


Cite this: *RSC Adv.*, 2020, 10, 33455

Received 23rd June 2020

Accepted 1st September 2020

DOI: 10.1039/d0ra05497f

rsc.li/rsc-advances

One-pot synthesis of indoles and quinolinones from *ortho*-tosylaminophenyl-substituted *para*-quinone methides†

Junwei Wang,^{‡*} Xiang Pan,[‡] Quanjin Rong, Lei Zhao, Lin Zhao, Weichen Dai, Kun Zhao^{ID*} and Lihong Hu*

A facile one-pot synthesis has been developed through alkylation/acylation of *ortho*-tosylaminophenyl-substituted *para*-quinone methides followed by an intramolecular 1,6-conjugate addition and oxidation sequence. This cascade reaction occurs readily in good yield (up to 95%), providing a divergent synthetic approach to structurally diverse 2,3-disubstituted indoles and 3,4-diaryl-substituted quinolinones.

Nitrogen-containing heterocycles as privileged structural motifs are widely found in natural products and small molecule pharmaceuticals.¹ In particular, indoles and quinolinones are of great significance in drug discovery because of their diverse biological activities.^{2,3} For example, indometacin (I), a synthetic indole acetic acid derivative, is an effective non-steroidal anti-inflammatory drug.^{2a} Fluvastatin sodium (II) and compound III, two 3-aryl-substituted indole derivatives, have been designed as a HMG-CoA reductase inhibitor^{2b} and carbonic anhydrase inhibitor,^{2c} respectively. 4-Phenyl-substituted quinolinone derivatives such as IV, V and VI have been demonstrated to possess excellent antitumor activity (Fig. 1).^{3b-d} Thus, it is highly desirable to develop more efficient and facile methods to construct these nitrogen-containing heterocycles.

Recently, *para*-quinone methides (*p*-QMs) have emerged as versatile building blocks due to their intrinsic reactivities.⁴ A large number of transformations based on *p*-QMs have been achieved since the seminal reports by Fan⁵ and Jørgensen.⁶ For example, annulation reactions based on simple *p*-QMs and vinyl *p*-QMs have been reported by Yao, Fan, Zhao, and Waser groups.⁷ In 2016, Enders and co-workers pioneered the design and application of *ortho*-hydroxyphenyl-substituted *p*-QMs in [4 + 2] cyclizations.⁸ After that the use of *ortho*-hydroxyphenyl-substituted *p*-QMs in [4 + 1], [4 + 2] and [4 + 3] cyclizations reactions was extensively investigated,⁹⁻¹² allowing the synthesis of diverse oxygenous heterocyclic motifs (Scheme 1a). Quite recently our group designed *in situ* generated *ortho*-tosylaminophenyl-substituted *p*-QMs and successfully applied

this class of substrates in [4 + 2] and [4 + 1] annulation reactions to synthesize tetrahydroquinolines and 2,3-dihydroindoles, respectively (Scheme 1b).¹³

Although great progress has been made in the synthesis of oxygen-containing heterocyclic frameworks, the application of *p*-QMs in the construction of nitrogen-containing heterocyclic frameworks remains underdeveloped. Cyclizations using *ortho*-tosylaminophenyl-substituted *p*-QMs as building blocks are still rather limited. Whereas, the privileged status of indoles and quinolinones in organic synthesis and biological applications demands more efficient strategies for their preparation. In 2019, Anand and co-workers reported a one-pot synthesis of oxygen-based heterocycles from 2-hydroxyphenyl-substituted *p*-QMs, which provided an efficient method for the construction of 2,3-disubstituted benzo[*b*]furans, 2,3-dihydrobenzofurans and diaryl-substituted coumarin derivatives.¹⁰ Inspired by this work, we wondered whether this strategy could be extended to *ortho*-tosylaminophenyl-substituted *p*-QMs, so that we might

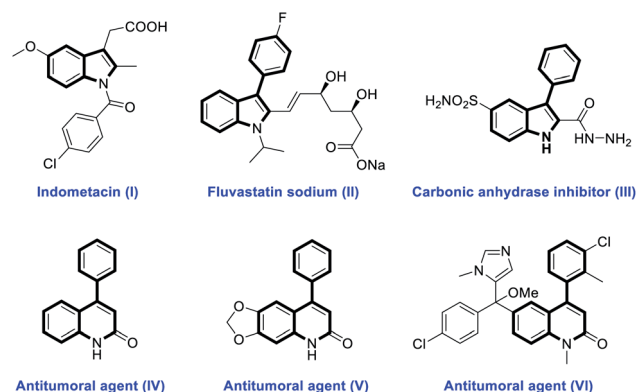


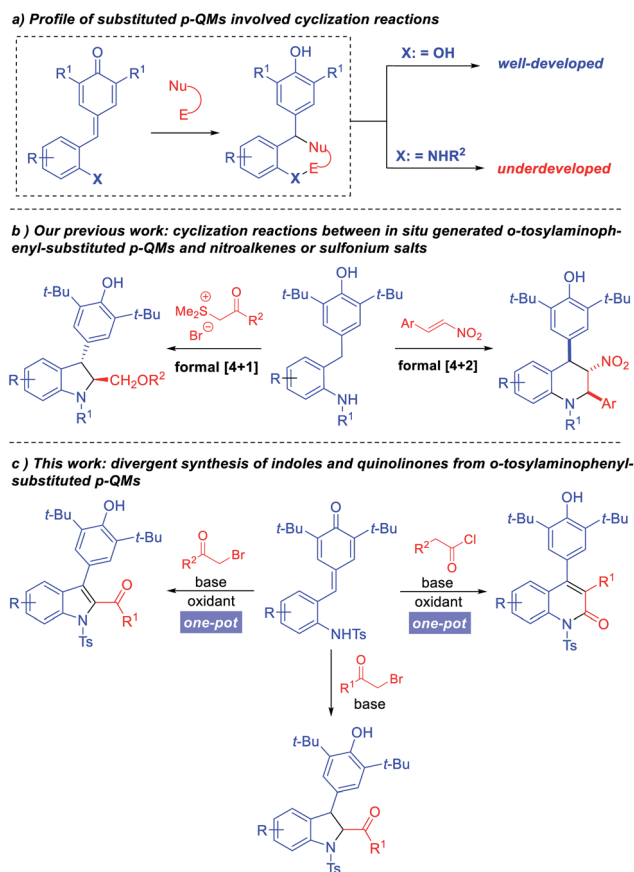
Fig. 1 Selected natural products and synthetic compounds containing indole and quinolinone frameworks.

Jiangsu Key Laboratory for Functional Substances of Chinese Medicine, School of Pharmacy, Nanjing University of Chinese Medicine, Nanjing, P. R. China. E-mail: jwwang@njucm.edu.cn; kunzhao13@gmail.com; lhhu@njucm.edu.cn

† Electronic supplementary information (ESI) available. CCDC 2009636. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/d0ra05497f

‡ Equally contributing authors.



Scheme 1 Reported reactions based on *p*-QMs and our design.

establish a powerful divergent cascade reaction to synthesize 2,3-dihydroindoles, indoles and quinolinone derivatives.

We hypothesized that assembly of 2,3-dihydroindoles could be realized through the union of *ortho*-tosylaminophenyl-substituted *p*-QMs and α -halo ketones *via* *N*-alkylation followed by intramolecular cyclization. Then, a suitable oxidant can promote the *in situ* generation of indoles. Although we have reported the synthesis of 2,3-dihydroindoles through a formal [4 + 1] annulation of *ortho*-tosylaminophenyl-substituted *p*-QMs with sulfur ylides,^{13b} the direct one-pot synthesis of 2,3-disubstituted indoles and 3,4-diaryl-substituted quinolinone derivatives from *ortho*-tosylaminophenyl-substituted *p*-QMs through *N*-alkylation/acylation followed by intramolecular 1,6-conjugate addition and oxidation strategy has not been reported yet (Scheme 1c).

To verify our hypothesis, we initially tried to identify the optimal conditions for the synthesis of 2,3-dihydroindoles before exploring the one-pot synthesis of indoles. *ortho*-Tosylaminophenyl-substituted *p*-QMs **1a** and 2-bromoacetophenone **2a** were chosen as the model substrates to optimize the reaction conditions (Table 1). To our delight, in the presence of Et₃N (1.5 equiv.) in CH₃CN at 20 °C, the expected reaction occurred and the desired product **3a** could be obtained, albeit with moderate yield (Table 1, entry 1). Encouraged by this promising result, different bases were evaluated, and we found that the inorganic base Cs₂CO₃ performed best, offering **3a** in

Table 1 Reaction condition optimization studies^a

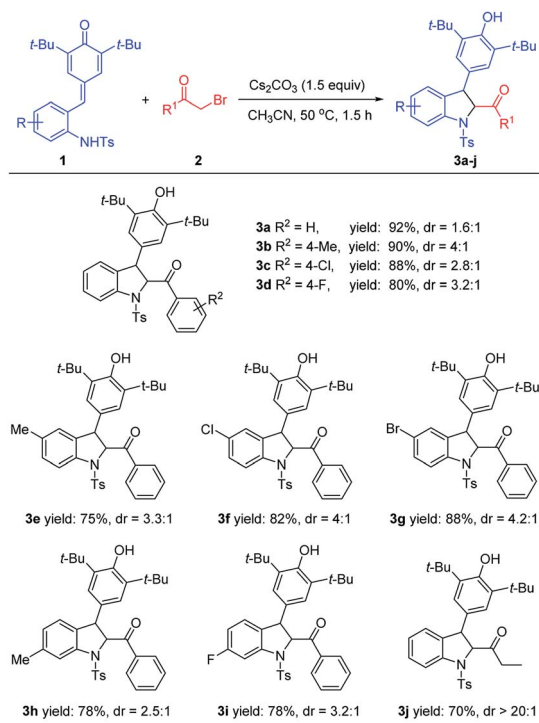
Entry	Base	<i>T</i> (°C)	Solvent	Yield ^b (%)
1	Et ₃ N	20	CH ₃ CN	54
2	DBU	20	CH ₃ CN	38
3	^t Pr ₂ NH	20	CH ₃ CN	7
4	Na ₂ CO ₃	20	CH ₃ CN	4
5	K ₂ CO ₃	20	CH ₃ CN	5
6	Cs ₂ CO ₃	20	CH ₃ CN	82
7	Cs ₂ CO ₃	20	CH ₂ Cl ₂	60
8	Cs ₂ CO ₃	20	CHCl ₃	57
9	Cs ₂ CO ₃	20	Acetone	80
10	Cs ₂ CO ₃	20	Toluene	53
11	Cs ₂ CO ₃	20	DCE	50
12 ^c	Cs ₂ CO ₃	20	CH ₃ CN	80
13 ^d	Cs ₂ CO ₃	20	CH ₃ CN	76
14 ^e	Cs ₂ CO ₃	20	CH ₃ CN	83
15	Cs ₂ CO ₃	35	CH ₃ CN	85
16	Cs ₂ CO ₃	50	CH ₃ CN	92

^a All reactions were conducted with **1a** (0.11 mmol), **2a** (0.10 mmol), base (1.5 equiv.), solvent (1.5 mL), 1.5 h. ^b Determined by ¹H NMR using 1,3,5-trimethoxybenzene as an internal standard; dr > 20 : 1. ^c 1.0 equiv. of base was used. ^d 2.0 equiv. of base was used. ^e *t* = 3 h.

82% yield (Table 1, entry 6). Striving for higher efficiency of this reaction, the effect of solvent was next investigated and we found that other solvents (*e.g.* CH₂Cl₂, CHCl₃, acetone, toluene and DCE) failed to improve the yield (entries 7–11). After establishing the optimal base and solvent, the dosage of the base was then evaluated and it was found that increasing or decreasing the amount of base is not beneficial for the reaction (entries 12 and 13). We further examined the reaction time and the reaction temperature (entries 14–16). Notably, when the temperature reached 50 °C, the expected product **3a** could be afforded in a good yield of 92%. Finally, the optimal reaction conditions were selected as those shown in entry 16 (1.5 equiv. of Cs₂CO₃ as base, CH₃CN as solvent and reaction at 50 °C for 1.5 h).

After establishing the optimal reactions conditions for 2,3-dihydroindoles, the substrate scope was explored. As shown in Table 2, a wide range of *p*-QMs **1** bearing different substituents on the benzene ring and different substituted bromomethyl aryl ketones and bromomethyl alkyl ketones could be smoothly processed to afford the expected products **3a–3j** in 70–92% yields. The reaction efficiency was less affected by the variations of the electronic properties or the position of substituents on the benzene ring. Based on this good result, we continued to investigate the one-pot synthesis of indoles, directly from the *in situ* dehydrogenative oxidation of 2,3-dihydroindoles by using suitable oxidant. After several attempts (*e.g.* Ag₂CO₃, Ag₂O,

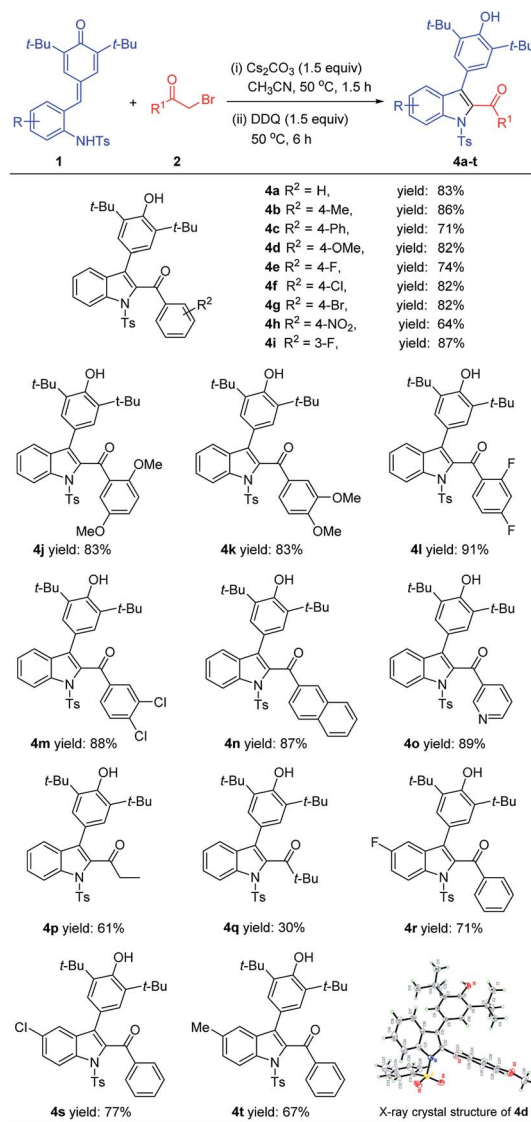


Table 2 Substrate scope for the synthesis of 2,3-dihydroindoles^a

^a All reactions were conducted with **1** (0.11 mmol), **2** (0.10 mmol), Cs_2CO_3 (1.5 equiv.), CH_3CN (1.5 mL). Yields are those of isolated products **3** after column chromatography.

DDQ, $\text{PhI}(\text{OAc})_2$ and MnO_2), we found that DDQ performed best and the corresponding product **4a** could be obtained in a total yield of 83% (not shown).

With the optimal one-pot reaction conditions in hand, we began to explore the substrate scope of this annulation reaction. The scope of bromomethyl ketones part was examined firstly and we were pleased to find that a wide range of bromomethyl aryl ketones **2** could readily react with *ortho*-tosylaminophenyl-substituted *p*-QM **1a** to afford **4a–4o** in good yields (Table 3). In detail, bromomethyl aryl ketones with electron-neutral ($\text{R} = \text{H}$), electron-donating ($\text{R} = \text{OMe}$, Me , Ph), or electron-withdrawing ($\text{R} = \text{Br}$, Cl , F , NO_2) groups at the C3 or C4 position of the benzene ring easily underwent this cascade reaction to provide the desired products **4a–4i** in 71–87% yields. Besides, the bromomethyl aryl ketones containing disubstituted groups on the benzene ring were also suitable substrates, and the corresponding products (**4j–4m**) were obtained in uniform high yields (83–91%). Moreover, the bromomethyl aryl ketones bearing a naphthyl or pyridinyl could also readily take part in this [4 + 1] annulation reaction to give the expected products **4n** and **4o** in 87% and 89% yields, respectively. In addition, bromomethyl alkyl ketones such as 1-bromo-2-butanone and bromopinacolone could also participate in the process to give the desired products **4p** and **4q** in 61% and 30% yields, respectively. However, bromomethyl alkyl ketone with an electron-

Table 3 Substrate scope for the synthesis of 2,3-disubstituted indoles^a

^a All reactions were conducted with **1** (0.11 mmol), **2** (0.10 mmol), Cs_2CO_3 (1.5 equiv.), DDQ (1.5 equiv.), CH_3CN (1.5 mL). Yields are those of isolated products **4** after column chromatography.

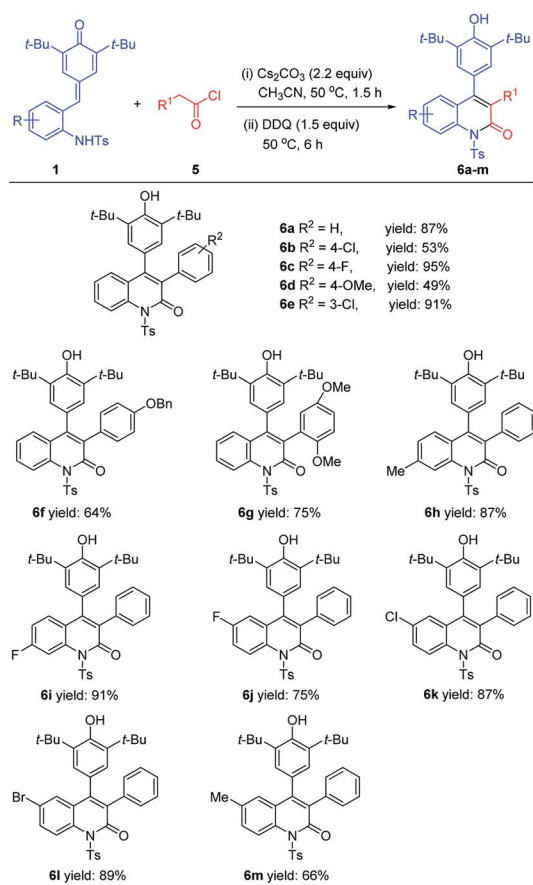
withdrawing group such as 1-bromo-3,3,3-trifluoroacetone was not suitable for this transformation.

Subsequently, the generality of this reaction was further evaluated by varying another reaction partner *ortho*-tosylaminophenyl-substituted *p*-QMs **1**. It was found that *p*-QMs bearing different substituents on the benzene ring could be smoothly converted into the expected products **4r–4t** in 67–77% yields, and the reaction efficiency was less affected by the electronic properties of substituents. The structure and relative configuration of **4d** was determined based on its HRMS, NMR spectroscopy and single-crystal X-ray analyses (Table 3).¹⁴

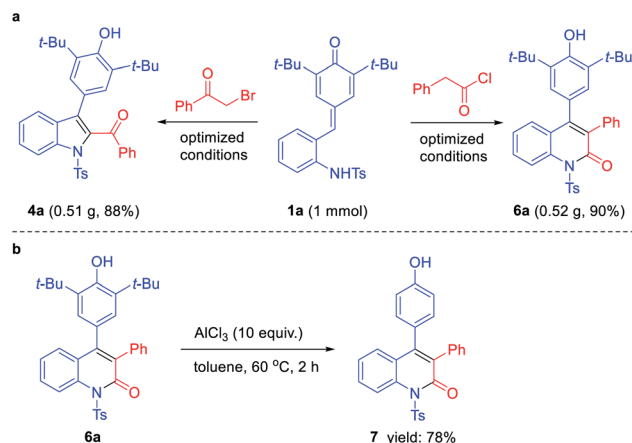


After accomplishing the [4 + 1] annulation reaction of *ortho*-tosylaminophenyl-substituted *p*-QMs with bromomethyl ketones for the synthesis of 2,3-disubstituted indole derivatives, we further tried to apply this methodology for the synthesis of other nitrogen-containing heterocycles. We envisioned that assembly of 3,4-diaryl-substituted quinolinone derivatives could be realized by treating *ortho*-tosylaminophenyl-substituted *p*-QMs with arylacetyl halides followed by one-pot dehydrogenative oxidation with DDQ. To verify the feasibility of our hypothesis, an initial experiment was carried out by treating **1a** with phenylacetyl chloride **5a** (1.2 equiv.) in the presence of Cs₂CO₃ (2.2 equiv.) in CH₃CN for 1.5 h followed by the addition of DDQ (1.5 equiv.) and reaction for another 6 h. As expected, the desired product **6a** was obtained in 87% isolated yield. Encouraged by this result, the substrate scope of this [4 + 2] annulation reaction was explored. As shown in Table 4, a wide range of arylacetyl chlorides **5** could readily react with **1a** to afford products **6a–6g** in acceptable yields. For instance, arylacetyl chlorides bearing electron-neutral (R = H), electron-donating (R = OMe, OBn), or electron-withdrawing (R = Cl, F) groups at the C3 or C4 position of the benzene ring were well-

Table 4 Substrate scope for the synthesis of quinolinone derivatives^a



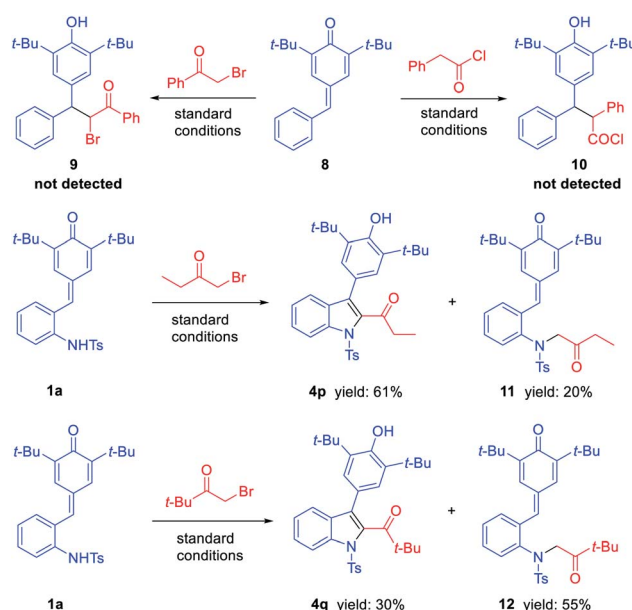
^a All reactions were conducted with **1** (0.1 mmol), **5** (0.12 mmol), Cs₂CO₃ (2.2 equiv.), DDQ (1.5 equiv.), CH₃CN (1.5 mL). Yields are those of isolated products **6** after column chromatography.



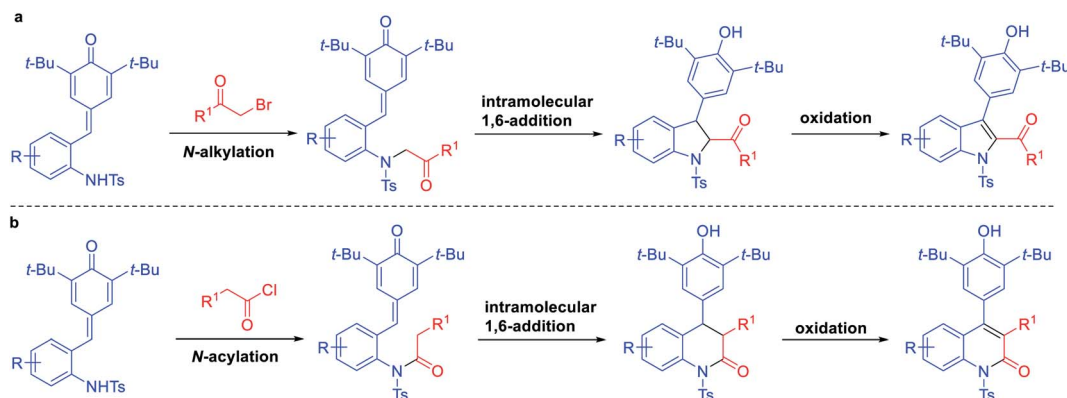
Scheme 2 Scale-up synthesis (a) and synthetic transformation (b).

tolerated and delivered the desired products **6a–6f** in 49–95% yields. Even arylacetyl chlorides bearing disubstituted groups on the benzene ring, the reaction also proceeded smoothly, giving the corresponding product **6g** in 75% yield. Furthermore, it was found that a variety of *p*-QMs **1** bearing different substituents on the benzene ring could be smoothly processed to afford the expected products **6h–6m** in 66–91% yields, and the reaction efficiency was less affected by variations of the electronic properties or the position of substituents on the benzene ring.

To evaluate the general utility and robustness of this novel protocol, we conducted a 1 mmol scale reaction under the standard conditions, and the products **4a** and **6a** could be isolated in 88% and 90% yields (Scheme 2a). Furthermore, the synthetic transformation of **6a** was carried out by treating it with excess of AlCl₃ (10 equiv.) in toluene at 60 °C, and the expected de-*tert*-butylation product **7** was obtained in 78% yield (Scheme 2b).



Scheme 3 Control experiments.



Scheme 4 The plausible reaction mechanism for the one-pot synthesis of 2,3-disubstituted indoles (a) and 3,4-diaryl-substituted quinolinones (b).

Finally, to understand the mechanism of this reaction, some control experiments were carried out (Scheme 3). Firstly, the reactions of phenyl substituted *p*-QM **8** with phenacyl bromide and phenylacetyl chloride were carried out individually under standard conditions. However, the corresponding products **9** and **10** were not detected, and the starting material **8** was not transformed in both cases. Further, in exploring the substrate scope of bromomethyl ketones, we obtained some by-products which may help explain the mechanism of this reaction. When treating **1a** with 1-bromo-2-butanone under standard conditions, in addition to product **4p**, *N*-alkylated product **11** was isolated in 20% yield. The similar phenomenon was observed when treating **1a** with bromopinacolone, *N*-alkylated product **12** was isolated in 55% yield, while the corresponding 1,6-adduct was only obtained in 30% yield. Based on above results, a plausible mechanism was suggested as shown in Scheme 4. The reaction proceeds through *N*-alkylation followed by intramolecular 1,6-conjugate addition/cyclization to form 2,3-dihydroindoles, which underwent the *in situ* dehydrogenative oxidation for the one-pot synthesis of 2,3-disubstituted indoles (Scheme 4a). Also, we can speculate that quinolinone derivatives were formed through *N*-acylation followed by intramolecular cyclization and one-pot oxidation (Scheme 4b).

In summary, we have developed an efficient and facile one-pot method for the synthesis of 2,3-disubstituted indoles and 3,4-diaryl-substituted quinolinones through alkylation/acylation of *ortho*-tosylaminophenyl-substituted *p*-QMs followed by intramolecular 1,6-conjugate addition/cyclization and oxidation sequence. This protocol could not only fulfill the task of developing new cyclization reactions of *ortho*-tosylaminophenyl-substituted *p*-QMs but also provide an easy access to structurally diverse nitrogen-containing heterocycles.

Conflicts of interest

The authors declare no competing financial interest.

Acknowledgements

This work was supported by the National Natural Science Foundation of China (grant: 81803342), the Natural Science

Foundation of Jiangsu Province (grant: BK20180826), the Natural Science Research of Jiangsu Higher Education Institutions of China (grants: 18KJB350008, 18KJD360001), the Graduate Research and Innovation Projects of Jiangsu Province (KYCX19_1259).

Notes and references

- For recent selected examples, see: (a) W. L. Huang, X. Q. Song, S. X. Peng and Z. Y. Huang, *Acta Pharmacol. Sin.*, 1990, **25**, 815; (b) G. W. Rewcastle, B. D. Palmer, A. J. Bridges, H. D. H. Showalter, L. Sun, J. Nelson, A. McMichael, A. J. Kraker, D. W. Fry and W. A. Denny, *J. Med. Chem.*, 1996, **39**, 918; (c) S. L. Cao, Y. P. Feng, Y. Y. Jiang, S. Y. Liu, G. Y. Ding and R. T. Li, *Bioorg. Med. Chem. Lett.*, 2005, **36**, 1915; (d) M. N. Noolvi, H. M. Patel, V. Bhardwaj and A. Chauhan, *Eur. J. Med. Chem.*, 2011, **46**, 2327; (e) K. B. Harikandei, P. Salehi, S. N. Ebrahimi, M. Bararjanian and A. Al-Harrasi, *Bioorg. Chem.*, 2019, **91**, 103116.
- (a) H. Sawaoka, S. Tsuji, M. Tsujii, E. S. Gunawan and M. Hori, *Lab. Invest.*, 1999, **79**, 1469; (b) K. Suzumura, M. Yasuhara, K. Tanaka and T. Suzuki, *Biochem. Pharmacol.*, 1999, **57**, 697; (c) O. Guzel, A. Innocenti, D. Vullo, A. Scozzafava and C. T. Supuran, *Curr. Pharm. Des.*, 2010, **16**, 3317; (d) A. Srivastava and S. N. Pandeya, *Asian J. Pharm. Clin. Res.*, 2011, **4**, 5; (e) C. R. Prakash and S. Raja, *Mini-Rev. Med. Chem.*, 2012, **12**, 98.
- (a) E. Ramesh, R. D. R. S. Manian, R. Raghunathan, S. Sainath and M. Raghunathan, *Bioorg. Med. Chem.*, 2009, **17**, 660; (b) J. M. Kraus, C. L. M. J. Verlinde, M. Karimi, G. I. Lepesheva, M. H. Gelb and F. S. Buckner, *J. Med. Chem.*, 2009, **52**, 1639; (c) Y. F. Chen, Y. C. Lin, P. K. Huang, H. C. Chan, S. C. Kuo, K. H. Lee and L. J. Huang, *Bioorg. Med. Chem.*, 2013, **21**, 5064; (d) B. X. Huang, K. Newcomer, K. Kevala, E. Barnaeva, W. Zheng, X. Hu, S. Patnaik, N. Southall, J. Marugan and M. Ferrer, *Sci. Rep.*, 2017, **7**, 11673.
- For selected reviews on *p*-QMs, see: (a) M. M. Toteva and J. P. Richard, *Adv. Phys. Org. Chem.*, 2011, **45**, 39; (b) C. Lorenzo, F. Mariafrancesca and B. Luca, *Molecules*, 2015,



- 20, 11733; (c) A. Parra and M. Tortosa, *ChemCatChem*, 2015, 7, 1524; (d) P. Chauhan, U. Kaya and D. Enders, *Adv. Synth. Catal.*, 2017, 359, 888.
- 5 W. D. Chu, L. F. Zhang, X. Bao, X. H. Zhao, C. Zeng, J. Y. Du, G. B. Zhang, F. X. Wang, X. Y. Ma and C. A. Fan, *Angew. Chem., Int. Ed.*, 2013, 52, 9399.
- 6 L. Caruana, F. Kniep, T. K. Johansen, P. H. Poulsen and K. A. Jorgensen, *J. Am. Chem. Soc.*, 2014, 136, 15929.
- 7 For selected examples, see: (a) Y. Lou, P. Cao, T. Jia, Y. Zhang, M. Wang, J. Liao, Y. Lou, P. Cao, T. Jia and Y. Zhang, *Angew. Chem., Int. Ed.*, 2015, 54, 12134; (b) Z. Wang, Y. F. Wong and J. Sun, *Angew. Chem., Int. Ed.*, 2015, 54, 13711; (c) Z. Yuan, X. Fang, X. Li, J. Wu, H. Yao and A. Lin, *J. Org. Chem.*, 2015, 80, 11123; (d) N. Dong, Z. P. Zhang, X. S. Xue, X. Li and J. P. Cheng, *Angew. Chem., Int. Ed.*, 2016, 55, 1460; (e) F. He, J. Jin, Z. Yang, X. Yu, J. S. Fossey and W. Deng, *ACS Catal.*, 2016, 6, 652; (f) S. Gao, X. Xu, Z. Yuan, H. Zhou, H. Yao and A. Lin, *Eur. J. Org. Chem.*, 2016, 3006; (g) X. Li, X. Xu, W. Wei, A. Lin and H. Yao, *Org. Lett.*, 2016, 18, 428; (h) C. Yang, S. Gao, H. Yao and A. Lin, *J. Org. Chem.*, 2016, 81, 11956; (i) Y.-H. Deng, X.-Z. Zhang, K.-Y. Yu, X. Yan, J.-Y. Du, H. Huang and C.-A. Fan, *Chem. Commun.*, 2016, 52, 4183; (j) X.-Z. Zhang, Y.-H. Deng, X. Yan, K.-Y. Yu, F.-X. Wang, X.-Y. Ma and C.-A. Fan, *J. Org. Chem.*, 2016, 81, 5655; (k) X.-Z. Zhang, J.-Y. Du, Y.-H. Deng, W.-D. Chu, X. Yan, K.-Y. Yu and C.-A. Fan, *J. Org. Chem.*, 2016, 81, 2598; (l) C. Ma, Y. Huang and Y. Zhao, *ACS Catal.*, 2016, 6, 6408; (m) Z. Yuan, L. Liu, R. Pan, H. Yao and A. Lin, *J. Org. Chem.*, 2017, 82, 8743; (n) L. Roiser and M. Waser, *Org. Lett.*, 2017, 19, 2338; (o) Z. Yuan, K. Gai, Y. Wu, J. Wu, A. Lin and H. Yao, *Chem. Commun.*, 2017, 53, 3485; (p) X.-Z. Zhang, Y.-H. Deng, K.-J. Gan, X. Yan, K.-Y. Yu, F.-X. Wang and C.-A. Fan, *Org. Lett.*, 2017, 19, 1752.
- 8 K. Zhao, Y. Zhi, T. Shu, A. Valkonen, K. Rissanen and D. Enders, *Angew. Chem., Int. Ed.*, 2016, 55, 12104.
- 9 For selected examples of [4 + 1] cyclization, see: (a) K. Zhao, D. Enders, Y. Zhi, C. von Essen and K. Rissanen, *Org. Chem. Front.*, 2018, 5, 1348; (b) B. Jiang, Y.-J. Xiong, S.-Q. Shi, W.-J. Hao and S.-J. Tu, *Org. Chem. Front.*, 2018, 5, 3483; (c) L. Liu, Z. Yuan, R. Pan, Y. Zeng, A. Lin, H. Yao and Y. Huang, *Org. Chem. Front.*, 2018, 5, 623; (d) Z. Jing, G. Liang, X. Hu, L. Zhou and Z. Hui, *Tetrahedron*, 2018, 74, 1492; (e) X. M. Chen, K. X. Xie, D. F. Yue, X. M. Zhang, X. Y. Xu and W. C. Yuan, *Tetrahedron*, 2018, 74, 600; (f) H. Lu, H.-X. Zhang, C.-Y. Tan, J.-Y. Liu, H. Wei and P.-F. Xu, *J. Org. Chem.*, 2019, 84, 10292; (g) J.-P. Tan, P. Yu, J.-H. Wu, Y. Chen, J. Pan, C. Jiang, X. Ren, H.-S. Zhang and T. Wang, *Org. Lett.*, 2019, 21, 7298.
- 10 G. Singh, S. Kumar, A. Chowdhury and R. V. Anand, *J. Org. Chem.*, 2019, 84, 15978.
- 11 For selected examples of [4 + 2] cyclization, see: (a) G. J. Mei, S. L. Xu, W. Q. Zheng, C. Y. Bian and F. Shi, *J. Org. Chem.*, 2018, 83, 1414; (b) X.-L. Jiang, S.-F. Wu, J.-R. Wang, G.-J. Mei and F. Shi, *Adv. Synth. Catal.*, 2018, 360, 4225; (c) J.-R. Zhang, H.-S. Jin, R.-B. Wang and L.-M. Zhao, *Adv. Synth. Catal.*, 2019, 361, 4811; (d) Y.-C. Cheng, C.-S. Wang, T.-Z. Li, F. Gao, Y. Jiao and F. Shi, *Org. Biomol. Chem.*, 2019, 17, 6662; (e) Z. Li, W. Wang, H. Jian, W. Li, B. Dai and L. He, *Chin. Chem. Lett.*, 2019, 30, 386–388; (f) Y. You, T.-T. Li, S.-P. Yuan, K.-X. Xie, Z.-H. Wang, J.-Q. Zhao, M.-Q. Zhou and W.-C. Yuan, *Chem. Commun.*, 2020, 56, 439; (g) B. Jiang, H.-M. Huang, X.-Y. Wu, B.-R. Leng, X.-C. Meng, Y. Hong, B. Jiang and D.-C. Wang, *Org. Chem. Front.*, 2020, 7, 414.
- 12 For selected examples of [4 + 3] cyclization, see: (a) F. Jiang, F. Yuan, L. Jin, G. Mei and F. Shi, *ACS Catal.*, 2018, 8, 10234; (b) L. Qiang, L. Sun, C. Xiang-Yu, R. Kari and E. Dieter, *Org. Lett.*, 2018, 20, 3622; (c) W. Li, H. Yuan, Z. Liu, Z. Zhang, Y. Cheng and P. Li, *Adv. Synth. Catal.*, 2018, 360, 2460; (d) B. Jiang, K. Chen, W.-J. Hao and S.-J. Tu, *Green Chem.*, 2019, 21, 675.
- 13 For selected examples of *ortho*-tosylaminophenyl-substituted *p*-QMs, see: (a) J. Wang, X. Pan, J. Liu, L. Zhao, Y. Zhi, K. Zhao and L. Hu, *Org. Lett.*, 2018, 20, 5995; (b) J. Wang, X. Pan, L. Zhao, L. Zhao, J. Liu, Y. Zhi, A. Wang, K. Zhao and L. Hu, *Org. Biomol. Chem.*, 2019, 17, 10158.
- 14 CCDC 2009636 (4d) contains the supplementary crystallographic data for this paper.†

