



Synthesis of functionalized carbamates and quinones via sequential oxidation of salicylaldehydes using TBHP as the oxidant



K. Rajendra Prasad, P. Suresh, B. Ravikumar, N. Veera Reddy, K. Rajender Reddy*

Inorganic and Physical Chemistry Division, CSIR-Indian Institute of Chemical Technology, Tarnaka, Hyderabad 500 607, India

ARTICLE INFO

Article history:

Received 14 August 2014

Revised 16 September 2014

Accepted 16 September 2014

Available online 20 September 2014

Keywords:

Salicylaldehydes

Formamide

Carbamate

Oxidation

Quinones

ABSTRACT

A sequential oxidative approach was designed to functionalize salicylaldehyde derivatives and provide corresponding bi-functional amide-carbamate and amide-quinone units. A combination of metal/metal free conditions and TBHP as the external oxidant provided the products in moderate to excellent yields (49–91%).

© 2014 Elsevier Ltd. All rights reserved.

Cross coupling chemistry is an extremely useful strategy for making C–C and C–heteroatom bonds. Among them cross dehydrogenative couplings (CDC) involving C–H bond activations have found a wider interest in recent years owing to their synthetic advantage over the traditional methods, where the involvement of pre-functionalized substrates makes the synthetic route longer, less atom-economical and expensive.¹ Tremendous progress has been made in this area and the feasibility of these reactions was successfully demonstrated for C–C bond formations involving cross coupling between Csp³–H, Csp²–H and Csp–H bonds in the presence of various transition metal catalysts.² In parallel the CDC approach was also efficiently utilized in the construction of various C–heteroatom bond processes, notably the formation of C–N, C–O, C–S and C–P bonds. Majority of these reactions were performed in the presence of oxidants, which significantly contributes for the thermodynamic favourability of the reaction.^{3–6}

Phenols are readily available and versatile building blocks in synthetic organic chemistry. Although it is readily oxidized by chemical and biological oxidants, its cross coupling chemistry is particularly challenging because of the problems associated with self coupling as well as formations of polymeric products. However, recent investigations by several groups under CDC or oxidative cross coupling strategies have shown the application of phenols towards the synthesis of hemiacetals,⁷ spirolactones,⁷ dihydrobenzofurans,⁸ furanones,^{9a} coumestrol^{9b} and dihydrooxazinones¹⁰

under metal and metal-free conditions. Similarly, the cross coupling approach was successfully applied for aromatic aldehydes for the construction of C–C, C–N and C–O bond formations.^{11–13} Whereas, a bi-functional moiety such as salicylaldehyde, which is a highly functionalized aromatic molecule was scarcely been explored in cross coupling chemistry.¹⁴

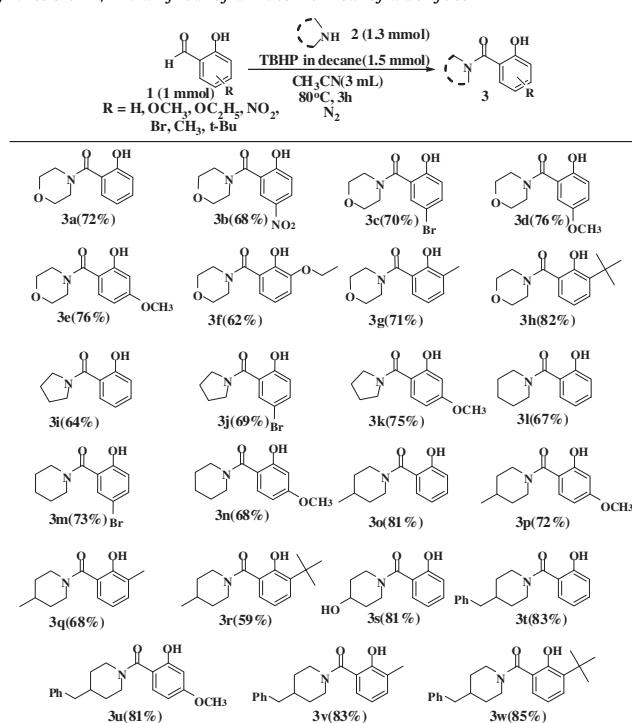
Our group has been working on oxidative couplings using metal and non-metal catalysts for the last couple of years.¹⁵ During these investigations it has been shown that direct coupling of aldehydes with amines and alcohols provides amides and esters.^{16,17} Similarly, synthesis of phenol- and enol-carbamates was demonstrated via oxidative cross coupling of formamides with phenols and β -keto esters using copper catalysts.¹⁸ Although the latter method allowed accessing the phenol carbamates, the substrate scope was limited to 2-carbonyl substituted derivatives. While extending this work to salicylaldehyde derivatives, surprisingly it has been observed that the aldehyde functionality was intact. This initial observation prompted us to look at the possibility of utilizing both phenolic and aldehyde functionalities under cross dehydrogenation strategies. During the execution of this work with salicylaldehydes, Chang and co-workers reported the formation of carbamates and acetals, where the sensitive aldehyde was retained.¹⁹ A similar observation is also made by Patel and co-workers in *o*-arylation of phenol with alkylbenzenes, where sensitive aldehyde functionality was intact and moreover used as directing group.²⁰ However, our interest was to activate both the functional groups either in one-pot or sequential manner to provide multi-functional chromophores.

* Corresponding author. Tel.: +91 040 27191532; fax: +91 040 27160921.

E-mail addresses: rajender@iict.res.in, rajenderkallu@yahoo.com (K.R. Reddy).

Chromophores having both carbamate and amide functionalities at *ortho*-position on aromatic rings have potential usefulness. For examples, these derivatives show pro-drug activity in inhibiting or modulating the activity of heat shock protein 90 (Hsp90) (Compound **A**)²¹ and also can be used in treatment of illnesses related to glycine uptake inhibitors (GLYT1) (Compound **B**).²² Moreover, some of these compounds are used as intermediates in the synthesis of semiovioxanthin and 4-functionalized estrone derivatives.²³ Based on our previous experience with amide and carbamate work under oxidative cross couplings, we envisaged that salicylaldehydes having both aldehyde and phenolic functionalities can be utilized under cross coupling strategy. In this Letter we report a direct route to access both carbamate and amide functionalities via sequential oxidative cross coupling of salicylaldehyde derivatives with amines and formamides (Scheme 1). Moreover by application of this procedure one can avoid the usage of isocyanates, amidoyl chlorides or acid chloride derivatives, which are generally used in traditional routes. The usefulness of sequential oxidations is also exploited in the synthesis of functionalized quinones by making use of one of the amide intermediates.²⁴

Regarding the amidation of salicylaldehydes, initially it was thought to investigate with KI/TBHP adopting our previously reported procedure of oxidative amidation of aldehydes with amines. However, it has been observed by our group that phenols undergo electrophilic iodination under KI/TBHP combination and a similar substitution with salicylaldehydes could hamper the catalytic activity of potassium iodide.²⁵ Among the several reported procedures in the literature, the best alternative we thought of for selective amidation of salicylaldehyde derivatives was oxidative cross coupling under metal-free system reported by Wolf and Kovi.²⁶ When this procedure was adapted for the reaction between salicylaldehyde and morpholine, interestingly the reactions work very well and amide product resulted in 72% isolated yield.²⁷ Subsequently, this metal-free cross coupling strategy was explored for the amidation with several substituted salicylaldehydes and amines. Both electron rich and electron deficient salicylaldehydes work very well and provided the respective amidation products in good to excellent yields. For example, reaction of morpholine with salicylaldehyde having *p*-NO₂, *p*-Br, *p*-OMe and *m*-OMe substitutions provided 70–76% of the amide product (Table 1, **3a–3e**). Similarly *o*-substitution with ethoxy-, methyl-

Table 1Synthesis of *N,N'*-dialkyl salicylamides from salicylaldehydes^a^a Isolated yield.

and *tert*-butyl groups provided 62–82% of amide product (Table 1, **3f–3h**). These results suggest that there is no regular pattern with respect to electronic and steric influence of substitution on salicylaldehydes. Further similar observations have been made by variation of amines with pyrrolidine, piperidine, 4-Me-piperidine and 4-OH-piperidine (Table 1, **3i–3s**). In case of 4-benzylpiperidine, the corresponding amides were formed in excellent yields (Table 1, **3t–3w**) and no oxidation of benzylic carbon was observed.

Formamides have been widely used in cross-coupling reactions in recent years.²⁸ Our previous work with formamides has shown the possibility of direct coupling of these groups with substituted phenols or amines to provide carbamates or ureas, respectively.^{15f,18} In case of phenols, the reactivity was limited to 2-carbonyl substituted derivatives and corresponding carbamates were synthesized successfully. Coordinating ability of carbonyl functionality with copper metal was attributed to the high reactivity of these derivatives. Moreover, formation of carbamate product with 2-hydroxy-*N*-phenylbenzamide provided the scope to extend for amide functionalities.¹⁸ When (2-hydroxyphenyl) (morpholino)methanone (**3a**) was treated with DMF under the previously reported conditions, the corresponding carbamate product **5a** formed in high yield.²⁹ Further substrate scope was investigated with various amide (**3a–3w**) and formamides and the results are summarized in Table 2. Irrespective of the substitutions on the aromatic ring of the amides the carbamate products (**5a–5t**) resulted in good to excellent yields. However, in certain combination of amides (**3**) with formamides, we encountered the isolation problem, because of the closer *R_f* values of reactants and products. This could be one of the reasons for the low isolated yield of diethylformamide products (**5r–5t**). The product formation was also not observed with sterically hindered amides **3h**, **3r** and **3w**.

Further investigations were focused on the functional group transformation of *N,N'*-dialkyl salicylamides (**3**). Since we were engaged in activation of C–H bonds adjacent to nitrogen heteroatom, we looked at the possibility of intra molecular oxidative

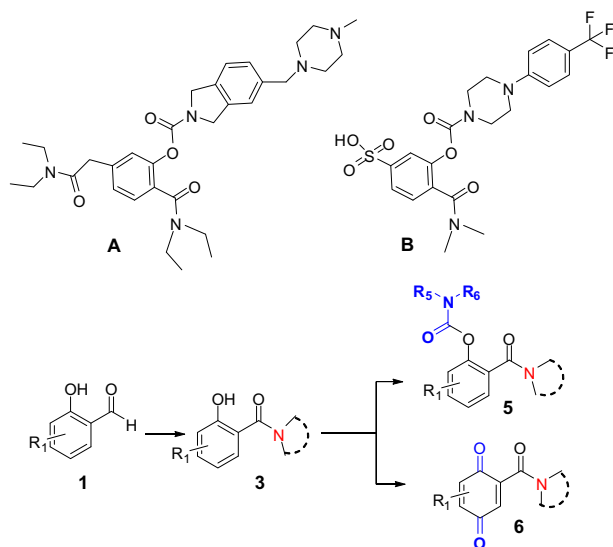
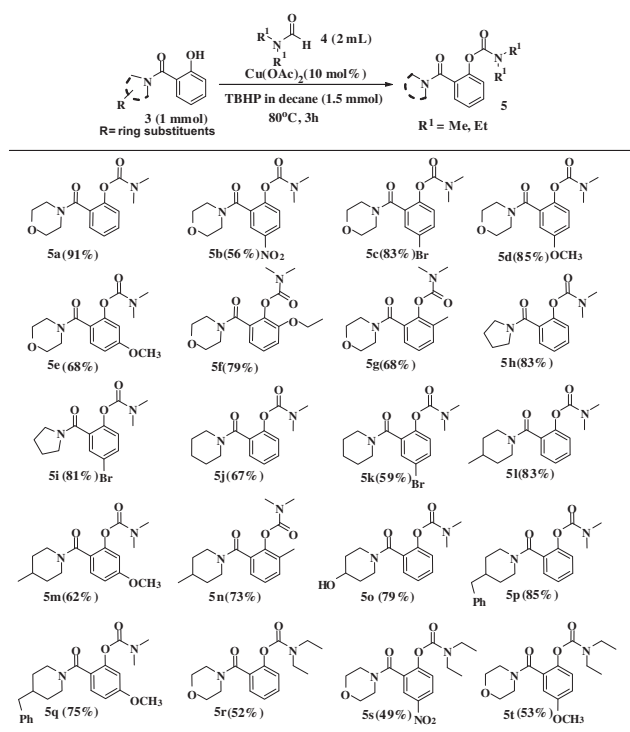
**Scheme 1.**

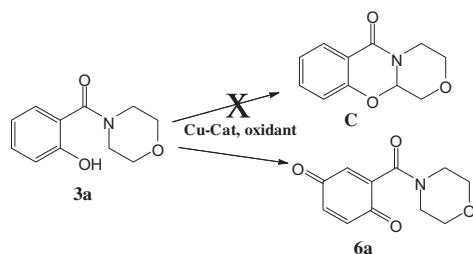
Table 2
Synthesis of *ortho* functionalized carbamates from *N,N'*-dialkyl salicylamides^a



^a Isolated yield.

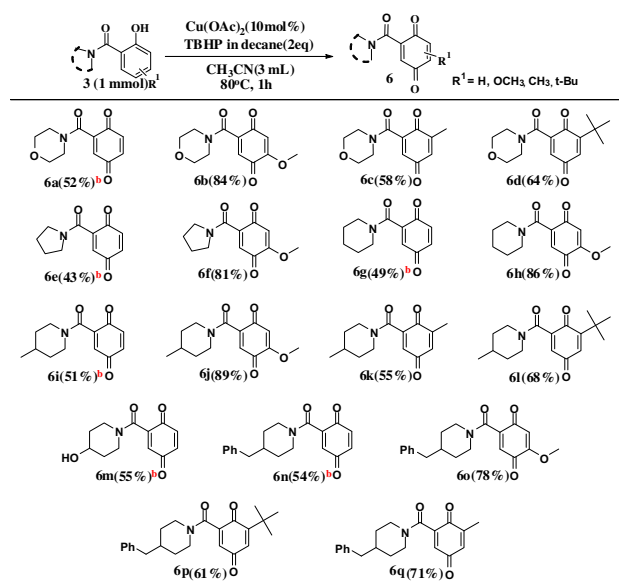
cross couplings in **3**, where phenolic –OH and C–H bond adjacent to nitrogen couples to generate cyclic product **C** (Scheme 2).^{10,30} Surprisingly the reaction with **3a** in the presence of copper catalyst and TBHP as the oxidant resulted in corresponding 1,4-benzoquinone derivative (**6a**) rather than the cyclic product. Although the oxidation of phenols to 1,4-benzoquinones is well known in the literature,³¹ the direct transformation of substituted salicylamide derivatives to quinones is not reported. Looking at the synthetic as well as biological importance of *para*-quinones, the scope of the reaction was tested with various salicylamide derivatives and the results are presented in Table 3.

The reaction of 2-hydroxyphenyl-morpholino methanone (**3a**) with 10 mol % of Cu(OAc)₂ catalyst resulted in 52% of the 1,4-benzoquinone product **6a** in acetonitrile solvent and TBHP as the external oxidant (Table 3).³² Salicylamide derivatives (**3**) having substitutions at *ortho*- and *meta*- to the phenolic functionality works very well and resulted in corresponding 1,4-benzoquinones in moderate to good yields (Table 3). Among them methoxy substitution at the *meta*-position provided higher *para*-quinone products **6b**, **6f**, **6j** and **6o** (Table 3). Even the substitution of the bulky *tert*-butyl group at *ortho*- to the phenolic functionality works very well and resulted in corresponding quinone product (**6d** and **6l**). No oxidation of benzylic carbon was observed during the synthesis of 4-benzylpiperidine derivatives (**6n–6q**). The reaction was not



Scheme 2.

Table 3
Synthesis *ortho* functionalized benzoquinones from *N,N'*-dialkyl salicylamides^a



^b Reaction was carried for 3 h.

^a Isolated yield.

successful with *N,N'*-dialkyl salicylamides having substitutions at *para*- to phenolic functional groups and moreover no *ortho*-quinones products were observed.

In conclusion, we have shown the selective and sequential oxidative cross couplings as one of the novel ways for functional group transformation involving multifunctional chromophores. As an example, we have demonstrated the activation of both aldehyde- and phenolic –OH of salicylaldehyde derivatives and transform them directly into amide and carbamate groups sequentially under metal/metal-free steps using TBHP as the oxidant. This method has the advantage over conventional routes by avoiding the use of hazardous reagents and additional steps. Moreover, we have also shown the synthesis of functionalized 1,4-benzoquinone by making use of one of the amide intermediates. The advantages of sequential oxidative cross coupling for functional group transformation on multifunctional chromophores are presently under investigation.

Acknowledgments

K.R.P., B.R.K. and N.V.R thank the Council of Scientific and Industrial Research (CSIR) for the award of Research Fellowships. K.R.P. thanks CSIR for financial support under net-work project CSC-0123.

Supplementary data

Supplementary data associated with this article can be found, in the online version, at <http://dx.doi.org/10.1016/j.tetlet.2014.09.080>.

References and notes

- For selected reviews of C–C coupling from C–H bonds, see: (a) Murahashi, S.-I.; Zhang, D. *Chem. Soc. Rev.* **2008**, 37, 1490–1501; (b) You, S.-L.; Xia, J.-B. *Top. Curr. Chem.* **2010**, 292, 165–194; (c) Li, Z.; Bohle, D.; Li, C.-J. *Proc. Natl. Acad. Sci. U.S.A.* **2006**, 103, 8928–8933; (d) Yeung, C. S.; Dong, V. M. *Chem. Rev.* **2011**, 111, 1215–1292; (e) Liu, C.; Zhang, H.; Shi, W.; Lei, A. *Chem. Rev.* **2011**, 111, 1780–1824; (f) Shi, W.; Liu, C.; Lei, A. *Chem. Soc. Rev.* **2011**, 40, 2761–2776; (g) Sun, C.-L.; Li, B.-J.; Shi, Z.-J. *Chem. Rev.* **2011**, 111, 1293; (h) Li, C.-J. *Acc. Chem. Res.* **2009**, 42, 335–344.

2. (a) Li, C. J. *Acc. Chem. Res.* **2009**, *42*, 335–344. and references therein; (b) Han, W.; Mayer, P.; Ofial, A. R. *Angew. Chem.* **2011**, *123*, 2226–2230. *Angew. Chem., Int. Ed.* **2011**, *50*, 2178–2182; (c) Deng, G.; Zhao, L.; Li, C. J. *Angew. Chem.* **2008**, *120*, 6374–6378. *Angew. Chem., Int. Ed.* **2008**, *47*, 6278–6282; (d) Lyons, T. W.; Hull, K. L.; Sanford, M. S. *J. Am. Chem. Soc.* **2011**, *133*, 4455–4464; (e) Li, Z.; Li, C. J. *J. Am. Chem. Soc.* **2006**, *128*, 56–57; (f) Engle, K. M.; Wang, D. H.; Yu, J. Q. *Angew. Chem.* **2010**, *122*, 6305–6309. *Angew. Chem., Int. Ed.* **2010**, *49*, 6169–6173; (g) Borduas, N.; Powell, D. A. *J. Org. Chem.* **2008**, *73*, 7822–7825; (h) Kitahara, M.; Umeda, N.; Hirano, K.; Satoh, T.; Miura, M. *J. Am. Chem. Soc.* **2011**, *133*, 2160–2162.
3. For C–N bond formation, see: (a) Bariwalab, J.; Eycken, E. V. *Chem. Soc. Rev.* **2013**, *42*, 9283–9303; (b) Xia, Q.; Chen, W.; Qiu, H. *J. Org. Chem.* **2011**, *76*, 7577–7582; (c) Zhang, C.; Xu, Z.; Zhang, L.; Jiao, N. *Angew. Chem., Int. Ed.* **2011**, *50*, 11088–11092.
4. For C–O bond formation, see: (a) Giri, R.; Liang, J.; Lei, J. G.; Li, J. J.; Wang, D. H.; Chen, X.; Naggar, I. C.; Guo, C.; Foxman, B. M.; Yu, J. Q. *Angew. Chem., Int. Ed.* **2005**, *44*, 7420–7424; (b) Dick, A. R.; Hull, K. L.; Sanford, M. S. *J. Am. Chem. Soc.* **2004**, *126*, 2300–2301; (c) Desai, L. V.; Hull, K. L.; Sanford, M. S. *J. Am. Chem. Soc.* **2004**, *126*, 9542–9543; (d) Zhang, Y.; Li, C. J. *J. Am. Chem. Soc.* **2006**, *128*, 4242–4243; (e) Li, Z.; Yu, R.; Li, H. *Angew. Chem.* **2008**, *120*, 7607–7610. *Angew. Chem., Int. Ed.* **2008**, *47*, 7497–7500; (f) Zhang, Y.; Li, C. J. *Angew. Chem.* **2006**, *118*, 1983–1986. *Angew. Chem., Int. Ed.* **2006**, *45*, 1949–1952.
5. For C–S bond formation, see: (a) Zhang, X.; Zeng, W.; Yang, Y.; Huang, H.; Liang, Y. *Org. Lett.* **2014**, *16*, 876–879; (b) Xu, H.-J.; Zhao, Y.-Q.; Feng, T.; Feng, Y.-S. *J. Org. Chem.* **2012**, *77*, 2878–2884; (c) Taniguchi, N. *J. Org. Chem.* **2006**, *71*, 7874–7876.
6. (a) Gao, Y.; Wang, G.; Chen, L.; Xu, P.; Zhao, Y.; Zhou, Y.; Han, L.-B. *J. Am. Chem. Soc.* **2009**, *131*, 7956–7957; (b) Basle, O.; Li, C.-J. *Chem. Commun.* **2009**, 4124–4126; (c) Fu, T.; Qiao, H.; Peng, Z.; Hu, G.; Wu, X.; Gao, Y.; Zhao, Y. *Org. Biomol. Chem.* **2014**, *12*, 2895–2902.
7. Parnes, R.; Kshirsagar, U. A.; Werbeloff, A.; Regev, C.; Pappo, D. *Org. Lett.* **2012**, *14*, 3324–3327.
8. (a) Huang, Z.; Jin, L.; Feng, Y.; Peng, P.; Yi, H.; Lei, A. *Angew. Chem., Int. Ed.* **2013**, *52*, 7151–7155; (b) Kshirsagar, U. A.; Regev, C.; Parnes, R.; Pappo, D. *Org. Lett.* **2013**, *15*, 3174–3177.
9. (a) Gao, Q.; Wu, X.; Liu, S.; Wu, A. *Org. Lett.* **2014**, *16*, 1732–1735; (b) Kshirsagar, U. A.; Parnes, R.; Goldstein, H.; Ofir, R.; Zarivach, R.; Pappo, D. *Chem. Eur. J.* **2013**, *19*, 13575–13583.
10. Modak, A.; Dutta, U.; Kancherla, R.; Maity, S.; Bhadra, M.; Mobin, S. M.; Maiti, D. *Org. Lett.* **2014**, *16*, 2602–2605.
11. (a) Jia, X.; Zhang, S.; Wang, W.; Luo, F.; Cheng, J. *Org. Lett.* **2009**, *11*, 3120–3123; (b) Wang, J.; Liu, C.; Yuan, J.; Lei, A. *Angew. Chem., Int. Ed.* **2013**, *52*, 2256–2259.
12. (a) Ghosh, S. C.; Ngiam, J. S. Y.; Seayad, A. M.; Tuan, D. T.; Chai, C. L. L.; Chen, A. J. *Org. Chem.* **2012**, *77*, 8007–8015; (b) Prasad, V.; Kale, R. R.; Mishra, B. B.; Kumar, D.; Tiwari, V. K. *Org. Lett.* **2012**, *12*, 2936–2939; (c) Ton, T. M. U.; Tejo, C.; Tania, S.; Chang, J. W. W.; Chan, P. W. H. *J. Org. Chem.* **2011**, *76*, 4894–4904; (d) Cadoni, R.; Porcheddu, A.; Giacomelli, G.; Luca, L. D. *Org. Lett.* **2012**, *14*, 5014–5017.
13. (a) Maki, B. E.; Scheidt, K. A. *Org. Lett.* **2008**, *10*, 4331–4334; (b) Sarkar, S. D.; Grimme, S.; Studer, A. J. *Am. Chem. Soc.* **2010**, *132*, 1190–1191.
14. (a) Shi, Z.; Schröder, N.; Glorius, F. *Angew. Chem., Int. Ed.* **2012**, *51*, 8092–8096; (b) De, S. K.; Gibbs, R. A. *Synthesis* **2005**, *8*, 1231–1233; (c) Rao, H. S. P.; Sivakumar, S. J. *Org. Chem.* **2006**, *71*, 8715–8723.
15. (a) Kumar, R. A.; Saidulu, G.; Sridhar, B.; Liu, S. T.; Reddy, K. R. *J. Org. Chem.* **2013**, *78*, 10240–10250; (b) Kumar, G. S.; Pieber, B.; Reddy, K. R.; Kappe, C. O. *Chem. Eur. J.* **2012**, *18*, 6124–6128; (c) Kumar, R. A.; Maheswari, C. U.; Ghantasala, S.; Jyothi, C.; Reddy, K. R. *Adv. Synth. Catal.* **2011**, *353*, 401–410; (d) Reddy, K. R.; Maheswari, C. U.; Venkateshwar, M.; Kantam, M. L. *Adv. Synth. Catal.* **2009**, *351*, 93–96; (e) Reddy, K. R.; Maheswari, C. U.; Venkateshwar, M.; Prashanthi, S.; Kantam, M. L. *Tetrahedron Lett.* **2009**, *50*, 2050–2053; (f) Kumar, G. S.; Kumar, R. A.; Kumar, P. S.; Reddy, N. V.; Kumar, K. V.; Kantam, M. L.; Prabhakar, S.; Reddy, K. R. *Chem. Commun.* **2013**, 6686–6688.
16. Reddy, K. R.; Maheswari, C. U.; Venkateshwar, M.; Kantam, M. L. *Eur. J. Org. Chem.* **2008**, 3619–3622.
17. Reddy, K. R.; Venkateshwar, M.; Maheswari, C. U.; Prashanthi, S. *Synth. Commun.* **2009**, *40*, 186–195.
18. Kumar, G. S.; Maheswari, C. U.; Kumar, R. A.; Kantam, M. L.; Reddy, K. R. *Angew. Chem., Int. Ed.* **2011**, *50*, 11748–11751.
19. (a) Barve, B. D.; Wu, Y.-C.; El-Shazly, M.; Chuang, D.-W.; Cheng, Y.-B.; Wang, J.-J.; Chang, F.-R. *J. Org. Chem.* **2014**, *79*, 3206–3214; (b) Barve, B. D.; Wu, Y.-C.; El-Shazly, M.; Chuang, D.-W.; Cheng, Y.-B.; Wang, J.-J.; Chang, F.-R. *Org. Lett.* **2014**, *16*, 1912–1915.
20. Rout, S. K.; Guin, S.; Banerjee, A.; Khatun, N.; Gogoi, A.; Patel, B. K. *Org. Lett.* **2013**, *15*, 4106–4109.
21. Jolidon, S.; Narquizean, R.; Nettekoven, M. H.; Norcross, R. D.; Pinard, E.; Stalder, H. WO, 2005014563, 2005.
22. Frederickson, M. WO, 2009125230, 2009.
23. (a) Schön, U.; Messinger, J.; Solodenko, W.; Kirschning, A. *Synthesis* **2012**, *44*, 3822–3828; (b) Kamila, S.; Mukherjee, C.; Mondal, S. S.; De, A. *Tetrahedron* **2013**, *59*, 1339–1348.
24. We have also performed the reactions in one-pot to achieve the quinones also. For example, reacting salicylaldehyde (1 mmol) and morpholine (1.3 mmol) with 10 mol % of Cu(OAc)₂-catalyst in the presence of TBHP for 3 h in acetonitrile resulted in <5% of quinone (**6a**) and 17% of amide (**3a**). We have observed mainly the unreacted starting material.
25. Reddy, K. R.; Venkateshwar, M.; Maheshwari, C. U.; Kumar, P. S. *Tetrahedron Lett.* **2010**, *51*, 2170–2173.
26. Ekoue-Kovi, K.; Wolf, C. *Org. Lett.* **2007**, *9*, 3429–3432.
27. General procedure for the synthesis of salicylamides: In a reaction vessel 1 mmol of salicylaldehyde and 1.3 equiv of secondary amine were dissolved in 3 mL of CH₃CN and 1.5 equiv of TBHP in decane was added dropwise at room temperature. The reaction mixture was heated to 80 °C and stirred for 3 h under nitrogen atmosphere and then cooled in to room temperature. The reaction mixture was poured into water and extracted with ethyl acetate. The organic layer was dried over anhydrous Na₂SO₄ and concentrated in vacuo. The residue was directly purified by column chromatography (hexane–ethyl acetate v/v 4:1) on silica gel to afford the desired product. The products were confirmed by ¹H, ¹³C, IR and Mass spectroscopic analysis. (2-(hydroxyphenyl)(morpholino)methanone (**3a**): Colorless solid, mp 152–154 °C. ¹H NMR (300 MHz, DMSO-d₆): δ 9.53 (s, 1H), 7.33 (dt, J = 7.324, 1.678 Hz, 1H), 7.23 (dd, J = 7.782, 1.678 Hz, 1H), 7.01 (dd, J = 8.240, 1.068 Hz, 1H), 6.86 (dt, J = 7.477, 1.221 Hz, 1H), 3.72–3.78 (m, 8H); ¹³C NMR (75 MHz, DMSO-d₆) δ 167.27, 153.23, 130.28, 128.21, 123.54, 119.19, 115.67, 66.23, 46.86, 41.73; IR (KBr, cm⁻¹): 2970, 2925, 2861, 1591, 1447, 1369, 1281, 1222, 1110, 1017, 844, 756, 640, 607, 556, 511; ESI-MS [M+Na]⁺ m/z 230; HRMS m/z (ESI) calcd for C₁₁H₁₄NO₃Na [M+H]⁺: 208.09681, found: 208.09676.
28. (a) He, T.; Li, H.; Li, P.; Wang, L. *Chem. Commun.* **2011**, 8946–8948; (b) Xu, K.; Hu, Y.; Zhang, S.; Zha, Z.; Wang, Z. *Chem. Eur. J.* **2012**, *18*, 9793–9797; (c) Liu, Z.; Chang, J.; Chen, S.; Shi, E.; Xu, Y.; Wan, X. *Angew. Chem., Int. Ed.* **2012**, *51*, 3231–3235; (d) Mai, W. P.; Wang, H. H.; Li, Z. C.; Yuan, J. W.; Xiao, Y. M.; Yang, L. R.; Mao, P.; Qu, L. B. *Chem. Commun.* **2012**, 10117–10119.
29. General procedure for the synthesis of ortho functionalized carbamates: To a reaction vessel were added 1 mmol of (2-hydroxyphenyl)(pyrrolidin-1-yl)methanone, 10 mol % of copper acetate and dissolved in 2 mL of formamide. To the above reaction mixture 1.5 equiv of TBHP in decane was added drop by drop at room temperature. The reaction temperature was raised to 80 °C and stirred for 3 h. After completion of the reaction, the reaction mixture was cooled to room temperature and extracted with ethyl acetate. The organic layer was dried over anhydrous Na₂SO₄ and concentrated in vacuo. The residue was purified by column chromatography (hexane–ethyl acetate v/v 7:3) to afford the corresponding product. The products were confirmed by ¹H, ¹³C, IR and Mass spectroscopic analysis. 2-(morpholine-4-carbonyl)phenyl isobutyrate (**5a**): ¹H NMR (300 MHz, CDCl₃): δ 7.38–7.44 (br, 1H), 7.19–7.29 (br, 3H), 3.48–3.82 (br, 6H), 3.29–3.35 (br, 2H), 3.09 (s, 3H), 3.00 (s, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 166.32, 153.43, 147.23, 129.66, 128.35, 126.74, 124.74, 122.59, 66.15, 66.07, 46.89, 41.42, 36.07, 35.87; IR (KBr, cm⁻¹): 2974, 2937, 2869, 1717, 1632, 1511, 1445, 1214, 1165, 753, 633, 489; ESI-MS [M+Na]⁺ m/z 301; HRMS m/z (ESI) calcd for C₁₄H₁₈O₄N₂Na [M+Na]⁺: 301.11588, found: 301.11525.
30. Deb, M. L.; Dey, S. S.; Bento, I.; Barros, M. T.; Maycock, C. D. *Angew. Chem., Int. Ed.* **2013**, *52*, 9791–9795.
31. Allen, S. E.; Walvoord, R. R.; Padilla-Salinas, R.; Kozłowski, M. C. *Chem. Rev.* **2013**, *113*, 6234–6458.
32. General procedure for the synthesis of ortho functionalized benzoquinones: To a reaction vessel were added (2-hydroxyphenyl)(pyrrolidin-1-yl)methanone (1 mmol), copper acetate (10 mol %) and dissolved in CH₃CN (3 mL). To the above reaction mixture TBHP in decane was added drop by drop at room temperature. The reaction temperature was raised to 80 °C and stirred for 1 h. After removal of solvent under reduced pressure, the crude product was purified by column chromatography (hexane: ethyl acetate v/v 1:1) to afford the corresponding product. The products were confirmed by ¹H, ¹³C, IR and Mass spectroscopic analysis. 2-(Morpholine-4-carbonyl) cyclohexa-2,5-diene-1,4-dione (**6a**): ¹H NMR (300 MHz, CDCl₃): δ 6.82–6.84 (m, 2H), 6.76–6.78 (m, 1H), 3.70–3.80 (br, 4H), 3.64–3.68 (br, 2H), 3.26–3.30 (br, 2H); ¹³C NMR (75 MHz, CDCl₃) δ 186.30, 184.28, 162.24, 142.64, 136.68, 135.97, 132.76, 66.43, 66.39, 47.25, 42.04; IR (KBr, cm⁻¹): 2962, 2924, 2851, 1631, 1442, 1265, 1201, 842, 543; ESI-MS [M+Na]⁺ m/z 244; HRMS m/z (ESI) calcd for C₉H₉NO₂Na [M+H]⁺: 222.07571, found: 222.07521.