Tetrahedron Letters 61 (2020) 151853

Contents lists available at ScienceDirect

Tetrahedron Letters

journal homepage: www.elsevier.com/locate/tetlet

Rh(II)-catalyzed formal [3+3] cycloaddition of diazonaphthoquinones and propargyl alcohols: Synthesis of 2,3-dihydronaphtho-1,4-dioxin derivatives

Mitsuru Kitamura *, Tomoaki Nishimura, Kota Otsuka, Hirokazu Shimooka, Tatsuo Okauchi

Department of Applied Chemistry, Kyushu Institute of Technology, 1-1 Sensuicho, Tobata, Kitakyushu 804-8550, Japan

ARTICLE INFO

Article history:
Received 29 February 2020
Revised 13 March 2020
Accepted 16 March 2020
Available online 19 March 2020

Keywords:
Cyclization
Diazo compounds
Diazonaphthoquinone
Propargyl alcohol
Rhodium

ABSTRACT

A Rh(II)-catalyzed formal [3+3] cyclization of diazonaphthoquinones and propargyl alcohol is reported to afford 2,3-dihydro-1,4-benzodioxins. Various terminal propargyl alcohols react with diazonaphthoquinone in the presence of $Rh_2(OAc)_4$ to give the corresponding dihydrodioxins in good to high yields. However, dihydrodioxins are not formed in the reaction of internal propargyl alcohols, and the O–H insertion product and 2,5-dihydrofurans are formed as the main product(s) depending on the terminal substituent. 2,3-Dihydro-1,4-benzodioxins are proposed to be formed *via* Rh(II)-catalyzed intermolecular oxonium ylide formation and subsequent 6-*exo*-*dig* cyclization with the internal alkynyl group.

© 2020 Elsevier Ltd. All rights reserved.

Introduction

α-Diazocarbonyl compounds react with various metal complexes to form metal carbenes, which are widely used as intermediates in organic synthesis [1]. One of the useful reactions of metal carbenes is the insertion reaction into X–H bonds (X = heteroatom) [1,2]. In particular, O—H insertion reactions between metal carbenes and alcohols are well studied [3], and the reaction mechanism is proposed to proceed *via* formation of an oxonium ylide followed by a proton transfer reaction [4]. Interestingly, when propargylic alcohols are used for the reaction with metal carbenes, allenes are occasionally formed *via* a tandem oxonium ylide formation followed by [2,3]/[3,3]-sigmatropic rearrangement (Scheme 1) [5]. Further cyclization of the formed allenes has been examined for the synthesis of heterocycles, namely, 2,5-dihydrofurans [6].

Previously, we developed an efficient synthetic method for the preparation of diazonaphthoquinones *via* diazo-transfer with 2-azido-1,3-dimethylimidazolinium salt [7], and we have subsequently been investigating a series of metal-catalyzed reactions using these products [8,9]. In the study of the Rh(II)-catalyzed O–H insertion reaction of diazonaphthoquinone and alcohols, we observed the formation of formal [3+3] cycloaddition product **2a** (2,3-dihydronaphtho[1,2-*b*]-1,4-dioxin) along with the expected O–H insertion product **3a** when 2-propyn-1-ol was used (Scheme 2) [9h]. Such formal [3+3] cycloaddition had not been previously reported for the metal-catalyzed reaction of diazocarbonyl compounds and propargyl alcohol. Only a related reaction was reported by Katukojvala and co-workers, which consists of the formation of 1,4-oxazines by the cooperative Rh (II)/Brønsted acid and Au(I)-catalyzed cyclization of enal diazocarbonyl compounds and propargylamine *via* a dienamine intermediate [10].

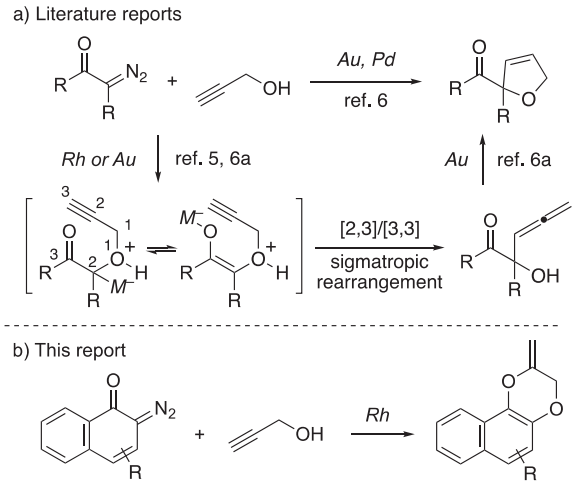
We were intrigued by this unexpected formal [3+3] cycloaddition and anticipated that this transformation could be a new and simple method for the synthesis of 2,3-dihydronaphtho[1,2-*b*]-1,4-dioxin derivatives, which are potentially attractive bioactive compounds similar to 2,3-dihydro-1,4-benzodioxins [11]. Therefore, the generality and efficiency of the Rh-catalyzed reaction of diazonaphthoquinones with propargylic alcohols were explored. In this letter, we describe these results in detail.

Results and discussion

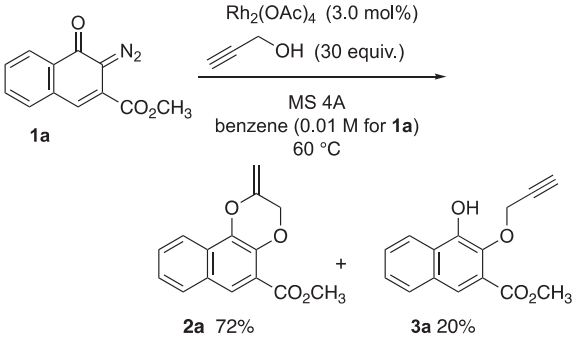
Initially, the model reaction of diazonaphthoquinone **1a** with 2-propyn-1-ol was examined in the presence of a Rh catalyst at 60 °C for 16 h (Table 1). When the reaction was carried out with $Rh_2(OAc)_4$ (3 mol%) in benzene under several concentrations (0.01–0.2 M for **1a**) (Entries 1–4), dihydrodioxin **2a** was obtained in the highest yield (94%) at the concentration of 0.1 M (Entry 3).

* Corresponding author.
E-mail address: kita@che.kyutech.ac.jp (M. Kitamura).

https://doi.org/10.1016/j.tetlet.2020.151853
0040-4039/© 2020 Elsevier Ltd. All rights reserved.



Scheme 1. Metal-catalyzed reaction of α-diazocarbonyl compounds and propargyl alcohol.



Scheme 2. Unexpected result in the Rh-catalyzed reaction of diazonaphthoquinone **1a** and propargyl alcohol.

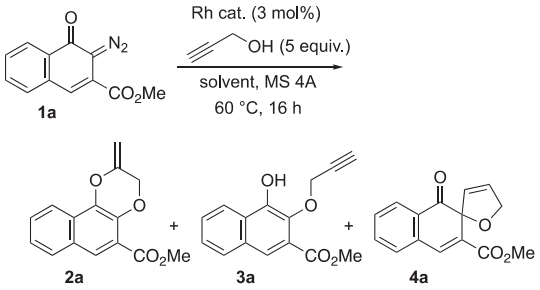
Nonpolar solvents were particularly suitable for the reaction (Entries 3 and 5–9), and benzene was determined to give the best results (Entry 3). In the screening of ligands for the Rh catalyst (Entries 3 and 10–14), $Rh_2(OAc)_4$ gave the best result for the formation of **2a** (Entry 3), and O–H insertion product **3a** was observed when the Rh catalyst contained electron-withdrawing ligands such as trifluoroacetate and perfluorobutyrate (Table 1, Entries 13 and 14).

Then, having established the optimized reaction conditions [5 equiv. of propargylic alcohol, 3 mol% $Rh_2(OAc)_4$ in benzene (0.1 M for **1**) at 60 °C], the scope of the Rh-catalyzed cyclization reaction of alkynes and diazonaphthoquinones was explored.

First, the reaction between various substituted diazonaphthoquinones **1** and 2-propyn-1-ol was examined (Table 2). The cyclization was strongly affected by the C-3 substituents of the diazonaphthoquinones **1**. When the C-3 substituent R^1 was a carbonyl group, the formal [3+3] cyclization proceeded efficiently (Entries 1–7). 3-Cyano- and alkoxylmethyl-substituted diazonaphthoquinones **1** also cyclized to dihydrodioxin **2** in good yields (Entries 8 and 9). However, the reaction of unsubstituted or alkyl-substituted diazonaphthoquinones **1** gave **2** in lower yields, and O–H insertion product **3** and/or oxy-spiro compounds **4** were mainly formed (Entries 10–12). In addition, the formation of allene **5m** was observed in the reaction of isopropyl-substituted diazonaphthoquinone (Entry 12). Interference in the dioxane formation was not observed upon introducing a methyl group at the C-4 position or a methoxy group at the C-8 position (Entries 13 and 14).

Next, the effect of substituents at the terminal and internal positions of the propargylic alcohol was examined (Table 3).

Table 1
Optimization of the formation of **2a** by the Rh-catalyzed reaction of **1a** and 2-propyn-1-ol.[a]



Entry	Solvent	Conc. (M)	Rh cat.[b]	Yield (%)[c]		
				2a	**3a**	**4a**
1	Benzene	0.01	$Rh_2(OAc)_4$	51	0	1
2	Benzene	0.05	$Rh_2(OAc)_4$	81	0	6
3	Benzene	0.1	$Rh_2(OAc)_4$	94	0	1
4	Benzene	0.2	$Rh_2(OAc)_4$	79	0	15
5	CH_3CN	0.1	$Rh_2(OAc)_4$	0	0	0
6	THF	0.1	$Rh_2(OAc)_4$	0	0	0
7	CH_2Cl_2	0.1	$Rh_2(OAc)_4$	41	18	0
8	CH_2ClCH_2Cl	0.1	$Rh_2(OAc)_4$	67	0	0
9	Toluene	0.1	$Rh_2(OAc)_4$	81	5	0
10	Benzene	0.1	$Rh_2(oct)_4$	76	0	0
11	Benzene	0.1	$Rh_2(esp)_2$	76	0	0
12	Benzene	0.1	$Rh_2(TPA)_4$	71	0	0
13	Benzene	0.1	$Rh_2(TFA)_4$	0	22	0
14	Benzene	0.1	$Rh_2(pfb)_4$	6	61	0

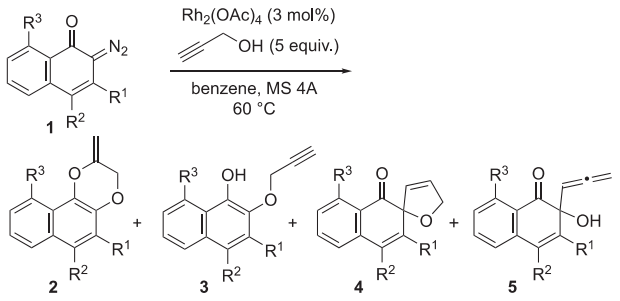
[a] Reagents and conditions: **1a** (0.3 mmol), 2-propyn-1-ol (1.5 mmol), $Rh_2(OAc)_4$ (3 mol%), solvent, 60 °C, 16 h.
[b] oct = octanoate, esp = α,α,α′,α′-tetramethyl-1,3-benzenedipropionate, TPA = triphenylacetate. TFA = trifluoro-acetate, pfb = perfluorobutyrate.
[c] Isolated yield.

In the reaction of 1-substituted-2-propyn-1-ol derivatives (terminal alkynes) with **1a**, dihydrodioxins **2** were formed exclusively. The yield of **2** decreased when the number of substituents increased (Entries 1 and 2).

In contrast, dihydrodioxins **2** were not obtained in the reaction of internal propargyl alcohols (Entries 3–7). Propargyl alcohols containing methyl, phenyl, or 1-alkynyl groups as the terminal substituent R^3 reacted with **1a** to afford a mixture of O–H insertion product **3** and spirocompounds **4** (Entries 3–5). O–H insertion product **3** was formed as the only product in the reaction of 3-trimethylsilyl-2-propyn-1-ol (Entry 6). When the terminal substituent R^3 was a hydroxymethyl group, dihydrodioxines **2** were formed as a sole product (Entries 7).

To gain insight into the reaction mechanism, several control experiments were conducted (Scheme 3). First, the three products **2a, 3a**, and **4a** were treated under the standard reaction conditions to investigate the occurrence of interconversion or transformation processes (Eqs. (1)–(3)). Compounds **2a** and **4a** were not converted to other forms (Eqs. (1) and (3)). In the case of O–H insertion product **3a**, formation of **2a** and **4a** was observed, albeit in low yields (Eq. (2)). These results suggest that the three products **2**, **3**, and **4** are not intermediates in the reaction. In the metal-catalyzed formation of 2,5-dihydrofuran derivatives *via* the reaction of diazocompounds and propargyl alcohol, α-hydroxy allenes were suggested as intermediates [5,6]. However, we ruled out the formation of hydroxy allene as intermediate in the reactions leading to cyclic compounds **2** and **4** because dihydrodioxin **2m** and spirocompound **4m** were not formed from hydroxy allene **5m** (Eq. (4)).

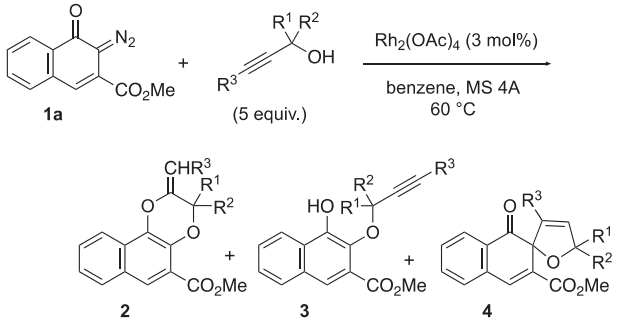
Table 2
Rh-catalyzed reaction of various diazonaphthoquinones **1** and 2-propyn-1-ol.[a]



Entry	R^1	R^2	R^3	Time (h)	Yield (%)[b]
1	CO_2Et	H	H	18	**2b** 90
2	CO_2Pr	H	H	17	**2c** 92
3	CO_2Ph	H	H	12	**2d** 76, **3d** 5
4	CO_2NHPh	H	H	24	**2e** 79
5	CHO	H	H	16	**2f** 54
6	COMe	H	H	12	**2g** 81
7	COPh	H	H	14	**2h** 82
8	CN	H	H	8	**2i** 40, **4i** 4
9	CH_2OMe	H	H	9	**2j** 60, **3j** 4, **4j** 14
10	H	H	H	6	**2k** 17, **3k** 33
11	Me	H	H	6	**2l** 31, **3l** 40, **4l** 25
12	^{i}Pr	H	H	16	**2m** 26, **3m** 33, **4m** 21, **5m** 17
13	CO_2Me	Me	H	12	**2n** 87
14	CO_2Me	H	OMe	18	**2o** 78, **3o** 6, **4o** 7

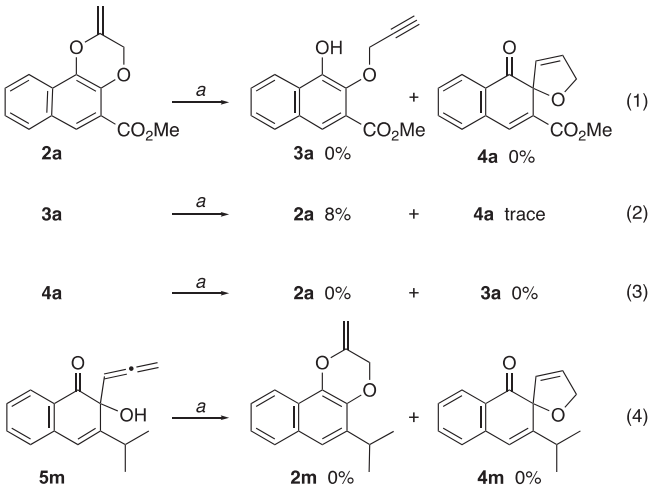
[a] Reagents and conditions: **1** (0.3 mmol), 2-propyn-1-ol (1.5 mmol), $Rh_2(OAc)_4$ (3 mol%), benzene (3 mL), 60 °C.
[b] Isolated yield.

Table 3
Substrate scope for internal propargyl alcohols.[a]



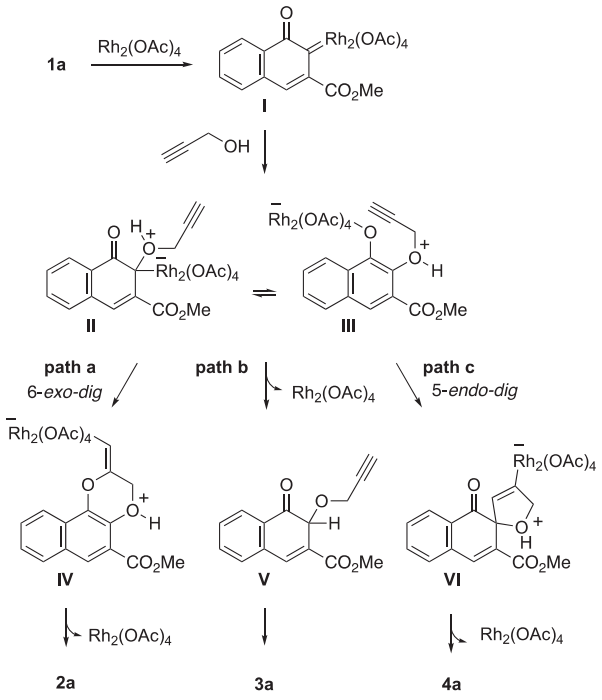
Entry	R^1	R^2	R^3	Time (h)	Yield (%)
1	CH_3	H	H	16	**2p** 66
2	CH_3	CH_3	H	16	**2q** 31
3	H	H	Me	17	**3r** 38, **4r** 34
4	H	H	Ph	16	**3s** 22, **4s** 6
5[b]	H	H	$C{\equiv}C(CH_2)_3CH_3$	10	**3t** 21, **4t** 23
6	H	H	TMS	16	**3u** 88
7[c]	H	H	CH_2OH	14	**2v** 58[d]

[a] Reagents and conditions: 1a (0.3 mmol), propargylic alcohol (1.5 mmol), Rh2(OAc)4 (3 mol%), benzene (3 mL), 60 °C.
[b] 1.2 equiv. of propargylic alcohol was used.
[c] $ClCH_2CH_2Cl$ was used as the solvent.
[d] Single geometric isomer. Geometry of the alkene in **2v** is not assigned.



a: $Rh_2(OAc)_4$ (3 mol%), CH≡C–CH_2OH (5 equiv.), benzene, 60 °C, 12 h.

Scheme 3. Investigation of the reaction mechanism.



Scheme 4. Possible reaction mechanism.

On the basis of the above results and literature reports, a plausible reaction mechanism for the Rh-catalyzed reaction of propargylic alcohol and diazonaphthoquinones **1a** is presented in Scheme 4. In the first step, the Rh(II) catalyst reacts with **1a** to form rhodium–carbene complex **I**. Then, the nucleophilic attack of propargylic alcohol on carbene complex **I** proceeds to form oxonium ylide **II**, which may be in equilibrium with Rh naphtholate **III**. In path a, dihydrodioxin **2a** is formed by oxy rhodation *via* 6-*exo-dig* cyclization. Meanwhile, **3a** and **4a** are formed from oxonium ylide **II** *via* a 1,2 proton shift (path b) and migratory insertion of the C≡C triple bond into the Rh–C bond (5-*endo-dig* cyclization, path c), respectively. Since transformation from **3a** to **2a** occurs in low yield as shown in Eq. (2), this interconversion would not be a main pathway for the formation of **2a**.

Conclusion

We have developed a novel $Rh_2(OAc)_4$-catalyzed formal [3+3] cyclization of diazonaphthoquinones and propargyl alcohol to afford 2,3-dihydro-1,4-benzodioxins, which are formed *via* an oxonium ylide and subsequent 6-*exo*-*dig* cyclization. In the reaction of terminal propargyl alcohols, dihydrodioxins are formed in good to high yields. However, in the reaction of internal propargyl alcohols, dihydrodioxins **2** were not necessarily formed, and the O–H insertion product and 2,5-dihydrofurans were formed as the main product(s) depending on the terminal substituent.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgement

This work was supported by a Grant in Aid for KAKENHI (17K19125).

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.tetlet.2020.151853.

References

[1] (a) For reviews, see: M.P. Doyle Chem. Rev. 86 (1986) 919–939;
(b) A. Padwa, K.E. Krumpe, Tetrahedron 48 (1992) 5385–5453;
(c) T. Ye, M.A. McKervey, Chem. Rev. 94 (1994) 1091–1160;
(d) A. Padwa, D.J. Austin, Angew. Chem. Int. Ed. Engl. 33 (1994) 1797;
(e) M.P. Doyle, T. Ye, M.A. McKervey, Modern Catalytic Methods for Organic Synthesis with Diazo Compounds, John Wiley & Sons, New York, 1998;
(f) H.M.L. Davies, R.E.J. Beckwith, Chem. Rev. 103 (2003) 2861–2903;
(g) Z. Zhang, J. Wang, Tetrahedron 64 (2008) 6577–6605;
(h) M.P. Doyle, R. Duffy, M. Ratnikov, L. Zhou, Chem. Rev. 110 (2010) 704–724;
(i) A. Ford, H. Miel, A. Ring, C.N. Slattery, A.R. Maguire, M.A. McKervey, Chem. Rev. 115 (2015) 9981–10080.
[2] A. Padwa, S.F. Hornbuckle, Chem. Rev. 91 (1991) 3263–3309.
[3] For a review, see: D.J. Miller, C.J. Moody Tetrahedron 51 (1995) 10811–10843.
[4] Y. Liang, H. Zhou, Z.-X. Yu, J. Am. Chem. Soc. 131 (2009) 17783–17785.
[5] (a) M.E. Jung, J. Pontillo, Org. Lett. 1 (1999) 367–369;
(b) G.A. Moniz, J.L. Wood, J. Am. Chem. Soc. 123 (2001) 5095–5097;
(c) Z. Li, V. Boyarskikh, J.H. Hansen, J. Autschbach, D.G. Musaev, H.M.L. Davies, J. Am. Chem. Soc. 134 (2012) 15497–15504.
[6] (a) J. Wang, X. Yao, T. Wang, J. Han, J. Zhang, X. Zhang, P. Wang, Z. Zhang, Org. Lett. 17 (2015) 5124–5127;
(b) , Related reaction, see:T. Shi, X. Guo, S. Teng, W. Hu Chem. Commun. 51 (2015) 15204–15207.
[7] (a) M. Kitamura, N. Tashiro, R. Sakata, T. Okauchi, Synlett (2010) 2503–2505;
(b) M. Kitamura, R. Sakata, N. Tashiro, A. Ikegami, T. Okauchi, Bull. Chem. Soc. Jpn. 88 (2015) 824–833.
[8] For a review, see: D.I.A. Othman, M. Kitamura Heterocycles 92 (2016) 1761–1783.
[9] (a) For selected examples: M. Kitamura, R. Sakata, T. Okauchi Tetrahedron Lett. 52 (2011) 1931–1933;
(b) M. Kitamura, M. Kisanuki, R. Sakata, T. Okauchi, Chem. Lett. 40 (2011) 1129–1131;
(c) M. Kitamura, M. Kisanuki, T. Okauchi, Eur. J. Org. Chem. (2012) 905–907;
(d) M. Kitamura, K. Araki, H. Matsuzaki, T. Okauchi, Eur. J. Org. Chem. (2013) 5045–5049;
(e) M. Kitamura, K. Kubo, S. Yoshinaga, H. Matsuzaki, K. Ezaki, T. Matsuura, D. Matsuura, N. Fukuzumi, K. Araki, M. Narasaki, Tetrahedron Lett. 55 (2014) 1653–1656;
(f) M. Kitamura, M. Kisanuki, K. Kanemura, T. Okauchi, Org. Lett. 16 (2014) 1554–1557;
(g) M. Kitamura, S. Takahashi, T. Okauchi, J. Org. Chem. 80 (2015) 8406–8416;
(h) M. Kitamura, K. Otsuka, S. Takahashi, T. Okauchi, Tetrahedron Lett. 58 (2017) 3508–3511;
(i) D.I.A. Othman, K. Otsuka, S. Takahashi, K.B. Selim, M.A. El-Sayed, A.S. Tantawy, T. Okauchi, M. Kitamura, Synlett 29 (2018) 457–462;
(j) S. Takahashi, H. Shimooka, T. Okauchi, M. Kitamura, Chem. Lett. 48 (2019) 28–31.
[10] J. Kalepu, S. Katukojvala, Angew. Chem. Int. Ed. 55 (2016) 7831–7835.
[11] O. Cruz-Lopez, M.C. Nunez, A. Conejo-Garcia, M. Kimatrai, J.M. Campos, Curr. Org. Chem. 15 (2011) 869–887.