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Selectfluor facilitated bridging of indoles to bis(indolyl)methanes using methyl *tert*-butyl ether as a new methylene precursor†

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A novel, green and efficient method is developed for the synthesis of methylene bridged bis(indolyl) methanes in good to excellent yields. The reaction employs methyl *tert*-butyl ether (MTBE) as the methylene source and selectfluor as an oxidizing agent. The scope and versatility of the methods have been successfully demonstrated with 48 examples. The metal-free transformation process is suitable for scale-up production. A selectfluor-promoted oxidative reaction mechanism is proposed based on the results of the experimental studies.

Introduction

Diarylmethanes and bis(heterocycle)methanes have attracted significant attention from organic chemists in recent years owing to their broad spectrum of biological activities.[1] For example, bis(indolyl)methanes (BIMs) are present in a large variety of natural products, and their derivatives exhibit diverse important biological and pharmacological activities (Fig. 1).[2] Moreover, BIMs are used as dietary supplements to help reduce the risk of developing breast and prostate cancer.[3] Furthermore, BIMs are used as active compounds against recurrent respiratory papillomatosis.[4] Recently, BIMs have been studied as potential treatment options for a variety of viral and bacterial infections owing to their innate immune modulating properties.[5] In addition, the oxidized forms of BIMs and their derivatives have been utilized as dyes, as well as colorimetric chemosensors.[6] Furthermore, bis-1,3-dicarbonyl compounds are valuable intermediates or precursors for organic synthesis and transition metal complexes.[7] Owing to the prevalence of methylene bridged compounds in natural products and their versatile biological activity, there has been significant interest in their synthesis.

Traditionally, BIMs can be prepared by reacting of indoles with various aromatic or aliphatic aldehydes in the presence of Lewis acids or Brønsted acids.[8] Although many reports are available that detail the synthesis of BIMs with substituents in the methylene group,[9] BIMs that possess a methylene bridge are difficult to synthesize using the usual method of coupling indoles with formaldehyde. Therefore, a variety of methylene donor or precursor molecules have been explored in this regard, such as the use of methanol as an alternative to formaldehyde (Scheme 1a).[10] Formic acid has also been used as a source for the methylene group in the synthesis of BIMs.

However, an additional external hydrosilane is required to provide the requisite hydrogen atoms (Scheme 1b).[11] In particular, the use of amines and amides, acting as a carbon source through C–N bond cleavage, has emerged as a useful strategy for the synthesis of BIMs (Scheme 1c).[12] In addition, DMSO has previously been used in the synthesis of BIMs using phosphoric acid as a promoter (Scheme 1d).[13] Despite these formidable achievements, certain problems are still unsolved, such as using metal catalysts, air sensitive reagents, harsh reaction conditions and non-environmentally friendly

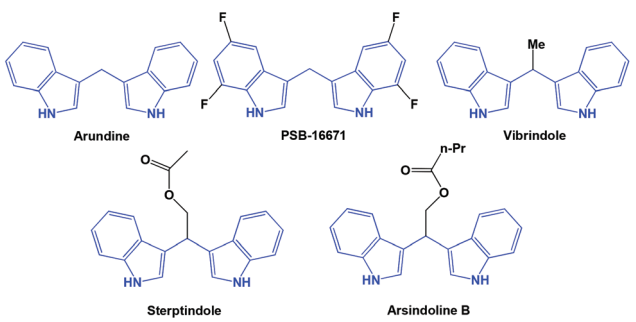

Fig. 1 Structures of some biologically active bis(indolyl)methane alkaloids.

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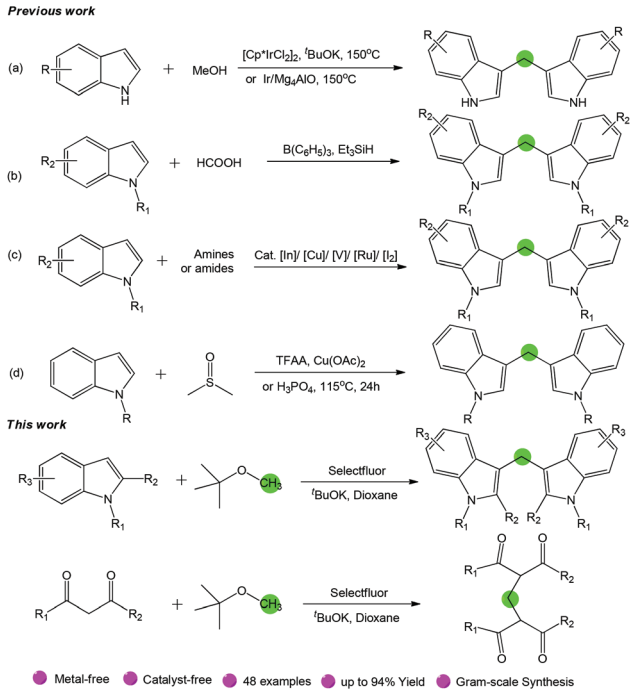
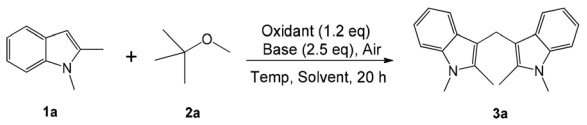


Scheme 1 Different strategies used to synthesize substituted BIMs.

Table 1 Optimization of the reaction conditions[a]



Entry	Oxidant	Base	Solvent	Temp (°C)	Yield[b] (%)
1	Selectfluor	^{t}BuOK	Dioxane	100	91
2	Selectfluor	^{t}BuOK	Dioxane	100	None[c]
3	$PhI(OAc)_2$	^{t}BuOK	Dioxane	100	None
4	$K_2S_2O_8$	^{t}BuOK	Dioxane	100	None
5	O_2	^{t}BuOK	Dioxane	100	None
6	NFSI	^{t}BuOK	Dioxane	100	None
7	Selectfluor	CsF	Dioxane	100	23
8	Selectfluor	K_2CO_3	Dioxane	100	57
9	Selectfluor	LiHMDS	Dioxane	100	21
10	Selectfluor	DBU	Dioxane	100	13
11	Selectfluor	^{t}BuOK	Toluene	100	71
12	Selectfluor	^{t}BuOK	DCE	100	79
13	Selectfluor	^{t}BuOK	THF	100	85
14	Selectfluor	^{t}BuOK	Dioxane	80	38
15	Selectfluor	^{t}BuOK	Dioxane	120	90

[a] Reaction conditions: **1a** (0.2 mmol), **2a** (0.6 mmol), oxidant (0.24 mmol), base (0.5 mmol), solvent (1.0 mL), air. [b] Isolated yield. [c] Without MTBE. NFSI = *N*-fluorobenzenesulfonimide, LiHMDS = lithium bis(trimethylsilyl)amide, DBU = 1,8-diazabicyclo[5.4.0]undec-7-ene, DCE = dichloroethane, THF = tetrahydrofuran.

methods. Therefore, the development of a more sustainable and mild protocol for the synthesis of BIMs is still a compelling area of research.

The cleavage of ethers is one of the most fundamental transformations in organic synthesis, mainly for the degradation or transformation of polyfunctional molecules, particularly in biologically active natural products.[14] Based on this, the utility of ethers as potential reactants in various organic transformations is an attractive prospect. As a minimally toxic, inexpensive and low-boiling point compound, methyl *tert*-butyl ether (MTBE) is usually used as a solvent.[15] However, to the best of our knowledge, selective C–O bond cleavage in MTBE and utilization of the released methyl groups as a methylene precursor agent has not been explored to date. Herein, we have developed a mild, simple, and environmentally friendly method for synthesizing methylene bridged compounds.

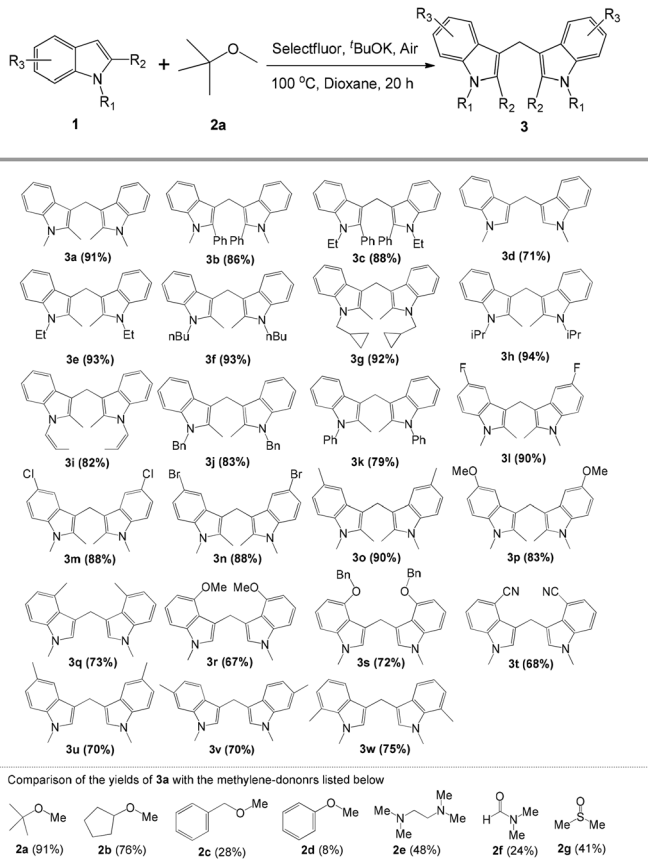
Results and discussion

All of the reactions were performed under air in 1 mL of solvent. In order to elucidate the optimal reaction conditions, 1,2-dimethylindole (**1a**) and MTBE (**2a**) were selected as the initial substrates and the effects of different oxidants, bases, solvents and temperatures on the product yield were investigated (Table 1). Based on the experimental results obtained, it was concluded that the reaction of substrates **1a** (0.2 mmol) and **2a** (0.6 mmol) in dioxane at 100 °C for 20 h provided optimal results, with the production of compound **3a** in a yield of up to 91% (entry 1). However, without the presence of MTBE, the desired product was not obtained (entry 2). When different oxidants, for example $PhI(OAc)_2$, $K_2S_2O_8$ and oxygen, were used in this coupling reaction the desired product was not observed (entries 3–5). Moreover, the transformation did not proceed when *N*-fluorobenzenesulphonimide (NFSI) was used (entry 6). These results reveal that the selectfluor reagent plays a paramount role in this transformation.

Other alkali salts and/or organic bases, such as CsF, K_2CO_3, lithium bis(trimethylsilyl)amide (LiHMDS) and 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU), afforded the product **3a** in lower yields (entries 7–10). Subsequently, the effect of various solvents, such as toluene, dichloroethane (DCE), tetrahydrofuran (THF) and dioxane were studied, and dioxane was found to be the optimal choice (entries 1 and 11–13). The effect of temperature was also investigated. The percentage conversion of indole was examined in a temperature range of 80–120 °C (entries 14 and 15), and a temperature of 100 °C was selected as the standard condition based on the transformation efficiency of compound **3a**. It was observed that a lower temperature decreased the yield dramatically, down to 38% at 80 °C (entry 14), and a higher temperature did not improve the efficiency of production (entry 15).

Using the optimal reaction conditions, we investigated the substrate scope and generality of the reaction (Table 2). Initially, we investigated *N*-methylindole with different substituents at the C-2 position. The yield of the methyl-substituted substrates was higher than that of the phenyl-substituted substrates (**3a**, **3b**); however, the yield was reduced for substrates without substitutes (**3c**). We used a variety of *N*-substituted indoles and to our delight the resultant BIMs were obtained in

Table 2 Scope of indoles with respect to the BIMs [a]



[a] Reaction conditions: **1** (0.2 mmol), **2a** (0.6 mmol), selectfluor (0.24 mmol), ^{t}BuOK (0.5 mmol), dioxane (1.0 mL), 100 °C, 20 h, air, isolated yield.

good to excellent yields (**3e–3k**) (Fig. 2a).[17] Interestingly, when 1-allyl-2-methyl-1*H*-indole weak electron-withdrawing groups were present on the C-5 position of 1,2-dimethylindole (**3l–3o**). Notably, the C–Cl and C–Br bonds remained intact during the reaction, which provided was used as the reaction substrate, the product **3i** was obtained, which had undergone a double bond rearrangement. High yields were also obtained if electron-donating groups and additional information for further elucidation of the products obtained (**3m**, **3n**). However, the methoxy substituent in the same position had a slightly lower yield (**3p**). We propose that this is because selectfluor could also break the methoxy C–O bond on the benzene ring of indole to reduce the contents of the substrate. Moreover, the

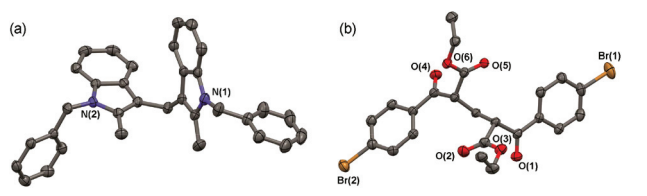
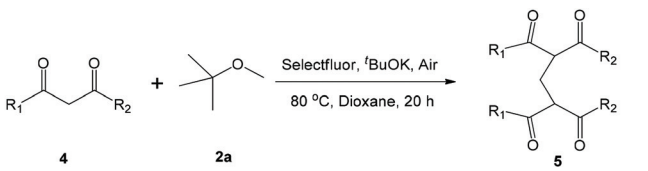


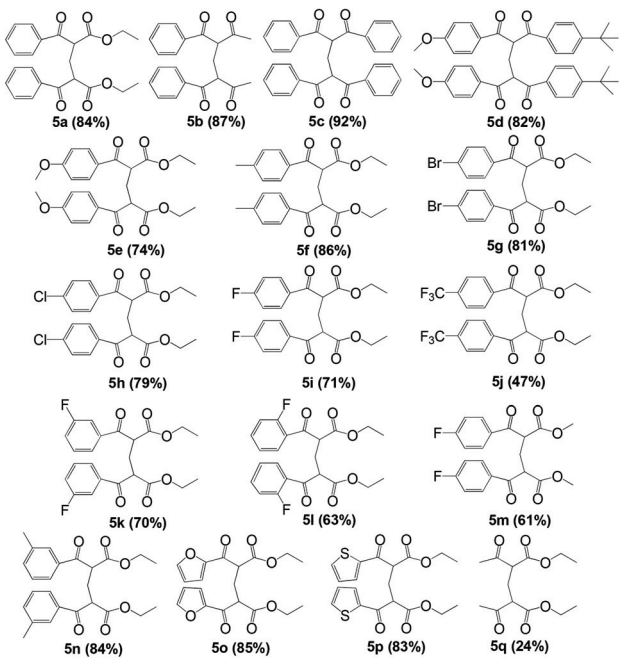
Fig. 2 Crystal structures of compounds **3j** (a) and **5g** (b).

effect of steric hindrance on the reaction was studied by employing a methyl group at different positions on the benzene ring (**3q**, **3u–3w**). The results demonstrated that the positions of the substituents did not appear to exert a significantly appreciable influence on the efficiency. Different substrates were then evaluated to determine the source of methylene in the methylenation. As shown in Table 2, the methyl ether, with a stronger electron-donating ability on the opposite side, provides a better yield in the reaction (**2a–2d**). *N*,*N*,*N*,*N*-Tetramethylethylenediamine (TMEDA), *N*,*N*-dimethylformamide (DMF) and dimethyl sulfoxide (DMSO), acting as methylene precursors, were also found to afford the methylene bridged products (**2e–2g**).

The success of the methylenation of the indoles encouraged us to further extend the substrate scope beyond the indoles. 1,3-dicarbonyl compounds are structurally unique and possess a variety of interesting chemical properties.[16] As shown in Table 3, a total of 17 examples were selected in order to analyse the reaction implications. The yield of 1,3-diphenylpropanedione, which possesses phenyl substituents on both sides, was higher than those obtained for compounds with substituents on only one side (**5a–5c**). Similarly, under the

Table 3 Scope of the 1,3-dicarbonyl compounds with respect to **5** [a]

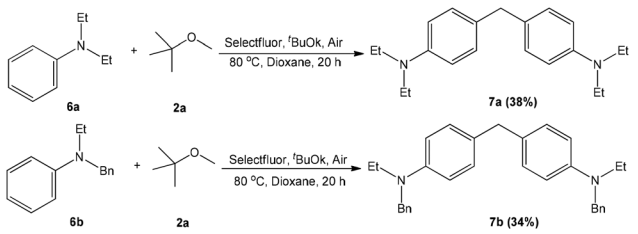




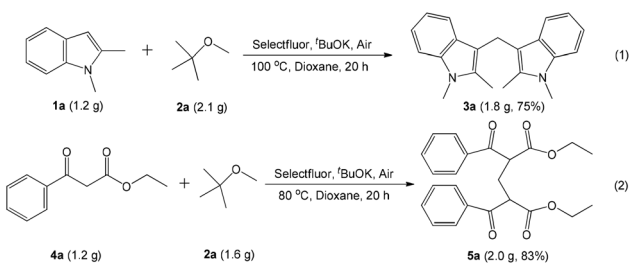
[a] Reaction conditions: **4** (0.2 mmol), **2a** (0.6 mmol), selectfluor (0.2 mmol), ^{t}BuOK (0.4 mmol), dioxane (1.0 mL), 80 °C, 20 h, air, isolated yield.

influence of the selectfluor, the reaction yield of the methoxy substituent on the benzene ring was lower than expected (**5d**, **5e**). High yields were also obtained when there were electron donating groups and weak electron withdrawing groups on the *para* position of the benzene ring of ethyl benzoylacetate (**5e**–**5i**, 71–86%). The electron-withdrawing fluoro group furnishes the product in a lower yield (**5i**, 71%) compared to the analogous bromo and chloro groups (**5g**, **5h**) (Fig. 2b).[17] However, if a strong electron withdrawing group, such as trifluoromethyl substituted ethyl 3-(4-trifluoromethylphenyl)-3-oxopropionate, is used for the reaction, the yield decreases significantly (**5j**). The steric hindrance of the reaction was then studied by utilising a fluoro group (**5i**, **5k**, **5l**) in the *para*-, *meta*- and *ortho*-positions. The results revealed that the reaction yields decreased from the substitution of the *para*-position (**5i**) to the *ortho*-position (**5l**). Meanwhile, the reaction of MTBE with ethyl 3-(furan-2-yl)-3-oxopropanoate and ethyl 3-oxo-3-(thiophen-2-yl)-propanoate gave the target products in good yields of 85% and 83%, respectively (**5o**, **5p**). Notably, the target product was also obtained when using ethyl acetoacetate as the reaction substrate (**5q**). Arylamines have also been used to investigate the availability of our protocol (Scheme 2). Very interestingly, the desired products were successfully obtained (**7a**, **7b**). In addition, to further demonstrate the practicality and efficiency of the developed methodology, a gram-scale reaction was performed. As shown in Scheme 3, **3a** (1.8 g, 75%) and **5a** (2.0 g, 83%) could be readily synthesized in a gram-scale reaction.

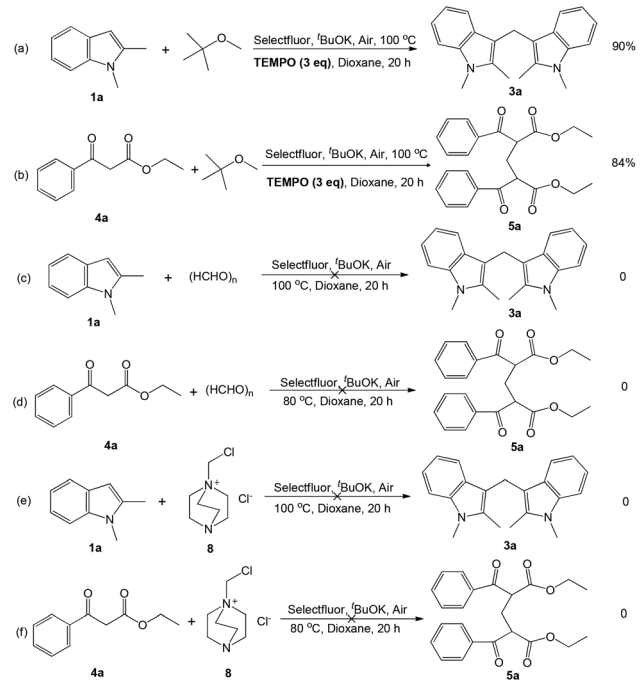
Several controlled experiments were conducted to gain further understanding about the reaction mechanism (Scheme 4). When a radical scavenger such as TEMPO was added ((a) and (b)), the product **3a** or **5a** was obtained in the nearly equal yield as that obtained without adding TEMPO.



Scheme 2 Reactions of different arylamines with MTBE.



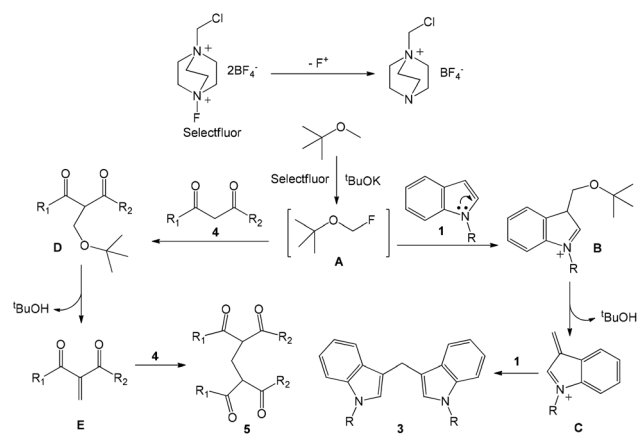
Scheme 3 Gram-scale synthesis of **3a** and **5a**.



Scheme 4 Schematic diagram of the controlled experiment.

Thus, we assume that the formation of neither the BIMs nor bis-1,3-dicarbonyl compounds are not involved free radical mediated processes. To examine the possibility of formaldehyde as an intermediate, the reaction of (c) and (d) was implemented by adding polyformaldehyde. However, the product **3a** or **5a** was not obtained. Considering the influence of chloromethyl group within selectfluor, we used **8** instead of MTBE to participate in the reaction under the best conditions. However, the desired product was not observed in the reaction ((e) and (f)).

On the basis of the above results, a possible mechanism was proposed in Scheme 5. Initially, the intermediate **A** is generated by oxidation of MTBE in the presence of selectfluor and ^{t}BuOK. Indoles **1** and 1,3-dicarbonyl compounds **4** then under-



Scheme 5 Schematic diagram of the possible reaction mechanism.

goes an electrophilic substitution with **A** to give unstable intermediate **B** and **D**, respectively. Finally, *in situ* elimination of *tert*-butanol from **B** and **D** produces reactive intermediate **C** and **E**. Azafulvalene **C** was ready for accepting another **1** to generate the final product **3**. The final product **5** was formed by reaction of intermediate **E** with the other portion of **4** *via* Michael addition process.

Conclusions

In summary, we have described a simple and efficient method for the synthesis of BIMs and bis-1,3-dicarbonyl compounds using MTBE as a methylene source. This work is superior to the traditional method of synthesis owing to the simple reaction conditions, the use of MTBE as a carbon source (that is abundantly available and cheap), the broad substrate scope and the relatively mild reaction conditions. Further studies investigating the reaction of MTBE with other nucleophiles are currently underway in our laboratory.

Experimental section

General experimental procedures

Synthesis of compounds 3. A mixture of indoles **1** (0.2 mmol), MTBE **2a** (0.6 mmol), selectfluor (0.24 mmol), and ^{t}BuOK (0.5 mmol) were placed in dioxane (1.0 mL) and stirred at 100 °C for 20 h. After cooling to room temperature, the reaction mixture was diluted with DCM (15 mL), filtered through a pad of silica gel and concentrated under reduced pressure. The crude product was purified using column chromatography on silica gel (eluent: petroleum ether/EtOAc = 5/1) to afford the product **3**.

Synthesis of compounds 5 and 7. A mixture of compounds **4** or **6** (0.2 mmol), MTBE **2a** (0.6 mmol), selectfluor (0.2 mmol), and ^{t}BuOK (0.4 mmol) were placed in dioxane (1.0 mL) and stirred at 80 °C for 20 h. After cooling to room temperature, the reaction mixture was diluted with DCM(15 mL), filtered through a pad of silica gel and concentrated under reduced pressure. The crude product was purified using column chromatography on silica gel (eluent: petroleum ether/EtOAc = 4/1) to afford the products **5** or **7**.

Conflicts of interest

There are no conflicts to declare.

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Notes and references

1 (*a*) A. Rosowsky, H. Chen, H. Fu and S. F. Queener, *Bioorg. Med. Chem.*, 2003, **11**, 59–67; (*b*) R. A. Forsch, S. F. Queener and A. Rosowsky, *Bioorg. Med. Chem. Lett.*, 2004, **14**, 1811–1815; (*c*) Y.-Q. Long, X.-H. Jiang, R. Dayam, T. Sanchez, R. Shoemaker, S. Sei and N. Neamati, *J. Med. Chem.*, 2004, **47**, 2561–2573; (*d*) D. Sarmah and U. Bora, *ChemistrySelect*, 2020, **5**, 8577–8603.

2 (*a*) T. R. Garbe, M. Kobayashi, N. Shimizu, N. Takesue, M. Ozawa and H. Yukawa, *J. Nat. Prod.*, 2000, **63**, 596–598; (*b*) Y. X. Gong, H. Sohn, L. Xue, G. L. Firestone and L. F. Bjeldanes, *Cancer Res.*, 2006, **66**, 4880–4887; (*c*) A. Roy, B. B. Das, A. Ganguly, S. B. Dasgupta, N. V. Khalkho, C. Pal, S. Dey, V. S. Giri, P. Jaisankar, S. Dey and H. K. Majumder, *Biochem. J.*, 2008, **409**, 611–622; (*d*) M. Shiri, M. A. Zolfigol, H. G. Kruger and Z. Tanbakouchian, *Chem. Rev.*, 2010, **110**, 2250–2293; (*e*) K. V. Sashidhara, A. Kumar, M. Kumar, A. Srivastava and A. Puri, *Bioorg. Med. Chem. Lett.*, 2010, **20**, 6504–6507; (*f*) K. V. Sashidhara, M. Kumar, R. Sonkar, B. S. Singh, A. K. Khanna and G. Bhatia, *J. Med. Chem.*, 2012, **55**, 2769–2779; (*g*) K. V. Sashidhara, R. K. Modukuri, R. Sonkar, K. B. Rao and G. Bhatia, *Eur. J. Med. Chem.*, 2013, **68**, 38–46; (*h*) S. Imran, M. Taha and N. H. Ismail, *Curr. Med. Chem.*, 2015, **22**, 4412–4433.

3 (*a*) P. Muti, H. L. Bradlow, A. Micheli, V. Krogh, J. L. Freudenheim, H. J. Schunemann, M. Stanulla, J. Yang, D. W. Sepkovic, M. Trevisan and F. Berrino, *Epidemiology*, 2000, **11**, 635–640; (*b*) K. M. Dalessandri, G. L. Firestone, M. D. Fitch, H. L. Bradlow and L. F. Bjeldanes, *J. Nutr. Cancer*, 2004, **50**, 161–167.

4 B. J. Wiatrak, *Curr. Opin. Otolaryngol. Head Neck Surg.*, 2003, **11**, 433–441.

5 L. Xue, J. J. Pestka, M. Li, G. L. Firestone and L. F. Bjeldanes, *J. Nutr. Biochem.*, 2008, **19**, 336–344.

6 (*a*) X. He, S. Hu, K. Liu, Y. Guo, J. Xu and S. Shao, *Org. Lett.*, 2006, **8**, 333–336; (*b*) H. J. Kim, H. Lee, J. H. Lee, D. H. Choi, J. H. Jung and J. S. Kim, *Chem. Commun.*, 2011, **47**, 10918–10920; (*c*) N. Kumari, S. Jha and S. Bhattacharya, *Chem. – Asian J.*, 2012, **7**, 2805–2812.

7 (*a*) A. Gogoll, C. Johansson, A. Axén and H. Grennberg, *Chem. – Eur. J.*, 2001, **7**, 396–403; (*b*) R. Karvembu and K. Natarajan, *Polyhedron*, 2002, **21**, 219–223; (*c*) H. Li, Z. He, X. Guo, W. Li, X. Zhao and Z. Li, *Org. Lett.*, 2009, **11**, 4176–4179; (*d*) J.-N. Tan, H. Li and Y. Gu, *Green Chem.*, 2010, **12**, 1772–1782; (*e*) L.-L. Wu, L. Tang, S.-G. Zhou, Y.-J. Peng, X.-D. He, Z. Guan and Y.-H. He, *Tetrahedron*, 2017, **73**, 6471–6478; (*f*) L. Xue, G. Cheng, R. Zhu and X. Cui, *RSC Adv.*, 2017, **7**, 44009–44012; (*g*) Y. Gao, D. Zhou and Y. Ma, *ChemistrySelect*, 2018, **3**, 9374–9377; (*h*) A. A. Smorodina, E. M. Buev, V. S. Moshkin and V. Y. Sosnovskikh, *Tetrahedron Lett.*, 2019, **60**, 1620–1623.

8 (*a*) A. Karam, J. C. Alonso, T. I. Gerganova, P. Ferreira and N. Bion, *Chem. Commun.*, 2009, **45**, 7000–7002; (*b*) T. M. Kubczyk, S. M. Williams, J. R. Kean, T. E. Davies, S. H. Taylor and A. E. Graham, *Green Chem.*, 2011, **13**,

2320–2325; (*c*) C. Karamia, H. Ahmadian, M. Nouri, F. Jamshidi, H. Mohammadi, K. Ghodrati, A. Farrokhi and Z. Hamidi, *Catal. Commun.*, 2012, **27**, 92–96; (*d*) A. Srivastava, A. Agarwal, S. K. Gupta and N. Jain, *RSC Adv.*, 2016, **6**, 23008–23011; (*e*) S. S. Mohapatra, Z. E. Wilson, S. Roy and S. V. Ley, *Tetrahedron*, 2017, **73**, 1812–1819; (*f*) A. Bahuguna, S. Kumar, V. Sharma, K. L. Reddy, K. Bhattacharyya, P. C. Ravikumar and V. Krishnan, *ACS Sustainable Chem. Eng.*, 2017, **5**, 8551–8567.

9 (*a*) S. Lancianesi, A. Palmieri and M. Petrini, *Adv. Synth. Catal.*, 2012, **354**, 3539–3544; (*b*) L. Ye, S.-H. Cai, D.-X. Wang, Y.-Q. Wang, L.-J. Lai, C. Feng and T.-P. Loh, *Org. Lett.*, 2017, **19**, 6164–6167; (*c*) K.-S. Du and J.-M. Huang, *Org. Lett.*, 2018, **20**, 2911–2915; (*d*) X. Peng, Y. Zen, Q. Liu, L. Liu and H. Wang, *Org. Chem. Front.*, 2019, **6**, 3615–3619.

10 (*a*) C. Sun, X. Zou and F. Li, *Chem. – Eur. J.*, 2013, **19**, 14030–14033; (*b*) W. Qiang, X. Liu and T.-P. Loh, *ACS Sustainable Chem. Eng.*, 2019, **7**, 8429–8439.

11 C. Qiao, X.-F. Liu, H.-C. Fu, H.-P. Yang, Z.-B. Zhang and L.-N. He, *Chem. – Asian J.*, 2018, **13**, 2664–2670.

12 (*a*) P. K. Pradhan, S. Dey, V. S. Giri and P. Jaisankar, *Synthesis*, 2005, 1779–1782; (*b*) C. Pal, S. Dey, S. K. Mahato, J. Vinayagam, P. K. Pradhan, V. S. Giri, P. Jaisankar, T. Hossain, S. Baruri, D. Ray and S. M. Biswas, *Bioorg. Med. Chem. Lett.*, 2007, **17**, 4924–4928; (*c*) L. Zhang, C. Peng, D. Zhao, Y. Wang, H.-J. Fu, Q. Shen and J.-X. Li, *Chem. Commun.*, 2012, **48**, 5928–5930; (*d*) D. Zhao, Y. Wang, M.-X. Zhu, Q. Shen, L. Zhang, Y. Du and J.-X. Li, *RSC Adv.*, 2013, **3**, 10272–10276; (*e*) F. Pu, Y. Li, Y.-H. Song, J. Xiao, Z.-W. Liu, C. Wang, Z.-T. Liu, J.-G. Chen and J. Lu, *Adv. Synth. Catal.*, 2016, **358**, 539–542; (*f*) P. Kaswan, N. K. Nandwana, B. DeBoef and A. Kumar, *Adv. Synth. Catal.*, 2016, **358**, 2108–2115; (*g*) M. L. Deb, P. J. Borpatra, C. D. Pegu, R. Thakuria, P. J. Saikia and P. K. Baruah, *ChemistrySelect*, 2017, **2**, 140–146; (*h*) M. L. Deb, P. J. Borpatra, P. J. Saikia and P. K. Baruah, *Org. Biomol. Chem.*, 2017, **15**, 1435–1443; (*i*) P. T. Ha, O. T. Nguyen, K. D. Huynh, T. T. Nguyen and N. T. Phan, *Synlett*, 2018, **29**, 2031–2034; (*j*) M. Yan, R. C. Hider and Y. Ma, *Org. Chem. Front.*, 2019, **6**, 1168–1172.

13 (*a*) T. Abe, T. Ikeda, T. Itoh and M. Ishikura, *Heterocycles*, 2014, **88**, 187–191; (*b*) P. Liu, Z. Shen, Y. Yuan and P. Sun, *Org. Biomol. Chem.*, 2016, **14**, 6523–6530.

14 (*a*) D. W. Kwon and Y. H. Kim, *J. Org. Chem.*, 2002, **67**, 9488–9491; (*b*) J. S. Yadav, B. V. S. Reddy, P. M. K. Reddy and M. K. Gupta, *Tetrahedron Lett.*, 2005, **46**, 8493–8495.

15 (*a*) A. Tuulmets and M. Sassian, *J. Organomet. Chem.*, 1999, **586**, 145–149; (*b*) M. Sassian and A. Tuulmets, *Helv. Chim. Acta*, 2003, **86**, 82–90.

16 (*a*) K. Maruyama, K. Kubo, Y. Toda, K. Kawase, T. Mashino and A. Nishinaga, *Tetrahedron Lett.*, 1995, **36**, 5609–5612; (*b*) R. Balamurugan and S. Manojveer, *Chem. Commun.*, 2011, **47**, 11143–11145; (*c*) W. J. Yoo, A. Tanoue and S. Kobayashi, *Chem. – Asian J.*, 2012, **7**, 2764–2767; (*d*) X.-J. Dai, X.-L. Xu, D.-P. Cheng and X.-N. Li, *Chin. Chem. Lett.*, 2014, **25**, 545–548; (*e*) X. Wang, Y. Wang, Y. Yuan and C.-H. Xing, *Tetrahedron*, 2014, **70**, 2195–2202; (*f*) L. Lu, S. Guo, Q. Xiong, S. Liu, X. Li and H. Cai, *Synthesis*, 2014, 2445–2450; (*g*) L.-J. Xing, X.-M. Wang, H.-Y. Li, W. Zhou, N. Kang, P. Wang and B. Wang, *RSC Adv.*, 2014, **4**, 26783–26786; (*h*) S. Guo, Z. Zhu, L. Lu, W. Zhang, J. Gong and H. Cai, *Synlett*, 2015, **26**, 543–546; (*i*) A. K. Jha, A. Kumari and S. Easwar, *Chem. Commun.*, 2020, **19**, 2949–2952.

17 Crystallographic data for the compound **3j** and **5g** have been deposited with the CCDC 2056480 and 2056483.†