Diastereoselective [Cu(MeCN)₄BF₄/BF₃·Et₂O]-Catalyzed Cyclopropenation of Alkynes: Asymmetric Synthesis of β-Amino-α-cyclopropenyl Phosphonates

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Abstract The diastereosepecific formation of β-amino-α-cyclopropenyl phosphonates has been achieved in moderate yields from the cyclopropenation of 1-alkynes with dialkyl α-diazo phosphonates. The reaction was performed by using a combined catalyst consisting of Cu(MeCN)₄BF₄ and BF₃·Et₂O as additive in dichloromethane at 40 °C. A possible mechanism for the reaction has been proposed to explain the origin of the activation and the asymmetric induction. This method provides a versatile approach to β-amino-α-cyclopropenyl phosphonates containing a quaternary stereogenic center with good efficiency and diastereoselectivity.

Key words cyclopropenation, α-diazo phosphonates, asymmetric synthesis, cyclopropenyl phosphonates, Cu(MeCN)₄BF₄/BF₃·Et₂O

Cyclopropenones are a unique class of the smallest ring compound with a double bond, and the combination of high strain and unsaturation renders cyclopropenones as versatile synthons in a wide variety of organic synthesis.¹ To enhance the synthetic potential of cyclopropenones further, the development of expeditious methods for their synthesis is highly desirable.² One of the most efficient catalytic asymmetric methods for their preparation involves the reaction of alkynes with diazo compounds using chiral copper(I),³ iridium(II),⁴ cobalt(II),⁵ or rhodium(II)⁶ catalysts. Diazo compounds are commonly used in formation of metallophanes, which can subsequently undergo diverse chemical transformations.⁷ In 1992, Doyle, Müller and co-workers reported the first cyclopropenation reactions of diazoacettes with terminal alkynes using [Rh₂(55-mepy)₄] as a chiral catalyst.⁸ Corey and co-workers also reported a significantly improved enantioselective cyclopropenation of ethyl diazoacetate with 1-alkynes using a new rhodium complex, Rh₂(OAc)(DPTI), as a catalyst.⁹ Although high levels of enantioselectivity (up to 99% ee) in cyclopropenations of terminal alkynes with aryl diazoacetates under catalysis by [Rh₂(S-dosp)₄] have been reported by Davies and co-workers,¹⁰ stereoselective syntheses of the corresponding cyclopropenylphosphonates using such a strategy remain scarce.¹¹

α-Diazo phosphonates are phosphorus analogues of α-diazo acetates, and therefore could undergo a range of chemical transformations and the synthesis of varieties of functionalized phosphorous compounds.¹² In 2013, Charette and co-workers reported the first catalytic asymmetric synthesis of bis-acceptor cyclopropophosphonates through the reaction of α-cyano diazophosphonates with allenes catalyzed by Rh₂(S-IBAZ)₄ under mild reaction conditions.¹³ Cyclopropophosphonates demonstrate a range of biological and biochemical properties.¹⁴ By analogy with cyclopropophosphonates,¹⁵ the development of efficient methods for the preparation of cyclopropenephosphonates is attracting increasing attention. In particular, the presence of a quaternary stereocenter in a highly substituted cyclopropenephosphonate can lead to interaction with certain proteases and a resistance to proteolytic degradation.¹⁶

Recently, we reported novel α-diazo phosphonophosphonate compounds prepared from natural amino acids that be used to could perform combined C–H functionalization and O–H insertion to form tertiary β-alkoxy-substituted β-amino phosphonates (Scheme 1, Eq. 1).¹⁶ As a natural extension of the combined C–H functionalization/O–H insertion reaction, we have developed a regioselective boron trifluoride-catalyzed C–H functionalization/S–H insertion reaction for
the synthesis of \(\text{NS\text{-}acetalts}\) containing quaternary centers (Scheme 1, Eq. 2). In a continuation of our interest in the chemistry of aminophosphorus derivatives, we herein report the first example of the conversion of dialkyl \(\alpha\)-diazo- phosphonates into cyclopropenylphosphonate derivatives catalyzed by tetrakis (acetonitrile)copper(I) tetrafluoroborate/boron trifluoride \([\text{Cu(MeCN)}_4\text{BF}_4/\text{BF}_3\cdot\text{Et}_2\text{O}]\) in a highly diastereoselective manner (Scheme 1, Eq. 3).

We began our investigations by studying the reaction of diethyl \(\alpha\)-diazo phosphonate \(1\text{a}\) with phenylacetylene \(2\text{a}\) in the presence of catalyst in dichloromethane at 25 °C (Table 1). The results revealed that transition-metal catalysts such as \(\text{Rh}_2(\text{OAc})_4\) and \(\text{Hg(OTf)}_2\) did not decompose \(1\text{a}\) in the presence of \(2\text{a}\) (entries 1 and 2). The other catalysts tested (e.g., \(\text{CuOTf}, \text{AgOTf}, \text{and Cu(MeCN)}_4\text{PF}_6\)) could be used to promote the reaction, resulting in low yields of product with moderate diastereoselectivities (entries 3–5). To our delight \(\text{Cu(MeCN)}_4\text{BF}_4\) catalyzed the decomposition of \(1\text{a}\), and diethyl[2-(phenyl-cycloprop-2-enyl)-2-(1,3-dioxoisoindolin-2-yl)ethyl]phosphonate \(3\text{a}\) was obtained with good diastereoselectivity \((\text{dr} = 12:1)\) in 29% yield (entry 6). In addition, a 1,2-hydrogen migration by-product \(\beta\text{-diazo phosphonate} (3\text{b})\) was obtained in 9% yield. The molecular structure of \(3\text{a}\) was determined based on \(\text{H}, \text{P}, \text{C}\) NMR, and 2D NMR spectroscopy and mass spectrometry. This result encouraged us to choose \(\text{Cu(MeCN)}_4\text{BF}_4\) as the catalyst for further optimization of the reaction conditions. To improve the reactivity and diastereoselectivity, the effects of different additives and solvents were investigated.

Initially, additives were evaluated to study the diastereoselectivity of this transformation. As shown in Table 1, both the diastereoselectivity and the ratio of the two products \(3\text{a}\) and \(4\text{a}\) was affected dramatically by the additive. In the presence of \(\text{Cu(MeCN)}_4\text{BF}_4\) as the catalyst (5 mol%) and \(\text{BF}_3\cdot\text{Et}_2\text{O} (20\text{ mol%})\) as the additive in dichloromethane, the reaction proceeded with an increased combined yield and good diastereoselectivity \((\text{dr} = 12:1)\) (entry 7). Furthermore, we found that high temperatures favored this reaction. When the reaction was carried out at 40 °C, the desired product \(3\text{a}\) could be obtained in 66% yield (entry 8). After screening \(\text{BF}_3\cdot\text{Et}_2\text{O}\), it was found that acetone, \(\text{CH}_3\text{CN}, \text{DMF}, \text{and iodine}\) did not give superior results in terms of either reactivity or stereoselectivity (entries 9–12).

With the optimum combination of \(\text{Cu(MeCN)}_4\text{BF}_4\) catalyst and \(\text{BF}_3\cdot\text{Et}_2\text{O}\) additive, we next carried out the reaction in different solvents to determine the best solvent for this reaction. Toluene, \(\text{THF}, \text{DME}, \text{and 1,2-dichloroethane}\) all provided lower yields of the desired products \(3\text{a}\) and \(4\text{a}\) with moderate diastereoselectivities (Table 1, entries 13–16). This screening therefore identified \(\text{CH}_2\text{Cl}_2\) as the optimal solvent for this reaction. Furthermore, a decrease in the catalyst loading to 2 mol% \(\text{Cu(MeCN)}_4\text{BF}_4\) and 10 mol% \(\text{BF}_3\cdot\text{Et}_2\text{O}\) led to a decrease in both yield and diastereoselectivity (entry 17). A similar result was obtained when the reaction was performed in \(\text{CH}_2\text{Cl}_2\) with increased catalyst loading to 10 mol% \(\text{Cu(MeCN)}_4\text{BF}_4\) and 30 mol% \(\text{BF}_3\cdot\text{Et}_2\text{O}\) (entry 18). Thus, the optimal reaction conditions for this transformation were determined to be 0.28 mmol \(\alpha\)-diazo phosphonate \(1\text{a}\), 5.0 equivalents of phenylacetylene \(2\text{a}\), 5 mol% \(\text{Cu(MeCN)}_4\text{BF}_4\) and 20 mol% \(\text{BF}_3\cdot\text{Et}_2\text{O}\) as co-catalyst in 6 mL of \(\text{CH}_2\text{Cl}_2\) as solvent at 40 °C.

Under the optimal reaction conditions, the substrate scope of this reaction was investigated (Table 2). The impact of different groups on the \(\beta\)-position of dialkyl \(\alpha\)-diazo phosphonates \(1\) was evaluated. \(\alpha\)-Diazophosphonates \(1\text{a}\text{e}\) with different substituents in the \(\beta\)-position, such as methyl, benzy1, isobutyl, ethyl, and 4-acetoxybenzyl groups, afforded moderate yields of the \(\beta\)-amino-\(\alpha\)-cyclopropenylphosphonates \(3\text{a}\text{e}\) and the 1,2-hydride migration products.
It is worth noting that diethyl \( \alpha \)-diazo-phosphonate \( 1f \), derived from methionine, did not undergo reaction to give the desired products, probably due to the fact that the sulfur atom coordinates with the copper(I) and hinders the reaction (entry 6). Instead, the starting material \( 1f \) decomposed under the reaction conditions. In addition to phenylacetylene, 3-methylphenyl acetylene and 4-methylphenylacetylene were also examined in the cycloprope-nation reaction with carbenoids derived from dialkyl \( \alpha \)-di-azophosphonates \( 1b \) and \( 1g \). Electron-rich phenylacetylene derivatives, substituted either at the meta-, or para-position, all provided good yields and diastereoselectivities of the corresponding \( \beta \)-amino-\( \alpha \)-cyclopropenylphosphonates (entries 7 and 8). Chiral cyclopropene derivatives \( 3i \) and \( 3j \), from reactions of aromatic alkynes containing both electron-withdrawing and –donating groups at the para-position could also be obtained in poor yields but with good diastereoselectivities (entries 9 and 10). The cyclopropenation could also be conducted on the internal alkyne prop-1-ynyl-benzene \( 2f \) with excellent diastereoselectivity (>30:1), albeit in diminished yield (11%), presumably due to the ste-ric effect (entry 11).

**Table 1** Optimization of the Reaction Conditions

<table>
<thead>
<tr>
<th>Entry</th>
<th>Catalysts</th>
<th>Additive</th>
<th>Solvent</th>
<th>(3a:4a) ratio ( ^b )</th>
<th>Overall yield (%) ( ^c )</th>
<th>Yield 3a (%) ( ^d )</th>
<th>Yield 4a (%) ( ^d )</th>
<th>dr ( ^e )</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Rh(_2)(OAc)_4</td>
<td>–</td>
<td>CH(_2)Cl (_2)</td>
<td>–</td>
<td>N.R.</td>
<td>N.R.</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>2</td>
<td>Hg(OTf)_2</td>
<td>–</td>
<td>CH(_2)Cl (_2)</td>
<td>–</td>
<td>N.R.</td>
<td>N.R.</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>3</td>
<td>CuOTf</td>
<td>–</td>
<td>CH(_2)Cl (_2)</td>
<td>63:37</td>
<td>&lt;10</td>
<td>&lt;10</td>
<td>8:1</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>AgOTf</td>
<td>–</td>
<td>CH(_2)Cl (_2)</td>
<td>57:43</td>
<td>&lt;10</td>
<td>&lt;10</td>
<td>10:1</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>Cu(MeCN)_4PF(_6)</td>
<td>–</td>
<td>CH(_2)Cl (_2)</td>
<td>60:40</td>
<td>23</td>
<td>14</td>
<td>12:1</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>Cu(MeCN)_4BF(_4)</td>
<td>BF(_3)·Et(_2)O</td>
<td>CH(_2)Cl (_2)</td>
<td>77:23</td>
<td>38</td>
<td>29</td>
<td>12:1</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>Cu(MeCN)_4BF(_4)</td>
<td>BF(_3)·Et(_2)O</td>
<td>CH(_2)Cl (_2)</td>
<td>78:22</td>
<td>42</td>
<td>33</td>
<td>12:1</td>
<td></td>
</tr>
<tr>
<td>8*</td>
<td>Cu(MeCN)_4BF(_4)</td>
<td>BF(_3)·Et(_2)O</td>
<td>CH(_2)Cl (_2)</td>
<td>82:18</td>
<td>81</td>
<td>66</td>
<td>12:1</td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>Cu(MeCN)_4BF(_4)</td>
<td>CH(_3)COCH(_3)</td>
<td>CH(_2)Cl (_2)</td>
<td>75:25</td>
<td>28</td>
<td>21</td>
<td>10:1</td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>Cu(MeCN)_4BF(_4)</td>
<td>–</td>
<td>CH(_2)CN</td>
<td>70:30</td>
<td>33</td>
<td>23</td>
<td>&gt;25:1</td>
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<tr>
<td>11</td>
<td>Cu(MeCN)_4BF(_4)</td>
<td>DMF</td>
<td>CH(_2)Cl (_2)</td>
<td>78:22</td>
<td>25</td>
<td>20</td>
<td>15:1</td>
<td></td>
</tr>
<tr>
<td>12</td>
<td>Cu(MeCN)_4BF(_4)</td>
<td>iodine</td>
<td>CH(_2)Cl (_2)</td>
<td>64:36</td>
<td>40</td>
<td>26</td>
<td>13:1</td>
<td></td>
</tr>
<tr>
<td>13(i)</td>
<td>Cu(MeCN)_4BF(_4)</td>
<td>BF(_3)·Et(_2)O</td>
<td>toluene</td>
<td>76:24</td>
<td>38</td>
<td>29</td>
<td>16:1</td>
<td></td>
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<tr>
<td>14(i)</td>
<td>Cu(MeCN)_4BF(_4)</td>
<td>BF(_3)·Et(_2)O</td>
<td>THF</td>
<td>80:20</td>
<td>47</td>
<td>38</td>
<td>15:1</td>
<td></td>
</tr>
<tr>
<td>15(i)</td>
<td>Cu(MeCN)_4BF(_4)</td>
<td>BF(_3)·Et(_2)O</td>
<td>DME(g)</td>
<td>78:22</td>
<td>42</td>
<td>33</td>
<td>10:1</td>
<td></td>
</tr>
<tr>
<td>16(i)</td>
<td>Cu(MeCN)_4BF(_4)</td>
<td>BF(_3)·Et(_2)O</td>
<td>1,2-dichloroethane</td>
<td>82:18</td>
<td>42</td>
<td>34</td>
<td>12:1</td>
<td></td>
</tr>
<tr>
<td>17(i)</td>
<td>Cu(MeCN)_4BF(_4)</td>
<td>BF(_3)·Et(_2)O</td>
<td>CH(_2)Cl (_2)</td>
<td>68:32</td>
<td>44</td>
<td>30</td>
<td>8:1</td>
<td></td>
</tr>
<tr>
<td>18(i)</td>
<td>Cu(MeCN)_4BF(_4)</td>
<td>BF(_3)·Et(_2)O</td>
<td>CH(_2)Cl (_2)</td>
<td>66:34</td>
<td>51</td>
<td>34</td>
<td>10:1</td>
<td></td>
</tr>
</tbody>
</table>

\( ^a \) Unless otherwise specified, all reactions were carried out using \( \alpha \)-diazo-phosphonate \( 1a \) (0.28 mmol, 1 equiv) and phenylacetylene \( 2a \) (1.40 mmol, 5 equiv) in the specified solvent (6 mL) with 5 mol% catalyst and 20 mol% additive at 25 °C for 3.5 h (addition over 1.5 h, then a further 2 h).

\( ^b \) The product ratio was determined by \( ^{31}\)P NMR spectroscopic analysis of the crude product.

\( ^c \) Overall yield of the mixture of 3a and 4a after silica gel chromatograph.

\( ^d \) Yield of isolated product.

\( ^e \) Diastereomeric ratio (dr) based on \( ^{31}\)P NMR spectroscopic analysis of the isolated product 3a.

\( ^f \) Reaction temperature 40 °C.

\( ^g \) DME = dimethoxyethane.

\( ^h \) 2 mol% Cu(MeCN)_4BF\(_4\) and 10 mol% BF\(_3\)·Et\(_2\)O were used.

\( ^i \) 10 mol% Cu(MeCN)_4BF\(_4\) and 30 mol% BF\(_3\)·Et\(_2\)O were used.
products were not obtained when diethyl α-diazophosphonate 1a was reacted with (triisopropyl)silylacetylene or 1-hexyne.

A stepwise mechanism for the formation of the cyclopropenylphosphonates is outlined in Scheme 2. Firstly, α-diazophosphonate 1 releases N₂ under the influence of the Cu catalyst on heating, affording Cu-carbenoid A. The role of the strong Lewis acids (BF₃·Et₂O) could be to coordinate to the copper to give metallocarbenoid B. The second C–C bond forms with inversion of the carbenoid center. This model is partly consistent with the observed sense of asymmetric induction, but there are a few anomalies. For instance, isopropyl phosphonate 1j leads to lower dr than methyl phosphonate 1i (Table 2, entries 13 and 14).

In conclusion, we have developed a Cu(MeCN)ₓBFₓ/BF₃·Et₂O-catalyzed cyclopropenation of 1-alkynes with dialkyl α-diazophosphonates to synthesize β-amino-α-cyclopropenyl phosphonates in moderate yields with good to excellent diastereoselectivities. The observed sense of asymmetric induction is rationalized by invoking steric hindrance between the phosphonate group and the Rᵢ group, with attack occurring on the back face of the carbenoid preferentially. In forming intermediate C, the terminal alkyne carbon is involved in C–C bond formation with the carbenoid carbon, while positive charge build-up occurs at the internal sp-carbon. Furthermore, the second C–C bond forms with inversion of the carbenoid center. This model is partly consistent with the observed sense of asymmetric induction, but there are a few anomalies. For instance, isopropyl phosphonate 1j leads to lower dr than methyl phosphonate 1i (Table 2, entries 13 and 14).

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cyclopropenyl phosphonates containing a quaternary stereogenic center. Further studies to explore the enantioselective synthesis of cyclopropenyl phosphonates are in progress in our laboratory.

All reactions and manipulations were performed using standard Schlenk techniques. Solvents were dried and distilled prior to use according to standard methods. Unless otherwise indicated, all materials were obtained from commercial sources, and used as purchased without dehydration. Flash column chromatography was performed on silica gel (particle size 10–40 μm, Ocean Chemical Factory of Qingdao, China). Nitrogen gas (99.999%) was purchased from Boc Gas Inc. 1H NMR, 13C NMR, and 31P NMR spectra were recorded in CDCl₃ with Bruker 400 MHz spectrometers, TMS served as internal standard (δ = 0 ppm) for 1H NMR and 13C NMR, H₃PO₄ served as internal standard (δ = 0 ppm) for 31P NMR. Mass spectra were recorded with a LCQ advantage spectrometer with ESI resource. HRMS were recorded with a PEXII and ZAB-HS spectrometer.

Preparation of 3 and 4; General Procedure
In an oven-dried Schlenk tube, [Cu(MeCN)₄]BF₄ (0.014 mmol) and BF₃·Et₂O (0.056 mmol) were dissolved in freshly distilled CH₂Cl₂ (4 mL) under nitrogen, the requisite phenylacetylene 2 (1.4 mmol) was added and the solution was stirred for 30 min at 25 °C. α-Diazo phosphonate 1 (0.28 mmol) dissolved in CH₂Cl₂ (2 mL) was then added to the reaction mixture dropwise over a period of 1.5 h by using a syringe pump. When the addition was complete, the reaction mixture was stirred for a further 2 h at 40 °C. The solvent was then removed under reduced pressure and the crude residue was purified by silica gel chromatography, eluting with CH₂Cl₂/EtOAc (15:1) to afford the corresponding products 3 and 4.

Diethyl[1-(phenylcycloprop-2-enyl)-2-(1,3-dioxoisoindolin-2-yl)ethyl]phosphonate (3a)
Yield: 0.085 g (66%); pale-yellow oil.
1H NMR (400 MHz, CDCl₃): δ = 7.61 (dd, J = 5.2, 3.2 Hz, 2 H), 7.56 (dd, J = 5.3, 3.1 Hz, 2 H), 7.49 (d, J = 7.1 Hz, 2 H), 7.16–7.25 (m, 3 H), 7.01 (d, J = 4.1 Hz, 1 H), 5.17–5.27 (m, 1 H, CH), 4.11 (dd, J = 12.8, 5.7 Hz, 4 H), 1.70 (d, J = 7.2 Hz, 3 H), 1.30 (td, J = 7.0, 4.2 Hz, 6 H).
13C NMR (101 MHz, CDCl₃): δ = 168.35, 133.57, 131.51, 129.77, 129.59, 128.30, 125.48, 116.00, 97.61, 62.02, 61.88, 47.44 (d, J = 36.5 Hz), 30.15, 28.17, 16.16.
31P NMR (162 MHz, CDCl₃): δ = 26.86.
HRMS (ESI): m/z [M + H]+ calcd for C₂₃H₂₄NO₅P: 426.1426; found: 426.1470.

Diethyl[1-(phenylcycloprop-2-enyl)-2-(1,3-dioxoisoindolin-2-yl)phenylethyl]phosphonate (3b)
Yield: 0.086 g (58%); pale-yellow oil.
1H NMR (400 MHz, CDCl₃): δ = 168.35, 133.57, 131.51, 129.77, 129.59, 128.30, 125.48, 116.00, 97.61, 62.02, 61.88, 47.44 (d, J = 36.5 Hz), 30.15, 28.17, 16.16.
13C NMR (101 MHz, CDCl₃): δ = 168.35, 133.57, 131.51, 129.77, 129.59, 128.30, 125.48, 116.00, 97.61, 62.02, 61.88, 47.44 (d, J = 36.5 Hz), 30.15, 28.17, 16.16.
31P NMR (162 MHz, CDCl₃): δ = 26.86.
Yield: 0.078 g (56%); pale-yellow oil.

1H NMR (400 MHz, CDCl3): δ = 7.50–7.60 (m, 4 H), 7.43 (d, J = 6.7 Hz, 2 H), 7.08–7.23 (m, 3 H), 6.97 (d, J = 4.2 Hz, 1 H), 5.17 (d, J = 12.2 Hz, 1 H), 4.31 (t, J = 6.7 Hz, 1 H), 4.04–4.15 (m, 4 H), 2.50 (t, J = 13.3 Hz, 1 H), 2.34 (t, J = 7.4 Hz, 1 H), 1.73 (dd, J = 13.2, 9.3 Hz, 3 H), 1.44 (dd, J = 15.4, 7.6 Hz, 3 H), 0.88–0.93 (m, 6 H).

13C NMR (101 MHz, CDCl3): δ = 168.65, 133.52, 129.68, 129.47, 128.85, 128.26, 125.45, 122.68, 115.62, 97.48, 65.58, 61.97, 50.16 (d, J = 36.2 Hz), 37.45, 29.71, 25.44, 23.59, 22.70, 21.11, 16.48, 14.13, 13.74.

31P NMR (162 MHz, CDCl3): δ = 26.80.


Yield: 0.097 g (60%); pale-yellow oil.

1H NMR (400 MHz, CDCl3): δ = 7.54–7.64 (m, 4 H), 7.47 (d, J = 6.7 Hz, 2 H), 7.15–7.24 (m, 3 H), 6.99 (d, J = 4.2 Hz, 1 H), 4.92–5.03 (m, 1 H), 4.10 (dd, J = 14.5, 11.7 Hz, 1 H), 4.23–4.24 (m, 1 H), 2.06–2.14 (m, 1 H), 1.34–1.49 (m, 3 H), 0.87 (dd, J = 15.3, 7.9 Hz, 6 H).

13C NMR (101 MHz, CDCl3): δ = 168.65, 133.56, 131.39, 129.72, 129.52, 128.29, 125.55, 122.71, 115.64, 97.46, 61.97, 53.99 (d, J = 36.1 Hz), 22.71, 22.11, 14.14, 11.20.

31P NMR (162 MHz, CDCl3): δ = 26.94.


1H NMR (400 MHz, CDCl3): δ = 7.42–7.49 (m, 5 H), 7.14–7.21 (m, 4 H), 6.96–7.11 (m, 2 H), 6.82–6.86 (m, 2 H), 5.35–5.42 (m, 1 H), 4.13 (dt, J = 7.1, 4.7 Hz, 1 H), 3.07–3.94 (m, 4 H), 3.69 (dd, J = 14.2, 12.6 Hz, 1 H), 3.47 (dd, J = 14.4, 4.2 Hz, 1 H), 2.20 (s, 3 H), 1.32 (s, 3 H), 1.18–1.24 (m, 6 H).

13C NMR (101 MHz, CDCl3): δ = 168.30, 133.67, 131.86, 131.78, 131.51, 122.74, 115.57 (d, J = 16.3 Hz, 97.17, 61.96 (d, J = 18.4, 6.9 Hz), 47.39 (d, J = 47 Hz), 47.30, 28.23, 16.42.

31P NMR (162 MHz, CDCl3): δ = 26.56.


Yield: 0.0109 g (19%); pale-yellow oil.

1H NMR (400 MHz, CDCl3): δ = 7.50–7.56 (m, 4 H), 7.41 (d, J = 7.4 Hz, 2 H), 6.82–6.89 (m, 3 H), 5.11 (d, J = 7.1 Hz, 1 H), 3.97–4.05 (m, 4 H), 1.60 (d, J = 1.6 Hz, 3 H), 1.18–1.24 (m, 6 H).

13C NMR (101 MHz, CDCl3): δ = 168.30, 133.67, 131.86, 131.78, 131.51, 122.74, 115.57 (d, J = 16.3 Hz, 97.17, 61.96 (d, J = 18.4, 6.9 Hz), 47.39 (d, J = 47 Hz), 47.30, 28.23, 16.42.

31P NMR (162 MHz, CDCl3): δ = 26.56.

HRMS (ESI): m/z [M + H]+ calcd for C30H30NO5P: 444.1371; found: 444.1378.

Yield: 0.0109 g (19%); pale-yellow oil.

1H NMR (400 MHz, CDCl3): δ = 7.70–7.80 (m, 3 H), 7.31–7.19 (m, 4 H), 7.09–7.10 (m, 1 H), 7.05 (t, J = 7.7 Hz, 1 H), 6.89 (d, J = 4.2 Hz, 1 H), 6.71–6.79 (m, 2 H), 5.38 (d, J = 4.2 Hz, 1 H), 4.12 (dd, J = 440 M Hz, 4 H), 3.72 (s, 3 H), 3.62–3.69 (m, 1 H), 3.44–3.53 (m, 1 H), 1.29–1.34 (m, 6 H).

13C NMR (101 MHz, CDCl3): δ = 160.63, 138.46, 133.38, 131.44, 128.70, 128.29, 126.19, 112.61, 115.03, 113.88, 94.80, 61.97, 55.23, 53.68 (d, J = 60.63 Hz), 34.99, 29.39, 27.40, 16.52, 16.45.

31P NMR (162 MHz, CDCl3): δ = 26.93.

Diethyl[(2-methyl-3-phenylcycloprop-2-enyl)-2-(1,3-dioxoisooindolin-2-yl)ethyl]phosphonate (3k)

Yield: 0.011 g (11%); pale-yellow oil.

$^{1}H$ NMR (400 MHz, CDCl$_3$): $\delta$ = 7.57–7.62 (m, 2 H), 7.45 (d, $J$ = 4.2 Hz, 1 H), 1.24–1.29 (m, 6 H).

$^{13}$C NMR (101 MHz, CDCl$_3$): $\delta$ = 137.14, 131.43, 133.67, 129.14, 128.25, 128.15, 125.67, 108.45, 108.05 61.41, 47.60 (d, $J$=74.60 Hz).

HRMS (ESI): m/z [M + H]+ calcd for C$_2$H$_2$NO$_2$P: 441.1621; found: 440.1613.

Dimethyl[(1-phenycycloprop-2-enyl)-2-(1,3-dioxoisooindolin-2-yl)ethyl]phosphonate (3l)

Yield: 0.066 g (55%); pale-yellow oil.

$^{1}H$ NMR (400 MHz, CDCl$_3$): $\delta$ = 7.47–7.54 (m, 4 H), 7.48 (d, $J$ = 6.7 Hz, 2 H), 7.17–7.26 (m, 3 H), 7.03 (d, $J$ = 4.2 Hz, 1 H), 5.16–5.25 (m, 1 H), 3.77 (dd, $J$ = 10.6, 5.5 Hz, 6 H), 1.72 (d, $J$ = 7.2 Hz, 3 H).

$^{1}C$ NMR (101 MHz, CDCl$_3$): $\delta$ = 168.34, 133.58, 131.46, 129.76, 129.69, 128.38, 125.26, 122.73, 115.73, 97.37, 52.84, 52.70, 47.40 (d, $J$ = 37.1 Hz), 16.07.

$^{31}$P NMR (162 MHz, CDCl$_3$): $\delta$ = 29.30.

HRMS (ESI): m/z [M + H]+ calcd for C$_2$H$_2$NO$_2$P: 398.1113; found: 398.1148.

Dimethyl[(1-phenycycloprop-2-enyl)-2-(1,3-dioxoisooindolin-2-yl)-2-phenyl-ethyl]phosphonate (3m)

Yield: 0.093 g (66%); pale-yellow oil.

$^{1}H$ NMR (400 MHz, CDCl$_3$): $\delta$ = 7.45–7.51 (m, 5 H), 7.13–7.24 (m, 7 H), 7.08 (dd, $J$ = 12.8, 5.7 Hz, 2 H), 5.39 (ddd, $J$ = 12.4, 4.3, 2.6 Hz, 1 H), 3.79–3.84(m, 6 H), 3.61–3.74 (m, 2 H), 3.46–3.50 (m, 1 H).

$^{13}$C NMR (101 MHz, CDCl$_3$): $\delta$ = 138.16, 133.49, 129.76, 129.73, 129.63, 128.70, 128.42, 128.35, 126.29, 125.10, 123.48, 122.66, 115.33, 97.46, 53.44 (d, $J$ = 37.0 Hz), 34.94.

$^{31}$P NMR (162 MHz, CDCl$_3$): $\delta$ = 29.11.

HRMS (ESI): m/z [M + H]+ calcd for C$_2$H$_2$NO$_2$P: 474.1426; found: 474.1468.

Diisopropyl[(1-phenycycloprop-2-enyl)-2-(1,3-dioxoisooindolin-2-yl)-2-phenyl-ethyl]phosphonate (3n)

Yield: 0.094 g (60%); pale-yellow oil.

$^{1}H$ NMR (400 MHz, CDCl$_3$): $\delta$ = 7.70 (dd, $J$ = 26.3, 19.1 Hz, 6 H), 7.37–7.51 (m, 3 H), 7.21 (d, $J$ = 4.3 Hz, 1 H), 7.00–7.09 (m, 4 H), 5.44 (d, $J$ = 8.9 Hz, 1 H), 4.52 (ddd, $J$ = 13.4, 11.0, 6.2 Hz, 2 H), 2.74–3.25 (m, 2 H), 2.55 (dd, $J$ = 14.0, 4.2 Hz, 1 H), 1.19 (d, $J$ = 6.2 Hz, 6 H), 1.03 (dd, $J$ = 16.5, 6.2 Hz, 6 H).

$^{13}$C NMR (101 MHz, CDCl$_3$): $\delta$ = 153.59, 140.51, 137.65, 133.50, 129.97, 128.85, 128.89,127.98, 127.57, 126.44, 126.29, 123.42, 116.36, 100.21, 70.03 (d, $J$ = 7.4 Hz), 52.71 (d, $J$ = 25.3 Hz), 35.70, 29.71, 23.78.

$^{31}$P NMR (162 MHz, CDCl$_3$): $\delta$ = 24.92.

HRMS (ESI): m/z [M + H]+ calcd for C$_2$H$_2$NO$_2$P: 530.2052; found: 530.2091.

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**Supporting Information**

Supporting information for this article is available online at [https://doi.org/10.1055/s-0036-1590969](https://doi.org/10.1055/s-0036-1590969).
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