Organic & Biomolecular Chemistry

ROYAL SOCIETY OF CHEMISTRY

COMMUNICATION

View Article Online
View Journal | View Issue

Cite this: *Org. Biomol. Chem.*, 2024, **22**, 5891

Received 7th June 2024,
Accepted 29th June 2024

DOI: 10.1039/d4ob00966e

rsc.li/obc

A HMPA–H_2O mediated oxygenative carbocyclization of 2-alkynylphenyl-substituted *p*-quinone methides to indenones†

Shaheen Fatma, Feroz Ahmad, Yogesh A. Pankhade, Pavit K. Ranga and Ramasamy Vijaya Anand *

Herein, we report a transition-metal and base-free protocol to access a wide range of functionalized indenone derivatives through a HMPA–H_2O-mediated oxygenative annulation of 2-alkynylphenyl-substituted *p*-quinone methides. This method worked effectively for most of the *p*-QMs investigated and the corresponding indenone derivatives were obtained in moderate to good yields. This methodology was further extended to the formal synthesis of one of the resveratrol based natural products, (±)-isopaucifloral F.

Introduction

Indenone is considered a privileged core that is an integral part of many natural products and also serves as an important structural motif in pharmaceutical chemistry and materials science.[1] Besides, indenone derivatives also serve as synthons/intermediates in the preparation of many important organic compounds including drug candidates.[2] Fig. 1 shows some indenone derivatives that show potential biological activities such as antitumor,[3] COX-2 inhibition,[4] and estrogen binding[5] activities.

The traditional method for indenone synthesis relies on intramolecular Friedel–Crafts type cyclization that often suffers from the need for harsh reaction conditions and a limited substrate scope.[6] Besides, some radical and other synthetic approaches have also been developed to produce indenone derivatives.[7] In recent years, transition metal catalysis has gained much attention in organic transformations and, to this end, many transition metal based protocols have also been documented in the literature for the synthesis of indenones,[8] which include catalytic annulations of alkynes with *ortho*-functionalized aromatic aldehydes, esters or nitriles (**a** & **b**, Scheme 1).[8b,c] However, the use of expensive transition metal catalysts such as Pd and Rh limits their synthetic utility. Recently, Yao and co-workers reported a transition metal free tandem annulation of 2-alkynylbenzaldehydes with phenols for the synthesis of 2,3-diarylindenones (**c**, Scheme 1).[9] However, their protocol is effective only for electron-poor aryl-substituted 2-alkynyl benzaldehydes. Moreover, both the regioisomers were formed in their method; of course, one would be the major product depending on the reaction conditions (**c**, Scheme 1). Considering the importance of indenone scaffolds in various fields, the development of more efficient and practical metal-free protocols to access these indenone derivatives are highly desirable.

In recent years, the synthetic utilities of *p*-quinone methides (*p*-QMs) have been widely explored.[10] Our group was also involved in the synthesis of various triarylmethanes,[11] carbocycles[12] and heterocycles[13] using *p*-QMs as synthons. Herein, we report a transition-metal and base-free HMPA-mediated oxygenative carbocyclization of 2-alkynylated *p*-QMs[14] to access substituted indenones (**d**, Scheme 1). In this

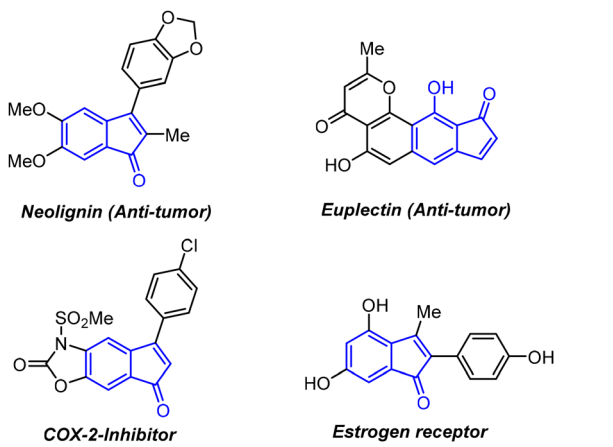
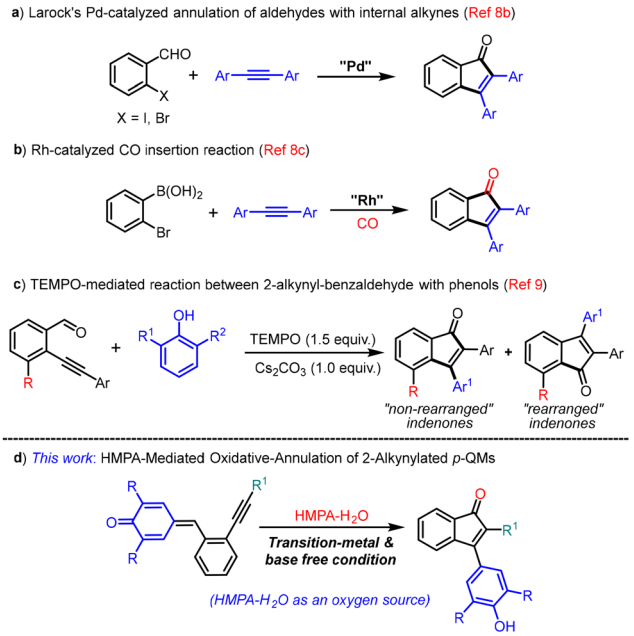


Fig. 1 Indenone-based bio-active molecules.

Department of Chemical Sciences, Indian Institute of Science Education and Research (IISER) Mohali, Sector 81, Knowledge City, S. A. S. Nagar, Manauli (PO), Punjab – 140306, India. E-mail: rvijayan@iisermohali.ac.in

†Electronic supplementary information (ESI) available. CCDC 2307508. For ESI and crystallographic data in CIF or other electronic format see DOI: https://doi.org/10.1039/d4ob00966e



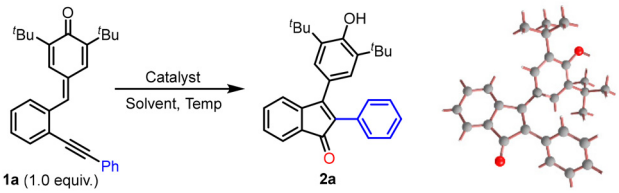
Scheme 1 Selected reported protocols and our hypothesis.

context, it should be noted that although HMPA has been utilized as an additive in many organic transformations[15] including in SmI_2 chemistry,[16] only a handful of reports are available in the literature on HMPA-mediated organic transformations, which include regioselective additions of organolithium reagents to enones and enals, conjugate additions of (phenylthio/phenylseleno)allylithium reagents to cyclopentenones, retro-aldol reactions, arylations of indenes, *etc.*[17]

Results and discussion

To find out the best reaction conditions, the 2-alkynylphenyl-substituted *p*-QM **1a** was chosen as the model substrate, and it was subjected to the cyclization reaction under different conditions (Table 1). Initially, we decided to use Au-based catalysts, as they are well known for activating the alkynes, and DMSO as the oxygenating source. However, the cyclization of **1a** with AuCl in DMSO did not yield the expected product **2a** even after 24 hours at room temperature (entry 1). Interestingly, when the reaction temperature was increased to 100 °C, the starting material **1a** was completely consumed (as observed by TLC) after 24 h, and product **2a** was isolated in 60% yield (entry 2). The structure of **2a** was unambiguously confirmed by NMR and X-ray analysis (CCDC 2307508†). Upon changing the catalyst from gold(I) chloride to $AuCl_3$, a slight decrease in the yield of **2a** was observed (entry 3). Later, a couple of other gold-based catalysts such as $(PPh_3)AuCl$ and PPh_3AuNTf_2 were examined (entries 4 & 5), and in these cases, only trace amounts of **2a** was observed. In addition, one reaction was conducted using a combination of gold and silver catalysts (entry 6); however, unfortunately, in that case too, only a

Table 1 Optimization study[a]



3 CCDC: 2307508

Entry	Catalyst (10 mol%)	Solvent	Temp. [°C]	Time [h]	Yield of **2a**[b] [%]
1	AuCl	DMSO	RT	24	0
2	AuCl	DMSO	100	24	60
3	$AuCl_3$	DMSO	100	12	40
4	$(PPh_3)AuCl$	DMSO	100	24	Trace
5	PPh_3AuNTf_2	DMSO	100	24	Trace
6	AuCl (5 mol%) AgOTf (5 mol%)	DMSO	100	24	Trace
7[c]	AuCl	HMPA	100	8	53
8[c]	—	HMPA	100	24	60
9[c]	—	HMPA	140	8	78
10	—	DMSO	130	48	0
11[d]	—	HMPA	140	24	0
12	—	H_2O	150	24	0
13	—	HMPA : H_2O (3 : 1)	140	24	30
14	—	NMP	130	24	10
15[c,e]	—	HMPA	140	8	75

[a] Reaction conditions: reactions were carried out with 0.10 mmol of **1a**. [b] Yields reported are isolated yields. [c] Non-anhydrous and commercially available HMPA with 98.5% purity (remaining 1.5% was water) was used as solvent. [d] Dry HMPA was used as solvent. [e] Reaction was carried out under a N_2 atmosphere. (HMPA = hexamethylphosphoramide; NMP = *N*-methylpyrrolidone).

trace amount of product formation was seen. When the reaction was performed using AuCl in commercially available HMPA (98.5% HMPA + 1.5% water) as a solvent, **2a** was obtained in 53% yield in 8 hours (entry 7). Excited by this result, further optimization experiments were conducted in HMPA. To our surprise, the reaction of **1a** in HMPA at 100 °C without any Au-catalyst also yielded the same product **2a** in 60% yield (entry 8). We found this result very interesting as the reaction worked without any external oxygenating source and it hinted that HMPA is probably promoting the reaction and also acting as an oxygenating agent. Since HMPA has not been utilized as a promoter for any cyclization reactions, including the cyclization of **1a** to **2a**, we became interested in investigating this transformation in detail. We found that reaction temperature plays an important role in the cyclization of **1a**. For example, increasing the temperature to 140 °C significantly improved the yield of **2a** to 78% (entry 9). Another experiment was conducted in DMSO at 130 °C without the Au-catalyst and, in that case, **2a** was not detected at all (entry 10). Interestingly, no product formation was observed when the reaction was conducted either in dry HMPA (entry 11) or in H_2O (entry 12) under reflux conditions. However, when a 3 : 1 mixture of dry HMPA and water was used as a solvent, **2a** was obtained in 30% yield (entry 13). Another experiment was also conducted

using the commercially available *N*-methylpyrrolidone (NMP); however, the desired product **2a** was formed only in 10% yield (entry 14). To exclude the effect of atmospheric oxygen on the outcome of the reaction, a reaction was conducted under inert conditions (entry 15) and in that case also, the product was obtained in 75% yield, clearly indicating that atmospheric oxygen is not playing any role in this transformation.

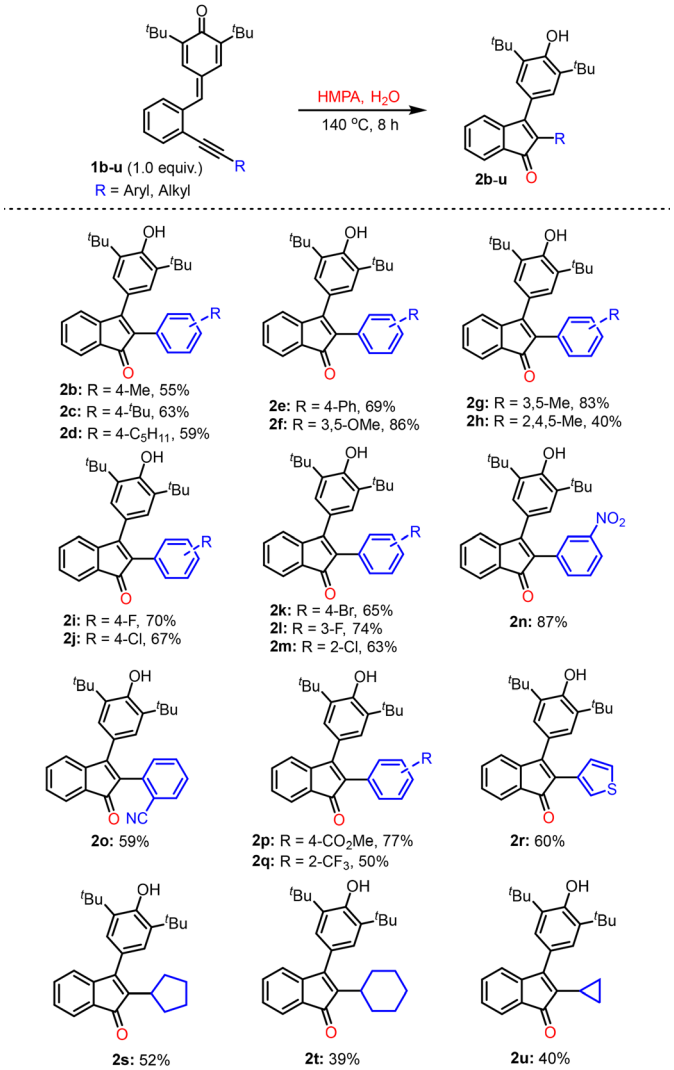
Next, the optimal reaction conditions (entry 9, Table 1) were employed to investigate the scope and limitations of this transformation (Table 2). The *para*-quinone methides (*p*-QMs) **1b–h**, where the alkyne was substituted with electron-rich arenes, produced the desired products **2b–h** in 40–86% yields. The halo-aryl alkyne-substituted *p*-QMs, **1i–m**, also reacted smoothly and afforded the desired products **2i–m** in 63–74% yields. In addition, the *p*-QMs **1n–q**, substituted with electron-withdrawing groups, also underwent cyclization under the optimal conditions and provided the corresponding products **2n–q** in the range of 50–87% yields. The 3-thienyl alkyne-substituted precursor **1r** afforded the desired product **2r** in 60% yield. The reaction also worked well with *p*-QMs **1s–u**, having cycloalkyl substituents (such as cyclopropyl, cyclopentyl, and cyclohexyl) on the alkyne, and in these cases, the desired products **2s–u** were isolated in 39–52% yields.

Later, the substrate scope investigation was extended to various substituted *p*-QMs **1v–1aa** and the results are summarized in Table 3. The *p*-QMs **1v–x**, having electron-rich substituents (–Me, –OMe, and 3,5-dimethoxy) on the aryl ring, afforded the corresponding products **3a–c** in yields ranging from 53–61%. The halo-arene-substituted *p*-QMs **1y** and **1z** also reacted under the standard reaction conditions and produced the desired indenones **3d** and **3e** in 35 and 60% yields, respectively. The indenone **3f** was isolated in 54% yield when the corresponding synthon **1aa** was subjected to oxygenative cyclization under standard conditions. The isopropyl containing 2-alkynylphenyl-substituted *p*-QM **1ab** also worked well under the optimized conditions and afforded product **3g** in 80% yield.

To show the feasibility of this methodology, a relatively large-scale reaction of **1a** was carried out under the standard reaction conditions, and in this case, **2a** was obtained in 62% yield (Scheme 2).

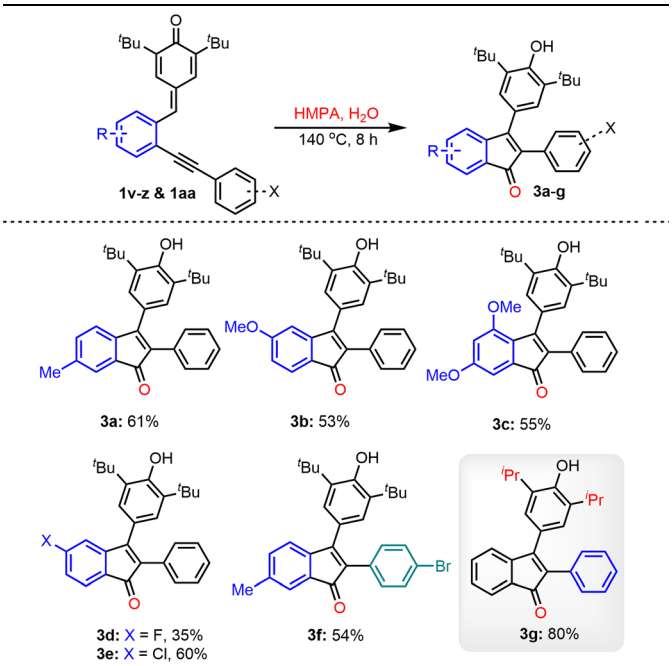
To demonstrate the practical applicability of this transformation, we targeted the formal synthesis of one of the resveratrol-derived natural products, isopaucifloral F (**8**),[18] starting from *p*-QM **4**.[12a] Upon treatment with the terminal alkyne **5**, *p*-QM **4** afforded the 2-alkynylphenyl-substituted *p*-QM **6** under Sonogashira conditions (Scheme 3). *p*-QM **6** was then sub-

Table 2 Substrate scope[a]

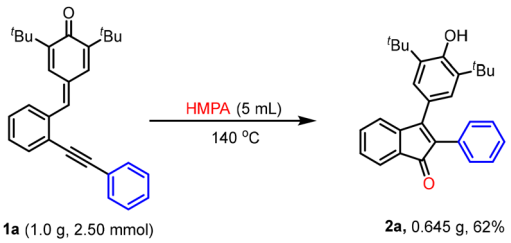


[a] Reactions were carried out at the 50 mg scale with **1b–u** in 1.0 mL of HMPA. Yields reported are isolated yields.

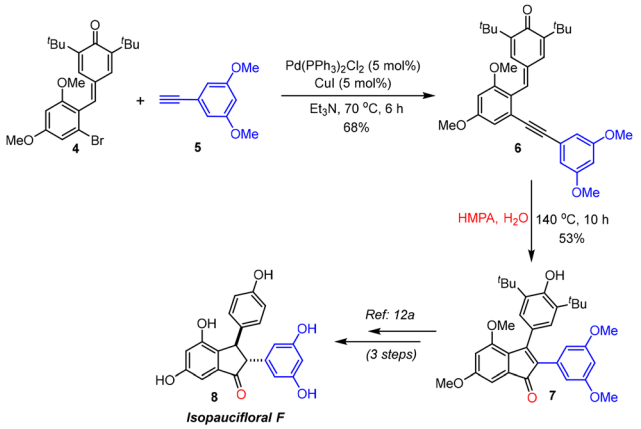
Table 3 Substrate scope[a]



[a] Reactions were carried out at the 50 mg scale with **1v–1aa** in 1.0 mL of HMPA. Yields reported are isolated yields.



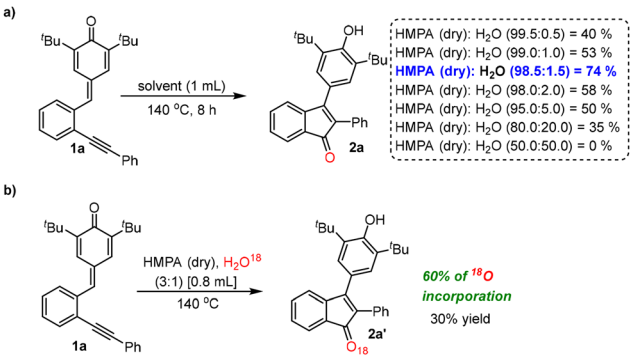
Scheme 2 Gram scale reaction of **1a**.



Scheme 3 Formal synthesis of (±)-isopaucifloral F **8**.

jected to oxygenative cyclization under the optimized reaction conditions to produce the indenone derivative 7 in 53% yield. Compound 7 can easily be converted to isopaucifloral F **8** in 3 steps through a known procedure involving reduction followed by demethylation/de-*tert*-butylation.[12a]

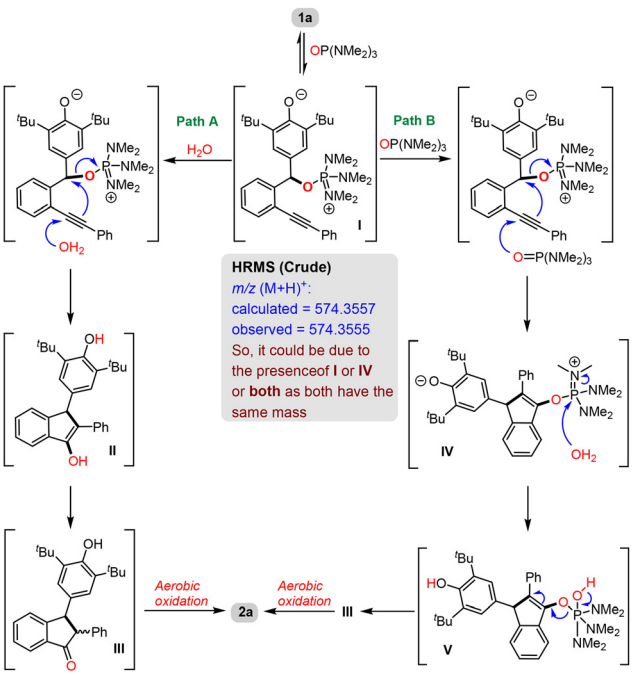
Next, we shifted our attention to find out the exact role of HMPA/water in this transformation. As discussed in the optimization table, the oxygenative cyclization of **1a** did not work either in anhydrous HMPA or in pure water (entries 11 & 12, Table 1). However, when the reaction was conducted in a mixture of dry HMPA and water in a 3 : 1 ratio, **2a** was obtained in 30% yield (entry 13, Table 1). These experiments clearly indicate that both HMPA and water are crucial to drive this transformation. The best result was obtained when the commercially available HMPA with 1.5% water content was used (entry 9, Table 1). To find out the optimal quantity of water required for this transformation, a few control experiments were performed in anhydrous HMPA by adding calculated amounts of water [0.5%, 1.0%, 1.5%, 2.0%, *etc.*] at 140 °C (**a**, Scheme 4). The reaction using 1.5% water gave product **2a** in 74% yield, which is very similar when compared to the optimal reaction conditions using commercially available HMPA (entry 9, Table 1). However, interestingly, product **2a** was obtained in much less yields when the water content in the reaction is less than or more than 1.5% (v/v) [Scheme 4]. These experiments clearly indicate that the optimal water quantity required for this transformation is approximately 1.5% (v/v). It is clear from these control experiments that the



Scheme 4 Control experiments.

yields of **2a** were decreasing gradually when the water content in the reaction was increased and, notably, no product formation was observed when the reaction was conducted in a 1 : 1 mixture of dry HMPA and water (**a**, Scheme 4). To further prove the involvement of water in the reaction, another control experiment was performed using a mixture of dry HMPA and ^{18}O labelled water (H_2O^{18}) and, in this case, **2a′** was obtained in 30% yield with 60% of ^{18}O incorporation (M − H, *m*/*z* = 411.2215) along with an unlabelled product (M − H, *m*/*z* = 409.2125) [**b**, Scheme 4]. We believe that the oxygen atom of the unlabelled product could have come from the HMPA, which explains the incorporation of the remaining 40% of ^{16}O in the product.

Based on the above-mentioned control experiments, a plausible mechanism for this transformation was proposed (Scheme 5). We presume that, initially, the oxygen-atom of



Scheme 5 Plausible mechanism.

HMPA reacts with **1a** in a 1,6-fashion to generate intermediate **I**. Now, there are two possibilities: (i) the attack of water on the alkyne moiety of **I** followed by cyclization with the expulsion of HMPA would lead to another intermediate **II**, which subsequently undergoes tautomerization (*via* **III**) followed by aerobic oxidation to generate product **2a** (Path A) or (ii) the attack of another molecule of HMPA on the alkyne of **I** followed by intramolecular cyclization would lead to intermediate **IV**, which then reacts with water to generate another intermediate **V**. The expulsion of HMPA from intermediate **V** would lead to **III**, which upon aerobic oxidation produces product **2a** (Path B). The HRMS analysis of the crude reaction mixture indicated the presence of either **I** or **IV** or both during the reaction as a peak was found at m/z $(M + H)^+ = 574.3555$, which corresponds to **I** and/or **IV**. So, based on this observation and the control experiment (Scheme 5), we assume that both the pathways (Paths A & B) are simultaneously operating during the reaction.

Conclusions

In conclusion, we have developed a HMPA–H_2O mediated simple method for the synthesis of functionalized indenone derivatives through the oxygenative carbocyclization of 2-alkynylphenyl-substituted *p*-QMs. Many indenone derivatives could be accessed in moderate to good yields using this protocol. In addition, this transformation was also extended to the formal synthesis of isopaucifloral F. Considering the importance of indenones in medicinal chemistry, we believe that this protocol will definitely find some applications in the synthesis of other indenone-based natural products in the near future.

Data availability

The data supporting this article have been included as part of the ESI.†

Conflicts of interest

There are no conflicts to declare.

Acknowledgements

The authors are grateful to the Science and Engineering Research Board (SERB) of the Department of Science and Technology (DST), Govt. of India (CRG/2022/005391) and IISER Mohali for the financial support. F. A. thanks UGC, New Delhi for a research fellowship. S. F., Y. P. and P. K. R. thank IISER Mohali for a research fellowship. We are grateful for the NMR and HRMS facilities at IISER Mohali.

References

1 For selected examples, please see: (*a*) R. Nigam, K. R. Babu, T. Ghosh, B. Kumari, D. Akula, S. N. Rath, P. Das, R. Anindya and F. A. Khan, *Bioorg. Med. Chem.*, 2018, **26**, 4100–4112; (*b*) J. H. Ahn, M. S. Shin, S. H. Jung, S. K. Kang, K. R. Kim, S. D. Rhee, W. H. Jung, S. D. Yang, S. J. Kim, J. R. Woo, J. H. Lee, H. G. Cheon and S. S. Kim, *J. Med. Chem.*, 2006, **49**, 4781–4784; (*c*) K. Morinaka, T. Ubukata and Y. Yokoyama, *Org. Lett.*, 2009, **11**, 3890–3893.

2 For selected examples, see: (*a*) N. Parui, T. Mandal and J. Dash, *Eur. J. Org. Chem.*, 2023, e202201285; (*b*) H. Lahousse, H. J. Martens, S. Toppet and G. J. Hoornaert, *J. Org. Chem.*, 1982, **47**, 2001–2005; (*c*) J. L. Jeffrey and R. Sarpong, *Org. Lett.*, 2009, **11**, 5450–5453.

3 (*a*) D. C. Harrowven, N. A. Newman and C. A. Knight, *Tetrahedron Lett.*, 1998, **39**, 6757–6760; (*b*) L. M. X. Lopes, M. Yoshida and O. R. Gottlieb, *Phytochemistry*, 1984, **23**, 2021–2024; (*c*) M. A. Ernst-Russell, C. L. L. Chai, J. H. Wardlaw and J. A. Elix, *J. Nat. Prod.*, 2000, **63**, 129–131.

4 C. H. Park, X. Siomboing, S. Yous, B. Gressier, M. Luyckx and P. Chavatte, *Eur. J. Med. Chem.*, 2002, **37**, 461–468.

5 R. E. McDevitt, M. S. Malamas, E. S. Manas, R. J. Unwalla, Z. B. Xu, C. P. Miller and H. A. Harris, *Bioorg. Med. Chem. Lett.*, 2005, **15**, 3137–3142.

6 (*a*) M. B. Floyd and G. R. Allen Jr, *J. Org. Chem.*, 1970, **35**, 2647–2653; (*b*) P. Galatsis, J. J. Manwell and J. M. Blackwell, *Can. J. Chem.*, 1994, **72**, 1656–1659; (*c*) G. Roberge and P. Brassard, *Synth. Commun.*, 1979, **9**, 129–139.

7 For selected recent examples, see: (*a*) For reviews on the radical cascade-based reactions to access indenones, see: Y. Zhang, K. Sun, Q. Lv, X. Chen, L. Qu and B. Yu, *Chin. Chem. Lett.*, 2019, **30**, 1361–1368; (*b*) X. Yan, S. Zou, P. Zhao and C. Xi, *Chem. Commun.*, 2014, **50**, 2775–2777; (*c*) P. Zhao, Y. Liu and C. Xi, *Org. Lett.*, 2015, **17**, 4388–4391; (*d*) S. K. Pagire, P. Kreitmeier and O. Reiser, *Angew. Chem., Int. Ed.*, 2017, **56**, 10928–10932; (*e*) J. Wen, W. Shi, F. Zhang, D. Liu, S. Tang, H. Wang, X. M. Lin and A. Lei, *Org. Lett.*, 2017, **19**, 3131–3134; (*f*) F. Jafarpour, M. Azizzade, Y. Golpazir-Sorkheh, H. Navid and S. Rajai-Daryasarei, *J. Org. Chem.*, 2020, **85**, 8287–8294; (*g*) L. Li and G.-W. Wang, *J. Org. Chem.*, 2021, **86**, 14102–14112; (*h*) W.-C. Yang, Y. Sun, L.-Y. Shen, X. Xie and B. Yu, *Mol. Catal.*, 2023, **535**, 112819; (*i*) X.-T. Zhu, T.-S. Zhang, Q. Zhao, P.-J. Cai, W.-J. Hao, S.-J. Tu and B. Jiang, *Chem. – Asian J.*, 2018, **13**, 1157–1164; (*j*) X.-T. Zhu, Q.-L. Lu, X. Wang, T.-S. Zhang, W.-J. Hao, S.-J. Tu and B. Jiang, *J. Org. Chem.*, 2018, **83**, 9890–9901.

8 For selected examples, see: (*a*) For reviews on transition-metal catalyzed synthesis of indenones, see: L. E. Hutchinson and D. J. Wilger, *Adv. Synth. Catal.*, 2022, **364**, 3441–3465; (*b*) R. C. Larock, M. J. Doty and S. Cacchi, *J. Org. Chem.*, 1993, **58**, 4579–4583; (*c*) Y. Harada, J. Nakanishi, H. Fujihara, M. Tobisu, Y. Fukumoto and N. Chatani, *J. Am. Chem. Soc.*, 2007, **129**, 5766–5771;

(*d*) H. Tsukamoto and Y. Kondo, *Org. Lett.*, 2007, **9**, 4227–4230; (*e*) T. Miura and M. Murakami, *Org. Lett.*, 2005, **7**, 3339–3341; (*f*) T. Morimoto, K. Yamasaki, A. Hirano, K. Tsutsumi, N. Kagawa, K. Kakiuchi, Y. Harada, Y. Fukumoto, N. Chatani and T. Nishioka, *Org. Lett.*, 2009, **11**, 1777–1780; (*g*) B.-J. Li, H.-Y. Wang, Q.-L. Zhu and Z.-J. Shi, *Angew. Chem., Int. Ed.*, 2012, **51**, 3948–3952; (*h*) Z. Qi, M. Wang and X. Li, *Org. Lett.*, 2013, **15**, 5440–5443; (*i*) L. Kong, X. Yang, X. Zhou, S. Yu and X. Li, *Org. Chem. Front.*, 2016, **3**, 813–816; (*j*) Y. Kuninobu, T. Matsuki and K. Takai, *Org. Lett.*, 2010, **12**, 2948–2950; (*k*) X. T. Zhu, Q. Zhao, F. Liu, A. F. Wang, P. J. Cai, W. J. Hao, S. J. Tu and B. Jiang, *Chem. Commun.*, 2017, **53**, 6828–6831; (*l*) F. Liu, Z. Dong, J. Wang and G. Dong, *Angew. Chem., Int. Ed.*, 2019, **58**, 2144–2148; (*m*) M. Miao, M. Jin, P. Chen, L. Wang, S. Zhang and H. Ren, *Org. Lett.*, 2019, **21**, 5957–5961.

9 T. Yao, S. Zhao, T. Liu, Y. Wu, Y. Ma, T. Li and X. Qin, *Chem. Commun.*, 2022, **58**, 4592–4595.

10 For recent reviews on the chemistry of *p*-QMs, see: (*a*) C. G. S. Lima, F. P. Pauli, D. C. S. Costa, A. S. de Souza, L. S. M. Forezi, V. F. Ferriera and F. de Carvalho da Silva, *Eur. J. Org. Chem.*, 2020, 2650–2692; (*b*) J.-Y. Wang, W.-J. Hao, S.-J. Tu and B. Jiang, *Org. Chem. Front.*, 2020, **7**, 1743–1778; (*c*) G. Singh, R. Pandey, Y. A. Pankhade, S. Fatma and R. V. Anand, *Chem. Rec.*, 2021, **21**, 4150–4173; (*d*) X. Liu, Y. Ren, L. Zhu, T. Li, W. Xu, Y. Liu, K.-W. Tang and B. Xiong, *Tetrahedron*, 2023, **148**, 133655; (*e*) Y. F. Gan, Y. Y. Li, X. Q. Chen, Y. Y. Guo and R. Wang, *Synthesis*, 2023, 1172–1186.

11 (*a*) V. Reddy and R. V. Anand, *Org. Lett.*, 2015, **17**, 3390–3393; (*b*) P. K. Ranga, F. Ahmad, P. Nager, P. S. Rana and R. V. Anand, *J. Org. Chem.*, 2021, **86**, 4994–5010.

12 (*a*) A. S. Jadhav, Y. A. Pankhade, R. Hazra and R. V. Anand, *J. Org. Chem.*, 2018, **83**, 10107–10119; (*b*) Y. A. Pankhade, R. Pandey, S. Fatma, F. Ahmad and R. V. Anand, *J. Org. Chem.*, 2022, **87**, 3363–3377.

13 (*a*) F. Ahmad, P. K. Ranga, Y. A. Pankhade, S. Fatma, A. Gouda and R. V. Anand, *Chem. Commun.*, 2022, **58**, 13238–13241; (*b*) F. Ahmad, P. K. Ranga, S. Fatma, A. Kumar and R. V. Anand, *Adv. Synth. Catal.*, 2023, **365**, 3271–3276.

14 For selected recent examples on the synthetic applications of 2-alkynylated *p*-quinone methides, see: (*a*) H.-D. Zuo, C.-C. Cui, C. Guo, W.-J. Hao, S.-J. Tu and B. Jiang, *Chem. – Asian J.*, 2020, **15**, 4070–4076; (*b*) H.-D. Zuo, W.-J. Hao, C.-F. Zhu, C. Guo, S.-J. Tu and B. Jiang, *Org. Lett.*, 2022, **22**, 4471–4477; (*c*) A. S. Jadhav, Y. A. Pankhade and R. V. Anand, *J. Org. Chem.*, 2018, **83**, 8615–8626.

15 For selected examples, see: (*a*) W. Wu, W. Dai, X. Ji and S. Cao, *Org. Lett.*, 2016, **18**, 2918–2921; (*b*) D.-P. Jin, P. Gao, D.-Q. Chen, S. Chen, J. Wang, X.-Y. Wang, X.-Y. Liu and Y.-M. Liang, *Org. Lett.*, 2016, **18**, 3486–3489.

16 (*a*) D. V. Sadasivam, P. K. S. Antharjanam, E. Prasad and R. A. Flowers II, *J. Am. Chem. Soc.*, 2008, **130**, 7228–7229; (*b*) K. A. Choquette, D. V. Sadasivam and R. A. Flowers II, *J. Am. Chem. Soc.*, 2010, **132**, 17396–17398; (*c*) H. Ohno, R. Wakayama, S.-I. Maeda, H. Iwasaki, M. Okumura, C. Iwata, H. Mikamiyama and T. Tanaka, *J. Org. Chem.*, 2003, **68**, 5909–5916.

17 (*a*) W. H. Sikorski and H. J. Reich, *J. Am. Chem. Soc.*, 2001, **123**, 6527–6535; (*b*) M. R. Binns and R. K. Haynes, *J. Org. Chem.*, 1981, **46**, 3790–3795; (*c*) M. R. Binns, R. K. Haynes, T. L. Houston and W. R. Jackson, *Tetrahedron Lett.*, 1980, **21**, 573–576; (*d*) P. R. Carlier, C. W.-S. Lo, M. M.-C. Lo, N. C. Wan and I. D. Williams, *Org. Lett.*, 2000, **2**, 2443–2445; (*e*) X. Ji, J. Li, M. Wu and S. Cao, *ACS Omega*, 2018, **3**, 10099–10106.

18 For selected examples, see: (*a*) M. H. Keylor, B. S. Matsuura and C. R. J. Stephenson, *Chem. Rev.*, 2015, **115**, 8976–9027; (*b*) C. Zhong, G. Zhu, J. Chang and X. Sun, *Tetrahedron Lett.*, 2011, **52**, 2815–2817; (*c*) S. Faiz, M. Yousaf, A. F. Zahoor, S. A. R. Naqvi, A. Irfan and Z. Zaman, *Synth. Commun.*, 2017, **47**, 1121–1135; (*d*) M.-L. Tang, P. Peng, Z.-Y. Liu, J. Jiang, J.-M. Yu and X. Sun, *Chem. – Eur. J.*, 2016, **22**, 14535–14539.

