Pergamon

Tetrahedron 58 (2002) 3493–3498

TETRAHEDRON

3-Phosphono-2-(*N*-cyanoimino)thiazolidine derivatives, new phosphorylating agents for alcohols

Naoyoshi Maezaki,[a] Akemi Furusawa,[a] Yuki Hirose,[a] Shuji Uchida[b] and Tetsuaki Tanaka[a,*]

[a]*Graduate School of Pharmaceutical Sciences, Osaka University, 1-6 Yamadaoka, Suita, Osaka 565-0871, Japan*
[b]*Faculty of Pharmaceutical Sciences, Setsunan University, 45-1 Nagaotogecho, Hirakata, Osaka 573-1041, Japan*

Received 23 January 2002; accepted 14 March 2002

Abstract—We have developed new phosphorylating agents, 3-phosphono-2-(*N*-cyanoimino)-thiazolidine derivatives (3-phosphono-NCTs), which were readily synthesized by phosphorylation of NCT, and transformed primary and secondary alcohols into phosphates in good yield. The transfer of three kinds of dialkylphosphono groups [$(PhO)_2P(O)$–, $(EtO)_2P(O)$–, $(Cl_3CCH_2O)_2P(O)$–] proceeded in excellent yields. Selective phosphorylation of various alcohols was also accomplished. © 2002 Elsevier Science Ltd. All rights reserved.

1. Introduction

Trialkyl phosphate is an important synthetic intermediate employed in various reactions[1–3] and also an important precursor of monoalkyl phosphate, which is found in a number of biologically important substances such as nucleic acids, phospholipids, and inositol phosphates. Phosphorochloridates [$(RO)_2P(O)Cl$] are widely used as phosphorylating agents for the synthesis of trialkyl phosphate. However, the reagents are moisture-sensitive and decompose to generate harmful hydrochloric acid. Therefore, they must be stored under nitrogen in a refrigerator.

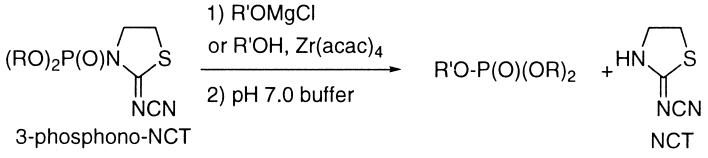
2-(*N*-Cyanoimino)thiazolidine (NCT) is a heterocyclic compound having a unique conjugate system and can be readily synthesized according to Neidlein's procedure.[4] We have reported that its *N*-substituted derivatives can be used as reagents for acylation[5,6] and sulfenylation.[7] These reagents are stable crystalline compounds and the NCT produced by the reactions is recovered for reuse. We also demonstrated that these reagents can be applied to asymmetric reactions using chiral NCT derivatives.[7–9] Next, we aimed at the development of a novel phosphorylating agent bearing NCT as a leaving group (Scheme 1).

In this paper, we describe the phosphorylation reaction of various alcohols using novel 3-phosphono-2-(*N*-cyanoimino)thiazolidine derivatives [$(RO)_2P(O)$–NCT].

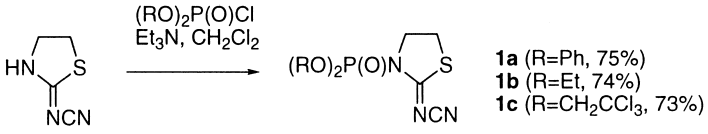
2. Results and discussion

2.1. Preparation of 3-phosphono-NCT

Phosphorylating agents **1a–c** were readily prepared by phosphorylation of NCT with the corresponding



Scheme 1.

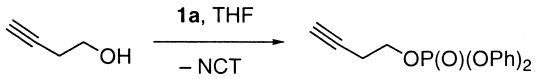


Scheme 2.

Keywords: phosphorylation; phosphoric acid and derivatives; thiazolidines.
* Corresponding author. Tel.: +81-6-6879-8210; fax: +81-6-6879-8214; e-mail: t-tanaka@phs.osaka-u.ac.jp

0040–4020/02/$ - see front matter © 2002 Elsevier Science Ltd. All rights reserved.
PII: S0040-4020(02)00312-5

Table 1. Phosphorylation of 3-butyn-1-ol with 3-phosphono–NCT **1a**



2

Entry	Conditions (epuiv.)	Temp. (°C)	Time (h)	Yield (%)[a]
1	*n*-BuLi (1.2)	0	0.25	89
2	NaH (1.2)	0	0.25	87
3	*t*-BuMgCl (1.2)	0	0.25	98
4	Et_3N (1.2)	Rt to reflux	24	0
5	Pyridine (1.2)	Rt to reflux	24	0
6	*p*-TsOH·H_2O (0.05)	Rt to reflux	24	0
7	PPTS (0.25)	Rt to reflux	24	0
8	$Cu(OTf)_2$ (0.25)	Rt	5	22
9	$Zr(acac)_4$ (0.25)	Rt	13	35
10	$Zr(acac)_4$ (1.0)	Rt	0.5	89

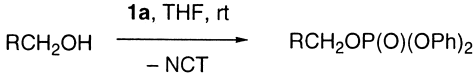
[a] Isolated yield.

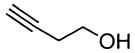
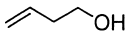
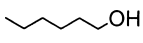
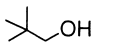
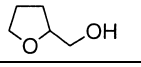
phosphorochloridates in the presence of Et_3N in CH_2Cl_2 at rt in good yields (Scheme 2). All the compounds are stable and odorless crystals, and are far less sensitive to moisture compared with the corresponding phosphorochloridates.

2.2. Phosphorylation of alcohols with 3-phosphono-NCT

Using $(PhO)_2P(O)$–NCT **1a**, we examined suitable reaction conditions for phosphorylation of 3-butyn-1-ol under basic and acidic conditions (Table 1). We found that activation of the alcohol with a strong base was effective to give the phosphate in good yields (entries 1–3). However, use of an amine base such as Et_3N or pyridine did not afford the product (entries 4 and 5). On the other hand, protic acids did not promote the reaction (entries 6 and 7), but some Lewis acids were effective (entries 8–10). Especially, the conditions using one equivalent of $Zr(acac)_4$[10] gave satisfactory yield (entry 10). As a result of the preliminary experiments, we adopted two promising reaction conditions, i.e. the *t*-BuMgCl and $Zr(acac)_4$ methods. In these reactions, the NCT is selectively replaced with alcohol, and no exchange

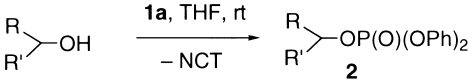
Table 2. Phosphorylation of various primary alcohols



Entry	Alcohol	Condition	Time (h)	Product	Yield (%)[a]
1		A	0.08	**2**	98
2		B	0.5	**2**	89
3		C	4	**2**	85
4		A	0.25	**3**	91
5		B	1.0	**3**	73
6		A	0.17	**4**	50
7		B	1.75	**4**	72
8		A	0.33	**5**	88
9		B	1.5	**5**	8
10		A	0.5	**6**	100
11		B	1.0	**6**	59

Method A: alcohol was activated with *t*-BuMgCl and reacted with **1a**. Method B: alcohol was reacted with **1a** in the presence of $Zr(acac)_4$. Method C: alcohol was activated with *t*-BuMgCl and reacted with $(PhO)_2P(O)Cl$.
[a] Isolated yield.

Table 3. Phosphorylation of various secondary alcohols



2

Entry	Alcohol	Condition	Time (h)	Product	Yield (%)[a]
1		A	1	**7**	92
2		B	14	**7**	19
3		C	2	**7**	85
4		A	0.25	**8**	88
5		A	0.5	**9**	87
6		A	9.5	**10**	23

Method A: alcohol was activated with *t*-BuMgCl and reacted with **1a**. Method B: alcohol was reacted with **1a** in the presence of $Zr(acac)_4$. Method C: alcohol was activated with *t*-BuMgCl and reacted with $(PhO)_2P(O)Cl$ in refluxing THF.
[a] Isolated yield.

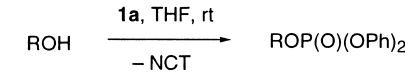
of the phenol part with the alcohol was detected. It is noted that the NCT was recovered for reuse in good yield (>80%).

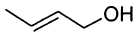
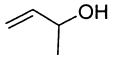
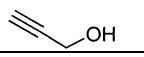
Then, we investigated phosphorylation of various primary alcohols using the established reaction conditions. The results are summarized in Table 2. Although satisfactory results were obtained in all cases except entry 9, the activation using *t*-BuMgCl almost exhibited higher yields than that using $Zr(acac)_4$. $(PhO)_2P(O)$–NCT **1a** exhibited better yield than $(PhO)_2P(O)Cl$ (entries 1–3).

Next, we examined phosphorylation of secondary alcohols with $(PhO)_2P(O)$–NCT (Table 3). Magnesium salts of the secondary alcohols were phosphorylated with **1a** at rt in good yield (entries 1, 4, and 5). We found that $(PhO)_2P(O)$–NCT can be sufficiently used in place of $(PhO)_2P(O)Cl$ even for secondary alcohols by using this method (entry 3). For secondary alcohols, phosphorylation using $Zr(acac)_4$ was sluggish and the yield was poor (entry 2). The reagent was not effective for phosphorylation of *tert*-butanol, and the phosphorylated product was obtained only in 23% yield (entry 6).

Phosphates of allylic[1] and propargylic alcohols[11] are important synthetic intermediates for various reactions. The 3-phosphono-NCT converted these alcohols into the corresponding phosphates in excellent yields (Table 4).

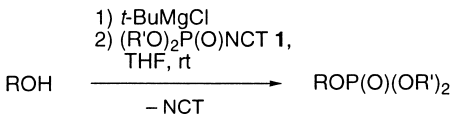
Table 4. Phosphorylaton of allylic and propargylic alcohols

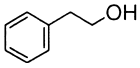
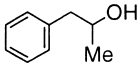


Entry	Alcohol	Time (h)	Product	Yield (%)[a]
1		0.25	**11**	85
2		0.5	**12**	85
3		0.25	**13**	100

Alcohol was activated with *t*-BuMgCl and reacted with **1a**.
[a] Isolated yield.

Table 5. Reactions of various 3-phosphono-NCTs



Entry	Alcohol	Reagent	R′	Time (h)	Product	Yield (%)[a]
1		**1a**	Ph	0.25	**14**	70
2		**1b**	Et	1.5	**15**	84
3		**1c**	Cl_3CCH_2	0.17	**16**	76
4		**1a**	Ph	0.25	**17**	98
5		**1b**	Et	1.5	**18**	97
6		**1c**	Cl_3CCH_2	0.25	**19**	78

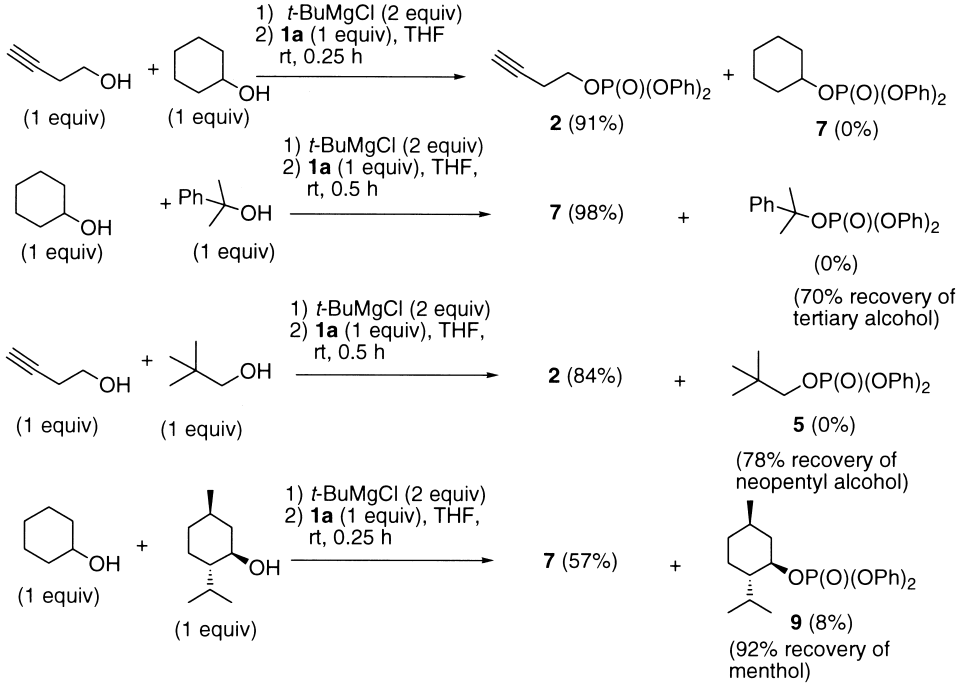
[a] Isolated yield.

Considerable attention has been paid towards the development of diversely protected phosphorylating agents, since conversion of trialkyl phosphates into the corresponding monoalkyl phosphates should take place under different conditions depending on the substrates.[12] Therefore, we examined the ability of 3-phosphono-NCTs **1b**, **c** as phosphorylating agents and found that these compounds smoothly converted both the primary and secondary alcohols into corresponding phosphates in good yields (Table 5). Phosphorylation using 3-phosphono-NCTs **1a** and **c** was completed faster than that using $(EtO)_2P(O)$–NCT **1b** presumably due to a resonance effect of the phenyl groups and inductive effect of the trichloroethyl groups, respectively.

Selective phosphorylation of alcohols is required for the synthesis of the monophosphate from polyol compounds without protection. We examined competitive phosphorylation toward two kinds of alkoxides using the 3-phosphono-NCT **1a** (Scheme 3). 3-Butyn-1-ol was selectively phosphorylated to **2** in the presence of cyclohexanol. Although volatile cyclohexanol could not be recovered, no phosphorylated cyclohexanol **7** was detected. Similarly, cyclohexanol was predominantly phosphorylated to give **7** with **1a** in the presence of 2-phenyl-2-propanol. Two primary alcohols with different steric demand were also differentiated clearly. Thus, 3-butyn-1-ol was exclusively phosphorylated to give **2** in the presence of neopentyl alcohol with **1a**. Similarly, differentiation of two secondary alcohols in cyclohexanol and L-menthol was accomplished, giving **7** and **9** in 57 and 8% yields, respectively.

3. Conclusions

3-Phosphono-NCTs **1a**–**c** can be used as a stable alternative to phosphorchloridates. Phosphorylation of primary and secondary alcohols proceeds in good yield. In addition, compound **1a** selectively phosphorylates different kinds of alcohols. As we have demonstrated with three kinds of phosphorylating agents **1a**–**c** in this paper, NCT would be a promising leaving group for other phosphorylating agents



Scheme 3.

having a variety of protection. Further studies along these lines are in progress.

4. Experimental

4.1. General

Melting points are uncorrected. Optical rotations were measured using a JASCO DIP-360 digital polarimeter. Unless otherwise stated, ^{1}H and ^{13}C NMR spectra were recorded in $CDCl_3$ solution. ^{1}H NMR spectra were recorded at 500 MHz with a JEOL JNM-GX500 spectrometer. ^{13}C NMR spectra were recorded at 68 or 75 MHz with a JEOL JNM-EX270 spectrometer or a JEOL JMN-AL-300, respectively. All signals are expressed as ppm downfield from tetramethylsilane used as an internal standard (δ value). IR spectra were measured with a Horiba FT-210 IR spectrometer. Mass spectra were taken with a Shimadzu QP-1000 mass spectrometer or a JMS-600 mass spectrometer. High-resolution mass spectra were measured by a JEOL JMS-600H. Merck Kieselgel 60 or Kanto silica gel 60 was used as an adsorbent for column chromatography. All air- or moisture-sensitive reactions were carried out in flame-dried glassware under N_2 atmosphere. All organic extracts were dried over anhydrous $MgSO_4$, filtered, and concentrated with a rotary evaporator under reduced pressure unless otherwise stated.

4.1.1. 3-(Diphenylphosphono)-2-(*N*-cyanoimino)thiazolidine (1a). $(PhO)_2P(O)Cl$ (8.67 g, 60.0 mmol) was added to a mixture of NCT (3.82 g, 30.0 mmol) and Et_3N (20.9 ml, 150 mmol) in CH_2Cl_2 (150 ml) with stirring at rt under N_2 and the stirring was continued at rt for 15 min. The mixture was partitioned between CH_2Cl_2 and water. The aqueous layer was extracted with CH_2Cl_2. The combined organic layers were washed with brine prior to drying and solvent evaporation. The crude was chromatographed on silica gel with *n*-hexane–AcOEt (1:1) to give **1b** (8.09 g, 75%) as a colorless powder. Mp 102.0–103.0°C (AcOEt). ^{1}H NMRδ: 3.33 (t, J=7.0 Hz, 2H, CH_2S), 4.19 (t, J=7.0 Hz, 2H, CH_2N), 7.24–7.40 (m, 10H, Ar-H). ^{13}C NMR δ: 30.2 (d, J(C,P)=8.1 Hz), 53.7 (d, J(C,P)=5.6 Hz), 114.3, 119.9 (d, J(C,P)=5.0 Hz, 4C), 126.0 (d, J(C,P)=1.2 Hz, 2C), 129.9 (4C), 149.1 (d, J(C,P)=6.9 Hz, 2C), 178.5. IR 2197 (CN), 1566 (Ph), 1234 (P–O–Ph), 1182 (P=O), 1138 (P–O). MS (FAB) *m/z*: 360 (MH^+). HRMS (FAB) Calcd $C_{16}H_{15}N_3O_3PS$ (MH^+): 360.0602. Found: 360.0587. Anal. calcd for $C_{16}H_{14}N_3O_3PS$: C, 53.48; H, 3.93; N, 11.69; S, 8.92. Found: C, 53.56; H, 3.95; N, 11.83, S, 8.83.

4.1.2. 3-(Diethylphosphono)-2-(*N*-cyanoimino)thiazolidine (1b). $(EtO)_2P(O)Cl$ (3.40 g, 23.6 mmol) was added to a mixture of NCT (1.50 g, 11.8 mmol) and Et_3N (8.20 ml, 59.0 mmol) in CH_2Cl_2 (30 ml) with stirring at rt under N_2 and the stirring was continued at rt for 30 min. The mixture was partitioned between CH_2Cl_2 and water. The aqueous layer was extracted with CH_2Cl_2. The combined organic layers were washed with brine prior to drying and solvent evaporation. The crude was chromatographed on silica gel with *n*-hexane–AcOEt (1:1) to give **1b** (2.28 g, 74%) as a colorless powder. Mp 81.0–82.0°C (AcOEt). ^{1}H NMR (acetone-d_6) δ: 1.32 (t, J=7.3 Hz, 6H, CH_3), 3.67 (t, J=7.3 Hz, 2H, CH_2S), 4.18 (m, 4H, CH_2O), 4.33 (t, J=7.3 Hz, 2H, CH_2N). ^{13}C NMR (methanol-d_4) δ: 16.4 (d, J(C,P)=6.7 Hz, 2C), 31.5 (d, J(C,P)=8.4 Hz), 55.1 (d, J(C,P)=5.0 Hz), 66.7 (d, J(C,P)=6.1 Hz, 2C), 116.0, 181.8 (d, J(C,P)=2.2 Hz). IR 2194 (CN), 1238 (P–O), 1144 (P–O). MS (EI) *m/z* (%) 263 (M^+, 31.9). HRMS (EI) Calcd $C_8H_{14}N_3O_3PS$ (M^+): 263.0493. Found: 263.0492.

4.1.3. 3-[Bis-(trichloroethyl)phosphono]-2-(*N*-cyanoimino)thiazolidine (1c). $(CCl_3CH_2O)_2P(O)Cl$ (226 mg, 0.60 mmol) was added to a mixture of NCT (64 mg, 0.50 mmol) and *i*-Pr_2NEt (0.26 ml, 1.50 mmol) in CH_2Cl_2 (2.5 ml) with stirring at rt under N_2 and the stirring was continued at rt for 30 min. The mixture was washed with 10% KOH prior to drying and solvent evaporation. The crude was washed with *n*-hexane to give **1c** (170 mg, 73%) as a colorless powder. Mp 161.0–162.0°C (AcOEt). ^{1}H NMR δ: 3.36 (t, J=7.3 Hz, 2H, CH_2S), 4.36 (t, J=7.3 Hz, 2H, CH_2N), 4.79 (d, J=7.3 Hz, 4H, CH_2O). ^{13}C NMR δ: 30.8 (d, J(C,P)=9.3 Hz), 53.2 (d, J(C,P)=5.6 Hz), 78.0 (d, J(C,P)=5.0 Hz, 2C), 94.1 (d, J(C,P)=9.3 Hz, 2C), 114.0, 180.0. IR 2199 (CN), 1236 (P–O), 1176 (P=O), 1107 (P–O). MS (FAB) *m/z*: 468 (MH^+). HRMS (FAB) Calcd $C_8H_9Cl_6N_3O_3PS$ (MH^+): 467.8262. Found: 467.8291.

4.1.4. General procedure for phosphorylation of alcohols (*t*-BuMgCl method). *t*-BuMgCl (0.97 M, THF solution) (0.25 ml, 0.24 mmol) was added to a solution of 3-butyn-1-ol (0.01 ml, 0.20 mmol) in THF (2 ml) with stirring at rt under N_2 and the stirring was continued at rt for 30 min. Then, $(PhO)_2P(O)$–NCT (86 mg, 0.24 mmol) was added to the mixture and the whole was stirred at rt for 15 min. The reaction was quenched with pH 7.0 sodium phosphate buffer and extracted with AcOEt. The extract was dried and the solvent was evaporated to give **2** (59 mg, 98%) as a colorless oil along with NCT (26 mg, 85%). ^{1}H NMR δ: 2.00 (t, J=2.7 Hz, 1H, C≡CH), 2.59 (td, J=6.7, 2.7 Hz, 2H, C≡CCH_2), 4.31 (dt, J=6.7, 6.7 Hz, 2H, CH_2O), 7.19–7.36 (m, 10H, Ar-H). ^{13}C NMR δ: 20.5 (d, J(C,P)=7.5 Hz), 66.4 (d, J(C,P)=5.6 Hz), 70.6, 77.8, 120.0 (d, J(C,P)=5.0 Hz, 4C), 125.4 (d, J(C,P)=1.3 Hz, 2C), 129.8 (4C), 150.3 (d, J(C,P)=7.5 Hz, 2C). IR 3295 (C≡CH), 2123 (C≡CH), 1589 (Ph), 1217 (P–O), 1190 (P=O), 1163 (P–O). MS (FAB) *m/z*: 303 (MH^+). HRMS (FAB) Calcd $C_{16}H_{16}O_4P$ (MH^+): 303.0810. Found: 303.0798.

4.2. General procedure for phosphorylation of alcohols [Zr(O*t*-Bu)$_4$ method]

$(PhO)_2P(O)$–NCT (86 mg, 0.24 mmol) was added to a mixture of 3-butyn-1-ol (0.01 ml, 0.20 mmol) and $Zr(acac)_4$ (98 mg, 0.20 mmol) in THF (2 ml) with stirring at rt under N_2 and the stirring was continued at rt for 30 min. The reaction was quenched with pH 7.0 sodium phosphate buffer and extracted with AcOEt. The extract was dried and the solvent was evaporated. The crude was chromatographed on silica gel with *n*-hexane–AcOEt (1:1) to give **2** (54 mg, 89%) as a colorless oil along with NCT (25 mg, 82%).

The phosphates **3**–**8**, **10**, **12**, **13**, and **15** are known

compounds, which were reported in Refs. 13, 14, 14, 15–18, 2b, 19, and 20, respectively.

4.2.1. L-Menthyl diphenyl phosphate (9). Colorless oil (87%). $[\alpha]_D^{25}=-37.4$ (*c* 0.86, $CHCl_3$). ^1H NMR δ: 0.72 (d, *J*=7.3 Hz, 3H, CH_3), 0.84 (d, *J*=7.3 Hz, 3H, CH_3), 0.89 (d, *J*=6.1 Hz, 3H, CH_3), 0.82–1.02 (m, 2H), 1.14 (m, 1H), 1.37–1.46 (m, 2H), 1.65 (d, *J*=12.2 Hz, 2H), 1.99–2.03 (m, 1H, C*H*$(CH_3)_2$), 2.21 (br d, 1H), 4.39 (ddt, *J*=11.0, 6.7, 4.3 Hz, 1H, CHO), 7.16–7.35 (m, 10H, Ar-H). ^{13}C NMR δ: 15.5, 20.7, 21.8, 22.7 (d, *J*(C,P)=1.2 Hz), 25.3, 31.4, 33.8, 42.3, 48.2 (d, *J*(C,P)=7.5 Hz), 81.4 (d, *J*(C,P)=6.9 Hz), 120.0 (d, *J*(C,P)=5.0 Hz, 4C), 125.0 (d, *J*(C,P)=1.2 Hz, 2C), 129.5 (4C), 150.6 (d, *J*(C,P)=1.9 Hz, 2C). IR 1591 (Ph), 1191 (P=O), 1163 (P–O). MS (FAB) *m/z*: 411 (MNa^+). HRMS (FAB) Calcd $C_{22}H_{29}NaO_4P$ (MNa^+): 411.1712. Found: 411.1723.

4.2.2. (*E*)-2-Butenyl diphenyl phosphate (11). Colorless oil (85%). ^1H NMR δ: 1.70 (br d, *J*=6.7 Hz, 3H, CH_3), 4.65 (dd, *J*=8.5, 6.7 Hz, 2H, CH_2O), 5.58 (dt, *J*=15.3, 6.7 Hz, 1H, CH_3CH=C*H*), 5.79 (dq, *J*=15.3, 6.7 Hz, 1H, CH_3C*H*=CH), 7.17–7.35 (m, 10H, Ar-H). ^{13}C NMR δ: 17.6, 69.7 (d, *J*(C,P)=6.2 Hz), 120.0 (d, *J*(C,P)=5.0 Hz, 4C), 124.8 (d, *J*(C,P)=6.3 Hz), 125.2 (d, *J*(C,P)=1.2 Hz), 129.6 (4C), 132.5, 150.4 (d, *J*(C,P)=6.9 Hz, 2C). IR 1591 (Ph), 1190 (P=O), 1163 (P–O). MS (FAB) *m/z*: 305 (MH^+). HRMS (FAB) Calcd $C_{16}H_{18}O_4P$ (MH^+): 305.0954. Found: 305.0966.

4.2.3. Diphenyl 2-phenylethyl phosphate (14). Colorless oil (70%). ^1H NMR δ: 3.00 (t, *J*=7.3 Hz, 2H, PhCH_2), 4.42 (dt, *J*=7.3, 7.3 Hz, 2H, CH_2O), 7.14–7.37 (m, 10H, Ar-H). ^{13}C NMR δ: 36.6 (d, *J*(C,P)=6.7 Hz), 69.4 (d, *J*(C,P)=6.7 Hz), 119.9 (d, *J*(C,P)=5.0 Hz, 4C), 125.2 (d, *J*(C,P)=1.7 Hz, 2C), 126.7 (2C), 128.4 (2C), 129.6 (d, *J*(C,P)=1.1 Hz, 4C), 129.7, 136.5, 150.2 (d, *J*(C,P)=7.3 Hz, 2C). IR 1591 (Ph), 1190 (P=O), 1163 (P–O). MS (FAB) *m/z*: 355 (MH^+). HRMS (FAB) Calcd $C_{20}H_{20}O_4P$ (MH^+): 355.1109. Found: 355.1104.

4.2.4. Bis-(2,2,2-trichloroethyl) 2-phenylethyl phosphate (16). Colorless oil (76%). ^1H NMR (500 MHz, $CDCl_3$) δ: 3.05 (t, *J*=7.0 Hz, 2H, $PhCH_2$), 4.42 (dt, *J*=7.0, 7.0 Hz, 2H, CH_2C*H*$_2$O), 4.44 (dd, *J*=11.0, 6.7 Hz, 2H, CH_2CCl_3), 4.48 (dd, *J*=11.0, 6.7 Hz, 2H, CH_2CCl_3), 7.24–7.34 (m, 5H, Ar-H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 36.5 (d, *J*(C,P)=6.9 Hz), 69.5 (d, *J*(C,P)=6.9 Hz), 76.9 (d, *J*(C,P)=9.9 Hz, 2C), 94.5 (d, *J*(C,P)=11.2 Hz, 2C), 127.0, 128.7 (2C), 129.0 (2C), 136.5. IR 1497 (Ph), 1298 (P=O), 1103 (P–O). MS (FAB) *m/z*: 463 (MH^+). HRMS (FAB) Calcd $C_{12}H_{14}Cl_6O_4P$ (MH^+): 426.8747. Found: 426.8754.

4.2.5. Diphenyl 1-phenylprop-2-yl phosphate (17). Colorless oil (98%). ^1H NMR δ: 1.34 (d, *J*=6.1 Hz, 3H, CH_3), 2.83 (dd, *J*=15.0, 6.7 Hz, 1H, $PhCH_2$), 3.00 (dd, *J*=15.0, 6.7 Hz, 1H, $PhCH_2$), 4.91 (m, 1H, CHO), 7.09–7.35 (m, 15H, Ar-H). ^{13}C NMR δ: 20.9 (d, *J*(C,P)=3.7 Hz), 43.5 (d, *J*(C,P)=6.2 Hz), 78.4 (d, *J*(C,P)=6.9 Hz), 119.9 (d, *J*(C,P)=5.0 Hz, 2C), 120.0 (d, *J*(C,P)=5.0 Hz, 4C), 125.1 (d, *J*(C,P)=1.2 Hz, 2C), 128.4 (2C), 129.3, 129.5 (d, *J*(C,P)=6.9 Hz, 4C), 136.5, 150.5 (d, *J*(C,P)=2.5 Hz, 2C). IR 1591 (Ph), 1192 (P=O), 1163 (P–O). MS (FAB) *m/z*: 369 (MH^+). HRMS (FAB) Calcd $C_{21}H_{22}O_4P$ (MH^+): 369.1280. Found: 369.1268.

4.2.6. Diethyl 1-phenylprop-2-yl phosphate (18). Colorless oil (97%). ^1H NMR δ: 1.21 (t, *J*=7.3 Hz, 3H, CH_3), 1.27 (t, *J*=7.3 Hz, 3H, CH_3), 1.33 (d, *J*=6.1 Hz, 3H, CH_3), 2.81 (ddd, *J*=14.0, 6.1, 1.8 Hz, 1H, PhCH_2), 2.97 (dd, *J*=14.0, 6.7 Hz, 1H, PhCH_2), 3.82 (m, 4H, CH_2CH_3), 4.67 (m, 1H, CHO), 7.21–7.31 (m, 5H, Ar-H). ^{13}C NMR δ: 15.9 (d, *J*(C,P)=1.9 Hz), 16.0 (d, *J*(C,P)=1.9 Hz), 21.1 (d, *J*(C,P)=3.1 Hz), 43.7 (d, *J*(C,P)=6.9 Hz), 63.2 (d, *J*(C,P)=5.0 Hz, 2C), 76.1 (d, *J*(C,P)=6.2 Hz), 126.4, 128.2 (2C), 129.4 (2C), 137.2. IR 1497 (Ph), 1273 (P–O), 1263 (P–O), 1167 (P=O), 1034 (P–O). MS (FAB) *m/z*: 273 (MH^+). HRMS (FAB) Calcd $C_{13}H_{22}O_4P$ (MH^+): 273.1296. Found: 273.1274.

4.2.7. Bis-(2,2,2-trichloroethyl) 1-phenylprop-2-yl phosphate (19). Colorless oil (78%). ^1H NMR δ: 1.47 (d, *J*=6.1 Hz, 3H, CH_3), 2.90 (ddd, *J*=14.0, 6.1, 3.1 Hz, 1H, PhCH_2), 2.98 (dd, *J*=14.0, 6.1 Hz, 1H, PhCH_2), 4.17 (dd, *J*=11.6, 6.1 Hz, 1H, CH_2CCl_3), 4.29 (dd, *J*=11.6, 6.1 Hz, 1H, CH_2CCl_3), 4.33 (dd, *J*=11.6, 6.1 Hz, 1H, CH_2CCl_3), 4.43 (dd, *J*=11.6, 6.1 Hz, 1H, CH_2CCl_3), 4.84 (m, 1H, CHO), 7.23–7.34 (m, 5H, Ar-H). ^{13}C NMR δ: 21.4 (d, *J*(C,P)=3.1 Hz), 43.6 (d, *J*(C,P)=6.9 Hz), 76.6 (d, *J*(C,P)=3.1 Hz, 2C), 78.9 (d, *J*(C,P)=6.9 Hz), 94.7 (d, *J*(C,P)=10.0 Hz, 2C), 127.0, 128.6 (2C), 129.5 (2C), 136.8. IR 1591 (Ph), 1190 (P=O), 1163 (P–O). MS (FAB) *m/z*: 477 (MH^+). HRMS (FAB) Calcd $C_{13}H_{16}Cl_6O_4P$ (MH^+): 476.8899. Found: 476.8908.

References

1. As a precursor of organometallic reagents, see: Kang, S.-K.; Kim, D.-Y.; Hong, R.-K.; Ho, P.-S. *Synth. Commun.* **1996**, *26*, 1493–1498. Nowotny, S.; Tucker, C. E.; Jubert, C.; Knochel, P. *J. Org. Chem.* **1995**, *60*, 2762–2772. Smith, J. G.; Henke, S. L.; Mohler, E. M.; Morgan, L.; Rajan, N. I. *Synth. Commun.* **1991**, *21*, 1999–2006. Araki, S.; Butsugan, Y. *Chem. Lett.* **1988**, 457–458. Araki, S.; Hatano, M.; Ito, H.; Butsugan, Y. *J. Organomet. Chem.* **1987**, *333*, 329–335. Matsubara, S.; Wakamatsu, K.; Morizawa, Y.; Tsuboniwa, N.; Oshima, K.; Nozaki, H. *Bull. Chem. Soc. Jpn* **1985**, *58*, 1196–1199.
2. As a leaving group: (a) nucleophilic substitution of allylic phosphates with carbon nucleophiles, see: Suzuki, A.; Butsugan, Y. *J. Chem. Soc., Perkin Trans. 1* **1984**, 969–972. Yanagisawa, A.; Nomura, N.; Yamamoto, H. *Tetrahedron* **1994**, *50*, 6017–6028 and references cited therein. (b) nucleophilic substitution of allylic phosphates with hetero nucleophiles, see: Araki, S.; Ohmori, K.; Butsugan, Y. *Synthesis* **1984**, 841–842. Itoh, A.; Ozawa, S.; Oshima, K.; Sasaki, S.; Yamamoto, H.; Hiyama, T.; Nozaki, H. *Bull. Chem. Soc. Jpn* **1980**, *53*, 2357–2362. (c) reaction via π-allyl palladium complex, see: Tanigawa, Y.; Nishimura, K.; Kawasaki, A.; Murahashi, S. *Tetrahedron Lett.* **1982**, *23*, 5549–5552. Imada, Y.; Fuji, M.; Kubota, Y.; Murahashi, S. *Tetrahedron Lett.* **1997**, *38*, 8227–8230. (d) conjugate addition–elimination: Alderdice, M.; Sum, F. W.; Weiler, L. *Org. Synth.* **1984**, *62*, 14–23.
3. For allylic rearrangemnt; see: Harusawa, S.; Miki, M.; Yoneda, R.; Kurihara, T. *Chem. Pharm. Bull.* **1985**, *33*,

2164–2167. Bartlett, P. A.; McQuaid, L. A. *J. Am. Chem. Soc.* **1984**, *106*, 7854–7860.
4. Neidlein, R.; Reuter, H. *Arch. Pharm.* **1972**, *305*, 731–737.
5. Iwata, C.; Watanabe, M.; Okamoto, S.; Fujimoto, M.; Sakae, M.; Katsurada, M.; Imanishi, T. *Heterocycles* **1988**, *27*, 323–326. Butsugan, Y.; Tsukamoto, H.; Morito, N.; Bito, T. *Chem. Lett.* **1976**, 523–524.
6. Tanaka, T.; Iwata, C. *J. Synth. Org. Chem. Jpn* **1998**, *56*, 182–191.
7. Tanaka, T.; Azuma, T.; Fang, X.; Uchida, S.; Iwata, C.; Ishida, T.; In, Y.; Maezaki, N. *Synlett* **2000**, 33–36.
8. Tanaka, T.; Fang, X.; Azuma, T.; Uchida, S.; Ishida, T.; In, Y.; Iwata, C.; Maezaki, N. *J. Chin. Chem. Soc.* **2000**, *47*, 865–868 *Chem. Abstr.* **2001**, *134*, 222653.
9. Maezaki, N.; Furusawa, A.; Uchida, S.; Tanaka, T. *Tetrahedron* **2001**, *57*, 9309–9315.
10. Nagamatsu, T.; Kunieda, T. *Tetrahedron Lett.* **1987**, *28*, 2375–2378.
11. Hojo, M.; Sakuragi, R.; Okabe, S.; Hosomi, A. *Chem. Commun.* **2001**, 357–358. Mikami, K.; Yoshida, A. *Tetrahedron* **2001**, *57*, 889–898. Yoshida, A.; Mikami, K. *Synlett* **1997**, 1375–1376. Mikami, K.; Yoshida, A.; Matsumoto, S.; Feng, F.; Matsumoto, Y.; Sugino, A.; Hanamoto, T.; Inanaga, J. *Tetrahedron Lett.* **1995**, *36*, 907–908.
12. Green, T. W.; Wuts, P. G. M. *Protective Groups in Organic Synthesis*; 3rd ed.; Wiley: New York, 1999 Chapter 9, pp 660–700.
13. Ye, M.; Li, L.; Zhao, Y.; Zhai, C. *Phosphorus Sulfur* **1988**, *39*, 79–87. Butsugan, Y.; Tsukamoto, H.; Morito, N.; Bito, T. *Chem. Lett.* **1976**, 523–524.
14. Gamrath, H. R.; Hatton, R. E.; Weesner, W. E. *Ind. Eng. Chem.* **1954**, *46*, 208–212.
15. Khatib, F. E.; Tachon, C.; Caminade, A.-M.; Koeng, M. *Tetrahedron Lett.* **1985**, *26*, 3007–3010.
16. Quast, H.; Dietz, T. *Synthesis* **1995**, *10*, 1300–1304.
17. Semenov, V. E.; Akamsin, V. D.; Enikeev, K. M.; Reznik, V. S. *Russ. J. Gen. Chem.* **1999**, *69*, 1386–1388.
18. Sosnovsky, G.; Zaret, E. H.; Schmitt, K. D. *J. Org. Chem.* **1970**, *35*, 336–340.
19. Watanabe, Y.; Mukaiyama, T. *Chem. Lett.* **1978**, 349–352.
20. Jung, A.; Engel, R. *J. Org. Chem.* **1975**, *40*, 3652–3654.