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Tetrasubstituted Olefinic Xanthene Dyes: Synthesis via Pd-Catalyzed 6-*exo-dig* Cyclization/C–H Activation of 2-Bromobenzyl-*N*-propargylamines and Solid State Fluorescence Properties

Avanashiappan Nandakumar and Paramasivan Thirumalai Perumal*

Organic Chemistry Division, CSIR-Central Leather Research Institute, Adyar,
Chennai-600 020, India

ptperumal@gmail.com

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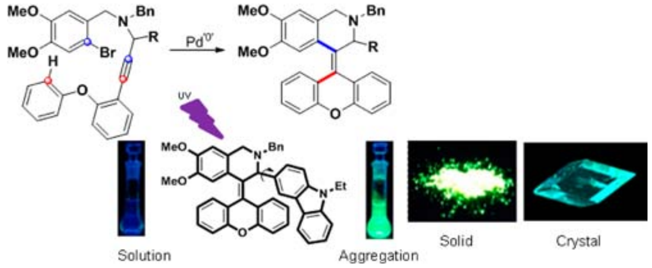
ABSTRACT



Tetrasubstituted olefin based new xanthene derivatives have been synthesized via palladium-catalyzed carbopalladation/C–*H* activation of 2-bromobenzyl-*N*-propargylamine derivatives. The synthesized compounds display a pronounced solid state fluorescence due to their restricted internal rotation of a C–Ar bond in the solid or aggregation state.

Conjugated tetrasubstituted olefins have attracted much attention from organic chemists due to their application in photoresponsive organic materials, molecular devices, and also in the field of biology.[1] A number of different methods have been developed to synthesize tetrasubstituted olefins, including the McMurry reaction,[2] Wittig reaction,[3] and transition metal catalyzed coupling reactions.[4] Recent approaches toward the synthesis of tetrasubstituted olefins involve palladium catalyzed intramolecular carbopalladation of an *in situ* formed oxidative addition adduct (Ar–Pd–X) to the internal alkyne followed by cross-coupling with a organocopper[5] or organostannane[6] or by direct C–*H* activation[7] (Scheme 1). These approaches enable chemists to construct tetrasubstituted olefins with high stereo- and regioselectivity.

Solid state organic luminescence materials find several applications in the field of optoelectronic devices including light emitting diodes, electroluminescence, and molecular sensors due to their phenomenal photophysical properties and significant photostability.[8] Several novel fluorescent compounds are being designed based on the concept of solid state luminescence.[5,9] It poses a great challenge to

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organic chemists to design a new core structure for fluorophores with tunable solid state emission despite the plethora of examples available for such molecules. Recently we reported an efficient stereo- and regioselective palladium-catalyzed protocol for the synthesis of trisubstituted olefins.[10] In this paper, we describe a convenient method for the synthesis of tetrasubstituted olefinic xanthene derivatives *via* palladium catalyzed intramolecular carbopalladation followed by C−*H* activation of substituted 2-bromobenzyl-*N*-propargylamines and their photophysical properties in both solid and aggregation states.

The requisite starting materials (**4a**−**h**) were synthesized using our previous A^3 coupling protocol,[10a] and the reaction yields are tabulated (Table 1). We studied the scope of the reaction by varying the aldehyde substrates. Generally the reaction proceeded smoothly and led to the desired products in good yields (Table 1, entries 1−8) of which 1,3,5-trioxane and naphthaldehyde displayed high reactivity (Table 1, entries 3 and 5). It is noteworthy to mention that aldehydes possessing heteroaromatic motifs provided the products in good yields (Table 1, entries 7 and 8).

Scheme 1. Concept for Synthesis of Tetrasubstituted Olefins

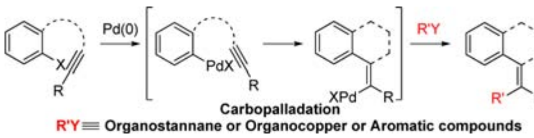
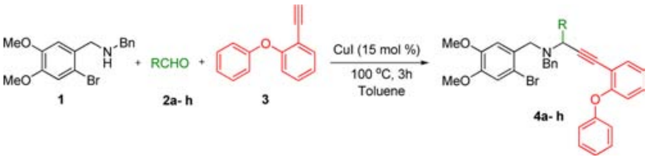


Table 1. Scope of A^3 Coupling Reaction for Synthesis of Propargylamine (**4a**−**h**)



entry	substrate (**2**)	product	yield^{a,b}
1	4-methylbenzaldehyde (**2a**)	**4a**	87
2	4-methoxybenzaldehyde (**2b**)	**4b**	89
3	1-naphthaldehyde (**2c**)	**4c**	90
4	1-pyrenecaboxaldehyde (**2d**)	**4d**	75
5	1,3,5-trioxane (**2e**)	**4e**	90
6	ferrocenecarboxaldehyde (**2f**)	**4f**	86
7	9-ethyl-9*H*-carbazole-3-carbaldehyde (**2g**)	**4g**	77
8	1,3-diphenyl-1*H*-pyrazole-4-carbaldehyde (**2h**)	**4h**	75

[a] The reactions were performed with amine **1** (0.5 mmol), aldehyde **2a**−**h** (0.55 mmol), and alkyne **3** (0.75 mmol). [b] Isolated yields.

Then we initiated our palladium catalyzed carbocyclization using *N*-benzyl-*N*-(2-bromo-4,5-dimethoxybenzyl)-3-(2-phenoxyphenyl)-1-*p*-tolylprop-2-yn-1-amine (**4a**). The reaction was carried out in the presence of Pd(OAc)$_2$ (5 mol %), PPh$_3$ (20 mol %), and Cs$_2$CO$_3$ (5 equiv) at 100 °C in DMF under a N$_2$ atmosphere (Table 2, entry 1). The desired cyclization product **5a** was obtained in 65% yield. This low yield prompted us to improve the reaction conditions to obtain better yields, for which bases and other solvents were investigated (Table 2, entries 2−6). Other Pd sources such as PdCl$_2$, Pd(CH$_3$CN)$_2$Cl$_2$, Pd(PPh$_3$)$_4$, and Pd$_2$(dba)$_3$ did not significantly affect the reaction yield (Table 2, entries 7−10). On increasing the stoichiometry of the Pd(OAc)$_2$ catalyst from 5 to 10 mol %, the yield of the product improved to 86% (Table 2, entry 11). A further increase in the amount of catalyst did not alter the yield (Table 2, entry 12). The effect of temperature on the reaction rate was also studied (Table 2, entry 13). Thus the desired carbocyclization product **5a** was obtained in maximum yield (86%), when the reaction was carried out with 10 mol % of Pd(OAc)$_2$, 20 mol % of PPh$_3$, and 5 equiv of K$_2$CO$_3$ at 100 °C in DMF (Table 2).

Product **5a** was isolated on completion of the reaction as indicated by TLC and characterized using spectroscopic techniques. The product **5a** did not show any characteristic property on the TLC plate under a UV lamp as soon as it was withheld from the solvent pool. But upon evaporation of solvent, the spot of **5a** on the TLC plate developed strong emission. We inferred that compound **5a** on the TLC plate exhibits a nonemissive property when it is exposed in organic solvents but becomes an intense green solid emitter under dry conditions. The PL spectrum of **5a** in dilute acetonitrile exhibits a flat line parallel to the abscissa confirming that it is nonemissive in the solution state. The solid state PL spectrum of **5a** shows an emission maximum at 523 nm. This anomalous behavior of **5a** is due to the phenomenon of aggregation induced emission

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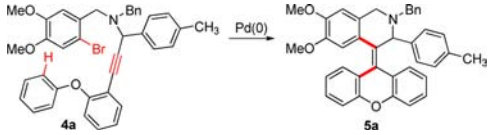
Table 2. Optimization of Palladium Catalyzed Carbocyclization



entry	catalyst (mol %) + ligand	base	solvent	time (h)	yield (%)[a]
1	$Pd(OAc)_2(5) + PPh_3$	Cs_2CO_3	DMF	5	65
2	$Pd(OAc)_2(5) + PPh_3$	K_2CO_3	DMF	5	70
3	$Pd(OAc)_2(5) + PPh_3$	NEt_3	DMF	5	55
4	$Pd(OAc)_2(5) + PPh_3$	K_2CO_3	dioxane	5	30
5	$Pd(OAc)_2(5) + PPh_3$	K_2CO_3	toluene	5	45
6	$Pd(OAc)_2(5) + PPh_3$	K_2CO_3	CH_3CN	5	60
7	$PdCl_2(5) + PPh_3$	K_2CO_3	DMF	5	55
8	$PdCl_2(CH_3CN)_2(5) + PPh_3$	K_2CO_3	DMF	8	trace
9	$Pd(PPh_3)_4(5) + PPh_3$	K_2CO_3	DMF	5	50
10	$Pd_2(dba)_3(5) + DPPF$[b]	K_2CO_3	DMF	5	45
11	**$Pd(OAc)_2(10) + PPh_3$**	**K_2CO_3**	**DMF**	**2**	**86**
12	$Pd(OAc)_2(15) + PPh_3$	K_2CO_3	DMF	2	85
13	$Pd(OAc)_2(10) + PPh_3$	K_2CO_3	DMF	2	86[c]

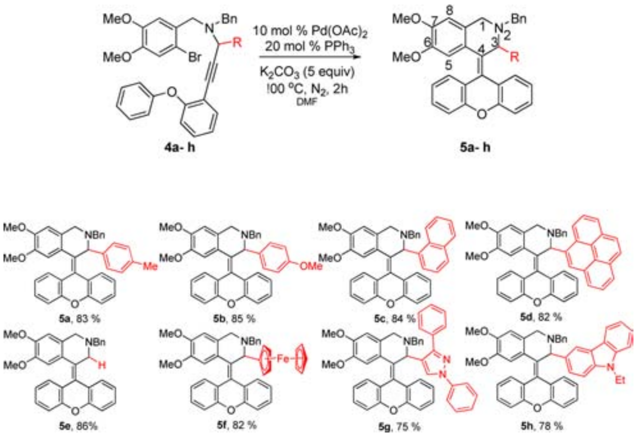
[a] The reactions were carried out with propargylamine **4a** (0.3 mmol) in the presence of a Pd source and base (5 equiv) at 100 °C under a N_2 atmosphere. [b] DPPF-1,1′-bis(diphenylphosphino)ferrocene. [c] The reaction was carried out at 120 °C.

(AIE),[9e] and this is observed only in the solid or aggregation state.

Having the optimal conditions in hand, we synthesized analogues of tetrasubstituted olefin based xanthenes (**5a**–**h**) in good yields (Scheme 2) and studied their photophysical properties in both solid and solution states (Table 3). All the derivatives showed an AIE phenomenon except compounds **5e** and **5f**. This further explains that the presence of a phenyl or fused aromatic or heteroaromatic group at the C-3 position in products (**5a**–**d**, **5g**, and **5h**) prompts the molecule to be AIE active. In solution, the intramolecular rotation of the C_3–Ar bond is active which causes nonradiative deactivation from its excited state, whereas in the solid state the intramolecular rotation is restricted and hence this activates the radiative decay pathway causing the molecule to exhibit an AIE phenomenon.

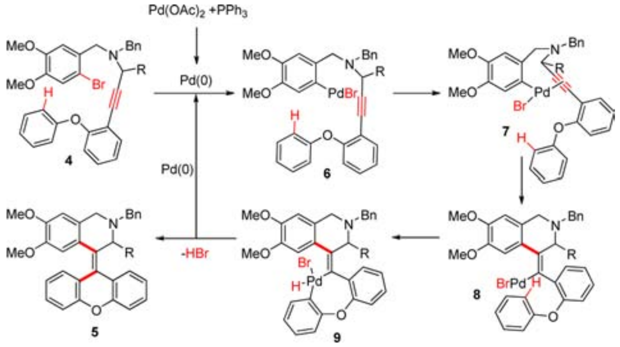
Mechanistically, the formation of product **5** consists of the following sequential steps. First, aryl bromide **4** undergoes oxidative addition to the *in situ* generated Pd(0) leads to aryl palladium complex **6** (Ar–Pd–Br). Insertion of an internal alkyne to aryl palladium complex **6** affords the carbopalladation complex **8**, and subsequent intramolecular C–*H* activation leads to seven-membered palladium ring **9**. Reductive elimination of **9** affords the tetrasubstituted olefin **5** with concomitant regeneration of the Pd(0) species (Scheme 3).

Scheme 2. Tetrasubstituted Olefinic Xanthene Derivatives (**5a**–**h**)[a]



[a] Isolated yields.

Scheme 3. Plausible Mechanism for Formation of **5**



Further, to confirm the AIE property of these compounds, we analyzed the PL spectra of compound **5h**. Compound **5h** at a 10 μM solution in acetonitrile did not show any variation of intensity with wavelength. The slower addition of a nonsolvent, e.g. water, made the solution visually emissive, and the solution consisting of a large fraction of water showed an enhancement in its emissive property. The PL spectrum of compound **5h** in an aqueous mixture initially starts to display emission intensity at 512 nm when the water content was a 65% volume fraction and reaches maximum at 75%. The intensity started to decrease as the water content was altered from 75 to 80% (Figure 1a and 1b). The plausible reason for this behavior could be due to the change in the packing order of the molecules in the aggregates. Low water content in the solution mixture may cause the molecules to arrange in an ordered fashion to form a more emissive crystalline aggregate, whereas at high water content the solubility of the molecules decreases which enforce the molecules to form lower emission agglomerated amorphous aggregates.[11] This confirms that, upon addition of water, the compound starts to exhibit a PL property due to formation of aggregation in aqueous mixtures. The normalized absorption and emission spectra of compound **5h** are shown in Figure 1c. The structure and optimized

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Table 3. Optical Properties of Compounds (**5a**−**d**, **5g**, and **5h**)

	$\lambda_{\max,ab}$, nm		$\lambda_{\max,em}$, nm		Stokes shift,[e] cm^{-1}		solid state fluorescent lifetime[f]			
compd	solid	solution[a] (ε cm^{-1})[b]	solid[c]	solution[a,d]	solid	solution[a]	τ_1 (ns)	τ_2 (ns)	τ_3 (ns)	$A_1/A_2/A_3$
5a	400	349 (10691)	523	516	5879	9273	1.50	–	4.37	0.32/0/0.68
5b	348	350 (12007)	522	519	9578	9303	1.12	1.32	4.04	0.11/0.33/0.56
5c	386	350 (9727)	532	532	7110	9774	1.72	–	4.61	0.36/0/0.64
5d	401	357 (26230)	534	533	6211	9249	1.81	2.31	4.38	0.32/0.06/0.62
5g	352	346 (12914)	518	510	9104	9294	1.27	2.45	3.80	0.37/0.14/0.49
5h	348	355 (16521)	526	517	9724	8826	1.98	–	4.77	0.30/0/0.70

[a] In CH_3CN/H_2O (1:99) mixture at 10 μM. [b] Recorded at 1×10^{-5} M. [c] Excitation wavelengh: 400 nm. [d] Excitation wavelength: 350 nm. [e] Stokes shift = $\lambda_{\max,abs} - \lambda_{\max,em}$ (cm^{-1}). [f] A and τ are the fractional amount and fluorescent lifetime of the shorter (1), medium (2), and longer (3) species.

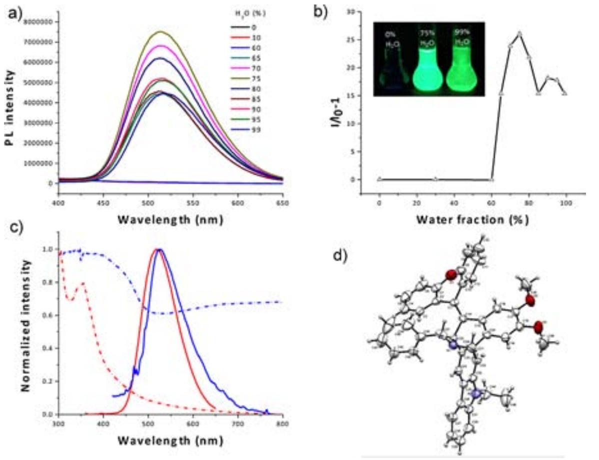

Figure 1. (a) PL spectra of **5h** in CH_3CN/H_2O mixtures with varying water fraction (f_w): concentration (μM), 10; excitation wavelength (nm), 350. (b) Plot of PL peak intensity vs water fractions in CH_3CN/H_2O mixtures of **5h**. I_0 was the PL intensity in pure CH_3CN solution. The inset in panel b: Photos of **5h** in CH_3CN/H_2O mixtures (f_w = 0, 75, and 99%) taken under UV luminescence. (c) Normalized absorption (dash line) and PL (solid line) spectra of compound **5h** in solid (blue) and aggregated solution (CH_3CN/H_2O (1:99) mixture) state (red). (d) Ortep of **5h**.

geometry of **5h** were studied using X-ray single crystal analysis (Figure 1d).[12] Molecular packing in the crystal state elucidates that the crystal geometry of **5h** is stabilized by the intermolecular C−H···O hydrogen bond with a distance of 2.529 Å, causing the structure to be rigid in the crystalline state (see Supporting Information). The presence of *N*-benzyl and carbazole at the C_2 and C_3 carbons respectively makes the molecule even more rigid. These collective effects rigidify the molecule in the crystal lattice and lock the molecular motion, thereby inducing emission in the visible region.

On the basis of the results obtained, compounds **5a**−**d**, **5g**, and **5h** were essentially nonluminescent in CH_3CN solution and displayed intense green to yellow fluorescence with a large Stokes shift in both the solid and aggregation states. Therefore, they prove to be promising candidates for a new class of AIE based dye materials with a rigid structure. The absorption maxima of all of the above compounds were measured in the solid state and 99% H_2O/CH_3CN solution mixture. All the compounds showed an intense absorption maximum in the range of 348−401 and 346−357 nm for solid and solution states respectively. The solid state photoluminescence study of **5a**−**d**, **5g**, and **5h** were carried out at rt. Introducing a fused aromatic group (naphthyl **5c** or pyrene **5d**) at the C_3 carbon center caused the emission maximum to show a red shift. Moreover, the presence of the pyrazole **5g** moiety in the C_3 position displayed a blue shift in emission spectra. The same results were obtained in 99% H_2O/CH_3CN solutions. All the compounds in the solid and aggregation states showed large Stokes shift values which occur in the range 5879−9774 cm^{-1}. The solid state fluorescent lifetimes of **5a**−**d**, **5g**, and **5h** were also analyzed (Table 3).

In summary, we have developed a palladium-catalyzed domino reaction involving a carbopalladation/C−*H* activation process that enables a new foundation for the synthesis of AIE materials. These novel AIE compounds are distinguishably featured by their intense solid state fluorescence with large Stoke shifts. Further studies to delineate this methodology are underway.

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Supporting Information Available. Experimental section, ^1H and ^{13}C NMR spectra, and UV−visible and PL spectra of all compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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[12] Crystallographic data of compound **5h** in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplemental publication no. CCDC 899105. Copies of the data can be obtained, free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: +44 01223 336033 or email: deposit@ccdc.cam.ac.uk).

The authors declare no competing financial interest.