesis of 2,4,6-triaryl pyridines **4**(**a**–**j**)



Entry	Compd	Ar	Yield[a] (%)	MP (°C)
1	**4a**	Ph	89	133–135
2	**4b**	4-Me-Ph	87	124–126
3	**4c**	4-OMe-Ph	91	98–99
4	**4d**	4-OH-Ph	89	194–196
5	**4e**	4-NO_2-Ph	92	195–197
6	**4f**	2-Cl-Ph	91	113–114
7	**4g**	4-Cl-Ph	93	127–128
8	**4h**	4-Br-Ph	89	102–104
9	**4i**	2-Thienyl	86	161–163
10	**4j**	2-Furyl	88	170–171

[a] Isolated Yields.

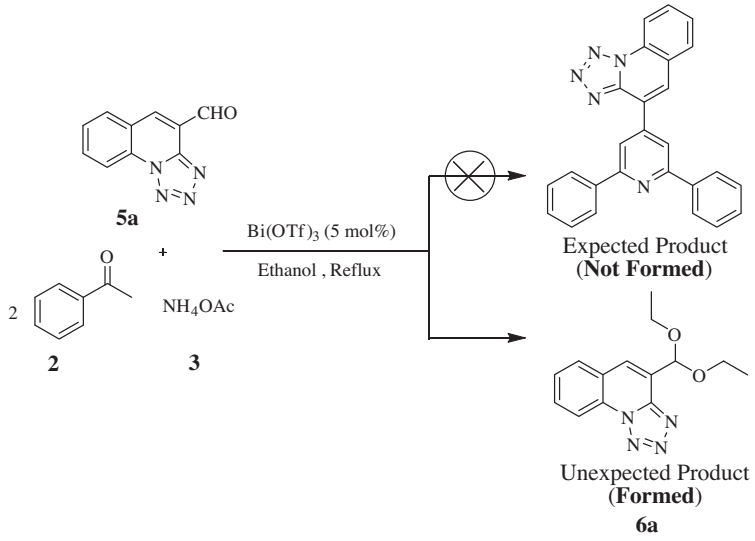
Success of bismuth triflate as an air/moisture tolerant and remarkably efficient catalyst for the synthesis of triaryl pyridines led us to investigate its efficacy for the formation of tetrazolo [1,5-*a*]quinoline based triaryl pyridines from a variety of tetrazolo [1,5-*a*]quinoline-4-carbaldehydes, acetophenone, and ammonium acetate. Initially, reaction between tetrazolo[1,5-*a*]quinoline-4-carbaldehyde **5a**, acetophenone **2**, and ammonium acetate **3** was performed in the presence of $Bi(OTf)_3$ with the hope to obtain tetrazolo[1,5-*a*]quinoline based 2,4,6-triarylpyridines (Scheme 2). But, unfortunately no reaction was observed even after longer reaction time (4 h).

In the next attempts, several solvents like water, ethanol, toluene, and THF were examined to achieve the targeted compounds. In all these solvents except ethanol no reaction was observed at their respective reflux temperatures. As noted, reaction carried out in ethanol as a solvent delivered the product after 3 h, but spectral analysis study of thus formed product revealed the unexpected results. It was observed that the obtained product was not the desired one, but unexpected acetal of tetrazolo[1,5-*a*]quinoline-4-carbaldehyde was formed. This observation reflected that tetrazolo[1,5-*a*]quinoline-4-carbaldehyde has greater affinity toward ethanol as compared to acetophenone.

$Bi(OTf)_3$ is a hard Lewis acid and is oxophilic. So, quite possibly in the presence of $Bi(OTf)_3$, the oxygen atom of EtOH solvent competes with the methylene carbon α- to carbonyl group of acetophenone for the nucleophilic attack on carbonyl carbon of the aldehyde and dominate over it, thereby eliminating the possibility of reaction between aldehyde and acetophenone.

It was thought that, this putative competition would be largely removed by omitting the use of ethanol. But, reaction under neat condition did not led to the formation of the desired product. Incidentally, it should be noted that use of various acid catalysts such as sulphanilic acid, sulfamic acid, *p*-TSA and boric acid under neat conditions as well as in the presence of ethanol as a solvent failed to deliver the desired product (i.e., triaryl pyridine), but, sulphanilic acid and *p*-TSA furnished the corresponding acetals in moderate yields. Finally, it was concluded that formation of the desired triaryl pyridine derivative was quite difficult, but, $Bi(OTf)_3$ efficiently forms the acetals of tetrazolo[1,5-*a*]quinoline-4-carbaldehyde. Therefore, we extended our study for the acetalization of series of tetrazolo[1,5-*a*]quinoline-4-carbaldehydes.

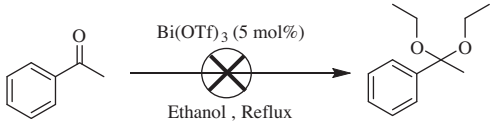
In this endevor, efforts were directed to determine the appropriate concentration of the catalyst ($Bi(OTf)_3$) for the acetalization reaction. Hence, model reaction was performed at different concentrations of ($Bi(OTf)_3$) such as 1, 2, 3, 5, and 10 mol %. Formation of the product was formed in 59%, 93%, 94%, 93%, and 91%



Scheme 2. Unexpected formation of 4-(diethoxymethyl)-tetrazolo[1,5-*a*]quinoline.

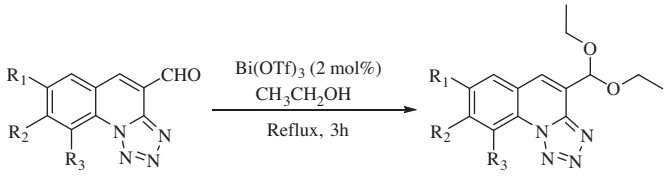
yield, respectively. This indicates that 2 mol % of $Bi(OTf)_3$ is sufficient to carry out the reaction effectively.

Results of our earlier work on the synthesis of triaryl pyridines involving simple aromatic aldehydes and literature report[40] involving the use of $Bi(OTf)_3$ reveals that there is a need of reagent trialkyl orthoformate for acetalization of aldehydes and ketones. In the absence of trialkyl orthoformate, acetalization of aldehydes, and ketones do not take place. To confirm this, reaction of acetophenone with ethanol in the presence of $Bi(OTf)_3$ was also performed (Scheme 3), but no reaction was observed even after 4 h. This study revealed that, selective acetalization of tetrazolo[1,5-*a*]quinoline-4-carbaldehyde takes place even in the presence of acetophenone.



Scheme 3. Reaction between acetophenone and ethanol.

Table 3
Acetalization of a series of tetrazolo[1,5-*a*]quinoline-4-carbaldehydes (**6a–h**)



Entry	Compd	R_1	R_2	R_3	Yield[a] (%)	MP (°C)
1	**6a**	H	H	H	93	95–97
2	**6b**	H	H	Me	91	117–119
3	**6c**	H	Me	H	89	110–111
4	**6d**	H	H	OMe	83	212–214(d)
5	**6e**	H	OMe	H	81	203–205(d)
6	**6f**	OMe	H	H	78	230–232(d)
7	**6g**	H	H	Et	89	148–150
8	**6h**	OEt	H	H	81	97–98

[a] Isolated yields; d = decompose.

The taming effect of ethanol and $Bi(OTf)_3$ on the reaction was confirmed by performing the acetalization reactions of various substituted tetrazolo[1,5-*a*]quinoline-4-carbaldehydes. In all the cases, similar results were observed for different substituents like Me, OMe, Et, and OEt affording the corresponding acetal in good to excellent yields. Complete results are summarized in Table 3. Formation of the product was confirmed with the help of ^1H NMR, ^{13}C NMR, and mass spectroscopic data.[42]

In summary, the procedure described here provides the opportunity to perform the selective acetal protection reaction of various substituted tetrazolo[1,5-*a*]quinoline-4-carbaldehydes in the presence of other carbonyl compounds. This protocol may be useful while carrying out diverse organic transformations on tetrazolo[1,5-*a*]quinoline-4-carbaldehydes.

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41. General experimental procedure for the synthesis of compounds **4**(**a**–**j**): A mixture of aldehyde 1 (0.001 mol), acetophenone 2 (0.002 mol), ammonium acetate 3 (0.0015 mol) and bismuth triflate (5 mol %) was heated at 120 (C for 2 h. Reaction progress was monitored by TLC (ethyl acetate/*n*-hexane, 1:9). After 2 h, reaction mass was allowed to cool down to room temperature. To the solid reaction mass thus obtained, was added aq. ethanol (water/ethanol, 7:3) (10 mL), reaction mixture was shaken well and then product was collected by simple filtration. This crude product 4 was purified by crystallization using aq. ethanol (water/ethanol, 3:7).
42. *General experimental procedure for the synthesis of compounds* **6**(**a**–**h**): To the solution of tetrazolo[1,5-*a*]quinoline-4-carbaldehyde 5 (0.001 mol) in ethanol (5 mL), bismuth triflate (2 mol %) was added and this reaction mass was subjected to reflux condition for 3 h. Progress of the reaction was monitored by TLC (ethyl acetate/*n*-hexane, 3:7). After 3 h, reaction mass was allowed to cool at room temperature and excess of ethanol was then removed on rotary evaporator to afford the crude product. Thus obtained solid product was purified by crystallization with 10% aq. ethanol to afford the pure product 6.
Experimental
All chemicals were purchased and used without any further purification. ^{1}H NMR and ^{13}C NMR spectra were recorded on Varian AS 400 MHz spectrometer and NMR spectrometer AC 200 in either DMSO-d_6 or $CDCl_3$. Chemical shifts (δ) are in (parts per million) ppm relative to TMS. Mass spectra were recorded on a macro mass spectrometer (waters) by electro-spray (ES) method.
Spectroscopic data for representative compound 2,4,6-triphenylpyridine (**4a**): ^{1}H NMR (400 MHz, DMSO-d_6): δ 7.46–7.58 (m, 9H), 8.03 (d, 2H, J = 7.2 Hz), 8.18 (s, 2H), 8.31 (d, 4H, J = 7.6 Hz); ^{13}C NMR (50 MHz, $CDCl_3$): δ 117.1, 127.1, 127.2, 128.7, 128.9, 129.0, 129.1, 139.1, 139.6, 150.2, 157.5; Mass (ES-MS): m/z 308.1 (M^+).
Spectroscopic data for compounds **6**(**a**–**h**). (Diethoxymethyl)tetrazolo[1,5-*a*]quinoline (**6a**): ^{1}H NMR (400 MHz, DMSO-d_6): δ 1.19 (t, 6H, J = 6.8 Hz), 3.70 (q, 4H, J = 6.8 Hz), 6.04 (s, 1H), 7.81 (t, 1H, J = 7.6 Hz), 7.97 (t, 1H, J = 7.6 Hz), 8.29 (s, 1H), 8.32 (d, 1H, J = 7.6 Hz), 8.60 (d, 1H, J = 8.4 Hz); ^{13}C NMR (100 MHz, DMSO-d_6): δ 15.8, 62.8, 97.8, 116.8, 124.1, 124.6, 128.9, 130.6, 130.7, 132.2, 146.9; Mass (ES-MS) m/z 273.2 (M^+).
4-(Diethoxymethyl)-9-methyltetrazolo[1,5-a]quinoline (**6b**): ^{1}H NMR (200 MHz, DMSO-d_6): δ 1.18 (t, 6H, J = 7.2 Hz), 2.64 (s, 3H,), 3.71 (q, 4H, J = 7.2 Hz), 6.02 (s, 1H), 7.78 (dd, 1H, J = 8.4 Hz), 7.91 (d, 1H, J = 8.4 Hz), 8.22 (s, 1H), 8.31 (d, 1H, J = 8.4 Hz); ^{13}C NMR (50 MHz, DMSO-d_6): δ 15.5, 18.1, 61.9, 99.0, 115.5, 124.8, 125.3, 128.5, 131.2, 131.7, 134.0, 147.5; Mass (ES-MS) m/z 287.3 (M^+).
4-(Diethoxymethyl)-8-methyltetrazolo[1,5-a]quinoline (**6c**): ^{1}H NMR (200 MHz, DMSO-d_6): δ 1.18 (t, 6H, J = 7.2 Hz), 2.64 (s, 3H,), 3.70 (q, 4H, J = 7.2 Hz), 6.01 (s, 1H), 7.74 (d, 1H, J = 8.4 Hz), 8.17 (d, 1H, J = 8.4 Hz) 8.27 (s, 1H), 8.53 (s, 1H); ^{13}C NMR (50 MHz, DMSO-d_6): δ 15.5, 21.7, 62.0, 99.8, 116.0, 125.2, 125.9, 128.9, 131.2, 131.8, 134.4, 147.1; Mass (ES-MS) m/z 287.3 (M^+).
4-(Diethoxymethyl)-9-methoxytetrazolo[1,5-a]quinoline (**6d**): ^{1}H NMR (200 MHz, DMSO-d_6 + $CDCl_3$): δ 1.21 (t, 6H, J = 7.6 Hz), 3.75 (q, 4H, J = 7.6 Hz), 3.88 (s, 3H,), 6.05 (s, 1H), 7.83 (dd, 1H, J = 7.6 Hz and 8.4 Hz), 7.91 (d, 1H, J = 7.6 Hz), 8.27 (s, 1H), 8.39 (d, 1H, J = 8.4 Hz); ^{13}C NMR (50 MHz, DMSO-d_6 + $CDCl_3$): δ 16.1, 59.6, 63.2, 101.0, 112.3, 116.6, 126.0, 128.7, 131.1, 133.1, 144.7, 152.5; Mass (ES-MS) m/z 303.3 (M^+).
4-(Diethoxymethyl)-8-methoxytetrazolo[1,5-a]quinoline (**6e**): ^{1}H NMR (200 MHz, DMSO-d_6 + $CDCl_3$): δ 1.19 (t, 6H, J = 7.2 Hz), 3.71 (q, 4H, J = 7.2 Hz), 3.84 (s, 3H,), 6.01 (s, 1H), 7.84 (d, 1H, J = 8.0 Hz), 7.97 (d, 1H, J = 8.0 Hz) 8.37 (s, 1H), 8.62 (s, 1H); ^{13}C NMR (50 MHz, DMSO-d_6 + $CDCl_3$): δ 16.0, 59.6, 63.0, 100.8, 111.9, 117.1, 125.9, 129.2, 130.8, 132.3, 147.7, 151.2; Mass (ES-MS) m/z 303.4 (M^+).
4-(Diethoxymethyl)-7-methoxytetrazolo[1,5-a]quinoline (**6f**): ^{1}H NMR (200 MHz, DMSO-d_6 + $CDCl_3$): δ 1.21 (t, 6H, J = 7.6 Hz), 3.69 (q, 4H, J = 7.6 Hz), 3.88 (s, 3H,), 6.11 (s, 1H), 7.57 (s, 1H), 7.89 (d, 1H, J = 8.4 Hz) 8.32 (s, 1H), 8.61 (d, 1H, J = 8.4 Hz); ^{13}C NMR (50 MHz, DMSO-d_6+CDCl3): δ 15.9, 59.0, 62.6, 100.8, 109.8, 117.5, 126.0, 129.7, 131.7, 133.4, 148.1, 151.5; Mass (ES-MS) m/z 303.3 (M^+).
4-(Diethoxymethyl)-9-ethyltetrazolo[1,5-a]quinoline (**6g**): ^{1}H NMR (200 MHz, DMSO-d_6): δ 1.15 (t, 6H, J = 7.6 Hz), 1.56 (t, 3H, J = 7.2 Hz), 3.56 (q, 4H, J = 7.6 Hz), 4.01 (q, 2H, J = 7.2 Hz), 5.98 (s, 1H), 7.67 (dd, 1H, J = 6.8 Hz and 7.6 Hz), 7.85 (d, 1H, J = 7.6 Hz), 8.18 (s, 1H), 8.41 (d, 1H, J = 6.8 Hz); ^{13}C NMR (50 MHz, DMSO-d_6): δ 14.9, 15.3, 26.4, 62.0, 98.7, 116.1, 125.9, 126.6, 129.0, 131.2, 131.9, 133.7, 146.1; Mass (ES-MS) m/z 301.2 (M^+).
4-(Diethoxymethyl)-7-ethoxytetrazolo[1,5-a]quinoline (**6h**): ^{1}H NMR (200 MHz, DMSO-d_6): δ 1.17 (t, 6H, J = 7.2 Hz), 1.51 (t, 3H, J = 7.6 Hz), 3.61 (q, 4H, J = 7.2 Hz), 4.08 (q, 2H, J = 7.6 Hz), 6.08 (s, 1H), 7.55 (s, 1H), 7.91 (d, 1H, J = 8.0 Hz) 8.28 (s, 1H), 8.56 (d, 1H, J = 8.0 Hz); ^{13}C NMR (50 MHz, DMSO-d_6): δ 15.1, 15.7, 60.6, 63.8, 101.1, 110.7, 118.2, 126.9, 130.1, 132.7, 134.0, 149.0, 152.1; Mass (ES-MS) m/z 317.4 (M^+).