Ruthenium-Catalyzed Synthesis of 1,2-Diketones from Alkynes

Yanan Miao, Antoine Dupé, Christian Bruneau, Cédric Fischmeister

DOI: 10.1002/ejoc.200((will be filled in by the editorial staff))

Ruthenium Catalyzed Synthesis of 1,2-diketones from Alkynes

Yanan Miao, Antoine Dupé, Christian Bruneau,* Cédric Fischmeister*

Keywords: Catalysis / Oxidation / Ruthenium / 1,2-diketones / alkynes

The ruthenium catalyzed synthesis of 1,2-diketones by oxidation of alkynes with sodium hypochlorite has been investigated. RuO_4 in situ generated from inexpensive $RuCl_3$,xH_2O and NaOCl demonstrated high performance at room temperature in diethyl carbonate as reaction medium. A variety of diketones were prepared in good yields using this environmentally friendly procedure.

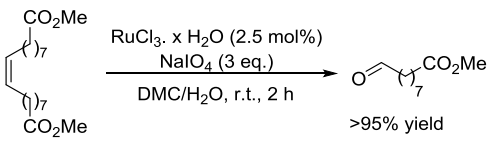
Yanan Miao, Dr. Antoine Dupé, Dr. Cédric Fischmeister, Dr. Christian Bruneau.
UMR CNRS 6226-Université de Rennes1
Institut des Sciences Chimiques de Rennes. Organometallics: Materials and Catalysis. Centre for Catalysis and Green Chemistry. Campus de Beaulieu. Avenue du général Leclerc. 35042 Rennes Cedex, France
Fax: (+) +33(0)223236939
E-mail: cedric.fischmeister@univ-rennes1.fr
christian.bruneau@univ-rennes1.fr
http://scienceschimiques.univ-rennes1.fr/catalyse/
Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/ejoc.xxxxxxxxx.

Introduction

1,2-Diketones are useful building blocks in organic synthesis in particular for the synthesis of heterocyclic compounds of biological interest.[1] 1,2-Dicarbonyl compounds are also precursors for the synthesis of *N*-Heterocyclic Carbenes (NHC), a prominent class of ligands in organometallic chemistry and catalysis.[2] During the past 15 years many examples of catalytic synthesis of 1,2-diketones have emerged in particular the oxidation of internal alkynes has received most attention as a result of the accessibility of a broad variety of substrates that can be obtained by Sonogashira cross-coupling reactions. These catalytic methods are undeniable progress making these protocols more environmentally friendly as compared to stoichiometric oxidation protocols employing for instance thallium, manganese, chromium or mercury salts.[3] A variety of transition metals have been reported for the oxidation of alkynes into 1,2-diketones. Rhenium[4] and Pd-catalyzed[5] processes employing hydrogen peroxide, dioxygen, sulfoxides or pyridine *N*-oxide as oxidant were reported. These catalysts displayed in general very good performances with diarylalkynes but they required high catalyst loading (5-10 mol-%) and/or high temperatures (60-140 °C).[6] An interesting Au/Ag catalytic system employing diphenylsulfoxide as oxidant was recently reported as an efficient system for the synthesis of benzil derivatives and α-keto imides.[7] However, best performances were obtained in refluxing dichloroethane, a solvent that is no longer usable in the pharmaceutical industry.[8] Iron catalysts have been reported since the early work by Sawyer in 1990[9,10] and recently, $FeCl_3$ (5 mol%)/H_2O_2 was found to be an efficient catalyst for room temperature oxidation of electron rich diarylalkynes.[11] Recently, an interesting copper catalyst operating under mild conditions with O_2/H_2O as the oxidant was disclosed. However, the use of selectfluor to generate the active catalyst might hamper the interest of this method.[12] Ruthenium catalysts in particular RuO_4 play a major role in oxidation catalysis.[13] In fact, regarding the oxidation of alkynes into diketones, a literature survey shows that RuO_4/$NaIO_4$ oxidation of alkyne into diketones is the most widespread procedure[14] despite the requirement for highly toxic solvent (CCl_4) and oxidant. For these reasons, decreasing the environmental impact of Ru-catalyzed oxidation reactions is a topic of high interest. In 2010, Wan reported a very efficient catalyst composed of [$RuCl_2$(*p*-cymene)] (0.001 mol-%)/I_2 (10 mol-%) and TBHP as oxidant.[15] However, this system required several hours in dioxane at 80 °C. Later on the same group reported a room temperature catalytic process consisting in a complex mixture of [$RuCl_2$(*p*-cymene)]$_2$, TEMPO, oxone, $NaHCO_3$ in nitromethane and water as reaction media.[16] As depicted in all these examples, oxidation of alkynes into 1,2-diketones still suffers in many cases from harsh conditions, high catalyst loadings and/or the use of oxidants and solvents of high environmental impact. Herein we present our studies aimed at decreasing the environmental impact of the ruthenium catalyzed oxidation of alkynes. In particular, we have focused our study on the use of carbonate solvents and sodium hypochlorite as oxidant.

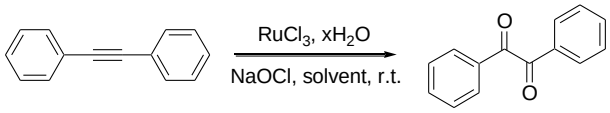
Results and Discussion

In our ongoing efforts on the sequential transformation reactions involving an initial metathesis transformation, we have been investigating tandem metathesis/oxidation reactions. Although the initial goals were not reached, we observed, as reported by Dragojlovic,[17] that dimethyl carbonate (DMC), a solvent recently introduced in olefin metathesis transformation as a greener alternative to toluene and dichloromethane,[18,19] was truly compatible with oxidant media.[20] This is particularly highlighted by the high yielding oxidative cleavage of alkene into aldehyde, a reaction usually carried out in CCl_4/H_2O media (Scheme 1).



Scheme 1 Alkene oxidative cleavage in DMC/H_2O

Following this result we turned our attention to the $RuCl_3,xH_2O$ catalyzed oxidation of diphenylacetylene (tolane) employing DMC as reaction media (Scheme 2). NaOCl was initially evaluated as the "greenest" oxidant that can be used without specific equipments[21] considering that H_2O_2 is not appropriate to generate RuO_4 from $RuCl_3,xH_2O$.



1 **2**

Scheme 2 $RuCl_3,xH_2O$ /NaOCl oxidation of tolane **1**

Table 1. Oxidation of tolane[a]

Entry	Solvent	NaOCl (equiv.)	*t* (h)	Conv. (%)[b]	Y (%)[c]
1	DMC	4	4	> 98%[f]	69
2	DMC	3	4	76	34
3[d]	DMC	3	4	65	51
4[e]	H_2O	4	4	0	0
5	DEC	4	4	>98[f]	86
6	DEC	2	4	46	n.d.[g]
7	DEC	3	4	>98[f]	86
8	DEC	3	2	>98	82
9[h]	DEC	3	8	46	n.d.[g,i]
10[j]	DEC	3	5.5	>98[f]	86
11[k]	DEC	3	2	62	39
12[l]	DEC	3	2	83	59
13[m]	DEC	3	2	0	0

[a] **1** (0.5 mmol), $RuCl_3.3H_2O$ (0.5 mol-%), [**1**] = 0.1 mol/L, r.t., argon atmosphere. [b] Monitored by GC using hexadecane as internal standard. [c] Isolated yields. [d] Buffer solution (Na_2HPO_4/NaOH, pH= 12). [e] No reaction. [f] **1** was not detected by gas chromatography. [g] n.d = not determined. [h] *T*= 5 °C. [i] Benzoic acid was detected. [j] 0.1 mmol-% $RuCl_3.3H_2O$. [k] [**1**]= 0.5 mol/L. [l] [**1**]= 0.02 mol/L. [m] no catalyst

Initial attempts were carried out in DMC at low $RuCl_3,xH_2O$ loading (0.5 mol%) employing 4 equiv. of sodium hypochlorite. Under these conditions the reaction proceeded with full conversion but diketone **2** was isolated in only 69 % (Table 1, entry 1). Careful analysis of the reaction mixture showed the presence of benzoic acid, a side product that was previously encountered in several studies on the oxidation of alkynes including the early report on RuO_2/NaOCl/CCl_4/H_2O oxidation of alkyne.[22] Reduction of the excess of oxidant was not efficient to suppress the formation of benzoic acid. In addition to benzoic acid, the dichloro derivative PhClC=CClPh was also detected by GC/MS. The formation of chlorinated product is often encountered upon using NaOCl but this issue is efficiently solved by using buffered solution with a pH>10.[23] Indeed when the reaction media was buffered at pH= 12 the chlorinated product formation was suppressed and the yield of **2** increased (Table 1, entry 2, 3). If water as reaction media was not suitable either (Table 1, entry 4), replacement of dimethyl carbonate by diethyl carbonate resulted in the reduction of the amount of benzoic acid side product ensuing the isolation of **2** in 86% and 82% after 4 and 2 h at room temperature, respectively (Table 1, entry 7, 8). Interestingly, no chlorinated product was formed when DEC was used as solvent. Further optimization attempts were implemented in order to improve the selectivity of the reaction. Hence low temperature experiments were performed (Table 1, entry 9). As one could expect the reaction rate slowed down but benzoic acid was yet detected. Decreasing the catalyst loading or altering the concentration conditions did not suppress formation of benzoic acid either (Table 1, entries 10-12). Despite the accessibility and low cost of $RuCl_3,xH_2O$, several ruthenium catalyst precursors including olefin metathesis catalysts were evaluated with the aim of improving catalytic performances. As depicted in Table 2, none of the tested precursors led to improved performances. Of note, the complex $[RuCl_2(p\text{-cymene})]_2$ that led to the best results with the Wan conditions[16] did not reach the performances of $RuCl_3,xH_2O$.

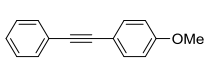
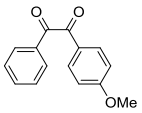
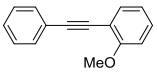
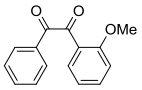
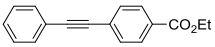
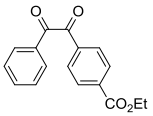
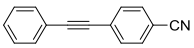
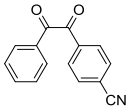
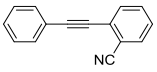
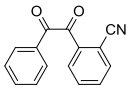
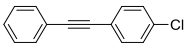
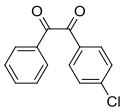
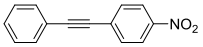
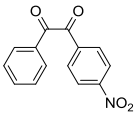
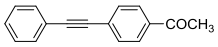
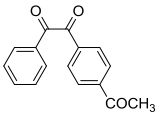
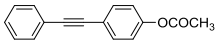
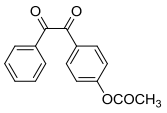
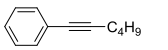
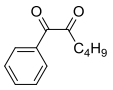
Table 2. Catalyst precursors screening[a]

Entry	Catalyst	Conv. (%)[b]	Yield[c]
1	$RuCl_3$, xH_20	>98[d]	82
2	$[Ru(COD)Cl_2]n$	90	79
3	$Ru(dppe)_2Cl_2$	73[e]	n.d.[f]
4	$[RuCl_2(p\text{-cymene})]_2$[g]	>98[d]	74
5	$RuCl_2(p\text{-cymene})PPh_3$	77	68
6	$RuCl_2(PCy_3)_2(=CHPh)$	90	79
7	$RuCl_2(SIMes)(PCy_3)(=CHPh)$	68	n.d. [f]
8	$IrCl_3.3H_2O$	0	0

[a] 1 (0.5 mmol), catalyst (0.5 mol-%), NaOCl (3 equiv.), DEC (5 mL), r.t., 2 h. [b] Determined by gas chromatography using hexadecane as internal standard. [c] Isolated yield. [d] 1 was not detected by gas chromatography. [e] after 6 h. [f] not determined. [g] 0.25 mol%

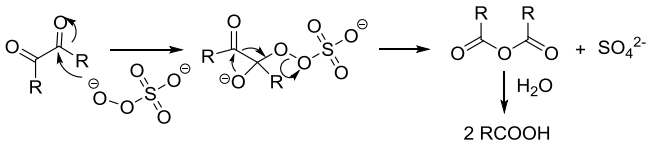
The scope of the reaction was explored with a variety of internal alkynes easily prepared by palladium catalyzed Sonogashira coupling. In particular, the influence of steric and electronic parameters was evaluated. Good yields were obtained with diphenylacetylene derivatives substituted with an electron donating group including a sterically hindered substrate. The situation was somewhat different when electron withdrawing group were installed on the substrates. In these cases (Table 3, entries 3-9) and despite the almost full conversion obtained, the 1,2-diketones were isolated in moderate to good yields. As it will be discussed later this feature could be rationalized with mechanistic considerations. However, it must be mentioned that this lower reactivity of electron withdrawing substituted alkynes is a general problem observed in the oxidation of alkynes.[5,11, 14d, 16] Likewise, aliphatic alkyne usually display lower reactivity leading to modest yield.

Table 3. Scope of the reaction[a]

Entry	Alkyne	Product	Conv. (%)[b]/Y (%)[c]
1	 **3**	 **13**	>98/83
2	 **4**	 **14**	>98/71
3	 **5**	 **15**	96/63
4	 **6**	 **16**	96/61
5	 **7**	 **17**	80/42 77/44[d]
6	 **8**	 **18**	98/79
7	 **9**	 **19**	>98/53
8	 **10**	 **20**	90/83
9	 **11**	 **21**	70/64
10	 **12**	 **22**	66/33 (90/28)[d]

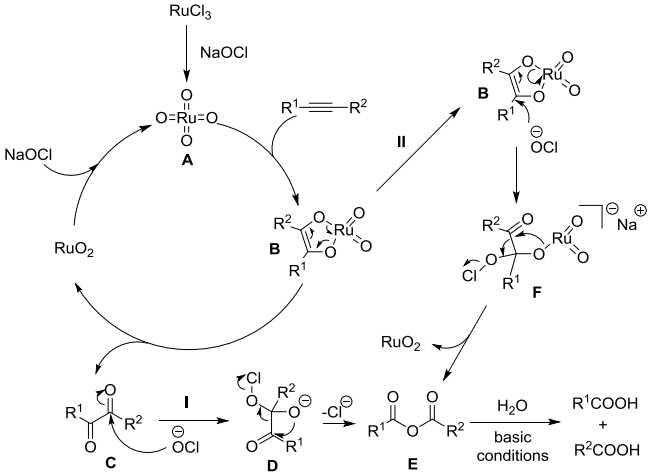
[a] Alkyne (0.5 mmol), $RuCl_3.3H_2O$ (0.5 mol-%), NaOCl (3 equiv.), DEC (5 mL), r.t., 4 h. [b] Monitored by GC. [c] Isolated yield. [d] 8 h

Based on the oxidation of alkenes mechanism, it was generally accepted that the RuO_4 oxidation of alkynes to 1,2-diketones involved a [3+2] cycloaddition.[13b] This hypothesis was confirmed in 2000 by Che et al. who presented the first evidence for [3+2] cycloaddition in the alkyne oxidation by a *cis*-dioxoruthenium(VI) complex.[24] In 2004, Yang et al. proposed a mechanism for the oxidation of alkynes into acids in which the generated 1,2-diketone undergoes a Baeyer-Villiger type oxidation by peroxymonosulfate leading to an acid anhydride which upon hydrolysis leads to a carboxylic acid (Scheme 3).[25]



Scheme 3 Suggested mechanism for formation of carboxylic acids from diketones

Based on these investigations, a tentative mechanism for the $RuCl_3.xH_2O$/NaOCl oxidation of alkynes is proposed in Scheme 4. A [3+2] cycloaddition between the in situ generated RuO_4 and the alkyne generates the metallacycle **B**, which undergoes a rapid electrocyclic fragmentation to the desired 1,2-diketone **C** and RuO_2. Similarly to Yang mechanism (Scheme 3), the cleavage of the diketone by NaOCl would proceed by a nucleophilic addition of the hypochlorite ion to the carbonyl functional group affording the intermediate **D**. A Baeyer-Villiger type rearrangement would further lead to the acid anhydride **E** and subsequently to the corresponding carboxylic acid. However, a test showed that benzil **2** was indeed converted into benzoic acid upon reaction with NaOCl under basic conditions with or without RuO_4[26,27] but these reactions were very slow and could not account for the total formation of benzoic acid. Hence other pathway(s) should be considered such as pathway **II**. Here, the ruthenacycle **B** undergoes a Baeyer-Villiger type rearrangement following addition of NaOCl (**F**) to furnish the anhydride **E**. Both mechanisms **I** and **II** are in agreement with experimental results as the nucleophilic addition of NaOCl on a carbonyl or alkenyl group should be facilitated by electron withdrawing substituent on the aromatic ring (R^1 in Scheme 4) hence leading to larger amounts of benzoic acid derivatives.



Scheme 4 Proposed mechanism for 1,2-diketone formation

Conclusion

We have demonstrated that the ruthenium-catalyzed oxidation of alkynes into 1,2-diketones could be performed under environmentally acceptable experimental conditions. In particular, the use of NaOCl as unique oxidant with low loading of

inexpensive $RuCl_3$,xH_2O enabled the room temperature synthesis of a variety of 1,2-diketones in diethyl carbonate solvent. As encountered in most of the transition-metal catalyzed oxidation of alkynes, the reaction performed particularly well when electron-rich diaryl alkynes were employed but performances dropped when electron-poor or aliphatic alkynes were employed. Despite this limitation, we believe that this protocol exhibits a favourable balance between cost and environmental impact on the one hand and yields on the other hand. Given the regulation strengthening regarding the use of toxic reagents and waste treatments, this protocol appears as an interesting alternative to the widespread oxidation process employing $NaIO_4$ in carbon tetrachloride.

References

[1] a) X. Deng, N. S. Mani, *Org. Lett*, **2005**, *8*, 269; b) S. E. Wolkenberg, D. D. Wisnoski, W. H. Leister, Y. Wang, Z. Zhao, C. W. Lindsley, *Org. Lett*. **2004**, *6*, 1453; c) J. M. McKenna, F. Halley, J. E. Souness, I. M. McLay, S. D. Pickett, A.J. Collis, K. Page, I. Ahmed, *J. Med. Chem.* **2002**, *45*, 2173; d) A.J. Herrera, M. Rondón, E. Suárez, *J. Org. Chem.* **2008**, *73*, 3384; e) R. M. Wadkins, J. L. Hyatt, X. Wei, K. J. P. Yoon, M. Wierdl, C. C. Edwards, C. L. Morton, J. C. Obenauer, K. Damodaran, P. Beroza, M. K. Danks, P. M. Potter, *J. Med. Chem.* **2005**, *48*, 2906; f) B. T. Ngadjui, S. F. Kouam, E. Dongo, G. W. F. Kapche, B. M. Abegaz, *Phytochem.* **2000**, *55*, 915; g) T. E. Barta, M.A. Stealey, P. W. Collins, R. M. Weier, *Bioorg. Med. Chem. Lett*. **1998**, *8*, 3443.

[2] b) L. Benhamou, E. Chardon, G. Lavigne, S. Bellemin-Laponnaz, V. César, *Chem. Rev*. **2011**, *111*, 2705 ;

[3] a) A. Mc Killop, O. H. Oldenziel, B. P. Swann, E. C. Taylor, R. L. Robey, *J. Am. Chem. Soc*. **1973**, *95*, 1296; b) N. S. Snirivasan, D. G. Lee, *J. Org. Chem.* **1979**, *44*, 1574; c) D. G. Lee, V. S. Chang, *Synthesis* **1978**, 462; d) H. Firouzabadi, A. R. Sardarian, H. moosavipour, G. M. Afshari, *Synthesis* **1986**, 285; e) M. E. Jung, G. Deng, *Org. Lett*. **2014**, *16*, 142.

[4] Z. L. Zhu, J. H. Espenson, *J. Org. Chem*. **1995**, *60*, 7728

[5] a) C. Mousset, O. Provot, A. Hamze, J. Bignon, J.-D. Brion, M. Alami, *Tetrahedron* **2008**, 4827; b) W. Ren, Y. Xia, S.-J. Ji, Y. Zhang, X. Wan, J. Zhao, *Org. Lett*. **2009**, *11*, 1841; c) S. Mori, M. Takubo, T. Yanase, T. Maegawa, Y. Monguchi, H. Sajiki, *Adv. Synth. Catal*. **2010**, *352*, 1630; d) S. Chandrasekhar, N. K. Reddy, V. P. Kumar, *Tetrahedron Lett*. **2010**, *51*, 3623; e) A. Gao, F. Yang, J. Li, Y. Wu, *Tetrahedron* **2012**, *68*, 4950; f) J. Liu, N. Zhang, Y. Yue, D. Wang, Y. Zhang, X. Zhang, K. Zhuo, *RSC Adv*. **2013**, *3*, 3865; g) Y. Sawama, M. Takubo, S. Mori, Y. Monguchi, H. Sajiki, *Eur. J. Org. Chem.* **2011**, 3361. For reviews, see: h) J. Muzart, J. *Mol. Catal. A: Chem*. **2011**, *338*, 7; i) R. Chinchilla, C. Najera, *Chem. Rev*. **2014**, *114*, 1783.

[6] S. Chandrasekhar, N. K. Reddy, V. P. Kumar, *Tetrahedron Lett*. **2010**, *51*, 3623

[7] C.-F. Xu, M. Xu, Y.-X. Jia, C.-Y. Li, *Org. Lett*. **2011**, *13*, 1556.

[8] a) R. K. Henderson, C. Jimenez-Gonzalez, D. J. C. Constable, S. R. Alston, G. G. A. Inglis, G. Fisher, J. Sherwood, S. P. Binks, A. Curzons, *Green Chem*. **2011**, *13*, 85; b) K. Alfonsi, J. Colberg, P. J. Dunn,T. Fevig, S. Jennings, T. A. Johnson, H. P. Kleine, C. Knight, M. A. Nagy, D. A. Perry, M. Stefaniak, *Green Chem*. **2008**, *10*, 31; c) B. W. Cue, J. Zhang, *Green Chem. Lett. Rev*. **2009**, 1

[9] a) C. Sheu, A. Sobkowiak, S. Jeon, D. T. Sawyer, *J. Am. Chem. Soc*., **1990**, *112*, 879; b) C. Sheu, S. A. Richert, P. Cofré, B. Ross, A. Sobkowiak, D. T. Sawyer, J. R. Ranofsky, *J. Am. Chem. Soc*. **1990**, *112*, 1936.

[10] (a) J. Y. Ryu, S. Heo, P. Park, W. Nam, J. Kim, *Inorg. Chem. Comm.* 2004, 7, 534; (b) A. Giraud, O. Provot, J.-F. Peyrat, M. Alami, J.-D. Brion, *Tetrahedron* **2006**, *62*, 7667

[11] S. Enthaler, *ChemCatChem*, **2011**, *3*, 1929.

[12] W. Zhang, J. Zhang, Y. Liu, Z. Xu, *Synlett* **2013**, *24*, 2709

[13] a) G.A. Barf, R.A. Sheldon, *J. Mol. Catal. A: Chem*. **1995**, *102*, 23; b) B. Plietker, *Synthesis* **2005**, *15*, 2453; c) S.-I. Murahashi, N. Komiya, (**2004**) Oxidation Reactions, in Ruthenium in Organic Synthesis (ed S.-I. Murahashi), Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim, pp. 53-93.

[14] a) S. Bensulong, J. Boonsombat, S. Ruchirawat, *Tetrahedron*, **2013**, *69*, 9335; b) K. Tsuchikama, J. Zhu, C. A. Lowery, G. F. Kaufmann, K. D. Janda, *J. Am. Chem. Soc.* **2012**, *134*, 13562; c) P. Magnus, M. A. H. Stent, *Org. Lett*. **2005**, *7*, 3853; d) J. Tummatorn, P. Khorphueng, A. Petsom, N. Muangsin, N. Chaichit, S. Roengsumran, *Tetrahedron* **2007**, *63*, 11878; e) N. Kulisic, S. Morea, A. Mateo-Alonso, *Chem. Commun*. **2011**, *47*, 514; f) J. Ishihara, T. Ishizaka, T. Suzuki, S. Hatakeyama, *Tetrahedron Lett*. **2004**, *45*, 7855; g) C. A. Lowery, J. Park, G. F. Kaufmann, K. D. Janda, *J. Am. Chem. Soc*. **2008**, *130*, 9200.

[15] W. Ren, J. Liu, L. Chen, X. Wan, *Adv. Synth. Catal*. **2010**, *352*, 1424.

[16] Y. Xu, X. Wan, *Tetrahedron Lett.* **2013**, *54*, 642.

[17] J. Cornely,L. M. Su Ham, D. E. Meade, V. Dragojlovic, *Green Chem.* **2003**, *5*, 34.

[18] a) X. Miao, C. Fischmeister, C. Bruneau, P. H. Dixneuf, *ChemSusChem*, **2008**, *1*, 813; (b) A. Keraani, T. Renouard, C. Fischmeister, C. Bruneau, M. Rabiller-Baudry, *ChemSusChem* **2008**, *1*, 927; (c) V. Le Ravalec, C. Fischmeister, C. Bruneau, *Adv. Synth. Catal*. **2009**, *351*, 1115; (d) V. Le Ravalec, A. Dupé, C. Fischmeister, C. Bruneau, *ChemSusChem* **2010**, *3*, 1291; (e) H. Bilel, N. Hamdi, F. Zagrouba, C. Fischmeister, C. Bruneau, *Green Chem*. **2011**, *13*, 1448; (f) A. Dupé, M. Achard, C. Fischmeister, C. Bruneau, *ChemSusChem* **2012**, 5, 2249; (g) H. Bilel, N. Hamdi, F. Zagrouba, C. Fischmeister, C. Bruneau, *RSC Adv.*, **2012**, *2*, 9584; (h) A. Dupé, V. Le Ravalec, C. Fischmeister, C. Bruneau, *Eur. J. Lipid. Sci. Technol*. **2013**, *115*, 490.

[19] (a) I. W. Ashworth, D. J. Nelson, J. M. Percy, *Dalton Trans*, **2013**, *42*, 4110; (b) K. Skowerski, J.Białecki, A.Tracza, K. Olszewski, *Green Chem*., **2014**, *16*, 1125.

[20] For a review on carbonates as solvents in catalysis, see: B. Schäffner, D. Schäffner, Sergey P. Verevkin, A. Börner, *Chem. Rev*. **2010**, *110*, 4554.

[21] Considering O_2 or O_3 as oxidants

[22] H. Gopal, A. J. Gordon, *Tetrahedron Lett*. **1971**, 2941.

[23] (a) W. Zhang, E. N. Jacobsen, *J. Org. Chem*. **1991**, *56*, 2296; (b) L. Goncalvi, I. W. C. E. Arends, P. Moilanen, R. A. Sheldon, *Adv. Synth. Catal*. **2003**, *345*, 1321.

[24] C. M. Che, W. Y. Yu, P. M. Chan, W. C. Cheng, S. M. Peng, K. C. Lau, W. K. Li, *J. Am. Chem. Soc*. **2000**, *122*, 11380

[25] D. Yang, F. Chen, Z. M. Dong, D. W. Zhang, *J. Org. Chem.* **2004**, *69*, 2221

[26] See Experimental Section for details

[27] Commercially available anhydride **E** was submitted to hydrolysis under neutral and basic conditions (NaOCl). The hydrolysis under neutral conditions was very slow as compared to the hydrolysis in a basic medium.

[28] a) H. Huang, H. L. Jiang , K. X. Chen, H. Liu, *J. Org. Chem.* **2008**, *73*, 9061; b) C. He, J. He, X. Xu, A. Lei, *Angew. Chem. Int. Ed.* **2013**, *52*, 1527; c) F. Xue, J. Zhao, T . S. A. Hor, Chem. Commun. **2013**, *49*, 10121.X. T. Pu, H. B. Li, T. J. Colacot, *J. Org. Chem*. **2013**, *78*, 568. d) J. R. Harjani, T. J. Abraham, A. T. Gomez, M. T. Garcia, R. D. Singer, P. J. Scammells, *Green Chem*, **2010**, *12*,650.

[29] J-H. Chu, Y-J. Chen, M-J. Wu, *Synthesis*, **2009**, *13*, 2155.

Experimental Section

General Methods

All reactions were conducted under an inert atmosphere of argon using standard Schlenk tube techniques, unless otherwise mentioned. DMC and DEC were distilled and stored over 4A molecular sieves before use. NEt_3 was used as received and degased. Organic reagents were obtained from commercial sources

and used as received. $RuCl_3$, xH_2O was purchased from Umicore Precious Metals. NMR spectra were recorded on Bruker 400 MHz spectrometers unless otherwise noted. Spectra are reported in ppm relative to residual chloroform (7.26 ppm for 1H NMRs and 77.0 ppm for ^{13}C NMRs). Coupling constants are reported in Hertz. GC-2014 Shimadzu Gas Chromatograph (Equity-5, 30m×0.25mm) were used to monitor the reaction. LRMS were recorded on GC-MS Shimadzu QP2010S apparatus. Products were purified by column chromatography on silica gel using mixtures of petroleum ether and ethyl acetate as eluent.

General procedure A: preparation of internal alkynes via Sonogashira coupling

A mixture of phenylacetylene (561.3 mg, 5.5 mmol, 1.1 equiv), halobenzene derivatives (5 mmol, 1.0 equiv), $PdCl_2(PPh_3)_2$ (35.1 mg, 1 mol%), PPh_3 (26.23 mg , 2 mol-%) in 20 mL of NEt_3 was stirred for 5 min under an atmosphere of argon at room temperature. CuI (9.5 mg, 1 mol-%) was added and the reaction was sealed and stirred overnight at 60°C. The reaction mixture was filtered and the filtrate was washed with Et_2O. The combined organic layers were washed with saturated NH_4Cl solution, HCl (1 N), NaOH (1 N), brine and dried over $MgSO_4$. After filtration the solvent was removed in vacuo. The residue was purified by silica gel chromatography to afford the pure alkynes.

General procedure B: oxidation of alkynes

A dry Schlenk tube was loaded with the solvent (DEC, 5 mL), hexadecane (gas chromatography standard; 20 µl) and the substrate (0.5 mmol). Catalyst $RuCl_3.3H_2O$ (0.5 mol%) in solution and oxidant 13 wt% NaOCl solution (3 equiv) were added subsequently. The mixture was stirred at 25 °C (regulated oil bath temperature) and monitored by gas chromatography. The reaction was quenched with a saturated aqueous solution of Na_2SO_3 and the organic layer was extracted with ethyl acetate (4×10 mL) and dried over Na_2SO_4. The combined organic layers were evaporated and the residue was purified by column chromatography on silica gel using a mixture of ethyl acetate and petroleum ether.

Procedure for the oxidation of benzil 2

In a first experiment, a dry Schlenk tube was loaded with the solvent (DEC, 5 mL), hexadecane (gas chromatography standard; 20 µl) and 2 (0.5 mmol). A 13 wt.-% NaOCl solution (3 equiv) was added subsequently. The mixture was stirred at 25 °C (regulated oil bath temperature) for 4 h. The reaction was quenched with a saturated aqueous solution of Na_2SO_3 and the organic layer was extracted with ethyl acetate (4×10ml) and dried over Na_2SO_4. Conversions were below 6 %. The aqueous phase was acidified to pH 4 by addition of 1N HCl and extracted with EtOAc. No benzoic acid could be detected in this organic phase.

A second experiment was carried out by first mixing for 2 h at r. t. $RuCl_3.3H_2O$ (0.5 mol-%) and 3 equiv. of NaOCl in 5 mL of DEC. 2 (1 equiv.) was then added and the reaction stirred for 2 h at r.t. Again, conversions were below 5% and only traces of benzoic acid could be detected.

Product analyses

1-methoxy-4-(phenylethynyl)benzene 3

3 was prepared according to the general procedure A. Yellow solid; Yield: 88 %. NMR data are consistent with reported data.[28] ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.51 (dd, J = 8.0, 2.0 Hz, 2H), 7.47 (d, J = 8.4 Hz, 2H), 7.35-7.30 (m. 3H), 6.88 (d, J = 8.8 Hz, 2H), 3.83 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) 159.6, 133.0, 131.4, 128.3, 127.9, 123.6, 115.4, 114.0, 89.4, 88.1, 55.3; LR-MS: $[M]^{+\cdot}$ ($C_{15}H_{12}O$) m/z th. = 208, m/z found = 208.

1-methoxy-2-(phenylethynyl)benzene 4

4 was prepared according to the general procedure A. Yellow oil; Yield: 70 %. NMR data are consistent with reported data.[28] ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.58 (d, J = 6.8 Hz, , 2H), 7.50 (dd, J = 7.6, 1.2 Hz, 1H), 7.40-7.25 (m, 4H), 6.96-6.90 (m, 2H), 3.92 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) 159.9, 133.5, 131.6, 129.7, 128.2, 128.0, 123.5, 120.4, 112.4, 110.7, 93.4, 85.7, 55.8; LR-MS: $[M]^{+\cdot}$ ($C_{15}H_{12}O$) m/z th. = 208, m/z found = 208.

Ethyl 4-(phenylethynyl)benzoate 5

5 was prepared according to the general procedure A. Yellow solid; Yield: 90 %. NMR data are consistent with reported data.[28] NMR (400 MHz,) δ (ppm) 8.03 (d, J = 8.3 Hz, 2H), 7.59 (d, J = 8.3 Hz, 2H), 7.56-7.54 (m, 2H), 7.41-7.31 (m, 3H), 4.39 (q, J = 7.1 Hz, 2H), 1.41 (t, J = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) 166.1, 131.7, 131.5, 129.9, 129.4, 128.7, 128.4, 127.8, 122.7, 92.2, 88.7, 61.1, 14.3; LR-MS: $[M]^{+\cdot}$ ($C_{17}H_{14}O_2$) m/z th. = 250, m/z found = 250.

4-(phenylethynyl)benzonitrile 6

6 was prepared according to the general procedure A. White solid; Yield: 83%. NMR data are consistent with reported data.[28] ^1H NMR (400 MHz, CDCl3) δ (ppm) 7.64 (d, J = 8.5 Hz, 2H), 7.61 (d, J = 8.5 Hz, 2H), 7.58 – 7.51 (m, 2H), 7.39-7.36 (m, 3H); ^{13}C NMR (ppm) (101 MHz, CDCl3) δ 132.1, 132.0, 131.8, 129.1, 128.5, 128.2, 122.2, 118.5, 111.5, 93.8, 87.7 LR-MS: $[M]^{+\cdot}$ ($C_{15}H_9N$) m/z th. = 203, m/z found = 203.

2-(phenylethynyl)benzonitrile 7

7 was prepared according to the general procedure A. Yellow oil; Yield: 82 %. NMR data are consistent with reported data.[28] ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.69-7.54 (m, 5H), 7.47-7.32 (m, 4H); ^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) 132.6, 132.3,132.1, 132.0, 129.2, 128.4, 128.2, 127.2, 122.0, 117.5, 115.3, 96.0, 85.6; LR-MS: $[M]^{+\cdot}$ ($C_{15}H_9N$) m/z th. = 203, m/z found = 203.

1-chloro-4-(phenylethenyl)benzene 8

8 was prepared according to the general procedure A. white solid; Yield 81%. NMR dada are consistent with reported data.[28] ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.55-7.50 (m, 2H), 7.46 (d, J = 8.5 Hz, 2H), 7.37-7.31 (m, 5H); ^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) 134.2, 132.8, 131.6, 128.7, 128.5, 128.4, 122.9, 121.8, 90.3, 88.2. LR-MS: $[M]^+$ ($C_{14}H_9{}^{35}Cl$) m/z th. = 212, m/z found = 212; ($C_{14}H_9{}^{37}Cl$) m/z th. = 214, m/z found = 214, ($C_{14}H_9{}^{35}Cl$)/($C_{14}H_9{}^{37}Cl$)= 2.8

1-nitro-4-(phenylethynyl)benzene 9

9 was prepared according to the general procedure A. Yellow solid; Yield: 85 %. NMR data are consistent with reported data.[28] ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.21 (d, J = 8.8 Hz, 2H), 7.66 (d, J = 8.8 Hz, 2H), 7.58-7.55 (m, 2H), 7.45-7.35 (m, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) 147.0, 132.2, 131.8, 130.3, 129.3, 128.5, 123.6, 122.1, 94.7, 87.5; LR-MS: $[M]^{+\cdot}$ ($C_{14}H_9NO_2$) m/z th. = 223, m/z found = 223.

1-[4-(2-phenylethynyl)phenyl]ethanone 10

10 was prepared according to the general procedure A. White solid; Yield: 95%. NMR data are consistent with reported data.[7] ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.94 (d, J = 8.3 Hz, 2H), 7.61 (d, J = 8.3 Hz, 2H), 7.58-7.53 (m, 2H), 7.40-7.35 (m, 3H), 2.62 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) 197.2, 136.2, 131.7, 131.6, 128.8, 128.4, 128.3, 128.2, 122.7, 92.7, 88.6, 26.6; LR-MS: $[M]^+$ ($C_{16}H_{12}O$) m/z th. = 220, m/z found 220.

[4-(2-phenylethynyl)phenyl] acetate 11

11 was prepared according to the general procedure. White solid; Yield: 89%. NMR data are consistent with reported data.[28] ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.56-7.52(m, 4H), 7.37-7.32(m, 3H), 7.10 (d, J = 8.4 Hz, 2H), 2.31 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) (ppm) 169.1, 150.5, 132.7, 131.6, 128.3, 128.3, 123.1, 121.7, 121.0, 89.4, 88.5, 21.1; LR-MS: $[M]^+$ ($C_{16}H_{12}O_2$) m/z th. = 236, m/z found 236.

Hex-1-yn-1-ylbenzene 12

12 was prepared according to the general procedure A. Light yellow oil; Yield: 81 %. NMR data are consistent with reported data.[28] ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.43 (d, J = 6.1 Hz, 2H), 7.32-7.22 (m, 3H), 2.44 (t, J = 6.9 Hz, 2H), 1.68-1.60 (m, 2H), 1.58-1.45 (m, 2H), 0.99 (t, J = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) 131.5, 128.1, 127.4, 124.1, 90.4, 80.5, 30.8, 22.0, 19.1, 13.6; LR-MS: $[M]^{+\cdot}$ ($C_{12}H_{14}$) m/z th. = 158, m/z found = 158.

1,2-diphenylethane-1,2-dione 2

2 was prepared according to the general procedure B. Yellow solid; Yield: 82 %. NMR data are consistent with reported data.[5a, 10b, 15] ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.98 (d, J = 7.3 Hz, 4H), 7.67 (t, J = 7.4 Hz, 2H), 7.52 (m, 4H); ^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) 194.7, 135.0, 133.2, 130.0, 129.2; LR-MS: $[M]^{+\cdot}$ ($C_{14}H_{10}O_2$) m/z th. = 210, m/z found = 210.

1-(4-methoxyphenyl)-2-phenylethane-1,2-dione 13

13 was prepared according to the general procedure B. Yellow oil; Yield: 83%. NMR data are consistent with reported data.[15] ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.96 (m, 4H), 7.63 (m, 1H), 7.50 (m, 2H), 6.98 (d, J = 8.1 Hz, 2H), 3.88 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) 194.8, 193.2, 165.0, 134.7, 133.3, 132.4, 129.9, 129.9, 126.2, 114.4, 55.7; LR-MS: $[M]^{+\cdot}$ ($C_{15}H_{12}O_3$) m/z th.=240, m/z found = 240.

1-(2-methoxyphenyl)-2-phenylethane-1,2-dione 14

14 was prepared according to the general procedure B. Yellow solid; Yield: 71%. NMR data are consistent with reported data.[5a] ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.02 (dd, J = 7.6, 2.1 Hz, 1H), 7.91 (d, J = 7.6 Hz, 2H), 7.60-7.58 (m, 2H), 7.52-7.45 (m, 2H), 7.15-7.10 (m, 1H), 6.93 (d, J = 8.4 Hz, 1H), 3.56 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) 194.8, 193.5, 160.4, 136.5, 133.7, 132.9, 130.4, 129.2, 128.6, 123.8, 121.5, 112.3, 55.6; LR-MS: $[M]^{+\cdot}$ ($C_{15}H_{12}O_3$) m/z th. = 240, m/z found = 240.

Ethyl 4-(2-oxo-2-phenylacetyl)benzoate 15

15 was prepared according to the general procedure B. Yellow solid; Yield: 63%. NMR data are consistent with reported data.[5a] ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.10 (d, J = 8.4 Hz, 2H), 8.03 (d, J = 8.4 Hz, 2H), 7.97 (dd, J = 7.3, 1.6 Hz, 2H), 7.68 (m, 1H), 7.53 (m, 2H), 4.11 (q, J = 7.1 Hz, 2H), 1.41 (t, J = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) 193.8, 193.7, 165.4, 136.0, 135.7, 135.1, 132.7, 130.0, 129.9, 129.7, 129.1, 61.6, 14.2; LR-MS: $[M]^{+\cdot}$ ($C_{17}H_{14}O_4$) m/z th. = 282, m/z found = 282.

4-(2-oxo-2-phenylacetyl)benzonitrile 16

16 was prepared according to the general procedure B. Yellow solid; Yield: 61%. NMR data are consistent with reported data.[16] ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.08 (d, J = 8.5 Hz, 2H), 7.987 (dd, J = 7.3, 1.6 Hz, 2H), 7.81 (d, J = 8.5 Hz, 2H), 7.70 (m, 1H), 7.54 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) 193.0, 192.4, 135.9, 135.4, 132.7, 132.4, 130.2, 130.0, 129.2, 117.9, 117.5; LR-MS: $[M]^{+\cdot}$ ($C_{15}H_9NO_2$) m/z th. = 235, m/z found = 235.

2-(2-oxo-2-phenylacetyl)benzonitrile 17

17 was prepared according to the general procedure B. Yellow solid; Yield 42%. NMR dada are consistent with reported data. [5a] ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.03 (d, J = 8.0 Hz, 2H), 7.94 -7.88 (m, 2H), 7.80-7.60 (m, 3H), 7.55 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) 192.1, 191.2, 135.6, 135.3, 135.1, 134.0, 132.7, 132.5, 132.3, 130.2, 129.2, 117.0, 112.0. LR-MS: $[M]^+$ ($C_{15}H_9NO_2$) m/z th. = 235, m/z found = 235.

1-(4-chlorophenyl)-2-phenylethane-1,2-dione 18

18 was prepared according to the general procedure B. Yellow solid; Yield 79%. NMR dada are consistent with reported data.[16] ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.98-7.92 (m, 4H), 7.67 (m, 1H), 7.65-7.44 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) 193.9, 193.1, 141.6, 135.0, 132.8, 131.3, 131.2, 129.9, 129.4, 129.1; LR-MS: $[M]^+$ ($C_{14}H_9{}^{35}ClO_2$) m/z th. = 244, m/z found = 244; ($C_{14}H_9{}^{37}ClO_2$) m/z th. = 246, m/z found = 246; ($C_{14}H_9{}^{35}ClO_2$)/($C_{14}H_9{}^{37}ClO_2$) = 3.0

1-(4-nitrophenyl)-2-phenylethane-1,2-dione 19

19 was prepared according to the general procedure B. Yellow solid; Yield: 53%. NMR data are consistent with reported data. [16] ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.36 (d, J = 8.8 Hz, 2H), 8.17 (d, J = 8.8 Hz, 2H), 7.99 (d, J = 7.3 Hz, 2H), 7.71 (m, 1H), 7.55 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) 192.8, 192.0, 151.2, 137.3, 135.4, 132.4, 130.9, 130.0, 129.2, 124.1; LR-MS: $[M]^{+\cdot}$ ($C_{14}H_9NO_4$) m/z th. = 255, m/z found = 255.

1-(4-acetylphenyl)-2-phenylethane-1,2-dione 20

20 was prepared according to the general procedure. Yellow solid; Yield: 83%. NMR data are consistent with reported data.[7] ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.07 (m, 4H), δ 7.98 (d, J = 7.2 Hz, 2H), 7.69 (t, J = 7.4 Hz, 1H), 7.53 (dd, J = 7.4 Hz, J = 7.4 Hz, 2H), 2.66 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) 197.2, 193.7, 193.6, 141.3, 136.0, 135.1, 132.7, 130.1, 130.0, 129.1, 128.7, 26.9; LR-MS: $[M]^+$ ($C_{16}H_{12}O_3$) m/z th. = 252, m/z found 252.

4-(2-oxo-2-phenylacetyl)phenyl acetate 21

21 was prepared according to the general procedure. Yellow solid; Yield: 64%. NMR data are consistent with reported data.[29] ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.02 (d, J = 8.4 Hz, 2H), 7.96 (d, J = 7.2 Hz, 2H), 7.66 (t, J = 7.6 Hz, 1H), 7.52 (m, 2H), 7.28-7.23 (m, 2H), 2.33 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) 194.2, 193.1, 168.5, 155.7, 134.9, 132.8, 131.6, 130.5, 129.9, 129.0, 122.3, 21.1; LR-MS: $[M]^+$ ($C_{16}H_{12}O_4$) m/z th. = 268, m/z found 268.

1-phenylhexane-1,2-dione 22

22 was prepared according to the general procedure B. Yellow oil; Yield: 33%. NMR data are consistent with reported data.[5a] ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97 (d, J = 7.8 Hz, 2H), 7.62 (m 1H), 7.50-7.45 (m, 2H), 2.87 (t, J = 7.4 Hz, 2H), 1.68 (m, 2H), 1.39 (m, 2H), 0.94 (t, J = 7.3 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 203.5, 192.6, 134.5, 132.0, 130.1, 128.8, 38.5, 24.9, 22.3, 13.8; LR-MS: $[M]^{+\cdot}$ ($C_{12}H_{14}O_2$) m/z th. = 190, m/z found = 190.

Acknowledgments

The authors are grateful to the CNRS and the Ministère de l'Enseignement Supérieur et de la Recherche for support. We thank the Fondation Rennes 1 for a grant to Y. M. The authors also thank ADEME (Agence de l'Environnement et de la Maîtrise de l'Energie) and Région Bretagne for a PhD grant to AD.

Entry for the Table of Contents ((Please choose one layout.))

Layout 1:

((Text for Table of Contents – max. 350 characters; not the same text as the Abstract))

((Please adjust TOC Graphic to the size of this area; max. width 5.5 cm; max. height 5.0 cm))

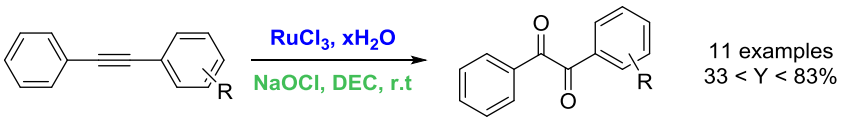
((Author(s), with * for Corresponding Author(s))) …….. Page No. – Page No.

((Title))

Keywords: ((Keyword 1 / Keyword 2 / Keyword 3 / Keyword 4 / Keyword 5))

Layout 2:

Oxidation of alkynes



The ruthenium catalyzed synthesis of 1,2-diketones by oxidation of alkynes with sodium hypochlorite has been investigated. The reaction operates under environmentally friendly conditions of oxidant, solvent and temperature.

A series of diketones have been prepared in good yields from electron rich alkynes whereas electron poor alkynes led to lower yields.

Y. Miao, A. Dupé, C. Bruneau,* C. Fischmeister* ……... Page No. – Page No.

Ruthenium Catalyzed Synthesis of 1,2-diketones from Alkynes

Keywords: Catalysis / Oxidation / Ruthenium / 1,2-diketones / alkynes