# Chemical Science

## EDGE ARTICLE



Cite this: Chem. Sci., 2022, 13, 13893

o All publication charges for this article have been paid for by the Royal Society of Chemistry

Received 29th July 2022 Accepted 11th October 2022

DOI: 10.1039/d2sc04229k

rsc.li/chemical-science

#### Introduction

Polyene cyclization, as one of the most powerful synthetic strategies, has been widely applied to the synthesis of complex polycyclic natural products and bioactive molecules.1 Since the elegant strategy was first successfully introduced for synthesizing diterpenes, many synthetic chemists have strived to explore more convenient and general synthetic approaches toward biologically active polycyclic terpenes<sup>2</sup> or the key 6/6/6 tricyclic skeleton.<sup>3</sup> During the process, many functional groups have been used as initiators to trigger this kind of cyclization procedure, such as alkene4 or alkyne,5 epoxide,6 allylic alcohol,7 propargylic ester8 and carbonyl-related groups.9 Nevertheless, it is still highly desirable to develop new activation patterns that can spontaneously introduce functional groups on the resulting polycyclic products to facilitate subsequent synthetic manipulations, in particular, the synthesis of corresponding bioactive molecules (Fig. 1).

Based on the pioneering work of polyene cyclization and in connection with our research interests in the development of efficient synthetic methodologies toward the synthesis of bioactive molecules, an Au(1)-catalyzed polyene cyclization strategy using propargylic ester as the initiator was developed by our group recently. In this procedure, an enol ester moiety at the C2-

"School of Pharmacy & State Key Laboratory of Applied Organic Chemistry, Lanzhou University, 730000, P. R. China. E-mail: zhudy@lzu.edu.cn; wangshh@lzu.edu.cn <sup>b</sup>School of Biotechnology and Health Science, Wuyi University, Jiangmen 529020, P. R.

### Inl<sub>3</sub>-catalyzed polyene cyclization of allenes and its application in the total synthesis of seven abietanetype diterpenoids<sup>†</sup>

Chen-Yu Huo,<sup>a</sup> Tian-Lu Zheng,<sup>a</sup> Wei-Hao Dai,<sup>a</sup> Zi-Hao Zhang,<sup>a</sup> Jin-Da Wang,<sup>a</sup> Dao-Yong Zhu,\*<sup>ac</sup> Shao-Hua Wang, 🕑 \*<sup>a</sup> Xiao-Ming Zhang 🔟 <sup>a</sup> and Xue-Tao Xu 🔟 <sup>b</sup>

A novel polyene cyclization using the allene group as the initiator has been successfully developed. This methodology provides an efficient strategy for the construction of an abietane-type tricyclic skeleton with a functionalizable C2-C3 double bond and features a wide substrate scope and excellent stereoselectivities. Potential utility of this approach has been well demonstrated by the collective total synthesis of seven abietane-type diterpenoids. Specifically,  $(\pm)$ -2,3-dihydroxyferruginol and  $(\pm)$ -2,3dihydroxy-15,16-dinor-ent-pimar-8,11,13-triene were synthesized for the first time.

> C3 site of the key 6/6/6 tricyclic skeleton can be readily installed and used as a functional handle for subsequent synthetic transformations (Scheme 1a), which has been shown through the divergent synthesis of five abietane-type diterpenoids encouraging us to carry out further investigation in this field.8 Over the past decades, the allene group, as a typical versatile synthon, has attracted broad attention from chemists.10 In particular, it has been applied to a series of cyclization modes to construct various ring systems with an alkene moiety.11 Inspired by these results, we envisioned that it should be viable to develop a new polyene cyclization mode using the allene functional group as the initiator to afford a 6/6/6 tricyclic cyclization product with a double bond at the C2-C3 position (Scheme 1b). Since the double bond can be readily transformed to structural moieties like vicinal diol or enone, realization of such a methodology should lead to a new synthetic strategy toward the collective total synthesis of some biological abietane-type diterpenoids with substituents at both C2 and C3-positions, such as  $(\pm)$ -shonanol,  $(\pm)$ -2,3-dihydroxy-



Fig. 1 Selected abietane-type diterpenoids.

**ROYAL SOCIETY** OF CHEMISTRY

China <sup>c</sup>Key Laboratory of Drug-Targeting of Education Ministry and Department of Medicinal

Chemistry, West China School of Pharmacy, Sichuan University, Chengdu, 610041, P. R. China

<sup>†</sup> Electronic supplementary information (ESI) available. CCDC [2171065, 2171067, 2171063]. For ESI and crystallographic data in CIF or other electronic format see DOI: https://doi.org/10.1039/d2sc04229k



15,16-dinor-*ent*-pimar-8,11,13-triene, and  $(\pm)$ -2,3-dihydroxyferruginol (Fig. 1). Herein, we present an InI<sub>3</sub>-catalyzed polyene cyclization of allenes and its application to the total synthesis of seven abietane-type diterpenoids.

#### **Results and discussion**

Initially, we attempted a model reaction of **1a** with various Lewis acids (see the ESI†). Fortunately, the desired product **2a** was obtained in 10% yield with  $In(OTf)_3$  (Table 1, entry 1), whereas other strong Lewis acids like  $Sn(OTf)_2$  and  $Zn(OTf)_2$  did not give product **2a** (Table 1, entries 2–3). Therefore, indium catalysts with different anions such as  $InCl_3$ ,  $InBr_3$ ,  $InI_3$  were further screened. Fortunately, the use of  $InI_3$  led to the best yield of 63% (Table 1, entry 6). Subsequently, several solvents were also tested, and



Entry	Cat.	Equiv.	Sol.	T (°C)	<i>t</i> /h	Yield (%) <sup>b</sup>
1	In(OTf) <sub>3</sub>	0.2	DCM	r.t.	18	10
2	$Sn(OTf)_2$	0.2	DCM	0	1	NR <sup>c</sup>
3	$Zn(OTf)_2$	0.2	DCM	r.t.	120	NR <sup>c</sup>
4	InCl <sub>3</sub>	0.2	DCM	r.t.	1	40
5	InBr <sub>3</sub>	0.2	DCM	r.t.	1	40
6	InI <sub>3</sub>	0.2	DCM	-20	4	63
7	InI <sub>3</sub>	0.2	$CH_3OH$	r.t.	120	NR <sup>c</sup>
8	InI <sub>3</sub>	0.2	DMF	r.t.	120	NR <sup>c</sup>
9	InI <sub>3</sub>	0.2	DCE	-20	3	45
10	InI <sub>3</sub>	0.2	Toluene	-20	3	20
11	InI <sub>3</sub>	0.2	CH <sub>3</sub> CN	r.t.	120	NR <sup>c</sup>
12	InI <sub>3</sub>	0.2	THF	r.t.	120	NR <sup>c</sup>
13	InI <sub>3</sub>	0.2	DCM	r.t.	0.5	45
14	InI <sub>3</sub>	0.2	DCM	0	1.5	54
15	InI <sub>3</sub>	0.2	DCM	-40	6	71
16	$InI_3$	0.2	DCM	-60	27	63

<sup>*a*</sup> Unless specified, all reactions were carried out with **1a** (0.1 mmol, 1.0 equiv.) and solvent (2 mL) in reaction tubes. <sup>*b*</sup> Isolated yield of product **2a**. <sup>*c*</sup> NR = no Reaction.

CH<sub>2</sub>Cl<sub>2</sub> was still the best choice after many trials, while other solvents were not efficient enough (Table 1, entries 7–12). Furthermore, examining different temperatures ranging from -60 °C to 0 °C revealed the best yield of 71% at -40 °C (Table 1, entries 13–16). Finally, the reaction was conducted in CH<sub>2</sub>Cl<sub>2</sub> at -40 °C (Table 1, entry 15).

With the optimal reaction conditions in hand, the substrate scope of this reaction was then investigated. As shown in Scheme 2, switching the *gem*-dimethyl moiety to cyclopentane and cyclohexane rings was feasible, giving the desired products **2b** and **2c** in 45% and 41% yields, respectively. The slightly decreased yields might be attributed to the steric hindrance of these moieties. Notably, a mono phenyl substituted substrate **1d** could deliver **2d** 



Scheme 2 Substrate scope investigation of the reaction<sup>a</sup>. <sup>a</sup>Unless specified, all reactions were carried out with 1 (0.1 mmol, 1.0 equiv.), InI<sub>3</sub> (20 mol%) and CH<sub>2</sub>Cl<sub>2</sub> (2 mL) in reaction tubes at -40 °C for 4 h. <sup>b</sup>Reaction temperature was 0 °C. <sup>c</sup>Reaction temperature was 25 °C. <sup>d</sup>Reaction temperature was -20 °C. <sup>e</sup>Yield obtained in a 2 mmol scale reaction.

smoothly in 50% yield with excellent diastereoselectivity, and the relative configuration of 2d was further determined by X-ray crystal diffraction. Next, changing the R<sup>3</sup> group of substrates from methyl to o-methylphenyl and p-methylphenyl was successful to give corresponding products 2e and 2f in moderate yields of 40% and 50% at 0 °C and room temperature, respectively. Subsequently, it was observed that bromo substituted substrate 1g was amenable to this reaction, albeit giving 2g with only 34% yield. Subsequently, substrates with electro-donating groups such as methyl, methoxy, tert-butyl and phenyl groups as R<sup>4</sup> at different positions on the phenyl ring were also investigated. All these substrates could produce the expected products in moderate to good yields (2h-2n). Generally, electron-donating substituents were beneficial for better yields of corresponding products (2g vs. 2h-2n). Consistent with the above observation, electron-donating substituents like TBS ether on the phenyl ring and the use of the naphthalene ring could also lead to the desired products 20 and 2p in good yields of 81% and 70%, respectively. It is worth mentioning that substrate 1r with two electron-donating substituents gave the best yield of 95%, whereas 1g bearing both electron-rich and electron-deficient substituents produced 2q in only 44% yield. Moreover, the electronic effect was also shown by comparison between 2r and 2t (40% vs. 83%). To further demonstrate the potential practicality of this reaction, a 2 mmol scale reaction of 1s was also conducted, and an excellent yield of 91% yield was obtained. Additionally, substrate 1u with a (Z)-1,4-enallene moiety was also tested under the standard conditions, and an inseparable mixture of 2a and 2u was obtained in 50% total yield and 1:1 diasteromeric ratio (trans/ cis). 12,4h,5e

To show the synthetic utility of the reaction, a collective total synthesis of seven abietane-type diterpenes, *i.e.*,  $(\pm)$ -2,3-dihydroxyferruginol,<sup>13</sup> (±)-shonanol,<sup>14</sup> (±)-2,3-dihydroxy-15,16-dinor*ent*-pimar-8,11,13-triene,<sup>15</sup>  $(\pm)$ -ferruginol,<sup>16</sup>  $(\pm)$ -sugiol methyl ether,<sup>17</sup> ( $\pm$ )-sugiol,<sup>18</sup> and ( $\pm$ )-acetylferruginol,<sup>19</sup> was then conducted from compounds 2s and 2t. As shown in Scheme 3, demethylation of 2s delivered 3 in 85% yield in the presence of NaSEt, and  $(\pm)$ -2,3-dihydroxyferruginol was facilely obtained through dihydroxylation of 3 in 50% yield along with its epimer 7. The relative configuration of  $(\pm)$ -2,3-dihydroxyferruginol was confirmed by X-ray diffraction (see the ESI<sup>+</sup>). In another successful example, selective oxidization of 2s with SeO<sub>2</sub> and further oxidization could give ketone 4 in 60% yield using DMP as the oxidant. Subsequently, the synthesis of  $(\pm)$ -shonanol was readily finished after simple demethylation, and the relative configuration was also confirmed by X-ray diffraction (see the ESI<sup>†</sup>). Other syntheses of abietane-type diterpenoids, such as (±)-ferruginol, (±)-sugiol methyl ether, (±)-sugiol, and (±)-acetylferruginol are also exhibited in Scheme 3 starting from a common advanced intermediate 5, which was easily prepared through hydrogenation of 2s in 81% yield. Next,  $(\pm)$ -ferruginol was obtained by demethylation of 5 in 90% yield in the presence of BBr<sub>3</sub>. Acylation of  $(\pm)$ -ferruginol gave  $(\pm)$ -acetylferruginol in 95% yield. Alternatively, compound 5 could be oxidized with  $CrO_3$  to give (±)-sugiol methyl ether in 83% yield, and demethylation of  $(\pm)$ -sugiol methyl ether with NaSEt afforded ( $\pm$ )-sugiol. Additionally, another natural product ( $\pm$ )-2,3-dihydroxy-15,16-dinor-ent-pimar-8,11,13-triene and its epimer 6 were



Scheme 3 Synthetic applications. (a) NaSEt, DMF, 140 °C; (b) OsO<sub>4</sub>, NMO, citric acid, t-BuOH/acetone/H<sub>2</sub>O = 1:1:1; (c) SeO<sub>2</sub>, 1,4-dioxane, 100 °C, then DMP, DCM, r.t.; (d) BBr<sub>3</sub>, DCM, -20 °C; (e) H<sub>2</sub>, Pd/C, CH<sub>3</sub>OH, r.t.; (f) CrO<sub>3</sub>, AcOH, r.t.; (g) Ac<sub>2</sub>O, Et<sub>3</sub>N, DMAP, DCM, r.t.

also rapidly prepared in 71% total yield through a dihydroxylation of compound **2t**. These synthetic applications well exhibit the utility of our newly developed polyene cyclization mode, in particular the usefulness of the retained C2–C3 double bond for further functionalization.

#### Conclusions

In conclusion, a new mode of polyene cyclization initiated by the allene moiety has been successfully realized under the catalysis of InI<sub>3</sub>, and the retained C2–C3 double bond provides the very crucial reaction site for further transformations, in particular, towards the synthesis of corresponding abietane diterpenes, such as  $(\pm)$ -2,3-dihydroxyferruginol,  $(\pm)$ -shonanol and  $(\pm)$ -2,3-dihydroxy-15,16-dinor-*ent*-pimar-8,11,13-triene. In addition, other diterpenes like  $(\pm)$ -ferruginol,  $(\pm)$ -sugiol methyl ether,  $(\pm)$ -sugiol, and  $(\pm)$ -acetylferruginol have also been collectively synthesized after simple operations. Currently, biological activity tests of these abietane diterpenes and their analogues along with the synthesis of other bioactive polycyclic terpenes using the same strategy are ongoing in the same laboratory.

#### Data availability

Experimental data has been uploaded as part of the ESI.†

#### Author contributions

SHW and DYZ directed this project. CYH, TLZ, WHD, ZHZ and JDW performed the experiments. XMZ, XTX, DYZ and SHW prepared the draft and SHW revised the manuscript.

### Conflicts of interest

There are no conflicts to declare.

#### Acknowledgements

This project was supported by the National Natural Science Foundation of China (21772071), the Science and Technology Program of Gansu Province (20JR10RA608), the Department of Education of Guangdong Province (No. 2019KZDXM035, 2021KCXTD044, and 2021KTSCX135), the Fundamental Research Funds for the Central Universities (lzujbky-2022-ct03, lzujbky-2022-sp09), the Collaborative Innovation Center for Northwestern Chinese Medicine of Lanzhou University and the Drug Research Project of Gansu Province (No.2022GSMPA0010).

#### References

- 1 (a) J. Justicia, L. Alvarez de Cienfuegos, A. G. Campana, D. Miguel, V. Jakoby, A. Gansauer and J. M. Cuerva, Chem. Soc. Rev., 2011, 40, 3525-3537; (b) S. A. Snyder and A. M. Levinson, in Comprehensive Organic Synthesis, ed. P. Knochel, Elsevier, Amsterdam, 2nd edn, 2014, pp. 268-292, DOI: 10.1016/B978-0-08-097742-3.00309-8; (c)C. N. Ungarean, E. H. Southgate and D. Sarlah, Org. Biomol. Chem., 2016, 14, 5454-5467; (d) A. Barrett, T.-K. Ma and T. Mies, Synthesis, 2019, 51, 67-82; (e) A. D'Hollander, L. Peilleron, T. Grayfer and K. Cariou, Synthesis, 2019, 51, 1753-1769; (f) B. Maji, Adv. Synth. Catal., 2019, 361, 3453-3489; (g) J. M. Feilner, F. L. Haut and T. Magauer, Chem.-Eur. J., 2021, 27, 7017-7021; (h) X.-S. Peng, H. N. C. Wong, Z. Zhong, M.-Y. Lyu and H.-R. Ma, Synlett, 2021, 32, 1796-1815; (i) G. Alachouzos and A. J. Frontier, Isr. J. Chem., 2021, 61, 469-485.
- 2 (a) M. A. Gonzalez, *Eur. J. Med. Chem.*, 2014, 87, 834–842; (b)
  M. A. Gonzalez, *Nat. Prod. Rep.*, 2015, 32, 684–704; (c)
  M. A. González, *Tetrahedron*, 2015, 71, 1883–1908.
- 3 (a) A. M. Gonzalez, *Curr. Bioact. Compd.*, 2007, 3, 1–36; (b)
  R. J. Peters, *Nat. Prod. Rep.*, 2010, 27, 1521–1530; (c)
  A. P. Wardana, N. S. Aminah, M. Rosyda, M. I. Abdjan,
  A. N. Kristanti, K. N. W. Tun, M. I. Choudhary and
  Y. Takaya, *Heliyon*, 2021, 7, e07777.
- 4 (*a*) K. Ishihara, H. Ishibashi and H. Yamamoto, *J. Am. Chem. Soc.*, 2001, **123**, 1505–1506; (*b*) K. Ishihara, H. Ishibashi and

H. Yamamoto, J. Am. Chem. Soc., 2002, 124, 3647-3655; (c) H. Ishibashi, K. Ishihara and H. Yamamoto, J. Am. Chem. Soc., 2004, 126, 11122-11123; (d) A. Sakakura, A. Ukai and K. Ishihara, Nature, 2007, 445, 900-903; (e) Y.-J. Zhao, S.-S. Chng and T.-P. Loh, J. Am. Chem. Soc., 2007, 129, 492-493; (f) Y.-J. Zhao and T.-P. Loh, J. Am. Chem. Soc., 2008, 130, 10024–10029; (g) S. A. Snyder and D. S. Treitler, Angew. Chem., Int. Ed., 2009, 48, 7899-7903; (h) S. A. Snyder, D. S. Treitler and A. P. Brucks, J. Am. Chem. Soc., 2010, 132, 14303-14314; (i) K. Surendra and E. J. Corey, J. Am. Chem. 2012, **134**, 11992–11994; (*j*) Y. Sawamura, Soc., H. Nakatsuji, A. Sakakura and K. Ishihara, Chem. Sci., 2013, 4, 4181–4186; (k) R. C. Samanta and H. Yamamoto, J. Am. Chem. Soc., 2017, 139, 1460-1463; (l) D. Vrubliauskas and C. D. Vanderwal, Angew. Chem., Int. Ed., 2020, 59, 6115-6121.

- 5 (a) H. Imagawa, T. Iyenaga and M. Nishizawa, Org. Lett., 2005, 7, 451–453; (b) W.-W. Qiu, K. Surendra, L. Yin and E. J. Corey, Org. Lett., 2011, 13, 5893–5895; (c) K. Surendra, W. Qiu and E. J. Corey, J. Am. Chem. Soc., 2011, 133, 9724–9726; (d) K. Surendra and E. J. Corey, J. Am. Chem. Soc., 2014, 136, 10918–10920; (e) J. Yao, C.-L. Li, X. Fan, Z. Wang, Z.-X. Yu and J. Zhao, CCS Chem., 2021, 3, 3133–3143.
- 6 (a) S. P. Morcillo, D. Miguel, S. Resa, A. Martin-Lasanta,
  A. Millan, D. Choquesillo-Lazarte, J. M. Garcia-Ruiz,
  A. J. Mota, J. Justicia and J. M. Cuerva, *J. Am. Chem. Soc.*,
  2014, 136, 6943–6951; (b) G. Rajendar and E. J. Corey, *J. Am. Chem. Soc.*, 2015, 137, 5837–5844; (c) Y. Tian, X. Xu,
  L. Zhang and J. Qu, *Org. Lett.*, 2016, 18, 268–271.
- 7 (a) M. A. Schafroth, D. Sarlah, S. Krautwald and E. M. Carreira, *J. Am. Chem. Soc.*, 2012, 134, 20276–20278;
  (b) F. Z. Zhang, Y. Tian, G. X. Li and J. Qu, *J. Org. Chem.*, 2015, 80, 1107–1115.
- 8 T.-L. Zheng, S.-Z. Liu, C.-Y. Huo, J. Li, B.-W. Wang, D.-P. Jin, F. Cheng, X.-M. Chen, X.-M. Zhang, X.-T. Xu and S.-H. Wang, *CCS Chem.*, 2020, **2**, 2795–2802.
- 9 (a) M. Uyanik, K. Ishihara and H. Yamamoto, Org. Lett., 2006,
  8, 5649–5652; (b) S. Rendler and D. W. C. MacMillan, J. Am. Chem. Soc., 2010, 132, 5027–5029; (c) Y.-J. Zhao, B. Li, L.-J.
  S. Tan, Z.-L. Shen and T.-P. Loh, J. Am. Chem. Soc., 2010,
  132, 10242–10244; (d) B. Li, Y. C. Lai, Y. Zhao, Y. H. Wong,
  Z. L. Shen and T. P. Loh, Angew. Chem., Int. Ed., 2012, 51,
  10619–10623; (e) L. Fan, C. Han, X. Li, J. Yao, Z. Wang,
  C. Yao, W. Chen, T. Wang and J. Zhao, Angew. Chem., Int. Ed., 2018, 57, 2115–2119.
- 10 (a) S. Ma, Chem. Rev., 2005, 105, 2829–2871; (b) S. Ma, Acc. Chem. Res., 2009, 42, 1679–1688; (c) T. Caneque,
  F. M. Truscott, R. Rodriguez, G. Maestri and M. Malacria, Chem. Soc. Rev., 2014, 43, 2916–2926; (d) J. Ye and S. Ma, Acc. Chem. Res., 2014, 47, 989–1000; (e) X. Huang and S. Ma, Acc. Chem. Res., 2019, 52, 1301–1312.
- 11 (a) S. Ma, Acc. Chem. Res., 2003, 36, 701–712; (b) B. Alcaide,
  P. Almendros and T. Martinez del Campo, Angew. Chem.,
  Int. Ed., 2007, 46, 6684–6687; (c) F. Zhao and T. P. Loh,
  Angew. Chem., Int. Ed., 2009, 48, 7232–7235; (d) W. Li,
  W. Yuan, M. Shi, E. Hernandez and G. Li, Org. Lett., 2010,

12, 64-67; (e) B. L. Lu and M. Shi, Angew. Chem., Int. Ed., 2011, 50, 12027-12031; (f) B. Bolte and F. Gagosz, J. Am. Chem. Soc., 2011, 133, 7696-7699; (g) S. Yu and S. Ma, Angew. Chem., Int. Ed., 2012, 51, 3074-3112; (h) B. Alcaide, P. Almendros, S. Cembellin, T. Martinez del Campo and I. Fernandez, Chem. Commun., 2013, 49, 1282-1284; (i) J. Ye and S. Ma, Org. Chem. Front., 2014, 1, 1210-1224; (f) D. Y. Li, Y. Wei, I. Marek, X. Y. Tang and M. Shi, Chem. Sci., 2015, 6, 5519-5525; (k) C. Ji, Q. Xu and M. Shi, Adv. Synth. Catal., 2017, 359, 974-983; (l) L.-P. Zhao, P.-J. Li, L. Wang and Y. Tang, Angew. Chem., Int. Ed., 2022, e202207360.

- 12 (a) G. Stork and A. W. Burgstahler, J. Am. Chem. Soc., 1955, 77, 5068–5077; (b) K. Ishihara, S. Nakamura and H. Yamamoto, J. Am. Chem. Soc., 1999, 121, 4906–4907; (c) S. Nakamura, K. Ishihara and H. Yamamoto, J. Am. Chem. Soc., 2000, 122, 8131–8140; (d) P. Alonso, P. Pardo, R. Fontaneda, F. J. Fananas and F. Rodriguez, Chem.—Eur. J., 2017, 23, 13158–13163; (e) S. J. Plamondon, J. M. Warnica, D. Kaldre and J. L. Gleason, Angew. Chem., Int. Ed., 2020, 59, 253–258; (f) S. J. Plamondon and J. L. Gleason, Org. Lett., 2022, 24, 2305–2309.
- 13 (a) R. E. Cox, S. Yamamoto, A. Otto and B. R. T. Simoneit, Biochem. Syst. Ecol., 2007, 35, 342–362; (b) H. Zhao, H. Li, G. Huang and Y. Chen, Nat. Prod. Rep., 2017, 31, 844–848.
- 14 (a) Y.-T. Lin and K.-T. Liu, J. Chin. Chem. Soc., 1965, 12, 51– 60; (b) T. Matsumoto, S. Imai and S. Yuki, Bull. Chem. Soc.

*Jpn.*, 1981, 54, 1448–1455; (*c*) J.-M. Fang, S.-T. Jan and Y.-S. Cheng, *Phytochemistry*, 1987, 26, 853–854.

- 15 H. Li, J. J. Zhao, J. L. Chen, L. P. Zhu, D. M. Wang, L. Jiang, D. P. Yang and Z. M. Zhao, *Phytochemistry*, 2015, **117**, 400–409.
- 16 (a) W. P. Campbell and D. Todd, J. Am. Chem. Soc., 1942, 64, 928–935; (b) C.-C. Wen, Y.-H. Kuo, J.-T. Jan, P.-H. Liang, S.-Y. Wang, H.-G. Liu, C.-K. Lee, S.-T. Chang, C.-J. Kuo, S.-S. Lee, C.-C. Hou, P.-W. Hsiao, S.-C. Chien, L.-F. Shyur and N.-S. Yang, J. Med. Chem., 2007, 50, 4087–4095; (c) Z. Tao, K. A. Robb, K. Zhao and S. E. Denmark, J. Am. Chem. Soc., 2018, 140, 3569–3573; (d) A. R. Jassbi, H. Hadavand Mirzaei, O. Firuzi, S. Pirhadi, M. Asadollahi, J. N. Chandran and B. Schneider, Nat. Prod. Rep., 2022, 36, 3183–3188.
- 17 (a) P. Sengupta, S. N. Choudhuri and H. N. Khastgir, *Tetrahedron*, 1960, 10, 45–54; (b) Z. Yang, Y. Kitano, K. Chiba, N. Shibata, H. Kurokawa, Y. Doi, Y. Arakawa and M. Tada, *Bioorg. Med. Chem.*, 2001, 9, 347–356.
- 18 (a) E. Wenkert, J. de Paiva Campello, J. D. McChesney and D. J. Watts, *Phytochemistry*, 1974, 13, 2545–2549; (b)
  I. Cordova, L. G. Leon, F. Leon, L. San Andres, J. G. Luis and J. M. Padron, *Eur. J. Med. Chem.*, 2006, 41, 1327–1332.
- 19 (a) H. Akita and T. Oishi, *Chem. Pharm. Bull.*, 1981, 29, 1567–1579; (b) C. Thommen, C. K. Jana, M. Neuburger and K. Gademann, *Org. Lett.*, 2013, 15, 1390–1393.