Tetrahedron: *Asymmetry* 21 (2010) 1569–1573

Contents lists available at ScienceDirect

Tetrahedron: *Asymmetry*

journal homepage: www.elsevier.com/locate/tetasy

Studies on the asymmetric, phosphine-promoted [3+2] annulations of allenic esters with 2-aryl-1,1-dicyanoalkenes

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ARTICLE INFO

Article history:
Received 9 March 2010
Accepted 12 April 2010
Available online 2 June 2010

Dedicated to Professor Henri Kagan on the occasion of his 80th birthday

ABSTRACT

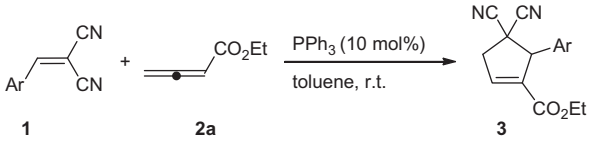
The first enantioselective variant of the phosphine-promoted [3+2] cycloaddition reaction between allenoates and 2-aryl-1,1-dicyanoethylenes has been developed. The use of (*S*)-*t*-butyl-Binepine as the chiral organocatalyst allows the synthesis of functionalized cyclopentenes with both aryl and heteroaryl substituents on the stereogenic carbon, in high yields and ees of up to 95%.

1. Introduction

Trivalent phosphines are known to promote a range of synthetically useful organocatalytic processes based on the activation of unsaturated substrates by the Lewis-basic phosphorus function.[1] Among others, electron-poor allenes have been suitably activated under phosphine catalysis to produce carbo- and heterocycles via their reactions with olefins, aldehydes, imines, etc.[2] Effective chiral catalysts have been developed for some of these reactions,[3] namely [4+2] annulations of allenoates with imines,[4] [3+2] annulations of allenoates, allenones, or allenylphosphonates with either imines,[5] α,β-unsaturated esters, or ketones.[6] Other classes of electron-deficient olefins were shown to be competent substrates for [3+2] annulations with allenoates, however, asymmetric variants of these reactions have not been reported so far. Examples include annulations on α,β-unsaturated α-aminoacid derivatives[7] and amides,[8] tropone,[9] chromones,[10] and acrylonitrile.[11] In this context, the aim of enlarging the scope of enantioselective cyclizations on allenoates prompted us to investigate the use of chiral phosphines as catalysts for [3+2] annulations on a special class of electron-deficient α,β-unsaturated olefins, that is, arylidene malononitriles. This paper reports our recent progresses in addressing this issue.

2. Results and discussion

The phosphine-promoted annulation between allenoates and electron-poor olefins initially disclosed by Lu[11] allows conversion of allenoates into highly functionalized cyclopentenes. A recent variant of this cyclization methodology involves highly activated 1,1-dicyanoolefins as the substrates[12] that are shown to be efficiently converted into the corresponding cyclopentenes **3** by catalytic amounts of triphenylphosphine (Scheme 1).[13]



Scheme 1. Phosphine-catalyzed [3+2] annulations of allenoates with arylidene malononitriles.[13]

The reaction takes place with high yields and good regioselectivity and the method has been conveniently developed into a one-pot, three component procedure starting from aryl aldehydes, malononitrile, and ethyl allenoate. Recently, the same reaction pathway has been demonstrated for reactions involving cumulene derivatives instead of allenes.[14]

The method represents an attractive tool for converting readily available and tunable α,α-dicyanoalkenes into multifunctional cyclopentene synthons. Therefore, enantioselective variant of these organocatalytic cyclization processes is a highly valuable goal, which has stimulated our recent studies.

We initiated our investigations by seeking a suitable chiral phosphine to promote a model [3+2] cyclization, the reaction of ethyl allenoate **2a**, and benzylidenemalononitrile **1a** shown in Table 1.

A variety of chiral phosphines have been surveyed. Most of them are either ineffective catalysts (entries 1–4) or give the expected cyclopentene **3a** in low enantiomeric excess (<30% ee, entries 5–10). However, the chiral P-*t*-butyl-substituted Binepine **4**[15] (entry 11) could catalyze the cyclization process with good conversion rate (61% isolated yield) and comparatively high enantioselectivity (72% ee). The annulation reaction takes place at room temperature and affords a single regioisomer which results from nucleophilic attack of the α-centered anionic form of the phosphine–allenoate adduct, **I**, on the olefinic substrate (Scheme 2).

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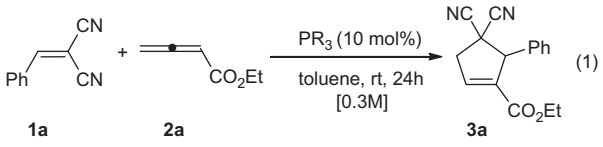
doi:10.1016/j.tetasy.2010.04.014

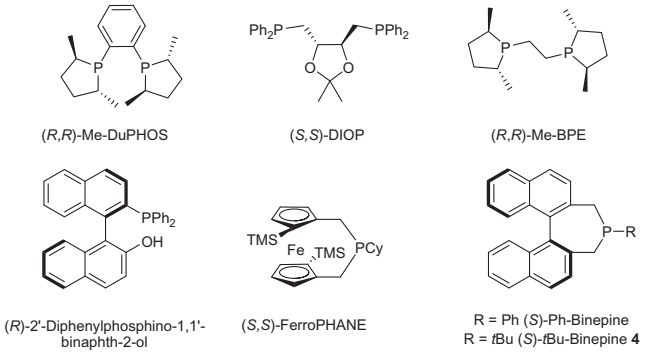
Table 1
Survey of chiral phosphine catalysts[a]



1a 2a 3a

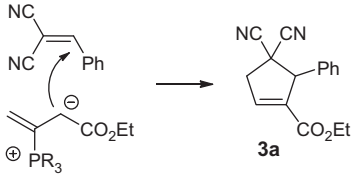
Entry	PR_3 catalyst	Yield[b] (%)	ee[c] (%)
1	(*R*)-BINAP	<10[d]	—
2	(*R*,*R*)-Et-FerroTANE	0	—
3	(*S*)-PHANEPHOS	0	—
4	(*R*)-Monophos	0	—
5	(*R*,*R*)-Me-DuPHOS	70	0
6	(*S*,*S*)-DIOP	48	2
7	(*R*,*R*)-Me-BPE	70	15
8	(*R*)-2′-Diphenylphosphino-1,1′-binaphth-2-ol	77	27
9	(*S*,*S*)-FerroPHANE	36	11
10	(*S*)-Ph-Binepine	23	12
11	(*S*)-*t*Bu-Binepine ((*S*)-**4**)	61	72

[a] Reaction conditions: **1a** (0.15 mmol), **2a** (0.18 mmol), and the phosphine were stirred at room temperature in toluene (0.5 mL) for 24 h.
[b] Isolated yields.
[c] Enantiomeric excesses have been measured by HPLC on a Chiralpak IA column. Yields and ees are an average of two experiments.
[d] Conversion rate.



With (*S*)-**4** as the catalyst, the enantiomeric excess could be increased to 80% for reactions carried out at 0 °C, the yield decreased, however, to 19% for reaction times of 66 h (entry 2 in Table 2). Consistent with this result, heating at 50 °C decreased the enantiomeric excess to 63%, while leading to quantitative conversion into the desired product **3a** (entry 3). Toluene afforded the most suitable reaction medium, in terms of both conversion rates and enantioselectivity, compared to the other solvents screened (acetone, THF, CH_2Cl_2, and MeOH). Finally, the conversion rate could be optimized by performing the cyclization at a 0.1M concentration of the reactants (entry 4 in Table 2), versus a 0.3M concentration applied in initial tests. Thus, in the optimized conditions, the chiral *t*-Bu-Binepine **4** allowed a 93% yield and a 73% ee to be attained in the annulation reaction leading to **3a**.

The above-mentioned results afford additional evidence for the efficiency of (*S*)-**4** as a chiral organocatalyst in [3+2] cyclizations on



Scheme 2. Sense of addition of the zwitterionic phosphine–allenoate adduct on the activated olefin.

Table 2
Optimization of the reaction conditions for the synthesis of **3a** by using (*S*)-**4** as the catalyst[a]

Entry	Solvent	Time (h)	Temp (°C)	Concn (M)	Yield[b] (%)	ee (%)
1	Toluene	24	rt	0.3	61	72
2	Toluene	66	0	0.3	19	80
3	Toluene	6	50	0.3	99	63
4	Toluene	24	rt	0.1	93	73
5	Toluene[c]	24	rt	0.1	57	74
6	CH_2Cl_2	24	rt	0.3	21	37
7	THF	24	rt	0.3	21	58

[a] Conditions: **1a**, 0.15 mmol; **2a**, 0.18 mmol; **4**,10 mol %.
[b] Isolated yields.
[c] Catalyst loading = 5 mol %.

allenoates. The same phosphine had been described previously to furnish high enantiomeric excesses in [3+2] cyclizations between allenoates and either enones[6b] or imines,[16] as well as in [4+2] cyclizations on imines.[4]

To further investigate the scope of the asymmetric cyclization methodology involving Binepine (*S*)-**4** as the catalyst, we examined the possibility of using olefins with either esters or cyano and ester groups as electron-withdrawing functions (Scheme 3).

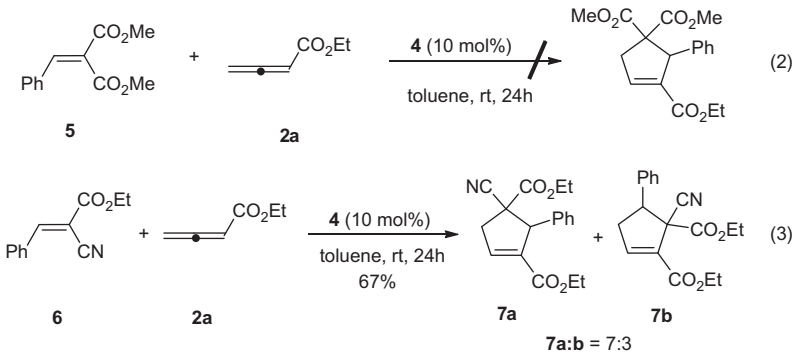
The benzylidene malonate **5** proved to be inert in the conditions mentioned above (Eq. 2) while ethyl *E*-α-cyanocinnamate **6**[17,19c] affords cyclopentene **7** in good yields, as a 7:3 mixture of two isomers (Eq. 3 in Scheme 3). The minor isomer has been assigned as the regioisomeric species **7b**, based on NMR data.[18] The enantiomeric excess of the major isomer proved to be of only 47%.

The low regio- and enantioselectivity make this process unpractical from a synthetic point of view. Therefore, in further studies, we focused our attention on cyclizations between allenoates and 1,1-dicyanoalkenes, promoted only by the chiral phosphepine (*S*)-**4**. We have expanded the scope of these annulations by investigating various 2-aryl-1,1-dicyanoalkenes as the reaction partners. Substrates **1a**–**k** have been prepared in high yields via Knoevenagel condensations of malononitrile with the desired aldehydes, according to published methods.[19] They have been engaged in the reaction with ethyl 2,3-butadienoate in the presence of 10 mol % of (*S*)-*t*-butylphosphepine **4** under the optimized conditions of Table 2 above. Results are displayed in Table 3.

Under this standard set of conditions, phosphepine **4** proved to be an efficient nucleophilic catalyst for the [3+2] cyclizations between ethyl allenoate and dicyanoolefins bearing various β-substituents, including substituted aryls and heteroaromatic groups. Low conversion rates have been noticed only for the *p*-nitrophenyl-substituted olefin (entry 4 in Table 3). Cyclopentenes **3a**–**k** were obtained in good yields and enantiomeric excesses higher than 70% in most cases. Especially high enantiomeric excesses were obtained from olefins with heteroaromatic substituents (entries 7–9 and 11), with the notable exception of the quinolyl-substituted olefin which afforded an ee of only 28% (entry 10). The highest 90% ee could be attained by starting from the 1,1-dicyano-2(2-*N*-methylindolyl)ethene **1k**.

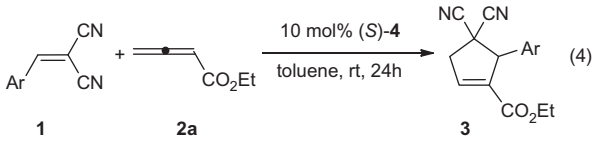
The scope of the reaction seems to be restricted to aryl-substituted olefins, since the attempted use of either 2-styryl- or 2-*sec*-butyl-substituted 1,1-dicyanoethene failed to produce the expected cyclopentenes.

With the aim of improving the method in terms of enantioselectivity, allenes with phenyl, benzyl, cyclohexyl, and *t*-butyl ester functions have been screened in the reaction with arylidene malononitrile. These variations of the allenic partners mostly did not significantly change the enantioselectivity levels. However, a notable exception is the reaction of 2-(2-thienyl)-1,1-dicyanoethylene shown in Scheme 4. In this case, the enantiomeric excess could be increased from 81% to 88% by using cyclohexyl 2,3-butadienoate **2b** as the reaction partner.



Scheme 3. Attempted [3+2] cyclizations on other electron-poor olefins.

Table 3
Synthesis of functionalized cyclopentenes through asymmetric cyclizations on arylidene malononitriles catalyzed by (*S*)-**4**[a]



Entry	Substrate	Ar	Product	Yield (%)	ee (%)
1	**1a**	Ph	**3a**	93	73
2	**1b**	*p*-$MeOC_6H_4$	**3b**	95	65
3	**1c**	*p*-ClC_6H_4	**3c**	99	74
4	**1d**	*p*-$NO_2C_6H_4$	**3d**	38[b]	74
5	**1e**	1-Naphthyl	**3e**	73	74
6	**1f**	2-Naphthyl	**3f**	75	70
7	**1g**	2-Furyl	**3g**	99	83
8	**1h**	2-Thiophenyl	**3h**	96	81
9	**1i**	2-Pyridyl	**3i**	77	82
10	**1j**	2-Quinolinyl	**3j**	86	28
11	**1k**	2-*N*-Methylindolyl	**3k**	77	90[c]

[a] **2a**:**1** ratio = 1.2:1. Substrate concentration = 0.1 M. All data are the average of two experiments. Enantiomeric excesses have been measured by HPLC in the conditions given in Section 4.
[b] After 48 h at rt, substrate concentration = 0.05 M.
[c] The ee could be increased to 94% by crystallization from $CHCl_3$.

For highly reactive substrates, the enantiomeric excess could be improved to some extent, while retaining a good conversion rate, by decreasing the reaction temperature to 0 °C. This is shown for instance in Eq. 6 in Scheme 4: a 95% ee could be attained in the annulation between ethyl 2,3-butadienoate and the 2-*N*-methylindolyl-substituted olefin **1k**. A sample of **3k** with 99% ee could be obtained by crystallization from chloroform.

The two examples in Scheme 4 demonstrate that, for selected substrates, the annulations between allenoates and 1,1-dicyanoolefins can be turned into synthetically useful enantioselective methods by fine tuning and optimization of the reaction parameters.

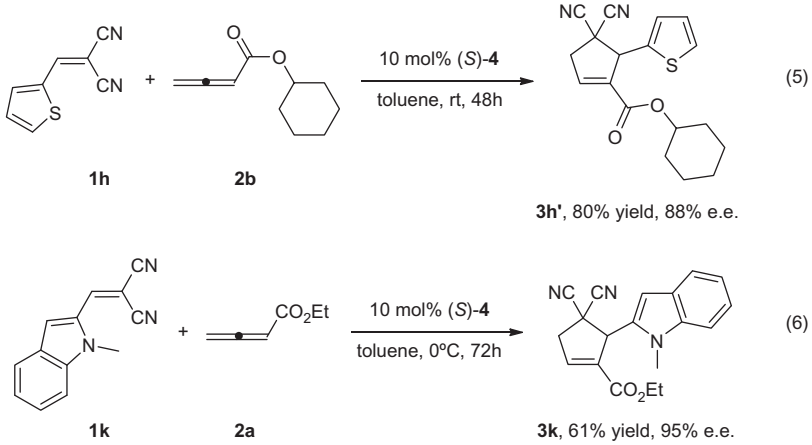
3. Conclusion

In conclusion, this work expands the currently limited range of enantioselective processes catalyzed by chiral phosphorus nucleophiles. It provides a convenient access to enantiomerically enriched aryl-substituted dicyanocyclopentenes via [3+2] annulations between allenoates and dicyanoolefins. High yielding, regioselective, and highly enantioselective procedures have been established by taking advantage of *t*-Bu-Binepine (*S*)-**4** as the chiral organocatalyst. These results thus complement previous studies on the use of **4** as a nucleophilic catalyst in [3+2] cyclization reactions.

4. Experimental

4.1. General remarks

All solvents were degassed under argon before use. All reactions were monitored by thin-layer chromatography (TLC) carried out on Merck Kiesegel 60 F_{254} plates, using UV light (254 nm) as a visualizing agent and $KMnO_4$ stain and heat as developing agent. Column chromatography was carried out on Merck silica gel Si60



Scheme 4. Optimized conditions for annulations reactions on **1h** and **1k**.

(40–63 μm). NMR spectra were recorded on Bruker AV500 or AV300 spectrometers, calibrated using residual undeuterated solvent as an internal reference. Chemical shifts are given in ppm. High resolution mass spectra (HRMS ESI$^+$) were recorded on LCT Waters equipment. IR spectra were recorded neat on a Perkin–Elmer FT-IR spectrophotometer. Melting points (mp) are uncorrected and recorded on a Buchi B-540 melting point apparatus. Optical rotations were determined with a JASCO P-1010 polarimeter. HPLC was performed at a column temperature of 30 °C on a Waters 2695 Separations Module equipped with a diode array UV detector. 2-Arylidenemalononitriles **1a**–**k** were prepared through phosphine- or potassium hydroxide-catalyzed Knoevenagel condensation of the corresponding aldehyde and malononitrile, according to the literature.[19] (*S*)-*t*-Bu-Binepine (*S*)-**4** was prepared according to Beller's procedure.[20] (*S*,*S*)-[Cy]-TMS-FerroPHANE was prepared according to our previous work.[6e]

4.2. General procedure for the synthesis of 3

To a solution of 2-arylidenemalononitrile **1** (0.15 mmol, 1 equiv) in degassed toluene (1.5 mL) were added ethyl 2,3-butadienoate **2a** (21 μL, 0.18 mmol, 1.2 equiv) and then the phosphine catalyst (10 mol %). The reaction vessel was purged with argon, and the reaction mixture was stirred at room temperature for 24 h. The solvent was evaporated then under reduced pressure and the crude mixture was purified by column chromatography on silica gel (heptane/AcOEt gradient from 100/0 to 70/30) to give the desired compound **3** as a single regioisomer.

4.2.1. Ethyl 4,4-dicyano-5-phenylcyclopent-1-ene-1-carboxylate 3a[13]

Yield: 93%. White solid (mp 82–83 °C), R_f 0.40 (Hept/AcOEt 70/30). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.40–7.34 (m, 3H), 7.22–7.17 (m, 2H), 6.94 (br s, 1H), 4.76 (br s, 1H), 4.14–4.03 (m, 2H), 3.37 (br s, 2H), 1.12 (t, J = 7.3 Hz, 3H). HRMS (ESI$^+$) m/z: calcd for $C_{16}H_{14}N_2NaO_2$ [M+Na]$^+$: 289.0953; found: 289.0959. HPLC (Chiralpak IA, heptane/*i*PrOH 92/8, 1 mL/min): t_r (minor) = 11.4 min; t_r (major) = 12.7 min. $[\alpha]_D^{25} = +153$ (c 0.95, $CHCl_3$, 73% ee).

4.2.2. Ethyl 4,4-dicyano-5-(4-methoxyphenyl)cyclopent-1-ene-1-carboxylate 3b[13]

Yield: 95%. Yellow oil. R_f 0.30 (heptane/AcOEt 70/30). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.11 (d, J = 8.6 Hz, 2H), 6.94–6.87 (m, 3H), 4.74 (br s, 1H), 4.15–4.05 (m, 2H), 3.79 (s, 3H), 3.36 (br s, 2H), 1.16 (t, J = 7.4 Hz, 3H). HRMS (ESI$^+$) m/z: calcd for $C_{17}H_{16}N_2NaO_3$ [M+Na]$^+$: 319.1059; found: 319.1068. HPLC (Chiralpak IA, heptane/*i*PrOH 92/8, 1 mL/min): t_r (minor) = 15.5 min; t_r (major) = 17.9 min. $[\alpha]_D^{24} = +148$ (c 0.92, $CHCl_3$, 65% ee).

4.2.3. Ethyl 5-(4-chlorophenyl)-4,4-dicyanocyclopent-1-ene-1-carboxylate 3c[13]

Yield: 99%. White solid (mp 102–103 °C). R_f 0.37 (heptane/AcOEt 70/30). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.42 (d, J = 8.5 Hz, 2H), 7.18 (d, J = 8.5 Hz, 2H), 7.00 (br s, 1H), 4.79 (br s, 1H), 4.21–4.10 (m, 2H), 3.46 (dd, J_{AB} = 18.5, J = 2.8 Hz, 1H), 3.40 (dd, J = 18.5 Hz, 1H), 1.19 (t, J = 7.2 Hz, 3H). HRMS (ESI$^+$) m/z: calcd for $C_{16}H_{13}ClN_2NaO_2$ [M+Na]$^+$: 323.0563; found: 323.0571. HPLC (Chiralpak IA, heptane/*i*PrOH 92/8, 1 mL/min): t_r (minor) = 12.8 min; t_r (major) = 13.9 min. $[\alpha]_D^{25} = +151$ (c 1.07, $CHCl_3$ 74% ee).

4.2.4. Ethyl 4,4-dicyano-5-(4-nitrophenyl)cyclopent-1-ene-1-carboxylate 3d

Yield: 38%. Orange oil. R_f 0.24 (heptane/AcOEt 70/30). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 8.26 (d, J = 8.2 Hz, 2H), 7.40 (d, J = 8.2 Hz, 2H), 7.02 (br s, 1H), 4.86 (br s, 1H), 4.17–4.05 (m, 2H), 3.48 (br d, J_{AB} = 18.6 Hz, 1H), 3.42 (br d, J_{AB} = 18.6 Hz, 1H), 1.15 (t, J = 7.2 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 161.6 (C), 148.7 (C), 141.2 (C), 139.3 (CH), 136.7 (C), 129.3 (CH), 124.7 (CH), 115.9 (C), 113.1 (C), 61.8 (CH_2), 59.8 (CH), 44.1 (CH_2), 39.9 (C), 14.1 (CH_3). IR (neat) (ν, cm^{-1}): 694, 737, 828, 847, 1013, 1099, 1246, 1346, 1520, 1606, 1712, 2248, 2932, 3096. HRMS (ESI$^-$) m/z: calcd for $C_{16}H_{12}N_3O_4$ [M−H]$^+$: 310.0828; found: 310.0843. HPLC (Chiralpak IA, heptane/*i*PrOH 90/10, 1 mL/min): t_r (minor) = 24.6 min; t_r (major) = 34.0 min. $[\alpha]_D^{25} = +151$ (c 1.29, $CHCl_3$, 74% ee).

4.2.5. Ethyl 4,4-dicyano-5-(naphthalen-1-yl)cyclopent-1-ene-1-carboxylate 3e[13]

Yield: 73%. Pale yellow solid (mp 85–86 °C). R_f 0.33 (heptane/AcOEt 70/30). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 8.14 (d, J = 8.5 Hz, 1H), 7.91 (d, J = 7.5 Hz, 1H), 7.88 (d, J = 8.0 Hz, 1H), 7.68 (t, J = 7.0 Hz, 1H), 7.57 (t, J = 7.5 Hz, 1H), 7.41 (t, J = 7.5 Hz, 1H), 7.17 (d, J = 7.0 Hz, 1H), 7.05 (br s, 1H), 5.70 (br s, 1H), 4.12–4.01 (m, 2H), 3.54 (dt, J = 18.2; 3.0 Hz, 1H), 3.46 (dm, J = 18.2 Hz, 1H), 1.05 (t, J = 7.1 Hz, 3H). HRMS (ESI$^+$) m/z: calcd for $C_{20}H_{16}N_2NaO_2$ [M+Na]$^+$: 339.1109. Found: 339.1125. HPLC (Chiralpak IA, heptane/*i*PrOH 95/5, 1 mL/min): t_r (minor) = 14.3 min; t_r (major) = 15.9 min. $[\alpha]_D^{24} = +58$ (c 1.07, $CHCl_3$, 74% ee).

4.2.6. Ethyl 4,4-dicyano-5-(naphthalen-2-yl)cyclopent-1-ene-1-carboxylate 3f

Yield: 75%. White solid (mp 122–123 °C). R_f 0.35 (heptane/AcOEt 70/30). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.86 (d, J = 8.6 Hz, 1H), 7.84–7.77 (m, 2H), 7.66 (br s, 1H), 7.53–7.44 (m, 2H), 7.27 (dd, J = 8.4; 1.8 Hz, 1H), 7.02–6.97 (m, 1H), 4.94 (br s, 1H), 4.08 (q, J = 7.1 Hz, 2H), 3.44–3.39 (m, 2H), 1.08 (t, J = 7.1 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 162.1 (C), 138.1 (CH), 137.5 (C), 133.7 (C), 133.3 (C), 131.2 (C), 129.4 (CH), 128.2 (CH), 127.9 (CH), 127.4 (CH), 126.9 (CH), 126.7 (CH), 125.2 (CH), 116.7 (C), 113.4 (C), 61.3 (CH_2), 60.3 (CH), 43.8 (CH_2), 40.1 (C), 13.9 (CH_3). IR (neat) (ν, cm^{-1}): 720, 744, 795, 824, 856, 1018, 1088, 1207, 1237, 1337, 1370, 1632, 1709, 2247, 2926. HRMS (ESI$^+$) m/z: calcd for $C_{20}H_{16}N_2NaO_2$ [M+Na]$^+$: 339.1109; found: 339.1122. HPLC (Chiralpak IA, heptane/*i*PrOH 95/5, 1 mL/min): t_r (minor) = 20.8 min; t_r (major) = 26.9 min. $[\alpha]_D^{24} = +183$ (c 1.05, $CHCl_3$, 70% ee).

4.2.7. Ethyl 4,4-dicyano-5-(furan-2-yl)cyclopent-1-ene-1-carboxylate 3g[13]

Yield: 99%. Orange oil. R_f 0.28 (heptane/AcOEt 70/30). ^{1}H NMR (500 MHz, $CDCl_3$) δ:7.45 (br s, 1H), 6.95 (br s, 1H), 6.41 (br s, 2H), 4.93 (br s, 1H), 4.28–4.13 (m, 2H), 3.54 (br d, J = 18.0 Hz, 1H), 3.40 (dd, J = 18.0; 3.0 Hz, 1H), 1.26 (t, J = 7.2 Hz, 3H). HRMS (ESI$^+$) m/z: calcd for $C_{14}H_{12}N_2NaO_3$ [M+Na]$^+$: 279.0746; found: 279.0765. HPLC (Chiralpak IA, heptane/*i*PrOH 95/5, 1 mL/min): t_r (minor) = 13.2 - min; t_r (major) = 15.2 min. $[\alpha]_D^{25} = +177$ (c 0.61, $CHCl_3$, 83% ee).

4.2.8. Ethyl 4,4-dicyano-5-(thiophen-2-yl)cyclopent-1-ene-1-carboxylate 3h

Yield: 96%. White solid (mp 66–67 °C). R_f 0.28 (heptane/AcOEt 70/30). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.33–7.28 (m, 1H), 7.07–7.02 (m, 2H), 6.93–6.90 (m, 1H), 5.06 (br s, 1H), 4.25–4.06 (m, 2H), 3.46 (dt, J = 18.3; 2.0 Hz, 1H), 3.36 (dd, J = 18.3; 3.0 Hz, 1H), 1.19 (t, J = 7.1 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 161.8 (C), 138.0 (C), 137.9 (CH), 136.2 (C), 128.1 (CH), 127.9 (CH), 126.9 (CH), 116.4 (C), 113.0 (C), 61.5 (CH_2), 54.9 (CH), 43.1 (CH_2), 40.5 (C), 14.1 (CH_3). IR (neat) (ν, cm^{-1}): 716, 791, 858, 1020, 1097, 1199, 1247, 1336, 1371, 1432, 1631, 1700, 2252, 2923, 3107. HRMS (ESI$^+$) m/z: calcd for $C_{14}H_{12}N_2NaO_2S$ [M+Na]$^+$: 295.0517. Found: 295.0522. HPLC (Chiralpak IA, heptane/*i*PrOH 80/20, 1 mL/min): t_r (minor) = 36.7 min; t_r (major) = 44.2 min. $[\alpha]_D^{25} = +204$ (c 0.93, $CHCl_3$, 81% ee).

4.2.9. Cyclohexyl 4,4-dicyano-5-(thiophen-2-yl)cyclo-pent-1-ene-1-carboxylate 3h′

Yield: 80%. Yellow solid (mp 76–77 °C). R_f 0.49 (heptane/AcOEt 70/30). ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 7.35–7.30 (m, 1H), 7.08–7.05 (m, 2H), 6.96–6.92 (m, 1H), 5.09–5.06 (br s, 1H), 4.85–4.75 (m, 1H), 3.47 (dt, J = 18.3; 2.1 Hz, 1H), 3.38 (dd, J = 18.3; 3.0 Hz, 1H), 1.83–1.21 (m, 10H). ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): 161.3 (C), 138.4 (C), 137.8 (CH), 136.5 (C), 128.1 (CH), 127.9 (CH), 126.8 (CH), 116.5 (C), 113.1 (C), 73.8 (CH), 55.1 (CH), 43.2 (CH_2), 40.5 (C), 31.4 (CH_2), 31.1 (CH_2), 25.3 (CH_2), 23.3 (CH_2), 23.1 (CH_2). IR (neat) (ν, cm^{-1}): 715, 726, 791, 934, 979, 1007, 1101, 1198, 1257, 1271, 1322, 1428, 1451, 1636, 1709, 2252, 2857, 2944. HRMS (ESI^+) m/z: calcd for $C_{18}H_{18}N_2O_2NaS$ $[M+Na]^+$: 349.0987; found: 349.0999. HPLC (Chiracel IC, heptane/EtOH 98/2, 1 mL/min): t_r (minor) = 20.1 min; t_r (major) = 21.2 min. $[\alpha]_D^{25} = +155$ (c 1.06, $CHCl_3$, 88% ee).

4.2.10. Ethyl 4,4-dicyano-5-(pyridin-2-yl)cyclopent-1-ene-1-carboxylate 3i[13]

Yield: 77%. Orange oil. R_f 0.21 (heptane/AcOEt 50/50). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 8.64 (d, J = 5.0 Hz, 1H), 8.51 (s, 1H), 7.53 (d, J = 8.0 Hz, 1H), 7.35 (dd, J = 8.0; 5.0 Hz, 1H), 7.00 (br s, 1H), 4.79 (br s, 1H), 4.17–4.04 (m, 2H), 3.46 (br d, J = 18.3 Hz, 1H), 3.40 (br d, J = 18.3 Hz, 1H), 1.14 (t, J = 7.2 Hz, 3H). HRMS (ESI^+) m/z: calcd for $C_{15}H_{14}N_3O_2$ $[M+H]^+$: 268.1086; found: 268.1086. HPLC (Chiralpak IC, heptane/EtOH 85/15, 1 mL/min): t_r (major) = 17.9 min; t_r (minor) = 59.0 min. $[\alpha]_D^{25} = +147$ (c 0.42, $CHCl_3$, 82% ee).

4.2.11. Ethyl 4,4-dicyano-5-(quinolin-2-yl)cyclopent-1-ene-1-carboxylate 3j

Yield: 86%. Orange solid (mp 103–105 °C). R_f 0.23 (heptane/AcOEt 70/30). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 8.17 (d, J = 8.4 Hz, 1H), 7.97 (br d, J = 8.7 Hz, 1H), 7.79 (br d, J = 8.1 Hz, 1H), 7.68 (ddd, J = 8.5; 7.0; 1.4 Hz, 1H), 7.52 (ddd, J = 8.1; 7.0; 1.1 Hz, 1H), 7.45 (d, J = 8.4 Hz, 1H), 6.97–6.94 (m, 1H), 4.96 (br s, 1H), 4.18–4.02 (m, 2H), 3.97 (dt, J = 17.7; 3.0 Hz, 1H), 3.44 (dd, J = 17.7, 3.0 Hz, 1H), 1.16 (t, J = 7.1 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 162.5 (C), 155.3 (C), 148.1 (C), 138.9 (CH), 137.7 (C), 137.4 (CH), 130.1 (CH), 129.7 (CH), 128.0 (C), 127.9 (CH), 127.3 (CH), 121.4 (CH), 117.2 (C), 113.8 (C), 61.4 (CH_2), 61.2 (CH), 45.2 (CH_2), 39.2 (C), 14.2 (CH_3). IR (neat) (ν, cm^{-1}): 724, 752, 784, 809, 834, 919, 990, 1009, 1027, 1099, 1206, 1244, 1338, 1371, 1418, 1503, 1592, 1635, 1699, 2255, 2924. HRMS (ESI^+) m/z: calcd for $C_{19}H_{16}N_3O_2$ $[M+H]^+$: 318.1243; found: 318.1245. HPLC (Chiralpak IA, heptane/iPrOH 95/5, 1 mL/min): t_r (minor) = 16.0 min; t_r (major) = 19.3 min. $[\alpha]_D^{25} = +44$ (c 1.05, $CHCl_3$, 28% ee).

4.2.12. Ethyl 4,4-dicyano-5-(1-methyl-1*H*-indol-2-yl)cyclopent-1-ene-1-carboxylate 3k

Yield: 77%. White solid (mp 161–162 °C). R_f 0.28 (heptane/AcOEt 70/30). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.52 (dm, J = 7.8 Hz, 1H), 7.34 (dd, J = 8.1; 0.6 Hz, 1H), 7.27–7.20 (m, 1H), 7.09 (ddd, J = 8.0; 7.1; 1.1 Hz, 1H), 6.96–6.93 (m, 1H), 6.30 (br s, 1H), 5.07 (s, 1H), 4.21–4.05 (m, 2H), 3.88 (s, 3H), 3.48 (dt, J = 18.0; 2.1 Hz, 1H), 3.35 (dd, J = 18.0; 3.0 Hz, 1H), 1.19 (t, J = 7.1 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 161.9 (C), 138.8 (C), 137.8 (CH), 136.7 (C), 131.5 (C), 127.1 (C), 122.9 (CH), 121.1 (CH), 120.3 (CH), 116.6 (C), 113.1 (C), 109.9 (CH), 102.0 (CH), 61.7 (CH_2), 52.1 (CH), 43.4 (CH_2), 38.7 (C), 30.4 (CH_3), 14.2 (CH_3). IR (neat) (ν, cm^{-1}): 900, 997, 1022, 1091, 1170, 1203, 1249, 1320, 1339, 1465, 1631, 1704, 2359, 2927. HRMS (ESI^+) m/z: calcd for $C_{19}H_{18}N_3O_2$ $[M+H]^+$: 320.1399; found: 320.1413. HPLC (Chiralpak IA, heptane/iPrOH 98/2, 1 mL/min): t_r (minor) = 27.9 - min; t_r (major) = 30.0 min. $[\alpha]_D^{25} = +272$ (c 0.87, $CHCl_3$, 99% ee (after crystallization in $CHCl_3$).

4.2.13. Diethyl 1-cyano-2-phenylcyclopent-3-ene-1,3-dicarboxylate 7a

Yield: 67%. Colorless oil. R_f 0.43 (Hept/AcOEt 70/30). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.38–7.27 (m, 3H), 7.19 (d, J = 7.0 Hz, 2H), 6.89 (br s, 1H), 4.70 (br s, 1H), 4.37–4.27 (m, 2H), 4.12–3.98 (m, 2H), 3.40 (dd, ^2J = 18.5 Hz, ^3J = 2.7 Hz, 1H), 3.19 (dt, ^2J = 18.5; $^3J = {}^4J$ = 2.4 Hz, 1H), 1.35 (t, J = 7.2 Hz, 3H), 1.09 (t, J = 7.3 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 168.4 (C), 163.1 (C), 148.4 (C), 139.9 (CH), 136.9 (C), 129.0 (CH), 128.7 (CH), 128.2 (CH), 117.8 (C), 63.8 (CH_2), 60.9 (CH_2), 58.7 (CH), 53.6 (C), 42.3 (CH_2), 14.2 (CH_3), 14.1 (CH_3). IR (neat) (ν, cm^{-1}): 699, 1023, 1055, 1240, 1260, 1331, 1710, 1742, 2247, 2982. HRMS (ESI^+) m/z: calcd for $C_{18}H_{19}NNaO_4$ $[M+Na]^+$: 336.1212; found: 336.1222. HPLC (Chiralpak IC, heptane/EtOH 95/5, 1mL/min): t_r (major) = 13.6 min; t_r (major) = 15.7 min (47% ee).

Acknowledgments

Authors warmly thank the Agence Nationale de la Recherche (ANR) for financial support to M.S. and the COST PhoSciNet Action for supporting research on phosphine organocatalysis.

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