A Convenient Approach to Enantioenriched Cyclopropanes Bearing Electron-Withdrawing Functionalities

Henryk Krawczyk,* Katarzyna Wąsek, Jacek Kędzia

Institute of Organic Chemistry, Technical University of Łódź, Żeromskiego 116, 90-924 Łódź, Poland
Fax +48(42)6365530; E-mail: henkrawc@p.lodz.pl

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Abstract: 1,2-Disubstituted cyclopropanes with different electron-withdrawing groups were accessed stereospecifically from similarly functionalized γ-hydroxy-α,β-unsaturated compounds.

Key words: cyclopropanation, intramolecular nucleophilic substitution, chiral allylic alcohols, stereoselective synthesis

Cyclopropane ring is a basic structural element in a wide range of biologically active natural products and their unnatural analogues.[1] With the offer of versatility both as intermediates, and as building blocks within organic synthesis,[2] the development of efficient methods to access these strained subunits is considered to be of significant importance. In recent years substantial synthetic effort has been focused on enantioselective synthesis of cyclopropanes.[3]

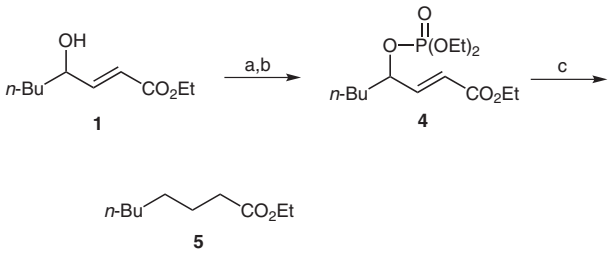
Although base-promoted intramolecular S_N2 substitution reaction of γ-haloalkanoates and their analogues with different leaving groups constitutes one of the simplest routes to the appropriate cyclopropane derivatives, it has not attracted much attention up to date.[4] On the other hand, this type of ring closure is a crucial step in a couple of more complex but commonly applied cyclopropanation reactions. For example, sequential conjugate addition of nucleophiles to γ-halo-α,β-unsaturated esters followed by the S_N2 intramolecular alkylation of the resulting adducts (MIRC) easily provides appropriate cyclopropanecarboxylates.[5] Homologous Horner–Wadsworth–Emmons (HWE) reaction of phosphonoacetate anions with epoxides leading to the same carboxylates involves similar ring forming process of γ-phosphoryloxyalkanoate intermediates.[6] Some time ago we demonstrated that these particular intermediates are easily produced and converted to the cyclopropane products by base-catalyzed ethanolysis of α-phosphono-γ-lactones.[7]

Guided by the presented knowledge, we envisioned that the reaction sequence consisting in enantioselective preparation of γ-hydroxyalkanoates followed by transformation of their hydroxy functionality in a good leaving group and further intramolecular S_N2 substitution reaction of the resulting alkanoate enolates would allow the enantiospecific synthesis of substituted cyclopropanecarboxylates.

We have recently described a method for the preparation of various γ-hydroxy-α,β-unsaturated compounds by HWE reaction of α-hydroxy aldehydes with differently activated methylphosphonates.[8] We have also found that this particular method can be easily used for the synthesis of enantiomerically enriched γ-hydroxy-α,β-unsaturated octenoates **1**, octenenitriles **2**, and heptenylphosphonates **3**. The latter approach required use of α-hydroxyhexanal of high optical purity as the starting material. Both enantiomeric α-hydroxyhexanals were obtained by asymmetric Sharpless dihydroxylation of (*E*)-hex-1-enyl methanesulfonate.

Outlined in this paper is the development of a highly efficient and general method for the transformation of enantioenriched compounds **1**, **2**, and **3** into the corresponding *trans*-2-*n*-butylcyclopropanecarboxylates **12**, cyclopropanenitriles **13**, and cyclopropanephosphonates **14** respectively, in a diastereoselective manner.

The requisite enatioenriched γ-hydroxy-α,β-unsaturated esters **1**, nitriles **2**, and phosphonates **3** were obtained according to the previously reported procedure.[8] The transformation of γ-hydroxyoctenoates **1** into γ-diethoxyphosphoryloxyoctanoates **9** was examined initially, however, routine phosphorylation of the hydroxyl group in esters **1** with diethyl chlorophosphate failed to yield the desired product. Nevertheless, we found that treatment of γ-hydroxyoctenoates **1** with diethyl chlorophosphite, followed by oxidation of the resulting phosphites with nitrogen dioxide in a one-pot process, gave rise to the desired γ-phosphoryloxyoctenoates **4** in good overall yield (Scheme 1).



Scheme 1 *Reagents and conditions*: (a) Et_3N (1.1 equiv), $(EtO)_2PCl$ (1 equiv), CH_2Cl_2, 0 °C, then r.t., 2 h; (b) 2 M N_2O_4 in CH_2Cl_2 (2 equiv), 0 °C, 20 h, 85%; (c) EtOH, 10% Pd/C (cat.), H_2, r.t., 3 h, 95%.

Subsequent catalytic hydrogenation of the unsaturated esters **4** did not provide the expected γ-phosphoryloxyoctanoates **9**, instead, ethyl octanoate (**5**) was isolated as the

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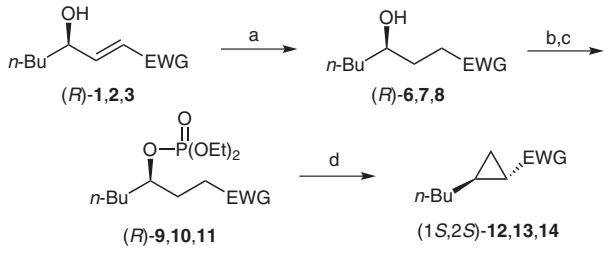
sole product. This, somewhat unexpected result can be explained by envisaging the reductive elimination of a phosphoryloxy group from the unsaturated ester **4** to afford the observed saturated ester **5**. Despite this unexpected result, the desired γ-phosphoryloxy saturated compounds **9**, **10**, and **11** were prepared from the γ-hydroxy-α,β-unsaturated compounds **1**, **2**, and **3** via catalytic hydrogenation of the C=C bond, followed by phosphorylation of the saturated alcohols **6**, **7**, and **8** using the protocol already described for the synthesis of γ-phosphoryloxy-α,β-unsaturated esters **4** (Scheme 2 and Scheme 3).

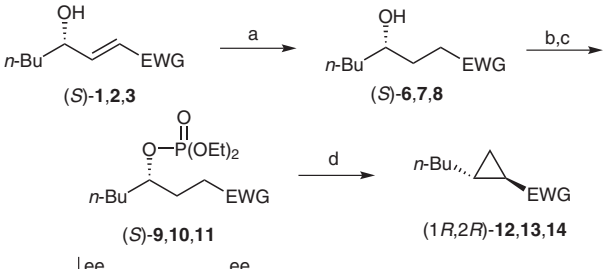


	ee		ee
(*R*)-**1**	91[a]	(1*S*,2*S*)-**12**	90[a]
(*R*)-**2**	91[a]	(1*S*,2*S*)-**13**	90[a]
(*R*)-**3**	86[b]	(1*S*,2*S*)-**14**	89[a]

1, **6**, **9**, **12** EWG = CO_2Et
2, **7**, **10**, **13** EWG = CN
3, **8**, **11**, **14** EWG = $P(O)(OEt)_2$

[a] ee determined by GC
[b] ee determined by ^1H NMR

Scheme 2 *Reagents and conditions*: (a) EtOH, 10% Pd/C (cat.), H_2, 3 h; (b) Et_3N (1.1 equiv), $(EtO)_2PCl$ (1 equiv), CH_2Cl_2, 0 °C, then r.t., 2 h; (c) 2 M N_2O_4 in CH_2Cl_2, 0 °C, then r.t., 20 h; (d) NaH (1 equiv), THF, reflux, 5 h or LDA (1 equiv), THF, r.t., 20 h.



	ee		ee
(*S*)-**1**	82[a]	(1*R*,2*R*)-**12**	80[a]
(*S*)-**2**	82[a]	(1*R*,2*R*)-**13**	80[a]
(*S*)-**3**	76[b]	(1*R*,2*R*)-**14**	79[a]

1, **6**, **9**, **12** EWG = CO_2Et
2, **7**, **10**, **13** EWG = CN
3, **8**, **11**, **14** EWG = $P(O)(OEt)_2$

[a] ee determined by GC
[b] ee determined by ^1H NMR

Scheme 3 *Reagents and conditions*: (a) EtOH, 10% Pd/C (cat.), H_2, 3 h; (b) Et_3N (1.1 equiv), $(EtO)_2PCl$ (1 equiv), CH_2Cl_2, 0 °C, then r.t., 2 h; (c) 2 M N_2O_4 in CH_2Cl_2, 0 °C, then r.t., 20 h; (d) NaH (1 equiv), THF, reflux, 5 h or LDA (1 equiv), THF, r.t., 20 h.

With phosphates **9**, **10** and **11** in hand**,** the applicability of these substrates in the intramolecular ring closure reaction was investigated**.** Thus, treatment of γ-phosphoryloxyesters (*R*)-**9** and (*S*)-**9** with sodium hydride in THF at reflux led to the expected cyclopropanecarboxylates (1*S*,2*S*)-**12**, and (1*R*,2*R*)-**12** respectively. In addition to this, reaction of nitriles (*R*)-**10** and (*S*)-**10**, as well as phosphates (*R*)- **11** and (*S*)-**11** with LDA resulted in an efficient cyclization at room temperature to afford cyclopropanenitriles (1*S*,2*S*)-**13** and (1*R*,2*R*)-**13**, and cyclopropanephosphonates (1*S*,2*S*)-**14** and (1*R*,2*R*)-**14**, respectively. In all the cases, the ring closure occurred in completely diastereoselective manner giving 1,2-disubstituted cyclopropanes as single diastereoisomers. The *trans* stereochemistry of the cyclopropanecarboxylates **12** obtained was confirmed by ^1H and ^{13}C NMR data and was in agreement with the results of our previous investigations.[7] The relative stereochemistry of the cyclopropanephosphonates **14** was established by ^1H NMR analysis. The observed value of coupling constant $^3J_{P,H\text{-}2} = 15.7$ Hz clearly proved the *trans* arrangement of the phosphoryl and butyl groups.[9] Unfortunately, the spectra of cyclopropenenitriles **13** could not be interpreted so unequivocally. Therefore, taking into account analogous method of preparation and structural similarity, we assigned *trans* stereochemistry to these compounds.

Chiral gas chromatography analysis revealed that the transformation of optically active γ-hydroxy-α,β-unsaturated compounds **1**, **2**, and **3** into the corresponding cyclopropanes **12**, **13**, and **14**, respectively, proceeded without change of the enantiopurity. Hydrolysis of (+)-*trans*-cyclopropenecarboxylate derived from ester (*R*)-**1** gave the known (1*S*,2*S*)-2-*n*-butylcyclopropenecarboxylic acid.[10] Thus, the *S*-absolute configuration of alkyl substituted stereogenic center in cyclopropanecarboxylate (1*S*,2*S*)-**12** although apparent from stereospecific S_N2 attack of the enolate could be confirmed by stereochemical correlation. Therefore, the cyclization of phosphoryloxyoctanoate (*S*)-**9** undoubtedly leads to (1*R*,2*R*)-**12** enantiomer. As a consequence of this, the absolute configurations of the cyclopropanes obtained from nitrile (*R*)-**10** and phosphonate (*R*)-**11** was assigned to be (1*S*,2*S*)-**13** and (1*S*,2*S*)-**14**, respectively. The cyclopropanes obtained from nitrile (*S*)-**10** and phosphonate (*S*)-**11** must be (1*R*,2*R*)-**14** and (1*R*,2*R*)-**15** isomers.

In summary, our studies have clearly demonstrated the potential of a synthetic strategy that employs various enantioenriched γ-hydroxy-α,β-unsaturated compounds for efficient enantiospecific synthesis of substituted cyclopropanes bearing the same electron-withdrawing group. We believe that broad access to highly enantioenriched starting materials of this type will be useful in the synthesis of a wide range of structurally and biologically interesting substituted cyclopropanes.

NMR spectra were recorded on a Bruker DPX 250 instrument at 250.13 MHz for ^1H and 62.9 MHz for ^{13}C and 101.3 MHz for ^{31}P NMR, respectively, using tetramethylsilane as internal and 85% H_3PO_4 as external standard. The multiplicities of carbons were determined by DEPT experiments. IR spectra were measured on a Specord M80 (Zeiss) instrument. Gas chromatographic analyses were obtained on a Hewlett-Packard 5890 II instrument equipped with γ-Dex 225 column. Elemental analyses were performed on a Perkin-Elmer PE 2400 analyzer.

Alcohols 6, 7, and 8; General Procedure

A corresponding olefin **1**, **2**, or **3** (5.0 mmol) was added to a stirred suspension of 10% Pd/C in EtOH (5 mL). The stirring was continued under H_2 atmosphere for 3 h. Then, the catalyst was filtered off

and the filtrate was concentrated under vacuum to give the crude product, which was used in the next step.

Ethyl 4-Hydroxyoctanoate (6)
Yield; 95%; colorless oil.

IR (film): 1748 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 0.87 (t, *J* = 6.7 Hz, 3 H, CH_3), 1.22 (t, *J* = 7.0 Hz, 3 H, CH_3CH_2O), 1.27–1.40 (m, 4 H, 2 × CH_2), 1.45–1.70 (m, 2 H, CH_2), 1.80–2.04 (m, 3 H, CH_2, OH), 2.25 (t, *J* = 7.2 Hz, 2 H, CH_2), 4.10 (q, *J* = 7.0 Hz, 2 H, CH_3CH_2O), 4.15–4.26 (m, 1 H, CH).

^{13}C NMR ($CDCl_3$): δ = 13.87 (CH_3), 14.08 (CH_3CH$_2$O), 22.12 (CH_2), 23.89 (CH_2), 28.15 (CH_2), 29.00 (CH_2), 32.69 (CH_2), 60.22 (CH_3CH_2O), 69.40 (CH), 172.93 (C=O),

4-Hydroxyoctanenitrile (7)[11]
Yield: 95%; colorless oil.

^1H NMR ($CDCl_3$): δ = 0.90 (t, *J* = 7.0 Hz, 3 H, CH_3), 1.22–1.48 (m, 6 H, 3 × CH_2), 1.67–1.80 (m, 2 H, CH_2), 2.00 (br s, 1 H, OH), 2.48 (t, *J* = 7.2 Hz, 2 H, CH_2), 3.63–3.74 (m, 1 H, CH).

Diethyl 3-(Hydroxy)heptanephosphonate (8)
Yield: 96%; pale-yellow oil.

IR (film): 1224, 1032 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 0.90 (t, *J* = 6.7 Hz, 3 H, CH_3), 1.33 (t, *J* = 7.0 Hz, 6 H, 2 × CH_3CH$_2$OP), 1.57–1.76 (m, 4 H, 2 × CH_2), 1.79–1.92 (m, 3 H, CH_2, OH), 4.18 (dq, $^3J_{H,H}$ = $^3J_{P,H}$ = 7.0 Hz, 4 H, 2 × CH_3CH_2OP), 4.20–4.29 (m, 1 H, CH).

^{13}C NMR ($CDCl_3$): δ = 12.94 (CH_3), 15.97 (d, $^3J_{C,P}$ = 6.0 Hz, 2 × CH_3CH$_2$OP), 20.34 (d, $^1J_{C,P}$ = 144.7 Hz, PCH_2), 21.41 (CH_2), 23.86 (CH_2), 26.57 (CH_2), 30.58 (CH), 33.61 (d, $^2J_{C,P}$ = 3.9 Hz, CH_2), 62.78 (d, $^2J_{C,P}$ = 7.0 Hz, 2 × CH_3CH_2OP), 71.08 (d, $^3J_{C,P}$ = 17.2 Hz, CH).

^{31}P NMR ($CDCl_3$): δ = 31.21.

Phosphates 9, 10, and 11; General Procedure
To a solution of a corresponding alcohol **6**, **8**, or **9** (3 mmol) in CH_2Cl_2 (10 mL) were added Et_3N (0.63 mL, 4.5 mmol) and diethyl chlorophosphite (0.64 g, 4.2 mmol) at 0 °C. The reaction mixture was stirred for 2 h at r.t. Then 2 M N_2O_4 in CH_2Cl_2 (2.1 mL, 9 mmol) was added at 0 °C. The stirring was continued for 20 h at r.t. Et_2O (10 mL) was added, the solid formed was collected by filtration, and the filtrate was evaporated. The residue was purified by column chromatography (eluent: $CHCl_3$–acetone 90:10).

Ethyl 4-(Diethoxyphosphoryloxy)octanoate (9)
Yield: 88%; colorless oil; R_f = 0.30 ($CHCl_3$–acetone, 90:10).

IR (film): 1764, 1254, 1024 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 0.90 (t, *J* = 6.7 Hz, 3 H, CH_3), 1.26 (t, *J* = 7.0 Hz, 3 H, CH_3CH$_2$O), 1.34 (t, *J* = 7.2 Hz, 6 H, 2 × CH_3CH$_2$OP), 1.30–1.40 (m, 4 H, 2 × CH_2), 1.48–1.70 (m, 2 H, CH_2), 1.80–2.16 (m, 2 H, CH_2), 2.45 (t, *J* = 7.5 Hz, 2 H, CH_2), 4.11 (dq, $^3J_{P,H}$ = $^3J_{H,H}$ = 7.2 Hz, 2 H, CH_3CH_2OP), 4.12 (dq, $^3J_{P,H}$ = $^3J_{H,H}$ = 7.2 Hz, 2 H, CH_3CH_2OP), 4.13 (q, $^3J_{H,H}$ = 7.0 Hz, 2 H, CH_3CH_2O), 4.34–4.46 (m, 1 H, CH).

^{13}C NMR ($CDCl_3$): δ = 13.74 (CH_3), 14.02 (CH_3CH$_2$O), 15.90 (CH_3CH$_2$OP), 16.01 (CH_3CH$_2$OP), 22.34 (CH_2), 26.80 (CH_2), 29.62 (CH_2), 29.86 (d, $^3J_{P,C}$ = 4.9 Hz, CH_2), 34.63 (d, $^3J_{P,C}$ = 3.7 Hz, CH_2), 60.22 (CH_3CH_2O), 63.41 (d, $^2J_{P,C}$ = 6.0 Hz, 2 × CH_3CH_2OP), 78.40 (d, $^2J_{P,C}$ = 6.2 Hz, CH), 172.93 (C=O).

^{31}P NMR ($CDCl_3$): δ = –1.18.

Anal. Calcd for $C_{14}H_{29}O_6P$: C, 51.84; H, 9.01. Found: C, 51.94; H, 9.05.

4-(Diethoxyphosphoryloxy)octanenitrile (10)
Yield: 85%; colorless oil; R_f = 0.33 ($CHCl_3$–acetone, 90:10).

IR (film): 2225 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 0.92 (t, *J* = 7.0 Hz, 3 H, CH_3), 1.35 (dt, *J* = 7.0 Hz, $^4J_{P,H}$ = 0.50 Hz, 6 H, 2 × CH_3CH$_2$OP), 1.36–1.48 (m, 2 H, CH_2), 1.54–1.75 (m, 2 H, CH_2), 1.91–2.03 (m, 2 H, CH_2), 2.51 (t, *J* = 7.5 Hz, 2 H, CH_2), 4.12 (dq, $^3J_{P,H}$ = 7.2 Hz, $^3J_{H,H}$ = 7.0 Hz, 2 H, CH_3CH_2OP), 4.14 (dq, $^3J_{P,H}$ = 7.2 Hz, $^3J_{H,H}$ = 7.0 Hz, 2 H, CH_3CH_2OP), 4.37–4.45 (m, 1 H, CH).

^{13}C NMR ($CDCl_3$): δ = 13.23 (CH_3), 13.84 (CH_2), 16.10 (d, $^3J_{C,P}$ = 6.8 Hz, 2 × CH_3CH$_2$OP), 22.39 (CH_2), 26.86 (CH_2), 30.91 (d, $^3J_{C,P}$ = 4.8 Hz, CH), 34.59 (d, $^3J_{C,P}$ = 3.2 Hz, CH_2), 63.92 (d, $^2J_{C,P}$ = 7.0 Hz, 2 × CH_3CH_2OP), 77.34 (CH_2), 119.30 (CN).

^{31}P NMR ($CDCl_3$): δ = –1.20.

Anal. Calcd for $C_8H_{15}NO$: C, 68.04; H, 10.71; N, 11.25. Found: C, 68.24; H, 10.66; N, 11.29.

Diethyl 3-(Diethoxyphosphoryloxyheptanephosphonate (11)
Yield: 82%; colorless oil; R_f = 0.15 ($CHCl_3$–acetone, 80:20).

IR (film): 1242, 1032 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 0.90 (t, *J* = 7.0 Hz, 3 H, CH_3), 1.33 (t, *J* = 7.0 Hz, 6 H, 2 × CH_3CH$_2$OP), 1.34 (t, *J* = 7.0 Hz, 6 H, 2 × CH_3CH$_2$OP), 1.57–1.70 (m, 4 H, 2 × CH_2), 1.79–1.92 (m, 2 H, CH_2), 4.16 (dq, $^3J_{H,H}$ = $^3J_{P,H}$ = 7.0 Hz, 8 H, 4 × CH_3CH_2OP), 4.34–4.42 (m, 1 H, CH).

^{13}C NMR ($CDCl_3$): δ = 12.94 (CH_3), 15.11 (d, $^3J_{C,P}$ = 6.7 Hz, 2 × CH_3CH$_2$OP), 15.40 (d, $^3J_{C,P}$ = 6.0 Hz, 2 × CH_3CH$_2$OP), 20.16 (d, $^1J_{C,P}$ = 143.2 Hz, PCH_2), 21.48 (CH_2), 23.48 (CH_2), 26.83 (CH_2), 30.58 (CH), 33.72 (d, $^2J_{C,P}$ = 3.80 Hz, CH_2), 60.83 (d, $^2J_{C,P}$ = 6.5 Hz, 2 × CH_3CH$_2$OP), 62.78 (d, $^2J_{C,P}$ = 5.8 Hz, 2 × CH_3CH$_2$OP), 78.19 (dd, $^3J_{C,P}$ = 18.5 Hz, $^2J_{C,P}$ = 6.30 Hz, PCH).

^{31}P NMR ($CDCl_3$): δ = 32.30, –1.20.

Anal. Calcd for $C_{15}H_{34}O_7P_2$: C, 46.39; H, 8.82. Found: C, 46.17; H, 8.78.

Cyclopropanes 12, 13, and 14; General Procedure
To a suspension of NaH (0.072g, 3 mmol) in THF (10 mL) was added the ester **9**, **10**, or **11** (3 mmol) at r.t. and the mixture was stirred at reflux for 5 h. H_2O (5 mL) was added and THF was evaporated under reduced pressure. The residue was extracted with Et_2O (3 × 10 mL) and dried ($MgSO_4$). Evaporation of the solvent afforded crude product, which was purified by column chromatography.

Ethyl *trans*-*n*-Butylcyclopropanecarboxylate (12)[7]
Yield: 75%; colorless oil; R_f = 0.63 ($CHCl_3$).

^1H NMR ($CDCl_3$): δ = 0.68 (ddd, ^3J = 9.7 Hz, ^3J = 5.7 Hz, ^2J = 4.0 Hz, 1 H, C*H*H), 0.89 (t, ^3J = 6.7 Hz, 3 H, CH_3), 1.11–1.17 (m, 1 H, CH*H*), 1.26 (t, ^3J = 7.2 Hz, 3 H, CH_3CH$_2$O), 1.30–1.38 (m, 8 H, CH, CH, 3 × CH_2), 4.11 (q, ^3J = 7.2 Hz, 2 H, CH_2O).

(1*S*,2*S*)-12
$[\alpha]_D^{20}$ +72.2 (*c* = 1.00, $CHCl_3$).

(1*R*,2*R*)-12
$[\alpha]_D^{20}$ –64.7 (*c* = 1.00, $CHCl_3$).

***trans*-2-*n*-Butylcyclopropanenitrile (13)**
Yield: 72%; colorless oil; R_f = 0.38 ($CHCl_3$).

IR (film): 2225 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 0.87–1.14 (m, 5 H, CH_3, CH_2), 1.24–1.54 (m, 8 H, 3 × CH_2, 2 × CH).

^{13}C NMR ($CDCl_3$): δ = 13.23 (s, CH_3), 17.64 (CH_2), 22.64 (CH_2), 25.28 (CH_2), 27.00 (CH_2), 29.14 (CH), 31.45 (CH), 118.11 (CN).

Anal. Calcd for $C_8H_{13}N$: C, 77.99; H, 10.64. Found: C, 77.71; H, 10.60.

(1*S*,2*S*)-13
$[\alpha]_D^{20}$ +58.4 (*c* = 1.05, $CHCl_3$).

(1*R*,2*R*)-13
$[\alpha]_D^{20}$ –52.9 (*c* = 1.05, $CHCl_3$).

Diethyl *trans*-2-*n*-Butylcyclopropanephosphonate (14)
Yield: 70%; colorless oil; R_f = 0.28 ($CHCl_3$–acetone, 90:10).

IR (film): 1224, 1048 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 0.89–1.18 (m, 5 H, CH_3, CH_2), 1.21 (dt, *J* = 7.2 Hz, $^4J_{P,H}$ = 0.5 Hz, 6 H, 2 × C*H*$_3$CH$_2$OP), 1.30–1.38 (m, 8 H, 3 × CH_2, 2 × CH), 4.19 (dq, $^3J_{H,H}$ = $^3J_{P,H}$ = 7.2 Hz, 4 H, 2 × CH_3CH_2OP).

^{13}C NMR ($CDCl_3$): δ = 13.23 (CH_3), 16.10 (d, $^3J_{C,P}$ = 6.5 Hz, 2 × *C*H_3CH$_2$OP), 17.64 (d, $^2J_{P,C}$ = 10.0 Hz, CH_2), 21.84 (CH_2), 22.64 (CH_2), 25.28 (CH_2), 27.00 (CH_2), 29.14 (d, $^2J_{P,C}$ = 17.1 Hz, CH), 31.45 (d, $^1J_{P,C}$ = 141.2 Hz, PCH), 62.92 (d, $^2J_{C,P}$ = 7.1 Hz, 2 × CH_3*C*H$_2$OP).

^{31}P NMR ($CDCl_3$): δ = 25.18.

Anal. Calcd for $C_{11}H_{23}O_3P$: C, 56.39; H, 9.90. Found: C, 56.27; H, 9.97.

(1*S*,2*S*)-14
$[\alpha]_D^{20}$ +56.4 (*c* = 1.20, $CHCl_3$).

(1*R*,2*R*)-14
$[\alpha]_D^{20}$ –50.1 (*c* = 1.20, $CHCl_3$).

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References

(1) (a) Wessjohann, L. A.; Brandt, W.; Thiemann, T. *Chem. Rev.* **2003**, *103*, 1625. (b) Faust, D. *Angew. Chem. Int. Ed.* **2001**, *40*, 2251. (c) Tombo, G. M. R.; Belluš, D. *Angew. Chem., Int. Ed. Engl.* **1991**, *30*, 703. (d) Liu, H.-W.; Walsh, C. T. In *The Chemistry of the Cyclopropyl Group*; Rappoport, Z., Ed.; Wiley: Chichester, **1987**, Chap. 16, 959.
(2) (a) Donaldson, W. A. *Tetrahedron* **2001**, *57*, 8559. (b) Reissig, H.-U.; Zimmer, R. *Chem. Rev.* **2003**, *103*, 1151. (c) Wong, H. N. C.; Hon, M.-Y.; Tse, C.-H.; Yip, Y.-C.; Tanko, J.; Hudlicky, T. *Chem. Rev.* **1989**, *89*, 165. (d) Davis, H. M. L. *Tetrahedron* **1993**, *49*, 5203. (e) Salaün, J. In *The Chemistry of the Cyclopropyl Group*; Rappoport, Z., Ed.; Wiley: Chichester, **1987**, Chap. 13, 809.
(3) (a) Salaün, J. *Chem. Rev.* **1989**, *89*, 1247. (b) Reissig, H.-U. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 971. (c) Lebel, H.; Marcoux, J.-F.; Molinaro, C.; Charette, A. B. *Chem. Rev.* **2003**, *103*, 977. (d) Pellissier, H. *Tetrahedron* **2008**, *64*, 7041.
(4) (a) Arlt, D.; Jautelat, M.; Lantzsch, R. *Angew. Chem., Int. Ed. Engl.* **1981**, *20*, 703. (b) Lantzsch, R. *Synthesis* **1982**, 955. (c) Fujimoto, Y.; Kimura, M.; Terasawa, T.; Khalifa, F. A. M.; Ikekawa, N. *Tetrahedron Lett.* **1984**, *25*, 1805. (d) Nakamura, E.; Kuwajima, I. *J. Am. Chem. Soc.* **1985**, *107*, 2138. (e) Nakamura, E.; Oshino, H.; Kuwajima, I. *J. Am. Chem. Soc.* **1986**, *108*, 3745. (f) Henniges, H.; Militizer, H.-C.; de Meijere, A. *Synlett* **1992**, 735. (g) Saito, A.; Ito, H.; Taguchi, T. *Tetrahedron* **2001**, *57*, 7487.
(5) Caine, D. *Tetrahedron* **2001**, *57*, 2643.
(6) (a) Wadsworth, W. S.; Emmons, W. D. *J. Am. Chem. Soc.* **1961**, *83*, 1733. (b) Tömösközi, I. *Tetrahedron* **1963**, *19*, 1969. (c) Izydore, R. A.; Ghirardelli, R. G. J. *J. Org. Chem.* **1973**, *38*, 1790.
(7) Krawczyk, H.; Wąsek, K.; Kędzia, J.; Wojciechowski, J.; Wolf, W. M. *Org. Biomol. Chem.* **2008**, *6*, 308.
(8) Krawczyk, H.; Wąsek, K.; Kędzia, J. *Synthesis* **2008**, 3299.
(9) Jubault, P.; Goumain, S.; Feason, C.; Collignon, N. *Tetrahedron* **1998**, *54*, 14767.
(10) Sakaguchi, K.; Mano, H.; Ohfune, Y. *Tetrahedron Lett.* **1998**, *39*, 4311.
(11) Taylor, S. K.; Young, D. D.; Simons, L. J.; Vyvyan, J. R.; Wemple, A. M.; Wood, K. N. *Synth. Commun.* **1998**, *28*, 1691.