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# [3+2] regioselective annulation reaction of 2-arylidene-1,3-indandiones towards synthesis of spirocyclopentenes: understanding the mechanism of $\gamma$ -attack vs. $\alpha$ -attack using DFT studies†

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A regioselective [3+2] cyclisation reaction between 2-arylidene-1,3-indanedione and ethyl 2,3-butadienoate catalysed by triphenylphosphine has been demonstrated to synthesize functionalised spirocyclic cyclopentenes. The reaction tolerated various electron-rich and electron-deficient aryl substituted 2-arylidene-1,3-indanediones with high to excellent chemical yields (up to 99%) and moderate to good regioselectivity (up to 5 : 1). DFT studies have also been carried out to understand the regioselective nature of this reaction. The results of Frontier molecular orbital calculations and the activation energy ( $E_a$ ) favour the formation of compound **3a** via  $\gamma$ -attack compared to that of **4a** via  $\alpha$ -attack.

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## Introduction

Nucleophilic phosphine-catalysed annulation of allenes has emerged as a powerful tool for the construction of diverse carbocycles and heterocycles.<sup>1</sup> Various electrophiles such as activated alkenes,<sup>2</sup> enones,<sup>3</sup> ketones,<sup>4</sup> imines,<sup>5</sup> oxo-dienes,<sup>6</sup> cyclic ketimines,<sup>7</sup> chromenones,<sup>8</sup> azomethine imines,<sup>9</sup> salicyl *N*-thio-phosphinyl imines,<sup>10</sup> alkylidene malononitriles,<sup>11</sup> exocyclic enones,<sup>12</sup> aldehydes,<sup>13</sup> *N*-acyldiazenes,<sup>14</sup> naphthaquinones,<sup>15</sup> *p*-quinine methide,<sup>16</sup> amino esters,<sup>17</sup> and diones<sup>18</sup> have been used for the annulation reaction. The first [3+2] asymmetric process was reported by Zhang *et al.*<sup>19</sup> Later on several chiral annulation reactions were investigated.<sup>20</sup>

1,3-Indandione is an important constituent of numerous natural products and bioactive skeletons (Fig. 1)<sup>21</sup> and has been used as a reaction substrate extensively.<sup>22</sup> Some of these natural products display activity due to spirocyclic moieties<sup>23</sup> of various sizes. In recent years, a readily accessible material *i.e.* 2-arylidene-1,3-indandiones<sup>24</sup> has started gaining importance in the

field of phosphine catalysed annulations.<sup>25</sup> A regioselective [4+2]<sup>26</sup> cyclisation between 2-arylidene-1,3-indandiones and  $\gamma$ -substituted allenoates was carried out explicitly by Huang and co-workers towards synthesis of spiro[4.5]dec-6-ene skeletons as  $\delta$ -adduct (eqn (a), Scheme 1).<sup>27</sup> Very recently, Zheng and Er-Qing carried out a phosphine catalysed [3+2] cyclisation with  $\gamma$ -methyl allenoates for the synthesis of spirocyclopentene as  $\alpha$ -adduct (eqn (b), Scheme 1).<sup>28</sup> In continuation with our interest towards the synthesis of spiro carbocycles,<sup>29</sup> we herein report a regioselective [3+2] cyclisation of 2-arylidene-1,3-indandiones and 2,3-butadienoate catalysed by triphenylphosphine (eqn (c), Scheme 1). To the best of our knowledge, this is the first report

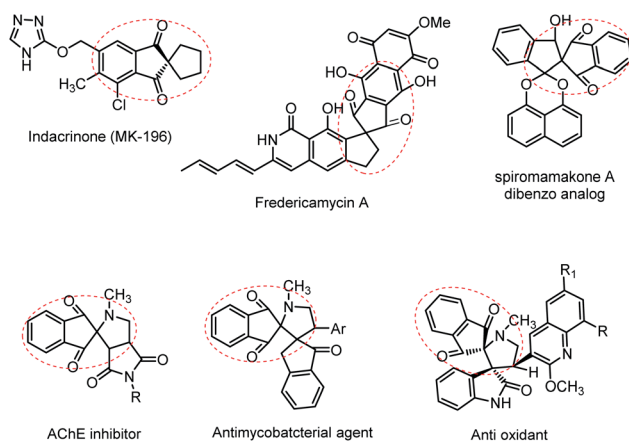


Fig. 1 Natural and bioactive molecules containing Indanedione based spirocarbocycles and spiroheterocycles.

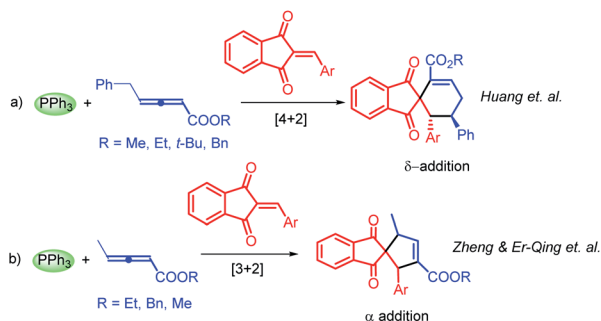
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† Electronic supplementary information (ESI) available: Experimental procedure, spectral data of products 3/4 and X-ray crystallographic data for **3e** and **4e**. CCDC 921839, 921702 and 2110327–2110330. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/d1ra07165c



## Previous Work: [4+2] and [3+2] Annulation Reactions



## Present Work: [3+2] Annulation reaction

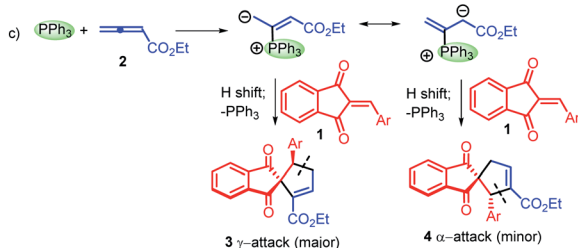
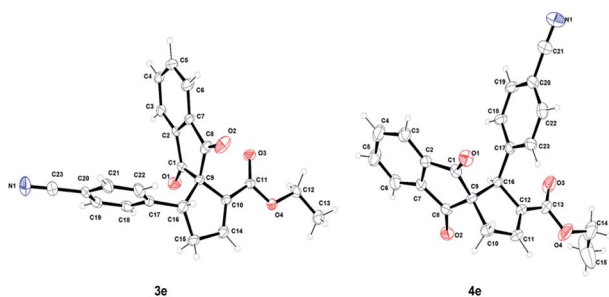
Scheme 1 PPh<sub>3</sub> driven annulation reaction of 2-arylidene-1,3-indanedione using allenates.

Fig. 2 Crystal structures of 3e (CCDC 921839) and 4e (CCDC 921702).

for the synthesis of functionalised spirocyclopentenes as  $\gamma$ -addition as well as  $\alpha$ -addition adduct.

Interestingly, spirocyclopentene 3 was obtained predominantly *via*  $\gamma$ -attack along with 4 as a minor product through  $\alpha$ -attack of ethyl-2,3-butadienoate 2 on benzylidene-1,3-indanedione 1 using PPh<sub>3</sub> (eqn (c), Scheme 1). The structures of both the products were further confirmed by single X-ray crystallography (Fig. 2).

## Results and discussion

We initially carried out the reaction of 2-(benzylidene)-1,3-indanedione 1a with allenate 2 using Ph<sub>3</sub>P (Table 1). The reaction was carried out in CH<sub>3</sub>CN at ambient temperature to give separable products 3a and 4a with a total chemical yield of 22% (Table 1, entry 1). The isolated yield of the reaction was improved to 41% when THF was used (Table 1, entry 2). A relatively electron-rich catalyst such as Bu<sub>3</sub>P showed the same reactivity with a marginal increase in yield using toluene as

Table 1 Optimization of reaction conditions<sup>a</sup>

Entry	Catalyst (mol%)	Solvent	Time (h)	(3a : 4a) <sup>b</sup>	Yield <sup>c</sup>
1	PPh <sub>3</sub>	CH <sub>3</sub> CN	24	n.d.	22
2	PPh <sub>3</sub>	THF	24	n.d.	41
3	PBu <sub>3</sub>	Toluene	24	5 : 1	44
4	PPh <sub>3</sub>	Toluene	12	5 : 1	51
5	PPh <sub>3</sub>	Toluene	24	5 : 1	55
6 <sup>d</sup>	PPh <sub>3</sub>	Toluene	24	6 : 1	76
7 <sup>e</sup>	PPh <sub>3</sub>	Toluene	24	5 : 1	88
8 <sup>f</sup>	PPh <sub>3</sub>	Toluene	24	5 : 1	99

<sup>a</sup> Unless otherwise noted, reactions were carried out with (0.1 mmol) of 1a with (0.2 mmol) of 2 using 20 mol% of catalyst in 400  $\mu\text{L}$  solvent under N<sub>2</sub> atmosphere. <sup>b</sup> Determined by <sup>1</sup>H-NMR analysis of crude reaction mixture. <sup>c</sup> Total isolated yield of products 3a and 4a. <sup>d</sup> Reaction was carried out at 0.1 M conditions (2.0 mL solvent). <sup>e</sup> Reaction was carried out at 0.05 M conditions (4.0 mL solvent). <sup>f</sup> Reaction was carried out at 0.03 M conditions (6.0 mL solvent).

solvent (Table 1, entry 3). Improvement in the yield of the reaction was observed using Ph<sub>3</sub>P in toluene that resulted in good regioselectivity of 5 : 1 (Table 1, entries 4 and 5). Drastic improvement in the chemical yield of the reaction was observed when the reaction was performed under dilute conditions (Table 1, entries 6 and 7). A culminating point was observed in the yield of the reaction on a further increase in the volume of the reaction (Table 1, entry 8).

Table 2 Substrate Scope towards cascade formal [3+2] annulation<sup>a</sup>

Entry	Ar	Product	(3 : 4) <sup>b</sup>	Yield <sup>c</sup>
1	C <sub>6</sub> H <sub>5</sub>	3a/4a	5 : 1	99
2	4-NO <sub>2</sub> C <sub>6</sub> H <sub>4</sub>	3b/4b	4 : 1	99
3	4-MeCO <sub>2</sub> C <sub>6</sub> H <sub>4</sub>	3c/4c	1 : 1	84
4	4-CF <sub>3</sub> C <sub>6</sub> H <sub>4</sub>	3d/4d	3 : 2	87
5	4-CNC <sub>6</sub> H <sub>4</sub>	3e/4e	5 : 1	99
6	4-FC <sub>6</sub> H <sub>4</sub>	3f/4f	2 : 1	96
7	4-ClC <sub>6</sub> H <sub>4</sub>	3g/4g	7 : 2	98
8	4-BrC <sub>6</sub> H <sub>4</sub>	3h/4h	3 : 2	88
9	4-AcOC <sub>6</sub> H <sub>4</sub>	3i/4i	4 : 1	89
10	4-CH <sub>3</sub> C <sub>6</sub> H <sub>4</sub>	3j/4j	4 : 1	95
11	4-CH <sub>3</sub> OC <sub>6</sub> H <sub>4</sub>	3k/4k	3 : 1	77
12	4-N(CH <sub>3</sub> ) <sub>2</sub> C <sub>6</sub> H <sub>4</sub>	3l/4l	2 : 1	63
13	3-Thienyl	3m/4m	3 : 2	82
14	2-Thienyl	3n/4n	1 : 2	91

<sup>a</sup> Unless otherwise noted, all reactions were carried out with 0.1 mmol of 1 with 0.2 mmol of 2 using 20 mol% of PPh<sub>3</sub> in 6.0 mL toluene (0.03 M conditions) under N<sub>2</sub> atmosphere. <sup>b</sup> Determined by <sup>1</sup>H-NMR analysis of crude reaction mixture. <sup>c</sup> Total isolated yield of products 3 & 4.



With the optimised reaction conditions realised, we carried out the generalisation of the present protocol using various substituted 2-arylidene-1,3-indanediones **1b–n**. It was observed that both electron-donating and electron-withdrawing groups were tolerable in the *para*-position of the phenyl ring in **1** (Table 2). The use of electron-withdrawing groups did not alter the reactivity of the reaction and the regioselectivity with quantitative yields was maintained (Table 2, entries 1 and 2). The chemical structures of  $\gamma$ - and  $\alpha$ -substituted products were initially assigned by  $^1\text{H}$ ,  $^{13}\text{C}$ -NMR, and HRMS analysis and were unambiguously assigned by single crystal X-ray diffraction for products **3e** and **4e** (Fig. 2).<sup>30</sup>

The methyl ester group on the phenyl ring decreased the regioselectivity of the reaction presumably due to a decrease in electrophilicity of Michael acceptor **1c** (Table 2, entry 3). The use of the  $-\text{CN}$  group demonstrated better regioselectivity and reactivity when compared to that of the  $-\text{CF}_3$  group (Table 2, entries 4–5). The presence of halogen-substituents in *para*-position of the phenyl ring was well tolerated with moderate regioselectivity and high chemical yields (Table 2, entries 6–8). The use of an acetoxy group was also compatible under the present reaction conditions (Table 2, entry 9). The use of electron-donating groups such as methyl, methoxy, and *N,N*-dimethyl on phenyl ring decreased the yield and regioselectivity for the formation of products **3j/4j** to **3l/4l** presumably due to the creation of electron density at the electrophilic carbon atom (Table 2, entries 10–12). Excellent chemical yields albeit with moderate regioselectivity when heteroaromatic substrates were used (Table 2, entries 13 and 14).

## DFT studies

### Computational methods

The computations were carried out using the Gaussian 09 suite of program.<sup>31</sup> All the optimisations, transition states and single point energy calculations have been carried out at B3LYP/6-31g(d)<sup>32</sup> level in the gas phase. The optimised conformation of reactants, intermediates and products were further confirmed that there is no imaginary frequency. Moreover, all the transition states were confirmed with a minimum of one imaginary frequency and the values are used in the discussion below.

**Results and discussion.** To corroborate the formation of major product spiro cyclopentene **3a** among two possible regioisomers **3a** and **4a**, Density Functional Theory (DFT) calculations were exclusively studied. The key step involved in this reaction is the formation of highly reactive zwitterions **A** and **B** (see ESI †). Zwitterion **A** and **B** were produced by the attack of  $\text{PPh}_3$  on 2,3-butadienoate **2**. 2-Benzylidene-1,3-indanedione **1a**, zwitterions **A** and **B** were chosen as precursors for DFT calculations. Moreover, the HOMO–LUMO gap (see Fig. 3) for the zwitterions **A** and **B** was observed to be 3.17 and 2.74 eV, respectively, which confirms the lower band gap for the zwitterion **B** and its high reactivity (Fig. 3). The HOMO–LUMO gap has been calculated based on the higher oscillator strength observed for both zwitterions.

The transition states were computed for the two possible products and the results were explained in Fig. 4. As shown in

Fig. 4 (potential energy surface), initially, **1a** was allowed to interact with **A** and has formed **1a–A** complex with the binding energy of  $-6.35 \text{ kcal mol}^{-1}$ . Similarly, **1a** was allowed to interact with **B** resulting in **1a–B** complex with the binding energy of  $-7.04 \text{ kcal mol}^{-1}$ . The binding energy difference between the two complexes was observed to be minimal *i.e.*,  $0.69 \text{ kcal mol}^{-1}$ . The results show the competitive nature of zwitterions towards the formation of products **3a** and **4a**. The attack of methylene anion of **B** on  $\alpha$ -carbon of 2-benzylidene-1,3-indandione **1a** has produced TS1a with the vibrational frequency of  $-284.23 \text{ cm}^{-1}$  and the barrier energy of  $9.95 \text{ kcal mol}^{-1}$ . Whereas, the attack of methine anion of **A** on  $\alpha$ -carbon of 2-benzylidene-1,3-indandione **1a** has produced TS1 with the vibrational frequency of  $-196.10 \text{ cm}^{-1}$  and the barrier energy of  $6.72 \text{ kcal mol}^{-1}$ . The barrier energy difference between TS1 and TS1a was observed to be  $2.54 \text{ kcal mol}^{-1}$ . This Michael addition leads to **Int 1** and **Int 1a** with enthalpies of formation ( $\Delta H_f$ )  $-9.39 \text{ kcal mol}^{-1}$  and  $-16.49 \text{ kcal mol}^{-1}$ , respectively. It was observed that **Int 1a** is more stable than that of **Int 1** with an energy difference of  $4.56 \text{ kcal mol}^{-1}$ . The intermediates, **Int 1a** and **Int 1**, produced TS2a and TS2 with the barrier energies of  $8.81$  and  $7.69 \text{ kcal mol}^{-1}$ . The difference in barrier energies for both TS2 and TS2a was observed to be  $1.12 \text{ kcal mol}^{-1}$ . Intramolecular Michael addition of **Int 1a** and **Int 1** resulted in **Int 2a** and **Int 2** respectively. The enthalpy of formation ( $\Delta H_f$ ) of **Int 2a** and **Int 2** was observed to be  $10.21$  and  $10.77 \text{ kcal mol}^{-1}$ , respectively. **Int 2a** and **Int 2** undergoes 1,2-proton transfer resulting in TS3a and TS3 having the barrier energies  $47.11 \text{ kcal mol}^{-1}$  and  $73.31 \text{ kcal mol}^{-1}$ , respectively. It is clearly evident that TS3a is more stable than TS3 with a difference of  $29.08 \text{ kcal mol}^{-1}$ .

The less barrier energy observed for TS3a leads to the formation of **3a** in line with the experimental observation of higher yield than that of **4a** with the elimination of  $\text{PPh}_3$ . For products **3a** and **4a**, the enthalpy energy was observed to be  $74.28$  and  $100.51 \text{ kcal mol}^{-1}$ , respectively. It can be concluded that product formation **3a** shows low barrier energy (Blue line) in all the steps except TS1a. Moreover, the computational results explained the cause of the major and minor products for this reaction.

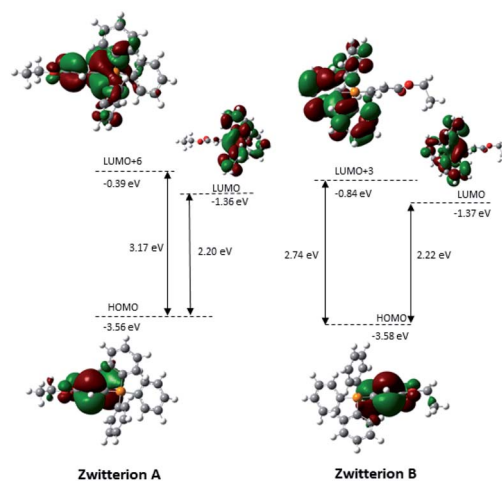


Fig. 3 Frontier molecular orbital diagram of **A** and **B** obtained at B3LYP/6-31(d) level in gas phase.



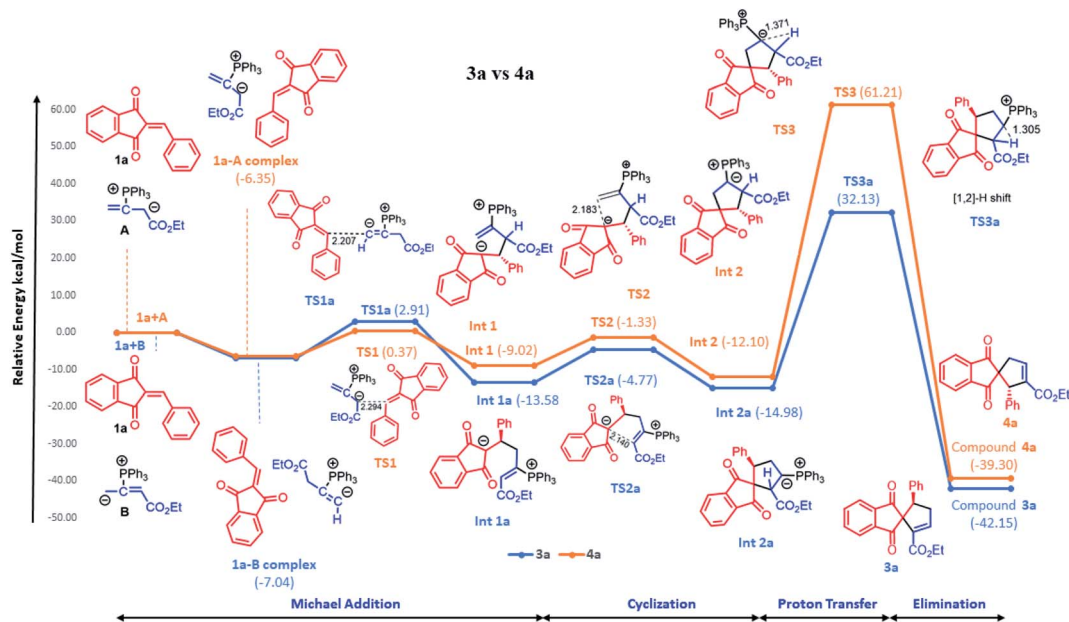
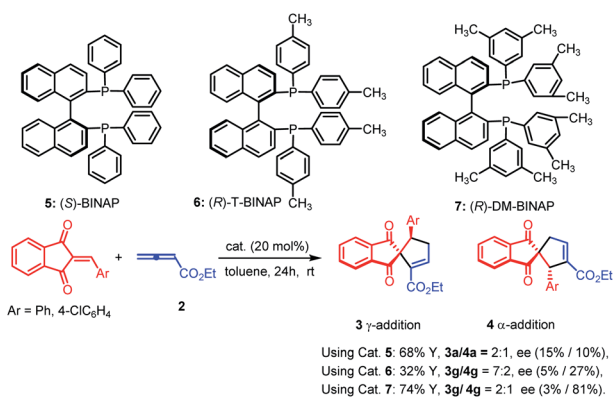
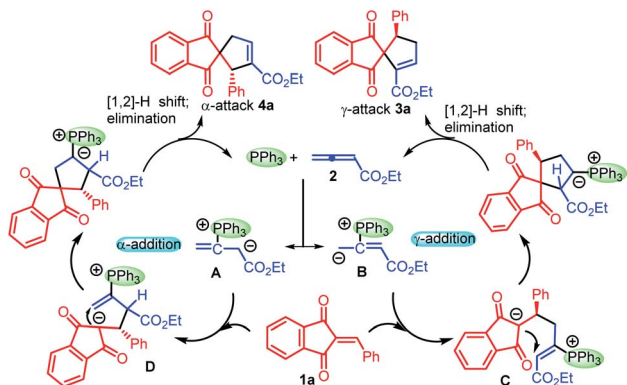


Fig. 4 Energy barrier diagram for the formation of regioisomers **3a** and **4a**.



Scheme 2 Asymmetric annulation catalysed by chiral catalysts.

No other product was detected from the <sup>1</sup>H NMR analysis of the crude products, which demonstrated the efficiency of the current [3+2] cyclisation. With the standard protocol



Scheme 3 Possible catalytic cycle for products **3a** and **4a**.

established for the synthesis of spirocyclopentenes, we next focused our attention on asymmetric variants by using various axially chiral trivalent phosphorus catalysts 5–7.

The use of chiral (*S*)-BINAP **5** gave a moderate yield of 68% with low regioselectivity (*i.e.*, 2 : 1) and enantioselectivity for **3a/4a** (*i.e.* 15 and 10% ee, respectively). The use of chiral (*R*)-T-BINAP **6** resulted in poor chemical yield for **3g/4g** even after 10 d of the reaction period. Finally, (*R*)-DM-BINAP **7** showed promising results with 74% yield for the formation of **3g/4g** with high enantioselectivity of 81% for  $\alpha$ -attack product **4g** (Scheme 2).

A reasonable mechanism can be given for this regioselective [3+2] annulation reaction as shown in Scheme 3, catalyst Ph<sub>3</sub>P attacks the central sp carbon of ethyl-2,3-butadienoate **2** to generate Ph<sub>3</sub>P-allenoate zwitterionic intermediates **A** and **B**. The dipole **A** with the anion at the  $\alpha$ -carbon position is believed to be more stable than dipole **B** with anion residing on  $\gamma$ -carbon position. This can be evident from the regioselectivity of products **3** and **4**. These dipole intermediates then react with the Michael acceptor **1** in a [3+2] cyclisation fashion to form **C** and **D**. Subsequent ring closure, 1,2-proton transfer and further elimination of PPh<sub>3</sub> gives the cyclopentenes **3** and **4** as major and minor products (Scheme 3).

## Conclusions

In conclusion, we have demonstrated a regioselective [3+2] annulation reaction for the formation of spirocyclic cyclopentenes with high to excellent levels of chemical yield and regioselectivity. Previous work carried out using  $\gamma$ -substituted allenates with 2-arylidene-1,3-indandiones in the presence of triphenylphosphine resulted in spiro[4.5]decene (*i.e.*  $\delta$ -addition)<sup>27</sup> and spiro[4.4]non-7-ene skeletons (*i.e.*  $\alpha$ -addition).<sup>28</sup> On



the other hand, the current work also involves the use of 2-arylidene-1,3-indandiones which on reaction with simple allenolate such as ethyl-2,3-butadienoate in the presence of triphenylphosphine gives  $\gamma$ -addition spiro[4.4]non-6-ene adduct as the major product and  $\alpha$ -addition spiro[4.4]non-7-ene adduct as the minor product. This triphenylphosphine mediated catalysis towards the synthesis of functionalized spirocarbocyclic derivatives results in the formation of asymmetric carbon centre as well as quaternary stereocentre. The result of DFT studies of frontier molecular orbital calculation on the regioselective reaction of 2-arylidene-1,3-indanedione and ethyl 2,3-butadienoate catalysed by triphenylphosphine shows a lower HOMO–LUMO gap for zwitterion **B** compared to that of **A**. Moreover, the activation energy has also been observed to be lower for **3a** compared with that of **4a** which shows the reactivity of zwitterion **B** which favours the formation of compound **3a** as the major product.

## Conflicts of interest

There are no conflicts to declare.

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## Notes and references

- For original publications, see: (a) C. Zhang and X. Lu, *J. Org. Chem.*, 1995, **60**, 2906; (b) Y. Fujiwara and G. C. Fu, *J. Am. Chem. Soc.*, 2011, **133**, 12293. For review articles, see: (c) X. Lu, C. Zhang and Z. Xu, *Acc. Chem. Res.*, 2001, **34**, 535; (d) B. J. Cowen and S. C. Miller, *Chem. Soc. Rev.*, 2009, **38**, 3102; (e) L.-W. Ye, J. Zhou and Y. Tang, *Chem. Soc. Rev.*, 2008, **37**, 1140; (f) Y. Wei and M. Shi, *Chin. J. Chem.*, 2020, **38**, 1395; (g) Y. Zhu and Y. Huang, *Synthesis*, 2020, **52**, 1181; (h) Q.-Y. Zhao, Z. Lian, Y. Wei and M. Shi, *Chem. Commun.*, 2012, **48**, 1724; For selected examples, see: (i) X. Tang, C. X. A. Tan, W. –L. Chan, F. Zhang, W. Zheng and Y. Lu, *ACS Catal.*, 2021, **11**, 1361; (j) S. Debanath, A. S. Kumar, S. Chauhan and K. C. K. Swamy, *J. Org. Chem.*, 2021, **86**, 11583; (k) T. Xu, D. Wang, W. Liu and X. Tong, *Org. Lett.*, 2019, **21**, 1944; (l) C. Cheng, X. Sun, Z. Wu, Q. Liu, L. Xiong and Z. Miao, *Org. Biomol. Chem.*, 2019, **17**, 3232; (m) Z. Wang, Y. Fei, C. Tang, L. Cui, J. Shen, K. Yin, S. Lu and J. Li, *Org. Lett.*, 2021, **23**, 4094.
- (a) J.-H. Wu, L. Pan, J. Du, X. Wang, X. Wang, C. Jiang and T. Wang, *Org. Lett.*, 2020, **22**, 395; (b) E. Li, H. Jin and Y. Huang, *ChemistrySelect*, 2018, **3**, 12007; (c) Q.-Z. Xi, Z. –
- J. Gan, E.-Q. Li and Z. Duan, *Eur. J. Org. Chem.*, 2018, **2018**, 4917.
- (a) J. E. Wilson and G. C. Fu, *Angew. Chem., Int. Ed.*, 2006, **45**, 1426; (b) A. Voituriez, A. Panossian, N. F. Bregeot, P. Retailleau and A. Marinetti, *Adv. Synth. Catal.*, 2009, **351**, 1968; (c) N. Pinto, P. Retailleau, A. Voituriez and A. Marinetti, *Chem. Commun.*, 2011, **47**, 1015.
- (a) Q.-Y. Zhao, L. Huang, Y. Wei and M. Shi, *Adv. Synth. Catal.*, 2012, **354**, 1926; (b) T. Wang and S. Ye, *Org. Lett.*, 2010, **12**, 4168.
- (a) J. Tian and Z. He, *Chem. Commun.*, 2013, **49**, 2058; (b) R. P. Wurz and G. C. Fu, *J. Am. Chem. Soc.*, 2005, **127**, 12234; (c) X. F. Zhu, J. Lan and O. Kwon, *J. Am. Chem. Soc.*, 2003, **125**, 4716; (d) Z. Yu, Z. Jin, M. Duan, R. Bai, Y. Lu and Y. Lan, *J. Org. Chem.*, 2018, **83**, 9729; (e) X. Kong, L. Liu, S. Luo, S. Fan, H. Qian and H. Xiao, *Synlett*, 2018, **29**, 1244.
- X. Wang, T. Fang and X. Tong, *Angew. Chem., Int. Ed.*, 2011, **50**, 5361.
- X.-Y. Chen, R.-C. Lin and S. Ye, *Chem. Commun.*, 2012, **48**, 1317.
- Y. Wang, Z.-H. Yu, H.-F. Zheng and D.-Q. Shi, *Org. Biomol. Chem.*, 2012, **10**, 7739.
- R. Na, C. Jing, Q. Xu, H. Jiang, X. Wu, J. Shi, J. Zhong, M. Wang, D. Benitez, E. Tkatchouk, W. A. Goddard III, H. Guo and O. Kwon, *J. Am. Chem. Soc.*, 2011, **133**, 13337.
- X. Meng, Y. Huang and R. Chen, *Org. Lett.*, 2009, **11**, 137.
- Z. Lu, S. Zheng, X. Zhang and X. Lu, *Org. Lett.*, 2008, **10**, 3267.
- D. J. Wallace, R. L. Sidda and R. A. Reamer, *J. Org. Chem.*, 2007, **72**, 1051.
- (a) X.-F. Zhu, C. E. Henry, J. Wang, T. Dudding and O. Kwon, *Org. Lett.*, 2005, **7**, 1387; (b) R. Ma, S. Xu, X. Tang, G. Wu and Z. He, *Tetrahedron*, 2011, **67**, 1053; (c) S. Xu, L. Zhou, R. Ma, H. Song and Z. He, *Chem.–Eur. J.*, 2009, **15**, 8698.
- X. Guo, X. Chen, Y. Cheng, X. Chang, X. Li and P. Li, *Org. Biomol. Chem.*, 2021, **19**, 1727.
- L. Zhou, C. Wang, C. Yuan, H. Liu, C. Zhang and H. Guo, *Org. Lett.*, 2018, **20**, 6591.
- (a) Y. Zhu, D. Wang and Y. Huanf, *Org. Lett.*, 2019, **21**, 908; (b) V. R. Reddy, N. Maripally, R. Mutyala, J. B. Nanubolu and R. Chandra, *Tetrahedron Lett.*, 2018, **59**, 2631; (c) D. Wang, Z.-F. Song, W.-J. Wang and T. Xu, *Org. Lett.*, 2019, **21**, 3963.
- M. Steurer, K. L. Jensen, D. Worgull and K. A. Jørgensen, *Chem.–Eur. J.*, 2012, **18**, 76.
- A. Jose, K. C. S. Lakshmi, E. Suresh and V. Nair, *Org. Lett.*, 2013, **15**, 1858.
- G. Zhu, Z. Chen, Q. Jiang, D. Xiao, P. Cao and X. Zhang, *J. Am. Chem. Soc.*, 1997, **119**, 3836.
- For review articles, see: (a) H. Ni, W.-L. Chan and Y. Lu, *Chem. Rev.*, 2018, **118**, 9344; (b) H. Guo, Y. C. Fan, Z. Sun, Y. Wu and O. Kwon, *Chem. Rev.*, 2018, **118**, 10049; For selected examples, see: (c) D. Wang, Y. Wei and M. Shi, *Chem. Commun.*, 2012, **48**, 2764; (d) H. Xiao, Z. Chai, D. Cao, H. Wang, J. Chen and G. Zhao, *Org. Biomol. Chem.*, 2012, **10**, 3195; (e) Y.-Q. Fang and E. N. Jacobsen, *J. Am. Chem. Soc.*, 2008, **130**, 5660; (f) Y. Du, X. Lu and Y. Yu, *J. Org. Chem.*, 2002, **67**, 8901; (g) W. Luo, B.-X. Shao, J. Li,



- X. Xiao, D. Song, F. Ling and W. Zhong, *Org. Chem. Front.*, 2020, 7, 1016; (h) P. Aillard, M. Gicquel, K. Yavari, P. Retailleau, A. Voituriez and A. Marinetti, *Eur. J. Org. Chem.*, 2018, **2018**, 5853.
- 21 (a) O. W. Woltersdorf Jr, S. J. deSolms, G. E. Stokker and E. J. Cragoe Jr, *J. Med. Chem.*, 1984, **27**, 840; (b) S. Kotha and A. Fatma, *Asian J. Org. Chem.*, 2021, **10**, 129; (c) C. Bharkavi, S. V. Kumar, M. A. Ali, H. Osman, S. Muthusubramanian and S. Perumal, *Bioorg. Med. Chem. Lett.*, 2017, **27**, 3071; (d) A. C. Wei, M. A. Ali, Y. K. Yoon, R. Ismail, T. S. Choon, R. S. Kumar, N. Arumugam, A. I. Almansour and H. Osman, *Bioorg. Med. Chem. Lett.*, 2012, **22**, 4930; (e) S. Mathusalini, T. Arasakumar, K. Lakshmi, C.-H. Lin, P. S. Mohan, M. G. Ramnath and R. Thirugnanasampandan, *New J. Chem.*, 2016, **40**, 5164.
- 22 (a) M. Li, W. L. Yang, L. R. Wen and F. Q. Li, *Eur. J. Org. Chem.*, 2008, **2008**, 2751; (b) S. J. Tu, B. Jiang, J. Y. Zhang, R. H. Jia, Y. Zhang and C. S. Yao, *Org. Biomol. Chem.*, 2006, **4**, 3980; (c) D. Pizzirani, M. Roberti and M. Recanatini, *Tetrahedron Lett.*, 2007, **48**, 7120; (d) D. B. Ramachary, C. Venkaiah and P. M. Krishna, *Chem. Commun.*, 2012, **48**, 2252.
- 23 (a) A. Ding, M. Meazza, H. Guo, J. W. Yang and R. Rios, *Chem. Soc. Rev.*, 2018, **47**, 5946; (b) E. Chupakhin, O. Babich, A. Prosekov, L. Asyakina and M. Krasavin, *Molecules*, 2019, **24**, 4165.
- 24 (a) D. B. Ramachary and P. M. Krishna, *Asian J. Org. Chem.*, 2016, **5**, 729; (b) U. Das, Y.-L. Tsai and W. Lin, *Org. Biomol. Chem.*, 2013, **11**, 44; (c) J. Qi, J. Zheng and S. Cui, *Org. Chem. Front.*, 2018, **5**, 222; (d) G. Zhan, M. L. Shi, Q. He, W. J. Lin, Q. Ouyang, W. Du and Y. C. Chen, *Angew. Chem., Int. Ed.*, 2016, **55**, 2147; (e) J. Duan, J. Cheng and P. Li, *Org. Chem. Front.*, 2015, **2**, 1048; (f) N. L. Ahlburg, P. G. Jones and D. B. Werz, *Org. Lett.*, 2020, **22**, 6404; (g) Y.-R. Chen, M. R. Ganapuram, K.-H. Hsieh, K.-H. Chen, P. Karanam, S. S. Vagh, Y.-C. Liou and W. Lin, *Chem. Commun.*, 2018, **54**, 12702.
- 25 (a) R. Chen, X. Fan, J. Gong and Z. He, *Asian J. Org. Chem.*, 2014, **3**, 877; (b) F. Hu, Y. Wei and M. Shi, *Tetrahedron*, 2012, **68**, 7911; (c) C.-Z. Liu, Y. Han, W.-J. Qi and C.-G. Yan, *Heterocycl. Commun.*, 2016, **22**, 301.
- 26 W. Shi, B. Mao, J. Xu, Q. Wang, W. Wang, Y. Wu, X. Li and H. Guo, *Org. Lett.*, 2020, **22**, 2675.
- 27 E. Li, Y. Huang, L. Liang and P. Xie, *Org. Lett.*, 2013, **15**, 3138.
- 28 M. Rong, S. Gege, X. Qiuzhen, Y. Liu, L. Er-Qing and D. Zheng, *Chin. J. Org. Chem.*, 2019, **39**, 2196.
- 29 (a) S. Roy, M. Amireddy and K. Chen, *Tetrahedron*, 2013, **69**, 8751; (b) H.-H. Kuan, C.-H. Chien and K. Chen, *Org. Lett.*, 2013, **15**, 2880; (c) S. Anwar, S. M. Li and K. Chen, *Org. Lett.*, 2014, **16**, 2993; (d) M. Amireddy and K. Chen, *Tetrahedron*, 2015, **71**, 8003; (e) V. B. Gudise, P. C. Settipalli, E. K. Reddy and S. Anwar, *Eur. J. Org. Chem.*, 2019, **2019**, 2234; (f) Y. P. Reddy, V. B. Gudise, P. C. Settipalli and S. Anwar, *ChemistrySelect*, 2021, **6**, 4456.
- 30 Detailed X-ray crystallographic data are available from CCDC, 12 Union Road, Cambridge CB2, 1EZ, UK for product **3e** (CCDC-921839) and **4e** (CCDC-921702)†
- 31 M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, G. Scalmani, V. Barone, B. Mennucci, G. A. Petersson, H. Nakatsuji, M. Caricato, X. Li, H. P. Hratchian, A. F. Izmaylov, J. Bloino, G. Zheng, J. L. Sonnenberg, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, T. Vreven, J. A. Montgomery, J. E. Peralta Jr, F. Ogliaro, M. Bearpark, J. J. Heyd, E. Brothers, K. N. Kudin, V. N. Staroverov, R. Kobayashi, J. Normand, K. Raghavachari, A. Rendell, J. C. Burant, S. S. Iyengar, M. Tomasi, N. Cossi, J. M. Rega, M. Millam, J. E. Klene, J. B. Knox, V. Cross, C. Bakken, J. Adamo, J. Jaramillo, R. Gomperts, R. E. Stratmann, O. Yazyev, A. J. Austin, R. Cammi, C. Pomelli, J. W. Ochterski, R. L. Martin, K. Morokuma, V. G. Zakrzewski, G. A. Voth, P. Salvador, J. J. Dannenberg, S. Dapprich, A. D. Daniels, O. Farkas, J. B. Foresman, J. V. Ortiz, J. Cioslowski and D. J. Fox, *Revision A. 02*, Gaussian Inc., Wallingford CT, 2009.
- 32 (a) A. D. Becke, *Phys. Rev. A*, 1993, **98**, 5648; (b) C. Lee, W. Yang and R. G. Parr, *Phys. Rev. B: Condens. Matter Mater. Phys.*, 1988, **37**, 785.

