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Transformation of γ-ketoaldehyde acetals into 3-substituted-2-cyclopentenones via cyanophosphates under mild conditions

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ABSTRACT

The reaction of cyanophosphates, which are readily derived from γ-ketoaldehyde acetals, with $TMSN_3$ (3 eq)/Bu_2SnO (0.3 eq) in refluxing toluene directly furnished 3-substituted-2-cyclopentenones in modest to good yield under mild conditions. The present method was further applied toward the synthesis of dechlorotrichodenone C isolated from Trichoderma asperellum.

1. Introduction

Cyanophosphates (**2**, CPs) [1] were initially developed by our group in 1983 as a novel intermediate for one-carbon homologation [2]. Since then, CPs have been extensively utilized as useful synthetic intermediates in organic synthesis [1]. That is based on the facile preparation of CPs from carbonyl compounds **1** using diethyl phosphorocyanidate [$(EtO)_2P(O)CN$, DEPC] [1] in the presence of a catalytic amount of lithium cyanide [2b]. On the other hand, α-hydroxy-tetrazoles [3] and α-cyano-mesylates [4] have been reported to generate alkylidene carbenes [5] via the decomposition of their tetrazole-intermediates, but they have some drawbacks such as the need for a strong base, substrate dependence, and high cost of reagents [5]. We recently clarified the potential of CPs as latent alkylidene carbenes, as illustrated in Scheme 1, in which the two-step transformation of carbonyl compounds **1** into homologous alkynes **7** [6a,d] as well as five-membered unsaturated cyclic compounds **8** [6b,c] have been conducted efficiently under nearly neutral conditions [1b,7]. The reactions of CPs **2** with trimethylsilyl azide ($TMSN_3$) in the presence of a catalytic amount of dibutyltin oxide (Bu_2SnO) generates alkylidene carbenes **6** via fragmentation of putative tetrazolylphosphate intermediate **3** with the elimination of diethyl trimethylsilylphosphate (TMS-phosphate, **4**) and 2 mol of dinitrogen [6,7].

The intramolecular [1,5]-C–H bond insertion reaction of alkylidene carbenes is a useful method for the construction of cyclopentene skeletons [5]. In 2000, Shioiri and co-workers revealed that the reaction of γ-ketoaldehyde acetals **9** with lithium trimethylsilyldiazomethane [$TMSC(Li)N_2$] [8], which was prepared upon the reaction of trimethylsilyldiazomethane ($TMSCHN_2$) [9] with *n*-BuLi, efficiently affords ketal-protected 2-cyclopentenones **12** via a [1,5]-C–H insertion reaction of their alkylidene carbenes **11** into acetals bearing a stereogenic center; and the ketal protecting group in **12** was removed using 1 *N* aqueous HCl to furnish 3-substituted 2-cyclopentenones **13**, as shown at the bottom of Scheme 2 [10]. This inspired our group to study the transformation of CPs **10** bearing a 1,3-dioxane functionality into cyclopentenones **13** (Scheme 2, the top). Herein we report the transformation of γ-ketoaldehyde acetals **9** into 3-substituted-2-cyclopentenones **13** via CPs **10** under mild conditions. Interestingly, the deprotection of ketal intermediate **12** was spontaneously caused by the secondary action of TMS-phosphate **4** formed *in situ*. In addition, the present method has been applied to the synthesis of dechlorotrichodenone C (**21**) isolated from *Trichoderma asperellum*.

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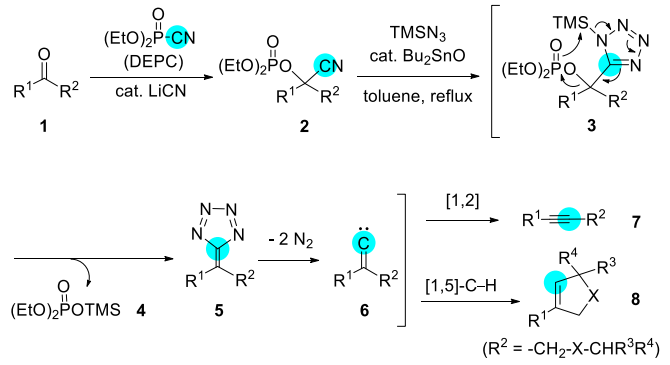
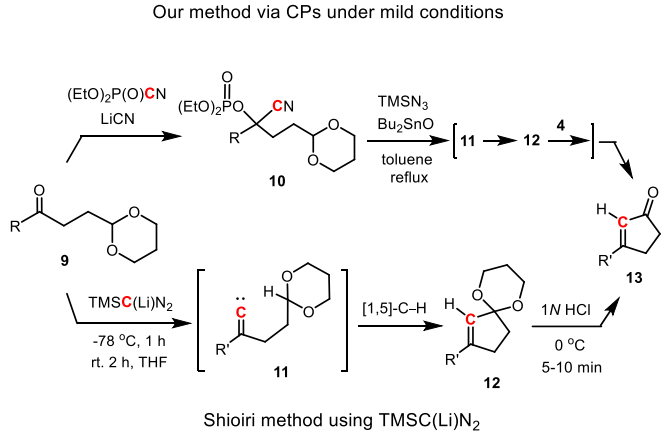


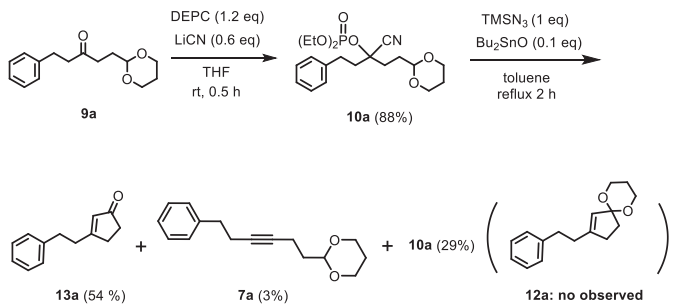
Scheme 1. Synthesis of homologous alkynes **7** and five-membered cyclic compounds **8** from carbonyl compounds **1** using CPs **2**.



Scheme 2. A comparison of the present and Shioiri methods used for the transformation of γ-ketoaldehyde acetals **9** into cyclopentenones **13**.

2. Results and discussion

When we first performed the reaction of CP **10a**, which was readily prepared via conventional cyanophosphorylation [2b,6a] of γ-ketoaldehyde acetal **9a**, with $TMSN_3$ [1 equivalent (eq)] in the presence of a catalytic amount of Bu_2SnO (0.1 eq) in refluxing toluene for 2 h, 3-phenethyl-2-cyclopentenone **13a** was obtained in 54% yield, accompanied by homologous alkyne **7a** (3%) and recovered CP **10a** (29%), as shown in Scheme 3. In contrast to the $TMSC(Li)N_2$ method, the transformation using CP **10a** indicates that it can directly provide cyclopentenone **13a** without the need of an acid-treatment step for ketal-protected intermediate **12a**.



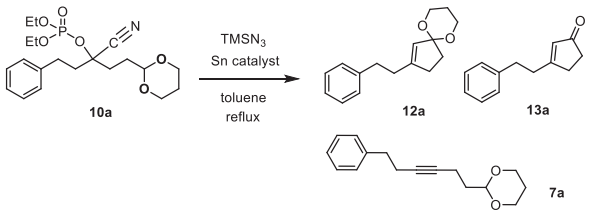
Scheme 3. Reaction of CP **10a** with $TMSN_3/Bu_2SnO$.

Subsequently, the reaction conditions used in the CP method were further investigated, as shown in Table 1. Increasing the amount of Bu_2SnO (0.1–0.3 eq) was effective and provided an improved yield of **13a** (80%) (entry 4), accompanied by a small amount of the [1,2]-rearrangement product **7a** (7%). On the other hand, we recently revealed a modified reagent system used for the synthesis of tetrazoles, in which the treatment of various nitriles with $TMSN_3$ and $Bu_2Sn(OAc)_2$ at 30 °C yielded their corresponding 5-substituted 1*H*-tetrazoles in excellent yield [11]. Application of this reagent system [$TMSN_3$ (3 eq) and $Bu_2Sn(OAc)_2$ (0.3 eq)] to CP **10a** in refluxing toluene for 2 h yielded cyclopentenone **13a** in 78% yield (entry 6). Accordingly, $Bu_2Sn(OAc)_2$ may be used as a Sn-based catalyst for the formation of cyclopentenones **13**, while the reaction at 30 °C proceeded sluggishly (60 h) to give a ketal-protected intermediate **12a** in 21% yield along with a large amount of recovered CP **10a** (65%) (entry 8).

Furthermore, we investigated the effect of the acetal moiety on the formation of cyclopentene product. Among the acetal functionalities studied, such as 1,3-dioxane, 1,3-dioxolane, dimethyl acetal, and 1,3-dithiane derivatives **10a**, **14**, **15**, and **16**, respectively (Table 2), 1,3-dioxane-protected CP **10a** was preferable to the other acetal-containing CPs as the acetal functionality in the starting γ-ketoaldehyde **9**, as indicated by Shioiri [8]. In addition, 1,3-dithiane-protected CP **16** gave only 1,3-dithiane protected 2-cyclopentenone in low yield (11%)(entry 4).

To study the scope and limitations of this transformation, the formation of cyclopentenones **13** from γ-ketoaldehyde acetals **9** was carried out upon the reaction of CP **10** with $TMSN_3/Bu_2SnO$, as shown in Table 3, using the synthetic procedure described above (Table 1, entry 4) [12]. First, phenethyl ketone CPs **10b–e**, which contain *para*-substituent on the phenyl ring (R^2 = Me, Cl, CH_3O, or CF_3), appear to afford their corresponding cyclopentenones **13b–e** in modest to high yield (48–85%), accompanied by a small amount of the [1,2]-rearrangement product **7b–e** (4–8%). (Table 3, entries 2–5). However, the reaction was dependent on the type of substrate used. The transformations of furan-2-yl-ethyl, thiophen-2-yl-ethyl, and indol-2-yl-ethyl ketone CPs **10f**, **10g**, and **10h** resulted in low yields of cyclopentenones **13f** (21%), **13g** (31%), and **13h** (11%),

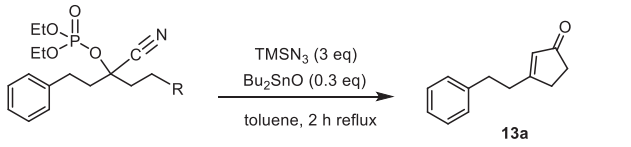
Table 1
Investigation of the reaction conditions used for the transformation of CP **10a** into cyclopentenone **13a**.



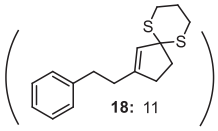
Entry	$TMSN_3$ (eq.)	Sn catalyst (eq.)	Time (h)	Yield (%) 12a	13a	7a	10a
		Bu_2SnO					
1	1	0.1	2	0	54	3	29
2	1	0.1	6	0	56	5	13
3	2	0.2	2	0	72	6	trace
4	3	0.3	2	0	80	7	trace
		$Bu_2Sn(OAc)_2$					
5	2	0.2	2	0	71	5	19
6	3	0.3	2	0	78	7	12
7	3	0.3	6	0	57	9	trace
8[a]	3	0.3	60	21	0	0	65

[a] Reaction temperature: 30 °C.

Table 2
Investigation of the acetal functionality for cyclopentenone formation.



entry	acetal-bearing CP		**13a** (%)
1	**10a:**		80[a]
2	**14:**		50
3	**15:**		17
4	**16:**		0



[a]see Table 1, entry 4

respectively (entries 6-8). The reaction of methyl ketone CP **10i** (R^1 = CH_3) proceeded successfully, but the isolated yield of 3-methylcyclopentenone **13i** was 63% due to its low boiling point (150–160 °C) (entry 9). In the cases of CPs **10j** (R^1 = pentyl) and **10k** (R^1 = isopentyl) bearing linear alkyl groups, the competitive acetal C–H and alkyl C–H insertion reactions of the alkylidene carbene occurred (entries 10 and 11), which is similar to that observed using the TMSC(Li)N_2 method [8], that is, the reaction of CP **10j** shows selectivity toward acetal C–H insertion to produce cyclopentenone **13j** (53%) and cyclopentene **17j** (11%), respectively (entry 10), while that of CP **10k** was slightly selective toward tertiary alkyl C–H insertion, yielding **13k** (37%) and **17k** (42%) (entry 11) [13]. The reaction of cyclohexylketone-CP **10l** with $TMSN_3$/Bu_2SnO in refluxing toluene for 10 h gave its corresponding cyclopentene product **13l** in 38% yield (entry 12). The presence of the *tert*-butyl group in CP **10m** was not compatible with these reaction conditions with recovery of **10m** (98%) (entry 13), probably which was attributed to steric hindrance. The reaction of **10m** with the alternative reagent system [$TMSN_3$/$Bu_2Sn(OAc)_2$] did not occur. In contrast, the TMSC(Li)N_2 method furnished **13l** (89%) and **13m** (54%) in good yield from their respective secondary and tertiary ketones **9l** and **9m** (entries 12 and 13) [8]. CP **10n** derived from cyclohexanone **9n** afforded a two-ring fused 2-cyclopentenone product **13n** in 12% yield along with a dephosphorylated compound **18** (15%) (entry 14). In addition, phenyl ketone CP **10o** gave only the [1,2]-rearrangement-product **7o** in 78% yield (entry 15), which was in accordance with that reported by Shioiri [8]. The reaction of methoxyethylketone CP **10p** with $TMSN_3$/Bu_2SnO afforded only a trace amount of cyclopentenone **13p** (entry 16), along with an unexpected azide derivative **19** (28%) [see Supplementary data (S.D.)].

(−)-Trichodenone C (**22**) was first isolated in 1998 in our laboratory from a strain of *Trichoderma harzianum* (OUPS—N115), which exhibits cytotoxicity against cultured P388 cells [14]. Furthermore, we determined the stereochemistry of trichodenones A–C using a synthetic study starting from optically active cyclopentenones, in which **22** was prepared via the chlorination of dechlorotrichodenone C (**21**) [15]. Shioiri and co-workers have also efficiently synthesized trichodenone C using the TMSC(Li)N_2 method over eight steps from methyl (*R*)-lactate [8]. In 2018, Ji and co-workers isolated dechlorotrichodenone C (**21**) from *Trichoderma asperellum* cf44-2 [16]. In this context, our attention was turned to the application of the present method to **21**, as shown in Scheme 4. Ketone **9q** was prepared upon the reaction of commercially available (*R*)-2-acetoxypropionic acid chloride (**20**) with 2-(1,3-dioxan-2-yl)ethylmagnesium bromide in 89% yield. Treatment of **9q** with DEPC in the presence of LiCN gave CP **10q** (quant). The reaction of **10q** with $TMSN_3$/Bu_2SnO in refluxing toluene for 4 h afforded the desired 2-cyclopentenone **13q** in 46% yield. Then, acid hydrolysis of **13q** yielded dechlorotrichodenone C [**21**, 82%; $[\alpha]_D$ −1.6 (c 1.00, $CHCl_3$)] [17] in a 33.6% overall yield in four steps from the starting acid chloride **20**. Synthetic **21** was identical to that of natural dechhlorotrichodenone C based on a comparison of their ^{1}H NMR, ^{13}C NMR, and HRMS data [15,16]. Thus, chlorination (Cl_2, Et_3N) [15] of **21** as previously described may provide **22**.

A plausible mechanism for the present reaction is proposed in Scheme 5. As this procedure does not require an acid treatment step, we focused on the role of TMS-phosphate **4** [18] which was excluded through the fragmentation of tetrazolylphosphates **3**, as indicated in Scheme 1. TMS-phosphate **4** can activate the C–O bond in 1,3 dioxane **12** to form an oxonium-cation intermediate **23**. Subsequent elimination of oxetane from **23** produces 2-cyclopentenone **13** (eq. 1 in Scheme 5). Indeed, the reaction of protected 2-cyclopentenone **12a** with **4** (1 eq) readily provides cyclopentenone **13a** in 93% yield in refluxing toluene for 1 h (eq. 2), while that of **12a** with $TMSN_3$ did not give **13a** (eq. 3). Although TMS-phosphate **4** has not been greatly documented in the literature [18], it should be noted that TMS-phosphate may be used as an activating agent for the cleavage of cyclic acetals [19].

3. Conclusions

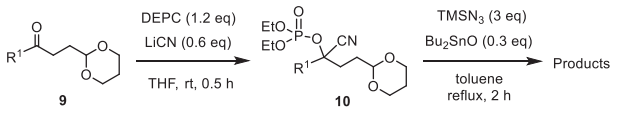
In this study, we have demonstrated that the reaction of CPs **10**, which are readily derived from γ-ketoaldehyde acetals **9**, with $TMSN_3$/Bu_2SnO in refluxing toluene directly affords 3-substituted-2-cyclopentenones **12** under nearly neutral conditions in modest to good yield, with a reasonable substrate scope. The present method complements the TMSC(Li)N_2 method, which requires strong basic and acidic conditions. The procedure was further applied to the synthesis of dechlorotrichodenone C. In addition, the role of TMS-phosphate **4** as the cleavage agent of 1,3-dioxane ketals was indicated. Furthermore, this study contributes to the diversity of CPs as key intermediates in a variety of organic synthesis [1].

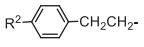
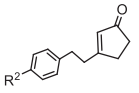
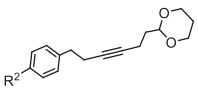
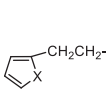
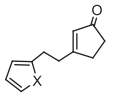
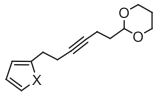
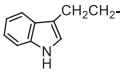
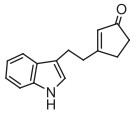
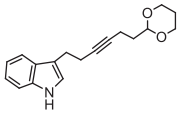
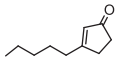
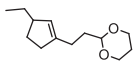
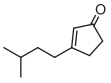
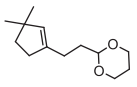
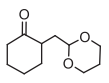
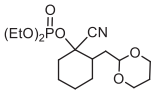
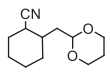
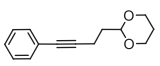
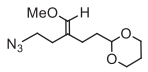
4. Experimental

4.1. General information

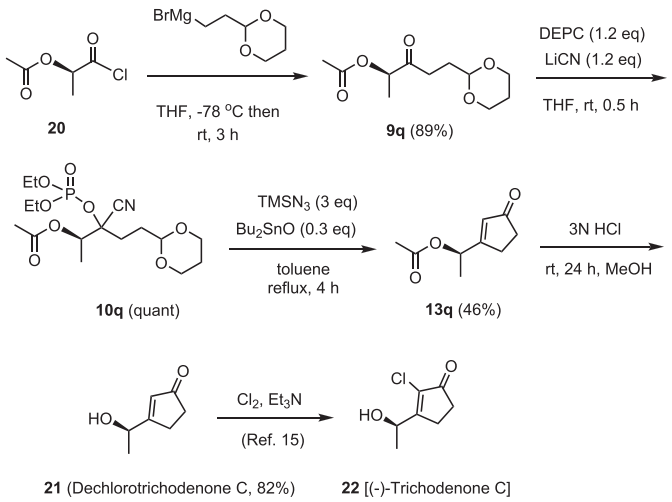
All reactions were carried out under an argon atmosphere. Super dehydration solvents (toluene and THF) were purchased from the WAKO Chemical Company. Fuji Silysia FL-60D silica gel was used for flash column chromatography. Thin layer chromatography was performed using pre-coated plates (WAKO silica gel 70 F_{254}). ^{1}H NMR spectroscopy was recorded on an Agilent 400-MR-DD2 spectrometer in $CDCl_3$ using tetramethylsilane (TMS) as an internal standard. Coupling constants (*J*) were reported in Hertz (Hz). For multiplicities the following abbreviations were used: s (singlet), d (doublet), t (triplet), q (quartet), quint (quintet), sext (sextet), sept (septet), m (multiplet), and br (broad). ^{13}C NMR spectroscopy was recorded on an Agilent 400-MR-DD2 spectrometer in $CDCl_3$.

Table 3
Synthesis of 2-cyclopentenes **13** from acyclic γ-ketoaldehyde acetals **9**.

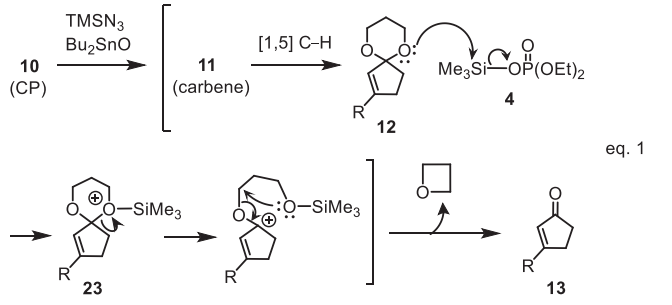


	9: R^1	10 (%)	product (%)[a]	
				
1	**9a** (R^2 = H) :	**10a** : 88	**13a** : 80 (82)[b]	**7a** : 7
2	**9b** (R^2 = CH_3) :	**10b** : 82	**13b** : 48	**7b** : 5
3	**9c** (R^2 = Cl) :	**10c** : 88	**13c** : 85	**7c** : 4
4	**9d** (R^2 = CH_3O) :	**10d** : 86	**13d** : 76	**7d** : 4
5	**9e** (R^2 = CF_3) :	**10e** : 86	**13e** : 58	**7e** : 8
				
6	**9f** (X = O) :	**10f** : 99	**13f** : 21	**7f** : 3
7	**9g** (X = S) :	**10g** : 98	**13g** : 31	**7g** : 12
				
8	**9h**	**10h** : 99	**13h** : 11	**7h** : 6
				
9	**9i** : CH_3-	**10i** : 83	**13i** : 63	–
				
10	**9j** : CH_3-$(CH_2)_4$-	**10j** : quant	**13j** : 53 (82)[b]	**17j** : 11 (7)[b]
				
11	**9k** : 	**10k** : quant	**13k** : 37 (41)[b]	**17k** : 42 (46)[b]
				
12	**9l** : 	**10l** : 84	**13l** : 38[c] (89)[b]	**10l** : 72
				
13	**9m** : ^{t}Bu-	**10m** : 98	**13m** : trace (54)[b]	**10m** : 98
				
14	**9n**	**10n** : quant	**13n** : 12 (15)[b,d]	**18** :15%[d]
15	**9o** : 	**10o** : 98	–	 **7o** : 78 (73)[b]
16	**9p** : $MeOCH_2CH_2$-	**10p** : 93	**13p** : (trace)	 **19** : 28%[e]

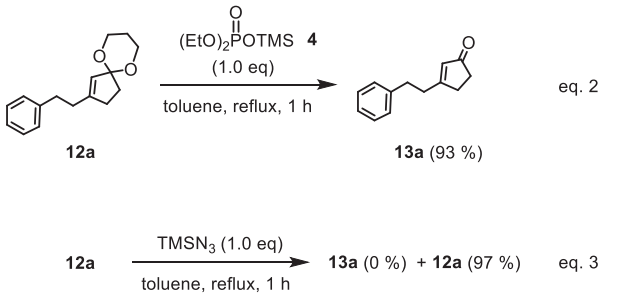
[a]Isolated yield. [b]The numbers in the parentheses are the yields obtained from **9** by using the TMSC(Li)N_2 method (Ref. 8). [c]Heated at reflux for 10 h in toluene. [d]**13n** and **18** (S.D.) was obtained as a mixture. [e]Azide compound **19** was obtained as a by-product (see S.D.).



Scheme 4. Synthesis of dechlorotrichodenone (**21**) using the present method.



Cf.) Reaction of 1,3-dioxane-protected cyclopentenone **12a** with TMS-phosphate



Scheme 5. A plausible mechanism for the formation of cyclopentenones **13** from ketal-protected intermediate **12**.

Chemical shifts (δ) were given relative to $CDCl_3$ (77.0 ppm). High-resolution mass spectra were obtained using a JMS-700(2) double-focusing magnetic sector mass spectrometer (JOEL Ltd., Tokyo, Japan) operated in positive-ion mode, with 3-nitrobenzyl alcohol (NBA)-NaCl. Infrared spectroscopy was recorded on an IR Affinity-1S Fourier transformation-infrared spectrometer (Shimadzu, Kyoto, Japan). Specific rotations were measured using a JASCO P-2300 spectrometer (JASCO Co., Tokyo, Japan).

4.2. General procedure for the synthesis of CPs **10** [2b,6a]

DEPC (0.18 mL, 1.2 mmol) and LiCN (20 mg, 0.6 mmol) were added to a solution of ketone **9** (1 mmol) in THF (5 mL). The reaction mixture was stirred for 0.5 h at room temperature (rt). Then, the reaction mixture was diluted with AcOEt and washed using saturated NH_4Cl and brine. The organic layer was dried over Na_2SO_4, filtered and evaporated to give a crude residue, which was purified by column chromatography (Hexane–AcOEt = 1:1) to give CP **10**.

4.2.1. 3-Cyano-1-(1,3-dioxan-2-yl)-5-phenylpentan-3-yl diethyl phosphate (**10a**)

Yield: 88% (360 mg); oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.32–1.40 (m, 7H), 1.80–1.95 (m, 2H), 2.00–2.24 (m, 1H), 2.25–2.42 (m, 4H), 2.79–2.94 (m, 2H), 3.72–3.80 (m, 2H), 4.07–4.23 (m, 6H), 4.61 (t, J = 4.8 Hz, 1H), 7.19–7.33 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 16.0 (15.96), 16.0 (16.03), 16.1, 25.6, 28.6 (28.57), 28.6 (28.62), 29.5, 30.1, 33.0, 33.1, 40.5 (40.48), 40.5 (40.52), 63.6 (63.56), 63.6 (63.61), 64.4, 64.5 (64.48), 64.5 (64.50), 64.5 (64.54), 67.0, 77.7, 77.8, 100.7, 117.7, 117.8, 126.4, 128.3, 128.6, 128.7, 139.7; HRMS (EI): *m/z* calcd for $C_{20}H_{29}NO_6P$ $[M - H]^+$ 410.1734, found 410.1732.

4.2.2. 3-Cyano-1-(1,3-dioxan-2-yl)-5-(4-methylphenyl)pentan-3-yl diethyl phosphate (**10b**)

Yield: 82% (350 mg); oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.32–1.40 (m, 7H), 1.80–1.94 (m, 2H), 2.00–2.11 (m, 1H), 2.12–2.40 (m, 4H), 2.32 (s, 3H), 2.74–2.90 (m, 2H), 3.72–3.80 (m, 2H), 4.06–4.23 (m, 6H), 4.61 (t, J = 4.8 Hz, 1H), 7.10 (s, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 16.0 (15.97), 16.0 (16.04), 16.1, 21.0, 25.6, 28.6 (28.57), 28.6 (28.62), 29.5, 29.6, 33.0, 33.1, 40.6. 40.7, 63.6, 64.4, 64.5 (64.49), 64.5 (64.54), 66.8, 77.7, 77.8, 100.7, 117.7, 117.8, 128.2, 129.2, 135.9, 136.6; HRMS (EI): *m/z* calcd for $C_{21}H_{33}NO_6P$ $[M - H]^+$ 426.2045, found 426.2043.

4.2.3. 5-(4-Chlorophenyl)-3-cyano-1-(1,3-dioxan-2-yl)pentan-3-yl diethyl phosphate (**10c**)

Yield: 88% (390 mg); oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.32–1.40 (m, 7H), 1.79–1.94 (m, 2H), 2.00–2.40 (m, 5H), 2.77–2.92 (m, 2H), 3.72–3.80 (m, 2H), 4.07–4.23 (m, 6H), 4.61 (t, J = 4.8 Hz, 1H), 7.15 (d, J = 8.4 Hz, 2H), 7.26 (d, J = 8.4 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 16.0, 16.1 (16.06), 16.1 (16.14), 25.6, 29.5, 33.0, 33.1, 40.3, 40.4, 64.5, 64.6 (64.57), 64.6 (64.60), 64.6 (64.63), 66.8, 76.8, 77.2, 77.6, 77.7, 100.6, 117.6, 117.7, 128.7, 129.7, 132.2, 138.2; HRMS (EI): *m/z* calcd for $C_{20}H_{28}{}^{35}ClNO_6P$ $[M - H]^+$ 444.1342, found 444.1344.

4.2.4. 3-Cyano-1-(1,3-dioxan-2-yl)-5-(4-methoxyphenyl)pentan-3-yl diethyl phosphate (**10d**)

Yield: 86% (380 mg); oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.32–1.40 (m, 7H), 1.80–1.94 (m, 2H), 2.00–2.38 (m, 5H), 2.73–2.88 (m, 2H), 3.72–3.80 (m, 2H), 3.79 (s, 3H), 4.07–4.23 (m, 6H), 4.61 (t, J = 4.8 Hz, 1H), 6.84 (d, J = 8.8 Hz, 2H), 7.13 (d, J = 8.8 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 16.0 (15.97), 16.0 (16.04), 16.1, 25.6, 29.2, 33.0, 33.1, 40.7, 40.8, 55.2, 64.5 (64.47), 64.5 (64.54), 66.8, 77.7, 77.8, 400.7, 114.0, 117.7, 117.8, 129.3, 131.7, 158.1; HRMS (EI): *m/z* calcd for $C_{21}H_{32}NO_7P$ $[M]^+$ 441.1916, found 441.1914.

4.2.5. 3-Cyano-1-(1,3-dioxan-2-yl)-5-(4-trifluoromethylphenyl) pentan-3-yl diethyl phosphate (**10e**)

Yield: 86% (410 mg); oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.32–1.40 (m, 7H), 1.80–1.95 (m, 2H), 2.00–2.44 (m, 5H), 2.87–3.01 (m, 2H), 3.73–3.80 (m, 2H), 4.07–4.24 (m, 6H), 4.62 (t, J = 4.8 Hz, 1H), 7.35 (d, J = 8.0 Hz, 2H), 7.56 (d, J = 8.0 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 15.9 (15.86), 15.9 (15.93), 16.0 (15.95), 16.0 (16.02), 16.1, 16.2, 25.5, 28.5 (28.47), 28.5 (28.51), 29.4, 29.9, 32.9, 33.0, 40.0, 40.1, 63.5 (63.47), 63.5 (63.52), 64.3, 64.4, 64.5 (64.46), 64.5 (64.51), 64.6, 66.7, 77.4, 77.5, 100.5, 117.5 (117.47), 117.5 (117.52), 124.1 (q, J = 271 Hz), 125.4 (q, J = 3.8 Hz), 128.7, 128.7 (q, J = 31.9 Hz), 143.8; HRMS (EI): *m/z* calcd for $C_{21}H_{28}F_3NO_6P$ $[M - H]^+$ 478.1606, found 478.1603.

*4.2.6. 3-Cyano-1-(1,3-dioxan-2-yl)-5-(furan-2-yl)pentan-3-yl diethyl phosphate (**10f**)*

Yield: 99% (398 mg); oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.31–1.38 (m, 7H), 1.79–1.93 (m, 2H), 2.00–2.46 (m, 5H), 2.83–2.98 (m, 2H), 3.72–3.80 (m, 2H), 4.06–4.22 (m, 6H), 4.60 (t, J = 4.8 Hz, 1H), 6.05 (dd, J = 3.2, 0.8 Hz, 1H), 6.28 (dd, J = 3.2, 1.6 Hz, 1H), 7.31 (dd, J = 3.2, 0.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 15.9, 16.0, 16.1 (16.05), 16.1 (16.12), 22.7, 25.6, 29.4, 33.0 (33.00), 33.0 (33.04), 37.0 (36.97), 37.0 (37.01), 64.5, 64.6, 66.8, 100.6, 105.6, 110.2, 117.4, 117.5, 141.3, 153.1; HRMS (EI): *m/z* calcd for $C_{18}H_{27}NO_7P$ $[M-H]^+$ 400.1525, found 400.1523.

*4.2.7. 3-Cyano-1-(1,3-dioxan-2-yl)-5-(thiophen-2-yl)pentan-3-yl diethyl phosphate (**10g**)*

Yield: 98% (406 mg); oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.32–1.40 (m, 7H), 1.80–1.94 (m, 2H), 2.00–2.49 (m, 5H), 3.02–3.18 (m, 2H), 3.72–3.80 (m, 2H), 4.06–4.24 (m, 6H), 4.61 (t, J = 4.8 Hz, 1H), 6.84 (dd, J = 3.6, 1.2 Hz, 1H), 6.92 (dd, J = 4.8, 3.6 Hz, 1H), 7.15 (dd, J = 4.8, 1.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 15.9, 16.0, 16.1, 24.3, 25.6, 28.5, 29.5, 33.0, 33.1, 40.5, 40.6, 63.5, 63.6, 64.4, 64.5, 64.6, 66.8, 77.3, 100.6, 117.4, 117.5, 123.6, 124.7, 126.9, 142.0; HRMS (EI): *m/z* calcd for $C_{18}H_{27}NO_6PS$ $[M-H]^+$ 416.1297, found 416.1291.

*4.2.8. 3-Cyano-1-(1,3-dioxan-2-yl)-5-(1H-indol-3-yl)pentan-3-yl diethyl phosphate (**10h**)*

Yield: 99% (444 mg); oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.30–140 (m, 7H), 1.82–1.94 (m, 2H), 2.00–2.14 (m, 2H), 1.98–2.53 (m, 3H), 2.94–3.10 (m, 2H), 3.72–3.80 (m, 2H), 4.07–4.30 (m, 6H), 4.61 (t, J = 4.8 Hz, 1H), 7.01 (brs, 1H), 7.12 (td, J = 7.6, 1.2 Hz, 1H), 7.19 (td, J = 7.6, 1.2 Hz, 1H), 7.37 (dt, J = 7.6, 1.2 Hz, 1H), 7.61 (d, J = 7.6 Hz, 1H), 8.25 (brs, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 15.9, 16.0 (15.96), 16.0 (15.99), 16.1, 19.8, 25.6, 29.5, 33.0, 33.1, 39.2, 39.3, 64.5, 64.6, 65.2, 66.8, 77.9, 78.0, 100.7, 111.2, 113.9, 117.9, 118.5, 119.3, 121.4, 122.0, 127.0, 136.3; HRMS (EI): *m/z* calcd for $C_{22}H_{31}N_2O_6P$ $[M]^+$ 450.1920, found 450.1917.

*4.2.9. 3-Cyano-1-(1,3-dioxan-2-yl)butan-3-yl diethyl phosphate (**10i**)*

Yield: 83% (265 mg); oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.32–1.40 (m, 7H), 1.79–1.94 (m, 1H), 1.85 (s, 3H), 2.00–2.19 (m, 3H), 3.72–3.82 (m, 2H), 4.07–4.23 (m, 6H), 4.61 (t, J = 4.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 15.9, 16.0 (15.99), 16.0 (16.04), 16.1, 25.6, 26.3 (26.30), 26.3 (26.33), 29.6, 35.8 (35.76), 35.8 (35.82), 63.5, 63.6, 64.3, 64.4, 64.5, 66.8, 74.2, 74.3, 100.6, 118.5 (118.47), 118.5 (118.51); HRMS (EI): *m/z* calcd for $C_{13}H_{23}NO_6P$ $[M-H]^+$ 320.1263, found 320.1262.

*4.2.10. 3-Cyano-1-(1,3-dioxan-2-yl)octan-3-yl diethyl phosphate (**10j**)*

Yield: quant (380 mg); oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.90 (t, J = 6.8 Hz, 3H), 1.30–1.41 (m, 10H), 1.44–1.60 (m, 2H), 1.80–2.16 (m, 8H), 3.72–3.81 (m, 2H), 4.06–4.22 (m, 6H), 4.60 (t, J = 4.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 13.8, 15.9, 16.0 (15.95), 16.0 (16.01), 16.1, 22.3, 23.4, 25.6, 28.5, 28.6, 29.4, 31.2, 32.9 (32.89), 32.9 (32.94), 38.5 (38.47), 38.5 (38.51), 63.5, 63.6, 64.3, 64.4, 66.8, 71.2, 71.3, 78.1, 78.2, 100.8, 117.9, 118.0, 119.4 (119.35), 119.4 (119.39); HRMS (EI): *m/z* calcd for $C_{17}H_{31}NO_6P$ $[M-H]^+$ 376.1889, found 376.1888.

*4.2.11. 3-Cyano-1-(1,3-dioxan-2-yl)-6-methylheptan-3-yl diethyl phosphate (**10k**)*

Yield: quant (380 mg); oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.92 (d, J = 5.6 Hz, 6H), 1.32–1.50 (m, 8H), 1.59 (quint, J = 5.6 Hz, 1H), 1.80–2.16 (m, 8H), 3.72–3.80 (m, 2H), 4.06–4.22 (m, 6H), 4.60 (t, J = 4.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 15.9, 16.0 (16.00), 16.0 (16.04), 22.3, 22.4, 25.6, 27.8, 28.6 (28.56), 28.6 (28.60), 29.4, 32.5, 32.9, 33.0, 36.6 (36.61), 36.6 (36.64), 64.4 (64.38), 64.4 (64.43), 66.8, 71.2, 71.3, 78.2, 78.3, 100.8, 117.9, 118.0; HRMS (EI): *m/z* calcd for $C_{17}H_{31}NO_6P$ $[M-H]^+$ 376.1889, found 376.1889.

*4.2.12. 3-Cyano-3-cyclohexyl-1-(1,3-dioxan-2-yl)propyl diethyl phosphate (**10l**)*

Yield: 84% (325 mg); oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.12–1.40 (m, 12H), 1.66–2.22 (m, 11H), 3.75 (td, J = 12.0, 2.4 Hz, 2H), 4.06–4.23 (m, 6H), 4.58 (t, J = 4.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 16.0 (15.97), 16.0 (16.03), 16.1, 21.1, 25.6, 25.7, 25.8, 26.8, 29.0, 30.0, 30.1, 44.2, 44.3, 63.6, 63.7, 64.4, 64.5 (64.45), 64.5 (64.51), 66.8, 81.5, 81.6, 101.0, 117.5 (117.45), 117.5 (117.49); HRMS (EI): *m/z* calcd for $C_{18}H_{31}NO_6P$ $[M-H]^+$ 388.1889, found 388.1891.

*4.2.13. 3-Cyano-1-(1,3-dioxan-2-yl)-4,4-dimethylpentan-3-yl diethyl phosphate (**10m**)*

Yield: 98% (355 mg); oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.15 (s, 9H), 1.34–1.38 (m, 6H), 1.92–2.16 (m, 4H), 3.72–3.80 (m, 2H), 4.06–4.23 (m, 6H), 4.62 (t, J = 4.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 16.0 (15.96), 16.0 (15.97), 16.0 (16.02), 16.1, 25.3, 25.7, 29.4 (29.35), 29.4 (29.37), 30.7, 40.2 (40.15), 40.2 (40.19), 64.5 (64.47), 64.5 (64.54), 66.8 (66.79), 66.8 (66.80), 84.5, 84.7, 101.1, 116.7, 116.8; HRMS (EI): *m/z* calcd for $C_{16}H_{29}NO_6P$ $[M-H]^+$ 362.1733, found 362.1732.

*4.2.14. 2-[(1,3-Dioxan-2-yl)methyl]-1-cyanocyclohexyl diethyl phosphate (**10n**)*

Yield: quant (360 mg); oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.32–1.42 (m, 7H), 1.54–1.74 (m, 3H), 1.79–1.89 (m, 2H), 1.98–2.20 (m, 4H), 2.68–2.74 (m, 1H), 3.70–3.82 (m, 2H), 4.06–4.25 (m, 6H), 4.62–4.68 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 15.9 (15.91), 15.9 (15.92), 16.0 (15.98), 16.0 (16.00), 16.1, 20.1, 23.2, 24.1, 25.6, 26.4, 28.5, 28.6, 29.3, 35.6, 35.8, 36.1, 36.8, 41.0, 41.1, 42.3 (42.26), 42.3 (42.33), 63.5, 63.6, 64.2, 64.3, 64.4 (64.35), 64. 4 (64.41), 66.8, 76.8, 80.0, 80.1, 100.3 (100.26), 100.3 (100.34), 116.6, 116.7; HRMS (EI): *m/z* calcd for $C_{16}H_{27}NO_6P$ $[M-H]^+$ 360.1576, found 360.1577.

*4.2.15. 3-Cyano-1-(1,3-dioxan-2-yl)-3-phenylpropyl diethyl phosphate (**10o**)*

Yield: 98% (375 mg); oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.20–1.34 (m, 7H), 1.65 (ddt, J = 13.6, 12.4, 4.8 Hz, 1H), 1.82 (ddt, J = 13.2, 12.4, 4.8 Hz, 1H), 2.02 (qt, J = 12.4, 4.8 Hz, 1H), 2.32 (dddd, J = 14.0, 12.0, 4.8, 2.0 Hz, 1H), 2.48 (ddd, J = 14.0, 12.4, 4.8 Hz, 1H), 3.67–3.74 (m, 2H), 3.89–420 (m, 6H), 4.53 (t, J = 5.2 Hz, 1H), 7.39–7.45 (m, 3H), 7.58–7.62 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 15.8, 15.9 (15.86), 15.9 (15.92), 25.6, 29.9, 37.8 (37.76), 37.8 (37.83), 64.3, 64.4, 66.8, 79.3, 79.4, 100.6, 117.2 (117.21), 117.2 (117.24), 125.6, 128.7, 129.6, 136.4 (136.39), 136.4 (136.41); HRMS (EI): *m/z* calcd for $C_{18}H_{26}NO_6P$ $[M]^+$ 383.1497, found 383.1496.

*4.2.16. 3-Cyano-1-(1,3-dioxan-2-yl)-5-methoxypentan-3-yl diethyl phosphate (**10p**)*

Yield: 93% (365 mg); oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.32–1.39 (m, 6H), 1.83–1.90 (m, 2H), 1.93–2.13 (m, 2H), 2.14–2.20 (m, 2H), 2.28 (dt, J = 14.4, 6.4 Hz, 1H), 2.41 (dt, J = 14.4, 6.4 Hz, 1H), 3.45 (s, 3H), 3.62 (t, J = 6.4 Hz, 2H), 3.72–3.81 (m, 2H), 4.07–4.22 (m, 6H), 4.59 (t, J = 5.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 15.9, 16.0, 16.1 (16.05), 16.1 (16.12), 25.6, 25.7, 29.5, 33.8 (33.79), 33.8 (33.83), 35.8, 35.9, 38.2 (38.20), 38.2 (38.23), 58.8, 63.1, 63.2, 63.6, 63.7, 64.4, 64.5, 64.6, 66.8, 67.4, 76.5, 76.6, 98.9, 100.8, 117.5, 117.6; HRMS (EI): *m/z* calcd for $C_{15}H_{27}NO_7P$ $[M-H]^+$ 364.1525, found 364.1522.

4.3. General procedure for the reaction of CPs (**10**) with $TMSN_3$/Bu_2SnO

$TMSN_3$ (0.39 mL, 3 mmol) and Bu_2SnO (75 mg, 0.3 mmol) were added to a solution of CP **10** (1 mmol) in toluene (10 mL). The reaction mixture was refluxed for 2 h. The solvent was evaporated to give a crude residue, which was purified by column chromatography (Hexane–AcOEt = 9:1 to 7:3) to give cyclopentenone **13** together with alkyne **7**.

4.3.1. 2-(6-Phenylhex-3-yn-1-yl)-1,3-dioxane (**7a**)

Yield: 7% (17 mg); oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.33 (dsept, J = 13.2, 2.0 Hz, 1H), 1.74 (td, J = 7.2, 5.2 Hz, 2H), 2.06 (qt, J = 13.2, 5.2 Hz, 1H), 2.24 (tt, J = 7.6, 2.4 Hz, 2H), 2.44 (tt, J = 7.6, 2.4 Hz, 2H), 2.80 (t, J = 7.2 Hz, 2H), 3.75 (tdd, J = 11.2, 2.4, 1.6 Hz, 2H), 4.08 (ddt, J = 11.2, 4.8, 1.6 Hz, 2H), 4.57 (t, J = 5.2 Hz, 1H), 7.16–7.32 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 13.6, 20.9, 25.8, 34.3, 34.8, 35.4, 66.8, 69.6, 80.0, 100.9, 125.8, 126.1, 128.3 (128.27), 128.3 (128.31), 128.4, 140.9, 141.5; HRMS (EI): m/z calcd for $C_{16}H_{20}O_2$ $[M]^+$ 244.1463, found 244.1460.

4.3.2. 3-Phenethylcyclopent-2-en-1-one (**13a**)

Yield: 80% (149 mg); wax. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.39–2.42 (m, 2H), 2.57–2.65 (m, 2H), 2.74 (t, J = 8.0 Hz, 2H), 2.92 (t, J = 8.0Hz, 2H), 5.99 (quint, J = 1.6 Hz, 1H), 7.18–7.35 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 31.7, 33.2, 35.0, 35.2, 126.3, 128.1, 128.5, 129.8, 140.4, 181.8, 210.0; HRMS (EI): m/z calcd for $C_{13}H_{14}O$ $[M]^+$ 186.1045, found 186.1041.

4.3.3. 2-[6-(p-Tolyl)hex-3-yn-1-yl]-1,3-dioxane (**7b**)

Yield: 5% (13 mg); oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.34 (dsept, J = 12.8, 2.4 Hz, 1H), 1.74 (td, J = 7.2, 5.6 Hz, 2H), 2.06 (qt, J = 12.8, 4.8 Hz, 1H), 2.24 (tt, J = 7.2, 2.4 Hz, 2H), 2.32 (s, 3H), 2.42 (tt, J = 7.6, 2.4 Hz, 2H), 2.76 (t, J = 7.6 Hz, 2H), 3.70–3.78 (m, 2H), 4.09 (qt, J = 5.2, 1.2 Hz, 2H), 4.57 (t, J = 5.2 Hz, 1H), 7.11 (s, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 13.6, 21.0, 25.8, 34.3, 35.0, 66.8, 66.9, 79.7, 79.8, 100.9, 128.2, 128.3, 129.0, 135.6, 137.9; HRMS (EI): m/z calcd for $C_{17}H_{20}O_2$ $[M]^+$ 258.1620, found 258.1621.

4.3.4. 3-(4-Methylphenethyl)cyclopent-2-en-1-one (**13b**)

Yield: 48% (96 mg); oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.32 (s, 3H), 2.38–2.42 (m, 2H), 2.57–2.60 (m, 2H), 2.72 (t, J = 8.0 Hz, 2H), 2.87 (t, J = 8.0Hz, 2H), 5.98 (quint, J = 1.6 Hz, 1H), 7.08 (d, J = 8.0 Hz, 2H), 7.11 (d, J = 8.0 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.0, 31.7, 32.8, 35.1, 35.2, 128.0, 129.2, 129.8, 135.8, 137.4, 182.0, 210.1; HRMS (EI): m/z calcd for $C_{14}H_{16}O$ $[M]^+$ 200.1201, found 200.1203.

4.3.5. 2-[6-(4-chlorophenyl)hex-3-yn-1-yl]-1,3-dioxane (**7c**)

Yield: 4% (11 mg); oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.28 (dsept, J = 12.8, 1.2 Hz, 1H), 1.73 (td, J = 7.2, 5.2 Hz, 2H), 2.06 (qt, J = 12.8, 5.2 Hz, 1H), 2.22 (tt, J = 7.2, 2.4 Hz, 2H), 2.42 (tt, J = 7.2, 2.4 Hz, 2H), 2.76 (t, J = 7.2 Hz, 2H), 3.68–3.76 (m, 2H), 4.09 (ddt, J = 10.8, 4.8, 1.2 Hz, 2H), 4.52 (t, J = 5.2 Hz, 1H), 7.15 (d, J = 8.4 Hz, 2H). 7.26 (d, J = 8.4 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 13.5, 20.7, 25.8, 34.2, 34.6, 66.8, 79.1, 80.4, 100.8, 128.3, 129.9, 131.9, 139.3; HRMS (EI): m/z calcd for $C_{16}H_{19}{}^{35}ClO_2$ $[M]^+$ 278.1073, found 278.1072.

4.3.6. 3-(4-Chlorophenethyl)cyclopent-2-en-1-one (**13c**)

Yield: 85% (188 mg); oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.39–2.45 (m, 2H), 2.57–2.65 (m, 2H), 2.71 (t, J = 8.0 Hz, 2H), 2.89 (t, J = 8.0 Hz, 2H), 5.97 (quint, J = 1.6 Hz, 1H), 7.13 (d, J = 8.4 Hz, 2H), 7.27 (d, J = 8.4 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 31.6, 32.5, 34.8, 35.2, 128.6, 129.5, 129.9, 132.1, 138.9, 181.2, 209.8; HRMS (EI): m/z calcd for $C_{13}H_{13}{}^{35}ClO$ $[M]^+$ 220.0655, found 220.0651.

4.3.7. 2-[6-(4-Methoxyphenyl)hex-3-yn-1-yl]-1,3-dioxane (**7d**)

Yield: 4% (11 mg); oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.33 (dsept, J = 13.2, 1.2 Hz, 1H), 1.74 (td, J = 7.2, 5.6 Hz, 2H), 2.06 (qt, J = 13.2, 4.8 Hz, 1H), 2.24 (tt, J = 7.2, 2.4 Hz, 2H), 2.40 (tt, J = 7.6, 2.4 Hz, 2H), 2.74 (t, J = 7.2 Hz, 2H), 3.70–3.80 (m, 2H), 3.79 (s, 3H), 4.09 (qt, J = 5.2, 1.2 Hz, 2H), 4.57 (t, J = 5.2 Hz, 1H), 6.84 (d, J = 8.4 Hz, 2H), 7.14 (d, J = 8.4 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 13.6, 21.2, 25.8, 34.3, 34.5, 55.2, 66.8, 79.7, 79.9, 100.6, 113.7, 129.4, 133.1, 157.9; HRMS (EI): m/z calcd for $C_{17}H_{22}O_3$ $[M]^+$ 274.1569, found 274.1568.

4.3.8. 3-(4-Methoxyphenethyl)cyclopent-2-en-1-one (**13d**)

Yield: 76% (164 mg); oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.38–2.42 (m, 2H), 2.56–2.60 (m, 2H), 2.70 (t, J = 7.6 Hz, 2H), 2.86 (t, J = 7.6 Hz, 2H), 3.79 (s, 3H),5.97 (quint, J = 1.6 Hz, 1H), 6.84 (d, J = 8.4 Hz, 2H), 7.11 (d, J = 8.4 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 31.7, 32.4, 35.2, 35.3, 55.2, 113.9, 129.0, 129.8, 132.5, 158.0, 181.9; HRMS (EI): m/z calcd for $C_{14}H_{16}O_2$ $[M]^+$ 216.1150, found 216.1149.

4.3.9. 2-[6-(4-Trifluoromethylphenyl)hex-3-yn-1-yl]-1,3-dioxane (**7e**)

Yield: 8% (20 mg); oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.30–1.36 (m, 1H), 1.70–1.76 (m, 2H), 2.02–2.13 (m, 1H), 2.23 (t, J = 7.2 Hz, 2H), 2.47 (t, J = 7.2 Hz, 2H), 2.85 (t, J = 7.2 Hz, 2H), 3.66–3.74 (m, 2H), 4.05–4.12 (m, 2H), 4.53 (t, J = 5.2 Hz, 1H), 7.34 (d, J = 8.0 Hz, 2H), 7.55 (d, J = 8.0 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 13.5, 20.5, 25.8, 34.3, 35.1, 66.8, 78.8, 80.6, 100.8, 124.3 (q, J = 270.2 Hz), 125.2 (q, J = 3.8 Hz), 128.5 (q, J = 34.9 Hz), 128.7, 128.8, 141.9; HRMS (EI): m/z calcd for $C_{17}H_{19}F_3O_2$ $[M]^+$ 258.1620, found 258.1621.

4.3.10. 3-(4-Trifluoromethylphenethyl)cyclopent-2-en-1-one (**13e**)

Yield: 58% (147 mg); oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.40–2.44 (m, 2H), 2.59–2.63 (m, 2H), 2.76 (t, J = 8.0 Hz, 2H), 2.99 (t, J = 8.0Hz, 2H), 5.99 (quint, J = 1.6 Hz, 1H), 7.32 (d, J = 8.0 Hz, 2H), 7.56 (d, J = 8.0 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 31.6, 32.9, 34.5, 35.2, 124.1 (q, J = 270.2 Hz), 125.5 (q, J = 3.8 Hz), 128.5, 128.7 (q, J = 32.6 Hz), 129.9, 144.5, 180.8, 209.7; HRMS (EI): m/z calcd for $C_{14}H_{13}F_3O$ $[M]^+$ 254.0918, found 254.0916.

4.3.11. 2-[6-(Furan-2-yl)hex-3-yn-1-yl]-1,3-dioxane (**7f**)

Yield: 3% (7 mg); oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.32–1.38 (m, 1H), 1.74 (td, J = 7.2, 5.2 Hz, 2H), 2.02–2.12 (m, 1H), 2.24 (tt, J = 7.2, 2.4 Hz, 2H), 2.48 (tt, J = 7.2, 2.4 Hz, 2H), 2.82 (t, J = 7.6 Hz, 2H), 3.72–3.81 (m, 2H), 4.07–4.14 (m, 2H), 4.60 (t, J = 5.2 Hz, 1H), 6.07 (dd, J = 3.2, 0.8 Hz, 1H), 6.29 (dd, J = 3.2, 1.6 Hz, 1H), 7.31 (dd, J = 1.6, 0.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 13.6, 18.0, 25.8, 27.9, 34.3, 66.9, 79.1, 80.0, 100.9, 105.4, 110.1, 141.0, 154.6; HRMS (EI): m/z calcd for $C_{14}H_{18}O_3$ $[M]^+$ 234.1256, found 234.1255.

4.3.12. 3-[2-(Furan-2-yl)ethyl]cyclopent-2-en-1-one (**13f**)

Yield: 21% (37 mg); oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.39–2.42 (m, 2H), 2.57–2.61 (m, 2H), 2.77 (t, J = 7.6 Hz, 2H), 2.94 (t, J = 7.6 Hz, 2H), 5.98 (quint, J = 1.6 Hz, 1H), 6.03 (dd, J = 3.2, 0.8 Hz, 1H), 6.28 (dd, J = 3.2, 1.6 Hz, 1H), 7.31 (dd, J = 1.6, 0.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 25.6, 31.4, 31.7, 35.2, 105.5, 110.2, 129.8, 141.2, 153.9, 181.0, 209.9; HRMS (EI): m/z calcd for $C_{11}H_{12}O_2$ $[M]^+$ 176.0837, found 176.0835.

4.3.13. 2-[6-(Thiophen-2-yl)hex-3-yn-1-yl]-1,3-dioxane (**7g**)

Yield: 12% (29 mg); oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.31–1.38 (m, 1H), 1.76 (td, J = 7.2, 5.2 Hz, 2H), 2.02–2.14 (m, 1H), 2.25 (tt, J = 7.2, 2.4 Hz, 2H), 2.49 (tt, J = 7.2, 2.4 Hz, 2H), 3.01 (t, J = 7.2 Hz, 2H), 3.72–3.80 (m, 2H), 4.07–4.15 (m, 2H), 4.60 (t, J = 5.2 Hz, 1H), 6.85 (dd, J = 3.2, 1.2 Hz, 1H), 6.93 (dd, J = 5.2, 3.2 Hz, 1H), 7.14 (dd, J = 5.2, 1.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 13.6, 21.4, 25.8, 29.7, 34.3, 66.9, 79.1, 80.5, 100.9, 123.4, 124.6, 126.6, 143.5; HRMS

(EI): *m/z* calcd for $C_{14}H_{18}O_2S$ $[M]^+$ 250.1027, found 250.1024.

*4.3.14. 3-[2-(Thiophen-2-yl)ethyl]cyclopent-2-en-1-one (**13g**)*

Yield: 31% (60 mg); oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.40–2.43 (m, 2H), 2.58–2.62 (m, 2H), 2.81 (t, *J* = 8.0 Hz, 2H), 3.14 (t, *J* = 8.0 Hz, 2H), 6.00 (quint, *J* = 1.6 Hz, 1H), 6.82 (dd, *J* = 3.6, 1.2 Hz, 1H), 6.92 (dd, *J* = 5.2, 3.6 Hz, 1H), 7.14 (dd, *J* = 5.2, 1.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 27.4, 31.6, 35.2, 35.3, 123.5, 124.6, 126.9, 130.0, 143.1, 180.8, 209.8; HRMS (EI): *m/z* calcd for $C_{11}H_{12}OS$ $[M]^+$ 192.0609, found 192.0606.

*4.3.15. 3-[6-(1,3-Dioxan-2-yl)hex-3-yn-1-yl]-1H-indole (**7h**)*

Yield: 6% (17 mg); oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.32 (dsept, *J* = 13.6, 2.4 Hz, 1H), 1.75 (td, *J* = 7.2, 5.2 Hz, 2H), 2.05 (qt, *J* = 13.6, 4.8 Hz, 1H), 2.25 (tt, *J* = 7.6, 2.4 Hz, 2H), 2.53 (tt, *J* = 7.6, 2.4 Hz, 2H), 2.97 (t, *J* = 7.6 Hz, 2H), 3.67–3.75 (m, 2H), 4.05–4.11 (m, 2H), 4.58 (t, *J* = 5.2 Hz, 1H), 7.07 (q, *J* = 3.2 Hz, 1H), 7.11 (td, *J* = 8.0, 2.4 Hz, 1H), 7.18 (td, *J* = 8.0, 2.4 Hz, 1H), 7.36 (d, *J* = 8.0 Hz, 1H), 7.61 (d, *J* = 8.0 Hz, 1H), 8.19 (brs, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 13.6, 20.0, 25.2, 25.8, 34.3, 66.8, 79.6, 80.4, 100.9, 111.1, 115.3, 118.7, 119.1, 121.5, 121.8, 127.3, 136.2; HRMS (EI): *m/z* calcd for $C_{18}H_{21}NO_2$ $[M]^+$ 283.1572, found 283.1571.

*4.3.16. 3-[2-(1-Oxocyclopent-2-en-3-yl)ethyl]-1H-indole (**13h**)*

Yield: 11% (25 mg); oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.39–2.43 (m, 2H), 2.60–2.64 (m, 2H), 2.85 (t, *J* = 7.6 Hz, 2H), 3.07 (t, *J* = 7.6 Hz, 2H), 6.04 (S, 1H), 6.99 (s, 1H), 7.13 (t, *J* = 8.0 Hz, 1H), 7.21 (t, *J* = 8.0 Hz, 1H), 7.37 (d, *J* = 8.0 Hz, 1H), 7.60 (d, *J* = 8.0 Hz, 1H), 8.06 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 22.9, 31.7, 33.9, 35.3, 111.2, 114.9, 118.5, 119.4, 121.3, 122.2, 127.0, 129.7, 136.3, 182.7, 210.2; HRMS (EI): *m/z* calcd for $C_{15}H_{15}NO$ $[M]^+$ 225.1154, found 225.1157.

*4.3.17. 3-Methylcyclopent-2-en-1-one (**13i**) [20]*

Yield: 63% (60 mg); oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.14 (s, 3H), 2.41–2.44 (m, 2H), 2.56–2.60 (m, 2H), 5.95 (sext, *J* = 1.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 19.4, 33.0, 35.7, 130.7, 179.0, 210.3.

*4.3.18. 3-Pentylcyclopent-2-en-1-one (**13j**)*

Yield: 53% (80 mg); oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.91 (t, *J* = 7.2 Hz, 3H), 1.29–1.38 (m, 4H), 1.59 (quint, *J* = 7.2 Hz, 2H), 2.38–2.44 (m, 4H), 2.56–2.60 (m, 2H), 5.95 (quint, *J* = 1.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.9, 22.4, 26.7, 31.4, 31.5, 33.5, 35.3, 129.4, 183.4, 210.3; HRMS (EI): *m/z* calcd for $C_{10}H_{16}O$ $[M]^+$ 150.1201, found 150.1203.

*4.3.19. 2-[2-(3-Ethylcyclopent-1-en-1-yl)ethyl]-1,3-dioxane (**17j**)*

Yield: 11% (23 mg); oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.87 (t, *J* = 7.6 Hz, 3H), 1.20–1.45 (m, 5H), 1.71–1.78 (m, 2H), 1.98–2.25 (m, 5H), 2.48–2.58 (m, 2H), 3.76 (td, *J* = 12.4, 2.4 Hz, 2H), 4.11 (qt, *J* = 5.2, 1.2 Hz, 2H), 4.52 (t, *J* = 5.2 Hz, 1H), 5.30 (q, *J* = 1.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 12.1, 25.5, 25.8, 29.0, 29.9, 33.4, 34.6, 47.2, 66.9, 102.0, 127.9, 143.4; HRMS (EI): *m/z* calcd for $C_{13}H_{22}O_2$ $[M]^+$ 210.1620, found 210.1617.

*4.3.20. 3-Isopentylcyclopent-2-en-1-one (**13k**)*

Yield: 37% (56 mg); oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.93 (d, *J* = 6.8 Hz, 6H), 1.44–1.50 (m, 2H), 1.60 (nonet, *J* = 6.8 Hz, 1H), 2.38–2.44 (m, 4H), 2.57–2.61 (m, 2H), 5.95 (quint, *J* = 1.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 22.3, 27.8, 31.4, 31.5, 35.3, 129.3, 183.5; HRMS (EI): *m/z* calcd for $C_{10}H_{16}O$ $[M]^+$ 152.1201, found 152.1201.

*4.3.21. 2-[2-(3,3-Dimethylcyclopent-1-en-1-yl)ethyl]-1,3-dioxane (**17k**)*

Yield: 42% (88 mg); oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.01 (s, 6H), 1.34 (dsept, *J* = 13.6, 1.2 Hz, 1H), 1.65 (t, *J* = 7.2 Hz, 2H), 1.70–1076 (m, 2H), 2.20–2.13 (m, 3H), 2.23–2.28 (m, 1H), 3.71–3.79 (m, 2H), 4.10 (ddt, *J* = 10.8, 4.8, 1.2 Hz, 2H), 4.51 (t, *J* = 5.2 Hz, 1H), 5.12 (quint, *J* = 1.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 25.4, 25.8, 28.6, 33.3, 34.2, 39.3, 66.9, 102.0, 134.6, 140.8; HRMS (EI): *m/z* calcd for $C_{13}H_{22}O_2$ $[M]^+$ 210.1620, found 210.1621.

*4.3.22. 3-Cyclohexylcyclopent-2-en-1-one (**13l**)*

Yield: 38% (62 mg); oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.20–1.42 (m, 5H), 1.70–1.76 (m, 1H), 1.78–1.94 (m, 4H), 2.31 (tt, *J* = 7.2, 3.2 Hz, 1H), 2.37–2.42 (m, 2H), 2.58–2.63 (m, 2H), 5.92 (q, *J* = 1.6 z, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 25.9, 26.0, 29.5, 31.2, 35.0, 41.9, 127.9, 187.7, 210.5; HRMS (EI): *m/z* calcd for $C_{11}H_{16}O$ $[M]^+$ 164.1201, found 164.1202.

*4.3.23. 2-(4-Phenylbut-3-yn-1-yl)-1,3-dioxane (**7o**)*

Yield: 78% (169 mg); oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.35 (dsept, *J* = 13.6, 1.2 Hz, 1H), 1.89 (td, *J* = 7.2, 5.2 Hz, 2H), 2.09 (qt, *J* = 13.6, 5.2 Hz, 1H), 2.51 (t, *J* = 7.2 Hz, 2H), 3.75–3.83 (m, 2H), 4.11 (ddt, *J* = 10.8, 4.8, 1.2 Hz, 2H), 4.71 (t, *J* = 5.2 Hz, 1H), 7.25–7.30 (m, 2H), 7.38–7.41 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.2, 25.8, 34.1, 66.9, 80.6, 89.3, 100.8, 123.8, 127.5, 128.1, 131.5; HRMS (EI): *m/z* calcd for $C_{14}H_{16}O_2$ $[M]^+$ 216.1151, found 216.1148.

*4.3.24. (Z)-2-[5-Azido-3-(methoxymethylene)pentyl]-1,3-dioxane (**19**)*

Yield: 28% (67 mg); oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.34 (dsept, *J* = 13.6, 1.2 Hz, 1H), 1.62–1.70 (m, 2H), 1.98–2.18 (m, 3H), 2.34 (t, *J* = 7.2 Hz, 2H), 3.29 (t, *J* = 7.2 Hz, 2H), 3.55 (s, 3H), 3.72–3.80 (m, 2H), 4.10 (ddt, *J* = 10.8, 5.2, 1.2 Hz, 2H), 4.50 (t, *J* = 5.2 Hz, 1H), 5.87 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 25.8, 26.0, 26.8, 34.0, 49.2, 59.4, 66.8, 101.6, 112.8, 144.5; HRMS (EI): *m/z* calcd for $C_{11}H_{18}N_3O_3$ $[M - H]^+$ 240.1348, found 240.1346; FTIR (NaCl, cm^{-1}): 2095(N_3), 1675(C═C–O-).

4.4. Reaction of CP **10n** with $TMSN_3$/Bu_2SnO

$TMSN_3$ (0.39 mL, 3 mmol) and Bu_2SnO (75 mg, 0.3 mmol) were added to a solution of CP **10n** (360 mg, 1 mmol) in toluene (10 mL). The reaction mixture was heated at reflux for 2 h and then evaporated to give a crude residue, which was purified by chromatography (Hexane/AcOEt = 9/1) to give a 1:1 mixture (96 mg) of cyclopentenone **13n** [21] and dephosphorylated compound **18**, the latter of which was further purified.

*4.4.1. 2-[(1,3-Dioxan-2-yl)methyl]cyclohexane-1-carbonitrile (**18**)*

^{1}H NMR (400 MHz, $CDCl_3$): δ 1.22–1.39 (m, 3H), 1.52–1.87 (m, 7H), 1.91–2.14 (m, 3H), 3.00–3.05 (m, 1H), 3.71–3.81 (m, 2H), 4.06–4.13 (m, 2H), 4.62 (t, *J* = 5.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 22.0, 25.3, 25.7, 28.7, 29.2, 33.0, 34.0, 39.7, 66.8, 66.9, 100.1, 120.7; HRMS (EI): *m/z* calcd for $C_{12}H_{19}NO_3$ $[M]^+$ 209.1416, found 209.1416; FTIR (NaCl, cm^{-1}): 2234 (CN).

4.5. Synthesis of dechlorotrichodenone **21**

*4.5.1. (R)-5-(1,3-Dioxan-2-yl)-3-oxopentan-2-yl acetate (**9q**)*

A solution of 2-(2-bromoethyl)-1,3-dioxane (0.54 mL, 4 mmol) in THF (5 mL) was added to a suspension of magnesium (96 mg, 4 mmol) in THF (5 mL) with stirring and stirred at rt for 0.5 h. After the magnesium was consumed by the exothermic reaction, the solution of the generated Grignard reagent was injected dropwise over 15 min via a syringe to a solution of (R)-(+)-2-acetoxypropionyl chloride **20** (0.64 mL, 5 mmol) in THF (15 mL) in another flask at −78 °C. The mixture was allowed to warm to rt and stirred for 3 h at the same temperature. The reaction mixture was quenched with saturated NH_4Cl and extracted with AcOEt. The

organic layer was washed with saturated NH_4Cl, saturated $NaHCO_3$, and brine, dried over anhydrous Na_2SO_4, filtered and then evaporated. The residual oil was purified by column chromatography (Hexane/AcOEt = 4/1) to give **9q** (821 mg 89%) as an oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 1.34 (dsept, J = 13.6, 1.2 Hz, 1H), 1.40 (d, J = 7.2 Hz, 3H), 1.90 (td, J = 7.2, 5.2 Hz, 2H), 2.05 (qt, J = 13.6, 5.2 Hz, 1H), 2.14 (s, 3H), 2.57 (dt, J = 18.0, 7.2 Hz, 1H), 2.64 (dt, J = 18.0, 7.2 Hz, 1H, 3.70–3.79 (m, 2H), 4.07 (ddt, J = 12.0, 5.2, 1.2 Hz, 2H), 4.57 (t, J = 5.2 Hz, 1H), 5.10 (q, J = 7.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 16.1, 20.8, 25.7, 28.4, 32.1, 66.8, 74.6, 100.5, 170.3, 207.1; HRMS (EI): *m/z* calcd for $C_{11}H_{17}O_5$ $[M - H]^+$ 229.1076, found 229.1080.

*4.5.2. (2R)-3-Cyano-3-[(diethoxyphosphoryl)oxy]-5-(1,3-dioxan-2-yl)pentan-2-yl acetate (**10q**)*

DEPC (1.4 mL, 8.9 mmol) and LiCN (147 mg, 4.4 mmol) were added to a solution of ketone **9q** (1.70 mg, 7.4 mmol) in THF (20 mL) and the reaction mixture was stirred for 0.5 h at rt. The resulting mixture was diluted with AcOEt, washed with saturated NH_4Cl and brine. The organic layer was dried over Na_2SO_4, filtered, and evaporated to give a crude residue, which was purified by column chromatography (Hexane/AcOEt = 1/1) to give **10q** (3.00 g, quant).

^{1}H NMR (400 MHz, $CDCl_3$): δ 1.33–1.45 (m, 10H), 1.80–1.92 (m, 2H), 2.00–2.30 (m, 3H), 2.11 (s, 1.5H), 2.12 (s, 1.5), 3.71–3.80 (m, 2H), 4.05–4.24 (m, 6H), 4.57–4.62 (m, 1H), 5.21 (q, J = 5.6 Hz, 0.5H), 5.31 (q, J = 5.6 Hz, 0.5H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.9, 15.0, 15.9, 16.0, 21.0, 25.6, 28.9, 29.6, 29.7, 64.7, 64.8, 66.8, 70.9, 71.0, 79.0, 79.1, 100.5, 100.6, 115.9, 169.4, 169.5; HRMS (EI): *m/z* calcd for $C_{16}H_{27}NO_8P$ $[M - H]^+$ 392.1475, found: 392.1471.

*4.5.3. (R)-1-(3-Oxocyclopent-1-en-1-yl)ethyl acetate (**13q**)*

$TMSN_3$ (0.39 mL, 3 mmol) and Bu_2SnO (75 mg, 0.3 mmol) were added to a solution of CP **10q** (393 mg, 1 mmol) in toluene (10 mL). The reaction mixture was heated at reflux for 4 h. After evaporation of the solvent, the residue was purified by column chromatography (Hexane/AcOEt = 3/1) to give **13q** (77 mg, 46%).

$[\alpha]_D$ = +56.5° (*c* 1.00, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.47 (d, J = 6.8 Hz, 3H), 2.12 (s, 3H), 2.46 (t, J = 4.8 Hz, 2H), 2.56–2.72 (m, 2H), 5.64 (q, J = 6.8 Hz, 1H), 6.07 (q, J = 1.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 18.9, 20.9, 27.9, 34.9, 69.3, 128.7, 169.9, 179.4, 208.7; HRMS (EI): *m/z* calcd for $C_9H_{12}O_3$ $[M]^+$ 168.0787, found 168.0787.

*4.5.4. Dechlorotrichodenone (**21**) [14,15]*

3 *N* HCl (2 mL) was added to a solution of **13q** in MeOH (10 mL). The reaction mixture was stirred for 24 h at rt. The solvent was evaporated to give a crude residue, which was purified by column chromatography (Hexane/AcOEt = 1/9) to give dechlorotrichodenone **21** (103 mg, 82%).

$[\alpha]_D$ = −1.6° (*c* 1.00, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.45 (d, J = 6.8 Hz, 3H), 2.44–2.48 (brm, 2H), 2.63–2.68 (brm, 2H), 4.66 (q, J = 6.8 Hz, 1H), 6.14 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.9, 21.8, 35.2, 67.6, 127.7, 185.6, 210.3.

*4.6. Reaction of ketal-protected cyclopentenone **12a** with TMS-phosphate (**4**)*

Diethyl phosphate (0.18 mL, 1.5 mmol) was added to a mixture of TMSCl (0.39 mL, 3 mmol) and Et_3N (0.84 mL, 6 mmol) at 0 °C. The reaction mixture was warmed to rt, and stirred for 24 h at the same temperature, and then distilled under reduced pressure (57–59 °C, 7 mmHg) to give TMS-phosphate (**4**). **4** (9 μL, 0.04 mmol) was added to a solution of ketal **12a** (10.0 mg, 0.04 mmol) in toluene (2 mL). After heating under reflux for 1 h, the reaction mixture was evaporated to give a crude residue, which was purified by column chromatography (Hexane/AcOEt = 7/3) to afford 3-phenethylcyclopent-2-en-1-one **13a** (6.9 mg, 93%) as an oil.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.tet.2020.131914.

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