A Convenient Route to Synthesize 1,2,4-Triazolo[1,5-*a*]pyrimidine Derivatives and Their One and Two-photon Absorption Spectral Properties

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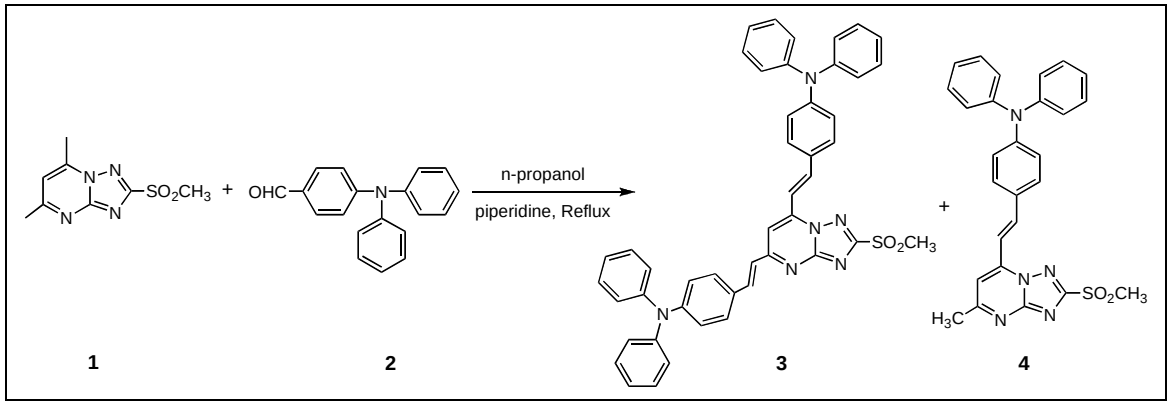

A convenient method for synthesizing α-(1,2,4-triazolo[1,5-*a*]pyrimidine-2-sulfonyl)methane derivatives, **3** and **4**, by the well known Knoevenagel reaction, in one step, is described. The two chromophores are stilbene-type chromophores containing the same D-π-A structures and end-capped with aromatic group as their donors. Measured with femtosecond multipass Ti:sapphire amplifier as irradiation source (pumped by the laser at 800 nm), the two chromophores show efficient two-photon induced orange red fluorescence emission. The experimental results indicate that the numbers of branches of the two chromophores affect their one-photon properties and two-photon up-conversion emission behaviors, and with the increasing numbers of branches, their wavelengths of λ^{abs}_{max}, λ^{spf}_{max} and λ^{tpf}_{max} exhibit bathochromic shifts.

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INTRODUCTION

In molecular non-linear optics (NLO), the well-recognized two-photon absorption (TPA) has attracted much attention recently [1]. Until now, increasing attention has been devoted to the TPA based applications in photonics and biophotonics areas, such as optical limiting [2,3], three-dimensional (3D) fluorescence microscopy [4-7], 3D microfabrication [4-7] and optical data storage [8] *etc*. It is found that the molecular structure has a significant influence on the TPA property of a molecule, so various design strategies have been employed to enhance the magnitude of the TPA properties of dyes. The search for molecules endowed with good TPA properties has mainly focused on push-pull (D-π-A) molecules as well as pull-pull (A-π-A), push-push (D-π-D) or quadrupolar molecules [9-12]. And new TPA compounds are still in great demand for developing novel opto-electronic materials.

On the other hand, the chemistry of 1,2,4-triazolo[1,5-*a*]-pyrimidine derivatives have been of considerable interest for many years, its various derivatives have found applications in pharmaceutical, agricultural and other areas [13-15]. Recently, we become interested in the synthesis of new 1,2,4-triazolo[1,5-*a*]pyrimidines, and their use as TPA materials, especially, it is of utmost importance to synthesize some pyrimidine derivatives by a simple and effective method.

Among many classical reactions, the well-known Knoevenagel condensation reaction is usually conducted between a carbonyl compound (aldehyde or ketone) and an active methylene compound of the type Z-CH_2-Z'. This classical reaction is usually catalyzed by organic bases (primary, secondary and tertiary amines), ammonia and ammonium salts or by Lewis acids such as $ZnCl_2$. It is widely used in the synthesis of intermediates or end-products for perfumes, pharmaceuticals and polymers. For example, (dicyanomethylene)pyran derivatives were reported as nonlinear optical chromophores, and it was synthesized by the Knoevenagel condensation reaction [16]. Donor-substituted 3,5-dicyano-2,4,6-tristyryl-pyridine derivatives, synthesized by the Knoevenagel condensation reaction, have been shown to be relatively effective as TPA materials [17].

And the above two former syntheses give us examples to synthesize the aimed D-π-A structural pyrimidine derivatives. We aimed at synthesizing push-pull (D-π-A) structure design molecules for TPA materials, chosing 1,2,4-triazolo[1,5-*a*]pyrimidine as the acceptor and 4-diphenylaminobenzyl group as the acceptor, and we have developed a convenient and efficient synthetic route to synthesized compounds **3** and **4** from α-(5,7-dimethyl-1,2,4-triazolo[1,5-*a*]pyrimidine-2-sulfonyl)methane (**1**) and aromatic aldehyde (**2**) directly by the Knoevenagel reaction (Scheme 1) in one step. The different numbers of branches of the two chromophores result in their different single-photon and two-photon properties. Especially, measured with femto-second laser at 800 nm by the two-photon-induced fluorescence, the two compounds show orange red fluorescence emission.

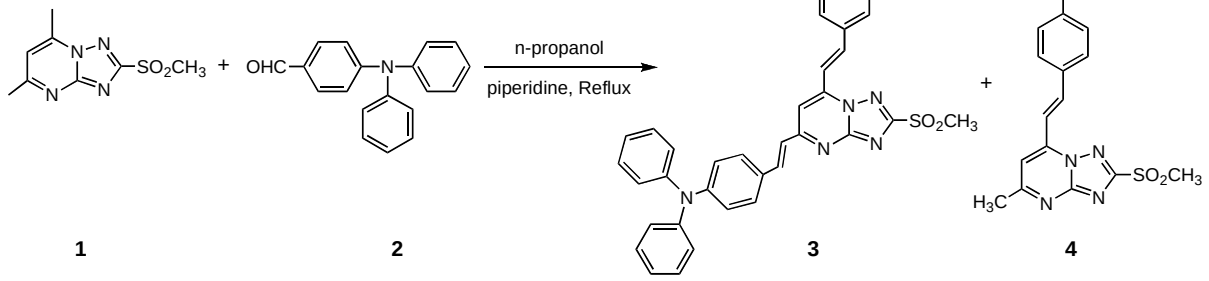
RESULTS AND DISCUSSION

Syntheses and structural characterization. Schemes 1 outline the synthetic sequence employed in our laboratories for preparation of the aimed products α-(5,7-di(triphenylaminostyryl)-1,2,4-triazolo[1,5-a]pyrimidine-2-sulfonyl) methane (**3**) and α-(7-dimethyl-5-triphenyl-aminostyryl-1,2,4-triazolo[1,5-*a*]pyrimidine-2-sulfonyl)-methane (**4**).

differs from other condensation reactions in that the starting material is the active methyl groups. In our experiment, the first step of the Knoevenagel condensation reaction is a piperidine-base reaction that converts 1,2,4-triazolo[1,5-*a*]pyrimidine into a nucleophilic anion. Namely, the protons of methyl group of α-(5,7-dimethyl-1,2,4-triazolo[1,5-*a*]pyrimidine-2-sulfonyl)methane (**1**) are acidic in piperidine which captures one proton of this methyl group. Then the intermediate carbanion is obtained, which is stabilized by the pyridine ring with delocalizing the base's negative charge, this is followed by carbonyl addition to obtain the desired products. Overall, the more stable the nucleophilic anion is, the easier the next nucleophilic reaction is to go on the Knoevenagel condensation reaction.

In the above mechanism of our Knoevenagel reaction, the single-substituted compound **4** was the first product and followed by its two-substituted derivative **3**. And if the molar ratio of the two reagents was 1:1.1 (compound **1**: **2**), the main product was single-substituted compound **4** with little amounts of **3**. In our experiment, the molar ratio was 1: 2.1, the main products were **3** and **4**. Their synthetical methods are very convenient, the crude products are separated easily, and can give simultaneously **3** and **4** in the yields for 46 % and 48 %, respectively (shown in Table 1), when reacted under nitrogen. Parallel experiments

Scheme 1



Synthetic routes to compounds **3** and **4**.

Our strategy for the synthesis of **3** and **4** was based on the Knoevenagel condensation reaction, this reaction indicated that this reaction could be carried out under either nitrogen or air, and the yields were almost the same. The

Table 1

Physical and Analytical Data of Compounds **3** and **4**

Compound	Time hours	Mp (°C)	Yield %	Molecular Formula	Analysis % Calcd./Found			
					C	H	N	S
3	6	270-271	46	$C_{46}H_{36}N_6SO_2$	75.00	4.89	11.41	4.35
		[a]			75.11	4.73	11.65	4.05
4	6	242-243	48	$C_{27}H_{23}N_5SO_2$	67.36	4.78	14.55	6.65
		[a]			67.52	4.43	14.28	6.82

[a] From chloroform.

above two compounds are characterized by ^{1}H NMR, FTIR, UV-Vis, elemental analysis.

In the ^{1}H NMR spectrum of the raw material (α-(5,7-dimethyl-1,2,4-triazolo[1,5-*a*]pyrimidine-2-sulfonyl) methane, **1**), the shifts at δ 2.74 ppm and δ 2.87 ppm were due to 5-methyl and 7-methyl protons, respectively, and in agreement with the reference [18], the 5-methyl appears as a single peak at high field (δ 2.74 ppm), which means that it has the stronger down-shielding effectiveness coming from the pyridine ring. While in the reference [21], the 4-methyl group of 3,5-dicyano-2,4,6-trimethylpyridine appears at 2.70 ppm (high field) and the 2- and 6-methyl groups appear at 2.76 ppm, according to our former experiment [17,22], the 4-methyl group is the most reactive group to go on the Knoevenagel reaction. So contrast the two methyl groups of α-(5,7-dimethyl-1,2,4-triazolo[1,5-*a*]pyrimidine-2-sulfonyl)methane and the three methyl groups of 3,5-dicyano-2,4,6-trimethylpyridine, we would have deduced that the 5-methyl group of the former is also the most reactive group. Therefore, in the ^{1}H NMR spectrum of compound **4**, there was only one unsubstituted methyl group (linked to the ring) being around 2.76 ppm (7-methyl group), and compared with the spectrum of **4**, there was no chemical shift of the unsubstituted methyl group of 5-methyl or 7-methyl in the spectrum of **3**, which proves the two methyl groups have already completed the Knoevenagel condensation reaction. Characteristic resonances of the vinylic protons of the two compounds at 8.03-7.40 ppm with large *trans* coupling constants were evident in their ^{1}H NMR spectra; the shift of the methyl groups linked to sulfonyl group of the two compounds were around 3.45 ppm. The absorption around 1333 cm^{-1} and 969 cm^{-1} of their FTIR spectra corresponded to SO_2 stretching and out-of-plane bending motions, respectively, of *trans*-vinylene. Both compounds are soluble in common organic solvents such as toluene, chloroform, acetone, THF, DMF and DMSO.

color change of the reaction mixture, for example, if the reaction takes place at the room temperature, there is not color change after stirring for six hours. While when the reactants were heated at refluxing temperature for only two hours, the mixture turned from colorless to orange, which would mean the product was formed. Thin layer chromatography showed that **1** and **2** were completely consumed after six hours at refluxing temperature when the mixture turned to red.

One-photon and two-photon absorption optical properties. With the increasing branches in their structures of compounds **3** and **4**, the absorption maxima become longer with the transition energy decreasing correspondingly and their profile curves are shown in Figures 1 (at the concentration of 1 x 10^{-5} M). Compared with di-armed structural chromophore **3** (between the two chromophores, it has the maximal λ_{max} at 486 nm, as shown in Table 2), the one-armed chromophore **4**, with the same 1,2,4-triazolo[1,5-*a*]pyrimidine moieties as its acceptor, demonstrated much better transparency (blue shifted 9 nm). This phenomenon is reasonable if we consider the numbers of their branches, which is associated with the much larger enhancements of electronic delocalization of di-armed molecules. Namely, the charge transfer and redistribution of chromophore **3** would occur along two axes, which leads to the extending of conjugation systems.

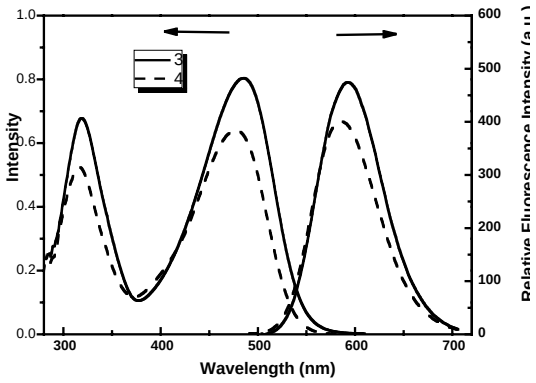


Figure 1. UV-Vis absorption spectra and Steady-state single-photon fluorescence spectra of compounds **3** and **4** in chloroform solution.

Table 2

Synthesis and Experimental Photophysical Properties of Compounds **3** and **4** in Chloroform Solution.

	$\lambda^{abs}{}_{max}$ [a]	$\lambda^{spf}{}_{max}$ [a]	$\lambda^{tpf}{}_{max}$ [a]	Φ_f (%) [b]
3	486	592	593	46
4	477	586	587	41

[a] $\lambda^{abs}{}_{max}$, $\lambda^{spf}{}_{max}$, $\lambda^{tpf}{}_{max}$: peak wavelengths in the linear absorption, single photon fluorescence emission, Two-photon absorption (at 800 nm) induced fluorescence emission. [b] Rhodamine B was used as the reference [20].

The one-photon fluorescence spectra of the two chromophores at the concentration of 1 x 10^{-6} M in chloroform are also displayed in Figure 1, and Table 2 summarizes the wavelengths of single-photon fluorescence ($\lambda^{spf}{}_{max}$) of the two compounds. Their fluorescence spectra exhibit the same tendency as above, that is $\lambda_3 > \lambda_4$, with enhancing the numbers of conjugated branches of molecules from one branch to two branches, the red shift is obvious from **4** to **3** by 6 nm (from 587 nm to 593 nm seen in Table 2). And the two compounds have relatively high Φ_f values up to 46 % in chloroform solution using Rhodamine B as the standard chromophore [20]. Especially, in this context, the two chromophores show orange red fluorescence and have high Φ_f values, they might have potential use in organic light-emitting devices, and the test of their electroluminescence properties is now under way.

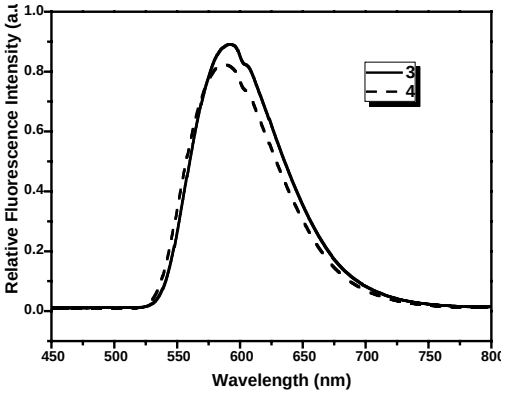


Figure 2. Two-photon absorption induced fluorescence emission spectra for compounds **3** and **4** in chloroform.

The TPA fluorescence experiments of the two compounds were conducted by a femtosecond Tsunami amplifier (Spectra-Physics, Mai Tai, pulse width 100 fs, repetition frequency 80 MHz) as irradiation source, and all the sample solutions were prepared in the same manner at concentration of 1.0 x 10^{-5} M in chloroform for this measurement. Figure 2 presents the two-photon induced fluorescence emission spectra of the two compounds at 800 nm, and Table 2 summarizes the corresponging wavelengths (λ^{tpf}_{max}) of the two compounds. Because there is no linear absorption at 800 nm, the emission excited by the laser wavelength at 800 nm would be attributed to the two-photon excited fluorescence spectra (TPEF) mechanism. The two chromophores in chloroform display manifest TPA induced frequency up-converted fluorescence emission.

Compared the TPEF spectra of the two chromophores (seen in Figure 2) with their corresponding SPEF spectra (seen in Figure 1), there are obviously many similarities. Obviously, the TPEF peak position of the two compounds is basically the same as the corresponding SPEF peak position (shown in Table 2). It is interesting to note that the branch numbers also affect the λ^{tpf}_{max} of the two compounds, with increasing the numbers of branches, compound **3** beholds the higher value of λ^{tpf}_{max} to be 593 nm, exhibiting the same sequence of $\lambda_3 > \lambda_4$ as those of SPEF. While the difference between TPEF spectra and SPEF spectra is mainly at the excitation process: two-photon absorption versus single-photon absorption.

Until now, multiphoton microscopy is currently a blooming field, owing to the advantages that it provides for in biological imaging. Besides the ongoing developments of optical systems, the design of novel fluorescence with optimized characteristics is of timely importance. In our work, the two chromophores, **3** and **4**, with elongated conjugated systems, display apparent two-photon absorption up-conversion fluorescence at 800 nm, which is in the visible-red/NIR region (700-900 nm), a spectral window of particular interest for the imaging of biological tissues.

CONCLUSIONS

This paper reports the synthesis of two donor-substituted 1,2,4-triazolo[1,5-*a*]pyrimidine derivatives, with dimensional D-π-A structures and ended with the same donor, as new two-photon absorption (TPA) chromophores. We have successfully converted pyrimidine **1** to its derivatives **3** and **4** simultaneously, and the whole synthetic procedure was fairly convenient and efficient, the reaction time was short and the yields were also satisfying. With the increasing numbers of branches, their wavelengths of λ^{abs}_{max} and λ^{spf}_{max}, λ^{tpf}_{max} exhibit bathochromic shifts, so the numbers of branches affect their one-photon properties and two-photon up-conversion emission behaviors. Although a number of push-pull polyenes and linear quadrupolar molecules have been synthesized and extensively studied because of their good TPA properties, in this context, an additional structural motif based on the 1,2,4-triazolo[1,5-*a*]pyrimidine derivatives was suggested and would be a promising direction for further developments of novel TPA chromophores, and the study of two-photon absorption properties of other derivatives are now under way.

EXPERIMENTAL

Chemicals and measurements. α-(5,7-Dimethyl-1,2,4-triazolo[1,5-*a*]pyrimidine-2-sulfonyl) methane (**1**)[18] and 4-diphenylaminobenzaldehyde (**2**) [19] were prepared as literature reported. Piperidine and *n*-propyl alcohol were AR grade, which were purchased from China National Medicines Group and were used without further purification.

^{1}H NMR and ^{13}C NMR spectra were recorded on a Varian-Mercury 300 spectrophotometer using $CDCl_3$ as a solvent and tetramethylsilane (TMS) as a reference. IR spectra were obtained as KBr pellets on a Nicolet-170 SKFT-IR spectrometer. UV-Vis absorption spectra were measured on a Shimadzu-12106 recording spectrophotometer. The steady-state fluorescence spectrum measurements were performed using a Hitachi 5000 spectrofluorimeter. Elemental analysis was performed using a PE 2400 elemental analyzer. The melting points were measured on Perkin Elmer DTA 1700 differential thermal analyzer. The two-photon-absorption up-conversion fluorescence experiments were determined using a femtosecond multipass Ti:sapphire amplifier (Quantronix Odin, pulse width 80 fs, repetition frequency 1 KHz, at 800 nm) as irradiation source.

Single photon photoluminescence and absorption measurements were conducted in chloroform, and the chloroform solvent was anhydrous grade after the further purification used for the single-photon fluorescence measurements. For these experiment the solvent was freshly prepared and kept in the dark before the measurements, and the solution concentration was 1 x10^{-6} M and 1 x10^{-5} M respectively. The fluorescence quantum yield was determined using Rhodamine B as the reference by the literature method [20]. And the two-photon absorption up-conversion fluorescence were measured at 800 nm, the intensity of the two-photon-induced fluorescence spectra of the samples were also dissolved

in $CHCl_3$ at concentration of 1.0 x10^{-5} M, emitted at the same excitation wavelength were determined.

Syntheses. The synthetic routes for compounds **3** and **4** are outlined in Scheme 1 and the details are described below.

α-(5,7-di(triphenylaminostyryl)-1,2,4-triazolo[1,5-*a*]pyrimidine-2-sulfonyl) methane (3) and α-(7-dimethyl-5-triphenylaminostyryl-1,2,4-triazolo[1,5-*a*]pyrimidine-2-sulfonyl)-methane (4). In a 100 mL round-bottomed flask equipped with a reflux condenser and nitrogen bubber were placed α-(5,7-dimethyl-1,2,4-triazolo[1,5-*a*]pyrimidine-2-sulfonyl)methane (**1**, 0.2 g, 0.885 mmol) and 3.1 equiv of aromatic benzylaldehydes (**2**) in 10 mL n-propyl alcohol, and piperidine (about 7 drops) was added to the mixture. The mixture was refluxed for six hours. After cooling to room temperature, some crude products were precipitated after the concentration of the reaction mixture to dryness *in vacuo*. The crude products were chromatographed over a silica gel column using chloroform as the eluent to collect the red band to get **3** as a red solid, it was obtained in 46 % yield (0.29 g), M.p. 270-271 ºC. ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 8.03 (d, 1 H, *J* = 15.5 Hz, -CH=CH-), 7.94 (d, 1 H, *J* = 15.5 Hz, -CH=CH-), 7.56-7.48 (m, 5 H, -CH=CH- and Ar-H), 7.37-7.32 (m, 12 H, Ar-H), 7.18-7.09 (m, 12 H, Ar-H), 7.05 (d, 2 H, *J* = 8.0 Hz, Ar-H), 3.46 (s, 3 H, CH_3). FTIR (cm^{-1}): 1661, 938 (CH=CH), 1335, 1165 (SO_2). Elemental analysis for $C_{46}H_{36}N_6SO_2$: Calculated C, 75.00; H, 4.89; N, 11.41; S, 4.35. Found: 75.11; H, 4.73; N, 11.65; S, 4.05%. The orange band gave compound **4** as an orange solid it yielded 0.20 g (48 % yield), M.p. 242-243 ºC. ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 7.91 (d, 1 H, *J* = 16.0 Hz, -CH=CH-), 7.54-7.48 (m, 2 H, -CH=CH- and Ar-H), 7.38-7.24 (m, 6 H, Ar-H), 7.20-7.13 (m, 6 H, Ar-H), 6.99 (d, 2 H, *J* = 8.0 Hz, Ar-H), 3.44 (s, 3 H, CH_3), 2.76 (s, 3 H, CH_3). FTIR (cm^{-1}): 1660, 936 (CH=CH), 1333, 1163 (SO_2). Elemental analysis for $C_{27}H_{23}N_5SO_2$: Calculated: C, 67.36; H, 4.78; N, 14.55; S, 6.65. Found: 67.52; H, 4.43; N, 14.28; S, 6.82%.

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