

Cite this: *Chem. Commun.*, 2011, **47**, 2628–2630

www.rsc.org/chemcomm

Palladium catalyzed bicyclization of 1,8-diiodonaphthalene and tertiary propargylic alcohols to phenalenones and their applications as fluorescent chemosensor for fluoride ions†

Xiaopeng Chen, Hongbo Wang, Xiaohan Jin, Jinwu Feng, Yanguang Wang* and Ping Lu*

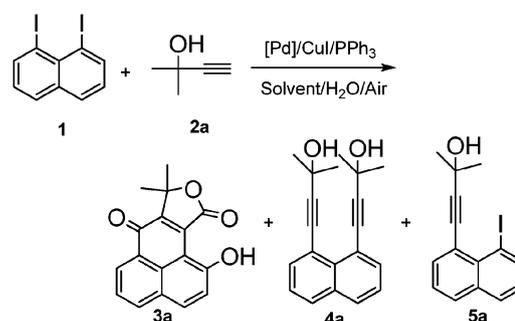
Received 9th November 2010, Accepted 14th December 2010

DOI: 10.1039/c0cc04875e

Phenalenone derivatives were efficiently constructed from 1,8-diiodonaphthalene and tertiary propynols via a one-pot domino reaction which eventually included Pd-catalyzed Sonogashira coupling, Pd-catalyzed allylic oxidation and Pd-catalyzed C_{sp2}-H activation. Moreover, the synthesized phenalenone derivative presented a practical application as a fluorescent chemosensor for fluoride anion with high sensitivity and selectivity.

The palladium-catalyzed Sonogashira coupling reaction has become a booming methodology to prepare arylalkynes and conjugated enynes, which are precursors for natural products, pharmaceuticals and optoelectronics materials.^{1–3} Our previous works on the synthesis of acetylene-linked light emitting materials confirmed further that this reaction deserved its importance in constructing fluorescent oligomers or dendrimers.⁴ However, while 1,8-diiodonaphthalene (**1**) and 2-methylbut-3-yn-2-ol (**2a**) were used as coupling substrates, varied from the normal Sonogashira coupling products (**4a** and **5a**) and the enyne formation product,⁵ an unexpected bicyclized phenalenone derivative **3a**^{6,7} was generated in the presence of trace amount of water and air. In this paper, we would like to report the systematic optimization of the reaction condition for this transformation, the diversity of the substrates, the possible mechanism, and its potential application of the product as fluorescent chemosensor for fluoride anion.

Exhaustive studies of reaction conditions for the formation of **3a** from **1** and **2a** were firstly processed. Pd(PPh₃)₂Cl₂ was found to be an efficient catalyst in comparison with other palladium catalysts, such as Pd(PPh₃)₄ and Pd(OAc)₂ (Table 1, entries 1, 8 and 9). Triethylamine was determined to be the most suitable solvent (Table 1, entries 1–5). When diisopropylethylamine or diisopropylamine was used as a solvent, **3a** could be obtained, but in relatively lower yields (Table 1, entries 2 and 3). However, when the reaction was conducted in pyrrolidine or piperidine, only trace amount of **3a** was detected by TLC (Table 1, entries 4 and 5). When the solvent was changed to THF adding with

Table 1 Optimization of reaction conditions for the preparation of **3a**^a

Entry	Catalyst	Solvent	T/°C	Yield (%)		
				3a	4a	5a
1	Pd(PPh ₃) ₂ Cl ₂	Et ₃ N	80	64	<5	18
2	Pd(PPh ₃) ₂ Cl ₂	<i>i</i> -Pr ₂ EtN	80	58	23	14
3	Pd(PPh ₃) ₂ Cl ₂	<i>i</i> -Pr ₂ NH	80	37	32	23
4	Pd(PPh ₃) ₂ Cl ₂	Pyrrolidine	80	<5	35	46
5	Pd(PPh ₃) ₂ Cl ₂	Piperidine	80	<5	38	40
6	Pd(PPh ₃) ₂ Cl ₂	THF/Bu ₄ NF ^b	65	0	75	12
7	Pd(PPh ₃) ₂ Cl ₂	THF/Bu ₄ NOH ^c	65	0	26	63
8	Pd(PPh ₃) ₄	Et ₃ N	80	53	23	18
9	Pd(OAc) ₂	Et ₃ N	80	20	12	63
10	Pd(PPh ₃) ₂ Cl ₂	Et ₃ N	rt	0	56	10
11	Pd(PPh ₃) ₂ Cl ₂	Et ₃ N	50	36	52	6
12 ^d	Pd(PPh ₃) ₂ Cl ₂	Et ₃ N	80	0	94	5
13 ^e	Pd(PPh ₃) ₂ Cl ₂	Et ₃ N	80	0	92	3
14 ^f	Pd(PPh ₃) ₂ Cl ₂	Et ₃ N	80	0	58	22
15 ^g	Pd(PPh ₃) ₂ Cl ₂	Et ₃ N	80	12	<5	—

^a Unless otherwise specified, the reaction was carried out in a sealed flask with the existence of water (10 μL) and air, and using **1** (1 mmol), **2a** (4 mmol), Pd catalyst (0.05 mmol), CuI (0.1 mmol), and PPh₃ (0.1 mmol) in solvent (40 mL). ^b Bu₄NOH (1.0 M in H₂O, 4 mmol). ^c Bu₄NF (1.0 M in THF, 4 mmol). ^d In the absence of water and air. ^e In the absence of water. ^f In the absence of air. ^g 1,8-Dibromonaphthalene was used as the substrate instead of **1**.

tetrabutylammonium fluoride or hydroxide, we didn't detect **3a** except that the normal Sonogashira products were obtained in different ratios (Table 1, entries 6 and 7). Further, **3a** could not be afforded either at room temperature (Table 1, entry 10), or in the absence of water and/or air (Table 1, entry 12–14). When **1** was altered as 1,8-dibromonaphthalene, **3a** was isolated in a yield of 12%, while 1-bromo-8-(phenylethynyl)naphthalene was isolated as a major product (Table 1, entry 15).

Department of Chemistry, Zhejiang University, Hangzhou 310027, P. R. China. E-mail: orgwyg@zju.edu.cn, pinglu@zju.edu.cn; Fax: +86 571-87952543; Tel: +86 571-87952543

† Electronic supplementary information (ESI) available: Detailed experimental procedures, characterization data, and copies of ¹H and ¹³C NMR spectra for all products. See DOI: 10.1039/c0cc04875e

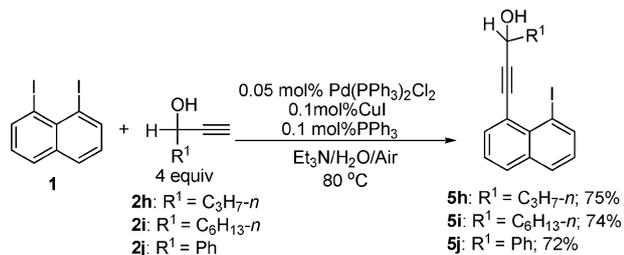
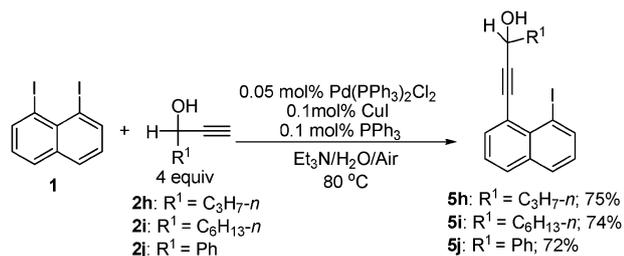
Table 2 Palladium catalyzed reaction of **1** with propynols **2a–2g**^a

Entry	Propynol	Product	Yield (%)
1	2a (R ₁ = R ₂ = Me)	3a (R ₁ = R ₂ = Me)	64
2	2b (R ₁ = Me, R ₂ = Et)	3b (R ₁ = Me, R ₂ = Et)	62
3	2c (R ₁ = Me, R ₂ = Pr- <i>n</i>)	3c (R ₁ = Me, R ₂ = Pr- <i>n</i>)	58
4	2d (R ₁ = R ₂ = Et)	3d (R ₁ = R ₂ = Et)	45
5	2e (R ₁ , R ₂ = -(CH ₂) ₄ -)	3e (R ₁ , R ₂ = -(CH ₂) ₄ -)	59
6	2f (R ₁ , R ₂ = -(CH ₂) ₅ -)	3f (R ₁ , R ₂ = -(CH ₂) ₅ -)	60
7	2g (R ₁ = Me, R ₂ = Bu- <i>i</i>)	3g (R ₁ = Me, R ₂ = Bu- <i>i</i>)	54

^a The reaction was carried out in a sealed flask with the existence of water (10 μ L) and air, and using **1** (1 mmol), **2** (4 mmol), Pd(PPh₃)₂Cl₂ (0.05 mmol), CuI (0.1 mmol), and PPh₃ (0.1 mmol) in Et₃N (40 mL).

In order to survey the substrate diversity of this one-pot reaction, various propynols **2a–2k** were examined under the optimized reaction condition. To tertiary propynols **2a–2g** (Table 2), bicyclic products **3a–3g** were obtained as major products in yields of 45–64%, respectively. However, when the secondary propynols **2h**, **2i** or **2j** (Scheme 1) were used as coupling substrates, the mono-Sonogashira coupling product **5h**, **5i** or **5j** were isolated as major products in moderate yields (72–75%). When primary propynol **2k** (Scheme 2) was used, an unexpected acenaphthylene product **6** was isolated in a yield of 76% (ESI⁺). The skeleton of **6** deserved multiple biological activities.⁸ More interestingly, **4a** did not go further bicyclization at all under the optimized reaction condition and was mostly recovered.

According to above investigations, it might be preliminarily concluded that the cleavage of one molar ketone from the mono-coupling intermediate **5a**⁵ played an important role in the reaction progress. It also well explained the majority

**Scheme 1** Palladium catalyzed reaction of **1** with propynols **2h–2j**.**Scheme 2** Palladium catalyzed reaction of **1** with propynols **2k**.

formations of **5h–5j** (Scheme 1) because the aldehyde cleavage is more difficult than ketone cleavage,⁹ similar to the relative reactivity of retro-aldol condensation. In this point of view, reactions of **5a** with **2a–2g** were conducted and bicyclic products **3a–3g** (Table 3) were obtained as we predicted.

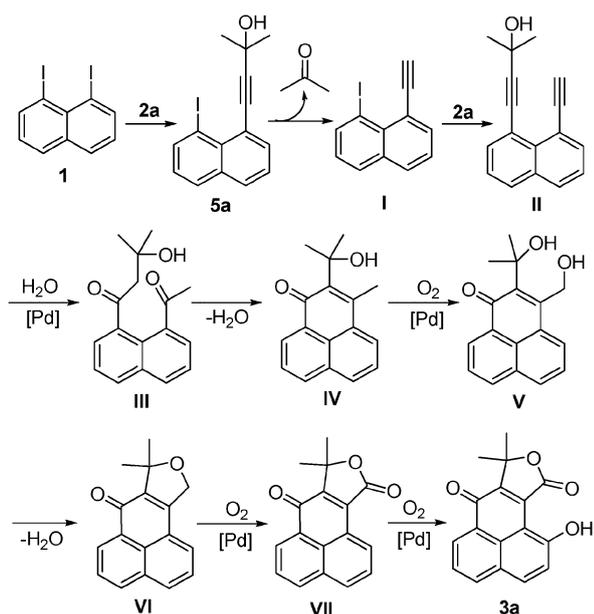
Based on the literature and the above substrate-controlled investigations, we proposed a possible mechanistic pathway shown in Scheme 3. **5a**, formed *via* normal Sonogashira coupling, was firstly postulated to undergo a base-catalyzed deacetonization to afford **I**, that is similar to retro-aldol condensation.⁹ Then **I** reacted further with **2a** to form **II**. Afterward, hydration of **II** and a sequential intramolecular aldol condensation generated the cyclized α,β -unsaturated ketone **IV**.¹⁰ A cyclic ether (**VI**) was obtained soon *via* Pd-catalyzed allylic oxidation¹¹ and immediate intramolecular dehydration. Sequentially, lactone (**VII**) was formed by further palladium catalyzed allylic oxidation of **VI**.^{11,12} Finally, by orientation of the carbonyl of ester group, palladium was inserted into aromatic C_{sp²}-H bond, and a palladium participated six membered ring was generated. Coordination with water in solution and followed by reductive elimination, **3a** was obtained.¹³

Not only the synthesis of **3a** is fascinating, but also its photophysical properties. **3a** (1 \times 10⁻⁵ M in THF) absorbs light at 432 nm and 454 nm, and emits light at 478 nm (Fig. 1). It might be assigned to the π - π^* transition of the phenalenone skeleton. Theoretical calculation supported this assignment (Table S1 in ESI⁺). Gradual addition of the fluoride anion produces a decreasing intensity of the absorption peaks at 432 nm and 454 nm, but an increasing intensity of the absorbance peaks at 502 nm and 536 nm. A clear isosbestic point is found to be at 468 nm, which suggests an interconversion between two species (Fig. S27, ESI⁺). At the same time, a noticeable change is also observed by the fluorescent measurement. No obvious change is found at 478 nm, but a new emission peak appears at 550 nm accompanied by a remarkable increment in intensity with the gradual addition of the fluoride anion (Fig. S28, ESI⁺). It might be explained that a photoinduced charge transfer (PCT) process occurs by the

Table 3 Main products of palladium catalyzed reactions of **5a** with propynols **2a–2g**^a

Entry	Propynol	Product	Yield (%)
1	2a	3a (R ₁ = R ₂ = Me)	68
2	2b	3b (R ₁ = Me, R ₂ = Et)	65
3	2c	3c (R ₁ = Me, R ₂ = Pr- <i>n</i>)	62
4	2d	3d (R ₁ = R ₂ = Et)	43
5	2e	3e (R ₁ , R ₂ = -(CH ₂) ₄ -)	61
6	2f	3f (R ₁ , R ₂ = -(CH ₂) ₅ -)	60
7	2g	3g (R ₁ = Me, R ₂ = Bu- <i>i</i>)	55

^a The reaction was carried out in a sealed flask with the existence of water (10 μ L) and air, and using **5a** (1 mmol), **2** (4 mmol), Pd(PPh₃)₂Cl₂ (0.05 mmol), CuI (0.1 mmol), and PPh₃ (0.1 mmol) in Et₃N (40 mL).



Scheme 3 The postulated mechanism.

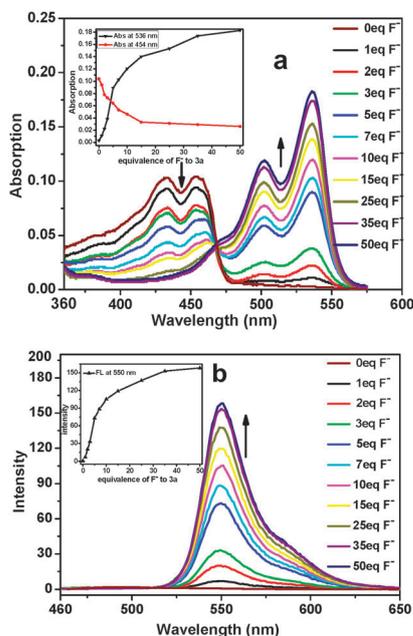


Fig. 1 (a) The absorption changes of **3a** (1×10^{-5} M in THF) with addition of F^- . Inset figure present the absorption intensity at 536 nm and 454 nm versus the concentration of F^- , respectively; (b) the fluorescent changes of **3a** (1×10^{-5} M in THF, excited at 454 nm) with addition of F^- . Inset figure present the emission at 550 nm versus the concentration of F^- .

addition of a fluoride anion which leads to a noticeably enhanced red-shifted emission and the red-shifted absorption as well.¹⁴ Furthermore, there were no significant changes in the emission spectra when other anions, such as AcO^- , Cl^- , Br^- , HPO_4^{2-} , $H_2PO_4^-$ were added (Fig. S29, ESI[†]). So we assume that **3a** might be used as a remarkable fluorescent chemosensor for the fluoride anion.¹⁵

In conclusion, phenalenone derivatives could be efficiently constructed from 1,8-diiodonaphthalene and tertiary propynols *via* a one-pot reaction which was catalyzed by $Pd(PPh_3)_2Cl_2/CuI$ in the presence of water and air. This domino process eventually combines nine sequential steps, including Pd-catalyzed Sonogashira coupling ($C_{sp}-H$ activation), Pd-catalyzed allylic oxidation ($C_{sp^3}-H$ activation) and Pd-catalyzed *ortho* activation of aromatic rings ($C_{sp^2}-H$ activation). Moreover, the resulting phenalenone derivatives could be a potential fluorescent chemosensor for the fluoride anion with high sensitivity and selectivity.¹⁵ Further studies to clearly understand the reaction mechanism and applications of this approach to phenalenones are ongoing in our laboratory.

This work has been supported by the National Nature Science Foundation of China (20972137; J0830413). Contributions from Prof. Shengmin Ma and Jinquan Yu in mechanism postulation and Jianming Gu and Xiurong Wu in structure elucidation are greatly appreciated.

Notes and references

- For a review of palladium-catalyzed Sonogashira coupling reaction, see: (a) H. Doucet and J.-C. Hierso, *Angew. Chem.*, 2007, **119**, 850 (*Angew. Chem., Int. Ed.*, 2007, **46**, 834); (b) R. Chinchilla and C. Nájera, *Chem. Rev.*, 2007, **107**, 874.
- Selected examples of the application of the Sonogashira coupling reaction: (a) M. Bock, R. Dehn and A. Kirschning, *Angew. Chem.*, 2008, **120**, 9274 (*Angew. Chem., Int. Ed.*, 2008, **47**, 9134); (b) K. Kanda, T. Koike, K. Endo and T. Shibata, *Chem. Commun.*, 2009, 1870; (c) Z. Chen, J. Zhu, H. Xie, S. Li, Y. Wu and Y. Gong, *Chem. Commun.*, 2010, **46**, 4184.
- (a) T. J. J. Müller and U. H. F. Bunz, *Functional Organic Material*, Wiley VCH, 2007, pp. 179–223, and references cited therein; (b) T. J. J. Müller and D. M. D'Souza, *Pure Appl. Chem.*, 2008, **80**, 609.
- (a) Z. Zhao, J.-H. Li, P. Lu and Y. Yang, *Adv. Funct. Mater.*, 2007, **17**, 2203; (b) Z. Zhao, X. Xu, H. Wang, P. Lu, G. Yu and Y. Liu, *J. Org. Chem.*, 2008, **73**, 594; (c) B. Hu, Y. Wang, X. Chen, Z. Zhao, Z. Jiang, P. Lu and Y. Wang, *Tetrahedron*, 2010, **66**, 7583.
- J. J. González, A. Francesch, D. J. Cárdenas and A. M. Echavarren, *J. Org. Chem.*, 1998, **63**, 2854.
- Patent of the compound **3a**: H. Wang and P. Lu, *CN 101230267 A*, 2008.
- CCDC 712668 contains the supplementary crystallographic data of **3a**.
- N. Haddad and E. Abu-Shqara, *J. Org. Chem.*, 1994, **59**, 6090.
- (a) K. Oisaki, D. Zhao, M. Kanai and M. Shibasaki, *J. Am. Chem. Soc.*, 2006, **128**, 7164; (b) P. R. Carlier, C. W.-S. Lo, M. M.-C. Lo, N. C. Wan and I. D. Williams, *Org. Lett.*, 2000, **2**, 2443.
- (a) J. Piera and J.-E. Bäckvall, *Angew. Chem.*, 2008, **120**, 3558 (*Angew. Chem., Int. Ed.*, 2008, **47**, 3506); (b) C. Zhang, D.-M. Cui, L.-Y. Yao, B.-S. Wang, Y.-Z. Hum and T. Hayashi, *J. Org. Chem.*, 2008, **73**, 7811; (c) A. Das, H.-K. Chang, C.-H. Yang and R.-S. Liu, *Org. Lett.*, 2008, **10**, 4061.
- (a) M. S. Chen and M. C. White, *Science*, 2007, **318**, 783; (b) D. J. Covell and M. C. White, *Angew. Chem.*, 2008, **120**, 6548 (*Angew. Chem., Int. Ed.*, 2008, **47**, 6448).
- B. A. Steinhoff, S. R. Fix and S. S. Stahl, *J. Am. Chem. Soc.*, 2002, **124**, 766.
- (a) S. Murai, F. Kakiuchi, S. Sekine, Y. Tanaka, A. Kamatani, M. Sonoda and N. Chatani, *Nature*, 1993, **366**, 529; (b) X. Li, P. Chen, J. W. Faller and R. H. Crabtree, *Organometallics*, 2005, **24**, 4810.
- (a) D. Tanaka, S. Horike, S. Kitagawa, M. Ohba, M. Hasegawa, Y. Ozawa and K. Toriumi, *Chem. Commun.*, 2007, 3142; (b) R. M. F. Batista, E. Oliveira, S. P. G. Costa, C. Lodeiro and M. M. M. Raposo, *Org. Lett.*, 2007, **9**, 3201; (c) S. Kumar, V. Luxami and A. Kumar, *Org. Lett.*, 2008, **10**, 5549.
- M. Cametti and K. Rissanen, *Chem. Commun.*, 2009, 2809.