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Synthesis of Functionalized Pyrazoles via Vanadium-Catalyzed C−N Dehydrogenative Cross-Coupling and Fluorescence Switch-On Sensing of BSA Protein

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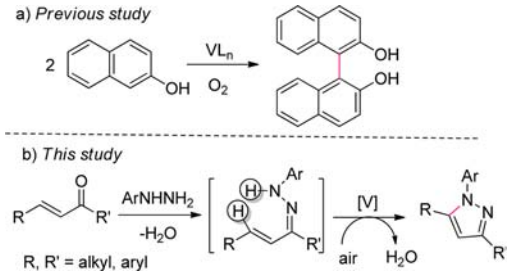
Supporting Information

ABSTRACT: Vanadium-catalyzed C−N dehydrogenative cross-coupling of alkenyl hydrazones leading to functionalized pyrazoles is described in a 1:1 mixture of toluene/H_2O using air as the terminal oxidant. Significant practical features include use of the commercial nontoxic $VOSO_4$ as a recyclable catalyst, mild reaction conditions, scalability, and the broad substrate scope. Some of the product pyrazoles exhibit interesting photophysical properties. Fluorescence light-up sensing of BSA protein by one of the pyrazoles is also highlighted.

Transition-metal-catalyzed oxidative C−H functionalization affords a powerful tool for regioselective C−C and C−heteroatom bond formation.[1] Transition metals such as Rh, Ru, Pd, and Cu have been significantly investigated for this purpose.[1] Vanadium is nontoxic, readily available, cheap, and also present in biological molecules.[2] Thus, its exploration for regioselective C−H functionalization via dehydrogenative cross-coupling, employing air[3] as the oxidant under environmentally benign aqueous organic reaction conditions,[4] would be valuable (Scheme 1a). Herein, we report the condensation of α,β-unsaturated ketones with aryl hydrazines followed by the C−N dehydrogenative cross-coupling[5] of alkenyl hydrazones using water-soluble $VOSO_4$ as the recyclable catalyst, leading to highly functionalized pyrazoles in a 1:1 mixture of toluene/water under air at room temperature (Scheme 1b).[6,7] Functionalized pyrazoles are the subject of recent research interest due to their widespread potential biological applications.[8] Also, pyrazoles are known to bind strongly with biomolecules.[9] Thus, synthesis of functionalized pyrazoles with a mild, atom economic, and simple process, and a study of their interaction properties with biomolecules such as bovine serum albumin (BSA) could find useful application in synthetic and medicinal sciences.[10]

Scheme 1. Vanadium-Catalyzed Dehydrogenative Coupling Reactions



We first commenced our optimization studies using α,β-unsaturated ketone **1a** and phenylhydrazine hydrochloride **2a** as model substrates with V catalysts (Supporting Information, Table 1). Gratifyingly, the reaction readily occurred to provide the functionalized pyrazole **3a** in 70% yield when the substrates **1a** and **2a** were stirred with NaOAc in a 1:1 mixture of toluene/H_2O at 60 °C for 1 h followed by rt for 18 h with 20% $VOSO_4$, using air as the oxidant (entry 1). Subsequent screening of $VO(acac)_2$ and V_2O_5 as the catalysts produced the target heterocycle **3a** in 55% and 54% yield, respectively (entries 2 and 3). Yet, lowering the quantity of $VOSO_4$ to 5 mol % led to an increase in the yield to 73% (entries 4−5). The reaction under N_2 provided **3a** in trace amount (entry 6). Control experiments confirmed that in the absence of a V catalyst the target heterocycle **3a** was not formed (entry 7).

Having identified the optimal reaction conditions, the scope of the procedure was explored. First, the reaction of a series of methyl alkenyl ketones **1b−p** was screened with phenylhydrazine **2a** (Scheme 2). The substrate **1b** underwent reaction to afford **3b** in 48% yield. The reactions of substrates **1c−j**

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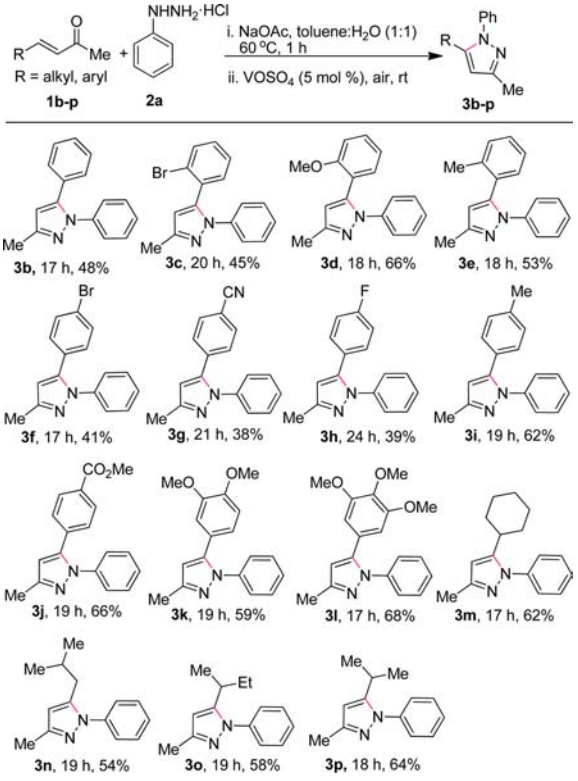
Scheme 2. Reaction of Different Methyl Alkenyl Ketones 1b–p with Phenylhydrazine 2a[a–c]

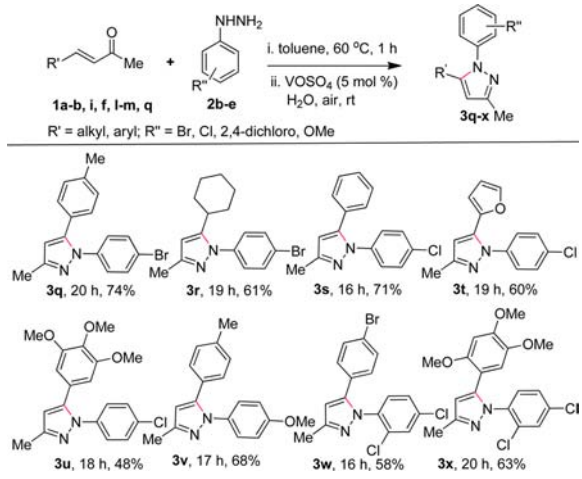


[a]Reaction conditions: **1b–p** (1.0 mmol), **2a** (1.2 mmol), NaOAc (2.9 mmol) toluene: H_2O (1:1, 3 mL), 60 °C, 1 h; $VOSO_4$ (0.05 mmol), rt, air. [b]Isolated yield. [c]Accompanied by ∼5–10% unreacted **1b–p** and **2a**.

bearing substituted aryl rings with 2-bromo, 2-methoxy, 2-methyl, 4-bromo, 4-cyano, 4-fluoro, 4-methyl, and 4-methyl carboxylate functionalities produced the corresponding pyrazoles **3c–j** in 38–66% yields, while **1k–l** having 2,4-dimethoxy and 3,4,5-trimethoxy substituents in the aryl ring underwent reaction to furnish **3k–l** in good yields. In addition, the reaction of **1m–p** bearing cyclohexyl, isobutyl, *sec*-butyl, and isopropyl substituents in the alkenyl position readily occurred to furnish the corresponding pyrazoles **3m–p** in 54–64% yields. Recrystallization of **3a** from CH_3CN gave a single crystal whose structure was determined by X-ray analysis.

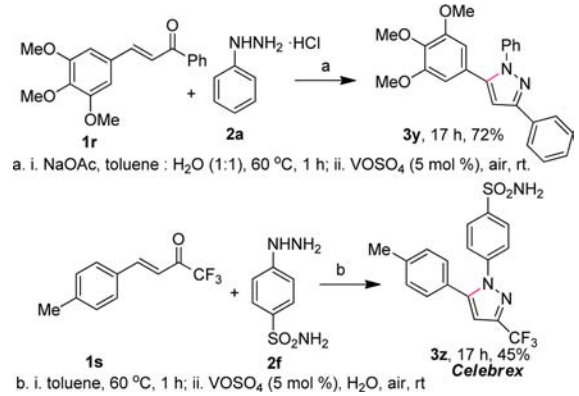
Next, the utility of the protocol was extended to the reaction of methyl alkenyl ketones **1a–b**, **1i**, **1f**, **1l–m**, and **1q** with different aryl hydrazines **2b–e** (Scheme 3). Ketones **1i** and **1m** underwent a reaction with (4-bromophenyl)hydrazine **2b** to give pyrazoles **3q** and **3r** in 74% and 61% yield, respectively, while **1b**, **1q**, and **1l** with (4-chlorophenyl)hydrazine **2c** produced the desired pyrazole derivatives **3s–u** in 48–71% yields. The reaction of the ketone **1i** with (4-methoxyphenyl)hydrazine **2d** gave **3v** in 68% yield, whereas **1f** and **1a** with (2,4-dichlorophenyl)-hydrazine **2e** furnished pyrazoles **3w** and **3x** in 58% and 63% yields, respectively. Also, the reaction of the chalcone **1r** with **2a** produced pyrazole **3y** in 72% yield (Scheme 4), whereas trifluoromethyl ketone with a *p*-tolyl substituent in the alkenyl position **1s** underwent reaction with hydrazine **2f** to produce celebrex **3z** in 45% yield. These results suggest that this procedure can be employed for the reactions of a broad range of substrates to afford diverse functionalized pyrazoles in good yields.

Scheme 3. Reaction of Methyl Alkenyl Ketones with Different Aryl Hydrazines 2b–e[a–c]



[a]Reaction conditions: ketone (1.0 mmol), aryl hydrazines **2b–e** (1.2 mmol), toluene (1.5 mL), 60 °C, 1 h; $VOSO_4$ (0.05 mmol), H_2O (1.5 mL), rt, air. [b]Isolated yield. [c]Accompanied 5–10% unreacted substrates.

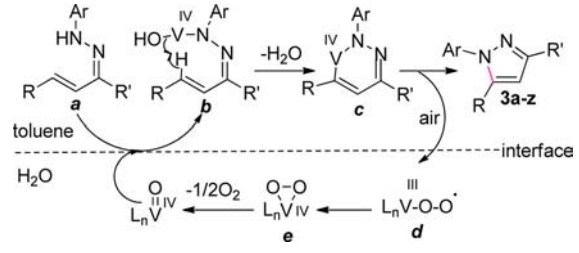
Scheme 4. Reaction of α,β-Unsaturated Ketones 1r–s with Hydrazines 2a and 2f



The reaction of **1a** with **2a** was also studied in gram scale as a representative example (Supporting Information (SI), Scheme S1). As mentioned above, the reaction took place readily to produce **3a** in 65% yield. Furthermore, the aqueous layer having the vanadium catalyst could be easily separated and recycled. For example, the reaction of **1a** with **2a** was studied over three runs with >64% yield (SI, Scheme S2).

The proposed catalytic cycle is shown in Scheme 5. Condensation of the ketones with aryl hydrazines may give hydrazones ***a***, which may react with $VOSO_4$ to yield the

Scheme 5. Proposed Reaction Pathway



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intermediate ***b***.[2a] Concerted metalation−deprotonation (CMD) of ***b*** may give the cyclic vanadium intermediate ***c***, which may undergo reductive elimination to produce the target pyrazole derivatives and V(II) species. The latter with air may oxidize to active catalysts via the peroxo species ***d*** and ***e*** to complete the catalytic cycle.

Finally, we studied the UV−visible and fluorescence photophysical properties of some of the synthesized pyrazoles and interaction of two of the compounds with the BSA biomolecule. Thus, pyrazole **3a** exhibited strong absorption bands at 260 and 302 nm as was revealed from UV−visible spectra. When excited at 302 nm it showed strong red-shifted emission (31 nm) at around 363−394 nm. In contrast, **3u**, in which the N-1 of pyrazole was substituted by the electron-withdrawing group, chlorophenyl, showed red-shifted (24 nm) emission at around 367−391 nm with decreased intensity as the solvent polarity increased when excited at its strong charge transfer absorption band at 301 nm. The emission was characterized as ICT emission. However, when pyrazole N-1 was substituted by the electron-withdrawing group, dichlorophenyl, the compound **3x** showed very weak emission with a strong red shift in the polar solvents compared to highly nonpolar hexane. The pyrazole derivative **3k** exhibited strong absorbance in various organic solvents at around 265 nm. Upon excitation at individual absorption maxima (λ_{ex} = 263−272 nm) of each solvent, **3k** showed strong emission behavior at around 365 nm with increased intensity as the solvent polarity increases from hexane to methanol. On the other hand, pyrazole **3l** containing the trimethoxyphenyl donor exhibited absorbance at around 265 and 325 nm. The charge transfer band at 325 nm showed increased intensity with red shifting behavior as solvent polarity was increased. However, upon excitation at around 260−270 nm it showed strong emission at around 370 nm in various organic solvents with no regular trend. The compound **3y** showed stronger absorbance at 255 and 335 nm than **3l**. The charge transfer band at 335 nm showed decreased intensity with a red shift as the solvent polarity was increased. Upon excitation at a longer absorption band, it showed strong red-shifted emission, characteristic of ICT at around 400 nm with a red shift of 39 nm as the solvent polarity was increased. The compound **3v** showed absorption at 260 nm in less polar solvent such as hexane with a shoulder at around 300 nm in polar solvents. It showed irregular emission behavior at around 373 nm when excited as 260 nm. On the other hand, compound **3q** showed a strong absorption band at around 262 nm which when excited at 262 nm showed structureless emission at around 375 nm with a red shift of 15 nm and decreased intensity as solvent polarity was decreased.

Looking at the microenvironment sensitive emission characteristics of pyrazoles, **3a** and **3y**, we were next interested in studying the interaction behavior with bovine serum albumin (BSA).[10] The absorption spectra of free **3a** and **3y** in phosphate buffer (20 mM, pH 7.0) showed maxima (λ_{max}) near 245, 299 nm and 243, 336 nm, respectively. Thus, upon addition of increasing concentration of BSA to the solution of pyrazole probe **3a**, we observed a hyperchromicity with a strong red shift of 12 nm in the UV−vis spectra indicating interactions between BSA and **3a** (SI, Figure 10a). On the other hand, pyrazole probe **3y** exhibited strong hypochromism with a red shift of about 8−10 nm of the absorbance band in the UV−vis spectra upon gradual addition of BSA. The band in the UV−visible spectra at around 335 nm vanished when the BSA concentration was 9 times the concentration of the probe. All these observations, along with an isosbestic point at 298 nm, clearly indicated strong ground state complex formation between **3y** and BSA (Figure 1a). Moreover, the nonperturbed nature of the isosbestic point

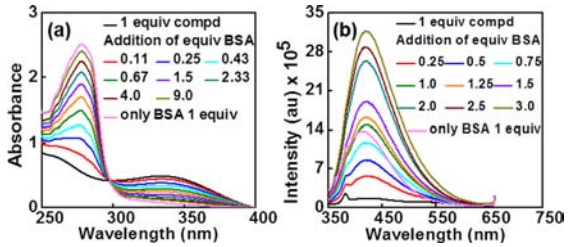

Figure 1. (a) UV−visible titration of probe **3y** with various concentrations of BSA. (b) Fluorescence titration of probe **3y** with various concentrations of BSA (5 mM phosphate buffer, pH 7.0, rt, λ_{ex} = 345 nm).

suggested only one binding stoichiometry. The Job plot for both probes suggested a 1:1 binding complex between probes and BSA (SI, Figure 16).

To investigate the protein sensing ability and insight into the binding event of the probes, we then investigated the change in fluorescence upon addition of increasing concentrations of BSA to the individual probe's solution. Thus, it was observed that both the fluorescence intensity and quantum yield of the probe pyrazole **3a** decreased slowly with a small blue shift of emission maxima when excited at 302 nm (SI, Figure 2a) indicating a binding of the probe in a relatively hydrophobic site of the BSA. This observation was also evident from a blue-shifted emission of the probe **3a** in various organic solvents as the solvent polarity decreases (SI, Figure 2c−d).[10,11] In contrast, upon excitation at 335 nm, a gradual increase in fluorescence intensity at about 420 nm was the result when an increasing concentration of BSA solution was added gradually to a solution of probe pyrazole **3y** (Figure 1b). This result indicated a binding interaction between the pyrazole **3y** and the BSA. Next, the fluorescence anisotropy was measured to confirm the binding event further. Thus, an enhancement of fluorescence anisotropy for the probe **3a** from 0.01 in aqueous buffer to 0.10 in the presence of BSA was observed. This indicated that the probe **3a** bound strongly inside the hydrophobic pocket of BSA and experienced a highly restricted rotational motion (SI, Figure 13).[12] On the other hand, upon addition of BSA to a solution of **3y**, the anisotropy value increased initially from 0.18 to 0.31 indicating a strong binding between BSA and the probe (SI, Figure 17).[12] An increase in the % α-helicity of BSA was observed from the CD spectra in the presence of both pyrazoles. This indicated a possible conformational adjustment of BSA upon association with the pyrazoles (SI, Figure 18).[10,11] The association constant of probe pyrazoles **3a** and **3y** with BSA was also determined fluorimetrically by a Stern−Volmer plot SI, Figure 11) and Benesi−Hildebrand plot (SI, Figure 15) respectively, which were found to be 4.9×10^3 and 1.64×10^4 M^{-1} respectively. The association constants reflected that the compound **3y** binds with BSA more strongly than **3a**. Therefore, it is clear from the above findings that the probe pyrazole **3y** is more efficient compared to **3a** in sensing the BSA protein biomolecule via the generation of enhanced fluorescence intensity. The low fluorescence intensity of the probe in phosphate buffer in the absence of biomolecules may be attributed to a radiationless channel assisted by intermolecular hydrogen bonding present in aqueous solution. However, in the presence of BSA the nonradiative channels are possibly blocked and are less effective, as the probe interacts strongly with the

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protein, which ultimately leads to a fluorescence switch-on signal of enhanced intensity and quantum yields.

In summary, vanadium(IV)-catalyzed C−N dehydrogenative cross-coupling of alkenyl hydrazones leading to functionalized pyrazoles has been described using air as the oxidant. Simplified product isolation, recyclability of the catalyst, mild reaction conditions, and the broad substrate scope are significant practical advantages. The binding studies of the target heterocycles toward protein have been demonstrated which showed that the pyrazole **3y** is an efficient fluorescence switch-on probe for the detection of BSA. This study will open new avenues for the further development in aerobic C−H functionalization strategy for the synthesis of biologically important small fluorescent heterocycles using vanadium catalysis in the water medium.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.orglett.5b02669.

Experimental procedure, crystal structure of **3a**, characterization data, photophysical studies, and NMR spectra (^{1}H and ^{13}C) of the products (PDF)
Crystallographic data for **3a** (CIF)

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Author Contributions

†A.Y. and S.S.B. contributed equally to the photophysical studies.

Notes

The authors declare no competing financial interest.

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■ REFERENCES

(1) For examples, see: (a) Ueda, S.; Nagasawa, H. *Angew. Chem., Int. Ed.* **2008**, *47*, 6411. (b) Brasche, G.; Buchwald, S. L. *Angew. Chem., Int. Ed.* **2008**, *47*, 1932. (c) Arockiam, P. B.; Bruneau, C.; Dixneuf, P. H. *Chem. Rev.* **2012**, *112*, 5879. (d) Kim, J. Y.; Park, S. H.; Ryu, J.; Cho, S. H.; Kim, S. H.; Chang, S. *J. Am. Chem. Soc.* **2012**, *134*, 9110. (e) Zhang, X.-G.; Dai, H.-X.; Wasa, M.; Yu, J.-Q. *J. Am. Chem. Soc.* **2012**, *134*, 11948. (f) Schröder, N.; Wencel-Delord, J.; Glorius, F. *J. Am. Chem. Soc.* **2012**, *134*, 8298. (g) Rosen, B. R.; Simke, L. R.; Thuy-Boun, P. S.; Dixon, D. D.; Yu, J.-Q.; Baran, P. S. *Angew. Chem., Int. Ed.* **2013**, *52*, 7317. (h) Kuninobu, Y.; Iwanaga, T.; Omura, T.; Takai, K. *Angew. Chem., Int. Ed.* **2013**, *52*, 4431. (i) Sadhu, P.; Alla, S. K.; Punniyamurthy, T. *J. Org. Chem.* **2013**, *78*, 6104. (j) Thirunavukkarasu, V. S.; Kozhushkov, S. I.; Ackermann, L. *Chem. Commun.* **2014**, *50*, 29. (k) Becker, P.; Priebbenow, D. L.; Pirwerdjan, R.; Bolm, C. *Angew. Chem., Int. Ed.* **2014**, *53*, 269. (l) Parthasarathy, K.; Bolm, C. *Chem. - Eur. J.* **2014**, *20*, 4896. (m) Zhao, D.; Lied, F.; Glorius, F. *Chem. Sci.* **2014**, *5*, 2869. (n) Yokoyama, Y.; Unoh, Y.; Hirano, K.; Satoh, T.; Miura, M. *J. Org. Chem.* **2014**, *79*, 7649.

(2) For examples, see: (a) Hirao, T. *Chem. Rev.* **1997**, *97*, 2707. (b) Zhang, S.; Nomura, K. *J. Am. Chem. Soc.* **2010**, *132*, 4960. (c) Ramos-Luna, M. A.; Cedeno-Caero, L. *Ind. Eng. Chem. Res.* **2011**, *50*, 2641. (d) Nomura, K.; Matsumoto, Y. *Organometallics* **2011**, *30*, 3610. (e) McLauchlan, C. C.; Crans, D. C. *Dalton Trans* **2013**, *42*, 11744. (f) Strassberger, Z.; Ramos-Fernandez, E. V.; Boonstra, A.; Jorna, R.; Tanase, S.; Rothenberg, G. *Dalton Trans* **2013**, *42*, 5546.

(3) For examples, see: (a) Ishii, Y.; Matsunaka, K.; Sakaguchi, S. *J. Am. Chem. Soc.* **2000**, *122*, 7390. (b) Hirao, T.; Morimoto, C.; Takada, T.; Sakurai, H. *Tetrahedron* **2001**, *57*, 5073. (c) Punniyamurthy, T.; Velusamy, S.; Iqbal, J. *Chem. Rev.* **2005**, *105*, 2329.

(4) For examples, see: (a) Narayan, S.; Muldoon, J.; Finn, M. G.; Fokin, V. V.; Kolb, H. C.; Sharpless, K. B. *Angew. Chem., Int. Ed.* **2005**, *44*, 3275. (b) Shapiro, N.; Vigalok, A. *Angew. Chem., Int. Ed.* **2008**, *47*, 2849. (c) Jammi, S.; Ali, M. A.; Sakthivel, S.; Rout, L.; Punniyamurthy, T. *Chem. - Asian J.* **2009**, *4*, 314. (d) Mellouli, S.; Bousekkine, L.; Theberge, A. B.; Huck, W. T. S. *Angew. Chem., Int. Ed.* **2012**, *51*, 7981. (e) Sengoden, M.; Punniyamurthy, T. *Angew. Chem., Int. Ed.* **2013**, *52*, 572.

(5) For some recent examples, see: (a) Girard, S. A.; Knauber, T.; Li, C.-J. *Angew. Chem., Int. Ed.* **2014**, *53*, 74. (b) Tran, B. L.; Driess, M.; Hartwig, J. F. *J. Am. Chem. Soc.* **2014**, *136*, 17292. (c) Zhao, J.; Fang, H.; Zhou, W.; Han, J.; Pan, Y. *J. Org. Chem.* **2014**, *79*, 3847. (d) Cheng, Y.; Dong, W.; Wang, L.; Parthasarathy, K.; Bolm, C. *Org. Lett.* **2014**, *16*, 2000.

(6) For traditional methods and importance of pyrazoles, see: (a) Knorr, L. *Ber. Dtsch. Chem. Ges.* **1883**, *16*, 2597. (b) Fustero, S.; Sanchez-Rosello, M.; Barrio, P.; Simon-Fuentes, A. *Chem. Rev.* **2011**, *111*, 6984.

(7) For synthesis of pyrazoles, see: (a) Kovelesky, A. C.; Shine, H. J. *J. Org. Chem.* **1988**, *53*, 1973. (b) Landge, S. M.; Schmidt, A.; Outerbridge, V.; Török, B. *Synlett* **2007**, *2007*, 1600. (c) Aggarwal, R.; Kumar, R. *Synth. Commun.* **2009**, *39*, 2169. (d) Neumann, J. J.; Suri, M.; Glorius, F. *Angew. Chem., Int. Ed.* **2010**, *49*, 7790. (e) Hu, J.; Chen, S.; Sun, Y.; Yang, J.; Rao, Y. *Org. Lett.* **2012**, *14*, 5030. (f) Desai, V. G.; Satardekar, P. C.; Polo, S.; Dhumaskar, K. *Synth. Commun.* **2012**, *42*, 836. (g) Li, X.; He, L.; Chen, H.; Wu, W.; Jiang, H. *J. Org. Chem.* **2013**, *78*, 3636. (h) Zhang, T.; Bao, W. *J. Org. Chem.* **2013**, *78*, 1317. (i) Ananthnag, G. S.; Adhikari, A.; Balakrishna, M. S. *Catal. Commun.* **2014**, *43*, 240. (j) Mane, V. D.; Mahajan, D. T.; Rajput, P. R. *Int. J. Pharm. Bio. Sci.* **2015**, *6*, 213. (k) Hamada, N. M. M.; Abdo, N. Y. M. *Molecules* **2015**, *20*, 10468. (l) Bharathiraja, G.; Sengoden, M.; Kannan, M.; Punniyamurthy, T. *Org. Biomol. Chem.* **2015**, *13*, 2786.

(8) (a) Chu, C. K.; Cutler, J. *J. Heterocycl. Chem.* **1986**, *23*, 289. (b) Larsen, J. S.; Zahran, M. A.; Pedersen, E. B.; Nielsen, C. *Monatsh. Chem.* **1999**, *130*, 1167. (c) Tewari, A. K.; Mishra, A. *Bioorg. Med. Chem.* **2001**, *9*, 715. (d) Mohammed, K. O.; Nissan, Y. M. *Chem. Biol. Drug Des.* **2014**, *84*, 473. (e) Ghorab, M. M.; Ragab, F. A.; Heiba, H. I.; El-Gazzar, M. G.; Zahran, S. S. *Eur. J. Med. Chem.* **2015**, *92*, 682.

(9) (a) Baraldi, P. G.; Balboni, G.; Pavani, M. G.; Spalluto, G.; Tabrizi, M. A.; Clercq, E. D.; Balzarini, J.; Bando, T.; Sugiyama, H.; Romagnoli, R. *J. Med. Chem.* **2001**, *44*, 2536. (b) Kulkarni, N. V.; Kamath, A.; Budagumpi, S.; Revankar, V. K. *J. Mol. Struct.* **2011**, *1006*, 580.

(10) For examples, see: (a) Tse, W. C.; Boger, D. L. *Acc. Chem. Res.* **2004**, *37*, 61. (b) Wu, J.; Liu, W.; Ge, J.; Zhang, H.; Wang, P. *Chem. Soc. Rev.* **2011**, *40*, 3483.

(11) For examples, see: (a) Xu, Y.; Li, Z.; Malkovskiy, A.; Sun, S.; Pang, Y. *J. Phys. Chem. B* **2010**, *114*, 8574. (b) Banerjee, M.; Pal, U.; Subudhhi, A.; Chakrabarti, A.; Basu, S. *J. Photochem. Photobiol., B* **2012**, *108*, 23. (c) Bag, S. S.; Kundu, R.; Jana, S. *Tetrahedron Lett.* **2013**, *54*, 2627.

(12) For examples, see: (a) Bi, S.; Song, D.; Tian, Y.; Zhou, X.; Liu, Z.; Zhang, H. *Spectrochim. Acta, Part A* **2005**, *61*, 629. (b) Lakowicz, J. R. *Principles of Fluorescence Spectroscopy*, 3rd ed.; Kluwer Academic/Plenum Publishers: New York, 2006.

DOI: 10.1021/acs.orglett.5b02669
Org. Lett. 2015, 17, 5308−5311