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Synthetic Approaches to Cyclopropyl Phosphorylmethyl Ketones and 1-Alkenyl Cyclopropyl Ketones

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Synthetic approaches to 1-diazo-3-phosphoryl-2-propanone, cyclopropyl phosphorylmethyl ketones, and 1-alkenyl cyclopropyl ketones are presented.

Acid-catalyzed ring opening of 1-alkenyl cyclopropyl ketones is immediately followed by an intramolecular olefin cyclization, in some cases further followed by additional cation cyclizations, to construct cyclopentanone or cyclohexenone skeletons.[1] On the other hand the 1-alkenyl cyclopropyl ketones derived from vinyl ethers undergo a ready ring opening under mild conditions using trifluoroacetic acid as a catalyst to give 4-oxo-5-alkenals or their dioxolane-protected derivatives.[1]

The starting 1-alkenyl cyclopropyl ketones **E** were prepared in the previous work by a sequence of cyclopropanations using 1-diazo-3-silyl-2-propanone **A** and Peterson olefinations of the resulting silylmethyl ketones **C**.[2] In this process high susceptibility of the silylmethyl

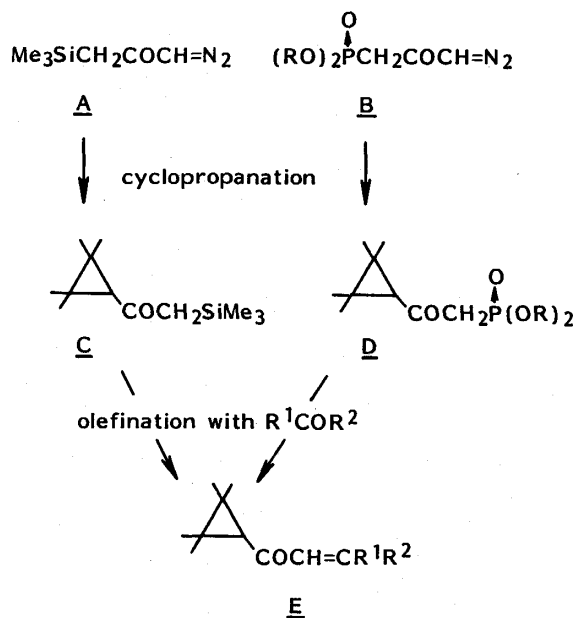

Chart 1.

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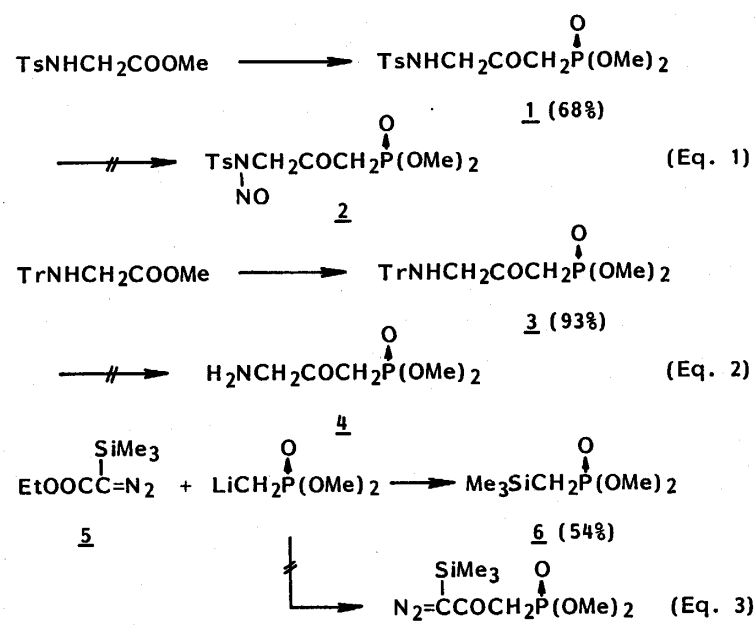
ketones **C** to moisture was a serious problem. Although partly solved by a one-flask procedure applied to the followed olefination step, this trouble still remains when cyclopropanation is a low-yield reaction or the final product **E** is too unstable to be separated from the complex mixture of many products. Therefore, we started a project aiming at the development of a synthetic equivalent of functionalized diazoketone **A** and its applications to the synthesis of 1-alkenyl cyclopropyl ketones.

As a candidate compound was selected 1-diazo-3-phosphoryl-2-propanone **B.** Its cyclopropanation is expected to produce phosphorylmethyl ketones **D,** the phosphoryl-stabilized carbanions generated from which would react with carbonyl compounds leading to 1-alkenyl cyclopropyl ketones **E.**

The present article describes our several attempts made for synthesizing 1-diazo-3-phosphoryl-2-propanone **B** and further 1-alkenyl cyclopropyl ketones **D.**

Results and Discussion

At an early stage of the present work, the following three methods (Eqs. 1–3) were examined in order to open the synthetic route to 1-diazo-3-phosporyl-2-propanone **B.** Eq. 1: Methyl *N*-(*p*-toluenesulfonyl)glycinate was readily converted by action with dimethyl lithiomethylphosphonate (3 equiv)[3] into 1-phosphoryl-3-(*p*-toluenesulfonylamino)-2-propanone **1** in 54% yield. However nitrosoation of **1** with $NaNO_2$+Ac_2O in acetic acid afforded no trace of the expected diazo compound **B,** but part of the methylene moiety activated by the two adjacent anion-stabilizing groups was involved in *C*-nitrosoation (^{1}H NMR). This indicates that the *N*-protecting group must not be such strongly electron-withdrawing as to decrease the basicity of this nitro-

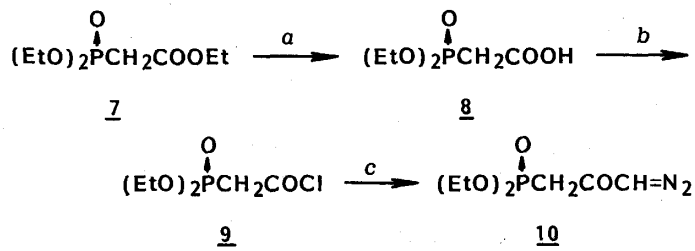


gen since the readily enolizable methylene moiety exists and is also reactive to electrophiles, NO^+ in this case.

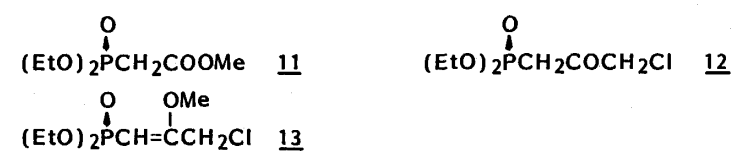
Eq. 2: Methyl *N*-tritylglycinate was employed instead of the *N*-tosylated derivative. Its transformation into 1-phosphoryl-3-(tritylamino)-2-propanone **3** was performed quantitatively by a similar method using the lithiomethylphosphonate. However deprotection of **3** with aqueous HCl in dichloromethane suspension resulted in complex mixture from which trityl alcohol was only isolated, indicating high instability of the resulting amino ketone **4.** Both deprotection and nitrosoation procedures were carried out in the same flask (5% HCl and then $NaNO_2$ or $NaNO_2$ and then 5% HCl, both in dichloromethane), but the results were complex mixture of many products or recovery of **3** (45%). Nitrosoation of **3** with ethyl nitrite in ethanol was not effective either, **3** being quantitatively recovered.

Eq. 3: Phosphorylmethylation of diazoacetate is one of the most direct accesses to the desired diazo ketone **B.** Accordingly silyl-protected diazoacetate **5** [4] was allowed to react with the lithiomethylphosphonate at −78°C in tetrahydrofuran (THF). The product obtained in 54% yield was silylmethylphosphonate **6,** [5] indicating that the silyl-protected **5** worked as silylating agent.

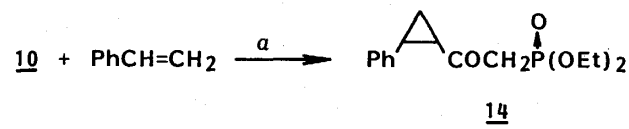
Finally 1-diazo-3-(diethoxyphosphoyl)-2-propanone (**10**) was synthesized according to the following route: Commercially available ethyl phosphorylacetate **7** was hydrolyzed with aqueous KOH in ethanol to give phosphorylacetic acid **8** [5] (Scheme 1). Treatment of **8** with oxalyl



a: aq. KOH in EtOH, rt, 20 h *b*: $(COCl)_2$ in CH_2Cl_2, rt, 22.5 h *c*: $CH_2=N_2$ in Et_2O, 0 °C



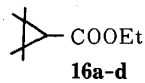
Scheme 1.



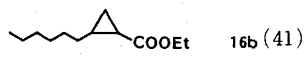
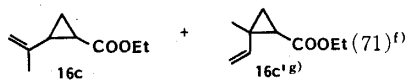
a: $Pd(OAc)_2$ (1 mol%) in styrene, rt, 2 h

Scheme 2.

Table 1. Synthesis of cycloprpanecarboxylates 16.

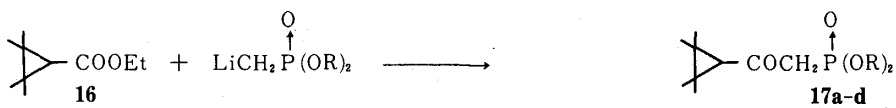
$N_2=CHCOOEt$ + olefin ⟶ 

15 **16a-d**

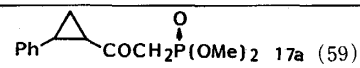
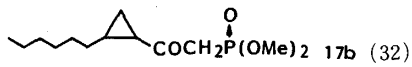
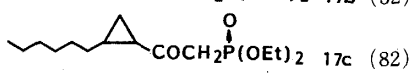
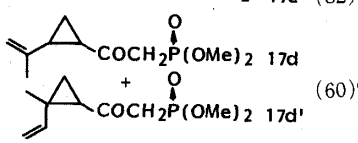
Olefin[a]	Cat.[b]	Conditions[c]	Product (yield/%)[d]
styrene	$Cu(OTf)_2$	80 ℃	 **16a** (75)[e]
1-octene	$Cu(acac)_2$	reflux	 **16b** (41)
2-methyl-1,3-butadiene	$Cu(OTf)_2$ or $Cu(acac)_2$	reflux	 **16c** + **16c'**[g] (71)[f]
3,4-dihydro-2*H*-pyran	$Cu(acac)_2$	80 ℃	 **16d** (98)[h]

a) Used as reaction solvent. b) Six mol % amount of catalyst was used. $Cu(OTf)_2$: copper trifluoromethanesulfonate. $Cu(acac)_2$: copper acetylacetonate. c) Diazo ester **15** was added to the heated olefin in a period of 1 h (2 mmol scale). d) Yield of isolated product. e) trans : cis = 2 : 1 (^{1}H NMR).
f) **16c** : **16c'** = 43 : 57 ($Cu(OTf)_2$), 75 : 25 ($Cu(acac)_2$), checked by GLC. g) trans : cis = 3 : 1 (^{1}H NMR).
h) Single isomer.

Table 2. Synthesis of cyclopropyl phosphorylmethyl ketones 17.



16 **17a-d**

Ester	Phosphonate[a]	Conditions[b]	Product (yield/%)[c]
16a	R = Me	−78℃, 0.5h	 **17a** (59)
16b	Me	〃	 **17b** (32)
16b	Et	〃	 **17c** (82)
16c+**16c'**	Me	〃	 **17d** + **17d'** (60)[d]

a) Two equivalents of the phosphonate were employed. b) Carried out in dry THF under nitrogen.
c) Yield of isolated products. d) **17d** : **17d'** = 2 : 3 (inseparable, ^{1}H NMR).

chloride in dichloromethane at room temperature followed by evaporation of excess the chlorinating agent afforded highly moisture-sensitive acid chloride **9** in a quantitative yield. Acylation of diazomethane with **9** produced the expected **10** in 57% yield.

Dry diazomethane has to be used in the above raction since the moisture-sensitive acyl chloride **9** is readily hydrolyzed into **8** which is then esterified under the reaction conditions to give **11.** Hydrogen chloride generated on the hydrolysis quickly reacts with diazo compound **10** to form chloromethyl ketone **12** whose enol form undergoes *O*-methylation leading to **13.** Not

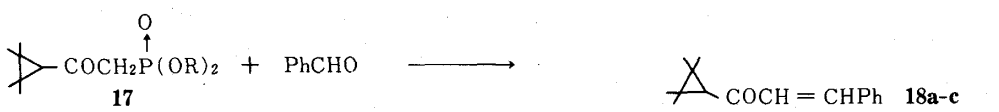
only these side reactions reduce the yield of **10**, but also their separation from **10** is difficult. Though **11** and **12** can be removed by column chromatography over silica gel pretreated with triethylamine, separation of **13** was unsuccessful. Under various conditions, the contamination by **11** – **13** was not avoided.

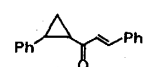
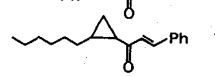
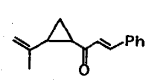
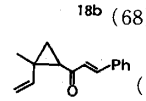
Cyclopropanations using diazo ketone **10** and styrene in the presence of a catalyst such as $Cu(acac)_2$, $Rh_2(OAc)_4$, or $Pd(OAc)_2$ were unfortunately not so fruitful as expected. Even when a large excess of styrene was used, both as substrate and solvent, yield of the expected cyclopropane **14** was still poor (44%, Scheme 2). The route of synthesizing cyclopropyl phosphorylmethyl ketones via diazo ketone **10** was thus abondoned.

Though a rather indirect route, an alternative synthesis starts with cyclopropanation of olefins with ethyl diazoacetate (**15**) as shown in Table 1. In the presence of a catalytic amount of $Cu(acac)_2$ or $Cu(OTf)_2$, cyclopropanations proceed smoothly to give cyclopropanecarboxylates **16a-d** as mixtures of *cis*- and *trans*-isomers. Ratio of two regioisomers **16c** and **16c'** changed depending upon the catalyst used (**16c**:**16c'**=43:57 ($Cu(OTf)_2$); 75:25 ($Cu(acac)_2$), checked by GLC).

Phosphorylmethylation [3] of cyclopropanecarboxylates **16** was easily carried out with 2 equivalents of lithiomethylphosphonates at −78°C in THF to give cyclopropyl phosphorylmethyl ketones **17a-d** and **17d'** (Table 2). As these ketones **17** are more stable than the corresponding silylmethyl ketones, they would serve as better starting compounds for synthesizing 1−alkenyl cyclopropyl ketones. However, the ester **16d** derived from 3,4−dihydro-2*H*-pyran produced a labile product **17e**. Though **17e** was assigned to be the expected phosphorylmethyl structure on the basis of ^1H NMR spectrum of the crude product, its separation was unsuccessful. Its use for the Horner-Emmons olefination with benzaldehyde, at −78°C in the presence of lithium

Table 3. Synthesis of 1-alkenyl cyclopropyl ketones 18.



Phosphonate	Base[a]	Conditions[b]	Product (yield/%)[c]
17a	$LiBr/NEt_3$	0℃, 0.5h → rt, 16h	 18a (85)
17b	〃	〃	 18b (82)
17c	〃	〃	18b (68)
17d+17d'	〃	0℃, 0.5h → rt, 14h	 18c +  18c' (79)[d]

a) Carried out in dry THF with LiBr (1.5 equiv) and NEt_3 (1.2 equiv). b) Phosphonates were treated with $LiBr/NEt_3$ at 0℃. After the addition of PhCHO, the mixture was stirred at room temperature. c) Yield of isolated product. d) **18c** : **18c'** = 58 : 42 (GLC).

diisopropylamide (LDA) failed either.

Horner-Emmons olefinations of phosphorylmethyl ketones **17** with benzaldehyde were smoothly performed by the method using such a weak base as triethylamine and lithium bromide.[6] Thus **17** were treated with lithium bromide (1.5 equiv) and triethylamine (1.2 equiv) in dry THF at 0°C for 30 min. The subsequent reactions with benzaldehyde at room temperature gave excellent yields of 1-alkenyl cyclopropyl ketones as *E*-isomers (Table 3).

In summary, 1-alkenyl cyclopropyl ketones are available via three steps of cyclopropanation with readily available ethyl diazoacetate (**15**), phosphorylmethylation with lithiomethylphosphonates, and Horner-Emmons olefinations under weakly basic conditions.

Experimental

General. Melting points were determined on a Yanagimoto melting point apparatus and are uncorrected. IR spectra were taken with a JASCO IRA-1 or a JASCO A-702 spectrometer. ^{1}H NMR spectra were recorded on a Hitachi R-40 (90MHz), a JEOL FX-100 (100MHz), or a JEOL GSX-270 instrument (270MHz), and ^{13}C NMR on a JEOL FX-100 (25.05MHz) or a JEOL GSX-270 spectrometer (67.94MHz). Chemical shifts are expressed in parts per million downfield from tetramethylsilane as an internal standard. Mass spectra were measured with a JEOL-01SG-2 spectrometer at 70 eV of ionization energy. High resolution mass spectra were obtained on the same instrument. Elemental analyses were performed on a Hitachi 026 CHN analyzer. Thin-layer chromatography (TLC) was accomplished on 0.2mm precoated plates of silica gel 60 F-254 (Merck) or of aluminum oxide 60 F-254 type-E (Merck). Visualization was made with ultraviolet light (254 and 365 nm), iodine, molybdophosphoric acid (5% in ethanol), or *p*-anisaldehyde (5% in ethanol containing 5% of sulfuric acid). For preparative column chromatography, Wakogel C-200, C-300 (Wako), Silica gel 60 (Merck), and Florisil (60-100 mesh, Wako) were employed. Flash chromatography was carried out on an EYELA EF-10 apparatus using a column (20×180mm) packed with Silicagel 60 (Merck, size: 0.04-0.063mm). Gas liquid chromatography (GLC) was accomplished on a Yanaco G-2800 gas chromatograph (Yanagimoto) with an ionization flame detector using a glass column (SE-30, 3×2000mm) or a glass capillary column (Silicone GE, SE-30, 0.25×50000mm). Micro vacuum distillation was carried out on a Sibata GTO-250R Kugelrohr distilling apparatus. Solvents were evaporated with a Tokyo Rikakikai rotary evaporator type-V at about 50°C unless otherwise stated.

1-(Dimethoxyphosphoryl)-3-(*p*-toluenesulfonylamino)-2-propanone (1). To a solution of butyllithium (1.64M in hexane, 1.88ml, 3mmol) in dry THF (3ml) was added dropwise dimethyl methylphosphonate (0.325ml, 3mmol) at −78°C under nitrogen. After 3h, methyl *N*-(*p*-toluenesulfonyl)glycinate (0.243g, 1mmol) in dimethoxyethane (DME, 3ml) was added and stirring was continued for 0.5h. The reaction mixture was poured into saturated aqueous ammonium

chloride and extractd with dichloromethane (20ml×2). The combined extracts were dried over magnesium sulfate and evaporated in vacuo. The residue (0.341g) was chromatographed over silica gel by using ethyl acetate to afford **1** (0.229g, 68%): Colorless needles (dichloromethane-benzene); mp 95–98°C; IR (KBr) 3147, 1734, 1328, 1255, 1232, 1045, and 1024cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=2.41 (3H, s, *p*-Me), 3.13 (2H, d, J=22.5Hz, PCH_2), 3.72 (6H, d, J=11.2Hz, MeOP), 3.93 (2H, d, J=5.6Hz, $NHCH_2$), 5.5–5.8 (1H, br s, NH), 7.28 (2H, d, J=8.6Hz, ArH), and 7.70 (2H, d, J=8.6Hz, ArH); ^{13}C NMR ($CDCl_3$) δ=21.47 (q, *p*-Me), 38.35 (td, J_{C-P}=129.0Hz, PCH_2), 52.66 (t, $NHCH_2$), 53.36 (qd, J_{C-P}=6.0Hz, MeOP), 127.24, 129.89 (each d, Ar), 136.77, 143.83 (each s, Ar), and 197.31 (s, CO); MS *m/z* (rel intensity, %) 335 (M^+, 0.2), 151 (24), 124 (base peak), 94 (32), and 91 (41). Anal. Calcd for $C_{12}H_{18}NO_6PS$: C, 42.99; H, 5.41; N, 4.18%. Found: C, 42.84; H, 5.36; N, 4.28%.

1-(Dimethoxyphosphoryl)-3-(tritylamino)-2-propanone (3). To a solution of butyllithium (1.64M in hexane, 12.6ml, 20mmol) in dry THF (30ml) was added dropwise dimethyl methylphosphonate (2.17ml, 20mmol) at −78°C under nitrogen. After 0.5h, methyl *N*-tritylglycinate (3.31g, 10mmol) in THF (30ml) was added and stirring was continued for 1h. The mixture was poured into saturated aqueous ammonium chloride, extracted with dichloromethane (30ml×2), the combined extracts were dried over magnesium sulfate, and evaporated in vacuo. The residue (5.21g) was subjected to column chromatography over silica gel with ethyl acetate to give **3** (3.95g, 93%): Colorless needles; mp 69–71°C; IR (KBr) 1715, 1250, 1010, and 1050cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=2.3–2.6 (1H, br s, NH), 2.94 (2H, d, J=23.0Hz, PCH_2), 3.39 (2H, s, NCH_2), 3.66 (6H, d, J=11.0Hz, MeOP), and 7.1–7.5 (15H, m, ArH); ^{13}C NMR ($CDCl_3$) δ=38.86 (td, J_{C-P}=128.0Hz, PCH_2), 52.74 (qd, J_{C-P}=7.0Hz, MeOP), 55.00 (t, NCH_2), 70.53 (s, Trt), 126.48, 127.89, 128.54 (each d, Ar), 145.48 (s, Ar), and 199.69 (s, CO); MS *m/z* (rel intensity, %) 423 (M^+, 8), 243 (34), 182 (base peak), 165 (32), 110 (25), 104 (39), 94 (26), 93 (20), 79 (23), 77 (55), 46 (24), and 44 (57). HRMS Calcd for $C_{24}H_{26}NO_4P$: M, 423.1598. Found: *m/z* 423.3102.

Reaction of 5 with Dimetyl Lithiomethyphosphonate Leading to Dimethyl (Trimethylsilyl)-methylphosphonate (6). To a solution of dimethyl methylphosphonate (0.216ml, 2mmol) was added butyllithium (1.64M in hexane, 1.25ml, 2mmol) at −78°C under nitrogen. After 0.5h, **5** [7] (0.186g, 1mmol) in THF (2ml) was added dropwise in a period of 10 min and the stirring was continued for 1h at the same temperature. The reaction mixture was poured into saturated aqueous ammonium chloride, extracted with dichloromethane (20ml×2), the combined extracts were dried over magnesium sulfate, and evaporated in vacuo. The residue (0.291g) was chromatographed over Florisil with ethyl acetate to give **6** (0.106g, 54%): Pale yellow liquid; IR (neat) 1240, 1050, 1025, and 845cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=0.17 (9H, s, $SiMe_3$), 1.15 (2H, d, J=22.5Hz, PCH_2), and 3.66 (4H, d, J=11.4Hz, MeOP); ^{13}C NMR ($CDCl_3$) δ=0.08 (qd, J_{C-P}=4.4Hz, $SiMe_3$), 13.89 (td, J_{C-P}=127.5Hz, PCH_2), and 52.36 (qd, J_{C-P}=5.9Hz, MeOP); MS *m/z*

(rel intensity, %) 196 (M^++1, 14), 183 (15), 181 (87), 151 (85), 105 (52), 89 (56), and 59 (56).

Diethoxyphosphorylacetic Acid (8). A mixture of aqueous KOH (4.5g in 4ml) and ethanol (10ml) was added to **7** (commercially available, 15g, 67mmol) in a period of 2 min. The mixture was stirred at room temperature for 20h and the solvent was evaporated in vacuo. After washed with diethyl ether (200ml×3), the residue was dissolved in water (10ml) and hydrochloric acid (6M) was added to this aqueous solution to become acidic (pH=1). The resulting mixture was extracted with dichloromethane (50ml×3). The combined extracts were dried over magnesium sulfate and evaporated in vacuo to give **8** (10.84g, 83%) as colorless liquid: ^{1}H NMR ($CDCl_3$) δ=1.32 (6H, t, J=6.5Hz, OEt), 2.95 (2H, d, J=22.0Hz, PCH_2), 4.14 (4H, qd, J= 7.0 and 6.5Hz, OEt), and 10.20 (1H, s, COOH).

1-Diazo-3-(diethoxyphosphoryl)-2-propanone (10). To a solution of **8** (1.96g, 10mmol) in dichloromethane (30ml) was added oxalyl chloride (3.6ml). The mixture was stirred at room temperature for 22.5h and the excess oxalyl chloride was removed off by evaporation in vacuo to give moisture-sensitive chloride **9** (^{1}H NMR ($CDCl_3$) δ=1.36 (6H, t, J=7.0Hz, OEt), 3.46 (2H, d, J=22.0Hz, PCH_2), and 4.17 (4H, qd, J=7.0 and 6.5Hz, OEt)). Diazomethane was prepared in another flask from *N*-methyl-*N*-nitroso-*p*-toluenesulfonamide (commercially available, 12.4g, 57mmol) in diethyl ether and dried over KOH pellets. To an etheral solution of the diazomethane was added **9** in dry diethyl ether (3ml) at 0°C. After 10 min, dry nitrogen was bubbled through the reaction mixture to remove the excess diazomethane and the solvent was evaporated in vacuo. The residue (1.922g) was chromatographed over silica gel by using hexane-ethyl acetate (1:4 v/v) containing triethylamine (1%) to give **10** (1.251g, 57%) and then **12** (0.515g, 22%). **10**: Yellow liquid; IR (neat) 2107, 1637, 1255, 1047, and 1024cm^{-1} ; ^{1}H NMR ($CDCl_3$) δ=1.32 (6H, td, J=7.0 and 0.7Hz, OEt), 2.95 (2H, d, J=22.0Hz, PCH_2), 4.15 (4H, dd, J=8.3 and 7.0Hz, EtOP), and 5.60 (1H, br s, $CH{=}N_2$); ^{13}C NMR ($CDCl_3$) δ=16.41 (qd, J_{C-P}=5.9Hz, EtOP), 40.18 (td, J_{C-P}=129.4Hz, PCH_2), 56.71 (d, $CH{=}N_2$), 62.83 (td, J_{C-P}=5.9 Hz, EtOP), and 185.57 (d, J_{C-P}=4.4Hz, COP); MS *m/z* (rel intensity, %) 192 (35), 164 (22), 136 (base peak), 81 (22), 65 (18), and 56 (47).

1-Chloro-3-(diethoxyphosphoryl)-2-propanone (12). A mixture of **10** (0.104g, 0.47mmol) and hydrochloric acid 5%, 1ml) in dichloromethane (1ml) was stirred at room temperature for 48h. After water was added, the mixture was extracted with dichloromethane (15ml×2). The combined extracts were dried over magnesium sulfate and evaporated in vacuo to give **12** (0.081 g, 35%): Colorless liquid; IR (neat) 1735, 1255, and 1024cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=1.34 (6H, t, J=7.0Hz, OEt), 3.25 (2H, d, J=22.8Hz, PCH_2), 4.15 (4H, qd, J=8.8 and 7.0Hz, EtOP), and 4.28 (2H, s, CH_2Cl); ^{13}C NMR ($CDCl_3$) δ=16.35 (qd, J_{C-P}=5.9Hz, EtOP), 39.74 (td, J_{C-P}= 127.9Hz, PCH_2), 49.18 (t, CH_2Cl), 63.00 (td, J_{C-P}=5.9Hz, EtOP), and 194.07 (d, J_{C-P}=5.9Hz,

COP); MS *m/z* (rel intensity, %) 228 (M^+, 15), 179 (base peak), 152 (31), 137 (21), 123 (67), 109 (76), 105 (26), 81 (45), and 65 (25). HRMS Calcd for $C_7H_{14}O_4ClP$: M, 228.0317. Found: *m/z* 228.0317.

This compound **12** was obtained above as a side product in the preparation of **10.**

3-Chloro-1-(diethoxyphosphoryl)-2-methoxypropene (13). A solution of diazomethane (ca 5–7mmol) in diethyl ether was added to **12** (0.444g, 1.94mmol) at 0°C and the mixture was stirred at room temperature for 4h. Evaporation of the solvent gave brown oil (0.455g) which was then chromatographed over silica gel with hexane-ethyl acetate (4:1 v/v) and then acetone to give **13** (0.204g, 43%) and then recovered **12** (38%). **13**: Colorless liquid; IR (neat) 1630, 1238, 1053, and 1028cm^{-1}; ^1H NMR ($CDCl_3$) δ=1.32 (6H, t, J=7.0Hz, OEt), 3.95 (3H, s, OMe), 4.06 (2H, d, J=2.0Hz, CH_2Cl), 4.08 (4H, qd, J=8.0 and 7.0 Hz, EtOP), and 4.93 (1H, d, J=8.8Hz, =CHP); ^{13}C NMR ($CDCl_3$) δ=16.11 (qd, J_{C-P}=7.3Hz, EtOP), 42.09 (td, J_{C-P}=19.5Hz, CH_2Cl), 57.18 (q, OMe), 61.57 (td, J_{C-P}=4.9Hz, EtOP), 94.04 (dd, J_{C-P}=192.9Hz, =CHP), and 165.57 (s, =COMe); MS *m/z* (rel intensity, %) 242 (M^+, 45), 207 (20), 179 (22), 177 (33), 157 (39), 149 (32), 133 (47), 121 (83), 98 (29), 95 (57), 86 (67), 84 (base peak), and 81 (34). HRMS Calcd for $C_8H_{16}O_4PCl$: M, 242.0474. Found: *m/z* 242.0479.

(Diethoxyphosphoryl)methyl 2-Phenylcyclopropyl Ketone (14). To a mixture of styrene (1.5ml, 13mmol) and paradium(I) acetate (1mg, 0.004mmol) was added dropwise **10** (0.105g, 0.47mmol) under nitrogen. After stirred for 2h at room temperature, the mixture was chromatographed over silica gel with ethyl acetate to give **14** (0.061g, 44%, trans : cis=10:1 (^1H NMR)). The trans isomer was separated in a pure form through column chromatography: *trans*-**14**: Colorless liquid; IR (neat) 1690, 1255, 1050, and 1025cm^{-1}; ^1H NMR ($CDCl_3$) δ=1.1-2.1 (8H, m, OEt and ring CH_2), 2.3–2.7 (2H, m, ring CH), 3.23 (2H, d, J=22.0Hz, PCH_2), 4.32 (4H, m, OEt), and 7.0–7.6 (5H, m, Ph); ^{13}C NMR ($CDCl_3$) δ=15.71 (qd, J_{C-P}=4.4Hz, EtOP), 19.13 (t, ring CH_2), 29.89, 32.58 (each d, ring CH), 43.03 (td, J_{C-P}=127.5Hz, PCH_2), 61.92 (td, J_{C-P}=4.4Hz, EtOP), 125.66, 126.07, 127.93 (each d, Ph), 139.41 (s, Ph), and 199.37 (d, J_{C-P}=5.9Hz, COP); MS *m/z* (rel intensity, %) 296 (M^+, base peak), 179 (89), 158 (23), 151 (59), 141 (29), 137 (25), 125 (21), 123 (67), 117 (91), 116 (42), 115 (93), 109 (48), 97 (23), 91 (62), and 81 (53). HRMS Calcd for $C_{15}H_{21}O_4P$: M, 296.1176. Found: *m/z* 296.1203. *cis*-**14**: ^1H NMR ($CDCl_3$) δ=1.2–1.6 (7H, m, OEt and ring CH_2), 1.8–2.1 (1H, m, ring CH_2), 2.7–3.2 (4H, m, ring CH and PCH_2), 3.7–4.4 (4H, m, OEt), and 7.22 (5H, s, Ph). This compound **14** was assigned by its conversion into **18a.**

General Procedure for the Synthesis of Cyclopropanecarboxylates 16 Using Diazoacetate 15. At 80°C or under reflux, ethyl diazoacetate (15, 1mmol) was added dropwise, in a period of 1h with the aid of a syringe, to the mixture of an olefin (20–40mmol) and a catalyst (0.06mmol).

After completion of the addition, the mixture was chromatographed over silica gel with hexane-ethyl acetate (19:1 to 4:1 v/v) to give a cyclopropane **16.** The reaction conditions as well as the results are listed in Table 1. All these compounds **16a-d** and **16c'** are known [8] while trans/cis rations are quite different from the reported results.

General Procedure for the Synthesis of Cyclopropyl Phosphorylmethyl Ketones 17. To a solution of butyllithium (1.64M in hexane, 1.25ml, 2mmol) in dry THF (15ml) was added dropwise in a period of 5 min dimethyl methylphosphonate (0.216g, 2mmol) at −78°C. A cyclopropanecarboxylate (1mmol) was added after 0.5h, the reaction mixture was stirred at the same temperature under nitrogen for 0.5h, and poured into diluted hydrochloric acid (5%). Products were extracted into dichloromethane (20ml×2), the combined extracts were washed with saturated aqueous sodium hydrogencarbonate and then with saturated aqueous sodium chloride, dried over magnesium sulfate, and finally evaporated in vacuo. The residue was subjected to column chromatography over silica gel by using hexane-ethyl acetate (0:1 to 1:2 v/v) to give **17.**

(Dimethoxyphosphoryl)methyl 2-Phenylcyclopropyl Ketone (17a). Both the isomers, *trans*-**17a** and *cis*-**17a,** can be separated from each other by column chromatography over silica gel with hexane-ethyl acetate (1:2 v/v). *trans*-**17a:** Pale yellow liquid; IR (neat) 1680, 1250, 1050, and 1025cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=1.3–1.6 (1H, m, ring CH_2), 1.6–1.9 (1H, m, ring CH_2), 2.3–2.7 (2H, m, ring CH), 3.23 (2H, d, J=22.5Hz, PCH_2), 3.69, 3.74 (each 3H, d, J=11.5Hz, MeOP), and 6.9–7.4 (5H, m, Ph); ^{13}C NMR ($CDCl_3$) δ=19.47 (t, ring CH_2), 30.47, 33.18 (each d, ring CH), 42.27 (td, J_{C-P}=127.9Hz, PCH_2), 52.86 (qd, J_{C-P}=7.4Hz, MeOP), 126.36, 126.77, 128.60 (each d, Ph), 140.01 (s, Ph), and 200.01 (d, J_{C-P}=5.9Hz, COP); MS *m/z* (rel intensity, %) 268 (M^+, 14), 151 (36), 109 (21), 58 (26), and 43 (base peak). HRMS Calcd for $C_{13}H_{17}O_4P$: M, 268.0863. Found: *m/z* 268.0817. *cis*-**17a:** Pale yellow liquid; IR (neat) 1690, 1250, and 1025cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=1.3–1.6 (1H, m, ring CH_2), 1.7–2.0 (1H, m, ring CH_2), 2.5–3.0 (2H, m, ring CH), 2.97, 3.01 (2H, each d, J=22.0Hz, PCH_2), 3.59, 3.64 (each 3H, d, J=1.4Hz, MeOP), and 7.20 (5H, s, Ph); ^{13}C NMR ($COCl_3$) δ=13.29 (t, ring CH_2), 30.24, 30.88 (each d, ring CH), 42.74 (td, J_{C-P}=127.9Hz, PCH_2), 53.00 (qd, J_{C-P}=5.9Hz, MeOP), 126.95, 128.10, 129.54 (each d, Ph), 135.66 (s, Ph), and 197.24 (d, J_{C-P}=5.9Hz, COP); MS *m/z* (rel intensity, %) 268 (M^+, 62), 165 (38), 151 (base peak) 138 (24), 124 (27), 117 (28), 115 (23), 110 (38), 109 (65), 94 (27), 78 (31), and 43 (59). HRMS Calcd for $C_{13}H_{17}O_4P$: M, 268.0863. Found: *m/z* 268.0779.

(Dimethylphosphoryl)methyl 2-Hexylcyclopropyl Ketone (17b). Only ^{1}H NMR spectrum was taken; its structure was confirmed by its conversion into **18b** as described below. ^{1}H NMR ($CDCl_3$) δ=0.7–1.6 (10H, m, *n*-C_6H_{13}, ring CH_2, and CH), 3.14 (2H, d, J=22.0Hz, PCH_2), and 3.72 (3H, d, J=10.8Hz, MeOP).

(Diethoxyphosphoryl)methyl 2-Hexylcyclopropyl Ketone (17c). Colorless liquid; IR (neat) 1685, 1250, 1045, and 1015cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=0.6–2.0 (23H, m, *n*-C_6H_{13}, ring CH_2, CH, and OEt), 3.16 (2H, d, J=22.1Hz, PCH_2), and 4.12 (4H, qd, J=7.8 and 7.1Hz, EtOP); ^{13}C NMR ($CDCl_3$) δ=14.06 (q, *n*-C_6H_{13}), 16.36 (qd, J_{C-P}=5.9Hz, EtO), 19.41 (t, ring CH_2), 22.65, 27.59, 29.06, 29.71, 31.83, 33.24, 48.38 (td, J_{C-P}=127.9Hz, PCH_2), 62.59 (td, J_{C-P}=5.9Hz, EtOP), and 201.71 (d, J_{C-P}=5.9Hz, COP); MS *m/z* (rel intensity, %) 304 (M^+, 13), 194 (55), 152 (40), 151 (48), 125 (62), 123 (98), 109 (47), 97 (39), 96 (31), 95 (29), 80 (49), and 41 (base peak). The structure of **17c** was confirmed on the basis of these data as well as its conversion into **18b** as described below.

(Dimethoxyphosphoryl)methyl 2-(1-Methylethenyl)cyclopropyl Ketone (17d) + (Dimethoxyphosphoryl)methyl 2-Ethenyl-2-methylcyclopropyl Ketone (17d'). These compounds were obtained as inseparable mixture of each two stereoisomers. Colorless liquid; ^{1}H NMR ($CDCl_3$) δ=1.1–2.4 (m including three singlets at 1.20, 1.34, and 1.65), 3.14, 3.18, 3.20 (2H, each d, J=22.5Hz, PCH_2), 3.73, 3.74, 3.75, 3.76 (6H, each d, J=11.5Hz, MeOP), and 4.6–6.0 (m including two doublet of doublets at 5.50 and 5.74 (J=17.0 and 10.5Hz)); ^{13}C NMR ($CDCl_3$) δ=13.65 (q, Me), 17.30, 20.24, 22.12, 22.88, 24.06, 29.65, 32.88, 33.06, 33.24, 36.65, 38.17, 42.33 (td, J_{C-P}=127.9Hz, PCH_2), 43.33 (td, J_{C-P}=127.9Hz, PCH_2), 53.06 (qd, J_{C-P}=5.9Hz, MeOP), 111.30, 112.71 (each t, $=CH_2$), 114.13, 138.25 (d, =CH), 143.01 (s, =CMe), 144.13 (d, =CH), 190.18, and 200.71 (each d, J_{C-P}=5.9Hz, COP); MS *m/z* (rel intensity, %) 232 (M^+, 26), 152 (93), 124 (base peak), 122 (35, 109 (64), 94 (59), 81 (23), and 79 (26).

General Procedure for the Synthesis of 1-Alkenyl Cyclopropyl Ketones 18. The mixture of a lithium bromide (0.131g, 1.5mmol) and a phosphonate **17** (1mmol) in dry THF (5ml) was stirred at room temperature under nitrogen for 0.5h. Triethylamine (0.167g, 1.2mmol) was added at 0°C and the mixture was stirred at room temperature for 1h. After benzaldehyde (0.101ml, 1mmol) was added, the stirring was continued for 14–16h. The reaction mixture was quenched with saturated aqueous ammonium chloride, extracted with diethyl ether (15ml× 2), the combined extracts were dried over magnesium sulfate, and evaporated in vacuo. The residue was chromatographed over silica gel with hexane-ethyl acetate (40:1 to 9:1 v/v) to give a 1-alkenylcyclopropyl ketone **18.** Both *trans*-**18a** and **18b** are known.[2]

(*E*)-2-Phenylcyclopropyl 2-Phenylethenyl Ketone (18a). Two isomers with respect to the ring configuration, *trans*-**18a** and *cis*-**18a**, were separated by column chromatography. *trans*-**18a**: Colorless needles (diethyl ether-hexane); mp 110–113°C (lit.[2] mp 80–81°C); IR (KBr) 1666 and 1602cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=1.48 (1H, ddd, J=9.0, 7.0, and 4.0Hz, ring CH_2), 1.98 (1H, ddd, J=9.0, 5.9, and 4.0Hz, ring CH_2), 2.4–2.8 (2H, m, ring CH), 6.86 (1H, d, J=16.3 Hz, =CH), 7.0–7.6 (10H, m, Ph), and 7.56 (1H, d, J=16.3Hz, =CH); ^{13}C NMR ($CDCl_3$) δ=19.18 (t, ring CH_2), 29.59, 31.71 (each d, ring CH), 126.24, 126.60, 128.42, 128.60, 129.01, 130.54, 134.66, 140.72, 142.42, and 197.74 (s, CO); MS *m/z* (rel intensity, %) 248 (M^+, 58), 157 (23),

131 (base peak), 115 (24), 103 (53), and 77 (32). *cis*-**18a**: Colorless needles (diethyl ether-hexane); mp 117–120°C; IR (KBr) 1675cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=1.39 (1H, dt, J=8.0 and 5.0 Hz, ring CH_2), 1.98 (1H, dt, J=6.2 and 5.0Hz, ring CH_2), 2.6–2.9 (2H, m, ring CH), 6.70 (1H, d, J=16.3Hz, =CH), 7.0–7.5 (10H, m, Ph), and 7.42 (1H, d, J=16.3 Hz, =CH); ^{13}C NMR ($CDCl_3$) δ=11.77 (t, ring CH_2), 28.47, 29.06 (each d, ring CH), 126.60, 127.42, 127.89, 128.18, 128.83, 129.30, 130.24, 134.66, 136.25, 141.83, and 195.48 (s, CO); MS *m/z* (rel intensity, %) 248 (M^+, 21), 157 (25), 131 (base peak), 116 (25), 115 (50), 103 (92), 91 (34), and 77 (71). Anal. Calcd for $C_{18}H_{16}O$: C, 87.06; H, 6.49%. Found: C, 87.23; H, 6.54%.

(*E*)-**2-(1-Methylethenyl)cyclopropyl 2-Phenylethenyl Ketone (18c) + (*E*)-2-Methyl-2-vinylcyclopropyl 2-Phenylethenyl Ketone (18c′).** A 58: 42 mixture (by GLC) of **18c** (trans: cis=3:2 (^{1}H NMR)) and **18c′** was obtained and their separation through column chromatography was unsuccessful. Colorless liquid; IR (neat) 1725 and 1720cm^{-1}; ^{1}H NMR ($CDCl_3$) *trans*-**18c**: δ= 1.15 (1H, dd, J=8.1 and 5.4Hz, ring CH_2), 1.21 (3H, s, Me), 1.65 (1H, dd, J=6.0 and 5.4Hz, ring CH_2), 2.36 (1H, dd, J=8.1 and 6.0Hz, ring CH), 5.07 (1H, dd, J=10.8 and 2.0Hz, CH_2=), 5.12 (1H, dd, J=17.3 and 2.0Hz, CH_2=), 5.59 (1H, dd, J=16.2 and 10.8 Hz, =CH), 6.87 (1H, d, J=16.2Hz, =CH), and 7.4–7.6 (6H, m, Ph and =CH); *cis*-**18c**: δ=1.0–2.5 (6H, m including one s at 1.39, Me, ring CH_2, and CH), 4.6–5.9 (3H, m, CH=CH_2), 6.86 (1H, d, J=16.2Hz, =CH), and 7.4–7.6 (6H, m, Ph and =CH); *trans*-**18c′**: δ=1.25 (1H, ddd, J=8.6, 7.0, and 3.8Hz, ring CH_2), 1.51 (1H, ddd, J=8.6, 4.8, and 3.8Hz, ring CH_2), 1.71 (3H, s, Me), 2.1–2.2 (1H, m, ring CH), 2.3–2.3 (1H, m, ring CH), 4.5–4.8 (2H, m, =CH_2), 6.89 (1H, d, J=16.2Hz, =CH), and 7.4–7.6 (6H, m, Ph and =CH); MS *m/z* (rel intensity, %) 212 (M^+, 16), 131 (base peak), 103 (38), and 76 (26). HRMS Calcd for $C_{15}H_{16}O$: M, 212.1200. Found: *m/z* 212.1200.

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