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## Graphical Abstract

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**Isopropanol and potassium *tert*-butoxide promoted intramolecular direct $sp^2$ C-H functionalization: An expedient synthesis of 1,2,3-triazole annulated chromens and quinolones**

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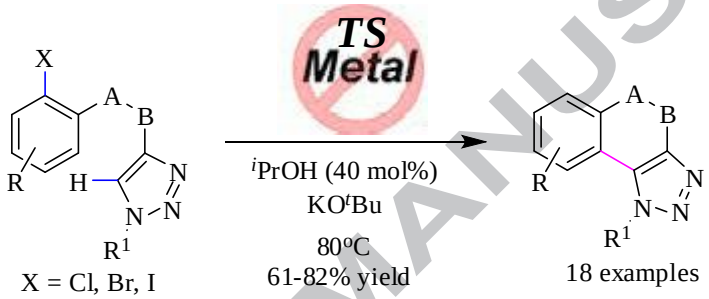

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# Isopropanol and potassium *tert*-butoxide promoted intramolecular direct $sp^2$ C-H functionalization: An expedient synthesis of 1,2,3-triazole annulated chromens and quinolones

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ABSTRACT

A series of 1,2,3-triazole annulated chromen and quinolone derivatives have been synthesized by means of direct $sp^2$ C-H functionalization in presence of *iso*-propanol and potassium *tert*-butoxide. The reaction proceeds through homolytic aromatic substitution (HAS). This efficient as well as simple C-H functionalization methodology offers a straightforward route to 1,2,3-triazole annulated oxygen and nitrogen heterocycles.



## Introduction

In recent years, the chemistry of 1,2,3-triazole derivatives has gained progressive attention in the field of chemical synthesis[1], material science[2], and biology[3-9]. 1,2,3-Triazole derivatives exhibit potential antibacterial[3], antifungal[4], anti-HIV[5a, b], and antimicrobial[5c] activities. Condensed 1,2,3-triazole derivatives acts against the hepatitis C virus[6a], inhibits benzodiazepine[6b] and adenosine[6b, 6c] receptors. Some 1,2,3-triazole derivatives are recognized as DNA cleaving agent[7] and potassium channel activator [8].

2*H*-chromene or 2*H*-benzopyran is a key structural unit of many biologically and pharmaceutically active compounds. For example, daurichromenic acid (**A**) exhibits anti-HIV properties[9] and coutareagenin shows antidiabetic activity[10]. Various 2*H*-benzopyran derivative shows potent antifungal activity [11]. 6-Substituted 2*H*-chromenyl (**B**)[12] shows potential antidiabetic activity as a $Na^+$-C-glucose co-transporter inhibitor (Fig. 1).

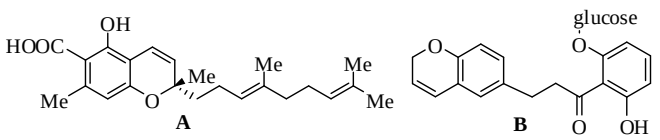
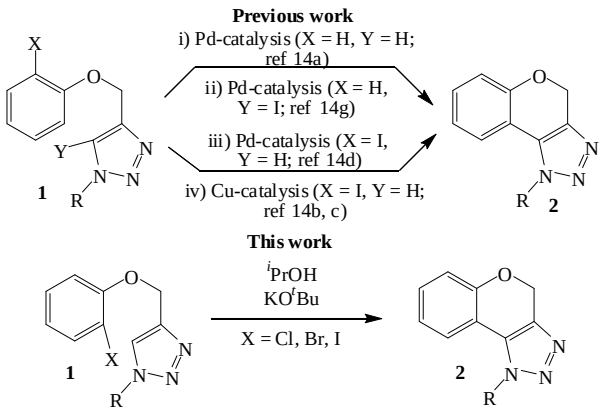



**Figure 1.** Biologically important 2*H*-chromene derivatives

On the other hand quinolone unit is considered as a big family of versatile drugs. Recently, fluoroquinolones are accepted as second-line drugs by the WHO to treat TB and thus their use in MDR-TB is growing due to their wide range of activity and even those drugs can also be taken orally[13]. Considering all those biological and pharmaceutical importance, we assumed that the synthesis of 1,2,3-triazole annulated chromens and quinolones might be promising.

Various reports are available for the synthesis of 1,2,3-triazole annulated oxygen and nitrogen heterocycles[14]. However, all of them followed transition metal-catalysed (Pd[14a, d] and Cu[14b, c, f]) methodology. Despite the significant advances in metal catalysed organic synthesis, the development of economical and environmentally compassionate protocols are still a challenge. In this perspective, transition metal-free C-H functionalization protocols appear to be particularly attractive[15-22].




**Scheme 1.** Synthesis of 1,2,3-triazole annulated chromens.

In last few years, C-H functionalization via homolytic aromatic substitution (HAS)[15, 16] has gained immense interest in chemical synthesis. These methodologies involves radical anion intermediates[16]. This low toxic and simple protocol might be very attractive and valuable alternatives to the transition metal-catalyzed C-H transformation. In 2006, Rossi et al. reported the synthesis of homoaporphine alkaloids by $^{t}$BuOK mediated photo induced ortho $sp^2$ C-H arylation under transition metal-free condition[17a]. After that in 2008, Itami et al. reported $^{t}$BuOK promoted C-H bond arylation of heterocycles using alry iodides under microwave condition[18a]. Following these ground breaking work, different groups developed a number of transition metal-free protocols *e.g.* photo induced $sp^2$ C-H functionalization[17], base mediated and organic electron donar ligand (phen, diamine, NHC etc) catalysed $sp^2$ C-H arylation[19-21] and alcohol $^{t}$BuOK promoted $sp^2$ C-H functionalization[22] for biaryl and heterocycle synthesis.

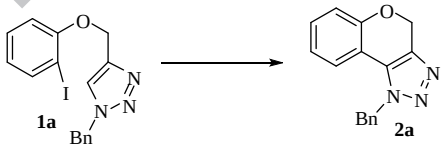
To the best of our knowledge, though there are few examples of base and ligand catalysed synthesis of heterocycles via $sp^2$ functionalization[20], base and acohol catalysed heterocycle synthesis is rare[22b] which must be a topic of immanse interest. In the continuation of our project, transition metal-free synthesis of heterocycles[18d, e]; herein, we report the synthesis of 1,2,3-triazole annulated chromen (**2**) and quinolone (**4**) derivatives with the aid of catalytic amount of *iso*-propanol in presence of potassium *tert*-butoxide through an HAS mechanism.

**Results and Discussion**

Initially, we started our investigation with 1-benzyl-4-((2-iodophenoxy) methyl)-1*H*-1,2,3-triazole (**1a**) (for synthesis of compound **1** and **3** see experimental section) as a model substrate and a set of reactions (Table 1) were performed. After surveying the literature[22], we choose 1 mmol of **1a** EtOH (20 mol %), potassium *tert*-butoxide (3 mmol) in dry DMF at 80 $^{o}$C as initial reaction conditions for this intramolecular coupling reaction. The reaction was continued for 6 h and only 5 % of the desired product **2a** was isolated, while 45 % conversion of the starting material (Table 1, entry 1) was observed. Then the use of a sublimed grade potassium *tert*-butoxide[23] instead of ordinary potassium *tert*-butoxide, offered 67 % yield of **2a** with 93 % conversion of the starting material (Table 1, entry 2). With sodium *tert*-butoxide a comparable yield (64 %) of **2a** was isolated during a longer reaction period (10 h) (Table 1, entry 3). Small amount (11 % yield of **2a** with 38 % conversion of **1a**) of **2a** was isolated with less basic lithium *tert*-butoxide (Table 1, entry 4). No product was obtained in absence of base, in presence of $Et_3N$ and $Na_2CO_3$ (Table 1, entries 5-7) and the starting material (**1a**) remain unchanged.

Noticing a steep improvement with sublime grade potassium *tert*-butoxide, different alcohols were examined under this reaction conditions. The use of $^{n}$BuOH (Table 1, entry 8) and $^{i}$PrOH (Table 1, entry 9) with sublimed potassium *tert*-butoxide provided 69 % and 76 % yields of **2a** respectively with total conversion of starting material, whereas with $^{t}$BuOH (Table 1, of entry 10) only 5 % yield of **2a** was recorded. Increasing of alcohol ($^{i}$PrOH) loading from 20 mol % to 40 mol % the yield of the reaction increased to 82 % (Table 1, entry 11). During optimization, different polar and non polar solvents were also ee continuened under this reaction conditions. With MeCN, only a trace amount of **2a** was obtained (Table 1, entry 12), but with 1,4-dioxane, toluene and mesitylene no sign of formation of **2a** was observed (Table 1, entries 13-15). In absence of $^{i}$PrOH (Table 1, entry 16) formation of **2a** was not found, when $^{i}$PrOH was used as solvent (Table 1, entry 17) 62 % yield of **2a** was noticed. Only a trace amount of **2a** (Table 1, entry 18) was isolated under open air condition and most of the starting material remain unreacted. Thus 40 mol % $^{i}$PrOH, 3 equiv. KO$^{t}$Bu in DMF at 80 $^{o}$C under $N_2$ atmosphere for 6 h was accepted as optimized reaction conditions. With the optimized reaction conditions in hand, we further explored the substrate scope (**1b-k**) of this methodology (Scheme 2).

**Table 1. Optimization of reaction conditions.**




| Entry | Cat (mol %) | Base | Solvent | Yield (%)[a] |
|---|---|---|---|---|
| 1 | EtOH (20) | KO$^{t}$Bu[b] | DMF | 5 |
| 2 | EtOH (20) | KO$^{t}$Bu | DMF | 67 |
| 3 | EtOH (20) | NaO$^{t}$Bu | DMF | 64[c] |
| 4 | EtOH (20) | LiO$^{t}$Bu | DMF | 11 |
| 5 | EtOH (20) | - | DMF | 0 |
| 6 | EtOH (20) | $Et_3N$ | DMF | 0 |
| 7 | EtOH (20) | $Na_2CO_3$ | DMF | 0 |
| 8 | $^{n}$BuOH (20) | KO$^{t}$Bu | DMF | 69 |
| 9 | $^{i}$PrOH (20) | KO$^{t}$Bu | DMF | 76 |
| 10 | $^{t}$BuOH (20) | KO$^{t}$Bu | DMF | 5 |
| **11** | **$^{i}$PrOH (40)** | **KO$^{t}$Bu** | **DMF** | **82** |
| 12 | $^{i}$PrOH (40) | KO$^{t}$Bu | MeCN | trace |
| 13 | $^{i}$PrOH (40) | KO$^{t}$Bu | 1,4-dioxan | 0 |
| 14 | $^{i}$PrOH (40) | KO$^{t}$Bu | toluene | 0 |
| 15 | $^{i}$PrOH (40) | KO$^{t}$Bu | mesytelene | 0 |
| 16 | - | KO$^{t}$Bu | DMF | 0 |
| 17 | $^{i}$PrOH | KO$^{t}$Bu | - | 62[d] |
| 18 | $^{i}$PrOH (40) | KO$^{t}$Bu | DMF | trace[e] |

**Reaction conditions:** 1.0 mmol of **1a**, 3.0 mmol base, alcohol and 10 mL solvent were heated for 6 h under $N_2$ atmosphere at 80 $^{o}$C.

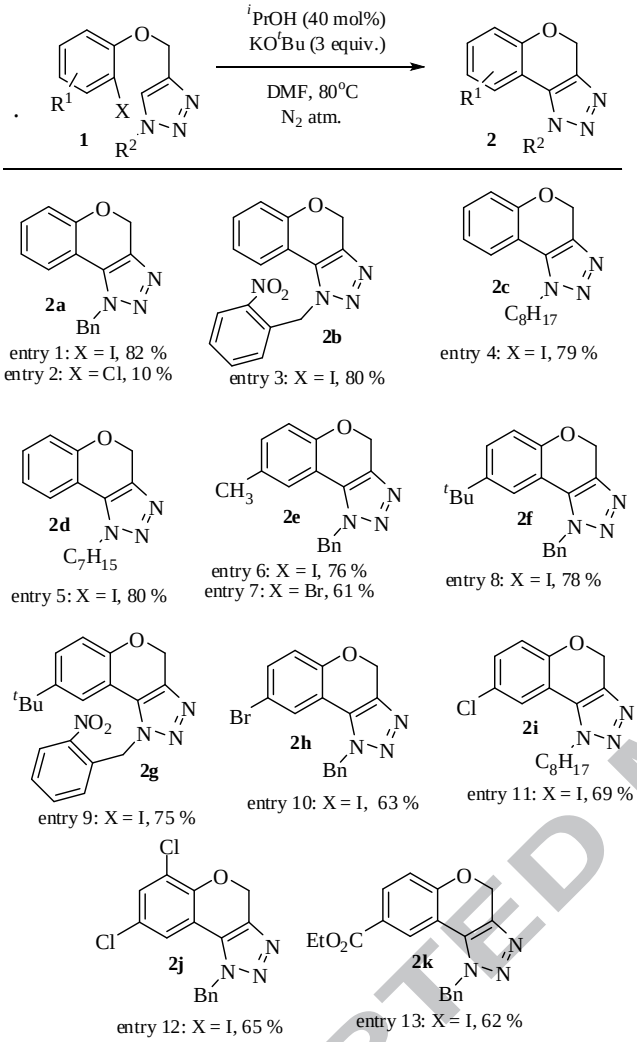
Bold values implies optimized reaction conditions.

[a] Yields were calculated after flash chromatography

[b] Ordinary KO$^{t}$Bu was used

[c] Reaction performed for 10 h

[d] Reaction performed in 10 mL $^{i}$PrOH, [e] Reaction performed under open air

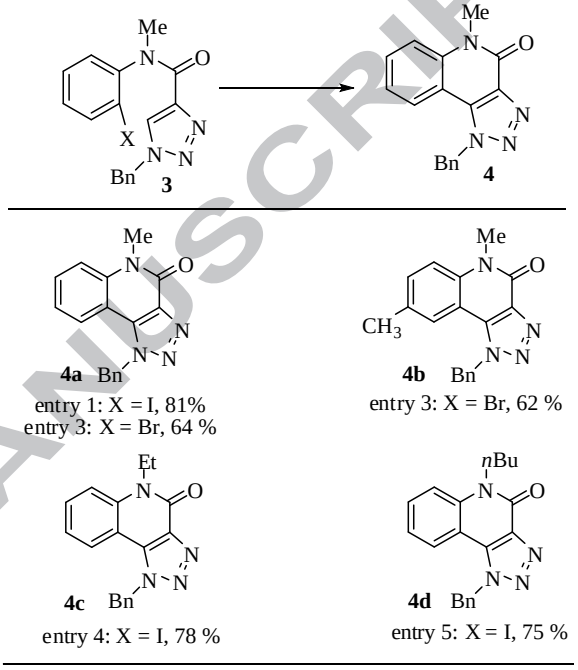



**Reaction condition:** A mixture of 1 mmol **1**, 3 mmol KO$^{t}$Bu, 40 mol % $^{i}$PrOH in 10 mL DMF was heated for 6 h under $N_2$ atmosphere at 80 $^{o}$C. Yields of isolated product based on **1**.

**Scheme 2.** Synthesis of *N*-substituted 1,4-dihydrochromeno[3,4-*d*][1,2,3]triazole.

In general, the yield of the reactions were good to very good (61-82 %). Alkyl and benzyl substitution on triazole nitrogen atom (**1a-d**) gave comparable and very good yield of desired product (**2a-d**). Alkyl substitution on phenyl ring has no effect on the yield of this reaction and also gave very good yield of **2e** (76 %), **2f** (78 %) and **2g** (75 %). The starting material (**1h**, **1i**, **1j**) with halogen (Br and Cl) substitution on phenyl ring were well tolerated and went efficiently under the optimized reaction conditions with a moderate yield. The phenyl ring with a bromo group (**1h**) gave somewhat lower yield (**2h**: 63%) than the chloro substituted starting material (**2i**: 69 %; **2j**: 65 %). Substrate **1k** with a strong electron withdrawing carboethoxy group on phenyl ring went smoothly under this reaction conditions with 62 % yield of **2k**. In case of **1j**; single product **2j** was isolated (entry-12) only by the substituting of iodo group and no other product was obtained corresponding to the substitution of chloro group was obtained. When X group on the substrate was changed from iodo to bromo or chloro, the yield of the reaction decreased. Chloro substrate gave very poor yield (10 %, entry-2), while bromo substrate afforded somewhat lower yield (61 %, entry-7) than the corresponding iodo compound.

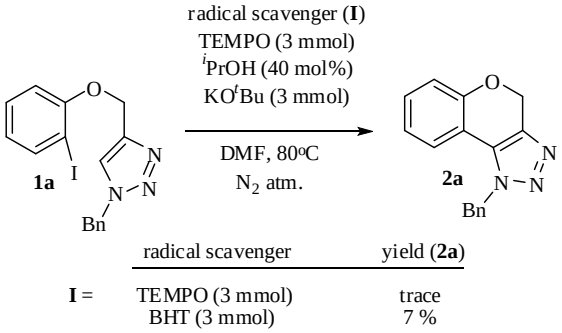
We also tested the validity of this methodology towards the synthesis of 1,2,3-triazolo fused quinolone ring systems **4** (Scheme 3). To our delight, the catalytic system also proved to be fruitful for the synthesis of *N*-substituted 1*H*-[1,2,3]triazolo[4,5-*c*]quinolin-4(5*H*)-ones (**4**).




**Reaction condition:** A mixture of 1 mmol **3**, 3 mmol KO$^{t}$Bu, 40 mol % $^{i}$PrOH in 10 mL DMF was heated at 80 $^{o}$C for 6 h under $N_2$ atmosphere. Yields were calculated after flash chromatography.

**Scheme 3.** Synthesis of *N*-substituted1*H*-[1,2,3]triazolo[4,5-*c*]quinolin-4(5*H*)-one derivatives.

All triazolo fused quinolone derivatives **4a-d** were isolated in good to very good yield (62-81 %). Substrate **3** with iodo group (**3a**) gave 81 % yield of **4a**, whereas with a bromo group gave 64 % yield of **4a**.

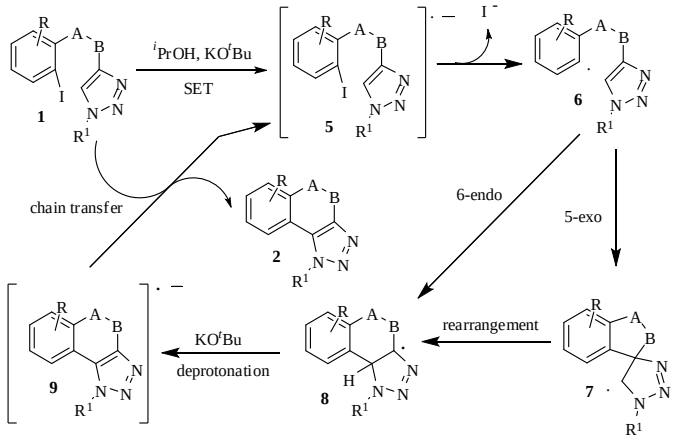



**Scheme 4.** Coupling reaction in presence of radical scavenger (TEMPO and BHT).

The yield difference between iodo, bromo and chloro substrates as well as solvent effect (Table 1, entry 12) led us to assume that the reaction might follow a radical pathway. Consequently we performed the reaction separately in presence of TEMPO (2,2,6,6-tetramethylpiperidine 1-oxyl) and BHT (butylated

hydroxy toluene) (Scheme 4) which produced a trace and 7 % yield of desired product **2a** respectively, supporting the radical pathway of the reaction.

Cosidering all the facts we assumed that aryl radical generation might be a step in this coupling reaction and following Murphy et al.[22e] we propose a plausible mechanistic pathway for this coupling reaction in Scheme 5.




**Scheme 5.** Plausible mechanistic pathway.

In presence of alcohol and KO$^t$Bu, compound **1** generates anion radical **5** through single electron transfer (SET)[22]. Radical anion **5** then transforms to aryl radical **6** through elimination of $I^-$. This aryl radical **6** then adds to the double bond of triazole ring to give 5-exo species **7** and/or 6-endo species **8**. Species **7** may rearranges to thermodynamically more stable **8**. In presence of KO$^t$Bu radical **8** gives another radical anion **9** via deprotonation. A radical chain transfer reaction between **9** and **1** result the desired product **2** along with regeneration of radical anion **5** and continues the cycle.

Thus from the mechanistic point of view, the yield difference from iodo to bromo to chloro [**1a** (X = I) Vs **1a**$^/$ (X = Cl); **1e** (X = I) Vs **1e**$^/$ (X = Br) and **3a** (X = I) Vs **3a**$^/$ (X = Br)] can be explained by the ease of generation of aryl radical. Arenes with lower absolute values of reduction potential or half-wave potential easily generate anion radicals. For halogens the order of lowering of absolute value of reduction potential is I>Br>Cl[24]. Hence, the iodo compound with lower value of absolute reduction potential generate anion radical **5** more readily and gives the desired product **2** in higher yield than the corresponding bromo and chloro compound.

## Conclusions

In conclusion, we have demonstrated a successful intramolecular $sp^2$ C-H functionalization methodology towards the synthesis of 1,2,3-triazolo annulated chromen and quinolone ring systems. This methodology is efficient, operationally simple and demands inexpensive $^i$PrOH and $^t$BuOK. Further development of transition metal-free C-H functionalization protocol for the synthesis of biologically attractive heterocycles is being explored in our lab.

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## Representative procedure for synthesis of compound 2a and NMR data:

### General procedure for the preparation of products (2 & 4):

Compound **1** (1 mmol), *iso*-propanol (40 mol %) and KO$^t$Bu (3 mmol) were added in preheated Schlenk tubes under $N_2$ atmosphere. 10 mL dry DMF was added into tubes by syringe. The mixture was stirred under $N_2$ atmosphere in sealed Schlenk tubes at 80 $^o$C for 6 h. The reaction was cooled down to room temperature. The mixture was filtered through a short plug of silica gel, washed with copious ethyl acetate. The combined organic layer was washed with $H_2O$ (3 ×10 mL) and saturated NaCl (aq) (1 ×10 mL). The organic part was dried over $Na_2SO_4$, concentrated under vacuum and purified by flash chromatography on 230-400 mesh silica gel using ethyl acetate/petroleum ether (2:8) as the eluent to afford product **2** .

### 1-Benzyl-1,4-dihydrochromeno[3,4-d][1,2,3]triazole (2a):

White solid; Yield: 82 % (X = I), 10 % (X = Cl)

$^1$H-NMR (400 MHz, $CDCl_3$, ppm): δ 5.49 (s, 2H); 5.82 (s, 2H); 6.90 (t, *J* = 7.2 Hz, 1H); 7.01 (d, *J* = 7.6 Hz, 1H), 7.18-7.23 (m, 4H); 7.29-7.38 (m, 3H).

$^{13}$C-NMR (100 MHz, $CDCl_3$, ppm): δ 53.0, 64.4, 113.8, 117.9, 122.1, 122.6, 126.5, 127.8, 128.4, 129.2, 130.6, 134.7, 139.7, 153.7.

HRMS calcd. for $C_{16}H_{14}N_3O$ $[M + H]^+$: 264.1137; found: 264.1142

## References

1. Moses, J. E.; Moorhouse, A. D. *Chem. Soc. Rev.* **2007**, *36*, 1249-1262.
2. Hawker, C. J.; Wooley, K. L. *Science* **2005**, *309*, 1200-1205.
3. Phillips, O. A.; Udo, E. E.; Abdel-Hamid, M. E.; Varghese, R. *Eur. J. Med. Chem.* **2009**, *44*, 3217-3227.
4. Aher, N. G.; Pore, V. S.; Mishra, N. N.; Kumar, A.; Shukla, P. K.; Sharma, A.; Bhat, M. K. *Bioorg. Med. Chem. Lett.* **2009**, *19*, 759-763.
5. a) Giffin, M. J.; Heaslet, H.; Brik, A.; Lin, Y.-C.; Cauvi, G.; Wong, C.-H.; McRee, D. E.; Elder, J. H.; Stout, C. D.; Torbett, B. E. *J. Med. Chem.* **2008**, *51*, 6263-6270; b) Whiting, M.; Muldoon, J.; Lin, Y.-C.; Silverman, S. M.; Lindstrom, W.; Olson, A. J.; Kolb, H. C.; Finn, M. G.; Sharpless, K. B.; Elder, J. H.; Fokin, V. V. *Angew. Chem. Int. Ed.* **2006**, *45*, 1435-1439; c) Demirbas, N.; Karaoglu, S. A.; Demirbas, A.; Sancak, K. *Eur. J. Med. Chem.* **2004**, *39*, 793-804.
6. a) Wang, P.; Du, J.; Rachakonda, S.; Chun, B.-K.; Tharnish, P. M.; Stuyver, L. J.; Otto, M. J.; Schinazi, R. F.; Watanabe, K. A. *J. Med. Chem.* **2005**, *48*, 6454-6460; b) Biagi, G.; Giorgi, I.; Livi, O.; Scartoni, V.; Betti, L.; Giannaccini, G.; Trincavelli, M. L. *Eur. J. Med. Chem*. **2002**, *37*, 565-571; c) Betti,V.; Biagi, G.; Giannaccini, G.; Giorgi, I.; Livi, O.; Lucacchini, A.; Manera, C.; Scartoni, V. *J. Med. Chem.* **1998**, *41*, 668-673.
7. Manfredini, S.; Vicentini, C. B.; Manfrini, M.; Bianchi, N.; Rutigliano, C.; Mischiati, C.; Gambari, R. *Bioorg. Med. Chem.* **2000**, *8*, 2343-2346.
8. Calderone, V.; Giorgi, I.; Livi, O.; Martinotti, E.; Mantuano, E.; Martelli, A.; Nardi, A. *Eur. J. Med. Chem.* **2005**, *40*, 521-528.
9. a) Iwata, N.; Wang, N.; Yao, X.; Kitanaka, S. *J. Nat. Prod.* **2004**, *67*, 1106-1109; b) Hu, H.; Harrison, T. J.; Wilson, P. D. *J. Org. Chem.* **2004**, *69*, 3782-3786.

10. Korec, R.; Heniz, S. K.; Zoukas, T. *Arzneimittel-Forschung* **2000**, *50*, 122-128.

11. Morandim, A. A.; Bergamo, D. C. B.; Kato, M. J.; Cavalheiro, A. J.; Bolzani, V. S.; Furlan, M. *Phytochem. Anal.* **2005**, *16*, 282-286.

12. Hongu, M.; Tanaka, T.; Funami, N.; Saito, K.; Arakawa, K.; Matsumoto, M.; Tsujihara, K. *Chem. Pharm. Bull.* **1998**, *46*, 22-33.

13. a) O'Brien, R. J. *Am J Respir Crit Care Med.* **2003**, *168*, 1266-1268; b) Mdluli, K.; Ma, Z. *Infect Disord Drug Targets.* **2007**, *7*, 159-168.

14. a) Ackermann, L.; Jeyachandran, R.; Potukuchi, H. K.; Novák, P.; Büttner, L. *Org. Lett.* **2010**, *12*, 2056-2059; b) Reddy, M. N.; Kumara Swamy, K. C. *Eur. J. Org. Chem.* **2012**, 2013-2022; c) Jeyachandran, R.; Potukuchiand, H. K.; Ackermann, L. *Beilstein J. Org. Chem.* **2012,** *8*, 1771-1777; d) Chen, C.-Y.; Yang, C.-H.; Hu, W.-P.; Vandavasi, J. K.; Chunga, M.-I.; Wang, J.-J. *RSC Advances* **2013**, *3*, 2710-2719; e) Habib, P. M.; Rama Raju, B.; Kavala, V.; Kuo, C.-W.; Yao, C.-F. *Tetrahedron* **2009**, *65*, 5799-5804; f) Cai, Q.; Yan, J.; Ding, K. *Org. Lett.* **2012**, *14*, 3332-3335; g) Schulman, J. M. ; Friedman, A. A.; Panteleev, J.; Lautens, M. *Chem. Commun.*, **2012**, *48*, 55–57.

15. a) Bolton, R.; Williams, G. H. *Chem. Soc. Rev.* **1986**, *15*, 261-289; b) Studer, A. Radicals in Organic Synthesis, Vol. 2, 1st ed. (Eds.: P. Renaud, M. P. Sibi), Wiley-VCH, Weinheim, **2001**, p. 44. c) Bowman, W. R.; Storey, J. M. D. *Chem. Soc. Rev.* **2007**, *36*, 1803-1822; d) Vaillard, S. E.; Schulte, B.; Studer, A. Modern Arylation Methods (Ed.: L. Ackermann), Wiley-VCH, Weiheim, **2009**, p. 475.

16. a) Studer, A.; Curran, D. P. *Angew. Chem. Int. Ed.* **2011**, *50*, 5018-5022; b) Sun, C.-L.; Shi, Z.-J. *Chem. Rev.* **2014**, *114*, 9219-9280.

17. a) Barolo, S. M.; Teng, X.; Cuny, G. D.; Rossi, R. A. *J. Org. Chem.* **2006**, *71*, 8493-8499; b) Buden, M. E.; Guastavino, J. F.; Rossi, R. A. *Org. Lett.* **2013**, *15*, 1174-1177; c) Guastavino, J. F.; Buden, M. E.; Rossi, R. A. *J. Org. Chem.* **2014**, *79*, 9104-9111; d) Prier, C. K.; MacMillan, D. W. C. *Chem. Sci.* **2014**, *5*, 4173-4178.

18. a) Yanagisawa, S.; Ueda, K.; Taniguchi, T.; Itami, K. *Org. Lett.* **2008**, *10*, 4673-4676; b) Masters, K.-S.; Bräse, S. *Angew. Chem. Int. Ed.*, **2013** *52*, 866-869; c) Liu, W.; Xu, L; Bi, Y. *RSC Advances*, **2014**, *4*, 44943-44947; d) Mondal, B.; Hazra. S.; Roy, B. *Tetrahedron Letters* **2014**, 55, 5625–5628; e) Mondal, B.; Roy, B. *RSC Adv.*, **2015**, 5, 69119-69123.

19. a) Sun, C.-L.; Li, H.; Yu, D. G.; Yu, M.; Zhou, X.; Lu, X. Y.; Huang, K.; Zheng, S. F.; Li, B. J.; Shi, Z.-J. *Nat. Chem.* **2010**, *2*, 1044-1049; b) Liu, W.; Cao, H.; Zhang, H.; Zhang, H.; Chung, K. H.; He, C.; Wang, H.; Kwong, F. Y.; Lei, A. *J. Am. Chem. Soc.* **2010**, *132*, 16737-16740; c) Shirakawa, E.; Itoh, K.; Higashino, T.; Hayashi, T. *J. Am. Chem. Soc.* **2010**, *132*, 15537-15539.

20. a) Roman, D. S.; Takahashi, Y.; Charette, A. B. *Org. Lett.* **2011**, *13*, 3242-3245; b) Sun, C.-L.; Gu, Y.-F.; Huang, W.-P.; Shi, Z.-J. *Chem. Commun.* **2011**, *47*, 9813-9815; c) Rueping, M.; Leiendecker, M.; Das, A.; Poisson, T.; Bui, L. *Chem. Commun.* **2011**, *47*, 10629-10631; d) Bhakuni, B. S.; Kumar, A.; Balkrishna, S. J.; Sheikh, J. A.; Konar, S.; Kumar, S. *Org. Lett.* **2012**, *14*, 2838-2841; e) De, S.; Ghosh, S.; Bhunia, S.; Sheikh, J. A.; Bisai, A. *Org. Lett.* **2012**, *14*, 4466-4469.

21. a) Qiu, Y.; Liu, Y.; Yang, K.; Hong, W.; Li, Z.; Wang, Z.; Yao, Z.; Jiang, S. *Org. Lett.* **2011**, *13*, 3556-3359; b) Yong, G.-P.; She, W.-L.; Zhang, Y.-M.; Li, Y.-Z. *Chem. Commun.* **2011**, *47*, 11766-11768; c) Chen, W.-C.; Hsu, Y.-C.; Shih, W.-C.; Lee, C.-Y.; Chuang, W. -H.; Tsai, Y.-F.; Chen, P. P.-Y.; Ong, T.-G. *Chem. Commun.* **2012**, *48*, 6702-6704; d) Tanimoro, K.; Ueno, M.; Takeda, K.; Kirihata, M.; Tanimori, S. *J. Org. Chem.* **2012**, *77*, 7844-7849.

22. a) Shirakawa, E.; Zhang, X.; Hayashi, T. *Angew. Chem. Int. Ed.* **2011**, *50*, 4671-4674; b) Wu, Y.; Wong, S. M.; Mao, F.; Chan, T. L.; Kwong, F. Y. *Org. Lett.* **2012**, *14*, 5306-5309; c) Liu, W.; Tian, F.; Wang, X.; Yu, H.; Bi, Y. *Chem. Commun.* **2013**, *49*, 2983-2985; d) Wu, Y.; Choy, P. Y.; Kwong, F. Y. *Org. Biomol. Chem.* **2014**, *12*, 6820-6823; e) Zhou, S.; Doni, E.; Anderson, G. M.; Kane, R. G.; MacDougall, S. W.; Ironmonger, V. M.; Tuttle, T.; Murphy, J. A. *J. Am. Chem. Soc.* **2014**, *136*, 17818−17826.

23. Sublimed grade (trace metal basis) Potassium *tert*-butoxide (CAS 865-47-4) was used for this reaction.

24. Sease, J. W.; Burton, F. G.; Nickol, S. L. *J. Am. Chem. Soc.* **1968**, *90*, 2595-2598.