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Oxidation of alkynes using $PdCl_2/CuCl_2$ in PEG as a recyclable catalytic system: one-pot synthesis of quinoxalines

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ABSTRACT

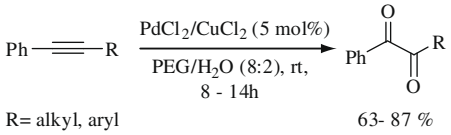
Alkynes were oxidized efficiently using the catalytic amount of $PdCl_2$ and $CuCl_2$ in PEG-400 in the presence of water, providing excellent yields of the corresponding 1,2-diketones. A variety of alkynes were well-suited substrates for the oxidation under the described conditions. Further, the optimized conditions were successfully utilized for the one-pot synthesis of 2,3-disubstituted quinoxaline derivatives.

Poly (ethylene glycol) (PEG) has been emerging as a promising green solvent and receiving more attention for both combinatorial as well as for heterogeneous catalysts.[1] The viscosity of PEG at ambient and higher temperatures gives them significant advantage to use for all general operations. PEG offers advantages such as unique solubility properties, low vapor pressure, ready availability, and low cost, which renders it a good solvent for various organic transformations, such as coupling,[2] oxidation,[3] addition,[4] reduction reactions.[5] We have also successfully demonstrated the use of PEG as a reusable solvent for asymmetric dihydroxylation,[6a] $Pd(OAc)_2$-catalyzed Heck reaction,[6b] DABCO-catalyzed Baylis–Hillman reaction,[6c] $Pd/CaCO_3$-catalyzed partial reduction of alkynes to *cis*-olefins,[6d] L-proline-catalyzed asymmetric Aldol reactions,[6e] one-pot conversion of amines to homologated esters.[6f] Further applications of PEG in organic transformations are still welcome.

Oxidation of substituted internal alkynes is one of the most useful methods among the reported methods for the synthesis of 1,2-diketones. The known oxidation methods include the use of $KMnO_4$,[7] transition metal catalysts,[8] DMSO,[9] Wacker-type oxidation using molecular oxygen,[10] oxone in trifluoroacetic acid,[11] or acid-promoted reactions.[12] However, most of these oxidation reactions suffer from a variety of disadvantages such as the use of toxic or expensive reagents, higher temperatures, or cryogenic reaction conditions. In continuation of our interest on the development of PEG-mediated reactions, we now report a mild oxidizing catalytic reagent system, $PdCl_2/CuCl_2$ in PEG/H_2O (8:2), for the oxidation of alkynes to 1,2-diketones as a recyclable system (Scheme 1).

Our studies started with the reaction of diphenylacetylene (**1a**) with catalytic amount (5 mol %) of $PdCl_2/CuCl_2$ in polyethylene glycol in the presence of water (8:2), which provided the corresponding ketone **2a** in 80% yield (Table 1, entry 1). The reaction proceeded at room temperature in 10 h for completion. We then explored the generality of the reaction by varying the substituent on the acetylene and the results are summarized in Table 1. All the substrates studied, diaryl acetylenes (**1b–g**), have been oxidized to the corresponding 1,2-diketones in good yields (Table 1, entries 2–7). Moreover, the reactions also proceeded with aryl alkyl acetylenes **1h** and **1i** (Table 1, entries 8 and 9), though slightly lower yields were obtained.[13]

The recycling performance of the present reagent system, $PdCl_2/CuCl_2$ in PEG, was investigated in the oxidation of 4-(phenylethynyl)benzonitrile (**1c**). The data presented in Table 2 show that the described reagent system could be recycled and reused five times without the loss of reactivity. Further, the reusability of the recycled reagent system was also tested for the different substrates. As the first experiment, the oxidation of **1e** gave diketone **2e** in 78% yield. The recycled reagent system from this reac-



R= alkyl, aryl — 63- 87 %

Scheme 1. Oxidation of alkynes to 1,2-diketones.

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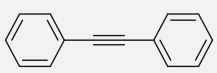
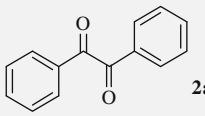
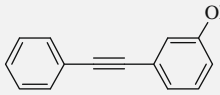
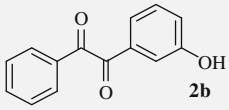
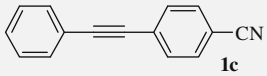
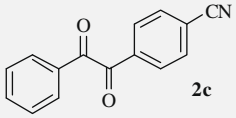
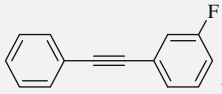
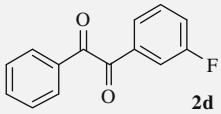
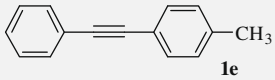
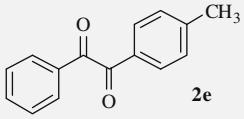
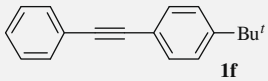
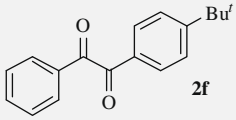
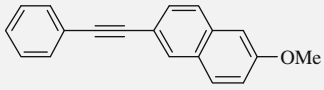
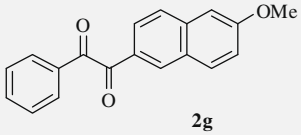
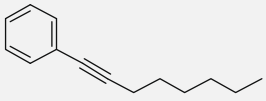
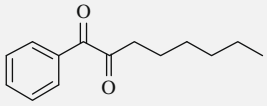
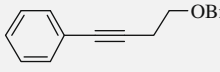
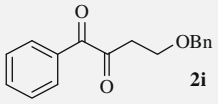
Table 1
Oxidation of alkyne with $PdCl_2/CuCl_2$ in PEG/H_2O[a]

S.No.	Alkyne	Time (h)	1,2-Diketone[b]	Yield[c] (%)
1	 **1a**	10	 **2a**	80
2	 **1b**	12	 **2b**	85
3	 **1c**	10	 **2c**	87
4	 **1d**	9	 **2d**	83
5	 **1e**	14	 **2e**	78
6	 **1f**	14	 **2f**	80
7	 **1g**	8	 **2g**	82
8	 **1h**	12	 **2h**	63
9	 **1i**	12	 **2i**	68

[a] Reaction conditions: Internal alkyne (1 mmol), $PdCl_2$ (5 mol %), $CuCl_2$ (5 mol %), PEG/H_2O (8:2), rt.
[b] Products were characterized by ^1H, ^{13}C NMR, and mass spectroscopy.
[c] Isolated yields.

Table 2
Recyclability for same substrate

Alkyne	Yield[a] (%)				
	1st	2nd	3rd	4th	5th
1c	87	87	80	80	75

[a] Isolated yield after column chromatography.

Table 3
Recyclability for different substrates

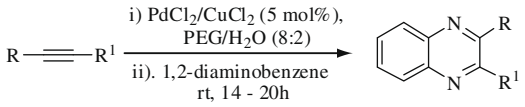
	Alkyne	Yield[a] (%)
1st Run	1e	78
2nd Run	1g	80

[a] Isolated yield after column chromatography.

tion was used for the oxidation of **1g**, which also furnished the corresponding diketone **2g** in 80% yield and no contaminants were observed (Table 3).

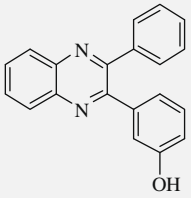
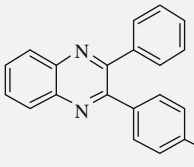
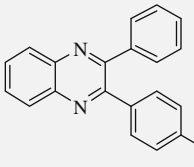
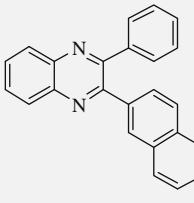
The obtained products in the above-described transformation, 1,2-diketones, are the useful compounds for the preparation of quinoxaline derivatives,[14] by reacting with 1,2-diaminobenzene. By taking this advantage, further, we have explored the one-pot synthesis of quinoxaline derivatives under the described conditions (Scheme 2).[15]

Accordingly, the oxidation of **1b** was carried out using 5 mol % of $PdCl_2/CuCl_2$ in PEG/H_2O (8:2) followed by the addition of 1,2-diaminobenzene. Interestingly, the expected quinoxaline **3a** was obtained in 80% yield at room temperature (Table 4, entry 1). To prove the generality of the reagent system for this one-pot transformation, a few more substrates **1c**, **1e**, and **1g** were studied



Scheme 2. Oxidation of alkynes to 1,2-diketones.

Table 4
One-pot synthesis of quinoxaline derivatives

S.No	Alkyne	Time (h)	Quinoxaline[a]	Yield[b] (%)
1	**Ib**	16	 **3a**	80
2	**Ic**	14	 **3b**	81
3	**Ie**	20	 **3c**	75
4	**Ig**	15	 **3d**	78

[a] Products were characterized by ^{1}H, ^{13}C NMR, and mass spectroscopy.
[b] Isolated yields.

and the results are summarized in Table 4. The reaction of alkynes **1c**, **1e**, and **1g** under the present reaction conditions in the presence of 1,2-diaminobenzene provided the 2,3-disubstituted quinoxaline derivatives in good yields (Table 4, entries 2–4).

In summary, an efficient recyclable catalytic system for the oxidation of internal alkynes to 1,2-diketones has been demonstrated. 5 mol % of $PdCl_2/CuCl_2$ in PEG/H_2O was used for the described transformation, and the recyclability has also been proved. Further, the efficiency of this reagent system in one-pot synthesis of 2,3-disubstituted quinoxaline derivatives was successfully explored.

Acknowledgments

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References and notes

1. Ji, C.; Spear, S. K.; Huddleston, J. G.; Rogers, R. D. *Green Chem.* **2005**, *7*, 64.
2. (a) Li, J.-H.; Hu, X.-C.; Liang, Y.; Xie, Y.-X. *Tetrahedron* **2006**, *62*, 31; (b) Yin, L.; Zhang, Z.-h.; Wang, Y.-M. *Tetrahedron* **2006**, *62*, 9359; (c) Li, J.-H.; Liu, W.-J.; Xie, Y.-X. *J. Org. Chem.* **2005**, *70*, 5409.
3. Alper, H. *Pure Appl. Chem.* **1988**, *60*, 35.
4. (a) Kumar, D.; Patel, G.; Mishra, B. G.; Varma, R. S. *Tetrahedron Lett.* **2008**, *49*, 6974; (b) Kouznetsov, V. V.; Arenas, D. R. M.; Bohorqez, A. R. R. *Tetrahedron Lett.* **2008**, *49*, 3097.
5. Zhou, H.-F.; Fan, Q.-H.; Tang, W.-J.; Xu, L. J.; He, Y.-M.; Deng, G.-J.; Zhao, L.-W.; Gu, L.-Q.; Chan, A. S. C. *Adv. Synth. Catal.* **2006**, *348*, 2172.
6. (a) Chandrasekhar, S.; Narsihmulu, Ch.; Sultana, S. S.; Reddy, N. R. *Chem. Commun.* **2003**, 1716; (b) Chandrasekhar, S.; Narsihmulu, Ch.; Sultana, S. S.; Reddy, N. R. *Org. Lett.* **2002**, *4*, 4399; (c) Chandrasekhar, S.; Narsihmulu, Ch.; Saritha, B.; Sultana, S. S. *Tetrahedron Lett.* **2004**, *45*, 5865; (d) Chandrasekhar, S.; Narsihmulu, Ch.; Chandrasekhar, G. *Tetrahedron Lett.* **2004**, *45*, 2421; (e) Chandrasekhar, S.; Narsihmulu, Ch.; Reddy, N. R. *Tetrahedron Lett.* **2004**, *45*, 4581; (f) Chandrasekhar, S.; Reddy, G. P. K.; Nagesh, Ch.; Reddy, Ch. R. *Tetrahedron Lett.* **2007**, *48*, 1269.
7. (a) Deng, X.; Mani, N. S. *Org. Lett.* **2006**, *8*, 269; (b) Lee, D.; Chang, V. S. *Synthesis* **1978**, 462.
8. (a) Li, P.; Cheong, F. H.; Chao, L. C. F.; Lin, Y. H.; Williams, I. D. *J. Mol. Catal. A* **1999**, *145*, 111; (b) Sheu, C.; Richert, S. A.; Cofre, P.; Ross, B., Jr.; Sobkowiak, A.; Sawyer, D. T.; Kanofsky, J. R. *J. Am. Chem. Soc.* **1990**, *112*, 1936; (c) Giraud, A.; Provot, O.; Peyrat, J. F.; Alami, M.; Brion, J. D. *Tetrahedron* **2006**, *62*, 7667.
9. (a) Wan, Z.; Jones, C. D.; Mitchell, D.; Pu, J. Y.; Zhang, T. Y. *J. Org. Chem.* **2006**, *71*, 826; (b) Yusubov, M. S.; Zholobova, G. A.; Vasilevsky, S. F.; Tretyakov, E. V.; Knight, D. W. *Tetrahedron* **2002**, *58*, 1607; (c) Rogatchov, V. O.; Filimonov, V. D.; Yusubov, M. S. *Synthesis* **2001**, 1001.
10. Ren, W.; Xia, Y.; Jun Ji, S.; Zhang, Y.; Wan, X. *Org. Lett.* **2009**, *11*, 1841.
11. Chu, J.; Chen, Y.; wu, M. *Synthesis* **2009**, 2155.
12. Gebeyehu, G.; McNelis, E. *J. Org. Chem.* **1980**, *45*, 4280.
13. *General procedure for 1,2-diketones*: To a stirred solution of alkyne (1 mmol) in 10 mL PEG/H_2O (8:2) were added $PdCl_2$ (5 mol %) and $CuCl_2$ (5 mol %). The solution was stirred at room temperature for the completion of the reaction (see Table 1). The solution was diluted with ether (2 × 20 mL) and cooled in ice bath. The ether layer was separated, dried over anhydrous Na_2SO_4, and concentrated under vacuum. The residue was purified by column chromatography to give the corresponding 1,2-diketone in good yield.
Spectral data of representative new products (**2b**): ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.95 (d, J = 7.3 Hz, 2H), 7.70–7.62 (t, J = 7.3 Hz, 1H), 7.55–7.45 (m, 4H), 7.40–7.32 (d, J = 7.9, 8.1 Hz, 1H), 7.17–7.12 (m, 1H), 5.89 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 194.8, 194.6, 156.4, 135.1, 134.1, 132.7, 130.4, 129.9, 129.0, 122.8, 122.6, 115.5; IR (KBr): ν 3421, 3060, 2924, 1660, 1618, 1477, 1176, 861, 710 cm^{-1}; MS-ESI: m/z 249 (M+Na)$^+$.
Compound (**2d**): ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.97 (d, J = 8.3 Hz, 2H), 7.77–7.64 (m, 3H), 7.58–7.45 (m, 3H), 7.41–7.32 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 193.6, 193.0, 164.4, 135.0, 132.6, 130.8, 130.7, 129.9, 129.0, 125.9, 122.1, 121.8, 116.1, 115.8; IR (KBr): ν 3325, 3070, 2923, 1670, 1587, 1446, 1241, 837, 717 cm^{-1}; MS-ESI: m/z 251 (M+Na)$^+$.
Compound (**2f**): ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.98–7.93 (m, 2H), 7.91–7.86 (m, 2H), 7.66–7.59 (m, 1H), 7.53–7.46 (m, 4H), 1.35 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 194.7, 194.2, 159.0, 134.7, 133.1, 130.4, 129.8, 128.9, 126.0, 35.3, 30.9, 29.6; IR (KBr): ν 3464, 2963, 1670, 1598, 1217, 1177, 882, 661 cm^{-1}; MS-ESI: m/z 289 (M+Na)$^+$.
Compound (**2g**): ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.98–7.93 (m, 2H), 7.91–7.86 (m, 2H), 7.66–7.59 (m, 1H), 7.53–7.46 (m, 4H), 1.35 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 194.7, 194.2, 160.4, 138.1, 134.6, 133.1, 133.0, 131.3, 129.8, 128.8, 128.1, 127.6, 127.4, 124.3, 119.9, 105.8, 55.3; IR (KBr): ν 3431, 3060, 2925, 2841, 1662, 1617, 1478, 1263, 860, 710 cm^{-1}; MS-ESI: m/z 313 (M+Na)$^+$.
14. (a) Nair, V.; Dhanya, R.; Rajesh, C.; Bhadbhade, M. M.; Manoj, K. *Org. Lett.* **2004**, *6*, 4743; (b) Aqad, E.; Lakshmikantham, M. V.; Cava, M. P. *Org. Lett.* **2003**, *5*, 4089; (c) Heravi, M. M.; Baghaernejad, B.; Oskooie, H. A. *Tetrahedron Lett.* **2009**, *50*, 767; (d) Madhav, B.; Murthy, S. N.; Reddy, V. P.; Rao, K. R.; Nageswar, Y. V. D. *Tetrahedron Lett.* **2009**, *50*, 6025.
15. *General procedure for quinoxalines*: To a stirred solution of alkyne (1 mmol) in 10 mL PEG/H_2O (8:2) were added $PdCl_2$ (5 mol %) and $CuCl_2$ (5 mol %) and the solution was stirred at room temperature. After the completion of alkyne (monitored by TLC), 1,2-diaminobenzene (1 mmol) was added and stirring was continued at room temperature (see Table 4). The solution was diluted with ether (2 × 20 mL) and cooled in ice bath. The ether layer was separated, dried over anhydrous Na_2SO_4, and concentrated in vacuo. The residue was purified by column chromatography to give the corresponding 2,3-disubstituted quinoxaline in good yield.
Spectral data of representative new products (**3a**): ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.21–8.12 (m, 2H), 7.81–7.71 (m, 2H), 7.53–7.42 (m, 2H), 7.30–7.20 (m, 3H), 7.10–6.96 (m, 2H), 6.91–6.83 (d, J = 7.5 Hz, 1H), 6.76–6.69 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 156.1, 153.4, 153.1, 141.1, 140.7, 139.7, 138.5, 130.1, 129.6, 129.3, 129.0, 128.8, 128.6, 128.1, 121.8, 116.8, 116.3; IR (KBr): ν 3053, 2924, 2853, 1581, 1347, 1273, 762, 695 cm^{-1}; MS-ESI: m/z 321 (M+Na)$^+$.
Compound (**3d**): ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.24–8.15 (m, 2H), 8.07 (s, 1H), 7.81–7.73 (m, 2H), 7.70 (d, J = 8.8 Hz, 1H), 7.63 (d, J = 8.7 Hz, 2H), 7.59–7.53 (m, 2H), 7.51–7.45 (dd, J = 1.7, 8.5 Hz, 1H), 7.38–7.26 (m, 3H), 7.17–7.08 (m, 2H), 3.92 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 158.3, 153.5, 153.3, 141.3, 141.1, 139.2, 134.5, 134.2, 130.1, 129.9, 129.7, 129.6, 129.1, 129.1, 128.7, 128.5, 128.3, 127.6, 126.4, 119.1, 105.5, 55.3; IR (KBr): ν 3446, 3053, 2921, 2853, 1342, 756, 696 cm^{-1}; MS-ESI: m/z 385 (M+Na)$^+$.