

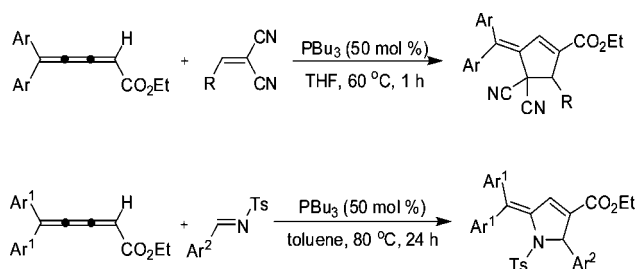
## Phosphine-Mediated [3+2] Cycloaddition Reactions of Ethyl 5,5-Diarylpenta-2,3,4-trienoates with Arylmethylenemalononitriles and *N*-Tosylimines

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Ethyl 5,5-diarylpenta-2,3,4-trienoates were synthesized and utilized in the phosphine-mediated [3+2] cycloaddition reactions with arylmethylenemalononitriles and *N*-tosylimines in the presence of tributylphosphine. These reactions provide an easy access to a variety of novel polysubstituted cyclopentenes or pyrrolidines in good to excellent yields under mild conditions.

### Introduction

Cumulene derivatives have attracted much attention in organic chemistry because of their high unique reactivities serving as nucleophiles, electrophiles, and occasionally as dienophiles in many reactions.<sup>1</sup> Among these derivatives, allenes have resulted in excellent regio- and stereoselectivities for many nucleophilic and electrophilic reactions if the electronic and steric nature of suitable catalysts were fine-tuned.<sup>2</sup> Although many fundamental reactions of butatrienes, such as oxidation, hydrogenation, halogenation, metalation, metal complexation, and sulfurization have been extensively investigated in the past years, much work on this unique cumulative system is still needed.<sup>3</sup> These reactions usually are focused on the symmetrical cumulene derivatives attached with alkyl or aryl groups on both sides of butatrienes. Thus far, there have been few reports regarding the reactivity of unsymmetrical cumulene derivatives.<sup>4</sup>

Recently, the phosphine-containing Lewis base-catalyzed cycloaddition and nucleophilic substitution reactions have been reported including several reviews after Lu's pioneering [3+2]

cycloaddition reactions between 2,3-butadienoates and *N*-tosylimines or arylmethylenemalononitriles catalyzed by tertiary phosphines were reported.<sup>5,6</sup> During our ongoing investigation on the phosphine or nitrogen-containing Lewis base-catalyzed reactions of allenic ketones and esters with a variety of electrophiles, we envisaged that ethyl 5,5-diarylpenta-2,3,4-trienoates, a family of unsymmetrical cumulene derivatives, would undergo cycloaddition reactions with arylmethylenemalononitriles or *N*-tosylimines if using tertiary phosphines or amines as the catalysts.<sup>7</sup> It is anticipated that introducing a double bond with two phenyl groups at the terminal of 2,3-butadienoates could affect the facial selectivity which should be important in asymmetric catalysis. The corresponding multifunctionalized [3+2] cycloaddition products could be more useful in organic synthesis. Herein, we would like to report the synthesis of ethyl 5,5-diarylpenta-2,3,4-trienoates and their [3+2] cycloaddition reactions with arylmethylenemalononitriles and *N*-tosylimines in the presence of tertiary phosphine under mild conditions.

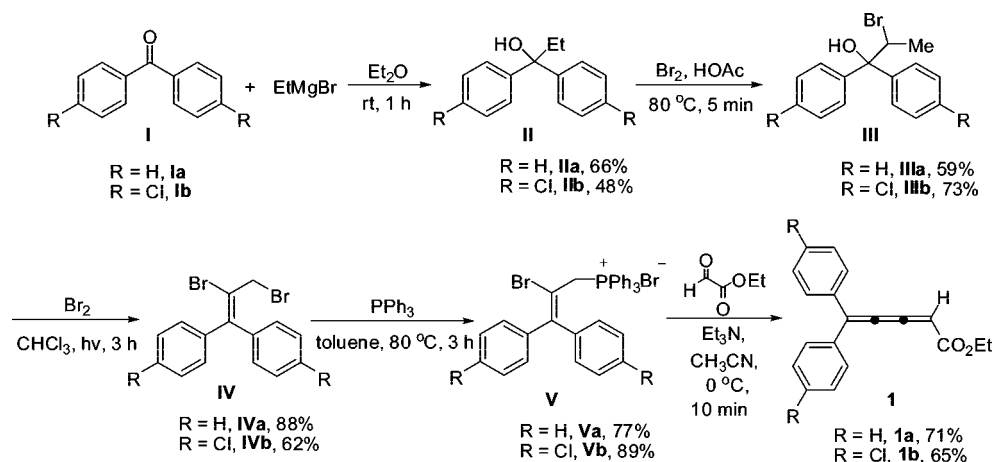
\* Corresponding author. Fax: 86-21-64166128.

(1) Furuta, T.; Asakawa, T.; Iinuma, M.; Fujii, S.; Tanakaa, K.; Kan, T. *Chem. Commun.* **2006**, 3648–3650.

(2) Ma, S. *Chem. Rev.* **2005**, *105*, 2829–2871.

(3) Tokitoh, N.; Hayakawa, H.; Goto, M.; Ando, W. *Tetrahedron Lett.* **1988**, *29*, 1935–1938, and references cited therein.

(4) (a) Asakawa, T.; Iinuma, M.; Furuta, T.; Fujii, S.; Kan, T.; Tanaka, K. *Chem. Lett.* **2006**, *35*, 512–513. (b) Toda, F.; Yamamoto, M.; Tanaka, K.; Mak, T. C. W. *Tetrahedron Lett.* **1985**, *26*, 631–634. (c) Vo-Quang, L.; Battioni, P.; Vo-Quang, Y. *Tetrahedron* **1980**, *36*, 1331–1336. (d) Saalfrank, R. W.; Welch, A.; Haubner, M. *Angew. Chem., Int. Ed.* **1995**, *34*, 2709–2710.

SCHEME 1. The Synthesis of **1a** and **1b**

## Results and Discussion

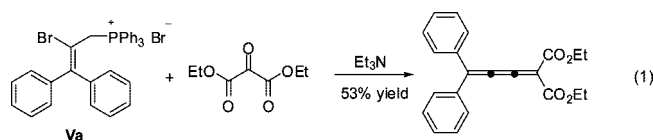
Since there has been no report on the preparation of ethyl 5,5-diarylpenta-2,3,4-trienoates, we attempted to synthesize these compounds according to the previously reported procedure by

(5) (a) Pyne, S. G.; Schafer, K.; Skelton, B. W.; White, A. H. *Chem. Commun.* **1997**, 2267–2268. (b) Ung, A. T.; Schafer, K.; Lindsay, K. B.; Pyne, S. G.; Amornraska, K.; Wouters, R.; Linden, I. V. d.; Biesmans, I.; Lesage, A. S. J.; Skelton, B. W.; White, A. H. *J. Org. Chem.* **2002**, *67*, 227–233. (c) Pham, T. Q.; Skelton, B. W.; White, A. H. *J. Org. Chem.* **2002**, *67*, 227–233. (d) Pham, T. Q.; Skelton, B. W.; White, A. H. *Tetrahedron Lett.* **2002**, *43*, 5953–5956. (e) Du, Y.; Lu, X.; Yu, Y. *J. Org. Chem.* **2002**, *67*, 8901–8905. (f) Du, Y.; Lu, X. *J. Org. Chem.* **2003**, *68*, 6463–6465. (g) Wang, L.-C.; Luis, A. L.; Agapiou, K.; Jang, H.-Y.; Krische, M. J. *J. Am. Chem. Soc.* **2002**, *124*, 2402–2403. (h) Frank, S. A.; Mergott, D. J.; Roush, W. R. *J. Am. Chem. Soc.* **2002**, *124*, 2404–2405. (i) Liu, B.; Davis, R.; Joshi, B.; Reynolds, D. W. *J. Org. Chem.* **2002**, *67*, 4595–4598. (j) Zhu, X.; Lan, J.; Kwon, O. *J. Am. Chem. Soc.* **2003**, *125*, 4716–4717. (k) Kuroda, H.; Tomita, I.; Endo, T. *Org. Lett.* **2003**, *5*, 129–131. (l) Wang, J.-C.; Ng, S.-S.; Krische, M. J. *J. Am. Chem. Soc.* **2003**, *125*, 3682–3683. (m) Wang, J.-C.; Krische, M. J. *Angew. Chem., Int. Ed.* **2003**, *42*, 5855–5857. (n) Couturier, M.; Ménard, F.; Ragan, J. A.; Riou, M.; Dauphin, E.; Andresen, B. M.; Ghosh, A.; Dupont-Gaudet, K.; Girardin, M. *Org. Lett.* **2004**, *6*, 1857–1860. (o) Methot, J. L.; Roush, W. R. *Adv. Synth. Catal.* **2004**, *346*, 1035–1050. (p) Tran, Y. S.; Kwon, O. *Org. Lett.* **2005**, *7*, 4289–4291. (q) Wurz, R. P.; Fu, G. C. *J. Am. Chem. Soc.* **2005**, *127*, 12234–12235. (r) Nair, V.; Biju, A. T.; Mohanan, K.; Suresh, E. *Org. Lett.* **2006**, *8*, 2213–2216. (s) Wilson, J. E.; Fu, G. C. *Angew. Chem., Int. Ed.* **2006**, *45*, 1426–1429. (t) Xia, Y.; Liang, Y.; Chen, Y.; Wang, M.; Jiao, L.; Huang, F.; Liu, S.; Li, Y.; Yu, Z.-X. *J. Am. Chem. Soc.* **2007**, *129*, 3470–3471. (u) Mercier, E.; Fonovic, B.; Henry, C.; Kwon, O.; Dudding, T. *Tetrahedron Lett.* **2007**, *48*, 3617–3620. (v) Wallace, D. J.; Sidda, R. L.; Reamer, R. A. *J. Org. Chem.* **2007**, *72*, 1051–1054. (w) Castellano, S.; Fijji, H. D. G.; Kinderman, S. S.; Watanabe, M.; de Leon, P.; Tamanoi, F.; Kwon, O. *J. Am. Chem. Soc.* **2007**, *129*, 5843–5845. (x) Tran, Y. S.; Kwon, O. *J. Am. Chem. Soc.* **2007**, *129*, 12632–12633. (y) Lu, Z.; Zheng, S.; Zhang, X.; Lu, X. *Org. Lett.* **2008**, *10*, 3267–3270. (z) Fang, Y.-Q.; Jacobsen, E. N. *J. Am. Chem. Soc.* **2008**, *130*, 5660–5661.

(6) (a) Lu, X.; Zhang, C.; Xu, Z. *Acc. Chem. Res.* **2001**, *34*, 535–544. (b) Zhang, C.; Lu, X. *Synlett* **1995**, 645–646. (c) Zhang, C.; Lu, X. *J. Org. Chem.* **1995**, *60*, 2906–2908. (d) Xu, Z.; Lu, X. *Tetrahedron Lett.* **1997**, *38*, 3461–3464. (e) Xu, Z.; Lu, X. *J. Org. Chem.* **1998**, *63*, 5031–5041. (f) Xu, Z.; Lu, X. *Tetrahedron Lett.* **1999**, *40*, 549–552. (g) Lu, X.; Lu, Z.; Zhang, X. *Tetrahedron* **2006**, *62*, 457–460.

(7) (a) Shi, M.; Zhao, G. *Tetrahedron Lett.* **2002**, *43*, 4499–4502. (b) Shi, M.; Zhao, G. *Tetrahedron Lett.* **2002**, *43*, 9171–9174. (c) Zhao, G.; Huang, J.; Shi, M. *Org. Lett.* **2003**, *5*, 4737–4739. (d) Shi, M.; Zhao, G. *Tetrahedron* **2004**, *60*, 2083–2089. (e) Shi, M.; Zhao, G. *Adv. Synth. Catal.* **2004**, *346*, 1205–1219. (f) Shi, Y.; Xu, Y.; Shi, M. *Adv. Synth. Catal.* **2004**, *346*, 1220–1230. (g) Zhao, G.; Shi, M. *Tetrahedron* **2005**, *61*, 7277–7288. (h) Zhao, G.; Shi, M. *J. Org. Chem.* **2005**, *70*, 9975–9984. (i) Zhao, G.; Shi, M. *Org. Biomol. Chem.* **2005**, *3*, 3686–3694. (j) Zhao, G.; Shi, M. *Org. Lett.* **2005**, *7*, 4527–4530. (k) Shi, Y.; Shi, M. *Synlett* **2005**, 17, 2623–2626. (l) Shi, Y.; Shi, M. *Org. Biomol. Chem.* **2005**, *3*, 1620–1621. (m) Shi, M.; Xu, Y.; Shi, Y. *Chem. Eur. J.* **2005**, *11*, 1794–1802. (n) Shi, Y.; Shi, M. *Org. Lett.* **2005**, *7*, 3057–3060. (o) Shi, M.; Dai, L.; Shi, Y.; Zhao, G. *Adv. Synth. Catal.* **2006**, *348*, 967–972. (p) Guo, Y.; Shi, Y.; Li, H.; Shi, M. *Tetrahedron* **2006**, *62*, 5875–5882. (q) Shi, Y.; Shi, M. *Tetrahedron* **2006**, *62*, 461–475. (r) Shi, Y.; Shi, M. *Chem. Eur. J.* **2006**, *12*, 3374–3378. (s) Dai, L.; Shi, Y.; Zhao, G.; Shi, M. *Chem. Eur. J.* **2007**, *13*, 3701–3706. (t) Shi, Y.; Shi, M. *Adv. Synth. Catal.* **2007**, *349*, 2129–2135. (u) Shi, Y.; Shi, M. *Eur. J. Org. Chem.* **2007**, *18*, 2905–2916. (v) Shi, Y.; Shi, M. *Org. Biomol. Chem.* **2007**, *5*, 1499–1504.

Ratts and Partos<sup>8</sup> in the preparation of Ph<sub>2</sub>C=C=C=PPh<sub>3</sub> via bromoalkenylphosphonium salt **Va**. Recently, Browne et al. have successfully prepared the corresponding cumulene diester from the reaction of **Va** with mesoxalic ester in 53% yield in the presence of triethylamine (eq 1).<sup>9</sup>

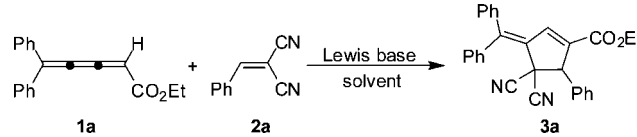


Therefore, the corresponding tertiary alcohols **IIa** and **IIb** were first prepared in moderate yields from the reaction of ketones **Ia** and **Ib** with ethylmagnesium bromide in diethyl ether at room temperature (20 °C). Then, the two alcohols were used to synthesize compounds **IIIa** and **IIIb** upon treating with bromine in acetic acid at 80 °C within 5 min (Scheme 1). Further treatment of compounds **IIIa** and **IIIb** with bromine in chloroform by photoirradiation afforded compounds **IVa** and **IVb** in 88% and 62% yield, respectively, which can be further transformed into the corresponding phosphonium salts **Va** and **Vb** in 77% and 89% yield, respectively, by treatment with PPh<sub>3</sub> in toluene at 80 °C for 3 h. The reactions of **Va** and **Vb** with ethyl glyoxylate in the presence of Et<sub>3</sub>N produced ethyl 5,5-diarylpenta-2,3,4-trienoates **1a** and **1b** as solid products in moderate yields in acetonitrile at 0 °C for 10 min (Scheme 1).

Initial examinations with ethyl 5,5-diphenylpenta-2,3,4-trienoate **1a** and benzylidenemalononitrile **2a** as the substrates in the presence of 50 mol % of PBu<sub>3</sub> in toluene at different temperatures were aimed at determining the optimal conditions and the results of these experiments are summarized in Table 1. When **1a**, **2a**, and 50 mol % of PBu<sub>3</sub> were stirred in toluene at 80 °C for 9 h, the polysubstituted cyclopentene derivative **3a** was obtained in 84% yield (Table 1, entry 1). Lowering the reaction temperature to 40 and 20 °C (room temperature) afforded **3a** in lower yields (Table 1, entries 2 and 3). A survey of the other reaction parameters was next performed and the results are also summarized in Table 1. The examination of a variety of phosphine-containing Lewis bases revealed that PPh<sub>2</sub>Me and PPhMe<sub>2</sub> (50 mol %) are more

(8) Ratts, K. W.; Partos, R. D. *J. Am. Chem. Soc.* **1969**, *91*, 6112–6115.

(9) Browne, N. R.; Brown, R. F. C.; Eastwood, F. W.; Fallon, G. D. *Aust. J. Chem.* **1987**, *40*, 1675–1686.

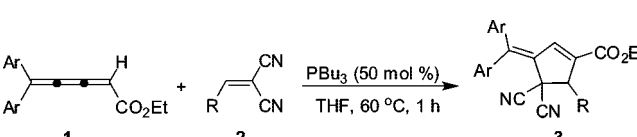
**TABLE 1.** Survey of the Reaction Parameters for the Phosphine-Mediated [3+2] Cycloaddition of **1a** and **2a**


| entry <sup>a</sup> | Lewis base                                | solvent            | temp (°C) | time (h) | yield (%) <sup>b</sup> |
|--------------------|---|--------------------|-----------|----------|------------------------|
| 1                  | PBu <sub>3</sub> (5.0 mol %)              | toluene            | 80        | 9        | 84                     |
| 2                  | PBu <sub>3</sub> (5.0 mol %)              | toluene            | 40        | 26       | 57                     |
| 3                  | PBu <sub>3</sub> (5.0 mol %)              | toluene            | rt        | 26       | 56                     |
| 4                  | PPh <sub>3</sub> (5.0 mol %)              | toluene            | 80        | 24       | 60                     |
| 5                  | PPh <sub>2</sub> Me (5.0 mol %)           | toluene            | 80        | 11       | 84                     |
| 6                  | PPhMe <sub>2</sub> (5.0 mol %)            | toluene            | 80        | 11       | 79                     |
| 7                  | P <sup>t</sup> Bu <sub>3</sub> (50 mol %) | toluene            | 80        | 22       | trace                  |
| 8                  | PMe <sub>3</sub> (5.0 mol %)              | toluene            | 80        | 11       | 65                     |
| 9                  | PBu <sub>3</sub> (5.0 mol %)              | DMF                | 80        | 1        | 61                     |
| 10                 | PBu <sub>3</sub> (5.0 mol %)              | 1,4-dioxane        | 80        | 1        | 93                     |
| 11                 | PBu <sub>3</sub> (5.0 mol %)              | THF                | 60        | 1        | 95                     |
| 12                 | PBu <sub>3</sub> (5.0 mol %)              | CH <sub>3</sub> CN | 80        | 1        | 70                     |
| 13                 | PBu <sub>3</sub> (5.0 mol %)              | DCE                | 80        | 1        | 93                     |
| 14                 | PBu <sub>3</sub> (2.0 mol %)              | THF                | 60        | 10       | 67                     |
| 15                 | PBu <sub>3</sub> (1.0 mol %)              | THF                | 60        | 10       | 49                     |

<sup>a</sup> All reactions were carried out with **1a** (0.1 mmol) and **2a** (0.1 mmol) in the presence of Lewis base in solvent (1.0 mL) under argon atmosphere. <sup>b</sup> Isolated yields.

effective catalysts than PPh<sub>3</sub> and PMe<sub>3</sub> under identical conditions, providing **3a** in 84% and 79% yield after 11 h, respectively, and P<sup>t</sup>Bu<sub>3</sub> did not catalyze the reaction presumably due to the steric hindrance (Table 1, entries 4–8). With use of PBu<sub>3</sub> as the optimized catalyst, the examination of solvent effects revealed that tetrahydrofuran (THF), 1,4-dioxane, and 1,2-dichloroethane (DCE) are suitable solvents to give **3a** in higher yields and the reaction could complete within 1 h in these solvents (Table 1, entries 9–13). Both of the employed amounts of the Lewis base and the reaction temperature in THF are crucial to the reaction outcomes. For example, using 20 mol % of PBu<sub>3</sub> as the catalyst afforded **3a** in 67% yield at 60 °C and carrying out the reaction at 60 °C with 10 mol % of PBu<sub>3</sub> as the catalyst provided **3a** in 49% yield under otherwise identical conditions (Table 1, entries 14 and 15). Accordingly, we also attempted to use some nitrogen-containing Lewis bases, such as 1,4-diazabicyclo[2.2.2]octane (DABCO), *N,N*-4-dimethylaminopyridine (DMAP), and imidazole, as the catalysts to promote the reaction under similar conditions. However, it was found that using DMAP as the catalyst afforded **3a** in only 36% yield, and using DABCO or imidazole as the catalyst, no reaction occurred.

Under these optimized reaction conditions, we next utilized 50 mol % of PBu<sub>3</sub> as the catalyst and THF as the solvent to examine the scope and limitations of this reaction using **1a** and **1b** as the substrates with a variety of arylmethylidenemalononitriles **2** bearing different substituents on the benzene rings and the results of these experiments are summarized in Table 2. As shown in Table 2, whether electron-withdrawing or electron-donating substituent was introduced at the ortho, meta, or para position of the benzene ring of **2** or the heterocycle-containing benzylidenemalononitriles were employed, the reactions proceeded smoothly to afford **3** in good to excellent yields (Table 2, entries 1–12). As for alkylmethylidenemalononitriles, the corresponding product **3n** was formed in 29% yield (Table 2, entry 13). Using butatriene **1b** bearing a electron-withdrawing group,

**TABLE 2.** Scope of the PBu<sub>3</sub>-Mediated [3+2] cycloaddition of **1** and **2**


| entry <sup>a</sup> | Ar  | R   | yield (%) <sup>b</sup> |
|--------------------|---|---|------------------------|
| 1                  | C <sub>6</sub> H <sub>5</sub>             | <i>p</i> -MeC <sub>6</sub> H <sub>4</sub>               | <b>3b</b> , 91         |
| 2                  | C <sub>6</sub> H <sub>5</sub>             | <i>p</i> -ClC <sub>6</sub> H <sub>4</sub>               | <b>3c</b> , 99         |
| 3                  | C <sub>6</sub> H <sub>5</sub>             | <i>p</i> -MeOC <sub>6</sub> H <sub>4</sub>              | <b>3d</b> , 98         |
| 4                  | C <sub>6</sub> H <sub>5</sub>             | <i>p</i> -NO <sub>2</sub> C <sub>6</sub> H <sub>4</sub> | <b>3e</b> , 73         |
| 5                  | C <sub>6</sub> H <sub>5</sub>             | <i>m</i> -MeC <sub>6</sub> H <sub>4</sub>               | <b>3f</b> , 82         |
| 6                  | C <sub>6</sub> H <sub>5</sub>             | <i>m</i> -FC <sub>6</sub> H <sub>4</sub>                | <b>3g</b> , 96         |
| 7                  | C <sub>6</sub> H <sub>5</sub>             | <i>o</i> -BrC <sub>6</sub> H <sub>4</sub>               | <b>3h</b> , 99         |
| 8                  | C <sub>6</sub> H <sub>5</sub>             | <i>o</i> -ClC <sub>6</sub> H <sub>4</sub>               | <b>3i</b> , 99         |
| 9                  | C <sub>6</sub> H <sub>5</sub>             | 3-pyridyl   | <b>3j</b> , 93         |
| 10                 | C <sub>6</sub> H <sub>5</sub>             | 2-furyl   | <b>3k</b> , 95         |
| 11                 | C <sub>6</sub> H <sub>5</sub>             | ( <i>E</i> )-C <sub>6</sub> H <sub>5</sub> CH=CH        | <b>3l</b> , 86         |
| 12                 | C <sub>6</sub> H <sub>5</sub>             | 1-naphthyl  | <b>3m</b> , 92         |
| 13                 | C <sub>6</sub> H <sub>5</sub>             | Et  | <b>3n</b> , 29         |
| 14 <sup>c</sup>    | <i>p</i> -ClC <sub>6</sub> H <sub>4</sub> | C <sub>6</sub> H <sub>5</sub>                           | <b>3o</b> , 52         |
| 15 <sup>d</sup>    | <i>p</i> -ClC <sub>6</sub> H <sub>4</sub> | C <sub>6</sub> H <sub>5</sub>                           | <b>3o</b> , 43         |

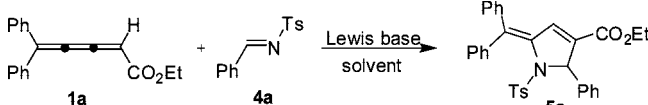
<sup>a</sup> All reactions were carried out with **1** (0.1 mmol) and **2** (0.1 mmol) in the presence of PBu<sub>3</sub> (50 mol %) in THF (1.0 mL) under argon atmosphere. <sup>b</sup> Isolated yields. <sup>c</sup> This reaction was carried out at 60 °C for 4 h. <sup>d</sup> This reaction was carried out at room temperature for 24 h.

such as Cl atom on the benzene ring, provided the corresponding product **3o** in 52% yield at 60 °C and 43% yield at 20 °C (room temperature), respectively (Table 2, entries 14 and 15). Moreover, the crystal structure of **3i** has been unambiguously determined by X-ray diffraction and its CIF data have been presented in the Supporting Information.<sup>10</sup>

Furthermore, ethyl 5,5-diarylpenta-2,3,4-trienoates could also react with *N*-tosylimines **4** smoothly to give the corresponding polysubstituted pyrrolidines in moderate to good yields in the presence of a variety of phosphine-containing Lewis bases. When this reaction was carried out at 80 °C in toluene with PBu<sub>3</sub> (50 mol %) as the catalyst, the corresponding [3+2] cycloaddition product **5a** was obtained in 72% yield after 20 h. The examination of the other reaction parameters revealed that PBu<sub>3</sub> is the best catalyst and the reaction should be carried out at 80 °C (Table 3, entries 1–5). To improve the yield of **5a**, we added some additives such as H<sub>2</sub>O (20 mol %) together with Et<sub>3</sub>N (5 mol %)<sup>3y</sup> as well as 4-nitrophenol (50 mol %) into the reaction system, but this provided no improvement on the reaction outcomes (Table 3, entries 6 and 7). Changing the employed solvent to THF, 1,4-dioxane, and DCE and raising the reaction temperature to 140 °C in DMF or *p*-xylene did not improve the yield of **5a** (Table 3, entries 8–12). Using DACBO or DMAP as the catalyst, no reaction occurred under the standard conditions. The best reaction conditions were found to be to carry out the reaction in toluene at 80 °C with PBu<sub>3</sub> (50 mol %) as the catalyst.

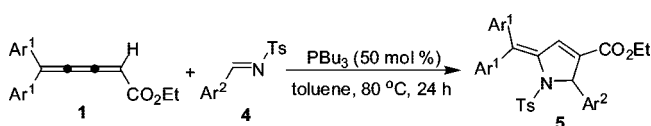
Under these optimized reaction conditions, we next similarly examined the scope and limitations of this reaction using a

(10) The crystal data of **3i** have been deposited in CCDC with no. 713030. Empirical formula: C<sub>20</sub>H<sub>21</sub>ClN<sub>2</sub>O<sub>2</sub>. Formula weight: 464.93. Crystal size: 0.503 × 0.450 × 0.378. Crystal color, habit: colorless, prismatic. Crystal system: triclinic. Lattice type: primitive. Lattice parameters: *a* = 10.2036(10) Å, *b* = 11.2203(11) Å, *c* = 11.5131(12) Å.  $\alpha$  = 84.328(2)°,  $\beta$  = 66.732(2)°,  $\gamma$  = 79.838(2)°, *V* = 1191.3(2) Å<sup>3</sup>. Space group: *P*1. *Z* = 2. *D*<sub>calcd</sub> = 1.296 g/cm<sup>3</sup>. *F*<sub>000</sub> = 484. *R*<sub>1</sub> = 0.0593, *wR*<sub>2</sub> = 0.1626. Diffractometer: Rigaku AFC7R.

TABLE 3. Survey of the Reaction Parameters for the Phosphine-Mediated [3+2] Cycloaddition of **1a** and **4a**


| entry <sup>a</sup> | Lewis base                     | solvent          | temp (°C) | time (h) | yield (%) <sup>b</sup> |
|--------------------|--------------------------------|------------------|-----------|----------|------------------------|
| 1                  | PBu <sub>3</sub> (50 mol %)    | toluene          | 80        | 20       | 72                     |
| 2                  | PBu <sub>3</sub> (50 mol %)    | toluene          | 40        | 26       | 46                     |
| 3                  | PPh <sub>3</sub> (50 mol %)    | toluene          | 80        | 24       | 35                     |
| 4                  | PPh <sub>2</sub> Me (50 mol %) | toluene          | 80        | 20       | 36                     |
| 5                  | PPhMe <sub>2</sub> (50 mol %)  | toluene          | 80        | 20       | 67                     |
| 6 <sup>c</sup>     | PBu <sub>3</sub> (50 mol %)    | toluene          | 80        | 24       | 52                     |
| 7 <sup>d</sup>     | PBu <sub>3</sub> (50 mol %)    | toluene          | 80        | 24       | 28                     |
| 8                  | PBu <sub>3</sub> (50 mol %)    | THF              | 60        | 20       | 69                     |
| 9                  | PBu <sub>3</sub> (50 mol %)    | 1,4-dioxane      | 80        | 20       | 65                     |
| 10                 | PBu <sub>3</sub> (50 mol %)    | DCE              | 80        | 20       | 65                     |
| 11                 | PBu <sub>3</sub> (50 mol %)    | DMF              | 140       | 20       | 33                     |
| 12                 | PBu <sub>3</sub> (50 mol %)    | <i>p</i> -xylene | 140       | 20       | 50                     |

<sup>a</sup> All reactions were carried out with **1a** (0.1 mmol) and **4a** (0.1 mmol) in the presence of Lewis base in solvent (1.0 mL) under argon atmosphere. <sup>b</sup> Isolated yields. <sup>c</sup> Et<sub>3</sub>N (5 mol %) and H<sub>2</sub>O (20 mol %) were added. <sup>d</sup> 4-Nitrophenol (50 mol %) was added.

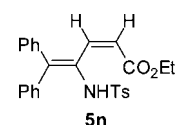
TABLE 4. Scope of the PBu<sub>3</sub>-Mediated [3+2] Cycloaddition of **1** and **4**

| entry <sup>a</sup> | Ar <sup>1</sup>                           | Ar <sup>2</sup>   | yield (%) <sup>b</sup> |
|--------------------|---|---|------------------------|
| 1                  | C <sub>6</sub> H <sub>5</sub>             | <i>p</i> -MeOC <sub>6</sub> H <sub>4</sub>                | <b>5b</b> , 74         |
| 2                  | C <sub>6</sub> H <sub>5</sub>             | <i>p</i> -ClC <sub>6</sub> H <sub>4</sub>                 | <b>5c</b> , 59         |
| 3                  | C <sub>6</sub> H <sub>5</sub>             | <i>p</i> -NO <sub>2</sub> C <sub>6</sub> H <sub>4</sub>   | <b>5d</b> , 48         |
| 4                  | C <sub>6</sub> H <sub>5</sub>             | <i>o</i> -MeOC <sub>6</sub> H <sub>4</sub>                | <b>5e</b> , 67         |
| 5                  | C <sub>6</sub> H <sub>5</sub>             | <i>o</i> -BrC <sub>6</sub> H <sub>4</sub>                 | <b>5f</b> , 73         |
| 6                  | C <sub>6</sub> H <sub>5</sub>             | <i>m</i> -FC <sub>6</sub> H <sub>4</sub>                  | <b>5g</b> , 59         |
| 7                  | C <sub>6</sub> H <sub>5</sub>             | <i>o,m</i> -Cl <sub>2</sub> C <sub>6</sub> H <sub>3</sub> | <b>5h</b> , 77         |
| 8                  | C <sub>6</sub> H <sub>5</sub>             | <i>m</i> -MeC <sub>6</sub> H <sub>4</sub>                 | <b>5i</b> , 71         |
| 9                  | C <sub>6</sub> H <sub>5</sub>             | ( <i>E</i> )-C <sub>6</sub> H <sub>5</sub> CH=CH          | <b>5j</b> , 75         |
| 10                 | C <sub>6</sub> H <sub>5</sub>             | 1-naphthyl  | <b>5k</b> , 68         |
| 11                 | C <sub>6</sub> H <sub>5</sub>             | 2-furyl   | <b>5l</b> , 66         |
| 12                 | <i>p</i> -ClC <sub>6</sub> H <sub>4</sub> | C <sub>6</sub> H <sub>5</sub>                             | <b>5m</b> , 57         |

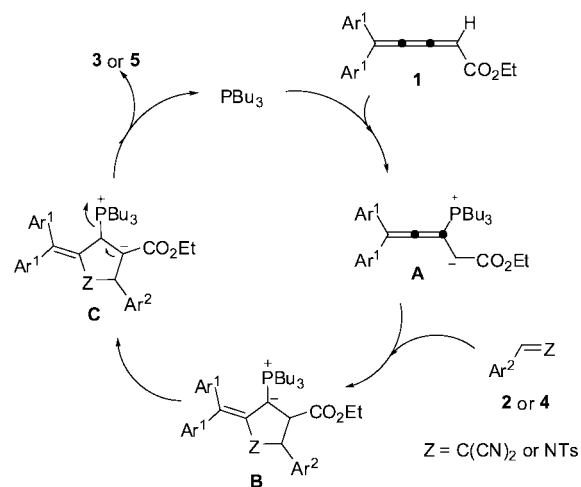
<sup>a</sup> All reactions were carried out with **1** (0.1 mmol) and **4** (0.1 mmol) in the presence of PBu<sub>3</sub> (50 mol %) in toluene (1.0 mL) under argon atmosphere. <sup>b</sup> Isolated yields.

variety of **4** bearing different substituents on the benzene ring and the results of these experiments are summarized in Table 4. As can be seen in Table 4, both aromatic and heterocyclic *N*-tosylimines are suitable substrates in this reaction, providing the corresponding [3+2] cycloaddition products **5** in moderate to good yields (Table 4, entries 1–11). Using butatriene **1b** as the substrate provided the corresponding product **5m** in 57% yield (Table 4, entry 12). The product structure of **5f** was further determined by X-ray diffraction and its CIF data are presented in the Supporting Information.<sup>11</sup> This reaction is sluggish as compared with the reaction of **1** with **2**, presumably due to the lower reactivity of *N*-tosylimines **4**. Moreover, since ethyl 5,5-diarylpenta-2,3,4-trienoates are not stable at 80 °C during a long reaction time, this could be the reason to explain why the yields of **5** in the reactions between **1** and **4** are lower.

(11) The crystal data of **5f** have been deposited in CCDC with no. 708170. Empirical formula: C<sub>33</sub>H<sub>28</sub>BrNO<sub>4</sub>S. Formula weight: 614.53. Crystal size: 0.470 × 0.303 × 0.167. Crystal color, habit: colorless, prismatic. Crystal system: triclinic. Lattice type: primitive. Lattice parameters: *a* = 10.0258(14) Å, *b* = 10.2798(15) Å, *c* = 16.313(2) Å, α = 88.121(3)°, β = 76.794(3)°, γ = 65.924(3)°, *V* = 1874.8(3) Å<sup>3</sup>. Space group: *P*1. *Z* = 2. *D*<sub>calc</sub> = 1.369 g/cm<sup>3</sup>. *F*<sub>000</sub> = 632. *R*<sub>1</sub> = 0.0627, *wR*<sub>2</sub> = 0.1457. Diffractometer: Rigaku AFC7R.

FIGURE 1. The structure of **5n**.

SCHEME 2. A Plausible Reaction Mechanism of These Two Reactions



We also utilized aliphatic *N*-tosylimines such as *N*-(cyclohexylmethylene)-4-methylbenzenesulfonamide and *N*-butylidene-4-methylbenzenesulfonamide in this reaction, but it was found that the product **5n** was formed in 36% and 31% yield, respectively, rather than the [3+2] cycloaddition product. This may be due to that the aliphatic *N*-tosylimine might decompose to give TsNH<sub>2</sub> and aldehyde under the reaction conditions. The direct nucleophilic addition of TsNH<sub>2</sub> to **1a** resulted in the formation of **5n** (Figure 1).

A plausible reaction mechanism is shown in Scheme 2 on the basis of the previously reported phosphine-catalyzed [3+2] cycloaddition reactions between 2,3-butadienoates and *N*-tosylimines or arylmethylidenemalononitriles.<sup>6</sup> The first step is the nucleophilic attack of PBu<sub>3</sub> to ethyl 5,5-diarylpenta-2,3,4-trienoate **1** to generate zwitterionic intermediate **A**. Nucleophilic attack of intermediate **A** to arylmethylidenemalononitrile **2** (or *N*-tosylimine **4**) followed by an intramolecular conjugate

addition produced the ylide-type intermediate **B**. The catalytic cycle completes to produce **3** or **5** via intermediate **C** after a proton transfer and the subsequent elimination of  $\text{PBu}_3$ .

## Experimental Section

**Compound 1a:** yellow solid, mp 83–85 °C;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 300 MHz, TMS)  $\delta$  1.36 (t, 3H,  $J = 7.2$  Hz), 4.25 (q, 2H,  $J = 7.2$  Hz), 5.81 (s, 1H), 7.40–7.44 (m, 6H), 7.55–7.58 (m, 2H), 7.67–7.70 (m, 2H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 75 MHz, TMS)  $\delta$  14.2, 60.8, 96.8, 128.5, 129.6, 129.7, 130.0, 134.8, 136.9, 137.2, 154.5, 165.5, 168.8; IR ( $\text{CH}_2\text{Cl}_2$ )  $\nu$  3056, 2980, 2925, 2359, 2341, 2053, 1733, 1699, 1489, 1446, 1365, 1329, 1243, 1185, 1150, 757, 692  $\text{cm}^{-1}$ ; MS (EI)  $m/z$  (%) 276 [ $\text{M}^+$ ] (73.2), 202 (100.0), 204 (78.0), 203 (73.5), 276 (73.2), 231 (25.7), 201 (25.1), 200 (21.5), 101 (17.8); HRMS (EI) calcd for  $\text{C}_{19}\text{H}_{16}\text{O}_2$  ( $\text{M}^+$ ) requires 276.1150, found 276.1153.

**Compound 1b:** yellow solid, mp 87–89 °C;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 300 MHz, TMS)  $\delta$  1.36 (t, 3H,  $J = 6.9$  Hz), 4.25 (q, 2H,  $J = 6.9$  Hz), 5.85 (s, 1H), 7.37–7.41 (m, 4H), 7.45–7.48 (m, 2H), 7.56–7.59 (m, 2H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 75 MHz, TMS)  $\delta$  14.3, 61.0, 98.1, 128.90, 128.94, 130.8, 131.0, 131.7, 135.0, 135.9, 136.1, 155.0, 165.1, 168.2; IR ( $\text{CH}_2\text{Cl}_2$ )  $\nu$  3053, 2980, 2359, 2341, 2053, 1702, 1585, 1488, 1405, 1366, 1322, 1300, 1244, 1189, 1152, 1092, 1012, 833, 749  $\text{cm}^{-1}$ ; MS (EI)  $m/z$  (%) 344 [ $\text{M}^+$ ] (8.0), 57 (100.0), 91 (63.4), 56 (49.5), 131 (43.6), 92 (39.7), 77 (29.8), 128 (29.3), 55 (27.4); HRMS (EI) calcd for  $\text{C}_{19}\text{H}_{14}\text{Cl}_2\text{O}_2$  ( $\text{M}^+$ ) requires 344.0371, found 344.0369.

**Compound 3a:** white solid, 42 mg (95% yield), mp 138–140 °C;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 300 MHz, TMS)  $\delta$  1.13 (t, 3H,  $J = 6.9$  Hz), 4.08–4.14 (m, 2H), 4.91 (s, 1H), 7.23–7.28 (m, 4H), 7.36–7.44 (m, 12H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 75 MHz, TMS)  $\delta$  13.9, 44.7, 61.2, 61.6, 111.3, 116.4, 128.0, 128.6, 128.8, 129.1, 129.37, 129.41, 129.5, 129.7, 129.9, 132.6, 134.7, 137.7, 138.1, 139.8, 140.1, 149.6, 162.9; IR ( $\text{CH}_2\text{Cl}_2$ )  $\nu$  3061, 3031, 2982, 2932, 2229, 1720, 1593, 1571, 1493, 1455, 1370, 1240, 1181, 1031, 771, 697, 615  $\text{cm}^{-1}$ ; MS (EI)  $m/z$  (%) 430 [ $\text{M}^+$ ] (7.9), 384 (100.0), 385 (33.8), 356 (22.5), 319 (20.0), 355 (16.9), 227 (11.3), 328 (10.9), 357 (10.7). Anal. Calcd for  $\text{C}_{29}\text{H}_{22}\text{N}_2\text{O}_2$ : C, 80.91; H, 5.15; N, 6.51. Found: C, 80.93; H, 5.05; N, 6.32.

**Compound 3i:** yellow oil, 39 mg (86% yield);  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 400 MHz, TMS)  $\delta$  1.02 (t, 3H,  $J = 7.2$  Hz), 1.31 (t, 3H,  $J = 7.2$  Hz), 1.99–2.10 (m, 2H), 3.78 (ddd, 1H,  $J_1 = 6.4$  Hz,  $J_2 = 4.4$  Hz,  $J_3 = 0.8$  Hz), 4.21–4.31 (m, 2H), 7.13 (d, 1H,  $J = 0.8$  Hz), 7.14–7.16 (m, 2H), 7.37–7.43 (m, 5H), 7.45–7.48 (m, 3H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 100 MHz, TMS)  $\delta$  10.1, 14.2, 24.5, 42.5, 56.3, 61.3, 111.9, 116.3, 128.5, 128.9, 129.3, 129.4, 129.6, 130.0, 133.1, 137.9, 138.4, 139.2, 140.1, 148.1, 163.4; IR ( $\text{CH}_2\text{Cl}_2$ )  $\nu$  3058, 2972, 2928, 2249, 1712, 1601, 1445, 1460, 1371, 1242, 1181, 1093, 769, 701  $\text{cm}^{-1}$ ; MS (EI)  $m/z$  (%) 382 [ $\text{M}^+$ ] (36.5), 84 (100.0), 308 (90.3), 86 (66.0), 382 (36.5), 307 (31.5), 293 (31.4), 309 (23.6), 149 (20.9); HRMS (EI) calcd for  $\text{C}_{25}\text{H}_{22}\text{N}_2\text{O}_2$  ( $\text{M}^+$ ) requires 382.1681, found 382.1679.

**Compound 5a:** yellow solid, 39 mg (72% yield), mp 219–221 °C;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 300 MHz, TMS)  $\delta$  1.05 (t, 3H,  $J = 6.6$  Hz), 2.43 (s, 3H), 4.00 (q, 2H,  $J = 6.6$  Hz), 6.06 (d, 1H,  $J = 0.9$  Hz), 7.02 (d, 1H,  $J = 0.9$  Hz), 7.11–7.18 (m, 5H), 7.23 (d, 4H,  $J = 8.4$

Hz), 7.33–7.40 (m, 8H), 7.56 (d, 2H,  $J = 8.7$  Hz);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 75 MHz, TMS)  $\delta$  13.9, 21.6, 60.7, 70.6, 127.4, 127.5, 127.7, 127.8, 128.3, 128.4, 128.7, 129.4, 130.4, 130.6, 134.4, 136.0, 138.2, 138.4, 139.3, 140.8, 141.3, 144.0, 162.6; IR ( $\text{CH}_2\text{Cl}_2$ )  $\nu$  3045, 2976, 2906, 1701, 1595, 1442, 1363, 1245, 1167, 1089, 988, 817, 769, 698, 660  $\text{cm}^{-1}$ ; MS (ESI)  $m/z$  (%) 558 ( $\text{M} + \text{Na}^+$ , 100), 574 ( $\text{M} + \text{K}^+$ , 40), 536 ( $\text{M} + \text{H}^+$ , 25). Anal. Calcd for  $\text{C}_{33}\text{H}_{29}\text{NO}_4\text{S}$ : C, 73.99; H, 5.46; N, 2.61. Found: C, 73.99; H, 5.45; N, 2.45.

**Compound 5n:** yellow oil, 16 mg (36% yield);  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 300 MHz, TMS)  $\delta$  0.99 (t, 3H,  $J = 7.2$  Hz), 2.34 (s, 3H), 3.88 (q, 2H,  $J = 7.2$  Hz), 6.32 (s, 1H), 7.20–7.24 (m, 4H), 7.30–7.37 (m, 7H), 7.41–7.45 (m, 3H), 7.70 (d, 2H,  $J = 8.4$  Hz);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 75 MHz, TMS)  $\delta$  13.9, 21.5, 61.5, 122.6, 123.0, 127.6, 128.2, 128.3, 128.4, 128.6, 128.8, 129.4, 130.6, 135.5, 136.1, 138.6, 141.3, 143.9, 151.9, 164.5; IR ( $\text{CH}_2\text{Cl}_2$ )  $\nu$  3252, 3058, 2981, 2927, 1709, 1616, 1494, 1446, 1410, 1370, 1338, 1265, 1240, 1166, 1091, 814, 771, 702, 670  $\text{cm}^{-1}$ ; MS (ESI)  $m/z$  (%) 470 ( $\text{M} + \text{Na}^+$ , 100), 448 ( $\text{M} + \text{H}^+$ , 25); HRMS (ESI) calcd for  $\text{C}_{26}\text{H}_{25}\text{NO}_4\text{SNa}$  ( $\text{M} + \text{Na}^+$ ) requires 470.1414, found 470.13965.

## Conclusion

Ethyl 5,5-diarylpenta-2,3,4-trienoates were successfully synthesized and utilized as a three-carbon source in the [3+2] cycloaddition reactions with arylmethylidenemalononitriles or *N*-tosylimines in the presence of  $\text{PBu}_3$  (50 mol %) in THF and toluene, respectively. These reactions show a broad substrate scope for a variety of arylmethylidenemalononitriles or *N*-tosylimines. In the reactions of ethyl 5,5-diarylpenta-2,3,4-trienoates with arylmethylidenemalononitriles, the corresponding [3+2] cycloaddition products could be obtained in 43–99% yields within 1 h at 60 °C, and in the reactions of ethyl 5,5-diarylpenta-2,3,4-trienoates with *N*-tosylimines, the cycloadducts were obtained in 57–74% yields after 24 h at 80 °C. Efforts are in progress to elucidate further mechanistic details of these reactions and to understand their scope and limitations. Moreover, the asymmetric [3+2] cycloaddition reactions of ethyl 5,5-diarylpenta-2,3,4-trienoates with arylmethylidenemalononitriles or *N*-tosylimines are in progress in our laboratory.

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**Supporting Information Available:**  $^1\text{H}$  NMR and  $^{13}\text{C}$  spectroscopic and analytic data for **1a**, **1b**, **3**, and **5**, and X-ray crystal structure of **3i** and **5f**. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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