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Transformation of Carbonyl Compounds into Homologous Alkynes under Neutral Conditions: Fragmentation of Tetrazoles Derived from Cyanophosphates

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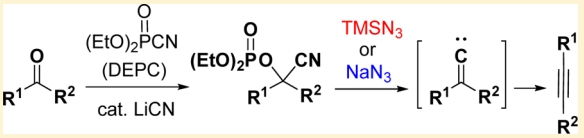
Supporting Information

ABSTRACT: Cyanophosphates (CPs) can be easily prepared from either ketones or aldehydes, and their reaction with NaN_3−Et_3N·HCl results in the formation of azidotetrazoles. Under microwave irradiation, successive fragmentation of the azidotetrazoles generates alkylidene carbenes that undergo [1,2]-rearrangement and are transformed into homologous alkynes. Treatment of ketone-derived CPs with $TMSN_3$ and Bu_2SnO as catalyst in toluene at reflux directly yields the corresponding internal alkynes, whereas the reaction of aldehyde-derived CPs with NaN_3−Et_3N·HCl in THF at reflux or $TMSN_3$−Bu_2SnO (cat.) in toluene at reflux provides homologous terminal alkynes in good yields. These reactions take place under neutral conditions and can be successfully extended to obtain alkynes that are not usually accessible from the corresponding carbonyl compounds by the Ohira−Bestmann or Shioiri procedures, which require basic conditions.



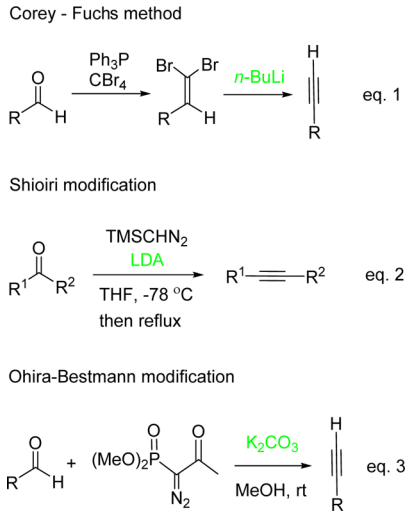
INTRODUCTION

The preparation of internal and terminal alkynes from carbonyl compounds is a very useful synthetic pathway. A widely used method for accessing alkynes is the one-carbon homologation of aldehydes or ketones.[1] Following Corey−Fuchs' pioneering two-step procedure for alkyne synthesis (Scheme 1, eq 1),[2] Colvin rearrangement using either trimethylsilyldiazomethane ($TMSCHN_2$) or dimethyl(diazomethyl)phosphonate (DAMP),[3] and Seyferth−Gilbert homologation (using DAMP) were developed.[1,4] Later, Shioiri and co-workers reinvestigated Colvin rearrangement and established general conditions for alkyne synthesis in the reaction of aldehydes or aryl alkyl ketones with lithium trimethylsilyldiazomethane [$TMSC(Li)N_2$] (eq 2).[5a] Aliphatic ketones failed to give the corresponding alkynes under these conditions.[5b] A common drawback of these methods is the necessity of a strong base, which is problematic for highly functionalized substrates.[1] Meanwhile, the Ohira−Bestmann procedure, in which DAMP is produced in situ from dimethyl-1-diazo-2-oxopropylphosphonate, has become the most popular method of transforming an aldehyde into the corresponding alkyne under mild basic reaction condition (K_2CO_3/MeOH) (eq 3).[6,7] However, using this method, ketones cannot be transformed into internal alkynes, and α,β-unsaturated aldehydes do not yield enynes.[1,7]

Tetrazoles have been successfully used in pharmaceutical development as lipophilic spacers and substituents of carboxylic acids. They are also used as components of explosives, ligands in coordination chemistry, and precursors in the preparation of a diverse heterocyclic compounds.[8] Synthesis of 5-substituted tetrazoles can be achieved directly by [2+3] cyclization of a nitrile and an azide, but the reactions are often slow and give poor yield in the case of less-reactive nitriles.[8a] Cyclization takes place at a sufficient rate only if electron-withdrawing groups are present on the nitrile or if the reaction can occur intramolecularly.[8a,9]

In 2012, Wardrop and Komenda reported successive fragmentation of 5-hydroxyalkyl-1*H*-tetrazoles **5** upon treatment with diisopropylcarbodiimide (DIC) under mild conditions.[10] The proposed mechanism, as illustrated in Scheme 2, describes the dehydration reaction of **5**, followed by the formation of an unstable tetraazafulvene **6**. Subsequent loss of 2 mol of N_2 generates an alkylidene carbene **7**,[11] which may undergo either

Scheme 1. Current Procedures for Homologous Alkyne Synthesis from Carbonyl Compounds



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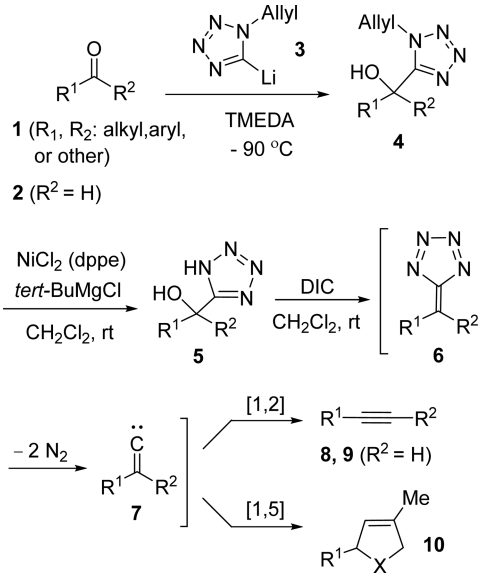
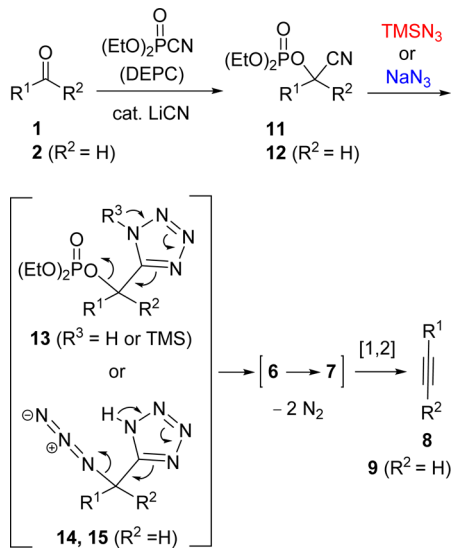
Scheme 2. Wardrop Alkyne Synthesis



[1,2]-rearrangement or [1,5]-C−H bond insertion to produce either alkynes **8** and **9** or cyclopentenes **10**, respectively. However, this methodology requires two additional steps for the preparation of the key intermediate **5**, i.e., the addition of 1-allyl-5-tetrazoyllithium **3** to carbonyl compounds **1** or **2** at −90 °C, followed by de-*N*-allylation of addition products **4**.[10] Behringer and Matner have previously described the thermolysis and rearrangement of tetrazoles **5** and their derivatives to form alkynes **8** or **9**.[12]

The reaction of diethyl phosphorocyanidate (DEPC)[13] with various ketones **1** or aldehydes **2** (R^2 = H) in the presence of a catalyst easily affords cyanohydrin-*O*-phosphates (or cyanophosphates, CPs) **11** or **12**,[14] which have been widely utilized as synthetic intermediates in organic synthesis (Scheme 3).[13a] Since the nitrile group of CPs is activated by the presence of an adjoining phosphate group, reaction of the CN moiety with an azide source may generate either tetrazolylphosphate **13** or azidotetrazoles **14** and **15**. The resulting tetrazoles **13**−**15** can spontaneously lead to alkynes **8** or **9** by a fragmentation mechanism

Scheme 3. Alkyne Synthesis Developed in This Study



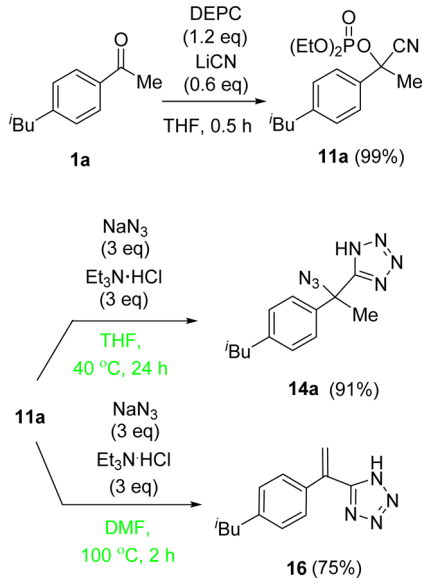
similar to the one illustrated in Scheme 3. In addition, Czernecki and Valéry showed that reaction of cyanohydrin-*O*-mesylate with sodium azide in DMF gave an unusual single formation of an acetylenic sugar,[15a] suggesting the formation of a presumed alkylidenecarbene species.[15]

Herein, we report the efficient and practical synthesis of alkynes by homologation of various carbonyl compounds, via fragmentation of tetrazole intermediates **13**−**15** that are derived from CPs under neutral conditions. The ease in handling of the reactants in toluene or THF is also noteworthy. This method was successfully extended to obtain alkynes not usually accessible from the corresponding carbonyl compounds by following the Ohira−Bestmann reaction[6,7] or Shioiri procedure[5] under basic conditions.[1]

RESULTS AND DISCUSSION

Formation of α-Azidotetrazoles and Their Transformation into Alkynes under MW Heating Condition. Excess DEPC (3 equiv) and LiCN (3 equiv) are routinely used for the cyanophosphorylation of different ketones **1** and aldehydes **2**.[13a,14] First, we optimized the reaction condition and demonstrated that 1.2 equiv of DEPC and 0.6 equiv of LiCN were sufficient for the synthesis of CPs **11** from ketones **1**, whereas 1.2 equiv of DEPC and 0.1 equiv of LiCN were required when aldehydes **2** were employed. Indeed, the treatment of 4-isobutylacetophenone **1a** with DEPC (1.2 equiv) in the presence of LiCN (0.6 equiv) afforded CP **11a** in 99% yield at room temperature (rt) within 0.5 h in THF (Scheme 4).

Scheme 4. Synthesis of α-AT 14a and VT 16 from CP 11a



The reaction of benzylic CP **11a** with sodium azide (NaN_3, 3 equiv) in the presence of triethylamine hydrochloride (Et_3N·HCl, 3 equiv),[9] gave α-azidotetrazole (AT) **14a** in 91% yield at 40 °C after 24 h in THF, as illustrated in Scheme 4. However, in the reaction of CP **11a** with the same reagent system, only vinyltetrazole (VT) **16** was obtained in 75% yield in DMF at 100 °C after 2 h.

The stability of AT **14a** was studied by differential scanning calorimetry (DSC) and the results indicated that it is thermally unstable at temperatures above its the melting point (mp 119−120 °C). However, it is not explosive (see SI) and could be stored

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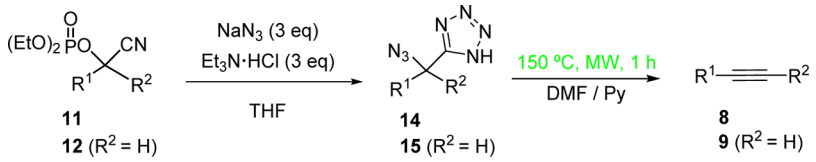
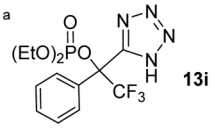
Table 1. Transformation of CPs 11 and 12 into Alkynes 8 and 9 under MW Condition



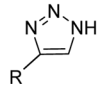
11
12 (R^2 = H)
14
15 (R^2 = H)
8
9 (R^2 = H)

entry		R^1	R^2	temp. (°C)	time (h)	**14** or **15** (%)		**8** or **9** (%)	
1	**11a**	*i*Bu	CH_3	40	24	**14a**	91	**8a**	76
2	**11b**	H_3C	CH_3	40	24	**14b**	91	**8b**	72
3	**11c**	Cl	CH_3	40	8	**14c**	88	**8c**	65
4	**11d**	MeO	CH_3	40	24	**14d**	96	**8d**	82
5	**11e**	O_2N	CH_3	40	24	**14e**	73	**8e**	40
6	**11f**		*n*-Pentyl	40	48	**14f**	82	**8f**	81
7	**11g**			60	48	**14g**	54	**8g**	88
8	**11h**	$(CH_2)_2$	CH_3	40	48	**14h**	82	**8h**	17
9	**11i**		CF_3	15	48	(**13i**	83)[a]	–	dec.
10	**12a**	*i*Bu	H	rt	24	**15a**	98	**9a**	62 (**17a**, 19)[b]
11	**12b**		H	rt	24	**15b**	81	–	– (**17b**, 33)[b]
12	**12c**		H	40	48	**15c**	71	–	– (**17c**, 25)[b]

[a] 

13i

[b]Triazoles **17** were obtained as by-products.



17a: R = *i*Bu-Ph-
17b: = Ph-
17c: = $PhCH_2$-

for over a year at rt. ^{1}H NMR and mp of the stored compound did not show any substantial decomposition, indicating that **14a** has long-term stability.

As shown in the entry 1 of Table 1, the reaction of AT **14a** under microwave (MW) irradiation condition with DMF-pyridine (5:2, v/v) as solvent at 150 ^{o}C (see SI) gave the expected alkyne **8a** in 76% yield after 1 h. This result indicated that carbonyl compounds could be converted into alkynes under MW activation. ATs **14b** and **14c** bearing electron donating groups at the *para*-position of phenyl groups, as well as AT **14d** with the 6-methoxy naphthalene moiety, similarly provided the alkynes **8b**–**d** in good yields (65–82%; entries 2–4). In the case of AT **14e** involving a nitro group, the reaction was suppressed, yield of alkyne **8e** was only 40% (entry 5). ATs **14f** and **14g**[16] prepared from hexaphenone and benzophenone CPs **11f** and **11g** respectively, provided the respective alkynes **8f** (81%) and **8g** (88%) in good yields (entries 6 and 7). However, AT **14h**, which was obtained from 4-phenyl-2-butanone CP **11h**, gave the corresponding alkyne **8h** in a low yield (17%, entry 8). The reaction of 2,2,2-trifluoroacetophene CP (**11i**) with NaN_3-Et_3N·HCl was interesting, as tetrazolylphosphate **13i** was obtained in 83% yield without further substitution of the azide anion (entry 9). Subsequently, **13i** was decomposed by the MW treatment. Formation of a terminal alkyne **9a** in yield of 62% was possible starting from 4-isobutylbenzaldehyde AT **15a**. The product mixture also contained a triazole **17a** (19%), which seems to have formed by a [2+3] cyclization of alkyne **9a** with hydrazoic acid (HN_3) generated in situ (entry 10). Other aldehyde derived ATs **15b** and **15c** gave triazoles **17b** (33%) and **17c** (25%) in low yields (entries 11 and 12).

Although one-pot synthesis of alkynes **8** and **9** from CPs **11** and **12**, respectively, could be carried out without isolation of corresponding ATs **14** and **15**, the yields of the alkynes were lower compared to the two-step method, as shown in Scheme 5.

In addition, hydrogenation of the aforementioned vinyl-tetrazole VT **16** and AT **15c**, afforded tetrazole analogues of ibuprofen **18**[17] and phenylalanine **19**[18] in 94% and 91% yields, respectively (Scheme 6). The former exhibits twice the analgesic

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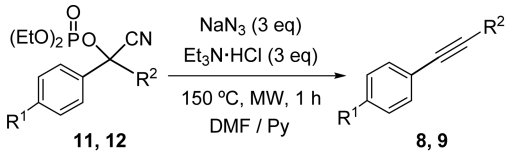
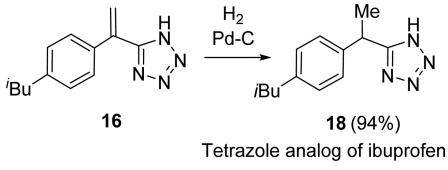
Scheme 5. One-Pot Synthesis of Alkynes 8 and 9 from CPs 11 and 12

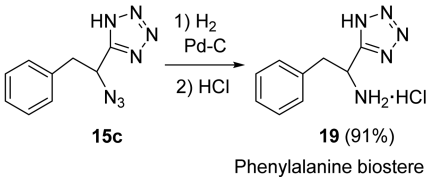


11a (R^1 = ^{i}Bu, R_2 = Me) **8a** (63%)
11c (R^1 = Cl, R_2 = Me) **8c** (28%)
12a (R^1 = ^{i}Bu, R_2 = H) **9a** (52%) + **17a** (19%)

activity of ibuprofen,[19] while the latter acts as a tyrosine hydroxylase inhibitor.[20]

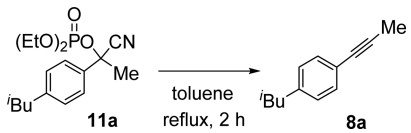
Scheme 6. Synthetic Application of VT 16 and AT 15c into Tetrazole Analogue 18 and Phenylalanine Biostere 19





Transformation of Ketones 1 into Homologous Alkynes 8 via CPs 11. The procedure outlined above still requires the isolation of unstable ATs and relatively harsh conditions in the MW reactor. In search for a milder variant (Table 2), we studied the reaction of CP **11a** with different organic azides such as tributyltin azide (Bu_3SnN_3, entries 1 and 2), diphenyl phosphorazidate (DPPA, entries 3 and 4), *p*-toluenesulfonyl azide (TsN_3, entries 5 and 6), and trimethylsilyl azide ($TMSN_3$, entries 7 and 8). From these experiments, it was found that CP **11a** could be transformed directly into the corresponding alkyne

Table 2. Investigation of Organic Azides for the Transformation of CP 11a to Alkyne 8a



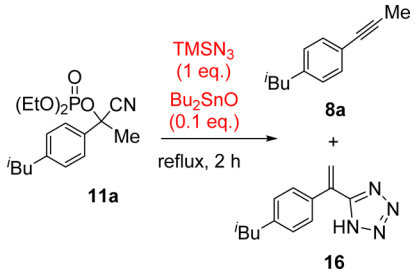
entry	reagent (eq)		8a (%)
1	Bu_3SnN_3 (1)		30
2	Bu_3SnN_3 (1)	Bu_2SnO (0.1)	33
3	DPPA (1)		NR[a]
4	DPPA (1)	Bu_2SnO (0.1)	0[b]
5	TsN_3 (1)		NR
6	TsN_3 (1)	Bu_2SnO (0.1)	NR
7	$TMSN_3$ (2)	Bu_2SnO (1.2)	59[c]
8	$TMSN_3$ (1)	Bu_2SnO (0.1)	60[c]

[a]NR: no reaction. [b]Only 2-(4-isobutylphenyl)acrylonitrile (18%) was obtained (ref 14). [c]VT**16** was obtained as a byproduct (see Table 3).

8a (60%) under Wittenberger conditions,[21] i.e., by using 1 equiv of $TMSN_3$ in the presence of a catalytic amount of Bu_2SnO (0.1 equiv) at reflux in toluene (entry 8 in Table 2).[15c−e]

The effect of the choice of solvent on the reaction was also investigated (Table 3). Using toluene, xylene, or cyclopentyl

Table 3. Formation of Alkyne 8a from CP11a in Various Solvents



entry	solvent	8a (%)	16 (%)
1	toluene	60	11
2	xylene	62	6
3	CPME[a]	59	13
4	benzene	22	42
5	CH_3CN	5	29

[a]Boiling point of CPME = 106 °C

methyl ether (CPME: bp = 106 °C) as solvents, alkyne **8a** was obtained in better yields (entries 1−3) compared to reactions performed in benzene or acetonitrile (entries 4 and 5). These results suggest that a solvent with boiling points >100 °C may be necessary for an efficient conversion to alkyne **8a**, while suppressing the formation of VT **16**.

Thus, several ketones **1** could be transformed into the corresponding alkynes **8** in moderate to high yields using $TMSN_3$−Bu_2SnO (cat.) in toluene at reflux (Table 4). Acetophenones **1c**, **e**, **j**−**l** (R = Cl, NO_2, CN, CF_3, and CO_2CH_3) and **1n**−**v** (R = OMe, NO_2, OMEM, OBn, OTs, NHTs, NHBoc, and OTBDMS) readily afforded the corresponding alkynes **8c**, **e**, **j**−**l** and **8n**−**v**, demonstrating that the reaction was relatively tolerant toward a range of functional groups on aromatic rings (entries 1−5 and 7−15). The reaction could not be applied only in the case of *p*-methoxyacetophenone (entry 6), because of the instability of the corresponding CP.

Notably, pyridine-containing ketones **1w**–**1z** were transformed into alkynes **8w**− **8z** in 73, 49, 80, and 41% overall yields in two steps (entries 16−19), respectively. In contrast, the overall yield of **8w** is merely 12% after a three-step of ketone **1w** following the Wardrop method.[10] A poor yield is obtained in this case because pyridines are known to undergo ring opening in the presence of carbodiimides.[22] Benzophenone CP (**11g**) and diketone CP **11aa** were efficiently converted into the respective alkynes **8g** (87%) and **8aa** (84%) (entries 20, 21).

The potential of the reaction methodology has been further explored by applying it to the synthesis of a selective mGlu5 receptor antagonist, 2-methyl-6-(phenylethynyl)pyridine (**8bb**: MPEP).[23] Starting from 6-methylpicolinaldehyde **2bb**, MPEP was obtained in 68% overall yield after four steps, as shown in Scheme 7.

Interestingly, *β*-ketoester **1cc**, which possesses readily enolizable *α*-protons, could also be converted into the corresponding alkyne **8cc** (68%) by the present method (Scheme 8). In contrast, the reaction of **1cc** under Shioiri conditions ($TMSCHN_2$/LDA)[5a] only resulted in the unreacted starting material **1cc**.

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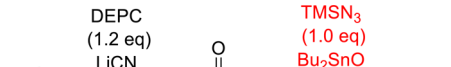
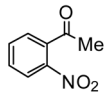
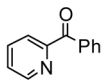
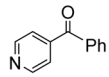
Table 4. Transformation of Ketones 1 into Alkynes 8 via CP 11

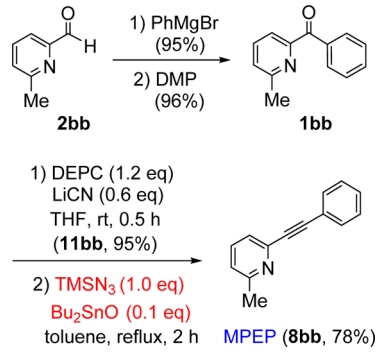


entry	1		CP 11 (%)[a]	product (%)[a]
1	**1c**	R = Cl	**11c** 86	**8c** 63
2	**1e**	R = NO_2	**11e** 97	**8e** 88
3	**1j**	R = CN	**11j** 99	**8j** 70
4	**1k**	R = CF_3	**11k** 99	**8k** 85
5	**1l**	R = CO_2CH_3	**11l** 93	**8l** 82
6	**1m**	R = OCH_3	dec	–
7	**1n**	R = OMe	**11n** 85	**8n** 72
8	**1o**	R = NO_2	**11o** 99	**8o** 85
9	**1p**	R = OMEM	**11p** 99[b]	**8p** 78[c]
10	**1q**	R = OBn	**11q** 98	**8q** 88[c]
11	**1r**	R = OTs	**11r** 95	**8r** 82[c]
12	**1s**	R = NHTs	**11s** 95	**8s** 72[d]
13	**1t**	R = NHBoc	**11t** 96	**8t** 47[d]
14	**1u**	R = OTBDMS	**11u** 67[e]	**8u** 80[c]
15	**1v**		**11v** 99	**8v** 50
16	**1w**		**11w** 97[b]	**8w** 75[f,g]
17	**1x**	R = CH_3	**11x** 81	**8x** 61
18	**1y**	R = Ph	**11y** 90[b]	**8y** 89[f]
19	**1z**		**11z** 71[b]	**8z** 58[f]
20	**1g**		**11g** 99	**8g** 87
21	**1aa**		**11aa** 85[h]	**8aa** 84[i]

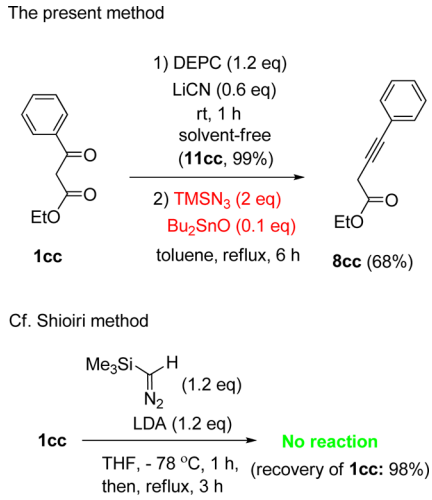
[a]Isolated yield. [b]DEPC (3.0 equiv) and LiCN (3.0 equiv). [c]$TMSN_3$ (3.0 equiv), Bu_2SnO (0.1 equiv), reflux, 4 h. [d]$TMSN_3$ (2.0 equiv), Bu_2SnO (0.2 equiv), reflux, 2 h. [e]DEPC (3.0 equiv) and LiCN (3.0 equiv), reflux, 0.5 h. [f]$TMSN_3$ (2.0 equiv), Bu_2SnO (0.2 equiv), reflux, 4 h. [g]See text. [h]DEPC (3.0 equiv) and LiCN (1.2 equiv). [i]$TMSN_3$ (3.0 equiv), Bu_2SnO (0.1 equiv), reflux, 21 h.

Colvin and Hamill's original procedure[3] using either $TMSCHN_2$ or DAMP, and its modifications cannot be applied to dialkyl ketones.[3,4] Furthermore, the Ohira–Bestmann reaction of ketones does not afford alkynes but instead enol ethers are formed.[6] As shown in Scheme 9, the method developed in this work furnished the corresponding 1,6-diphenylhexen-3-yne (**8dd**) from

Scheme 7. Synthesis of mGlu5 Receptor Antagonist, MPEP



Scheme 8. Transformation of β-Ketoester 1cc to Its Corresponding Ketone 8cc



1,5-diphenylpentan-3-one (**1dd**) in 77% overall yield (eq 1). In contrast, Ohira–Bestmann reaction of **1dd** gave methyl enol ether **20** in 40% yield (eq 2),[6] while the Shioiri procedure yielded allenylsilane **21** (31%),[24] a homologous aldehyde **22** (23%),[5b] as well as unreacted **1dd** (46%) (eq 3). The formation of allenylsilanes or homologous aldehydes from ketones utilizing $TMSCHN_2$ has been reported independently by Lee[24] and Shioiri groups.[5b] These results indicate the versatility of our method.

Furthermore, reaction of 12-membered cyclic ketone **1ee** yielded cyclotridecyne **8ee** in 64% overall yield via CP **11ee**. Bicyclo[8.2.1]tridecene **23ee** (13%) was also formed in this transformation, which is possibly due to a [1,5]-C–H insertion mediated by the alkylidene carbene **24**, as illustrated in Scheme 10. In contrast, when the same ketone **1ee** was subjected to Shioiri conditions, cyclotridecyne **8ee** was obtained in only 15% yield, along with the bicyclo compound **23ee** (9%), allenylsilane **25** (9%), homologous aldehyde **26** (33%), and the starting **1ee** (33%).

Transformation of aldehydes 2 into Alkynes 9 via CPs 12. The present method was successfully extended to the transformation of aldehydes **2** into homologous terminal alkynes **9**, as shown in Table 5. In our studies on the synthesis of novel triazole-containing RNA or DNA,[25] we sought access to alkynes **9d–g**, prepared from β-D-ribofuranosyl C_n-aldehydes **2d–f** (n = 0–2) and deoxyribofuranosyl carbaldehyde **2g**. Reaction of CP **12d** with NaN_3 (3 equiv) and Et_3N·HCl (3 equiv) gave β-ribofuranosyl alkyne **9d** in 68% yield (method A). Alternatively, treatment of **12d** with $TMSN_3$ (1 equiv) in the presence of

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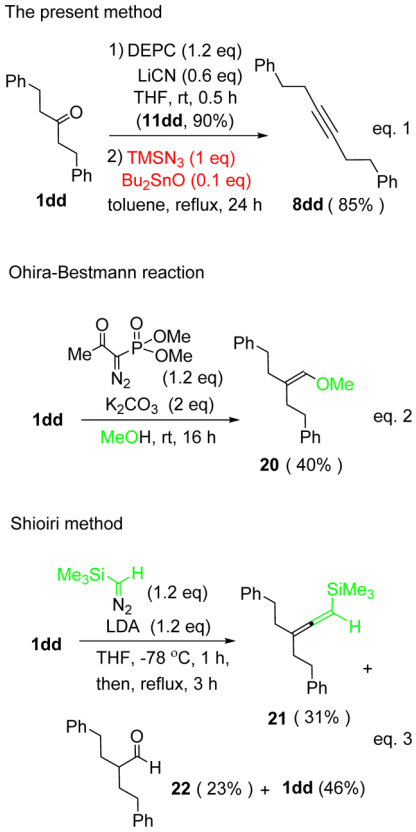
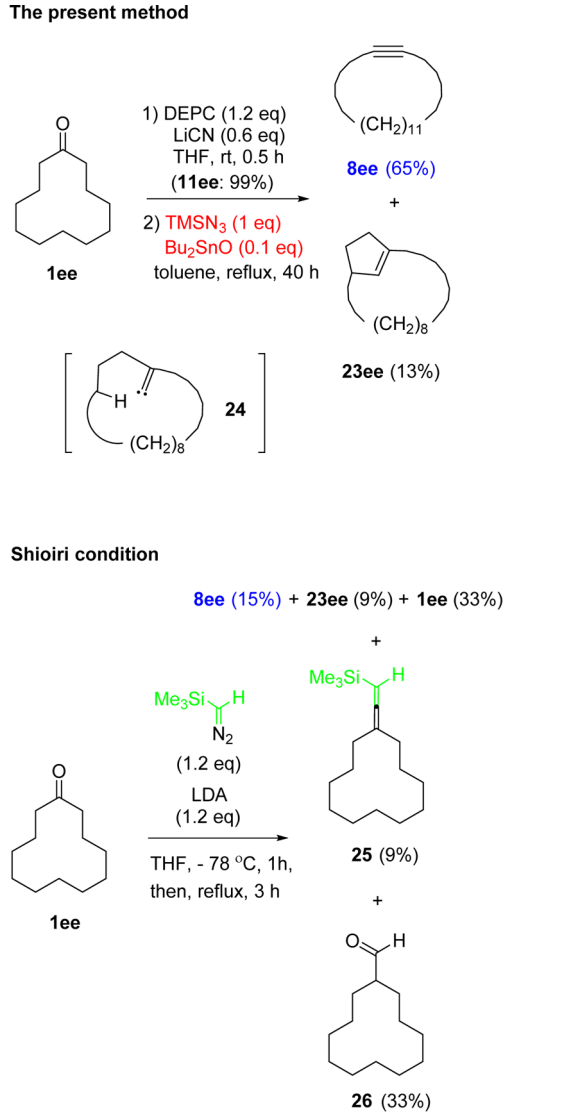
Scheme 9. Reactivity of Dialkyl Ketone 1dd under Three Different Conditions



Scheme 10. Transformation of Cyclic Ketone 1ee to Cyclic Alkyne 8ee



Bu_2SnO (0.1 equiv) gave **9d** in 47% yield (method B) (entry 1). Thus, method A was favored for the preparation of homologous alkynes **9e**−**g** from their corresponding aldehydes **2e**−**g** (entries 2−4). Both methods A and B may be employed equally for primary aldehydes **2h** (entry 5), but method A slightly more effective for aldehydes **2i**−**k** (entries 6−8). Furthermore, method A is remarkably superior to method B for the transformation of diphenylacetaldehyde **2l** into the corresponding alkyne **9l** (quantitative yield) (entry 9). Conversely, in the case of aromatic and α,β-unsaturated aldehyde CPs **12a** and **12n**, method B is favorable, providing the alkynes **9a** and **9n** in 71% and 80% yields, respectively (entries 10 and 12). An explanation for the preference toward either method A or B depending on the aldehyde is unknown at present. Homologation of geranial and neral CPs **12o** and **12p** using method B gave moderate yields of the alkynes **9o** and **9p**, i.e., 68%, E/Z = 15/1 and 53%, E/Z = 1/10, respectively (entries 13 and 14).

As shown in Scheme 11, the transformation of aldehyde **2e** into alkyne β-**9e** in overall 99% yield is of particular interest, since Ohira−Bestmann reaction and Shioiri modification procedures gave only inseparable 5:2 and 9:1 epimeric mixtures of β-**9e** and α-**9e**, respectively. The formation of the epimeric mixtures presumably occurs due to the extraction of α-acidic proton of **2e** followed by β-elimination under basic conditions. Phthalimide-containing propanal **2q** similarly provided the terminal alkyne **9q** in 68% from CP **12q**, but the Ohira−Bestmann reaction of **2q** gave **9q** in only 10% yield (Scheme 12).

As mentioned before, the Ohira−Bestmann reaction does not give enynes from α,β-unsaturated aldehydes.[1,7] In contrast, it is possible to synthesize the corresponding enyne **9n** from cinnamaldehyde **2n** in 78% overall yield following the method described in this work (Scheme 13).[26] Furthermore, the Ohira−Bestmann reaction using **2n** as substrate gave (1-methoxybut-3-nyl)benzene **27** in 10% yield, together with dimethyl acetal **28** (67%).

In conclusion, a novel two-step transformation of carbonyl compounds into homologous alkynes has been developed. Under neutral conditions, CPs react with azides to form tetrazole intermediates, which subsequently undergo successive fragmentation to give alkynes. This transformation is versatile and most of the functional motifs, such as β-ketoesters, dialkyl ketones, cyclic ketones, β-elimination-prone aldehydes, and α,β-unsaturated aldehydes, can be used. This demonstrates the superiority of this method over the Ohira−Bestmann and Shioiri procedures which require basic conditions. Meanwhile, CPs have been employed as key intermediates in a variety of organic synthesis,[13a] and the present study also contributes to the diversity of CPs.

■ EXPERIMENTAL SECTION

Reactions with air- and moisture-sensitive compounds were carried out under an inert argon atmosphere. MW-assisted reactions were performed in a Milestone MultiSYNTH multimodal reactor with thermal

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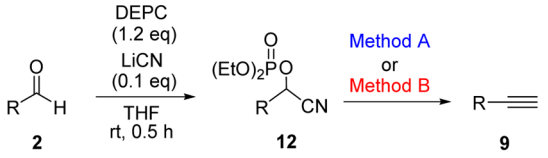
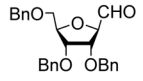
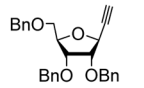
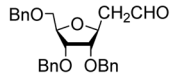
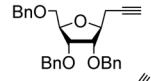
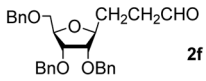
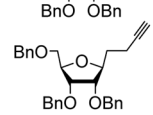
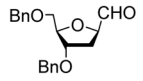
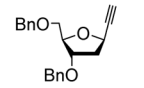
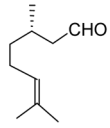
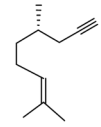
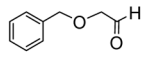
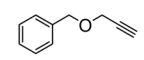
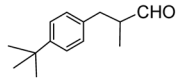
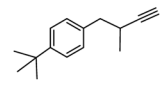
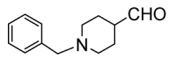
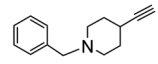
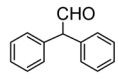
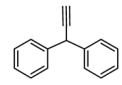
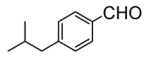
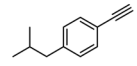
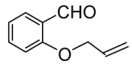
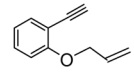
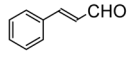
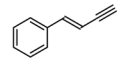
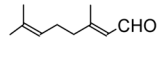
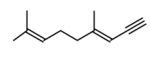
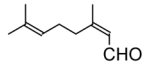
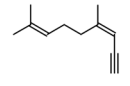
Table 5. Transformation of Aldehydes 2 into Terminal Alkynes 9 via CP 12



Method A :NaN_3 (3 eq), $Et_3N{\cdot}HCl$ (3 eq), THF, reflux, 16 h.

Method B : $TMSN_3$ (1eq), Bu_2SnO (0.1eq), toluene, reflux, 2 h.

entry	2		12 (%)[a]	Method	9		(%)[a]
1		**2d**	**12d** 91	A B		**9d**	68 47
2		**2e**	**12e** 99	A B		**9e**	quant 82
3		**2f**	**12f** 96	A B		**9f**	quant 86
4		**2g**	**12g** quant	A		**9g**	74
5		**2h**	**12h** 99	A B		**9h**	57 55
6		**2i**	**12i** 88	A B		**9i**	88 82
7		**2j**	**12j** quant	A B		**9j**	74 68
8		**2k**	**12k** 92	A B		**9k**	71 61
9		**2l**	**12l** quant	A B		**9l**	quant 64
10		**2a**	**12a** 98	A B[b]		**9a**	29 71
11		**2m**	**12m** quant	B		**9m**	88
12		**2n**	**12n** 98	A B[c]		**9n**	17 80
13		**2o**	**12o** 99	B[c]		**9o** (*E*/*Z*=15/1)	68
14		**2p**	**12p** 99	B[c]		**9p** (*E*/*Z*=1/10)	53

[a]Isolated yield. [b]Reflux, 0.5 h. [c]$TMSN_3$ (3 equiv), Bu_2SnO (0.1 equiv), reflux, 0.5 h.

control, its reaction vessels were sealed until 20 bar, and reaction internal temperature was monitored on an infrared thermometer.

Anhydrous solvents were either purchased from WAKO Chemical Company. During organic workup, solvent extracts were dried over Na_2SO_4 or $MgSO_4$ and subsequently removed in a rotary evaporator under reduced pressure. Fuji Silysia FL-60D silica gel was used for flash column chromatography. Thin layer chromatography (TLC) was performed using precoated plates (WAKO silica gel 70 F_{254}). ^1H- and ^{13}C NMR spectra were recorded on Varian Mercury-300 and Agilent 400-MR-DD2 spectrometer in $CDCl_3$ with tetramethylsilane (TMS) as an internal standard. ^{31}P NMR spectra were recorded at 121 MHz (Varian Mercury-300) and the chemical shifts were measured relative to

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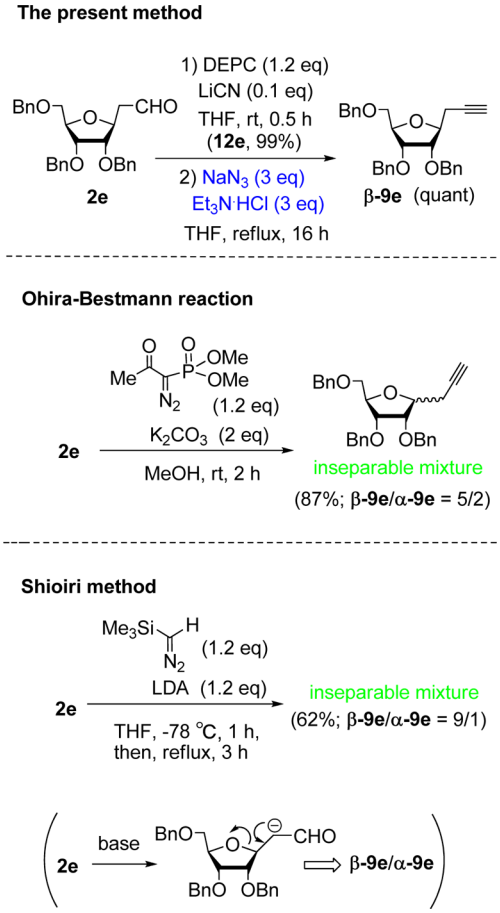
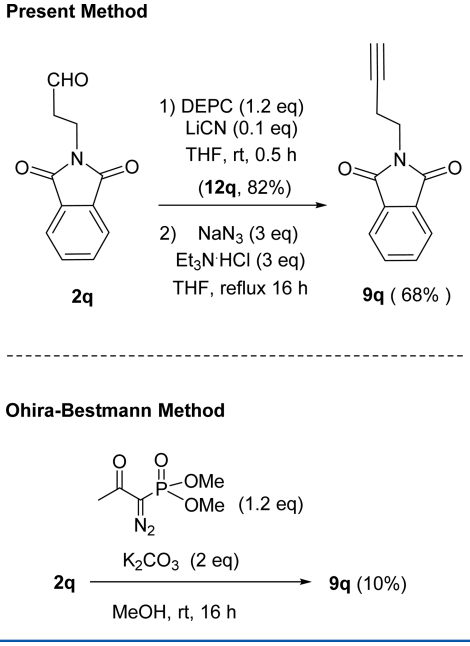
Scheme 11. Reactivity of β-D-Ribofuranosyl C_1-Carbaldehyde 2e under Different Conditions

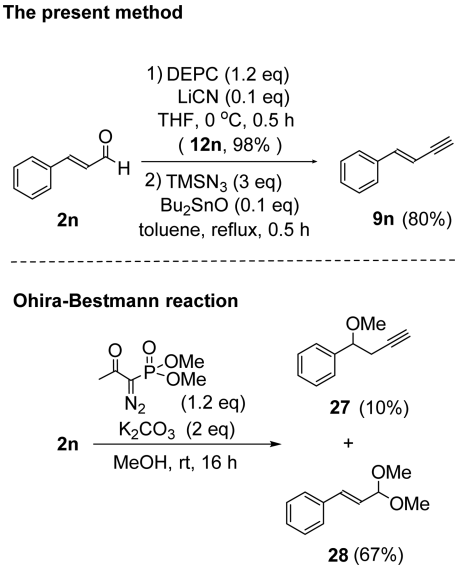


Scheme 12. Transformation of Phthalimide-Containing Propanal 2q into Alkyne 9q Using Present Method and Shioiri Procedure



85% H_3PO_4 as an external standard. High-resolution mass spectra were obtained using a JMS-700(2) double-focusing magnetic sector mass spectrometer (JEOL Ltd., Tokyo, Japan) operating in positive-ion

Scheme 13. Reactivity of Cinnamaldehyde 2n under Present and Ohira−Bestmann Methods



mode, with 3-nitrobenzyl alcohol (NBA) or triethanolamine (TEOA)-NaCl[27] as matrix. Melting points were determined on a Yanagimoto micromelting point apparatus and are uncorrected. IR spectra were recorded using a Shimazu IR-435 spectrometer.

Commercially available diethyl phosphorocyanidate[13a] (DEPC: WAKO Chemical Co.) was purified by distillation under reduced-pressure (21 mmHg, 55 °C), and kept under Ar atmosphere over 4 Å molecular sieves. Lithium cyanide (LiCN):[14,28] Acetone cyanohydrin (25 mL) was added dropwise to a solution of lithium hydride (2.74 g) in THF (250 mL) at 0 °C over a duration of 15 min. After the addition was complete, the reaction mixture was left to stir at rt for 2 h. Subsequently, the reaction mixture was concentrated by evaporating the solvent as much as possible to obtain a white residue. The white solid lithium cyanide residue was then dried in vacuo for 3 h until its color changed to pale orange, and was subsequently stored under an inert Ar atmosphere.

Synthesis of AT 14a and VT 16 rom CP 11a (Scheme 4). *1-Cyano-1-(4-isobutylphenyl)ethyl Diethylphosphate (**11a**: Scheme 4 and Table 1, entry 1).*[29] To a solution of 4-isobutylacetophenone (**1a**, 176 mg, 1 mmol) in THF (5 mL) were added DEPC (196 mg, 1.2 mmol) and LiCN (20 mg, 0.6 mmol) at rt. After stirring for 30 min, the reaction mixture was treated with water (50 mL), extracted with EtOAc:hexane (1:1, 75 mL), washed with brine (× 2), dried over Na_2SO_4, filtered, and concentrated to afford a crude residue. It was purified by silica gel column chromatography (EtOAc:hexane, 1:4) to give CP **11a** (335 mg, 99%) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.90 (d, 6H, J = 6.7 Hz), 1.25−1.34 (m, 6H), 1.87 (m, 1H), 2.14 (s, 3H), 2.50 (d, 2H, J = 7.1 Hz), 3.95−4.19 (m, 4H), 7.21 (d, 2H, J = 8.4 Hz), 7.53 (d, 2H, J = 8.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.9(15.86), 15.9(15.89), 15.9(15.93), 16.0, 22.3, 30.1(30.09), 30.1(30.14), 30.2, 44.9, 64.3(64.28), 64.3(64.34), 64.4, 64.5, 75.6, 75.7, 118.5, 118.6, 125.0, 129.5, 135.1, 135.2, 143.5; ^{31}P NMR (121 MHz, CD_3OD) δ - 5.2; HRMS (EI): m/z [M$^+$] calcd for $C_{13}H_{17}N_7$: 271.1545 ; found 271.1546.

*5-[1-Azido-1-(4-isobutylphenyl)ethyl]-1H-tetrazole (**14a**: Scheme 4 and Table 1, entry 1).* To a solution of CP **11a** (170 mg, 0.5 mmol) in THF (1 mL) were added NaN_3 (98 mg, 1.5 mmol), Et_3N·HCl (206 mg, 1.5 mmol) at 40 °C. After stirring for 24 h, the reaction mixture was treated with aq. 2 N HCl (5 mL) and extracted with EtOAc:hexane (1:1, 15 mL) and washed with brine (× 3), dried over $MgSO_4$, filtered, and concentrated to afford a crude residue. It was purified by silica gel column chromatography (EtOAc:hexane, 3:7) to give AT **14a** (124 mg, 91%) as a white powder (mp 119−120 °C). ^{1}H NMR (400 MHz, CD_3OD) δ 0.88 (d, 6H, J = 6.6 Hz), 1.85 (m, 1H), 2.14 (s, 3H), 2.48 (d, 2H, J = 7.2 Hz), 7.20 (d, 2H, J = 8.4 Hz), 7.25 (d, 2H, J = 8.4 Hz); ^{13}C NMR (400 MHz, CD_3OD) δ 22.6, 26.3, 31.3, 45.8, 64.6, 126.6, 130.7,

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138.6, 143.7, 161.8; HRMS (EI): m/z [M^+] calcd for $C_{13}H_{17}N_7$: 271.1545; found: 271.1546; FTIR (KBr, cm^{-1}): 2113.

*5-[1-(4-Isobutylphenyl)vinyl]-1H-tetrazole (**16**: Scheme 4).* NaN_3 (195 mg, 3 mmol) and Et_3N·HCl (411 mg, 3 mmol) were added to a solution of CP **11a** in DMF (2 mL). After the mixture was stirred at 100 °C for 2 h, aq. 2 N HCl (10 mL) was added to the mixture and extracted with EtOAc:hexane (1:1, 30 mL). The organic layer was washed with brine (× 2), dried over $MgSO_4$, filtered, and concentrated under vacuum to afford a crude residue. It was purified by silica gel column chromatography (EtOAc:hexane, 3:7) to give VT **16** (170 mg, 75%) as prisms (toluene); mp 121−122 °C. ^{1}H NMR (400 MHz, Acetone-d_6) δ 0.91 (d, 6H, J = 6.7 Hz), 1.90 (m, 1H), 2.53 (d,2H, J = 7.2 Hz), 5.97 (s, 1H), 6.16 (s, 1H), 7.24 (d, 2H, J = 8.2 Hz), 7.29 (d, 2H, J = 8.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 22.2, 30.0, 44.9, 122.1, 127.3, 129.3, 132.9, 133.5, 142.8, 155.8; HRMS (EI): m/z [M^+] calcd for $C_{13}H_{16}N_4$: 228.1375; found: 228.1377.

Transformation of CPs 11 and 12 into Alkynes 8 and 9 (Table 1). *General Procedure 1 (Synthesis of CPs 11 from Ketones 1).* To a solution of ketones **1** (1 mmol) in THF (5 mL), DEPC (196 mg, 1.2 mmol) and LiCN (20 mg, 0.6 mmol) were added at rt. After stirring for 30 min, the reaction mixture was diluted with water (50 mL), followed by extraction with EtOAc:hexane (1:1, 100 mL). The solvent was subsequently washed with brine (× 2), dried over Na_2SO_4, filtered, and concentrated on a rotary evaporator to give a crude residue. The residue was purified by silica gel column chromatography (EtOAc:hexane) to give CPs **11**.

*1-Cyano-1-(p-tolyl)ethyl Diethylphosphate (**11b**: Table 1, entry 2).* According to the above general procedure, 4-methylacetophenone **1b** (268 mg, 2 mmol) provided **11b** (590 mg, 99%) as a colorless oil, after purification by silica gel column chromatography (EtOAc:hexane, 2:3). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.26−1.35 (m, 6H), 2.13 (s, 3H), 2.38 (s, 3H), 3.97−4.19 (m, 4H), 7.24 (d, 2H, J = 8.6 Hz), 7.51 (d, 2H, J = 8.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.8, 15.9(15.87), 15.9(15.91), 15.9(15.94), 21.1, 30.2(30.16), 30.2(30.21), 64.3(64.28), 64.3(64.34), 64.4(64.37), 64.4(64.43), 75.5, 75.6, 118.4, 118.5, 125.1, 129.4, 134.9, 135.0, 139.7; ^{31}P NMR (121 MHz, $CDCl_3$) δ −5.20; HRMS (EI): m/z [M^+] calcd for $C_{14}H_{20}NO_4P$: 297.1130; found: 297.1138.

*1-(4-Chlorophenyl)-1-cyanoethyl Diethylphosphate (**11c**: Table 1, entry 3 and Table 4, entry 1).*[30] According to the above general procedure, 4-chloroacetophenone **1c** (773 mg, 5.0 mmol) provided **11c** (1365 mg, 86%, colorless oil), after purification by silica gel column chromatography (EtOAc:hexane, 1:4). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.28−1.36 (m, 6H), 2.12 (s, 3H), 4.09−4.21 (m, 4H), 7.42 (d, 2H, J = 8.6 Hz), 7.57 (d, 2H, J = 8.6 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.8, 15.9, 30.2(30.19), 30.2(30.24), 64.4, 64.5(64.46), 64.5(64.48), 64.5(64.54), 74.9(74.87), 74.9(74.94), 117.9 118.0, 126.6, 128.9, 135.7, 136.4, 136.5; ^{31}P NMR (121 MHz, $CDCl_3$) δ-5.12; HRMS (EI): m/z [M^+] calcd for $C_{13}H_{17}{}^{35}ClNO_4P$: 317.0583; found: 317.0579.

*1-Cyano-1-(6-methoxynaphthalen-2-yl)ethyl Diethylphosphate (**11d**: Table 1, entry 4).* According to the above general procedure, 2-acetyl-6-methoxynaphthalene **1d** (400 mg, 2 mmol) provided **11d** (690 mg, 95%) as a yellow oil, after purification by silica gel column chromatography (EtOAc:hexane, 2:3). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.25 (td, 3H, J = 7.1, 0.9 Hz), 1.31 (td, 3H, J = 7.1, 0.9 Hz), 2.24 (s, 3H), 3.94 (s, 3H), 3.97−4.19 (m, 4H), 7.15 (d, 1H, J = 2.4 Hz), 7.21 (dd, 2H, J = 9.1, 2.3 Hz), 7.63 (d, 1H, J = 8.8 Hz), 7.81 (dd, J = 8.8, 2.1 Hz), 8.05 (d, 1H, J = 2.1 Hz); HRMS (EI): m/z [M^+] calcd for $C_{18}H_{22}NO_5P$; 363.1235; found 363.1235.

*1-Cyano-1-(4-nitrophenyl)ethyl Diethylphosphate (**11e**: Table 1, entry 5 and Table 4, entry 2).*[30] According to the above general procedure, 4-nitroacetophenone **1e** (825 mg, 5.0 mmol) afforded **11e** (1591 mg, 97%, yellow oil), after purification by silica gel column chromatography (EtOAc:hexane, 1:4). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.31−1.38 (m, 6H), 2.15 (s, 3H), 4.09−4.25 (m, 4H), 7.82 (d, 2H, J = 8.8 Hz), 7.31 (d, 2H, J = 8.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 15.9(15.85), 15.9(15.92), 30.5(30.50), 30.5(30.54), 64.7, 64.8, 64.9, 74.6(74.55), 74.6(74.63), 117.4(117.41), 117.4(117.44), 124.1, 126.2, 144.6(144.58), 144.6(144.64), 148.4; ^{31}P NMR (121 MHz, $CDCl_3$) δ - 4.96; HRMS (EI): m/z [M^+] calcd for $C_{13}H_{17}N_2O_6P$: 328.0824; found: 328.0821.

*1-Cyano-1-phenylhexyl Diethylphosphate (**11f**: Table 1, entry 6).* According to the above general procedure, hexaphenone **1f** (352 mg, 2 mmol) provided **11f** (668 mg, 99%) as a colorless oil, after purification by silica gel column chromatography (EtOAc:hexane, 1:4). ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.83−0.87 (m, 3H), 1.19−1.31 (m, 11H), 1.50−1.56 (m, 1H), 2.16−2.21 (m, 1H), 2.32−2.40 (m, 1H), 3.88−4.14 (m, 4H), 7.39−7.46 (m, 3H), 7.59−7.62 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.7, 15.7, 15.8(15.78), 15.8(15.84), 22.1, 23.7, 30.9, 43.1, 43.2, 64.2(64.18), 64.2(64.24), 79.7, 79.8, 117.4(117.36), 117.4(117.39), 125.5, 128.6, 129.5, 136.6(136.61), 136.6(136.64); ^{31}P NMR (121 MHz, $CDCl_3$) δ - 5.10; HRMS (EI): m/z [M^+] calcd for $C_{17}H_{26}NO_4P$: 339.1599; found: 339.1598.

*Cyanodiphenylmethyl Diethylphosphate (**11g**: Table 1, entry 7 and Table 4, entry 20).*[29] According to the above general procedure, benzophenone **1g** (910 mg, 5.0 mmol) provided **11g** (1707 mg, 99%, colorless oil), after purification by silica gel column chromatography (EtOAc:hexane, 2:3). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.22−1.26 (m, 6H), 3.90−4.12 (m, 4H), 7.38−7.56 (m, 10H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.8, 15.9, 64.4(64.37), 64.4(64.43), 79.4(79.35), 79.4(79.44), 117.5(117.49), 117.5(117.51), 126.5, 128.7, 129.5, 138.3, 138.4; ^{31}P NMR (121 MHz, $CDCl_3$) δ - 5.03; HRMS (EI): m/z [M^+] calcd for $C_{14}H_{10}$:178.0783; found: 178.0782.

*2-Cyano-4-phenylbutan-2-yl Diethylphosphate (**11h**: Table 1, entry 8).*[31] According to the above general procedure, 4-phenyl-2-butanone **1h** (296 mg, 2 mmol) provided **11h** (602 mg, 97%, colorless oil), after purification by silica gel column chromatography (EtOAc:hexane, 1:4). ^{1}H NMR (CD_3OD) δ 1.36 (td, 3H, J = 7.1, 1.0 Hz), 1.37 (td, 3H, J = 7.1, 1.0 Hz), 1.89 (s, 3H), 2.21−2.36 (m, 2H), 2.80−2.93 (m, 2H), 4.13−4.22 (m, 4H), 7.17−7.31 (m, 5H); ^{13}C NMR ($CDCl_3$) δ 16.0(15.95), 16.0(16.02), 26.4, 26.5, 30.4, 43.2, 43.3, 64.4, 64.5(64.46), 64.5(64.52), 74.4, 74.5, 118.5(118.48), 118.5(118.52), 126.4, 128.3, 128.6, 139.6; ^{31}P NMR ($CDCl_3$) δ ppm -4.94; HRMS (EI): m/z [M+H] calcd for $C_{15}H_{23}NO_4P$; 312.1364 found 312.1363

*1-Cyano-2,2,2-trifluoro-1-phenylethyl Diethylphosphate (**11i**: Table 1, entry 9).* According to the general procedure 1, ketone **1i** (348 mg, 2.0 mmol) was treated for 5 min to provide, after purification by silica gel column chromatography (EtOAc:hexane, 1:4) to give **11i** (644 mg, 96%) as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.23−1.35 (m, 6H), 4.00−4.24 (m, 4H), 7.48−7.58 (m, 3H), 7.72−7.76 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.7, 15.8(15.75), 15.8(15.82), 15.9, 65.2, 65.3(65.29), 65.3(65.34), 65.4, 77.2, 77.5, 120.7 (quart, J = 285 Hz), 120.9 (quart, J = 285 Hz),122.4(122.38), 122.4(122.41), 127.2(127.23), 127.2(127.24), 128.9(128.88), 128.9(128.93), 131.5; HRMS (EI): m/z [M^+] calcd for $C_{13}H_{15}F_3NO_4P$: 337.0691; found: 337.0690.

General Procedure 2 (Synthesis of CPs 12 from Aldehydes 2). To a solution of aldehydes **2** (3 mmol) in THF (15 mL), DEPC (587 mg, 3.6 mmol) and LiCN (10 mg, 0.3 mmol) were added at rt. After stirring for 30 min, the reaction mixture was treated with water (50 mL), extracted with EtOAc:hexane (1:1, 100 mL). The organic layer was washed with brine, dried over Na_2SO_4, filtered, and concentrated to afford a crude residue, which was purified by silica gel column chromatography (EtOAc:hexane) to give CPs **12**.

*Cyano(4-isobutylphenyl)methyl Diethylphosphate (**12a**: Table 1, entry 10).* According to the general procedure 2, aldehyde **2a** (324 mg, 2 mmol) provided **12a** (606 mg, 98%, colorless oil), after purification by silica gel column chromatography (EtOAc:hexane, 1:4). ^{1}H NMR (400 MHz, CD_3OD) δ 0.91 (d, 6H, J = 6.6 Hz), 1.22−1.25 (m, 3H), 1.32−1.36 (m, 3H), 1.89 (m, 1H), 2.53 (d, 2H, J = 7.2 Hz), 4.00−4.23 (m, 4H), 6.24 (d, 1H, J = 8.8 Hz), 7.30 (d, 2H, J = 8.3 Hz), 7.49 (d, 2H, J = 8.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.7(15.66), 15.7(15.72), 15.8, 15.9, 22.1, 30.0, 45.0, 64.4, 64.5, 64.6, 64.7, 66.4(66.35), 66.4(66.39), 116.1, 116.2, 127.3, 129.7, 129.8(129.75), 129.8(129.81), 144.5; ^{31}P NMR (121 MHz, $CDCl_3$) δ - 1.69; HRMS (EI): m/z [M^+] calcd for $C_{16}H_{24}NO_4P$: 325.1443; found: 325.1445

*Cyano(phenyl)methyl Diethylphosphate (**12b**: Table 1, entry 11).*[31] According to the general procedure 2, a solution of benzaldehyde **2b** (212 mg, 2.0 mmol) was treated 10 min, a residue was purified by silica gel column chromatography (EtOAc:hexane, 1:9) to give **12b** (521 mg, 98%) as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.22−1.26 (m, 3H),

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1.37−1.41 (m, 3H), 3.95−4.29 (m, 4H), 6.06 (d, 1H, J = 8.8 Hz), 7.45−7.58 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.8(15.77), 15.8(15.84), 15.9, 16.0, 64.6, 64.7, 64.8, 64.9, 66.5(66.45), 66.5(66.50), 116.1(116.07), 116.1(116.13), 127.5, 129.2, 130.6, 132.4(132.37), 132.4(132.43); ^{31}P NMR (121 MHz, $CDCl_3$) δ - 1.68; HRMS (EI): m/z [M^+] calcd for $C_{12}H_{16}NO_4P$: 269.0817; found: 269.0816.

*1-Cyano-2-phenylethyl Diethylphosphate (**12c**: Table 1, entry 12).*[31] According to the general procedure 2, a solution of phenyl acetaldehyde **2c** (240 mg, 2.0 mmol) was treated 10 min, a residue was purified by silica gel column chromatography (EtOAc:hexane, 1:4) to give **12c** (539 mg, 95%) as a colorless oil. ^{1}H NMR (400 MHz, acetone-d_6) δ 1.19−1.23 (m, 3H), 1.25−1.29 (m, 3H), 3.25−3.38 (m, 2H), 3.87−4.13 (m, 4H), 5.38 (m, 1H), 7.30−7.42 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.9(15.86), 15.9(15.93), 40.4(40.37), 40.4(40.43), 64.6(64.55), 64.6(64.60), 64.6(64.62), 64.7, 65.4(65.36), 65.4(65.42), 116.4, 116.5, 127.9, 128.8, 129.6, 132.9; ^{31}P NMR (121 MHz, $CDCl_3$) δ - 1.81; HRMS (EI): m/z [M^+] calcd for $C_{13}H_{18}NO_4P$: 283.0973; found: 283.0972.

*General Procedure 3 [Formation of α-Azidotetrazole (AT) **14** or **15**].* To a solution of CPs **11** or **12** (0.5 mmol) in THF (1 mL), NaN_3 (98 mg, 1.5 mmol) and Et_3N·HCl (206 mg, 1.5 mmol) were added at 40 °C. After stirring for 24 h, the reaction mixture was treated with aq. 2 N HCl (5 mL) and extracted with EtOAc:hexane (1:1, 15 mL). The organic extract was washed with brine (× 3), dried over $MgSO_4$, filtered, and concentrated to give a crude residue. The residue was purified by silica gel column chromatography (EtOAc:hexane) to obtain ATs **14** or **15**.

*5-[1-Azido-1-(p-tolyl)ethyl]-1H-tetrazole (**14b**: Table 1, entry 2).* According to the general procedure 3, CP **11b** (149 mg, 0.5 mmol) provided **14b** (105 mg, 91%) as a yellow oil, after purification by silica gel column chromatography (EtOAc:hexane, 3:7). ^{1}H NMR (400 MHz, acetone-d_6) δ 2.16 (s, 3H), 2.30 (s, 3H), 7.13 (d, 2H, J = 8.0 Hz), 7.21 (d, 2H, J = 8.1 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.9, 25.6, 63.5. 125.7, 129.6, 136.7, 138.7, 161.5; HRMS (EI): m/z [M^+] calcd for $C_{10}H_{11}N_7$:229.1075; found: 229.1074; FTIR (film/NaCl, cm^{-1}): 2105.

*5-[1-Azido-1-(4-chlorophenyl)ethyl)-1H-tetrazole (**14c**: Table 1, entry 3).* According to the general procedure 3, CP **11c** (159 mg, 0.5 mmol) was treated for 8 h, a residue was purified by silica gel column chromatography (EtOAc:hexane, 3:7) to give **14c** (110 mg, 88%) as needles (CH_2Cl_2); mp 178−185 °C. ^{1}H NMR (400 MHz, CD_3OD) δ 2.15 (s, 3H), 7.37 (d, 2H, J = 9.0 Hz), 7.42 (d, 2H, J = 9.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 25.7, 62.9, 127.2, 129.2, 135.0, 137.9, 160.9; HRMS (EI): m/z [M^+] calcd for $C_9H_8{}^{35}ClN_7$: 249.0529; found: 249.0526; FTIR (KBr, cm^{-1}): 2105.

*5-[1-Azido-1-(6-methoxynaphthalen-2-yl)ethyl]-1H-tetrazole (**14d**: Table 1, entry 4).* According to the general procedure 3, CP **11d** (182 mg, 0.5 mmol) provided **14d** (142 mg, 96%) as needles (CH_2Cl_2, mp 136−137 °C), after purification by silica gel column chromatography (EtOAc:hexane, 2:8). ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.33 (s, 3H), 3.93 (s, 3H), 7.12 (d, 1H, J = 2.5 Hz), 7.19 (dd, 1H, J = 9.0, 2.6 Hz), 7.36 (dd, 1H, J = 8.8, 2.0 Hz), 7.73 (d, 1H, J = 4.9 Hz), 7.75 (d, 1H, J = 4.7 Hz), 7.81 (d, 1H, J = 1.9 Hz); ^{13}C NMR (100 MHz, CD_3OD) δ 26.1, 55.8, 64.8, 106.5, 120.6, 124.9, 125.7, 129.0, 129.7, 130.9, 135.9, 136.0, 160.0, 161.9; HRMS (EI): m/z [M^+] calcd for $C_{14}H_{13}N_7O$: 295.1181; found: 295.1180; FTIR (KBr, cm^{-1}): 2108.

*5-[1-Azido-1-(4-nitrophenyl)ethyl]-1H-tetrazole (**14e**: Table 1, entry 5).* According to the general procedure 3, CP **11e** (164 mg, 0.5 mmol) provided **14e** (95 mg, 73%) as yellow pillars (toluene, mp 88−90 °C), after purification by silica gel column chromatography (EtOAc:hexane, 3:7). ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.27 (s, 3H), 7.64 (d, 2H, J = 9.0 Hz), 8.24 (d, 2H, J = 9.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 26.0, 62.9, 124.2, 127.1, 146.6, 147.8, 161.3; HRMS (EI): m/z [M^+] calcd for $C_9H_8N_8O_2$: 260.0770; found: 260.0765; FTIR (KBr, cm^{-1}): 2135, 2110.

*5-(1-Azido-1-phenylhexyl)-1H-tetrazole (**14f**: Table 1, entry 6).* According to the general procedure 3, CP **11f** (170 mg, 0.5 mmol) was treated for 48 h, the residue was purified by silica gel column chromatography (EtOAc:hexane, 3:7) to give **14f** (112 mg, 82%) as a yellow oil. ^{1}H NMR (400 MHz, CD_3OD) δ 0.84 (t, 3H, J = 7.0 Hz), 1.16−1.33 (m, 6H), 2.43−2.57 (m, 2H), 7.29−7.38 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.8, 22.2, 23.2, 31.4, 38.2, 66.9, 126.0, 128.7, 128.9, 138.4, 160.3; HRMS (FAB): m/z [M+H]$^+$ calcd for $C_{13}H_{18}N_7$: 272.1624; found: 272.1630; FTIR (KBr, cm^{-1}): 2110.

*5-(Azidodiphenylmethyl)-1H-tetrazole (**14g**: Table 1, entry 7).* According to the general procedure 3, CP **11g** (173 mg, 0.5 mmol) was treated for 48 h at 60 °C, the residue was purified by silica gel column chromatography (EtOAc:hexane, 3:7) to give **14g** (75 mg, 54%) as a white amorphous solid. ^{1}H NMR (400 MHz, CD_3OD) δ 7.27−7.43 (m, 10H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 71.2, 127.8, 128.5, 128.7, 139.7, 162.322.7, 26.3, 31.3, 45.8, 64.5, 126.6, 130.7, 138.6, 143.7, 161.8; HRMS (EI): m/z [M^+] calcd for $C_{14}H_{11}N_7$: 277.1076; found: 277.1079; FTIR (film/NaCl, cm^{-1}): 2108.

*5-(2-Azido-4-phenylbutan-2-yl)-1H-tetrazole (**14h**: Table 1, entry 8).* According to the general procedure 3, CP **11h** (15 mg, 0.5 mmol) was treated for 48 h, the residue was purified by silica gel column chromatography (EtOAc:hexane, 3:7) to give **14h** (100 mg, 82%) as needles (toluene); mp 98−101 °C. ^{1}H NMR (400 MHz, CD_3OD) δ 1.84 (s, 3H), 2.25−2.38 (m, 2H), 2.41−2.48 (m, 1H), 2.61−2.68 (m, 1H), 7.12−7.16 (m, 3H), 7.22−7.26 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 24.9,, 30.3, 42.1, 61.4, 126.3, 128.2, 128.6, 139.9, 160.3; HRMS (EI): m/z [M+H]$^+$ calcd for $C_{11}H_{14}N_7$ 244.1310; found 244.1313.

*Diethyl 2,2,2-trifluoro-1-phenyl-1-(1H-tetrazol-5-yl)ethyl Phosphate (**13i**: Table 1, entry 9).* To a solution of CP **11i** (169 mg, 0.50 mmol) in THF (1 mL) were added NaN_3 (98 mg, 1.5 mmol), Et_3N·HCl (206 mg, 1.5 mmol). After the reaction mixture was stirred for 48 h at 15 °C, it was diluted with EtOAc and washed with H_2O (×2), brine. The organic phase was dried over Na_2SO_4, filtered and concentrated. The residue was purified by silica gel column chromatography (EtOAc:hexane, 1:1) to give tetrazole **13i** (158 mg, 83%) as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ1.26−1.40 (m, 6H), 4.08−4.33 (m, 4H), 7.37−7.47 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.7(15.71), 15.7(15.74), 15.8(15.78), 15.8(15.81), 65.4(65.38), 65.4(65.41), 65.4(65.44), 65.5, 81.4(81.36) (quart, J = 31.8 Hz), 81.4(81.43) (quart, J = 31.8 Hz), 122.6 (quart, J = 285 Hz), 126.9 (quart, J = 285 Hz), 127.6, 128.2, 130.1, 133.1(133.09), 133.1(133.13), 159.8; HRMS (EI): m/z [M^+] calcd for $C_{13}H_{16}F_3N_4O_4P$: 380.0861; found: 380.0862.

*5-[Azido(4-isobutylphenyl)methyl]-1H-tetrazole (**15a**: Table 1, entry 10).* According to the general procedure 3, CP **12a** (155 mg, 0.5 mmol) was treated at rt, the residue was purified by silica gel column chromatography (MeOH−CH_2Cl_2, 1:9) to give **15a** (126 mg, 98%) as needles (toluene); mp 130−131 °C. ^{1}H NMR (CD_3OD) δ 0.88 (d, 6H, J = 6.6 Hz), 1.86 (m, 1H), 2.49 (d, 2H, J = 7.2 Hz), 6.25 (s, 1H), 7.23 (d, 2H, J = 8.2 Hz), 7.49 (d, 2H, J = 8.2 Hz); ^{13}C NMR (CD_3OD) δ 22.6, 31.3, 45.9, 60.2, 128.6, 131.0, 134.0, 144.5, 158.2; HRMS (EI): m/z [M^+] calcd for $C_{12}H_{15}N_7$ 257.1389; found 257.1388.

*5-[Azido(phenyl)methyl]-1H-tetrazole (**15b**: Table 1, entry 11).* According to the general procedure 3, CP **12b** (135 mg, 0.5 mmol) was treated at rt, the residue was purified by silica gel column chromatography (EtOAc:hexane, 3:7) to give **15b** (82 mg, 81%) as prisms (toluene); mp 108−109 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.12 (s, 1H), 7.37−7.47 (m, 5H); ^{13}C NMR (100 MHz, CD_3OD) δ 60.3, 128.7, 130.3, 130.5, 136.7, 158.2; HRMS (EI): m/z [M^+] calcd for $C_8H_7N_7$: 201.0763; found: 201.0764; FTIR (KBr, cm^{-1}): 2111.

*5-(1-Azido-2-phenylethyl)-1H-tetrazole (**15c**: Table 1, entry 12).* According to the general procedure 3, CP **12c** (142 mg, 0.5 mmol) was treated for 48 h, the residue was purified by silica gel column chromatography (EtOAc:hexane, 2:8) to give **15c** (77 mg, 71%) as leaflets (toluene); mp 98−101 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.27 (dd, 1H, J = 14.1, 7.8 Hz), 3.50 (dd, 1H, J = 14.3, 5.1 Hz), 5.23 (m, 1H), 7.17−7.20 (m, 2H), 7.29−7.34 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 40.3, 57.3, 127.6, 128.9, 129.4, 134.8, 157.1; HRMS (EI): m/z [M^+] calcd for $C_9H_9N_7$: 215.0919; found: 215.0915; FTIR (KBr, cm^{-1}): 2137, 2097.

*General Procedure 4 (Transformation of ATs **14** into Alkynes **8** by Irradiation with MW Condition).* A solution of ATs **14** (0.5 mmol) in DMF/pyridine (5:2, v/v; 1 mL) was exposed to MW irradiation at 150 °C for 1 h. The reaction mixture was treated with aq 2 N HCl (5 mL) and extracted with methyl t-butyl ether (15 mL). The organic

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layer was washed with brine (×3), dried over $MgSO_4$, filtered, and concentrated to afford a crude residue. The residue was purified by silica gel column chromatography (hexane) to give alkynes **8**.

Caution: The MW container should be opened carefully to relieve the elevated internal pressure caused by release of N_2.

*1-Isobutyl-4-(prop-1-yn-1-yl)benzene (**8a**: Table 1, entry 1).* According to the general procedure 4, AT **14a** (136 mg, 0.50 mmol) provided **8a** (65 mg, 76%, colorless oil) after purification by silica gel column chromatography (hexane). ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.88 (d, 6H, J = 6.6 Hz), 1.84 (m, 1H), 2.04 (s, 3H), 2.44 (d, 2H, J = 7.3 Hz), 7.05 (d, 2H, J = 7.9 Hz), 7.29 (d, 2H, J = 7.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 4.3, 22.3, 30.1, 45.2, 79.7, 85.0, 121.1, 129.0, 131.2, 141.3; HRMS (EI): m/z [M$^+$] calcd for $C_{13}H_{16}$: 172.1252; found: 172.1252.

*1-Methyl-4-(prop-1-yn-1-yl)benzene (**8b**: Table 1, entry 2).*[32] According to the general procedure 4, AT **14b** (115 mg, 0.5 mmol) provided **8b** (47 mg, 72%, colorless oil) after purification by silica gel column chromatography (hexane). ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.04 (s, 3H), 2.33 (s,3H), 7.08 (d, 2H, J = 8.2 Hz), 7.28 (d, 2H, J = 8.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 4.2, 21.3, 79.7, 84.9, 120.9, 128.9, 131.3, 137.4; HRMS (EI): m/z [M$^+$] calcd for $C_{10}H_{10}$: 130.0783; found: 130.0779.

*1-Chloro-4-(prop-1-yn-1-yl)benzene (**8c**: Table 1, entry 3).*[32] According to the general procedure 4, AT **14c** (125 mg, 0.50 mmol) provided **8c** (49 mg, 65%, colorless oil) after purification by silica gel column chromatography (hexane). ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.03 (s, 3H), 7.24 (d, 2H, J = 8.8 Hz), 7.30 (d, 2H, J = 8.6 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 4.3, 78.7, 86.9, 122.5, 128.5, 132.7, 133.4; HRMS (EI): m/z [M$^+$] calcd for $C_9H_7{}^{35}Cl$: 150.0236; found: 150.0.237.

*2-Methoxy-6-(prop-1-yn-1-yl)naphthalene (**8d**: Table 1, entry 4).* According to the general procedure 4, AT **14d** (148 mg, 0.5 mmol) provided **8d** (80 mg, 82%) as leaflets (EtOH, mp 108−109 °C), after purification by silica gel column chromatography (hexane). ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.09 (s, 3H), 3.92 (s, 3H), 7.09 (d, 1H, J = 2.5 Hz), 7.13 (dd, 1H, J = 8.8, 2.5 Hz), 7.41 (dd, 1H, J = 8.4, 1.6 Hz), 7.64 (d, 1H, J = 9.4 Hz), 7.66 (d, 1H, J = 9.6), 7.82 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 4.3, 55.2, 80.1, 85.3, 105.6, 118.9, 119.1, 126.6, 128.5, 129.1, 130.8, 133.6, 157.9; HRMS (EI): m/z [M$^+$] calcd for $C_{14}H_{12}O$: 196.0888; found: 196.0886.

*1-Nitro-4-(prop-1-yn-1-yl)benzene (**8e**: Table 1, entry 5).*[33] According to the general procedure 4, AT **14e** (130 mg, 0.50 mmol) provided **8e** (32 mg, 40%) as yellow prisms [hexane, mp 105−106 °C (lit. mp 103−104 °C)], after purification by silica gel column chromatography (hexane). ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.10 (s, 3H), 7.51 (d, 2H, J = 8.9 Hz), 8.15 (d, 2H, J = 9.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 4.5, 78.4, 92.2, 123.5, 131.1, 132.2, 146.6.

*Hept-1-yn-1-ylbenzene (**8f**: Table 1, entry 6).*[10] According to the general procedure 4, AT **14f** (136 mg, 0.5 mmol) provided **8f** (70 mg, 81%, colorless oil) after purification by silica gel column chromatography (hexane). ^{1}H NMR (400 MHz, acetone-d_6) δ 0.92 (t, 3H, J = 7.2 Hz), 1.32−1.49 (m, 4H), 1.56−1.64 (m, 2H), 2.41 (t, 2H, J = 7.0 Hz), 7.30−7.40 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.0, 19.4, 22.2, 28.5, 31.1, 80.5, 90.4, 124.1, 127.4, 128.1, 131.5; HRMS (EI): m/z [M$^+$] calcd for $C_{13}H_{16}$: 172.1252; found: 172.1250.

*1,2-Diphenylethyne (**8g**: Table 1, entry 7).*[10] According to the general procedure 4, AT **14g** (139 mg, 0.50 mmol) provided **8g** (78 mg, 88%) as pillars [hexane, mp 55−57 °C (lit. 58−60 °C)] after purification by silica gel column chromatography (hexane). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31−7.55 (m, 10H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 89.4, 123.3, 128.2, 128.3, 131.6.

*Pent-3-yn-1-ylbenzene (**8h**: Table 1, entry 8).*[34] According to the general procedure 4, AT **14h** (122 mg, 0.5 mmol) provided **8h** (12 mg, 17%, oil), after purification by silica gel column chromatography (hexane). ^{1}H NMR ($CDCl_3$) δ 1.78 (t, 3H, J = 2.4 Hz), 2.38−2.45 (m, 2H), 2.80 (t, 2H, J = 7.6 Hz), 7.18−7.32 (m, 5H); ^{13}C NMR ($CDCl_3$) δ 3.5, 20.9, 35.5, 76.1, 78.6, 126.1, 128.3, 128.4, 141.0.

*1-Ethynyl-4-isobutylbenzene (**9a**) and 5-(4-Isobutylphenyl)-1H-1,2,3-triazole (**17a**: Table 1 entry 10).* According to the general procedure 4, AT **15a** (129 mg, 0.5 mmol) provided 1-ethynyl-4-isobutylbenzene **9a** (49 mg, 62%, colorless oil) and **17a** (19 mg, 19%, white solid), after purification by silica gel column chromatography (EtOAc:hexane, 3:7). **9a**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.89 (d, 6H, J = 6.6 Hz), 1.85 (m,1H), 2.47 (d, 2H, J = 7.2 Hz), 3.03 (s, 1H), 7.09 (d, 2H, J = 8.3 Hz), 7.40 (d, 2H, J = 8.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 22.3, 30.1, 45.3, 76.5, 83.9, 119.3, 129.1, 131.9, 142.7; HRMS (EI): m/z [M$^+$] calcd for $C_{12}H_{14}$: 158.1096; found: 158.1095; **17a**: ^{1}H NMR (400 MHz,$CDCl_3$): δ 0.93 (d, 6H, J = 6.6 Hz), 1.90 (m, 1H), 2.52 (d, 2H, J = 7.2 Hz), 7.24 (d, 2H, J = 8.4 Hz), 7.72 (d, 2H, J = 8.2 Hz), 7.95 (s, 1H), 11.62 (br, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 22.1, 29.6, 44.3, 125.4, 128.2, 129.5, 130.5, 141.2, 146.1.; HRMS (EI): m/z [M$^+$] calcd for $C_{12}H_{15}N_3$ 201.1266; found 201.1269.

*5-Phenyl-1H-1,2,3-triazole (**17b**: Table 1 entry 11).*[35] According to the general procedure 4, AT **15b** (101 mg, 0.5 mmol) provided **17b** (24 mg, 33%, white solid) after purification by silica gel column chromatography (EtOAc:hexane, 1:9). ^{1}H NMR (400 MHz, DMSO-d_6 + TFA, 1 drop): δ 7.33−7.38 (m, 1H), 7.43−7.48 (m, 2H), 7.85−7.87 (m, 2H), 8.34 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6 + TFA, 1 drop): δ 125.6, 127.5, 128.1, 129.0, 130.3, 145.1

*4-Benzyl-1H-1,2,3-triazole (**17c**: Table 1, entry 12).*[36] According to the general procedure 4, AT **15c** (108 mg, 0.5 mmol) provided **17c** (20 mg, 25%, yellow oil) after purification by silica gel column chromatography (EtOAc:hexane, 1:4). ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.15 (s, 2H), 7.21−7.38 (m, 5H), 7.43 (s, 1H); HRMS (EI): m/z [M$^+$] calcd for $C_9H_9N_3$ 159.0796 found 159.0796.

*Scheme 6, Synthesis of Tetrazole Analog **18** of Ibuprofen and Phenylalanine Biostere **19**. 5-[1-(4-Isobutylphenyl)ethyl]-1H-tetrazole (**18**).*[17] VT **16** (112 mg, 0.49 mmol) in EtOH (10 mL) was hydrogenated over 10% Pd on carbon (67 mg) at 3.0 kg/cm^2 for 2 h. After filtration through Celite, the filtrate was concentrated to afford a crude residue, which was purified by silica gel column chromatography (EtOAc:hexane, 1:4) to give **18** (106 mg, 94%) as a solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ 0.84 (d, 6H, J = 6.4 Hz), 1.64 (d, 3H, J = 7.3 Hz), 1.79 (m, 1H), 2.40 (d, 2H, J = 7.0 Hz), 4.50 (q, 1H, J = 7.2 Hz), 7.11 (d, 2H, J = 8.2 Hz), 7.15 (d, 2H, J = 8.2 Hz); ^{13}C NMR (100 MHz, CD_3OD) δ 20.7, 22.7, 31.4, 36.4, 45.9, 127.9, 130.7, 140.3, 142.1, 161.3.

*2-Phenyl-1-(1H-tetrazol-5-yl)ethanamine Hydrochloride (**19**).* AT **15c** (22 mg, 0.10 mmol) in EtOH (5 mL) was hydrogenated over 10% Pd on carbon (13 mg) at 3.0 kg/cm^2 for 2 h. After filtration of the reaction mixture though Celite, the filtrate was concentrated to afford a crude residue, which was dissolved in CH_2Cl_2 and extracted with aq 2 N HCl. The aqueous layer was evaporated to give **19** (21 mg, 91%) as a clear solid. ^{1}H NMR (400 MHz, CD_3OD) δ 3.36−3.48 (m, 2H), 5.05 (dd, 1H, J = 6.5 Hz), 7.12−7.14 (m, 2H), 7.22−7.30 (m, 3H); ^{13}C NMR (100 MHz, CD_3OD): δ 40.0, 128.8, 130.0, 130.3, 130.4, 135.4, 159.4; HRMS (EI): m/z [M$^+$] calcd for $C_9H_{11}N_5$ 189.1014; found 189.1007

*Transformation of Ketones **1** into Alkynes **8** (Table 4). 1-Cyano-1-(4-cyanophenyl)ethyl Diethylphosphate (**11j**: Table 4, entry 3).* According to the general procedure 1, ketone **1j** (435 mg, 3.0 mmol) provided **11j** (915 mg, 99%, colorless oil), after purification by silica gel column chromatography (EtOAc:hexane, 1:2). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.31−1.40 (m, 6H), 2.14 (s, 3H), 4.08−4.24 (m, 4H), 7.75−7.80 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.9, 16.0, 28.6(28.56), 28.6(28.61), 30.5(30.46), 30.5(30.51), 64.4(64.37), 64.4(64.43), 64.7, 64.8, 64.9, 74.7, 74.8, 113.7, 117.5(117.46), 117.5(117.49), 117.8, 125.9, 132.7, 142.9(142.88), 142.9(142.93); HRMS (EI): m/z [M$^+$] calcd for $C_{14}H_{17}N_2O_4P$: 308.0926; found: 308.0930.

*1-Cyano-1-(4-trifluoromethylphenyl)ethyl Diethylphosphate (**11k**: Table 4, entry 4).* According to the general procedure 1, ketone **1k** (564 mg, 3.0 mmol) provided **11k** (1042 mg, 99%, colorless oil), after purification by silica gel column chromatography (EtOAc:hexane, 1:4). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.29−1.36 (m, 6H), 2.15 (s, 3H), 7.72 (d, 2H, J = 8.8 Hz), 7.77 (d, 2H, J = 8.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.8(15.78), 15.8(15.81), 15.9(15.85), 15.9(15.88), 30.4, 30.5, 64.6(64.56), 64.6(64.62), 64.6(64.64), 64.7, 74.9(74.87), 74.9(74.94), 117.7, 117.8, 123.5 (q, J = 270.9 Hz), 125.5, 125.9 (q, J = 3.8 Hz), 131.7 (q, J = 32.6 Hz), 141.8(141.81), 141.8(141.82), 141.9; HRMS (EI): m/z [M$^+$] calcd for $C_{14}H_{17}F_3NO_4P$: 351.0847; found: 351.0851.

*Methyl 4-{1-Cyano-1-[(diethoxyphosphoryl)oxy]ethyl}benzoate (**11l**: Table 4, entry 5).* According to the general procedure 1, ketone **1l** (356 mg, 2.0 mmol) provided **11l** (634 mg, 93%, colorless oil), after

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purification by silica gel column chromatography (EtOAc:hexane, 1:2). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.29−1.40(m, 6H), 2.15 (s, 3H), 3.95 (s, 3H), 4.04−4.22 (m, 4H), 7.71 (dd, 2H, J = 8.8, 2.0 Hz), 8.12 (dd, 2H, J = 8.8, 2.0 Hz; ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.8, 15.9, 30.4, 30.5, 52.3, 64.5, 64.6(64.56), 64.6(64.58), 64.6(64.64), 75.1, 76.7, 117.8, 117.9, 125.1, 130.1, 131.3, 142.5(142.47), 142.5(142.53), 166.0; HRMS (EI): m/z [M$^+$] calcd for $C_{15}H_{20}NO_6P$: 341.1028; found: 341.1026.

*1-Cyano-1-(3-methoxyphenyl)ethyl Diethylphosphate (**11n**: Table 4, entry 7).* According to the general procedure 1, ketone **1n** (450 mg, 3.0 mmol) provided **11n** (798 mg, 85%, colorless oil), after purification by silica gel column chromatography (EtOAc:hexane, 1:2). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.28−1.36 (m, 6H), 2.13 (s, 3H), 3.84 (s, 3H), 4.01−4.22 (m, 4H), 6.95 (ddd, 1H, J = 8.4, 2.4, 0.8 Hz), 7.15 (dd, 1H, J = 2.4, 2.0 Hz), 7.20 (ddd, 1H, J = 7.6, 2.0, 0.8 Hz), 7.36 (dd, 1H, J = 8.4, 7.6 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.8, 15.9(15.85), 15.9(15.87), 15.9(15.91), 30.3, 30.4, 55.3, 64.3, 64.4(64.36), 64.4(64.40), 64.5, 75.3, 75.4, 110.9, 114.8, 117.1, 118.2(118.21), 118.2(118.24), 129.9, 139.4(139.39), 139.4(139.44), 159.7; HRMS (EI): m/z [M$^+$] calcd for $C_{14}H_{20}NO_5P$: 313.1079; found: 313.1079.

*1-Cyano-1-(3-nitrophenyl)ethyl Diethylphosphate (**11o**: Table 4, entry 8).* According to the general procedure 1, ketone **1o** (495 mg, 3.0 mmol) gave **11o** (974 mg, 99%, yellow oil), after purification by silica gel column chromatography (EtOAc:hexane, 2:3). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.34−1.38 (m, 6H), 2.19 (s, 3H), 4.12−4.26 (m, 4H), 7.70(t, 1H, J = 8.0 Hz), 8.00 (ddd, 1H, J = 8.0, 2.0, 0.8 Hz), 8.31 (ddd, 1H, J = 8.0, 2.0, 0.8 Hz), 8.48 (t, 1H, J = 2.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.8(15.75), 15.8(15.82), 30.3(30.25), 30.3(30.29), 64.6, 64.7, 64.8, 74.3, 74.4, 117.4(117.39), 117.4(117.42), 120.1, 124.4, 131.0, 131.1, 140.1, 140.2, 148.2; HRMS (EI): m/z [M$^+$] calcd for $C_{13}H_{17}N_2O_6P$: 328.0824; found: 328.0827.

*1-Cyano-1-{3-[(2-methoxyethoxy)methoxy]phenyl}ethyl Diethylphosphate (**11p**: Table 4, entry 9).* According to the general procedure 1, ketone **1p** (672 mg, 3.0 mmol) was treated with DEPC (1467 mg, 9 mmol) and LiCN (297 mg, 9.0 mmol) to provide **11p** (1149 mg, 99%, colorless oil) as a yellow oil, after purification by silica gel column chromatography (EtOAc:hexane, 1:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.28−1.36 (m, 6H), 2.13 (s, 3H), 3.38 (s, 3H), 3.55−3.57 (m, 2H), 3.82−3.84 (m, 2H), 4.02−4.23 (m, 4H), 7.11−7.14 (m, 1H), 7.25−7.28 (m, 2H), 7.33−7.37 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.9(15.89), 15.9(15.91), 16.0(15.96), 16.0(15.97), 30.3, 30.4, 59.0, 64.4, 64.5(64.47), 64.5(64.52), 64.6, 67.8, 71.5, 75.3, 75.4, 93.5, 113.6, 117.0, 118.3(118.25), 118.3(118.28), 118.4, 130.0, 139.5, 139.6, 157.5; HRMS (EI): m/z [M$^+$] calcd for $C_{17}H_{26}NO_7P$: 387.1447; found: 387.1446.

*1-[3-(Benzyloxy)phenyl]-1-cyanoethyl Diethylphosphate (**11q**: Table 4, entry 10).* According to the general procedure 1, ketone **1q** (678 mg, 3.0 mmol) provided **11q** (1144 mg, 98%, colorless oil), after purification by silica gel column chromatography (EtOAc:hexane, 1:2). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.26−1.35 (m, 6H), 2.12 (s,3H), 3.99−4.21 (m, 4H), 5.09 (s, 2H), 7.01 (ddd, 1H, J = 8.4, 2.4, 0.8 Hz), 7.20−7.24 (m, 2H), 7.31−7.45 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.8, 15.9(15.87), 15.9(15.91), 15.9(15.94), 30.4(30.35), 30.4(30.38), 64.4(64.36), 64.4(64.42), 64.5(64.46), 64.5(64.53), 70.1, 75.4(75.35), 75.4(75.44), 112.0, 115.7, 117.4, 118.2, 118.3, 127.5, 128.1, 128.6, 130.0, 136.3, 139.5(139.48), 139.5(139.54), 158.9; HRMS (EI): m/z [M$^+$] calcd for $C_{20}H_{24}NO_5P$: 389.1392; found: 389.1389.

*3-{1-Cyano-1-[(diethoxyphosphoryl)oxy]ethyl}phenyl 4-Methylbenzenesulfonate (**11r**: Table 4, entry 11).* According to the general procedure 1, ketone **1r** (911 mg, 3.1 mmol) provided **11r** (1351 mg, 95%) as a white solid (mp 66−67 °C), after purification by silica gel column chromatography (EtOAc:hexane, 2:3). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.29−1.35 (m, 6H), 2.03 (s, 3H), 2.46 (s, 3H), 4.03−4.22 (m, 4H), 7.09 (ddd, 1H, J = 8.0, 2.4, 0.8 Hz), 7.15 (t, 1H, J = 2.0 Hz), 7.34 (d, 2H, J = 8.0 Hz), 7.40 (t, 1H, J = 8.0 Hz), 7.53 (ddd, 1H, J = 8.0, 1.6, 0.8 Hz), 7.71 (ddd, 2H, J = 8.4, 2.0, 1.6 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.9(15.87), 15.9(15.94), 21.7, 30.2, 30.3, 64.5, 64.6(64.59), 64.6(64.63), 64.7, 74.5, 74.6, 117.7(117.67), 117.7(117.70), 119.3, 123.7, 128.5, 129.9, 130.2, 131.9, 140.0(139.98), 140.0(140.04), 145.8, 149.7; HRMS (EI): m/z [M$^+$] calcd for $C_{20}H_{24}NO_7PS$: 453.1011; found: 453.1013.

*3-{1-Cyano-1-[(diethoxyphosphoryl)oxy]ethyl}phenyl 4-Methylbenzenesulfonamide (**11s**: Table 4, entry 12).* According to the general procedure 1, ketone **1s** (867 mg, 3.0 mmol) provided **11s** (1288 mg, 95%, colorless oil), after purification by silica gel column chromatography (EtOAc:hexane, 1:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.24−1.39 (m, 6H), 2.04 (s, 3H), 2.37 (s, 3H), 3.97−4.23 (m, 4H), 7.20−7.35 (m, 6H), 7.71 (d, 2H, J = 8.0 Hz), 7.77 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.8, 15.9(15.89), 15.9(15.91), 16.0, 21.5, 28.6(28.59), 28.6(28.64), 30.3(30.26), 30.3(30.30), 64.7(64.66), 64.7(64.72), 64.8, 75.1, 75.2, 117.3, 118.0(117.99), 118.0(118.02), 121.1, 121.6, 127.3, 129.7, 129.8, 136.0, 137.8, 139.2(139.18), 139.2(139.23), 144.0; HRMS (EI): m/z [M$^+$] calcd for $C_{20}H_{25}N_2O_6PS$: 452.1171; found: 452.1180.

*t-Butyl {3-{1-cyano-1-[(diethoxyphosphoryl)oxy]ethyl}phenyl}-carbamate (**11t**: Table 4, entry 13).* According to the general procedure 1, ketone **1t** (470 mg, 2.0 mmol) provided **11t** (764 mg, 96%, colorless oil), after purification by silica gel column chromatography (EtOAc:hexane, 1:2). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.28−1.35 (m, 6H), 1.52 (s, 9H), 2.13 (s, 3H), 4.04−4.19 (m, 4H), 6.87 (s, 1H), 7.26 (ddd, 1H, J = 8.0, 4.0, 0.8 Hz), 7.34 (t, 1H, J = 8.0 Hz), 7.47−7.49 (brd, 1H, J = 8.0 Hz), 7.63 (t, 1H, J = 4.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.8, 15.8, 30.4, 30.5, 52.3, 64.5, 64.6(64.56), 64.6(64.58), 64.6(64.64), 75.1, 75.2, 117.8, 117.9, 125.1, 130.1, 131.3, 142.5(142.47), 142.5(142.53), 166.0; HRMS (EI): m/z [M$^+$] calcd for $C_{18}H_{27}N_2O_6P$: 398.1607; found:398.1604.

*1-[3-(t-Buthyldimethylsilyloxy)phenyl]-1-cyanoethyl Diethylphosphate (**11u**: Table 4, entry 14).* According to the general procedure 1, ketone **1u** (750 mg, 3.0 mmol) was treated with DEPC (1467 mg, 9.0 mmol), LiCN (297 mg, 9.0 mmol) and refluxed for 0.5 h to provide **11u** (830 mg, 67%, colorless oil), after purification by silica gel column chromatography (EtOAc:hexane, 1:2). ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.22 (s, 6H), 0.99 (s, 9H), 1.27−1.37 (m, 6H), 2.12 (s, 3H), 4.01−4.22 (m, 4H), 6.87 (ddd, 1H, J = 7.8, 2.1, 0.9 Hz), 7.08 (t, 1H, J = 2.1 Hz), 7.20 (ddd, 1H, J = 7.8, 2.1, 0.9 Hz), 7.30 (t, 1H, J = 7.8 Hz); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ −4.5, 15.9, 16.0, 18.1, 25.6, 30.4, 64.3, 64.4, 64.5, 64.6, 75.3, 75.4, 116.9, 117.8, 118.3(118.26), 118.3(118.31), 121.1, 129.9, 139.4, 139.5, 156.0; HRMS (EI): m/z [M$^+$] calcd for $C_{19}H_{32}NO_5PSi$: 413.1787; found:413.1785.

*1-Cyano-1-(2-nitrophenyl)ethyl Diethylphosphate (**11v**: Table 4, entry 15).* According to the general procedure 1, ketone **1v** (495 mg, 3.0 mmol) provided **11v** (974 mg, 99%, yellow oil), after purification by silica gel column chromatography (EtOAc:hexane, 2:3). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.33−1.38 (m, 6H), 2.40 (s, 3H), 4.13−4.25 (m, 4H), 7.56 (td, 1H, J = 7.6, 1.2 Hz), 7.67 (td, 1H, J = 7.6, 1.2 Hz), 7.70 (dd, 1H, J = 7.6, 1.2 Hz), 7.83 (dd, 1H, J = 7.6, 1.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.8, 15.9(15.85), 15.9(15.90), 15.9(15.92), 28.5, 28.6, 29.4(29.38), 29.4(29.41), 64.4(64.35), 64.4(64.41), 64.8(64.78), 64.8(64.84), 65.0(64.95), 65.0(65.01), 74.6, 74.7, 117.1(117.12), 117.1(117.14), 125.0, 127.5, 130.6, 130.8, 130.9, 132.2, 148.3; HRMS (EI): m/z [M+H$^+$] calcd for $C_{13}H_{18}N_2O_6P$: 329.0902; found: 329.0905.

*Cyano-phenyl-(pyridin-2-yl)methyl Diethylphosphate (**11w**: Table 4, entry 16).* According to the general procedure 1, ketone **1w** (366 mg, 2.0 mmol) was treated with DEPC (978 mg, 6.0 mmol) and LiCN (198 mg, 6.0 mmol) to provide **11w** (671 mg, 97%) as prisms (hexane/EtOAc, mp 98−101 °C), after purification by silica gel column chromatography (EtOAc:hexane, 1:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.24−1.28 (m, 6H), 4.00−4.19 (m, 4H), 7.31 (ddd, J = 1.2, 4.8, 7.6 Hz), 7.35−7.42 (m, 3H), 7.57−7.62 (m, 2H), 7.73−7.82 (m, 2H), 8.61 (dt, 1H, J = 1.2, 4.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.8, 15.9, 64.6, 64.7, 80.4, 80.5, 117.0, 117.1, 120.1, 124.0, 126.3, 128.7, 128.9, 129.5, 137.3(137.31), 137.3(137.34), 149.5, 156.7(156.66), 156.7(156.73); HRMS (EI): m/z [M$^+$] calcd for $C_{17}H_{19}N_2O_4P$: 346.1082; found: 346.1081.

*1-Cyano-1-(pyridin-3-yl)ethyl Diethylphosphate (**11x**: Table 4, entry 17).* According to the general procedure 1, ketone **1x** (605 mg, 5.0 mmol) provided **11x** (1150 mg, 81%, yellow oil), after purification by silica gel column chromatography (EtOAc:hexane, 1:1). ^{1}H NMR (400 MHz, CD_3OD) δ 1.26−1.34 (m, 6H), 2.19 (s, 3H), 4.04−4.23 (m, 4H), 7.57 (ddd, 1H, J = 8.4, 4.8, 0.8 Hz), 8.13 (ddd, 1H, J = 8.4, 2.4, 1.6 Hz), 8.66 (dd, 1H, J = 4.8, 1.6 Hz), 8.85 (dd, 1H, J = 2.4, 0.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.9, 16.0, 30.1, 30.2, 64.6, 64.7(64.68),

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64.7(64.72), 64.8, 73.9, 74.0, 117.5(117.49), 117.5(117.52), 123.4, 133.1, 133.8, 133.9, 146.7, 150.9; HRMS (EI): m/z [M^+] calcd for $C_{12}H_{17}N_2O_4P$: 284.0926; found: 284.0923.

*Cyano-phenyl-(pyridin-3-yl)methyl Diethylphosphate (**11y**: Table 4, entry 18).* According to the general procedure 1, ketone **1y** (366 mg, 2.0 mmol) was treated with DEPC (978 mg, 6.0 mmol) and LiCN (198 mg, 6.0 mmol) to provide **11y** (623 mg, 90%, yellow oil), after purification by silica gel column chromatography (EtOAc:hexane, 1:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.23−1.28 (m, 6H), 3.95−4.15 (m, 4H), 7.36 (ddd, 1H, J = 8.0, 4.8, 0.8 Hz), 7.41−7.47 (m, 3H), 7.53−7.57 (m, 2H), 7.87 (ddd, 1H, J = 8.0, 2.4, 1.6 Hz), 8.65 (dd, J = 4.8, 1.6 Hz), 8.77 (dd, 1H, J = 2.4, 0.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.8(15.75), 15.8(15.81), 64.5, 64.6, 77.7, 77.8, 116.7(116.70), 116.7(116.72), 123.2, 126.3, 128.9, 129.9, 134.3, 134.4(134.38), 134.4(134.44), 137.1, 137.2, 147.7, 150.6; HRMS (EI): m/z [M^+] calcd for $C_{17}H_{19}N_2O_4P$: 346.1082; found: 346.1084.

*Cyano-phenyl-(pyridin-4-yl)methyl Diethylphosphate (**11z**: Table 4, entry 19).* According to the general procedure 1, ketone **1z** (366 mg, 2.0 mmol) was treated with DEPC (978 mg, 6.0 mmol) and LiCN (198 mg, 6.0 mmol) to provide **11z** (491 mg, 71%, yellow oil), after purification by silica gel column chromatography (EtOAc:hexane, 1:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.23−1.28 (m, 6H), 3.94−4.17 (m, 4H), 7.45−7.48 (m, 5H), 7.52−7.55 (m, 2H), 8.69 (dd, 2H, J = 4.8, 1.6 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 15.8(15.78), 15.8(15.81), 15.9(15.85), 15.9(15.88), 64.7(64.66), 64.7(64.72), 78.2, 78.3, 116.5(116.50), 116.5(116.52), 120.5, 126.4, 129.0, 130.1, 136.7, 136.8, 147.2, 147.3, 150.4; HRMS (EI): m/z [M^+] calcd for $C_{17}H_{19}N_2O_4P$: 346.1082; found: 346.1080.

*1,4-Phenylenebis(1-cyanoethane-1,1-diyl) Tetraethyl Bisphosphate (**11aa**: Table 4, entry 21).* According to the general procedure 1, ketone **1aa** (162 mg, 1.0 mmol) was treated with DEPC (489 mg, 3.0 mmol) and LiCN (40 mg, 1.2 mmol) to provide **11aa** (416 mg, 85%, yellow wax) after purification by silica gel column chromatography (EtOAc:hexane, 4:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.30−1.37 (m, 12H), 2.15 (s, 6H), 4.06−4.23 (m, 8H), 7.71 (s, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.8, 15.9, 3.03(30.27), 3.03(30.30), 64.5(64.48), 64.5(64.54), 64.6(64.57), 64.6(64.63), 74.9(74.85), 74.9(74.92), 117.9(117.87), 117.9(117.90), 125.6, 139.6(139.55), 139.6(139.61); HRMS (EI): m/z [M^+] calcd for $C_{20}H_{30}N_2O_8P_2$: 488.1477; found: 488.1475.

*General Procedure 5 (Synthesis of Alkynes **8** from CPs **11**).* To a solution of CPs **11** (1.0 mmol) in toluene, $TMSN_3$ (116 mg, 1.0 mmol) and Bu_2SnO (25 mg, 0.1 mmol) were added, and the resulting mixture was refluxed for 2 h. Subsequently, the reaction mixture was evaporated to give a residue, which was purified by silica gel column chromatography (using hexane) to give alkynes **8**.

*1-Chloro-4-(prop-1-yn-1-yl)benzene (**8c**: Table 4, entry 1).*[32] According to the general procedure 5, CP **11c** (159 mg, 0.50 mmol) provided **8c** (47 mg, 63%, colorless oil) after purification by silica gel column chromatography (hexane).

*1-Nitro-4-(prop-1-yn-1-yl)benzene (**8e**: Table 4, entry 2).*[33] According to the general procedure 5, CP **11e** (164 mg, 0.50 mmol) provided **8e** (71 mg, 88%) as yellow prisms [hexane, mp 105−106 °C (lit. mp 103−104 °C)] after purification by silica gel column chromatography (hexane).

*1,2-Diphenylethyne (**8g**: Table 4, entry 20).* According to the general procedure 5, CP **11g** (173 mg, 0.50 mmol) provided **8g** (73 mg, 87%) as pillars (Hexane) after purification by silica gel column chromatography (hexane).

*4-(Prop-1-yn-1-yl)benzonitrile (**8j**: Table 4, entry 3).* According to the general procedure 5, CP **11j** (154 mg, 0.50 mmol) provided **8j** (54 mg, 70%) as white prisms (hexane, mp 112−115 °C) after purification by silica gel column chromatography (hexane). ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.08 (s, 3H), 7.45 (dd, 2H, J = 8.4, 2.0 Hz), 7.57 (dd, 2H, J = 8.4, 2.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 4.5, 78.6, 91.1, 110.8, 118.6, 129.1, 131.9, 132.0; HRMS (EI): m/z [M^+] calcd for $C_{10}H_7N$: 141.0578; found: 141.0577.

*1-(Prop-1-yn-1-yl)-4-(trifluoromethyl)benzene (**8k**: Table 4, entry 4).* According to the general procedure 5, CP **11k** (175 mg, 0.50 mmol) provided **8k** (78 mg, 85%, colorless oil) after purification by silica gel column chromatography (hexane). ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.06 (s, 3H), 7.47 (d, 2H, J = 8.4 Hz), 7.53 (d, 2H, J = 8.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 4.3, 78.7, 88.7, 124.0 (q, J = 270.9 Hz), 125.1 (q, J = 3.8 Hz), 127.9(127.88), 127.9(127.90), 129.3 (q, J = 32.6 Hz), 131.7; HRMS (EI): m/z [M^+] calcd for $C_{10}H_7F_3$: 184.0500; found: 184.0498.

*Methyl 4-(Prop-1-yn-1-yl)benzoate (**8l**: Table 4, entry 5).* According to the general procedure 5, CP **11l** (341 mg, 1.00 mmol) provided **8l** (142 mg, 82%) as a white powder (mp 58−59 °C) after purification by silica gel column chromatography (EtOAc:hexane, 1:19). ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.07 (s, 3H), 3.90 (s, 3H), 7.43 (dd, 2H, J = 8.0, 1.6 Hz), 7.95 (dd, 2H, J = 8.0, 1.6 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 4.4, 52.1, 79.2, 89.3, 128.8, 129.4, 131.4, 166.6; HRMS (EI): m/z [M^+] calcd for $C_{11}H_{10}O_2$: 174.0681; found: 174.0679.

*1-Methoxy-3-(prop-1-yn-1-yl)benzene (**8n**: Table 4, entry 7).* According to the general procedure 5, CP **11n** (157 mg, 0.50 mmol) provided **8n** (53 mg, 72%, colorless oil) after purification by silica gel column chromatography (hexane). ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.03 (s, 3H), 3.76 (s, 3H), 6.82 (ddd, 1H, J = 8.0, 2.4, 1.2 Hz), 6.92 (dd, 1H, J = 2.4, 1.2 Hz), 6.98 (dt, 1H, J = 8.0, 1.2 Hz), 7.19 (t, 1H, J = 8.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 4.2, 55.1, 79.6, 85.7, 114.0, 116.3, 124.0, 125.0, 129.2, 159.2; HRMS (EI): m/z [M^+] calcd for $C_{10}H_{10}O$: 146.0732; found: 146.0730.

*1-Nitro-3-(prop-1-yn-1-yl)benzene (**8o**: Table 4, entry 8).* According to the general procedure 5, CP **11o** (164 mg, 0.50 mmol) provided **8o** (68 mg, 85%) as yellow leaflets (hexane, mp 43−44 °C) after purification by silica gel column chromatography (EtOAc:hexane, 1:19). ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.08 (s, 3H), 7.45 (t, 1H, J = 8.0 Hz), 7.67 (dt, 1H, J = 8.0, 1.2 Hz), 8.11 (ddd, 1H, J = 8.0, 2.0, 1.2 Hz), 8.22 (t, 1H, J = 2.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 4.3, 77.6, 89.0, 122.2, 125.8, 126.3, 129.1, 137.2, 148.0; HRMS (EI): m/z [M^+] calcd for $C_9H_7NO_2$: 161.0477; found: 161.0478.

*1-[(2-Methoxyethoxy)methoxy]-3-(prop-1-yn-1-yl)benzene (**8p**: Table 4, entry 9).* According to the general procedure 5, CP **11p** (387 mg, 1.0 mmol) was treated with $TMSN_3$ (348 mg, 3.0 mmol) and Bu_2SnO (25 mg, 0.1 mmol) at reflux for 4 h to provide **8p** (184 mg, 78%, colorless oil), after purification by silica gel column chromatography (EtOAc:hexane, 1:19). ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.03 (s, 3H), 3.37 (s, 3H), 3.54−3.60 (m, 2H), 3.79−3.82 (m, 2H), 5.24 (s, 2H), 6.96 (ddd, 1H, J = 8.0, 2.4, 1.2 Hz), 7.03 (dt, 1H, J = 8.0, 1.2 Hz), 7.09 (dd, 1H, J = 2.4, 1.2 Hz), 7.18 (t, 1H, J = 8.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 4.2, 59.0, 67.6, 71.5, 79.4, 85.8, 93.3, 115.9, 119.1, 125.1(125.05), 125.1(125.10), 129.2, 156.9; HRMS (EI): m/z [M^+] calcd for $C_{13}H_{16}O_3$: 220.1099; found: 220.1101.

*1-(Benzyloxy)-3-(prop-1-yn-1-yl)benzene (**8q**: Table 4, entry 10).* According to the general procedure 5, CP **11q** (389 mg, 1.0 mmol) was treated with $TMSN_3$ (348 mg, 3.0 mmol) and Bu_2SnO (25 mg, 0.1 mmol) at reflux for 4 h to provide **8q** (226 mg, 88%) as a white solid (mp 58−59 °C) after purification by silica gel column chromatography (hexane). ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.03 (s, 3H), 5.02 (s, 2H), 6.87−6.90 (m, 1H), 6.99−7.05 (m, 2H), 7.19 (t 1H, J = 7.6 Hz), 7.29−7.42 (m, 5H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 4.3, 69.9, 79.6, 85.8, 114.9, 117.3, 124.3, 125.0, 127.4, 127.9, 128.5, 129.3, 136.7, 158.4; HRMS (EI): m/z [M^+] calcd for $C_{16}H_{14}O$: 222.1045; found: 222.1042.

*3-(Prop-1-yn-1-yl)phenyl 4-Methylbenzenesulfonate (**8r**: Table 4, entry 11).* According to the general procedure 5, CP **11r** (453 mg, 1.0 mmol) was treated with $TMSN_3$ (348 mg, 3.0 mmol) and Bu_2SnO (25 mg, 0.1 mmol) at reflux for 4 h to provide **8r** (252 mg, 82%, colorless oil), after purification by silica gel column chromatography (hexane). ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.01 (s, 3H), 2.44 (s, 3H), 6.86 (ddd, 1H, J = 8.0, 2.0, 1.2 Hz), 7.05 (t, 1H, J = 2.0 Hz), 7.17 (dd, 1H, J = 8.0, 7.6 Hz), 7.24 (dt, 1H, J = 7.6, 1.2 Hz), 7.31 (d, 2H, J = 8.0 Hz), 7.70 (dd, 2H, J = 8.0, 2.0 Hz); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 4.3, 21.7, 78.3, 87.5, 121.5, 125.3, 125.7, 128.4, 129.3, 129.8, 130.2, 132.1, 145.4, 149.3; HRMS (EI): m/z [M^+] calcd for $C_{16}H_{14}O_3S$: 286.0664; found: 286.0665.

*3-(Prop-1-yn-1-yl)phenyl 4-methylbenzenesulfonamide (**8s**: Table 4, entry 12).* According to the general procedure 5, CP **11s** (452 mg, 1.00 mmol) was treated with $TMSN_3$ (232 mg, 2.0 mmol) and Bu_2SnO (50 mg, 0.2 mmol) to provide **8s** (205 mg, 72%) as a white powder (mp 58−59 °C) after purification by silica gel column chromatography (EtOAc:hexane, 1:9). ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.01 (s, 3H), 2.37

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(s, 3H), 7.01−7.03 (m, 1H), 7.08−7.15 (m, 4H), 7.22 (d, 2H, J = 8.0 Hz), 7.68 (dd, 2H, J = 6.8, 1.6 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 4.3, 21.5, 78.9, 86.8, 120.3, 123.9, 125.1, 127.2, 128.2, 129.1, 129.7, 135.8, 136.6, 144.0; HRMS (EI): m/z [M^+] calcd for $C_{16}H_{15}NO_2S$: 285.0823; found: 285.0817.

*t-Buthyl [3-(prop-1-yn-1-yl)phenyl]carbamate (**8t**: Table 4, entry 13).* According to the general procedure 5, CP **11t** (199 mg, 0.50 mmol) was treated with $TMSN_3$ (116 mg, 1.0 mmol) and Bu_2SnO (25 mg, 0.10 mmol) to provide **8t** (54 mg, 47%) as a white powder (mp 71−72 °C) after purification by silica gel column chromatography (EtOAc:hexane, 3:97). ^{1}H NMR (400 MHz, CD_3OD) δ 1.50 (s, 9H), 1.99 (s, 3H), 6.96 (dt, 1H, J = 8.0, 1.2 Hz), 7.15 (t, 1H, J = 8.0 Hz), 7.30 (dd, 1H, J = 8.0, 1.2 Hz), 7.41 (s, 1H); ^{13}C NMR (100 MHz, CD_3OD): δ 3.7, 28.7, 80.5, 80.9, 86.1, 118.2, 122.4, 125.9, 126.7, 129.6, 140.6, 155.1; HRMS (EI): m/z [M^+] calcd for $C_{14}H_{17}NO_2$: 231.1259; found: 231.1256.

*1-(t-Buthylsilyloxy)-3-(prop-1-yn-1-yl)benzene (**8u**: Table 4, entry 14).* According to the general procedure 5, CP **11u** (413 mg, 1.00 mmol) was treated with $TMSN_3$ (348 mg, 3.0 mmol) and Bu_2SnO (25 mg, 0.10 mmol) at reflux for 4 h to provide **8u** (196 mg, 80%) after purification by silica gel column chromatography (hexane). ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.19 (s, 6H), 0.98 (s, 9H), 2.03 (s, 3H), 6.75 (ddd, 1H, J = 8.0, 2.4, 1.2 Hz), 6.87 (dd, 1H, J = 2.4, 1.2 Hz), 6.98 (dt, 1H, J = 8.0, 1.2 Hz), 7.12 (t, 1H, J = 8.0 Hz); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ −4.5, 4.3, 18.2, 25.6, 79.5, 85.6, 119.9, 123.0, 124.7, 124.9, 129.2, 155.3; HRMS (EI): m/z [M^+] calcd for $C_{15}H_{22}OSi$: 246.1440; found: 246.1435.

*1-Nitro-2-(prop-1-yn-1-yl)benzene (**8v**: Table 4, entry 15).* According to the general procedure 5, CP **11v** (164 mg, 0.50 mmol) provided **8v** (40 mg, 50%) as a yellow powder (mp 34−38 °C) after purification by silica gel column chromatography (EtOAc:hexane, 1:9). ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.13 (s, 3H), 7.39 (ddd, 1H, J = 8.0, 7.6, 1.6 Hz), 7.52 (td, 1H, J = 7.6, 1.2 Hz), 7.57 (dd, 1H, J = 7.6, 1.6 Hz), 7.96 (dd, 1H, J = 8.0, 1.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 4.8, 74.9, 94.8, 119.2, 124.3, 127.9, 132.5, 134.8, 150.0; HRMS (EI): m/z [M^+] calcd for $C_9H_7NO_2$: 161.0477; found: 161.0478.

*2-(Phenylethynyl)pyridine (**8w**: Table 4, entry 16).*[37] According to the general procedure 5, CP **11w** (364 mg, 1.0 mmol) was treated with $TMSN_3$ (232 mg, 2.0 mmol) and Bu_2SnO (50 mg, 0.2 mmol) at reflux for 4 h to provide **8w** (140 mg, 75%, yellow oil) after purification by silica gel column chromatography (EtOAc:hexane, 3:7). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.23 (ddd, 1H, J = 7.6, 4.8, 1.2 Hz), 7.35−7.38 (m, 3H), 7.52 (ddd, 1H, J = 7.6, 1.2, 0.8 Hz), 7.59−7.62 (m, 2H), 7.67 (td, 1H, J = 7.6, 1.6 Hz), 8.62 (ddd, 1H J = 4.8, 1.6, 0.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 88.5, 89.1, 122.2, 122.7, 127.1, 128.3, 128.9, 132.0, 136.1, 143.4, 150.0.

*3-(Prop-1-yn-1-yl)pyridine (**8x**: Table 4, entry 17).* According to the general procedure 5, CP **11x** (142 mg, 0.50 mmol, yellow oil) provided **8x** (36 mg, 61%) after purification by silica gel column chromatography (EtOAc:hexane, 3:7). ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.08 (s, 3H), 7.21 (ddd, 1H, J = 8.0, 4.8, 0.8 Hz), 7.66 (dt, 1H, J = 8.0, 2.0 Hz), 8.48 (dd, 1H, J = 4.8, 1.6 Hz), 8.62 (d, 1H, J = 1.6 Hz); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 4.4, 76.5, 89.4, 121.1, 122.9, 138.4, 147.9, 152.3; HRMS (EI): m/z [M^+] calcd for C_8H_7N: 117.0578; found: 117.0576.

*3-(Phenylethynyl)pyridine (**8y**: Table 4, entry 18).*[37] According to the general procedure 5, CP **11y** (346 mg, 1.0 mmol) was treated with $TMSN_3$ (232 mg, 2.0 mmol) and Bu_2SnO (50 mg, 0.2 mmol) at reflux for 4 h to provide **8y** (177 mg, 89%), after purification by silica gel column chromatography (EtOAc:hexane, 3:7). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29 (ddd, 1H, J = 8.0, 5.2, 0,8 Hz), 7.36−7.39 (m, 3H), 7.53−7.57 (m, 2H), 7.81 (dt, 1H, J = 8.0, 2.0 Hz), 8.55 (dd, 1H, J = 5.2, 1.6 Hz), 8.77 (dd, 1H, J = 5.2, 0.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 85.9, 92.6, 120.5, 122.5, 123.0, 128.4, 128.8, 131.7, 138.4, 148.5, 152.3.

*4-(Phenylethynyl)pyridine (**8z**: Table 4, entry 19).*[38] According to the general procedure 5, CP **11z** (346 mg, 1.00 mmol) was treated with $TMSN_3$ (232 mg, 2.0 mmol) and Bu_2SnO (50 mg, 0.2 mmol) at reflux for 4 h to provide **8z** (104 mg, 58%) after purification by silica gel column chromatography (EtOAc:hexane, 1:9). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36−7.40 (m, 5H), 7.54−7.57 (m, 2H), 8.60 (dd, 2H, J = 4.4, 1.1 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 86.6, 93.9, 122.0, 125.5, 128.5, 129.2, 131.4, 131.8, 149.7; HRMS (EI): m/z [M^+] calcd for $C_{13}H_9N$: 179.0735; found: 179.0735.

*1,4-Di(prop-1-yn-1-yl)benzene (**8aa**: Table 4, entry 21).*[39] According to the general procedure 5, CP **11aa** (244 mg, 0.50 mmol) was treated with $TMSN_3$ (174 mg, 1.5 mmol) and Bu_2SnO (12 mg, 0.05 mmol) at reflux for 21 h to provide **8aa** (65 mg, 84%, white powder) after purification by silica gel column chromatography (hexane). ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.05 (s, 6H), 7.29 (s, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 4.4, 79.5, 87.3, 123.1, 131.3.

Synthesis of mGlu5 Recepto Antagonist MPEP (Scheme 7). (6-Methylpyridin-2-yl) (phenyl)methanol.[40] PhMgBr (1 M) in THF (12 mL, 12 mmol) was added dropwise to a solution of 6-methyl-2-pyridinecarbaldehyde **2bb** (1210 mg, 10 mmol) in THF (50 mL) at 0 °C. After being stirred for 10 min at 0 °C, the mixture was stirred for 30 min at rt. It was quenched by aq sat. NH_4Cl and the aqueous layer was extracted with EtOAc. The organic layer was washed with brine, dried over $MgSO_4$, filtered, and concentrated under vacuum to afford crude residue, which was purified by silica gel column chromatography (EtOAc:hexane, 1:4) to give (6-methylpyridin-2-yl) (phenyl)methanol (1895 mg, 95%) as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.59 (s, 3H), 5.69 (s, 1H), 6.89 (d, 1H, J = 7.8 Hz), 7.04 (d, 1H, J = 7.2 Hz), 7.24−7.39 (m, 5H), 7.49 (dd, 1H, J = 7.9, 7.6); ^{13}C NMR (100 MHz, $CDCl_3$): δ 24.1, 74.5, 118.2, 121.7, 127.0, 127.6, 128.4, 137.0, 143.4, 156.5, 159.8

*(6-Methylpyridin-2-yl)(phenyl)methanone (**1bb**).*[41] Dess-Martin periodinane (4441 mg, 10.5 mmol) was added to a solution of (6-methylpyridin-2-yl)(phenyl)methanol (1895 mg, 9.5 mmol) in CH_2Cl_2 (50 mL) at 0 °C. After being stirred for 30 min at rt., the reaction mixture was quenched by aq. sat. $Na_2S_2O_3$ (50 mL) and aq. sat. $NaHCO_3$ (50 mL), and the aqueous layer was extracted with MTBE (50 mL × 2). The combined organic layer was washed with brine, dried over $MgSO_4$, filtered, and concentrated under vacuum to afford crude residue, which residue was purified by silica gel column chromatography (EtOAc:hexane, 1:19) to give **1bb** (1806 mg, 96%) as a yellow oil. ^{1}H NMR (400 mHz, $CDCl_3$) δ 2.64 (s, 3H), 7.35 (dd, 1H, J = 6.7, 2.4 Hz), 7.48 (app t, J = 7.9 Hz), 7.59 (app t, 1H, J = 7.5 Hz), 7.75−7.80 (m, 2H), 8.10 (app d, 2H, J = 8.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 24.4, 121.6, 125.7, 128.0, 131.1, 132.8, 136.2, 136.9, 154.6, 157.6, 193.8.

*Cyano-(6-methylpyridin-2-yl)-phenyl-methyl Diethylphosphate (**11bb**).* According to the general procedure 1, ketone **1bb** (394 mg, 2 mmol) provided CP **11bb** (686 mg, 95%) as prisms (isopropyl ether; mp 99−100 °C), after purification by silica gel column chromatography (EtOAc:hexane, 2:3). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.25−1.29 (m, 6H), 2.62 (s, 3H), 4.00−4.20 (m, 4H), 7.12 (d, 1H, J = 7.6 Hz), 7.34−7.41 (m, 3H), 7.50 (d, 1H, J = 7.1 Hz), 7.59−7.66 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.8(15.79), 15.8(15.81), 15.9(15.86), 15.9(15.89), 24.3, 64.5(64.47), 64.5(64.53), 80.6, 80.7, 116.9, 117.2(117.23), 117.2(117.25), 123.5, 126.3, 128.5, 129.4, 137.2, 137.5, 137.6, 155.7, 155.8, 158.6; ^{31}P NMR (121 MHz, $CDCl_3$) δ - 5.23; HRMS (EI): m/z [M^+] calcd for $C_{18}H_{21}N_2O_4P$: 360.1239; found: 360.1240.

*2-Methyl-6-(phenylethynyl)pyridine (**8bb**).*[42] According to the general procedure 5, CP **11bb** (158 mg, 0.44 mmol) was treated with $TMSN_3$ (102 mg, 0.88 mmol) and Bu_2SnO (22 mg, 0.09 mmol) at reflux for 4 h to provide MPEP (**8bb**:85 mg, 78%, yellow oil) after purification by silica gel column chromatography (EtOAc:hexane, 3:7). ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.59 (s, 3H), 7.12 (d, 1H, J = 7.4 Hz), 7.34−7.38 (m, 4H), 7.56−7.62 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 24.5, 88.7, 88.7, 122.3, 122.5, 124.3, 128.2, 128.8, 132.0, 136.3, 136.3, 142.6, 158.9.

*Transformation of β-Ketoester **1cc** into Alkyne **8cc** (Scheme 8). Ethyl 3-Cyano-3-[(diethoxyphosphoryl)oxy]-3-phenylpropanoate (**11cc**).* According to the general procedure 1, ketone **1cc** (384 mg, 2 mmol) was treated under solvent-free condition to provide **11cc** (700 mg, 99%) as a yellow oil after purification by silica gel column chromatography (EtOAc:hexane, 1:3). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.16−1.40 (m, 9H), 3.28 (d, 0.5H, J = 16.0 Hz), 3.29 (d, 0.5H, J = 16.0 Hz), 3.50 (d, 0.5H, J = 16.0 Hz), 3.51 (d, 0.5H, J = 16.0 Hz), 3.90−4.28 (m, 6H), 7.37−7.49 (m, 3H), 7.65−7.70 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.9, 14.2, 15.8(15.78), 15.8(15.84), 15.9, 16.0,

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46.8, 46.9, 60.3, 75.5, 75.6, 106.5(106.48), 106.5(106.54), 116.6(116.61), 116.6(116.64), 125.9, 126.9, 128.4, 128.7, 130.0, 130.7, 135.7(135.68), 135.7(135.71), 166.4; HRMS (EI): m/z [M$^+$] calcd for $C_{16}H_{22}NO_6P$: 355.1185; found: 355.1188.

*Ethyl 4-Phenylbut-3-ynoate (**8cc**).*[43] According to the general procedure 5, CP **11cc** (710 mg, 2.0 mmol) was treated with $TMSN_3$ (460 mg, 4.0 mmol) and Bu_2SnO (50 mg, 0.20 mmol) at reflux for 6 h to provide **8cc** (255 mg, 68%, yellow oil), after purification by silica gel column chromatography (EtOAc:hexane, 1:4). ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.31 (t, 3H, J = 6.9 Hz), 3.50 (s, 2H), 4.23 (quart, 2H, J = 6.9 Hz), 7.26−7.31 (m, 3H), 7.40−7.46 (m, 2H).

*Reactivity of Dialkyl Ketone **1dd** under Ohira−Bestmann Reaction and Shioiri Method (Scheme 9). 3-Cyano-1,5-diphenylpentan-3-yl Diethylphosphate (**11dd**).* According to the general procedure 1, ketone **1dd** (714 mg, 3 mmol) provided **11dd** (1087 mg, 90%) as a yellow oil, after purification by silica gel column chromatography (EtOAc:hexane, 1:3). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.36−1.41(m, 6H), 2.28−2.37(m, 2H), 2.40−2.48(m, 2H), 2.82−2.98(m, 4H), 4.18−4.26(m, 4H), 7.20−7.26(m, 6H), 7.29−7.33(m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 16.0, 16.1, 30.3, 40.7, 40.8, 64.6, 64.7, 77.9, 78.0, 117.7, 117.8, 126.5, 128.4, 128.7, 139.7; HRMS (FAB): m/z [M+H$^+$] calcd for $C_{22}H_{29}NO_4P$: 402.1834; found: 402.1832.

*1,6-Diphenylhex-3-yne (**8dd**).*[44] According to the general procedure 5, CP **11dd** (200 mg, 0.50 mmol) was treated with $TMSN_3$ (58 mg, 0.5 mmol) and Bu_2SnO (13 mg, 0.05 mmol) at reflux for 24 h to provide **8dd** (110 mg, 94%) as an oil after purification by silica gel column chromatography (hexane). ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.34(t, 4H, J = 7.6 Hz), 2.78(t, 4H, J = 7.6 Hz), 7.17−7.30(m, 10H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.9, 35.5, 80.2, 126.1, 128.4, 140.9.

*[3-(Methoxymethylene)pentane-1,5-diyl]dibenzene (**20**).*[24,45] To a solution of dimethyl (1-diazo-2-oxopropyl)phosphonate (0.18 mL, 1.2 mmol) in MeOH (3 mL) were added ketone **1dd** (238 mg, 1.0 mmol) in MeOH (2 mL) and potassium carbonate (276 mg, 2.0 mmol) at 0 °C. After stirred for 16 h at rt., the reaction mixture was quenched by H_2O (50 mL), and the aqueous layer was extracted with EtOAc (50 mL × 2). The combined organic layer was washed with brine, dried over Na_2SO_4, filtered, and concentrated under vacuum to afford a crude residue. It was purified by silica gel column chromatography (EtOAc:hexane, 1:9) to give **20** (107 mg, 40%) together with the recovery of **1dd** (129 mg, 54%).

*Trimethyl(3-phenethyl-5-phenylpenta-1,2-dien-1-yl)silane (**21**)*[24] *and 2-Phenethyl-4-phenylbutanal (**22**)*[5a] *(Scheme 9).* $TMSCHN_2$ solution (0.6 M) in hexane (2 mL, 1.2 mmol) was added dropwise to a solution of LDA, prepared from diisopropylamine (0.17 mL, 1.2 mmol) and 1.6 M n-butyllithium solution in hexane (0.75 mL, 1.2 mmol) in THF (6 mL) at −78 °C. After the reaction mixture was stirred at −78 °C for 30 min, a solution of ketone **1dd** (238 mg, 1.0 mmol) in THF (4 mL) was added dropwise at −78 °C. The mixture was stirred at −78 °C for 1 h, then heated under reflux for 3 h. The resulting mixture was quenched by H_2O (50 mL), and the aqueous layer was extracted with EtOAc (50 mL × 2). The combined organic layer was washed with brine, dried over Na_2SO_4, filtered, and concentrated under vacuum to afford a crude residue. It was purified by silica gel column chromatography (EtOAc:hexane, 1:19) to give **21**[24] (102 mg, 31%) and a 1:2 mixture (168 mg) of **22**[5a] (23%) and **1dd** (46%).

*Transformation of Cyclic Ketone **1ee** under Shioiri Method (Scheme 10). 1-Cyanocyclododecyl Diethylphosphate (**11ee**).* According to the general procedure 1, ketone **1ee** (910 mg, 5 mmol) provided **11ee** (1722 mg, 99%, yellow oil), after purification by silica gel column chromatography (EtOAc:hexane, 1:3). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.28−1.51 (m, 22H), 1.53−1.66 (m, 2H), 1.97−2.05 (m, 2H), 2.15−2.24 (m, 2H), 4.136−4.28 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 16.0(15.97), 16.0(16.04), 18.2, 21.9, 22.3, 25.5, 25.6, 33.3(33.25), 33.3(33.30), 64.4(64.37), 64.4(64.43), 77.4, 77.5, 118.7(118.70), 118.7(118.73); HRMS (FAB): m/z [M+H$^+$] calcd for $C_{17}H_{33}NO_4P$: 346.2147; found: 346.2146.

*Cyclotridecyne (**8ee**) and Bicyclo[8.2.1]tridec-1(13)-ene (**23ee**).* According to the general procedure 5, CP **11ee** (560 mg, 1.6 mmol) was treated with $TMSN_3$ (184 mg, 1.6 mmol) and Bu_2SnO (40 mg, 0.16 mmol) at reflux for 40 h to provide **23ee** (37 mg, 13%, oil) and **8ee** (185 mg, 65%, oil) after purification by silica gel column chromatography (hexane). **8ee**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.34−1.43 (m, 10H), 1.46−1.55(m, 8H), 2.14−2.19(m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 18.6, 25.3, 25.4, 25.7, 26.2, 27.6, 81.1; HRMS (EI): m/z [M]$^+$ calcd for $C_{13}H_{22}$: 178.1722; found: 178.1725. **23ee**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.09−1.70 (m, 14H), 1.97−2.25 (m, 4H), 2.36−2.64 (m, 2H), 2.90−2.98 (brm, 1H), 5.38 (brs, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.9, 24.7, 26.0(25.95), 26.0(25.99), 27.0, 27.1, 28.0, 32.2, 33.5, 35.4, 44.6, 131.3, 142.1; HRMS (EI): m/z [M]$^+$ calcd for $C_{13}H_{22}$: 178.1722; found: 178.1724.

*(2-Cyclododecylidenevinyl)trimethylsilane (**25**)*[24] *and Cyclododecanecarbaldehyde (**26**)*[5a,46] *(Scheme 10).* By the same procedure as used for the preparation of **21**, ketone **1ee** (182 mg, 1.0 mmol) provided **25**[24] (24 mg, 9%), **23ee** (16 mg, 9%), **8ee** (26 mg, 15%), and **26**[5a,46] (65 mg, 33%), together with recovery of **1ee** (60 mg, 33%) after purification by silica gel column chromatography (hexane).

*Transformation of Aldehyde **2** into Terminal Alkynes **9** (Table 5). Diethylphosphonooxy-(2,3,5-tri-O-benzyl-β-ribofuranosyl)-acetonitrile (**12d**: Table 5, entry 1).* According to the general procedure 2, β-ribofuranosyl aldehyde **2d** (1296 mg, 3 mmol) provided **12d** (1624 mg, 91%, colorless oil), after purification by silica gel column chromatography (EtOAc:hexane, 1:3). ^{1}H NMR (400 MHz, $CDCl_3$) δ1.27−1.39 (m, 6H), 3.46−3.57 (m, 2H), 3.90−4.23 (m, 6H), 4.27−4.35 (m, 2H), 4.42−4.67 (m, 6H), 5.03 (quart, 0.6H, J = 4.4 Hz), 5.12 (quart, 0.4H, J = 4.4 Hz), 7.22−7.38 (m, 15H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.9, 16.0(16.0), 16.0(16.03), 64.8, 64.9, 65.0(64.96), 65.0(65.01), 65.1, 65.7, 65.8, 69.5, 69.6, 69.9, 72.0, 72.1(72.05), 72.1(72.11), 72.3(72.27), 72.3(72.32), 73.5, 76.8, 77.2(77.17), 77.2(77.20), 77.5, 77.7, 78.8, 80.8, 81.3, 81.8, 82.2, 86.4, 114.7(114.70), 114.7(114.73), 115.2(115.18), 115.2(115.22), 127.6, 127.7(127.67), 127.7(127.69), 127.7(127.71), 127.7(127.74), 127.9, 128.0(127.95), 128.0(128.03), 128.1, 128.2(128.15), 128.2(128.22), 128.4(128.39), 128.4(128.44), 128.5, 137.0, 137.1, 137.2, 137.3(137.31), 137.3(137.34), 137.4, 137.8; HRMS (FAB): m/z [M+H$^+$] calcd for $C_{32}H_{39}NO_8P$:596.2413 ; found 596.2408.

*2-Diethylphosphonooxy-3-(2,3,5-tri-O-benzyl-β-ribofuranosyl)-propionitrile (**12e**: Table 5, entry 2).* According to the general procedure 2, β-ribofuranosyl acetaldehyde **2e** (892 mg, 2 mmol) provided **12e** (1200 mg, 99%, colorless oil), after purification by silica gel column chromatography (EtOAc:hexane, 1:3). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.29−1.39 (m, 6H), 1.84−2.07 (m, 1H), 2.19−2.29 (m, 1H), 3.42−3.50 (m, 2H), 3.60−3.65 (m, 1H), 3.90−3.96 (m, 1H), 4.08−4.22 (m, 6H), 4.42−4.62 (m, 6H), 5.12−5.21 (m, 1H), 7.24−7.38 (m, 15H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.9, 16.0, 38.1, 38.5, 61.7, 62.7, 64.6, 64.7, 70.0, 70.2, 71.8(71.76), 71.8(71.83), 72.2, 73.4, 73.5, 74.9, 75.7, 77.1, 80.8, 81.0, 82.1, 82.4, 116.5, 117.2, 127.6(127.58), 127.6(127.63), 127.7, 127.8, 127.9, 128.0(127.96), 128.0(127.98), 128.1(128.09), 128.1(128.12), 128.4(128.39), 128.4(128.41), 128.5, 137.4, 137.6, 137.8, 137.9; ^{31}P NMR (121 MHz, $CDCl_3$) δ - 2.27, −2.12; HRMS (FAB): m/z [M+H$^+$] calcd for $C_{33}H_{41}NO_8P$: 610.2570; found: 610.2575

*2-Diethylphosphonooxy-4-(2,3,5-tri-O-benzyl-β-ribofuranosyl)-butanenitrile (**12f**: Table 5, entry 3).* According to the general procedure 2, β-ribofuranosyl propionaldehyde **2f** (920 mg, 2 mmol) provided **12f** (1195 mg, 96%, colorless oil), after purification by silica gel column chromatography (EtOAc:hexane, 1:3). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.28−1.42 (m, 6H), 1.56−1.68 (m, 1H), 1.78−1.93 (m, 1H), 1.94−2.08 (m, 2H), 3.42−3.50 (m, 2H), 3.54−3.58 (m, 1H), 3.88−3.91 (m, 1H), 3.95−4.05 (m, 1H), 4.06−4.22 (m, 5H), 4.40−4.62 (m, 6H), 4.94−5.12 (m, 1H), 7.25−7.38 (m, 15H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.9, 16.0, 28.0, 28.1, 30.6, 30.7, 30.9, 31.0, 64.6, 64.7(64.65), 64.7(64.71), 64.8(64.78), 64.8(64.84), 70.4, 70.5, 71.7(71.70), 71.7(71.71), 72.1, 73.4(73.39), 73.4(73.42), 77.2(77.18), 77.2(77.21), 79.2, 79.4, 80.7, 80.9, 81.8, 81.9, 116.7(116.67), 116.7(116.71), 116.8(116.76), 116.8(116.80), 127.6(127.59), 127.6(127.62), 127.7(127.65), 127.7(127.67), 127.8, 127.9, 128.0, 128.1, 128.4(128.35), 128.4(128.39), 128.4(128.41), 137.6, 137.7, 140.0(137.97), 140.0(137.98); HRMS (FAB): m/z [M+H$^+$] calcd for $C_{34}H_{43}NO_8P$: 624.2726; found: 624.2727.

*Diethylphosphonooxy-(3,5-bis-O-benzyl-2-deoxy-β-ribofuranosyl)-acetonitrile (**12g**: Table 5, entry 4).* According to the general procedure 2, β-deoxyribofuranosyl aldehyde **2g** (360 mg, 1.10 mmol)

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provided **12g** (542 mg, quant, colorless oil), after purification by silica gel column chromatography (EtOAc:hexane, 1:3). ^{1}H NMR (400 MHz, $CDCl_3$) δ1.28−1.40 (m, 6H), 2.12−2.42 (m, 2H), 3.4−3.54 (m, 2H), 4.08−4.23 (m, 5H), 4.28−4.35 (m, 1H), 4.38−4.58 (m, 5H), 5.09 (dd, *J* = 8.4, 7.6 Hz, 0.6H), 5.24 (dd, *J* = 9.2, 8.0 Hz, 0.4H), 7.25−7.37 (m, 10H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.9, 16.0, 28.6(28.58), 28.6(28.62), 33.3, 34.1, 64.5, 64.6, 64.8(64.78), 64.8(64.81), 64.9, 66.5, 66.6, 67.2(67.18), 67.2(67.23), 70.3, 70.4, 71.4(71.36), 71.4(71.44), 73.4, 73.5, 78.5(78.46), 78.5(78.54), 79.1(79.06), 79.1(79.13), 79.3, 80.0, 83.8, 84.4, 115.7, 116.0(115.95), 116.0(115.97), 127.5, 127.7(127.68), 127.7(127.71), 127.7(127.74), 127.8(127.76), 127.8(127.82), 128.4(128.38), 128.4(128.40), 128.5, 137.4, 137.5, 137.8(137.80), 137.8(137.83); HRMS (FAB): *m*/*z* [M+H$^+$] calcd for $C_{25}H_{33}NO_7P$:490.1995 ; found 490.1996.

*(3S)-1-Cyano-3,7-dimethyloct-6-en-1-yl Diethylphosphate (**12h**: Table 5, entry 5).* According to the general procedure 2, aldehyde **2h** (385 mg, 2.5 mmol) provided **12h** (803 mg, quant) as a colorless oil, after purification by silica gel column chromatography (EtOAc:hexane, 1:2). ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.97−1.00(m, 3H), 1.19−1.30(m, 1H), 1.34−1.48(m, 7H), 1.61−1.84(m, 1H), 1.69(s, 3H), 1.70−1.84(m, 1H), 1.92−2.08(m, 3H), 4.12−4.24(m, 4H), 4.30−4.38(m, 1H), 5.00−5.10(m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.8, 15.9(15.88), 15.9(15.93), 16.0, 17.6, 18.7, 19.1, 25.0, 25.1, 25.6, 28.3, 28.6, 36.4, 36.6, 41.0, 41.1, 41.3(41.27), 41.3(41.33), 63.1, 63.2, 63.7(63.66), 63.7(63.72), 64.6, 64.7(64.65), 64.7(64.71), 66.0(65.96), 66.0(66.02), 116.9, 117.0, 117.2(117.20), 117.2(117.23), 123.8, 131.9; HRMS (FAB): *m*/*z* [M+H$^+$] calcd for $C_{15}H_{29}NO_4P$: 318.1835; found: 318.1843.

*2-(Benzyloxy)-1-cyanoethyl Diethylphosphate (**12i**: Table 5, entry 6).* According to the general procedure 2, aldehyde **2i** (750 mg, 5 mmol) provided **12i** (1380 mg, 88%, colorless oil), after purification by silica gel column chromatography (EtOAc:hexane, 1:2). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.30−1.39 (m, 6H), 3.80 (d, *J* = 5.6 Hz, 1H), 3.81 (d, *J* = 5.6 Hz, 1H), 4.08−4.24 (m, 4H), 4.62 (d, *J* = 12.0 Hz, 1H), 4.66 (d, *J* = 12.0 Hz, 1H), 5.15 (t, *J* = 5.6 Hz, 0.5H), 5.17 (t, *J* = 5.6 Hz, 0.5H), 7.29−7.40 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.9(15.87), 15.9(15.90), 15.9(15.94), 16.0, 28.6(28.56), 28.6(28.61), 63.9, 64.0, 64.8, 64.9, 69.3, 69.4, 73.7, 115.3(115.28), 115.3(115.31), 127.8, 128.2, 128.5, 136.6; HRMS (FAB): *m*/*z* [M+H$^+$] calcd for $C_{14}H_{21}NO_5P$: 314.1157; found: 314.1155.

*3-[4-(tert-Butyl)phenyl]-1-cyano-2-methylpropyl Diethylphosphate (**12j**: Table 5, entry 7).* According to the general procedure 2, aldehyde **2j** (613 mg, 3 mmol) provided **12j** (1103 mg, quant, colorless oil), after purification by silica gel column chromatography (EtOAc:hexane, 1:4). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.10 (d, *J* = 6.8 Hz, 1.5H), 1.13 (d, *J* = 6.4 Hz, 1.5H), 1.25−1.48 (m, 6H), 1.31 (s, 9H), 2.24−2.40 (m, 1H), 2.51 (dd, *J* = 13.6, 8.4 Hz, 0.5H), 2.60 (dd, *J* = 13.6, 8.0 Hz, 0.5H), 2.78 (dd, *J* = 13.6, 6.8 Hz, 0.5H), 2.94 (dd, *J* = 13.6, 5.6 Hz, 0.5H), 4.10−4.25 (m, 4H), 4.86 (dd, *J* = 8.4, 5.2 Hz, 0.5H), 4.95 (dd, *J* = 8.4, 4.0 Hz, 0.5H), 7.11(d, *J* = 8.0 Hz, 2H), 7.30−7.35 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.5(14.46), 14.5(14.49), 15.9, 16.0(15.98), 16.0(16.04), 16.1, 31.3, 34.4, 37.0, 37.8, 39.3, 39.4, 39.7, 39.8, 64.7(64.66), 64.7(64.71), 64.8, 68.3(68.25), 68.3(68.31), 68.8, 68.9, 115.6, 116.3(116.27), 116.3(116.30), 125.5, 125.6, 128.5, 128.8, 134.7, 135.1, 149.5, 149.7; HRMS (EI+): *m*/*z* [M$^+$] calcd for $C_{19}H_{31}NO_4P$: 368.1990; found: 368.1984.

*(1-Benzylpiperidin-4-yl)cyanomethyl Diethylphosphate (**12k**: Table 5, entry 8).* According to the general procedure 2, aldehyde **2k** (406 mg, 2 mmol) provided **12k** (673 mg, 92%, colorless oil), after purification by silica gel column chromatography (EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.34−1.42 (m, 6H), 1.45−1.60 (m, 2H), 1.75−2.03 (m, 5H), 2.93−3.00 (brm, 2H), 3.51 (s, 2H), 4.10−4.28 (m, 4H), 4.81 (d, *J* = 8.4 Hz, 0.5H), 4.83 (d, *J* = 8.4 Hz, 0.5H), 7.23−7.34 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 16.0(15.97), 16.0(16.04), 27.0, 27.3, 40.0, 40.1, 52.5, 52.6, 62.93, 64.69, 64.75, 68.70, 68.76, 115.93, 115.96, 127.03, 128.20, 128.97, 138.18; HRMS (EI): *m*/*z* [M$^+$] calcd for $C_{18}H_{27}N_2O_4P$: 366.1709; found: 366.1704.

*1-Cyano-2,2-diphenylethyl Diethylphosphate (**12l**: Table 5, entry 9).* According to the general procedure 2, aldehyde **2l** (589 mg, 3 mmol) provided **12l** (1080 mg, quant, colorless oil), after purification by silica gel column chromatography (EtOAc:hexane, 1:9). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.06−1.11 (m, 2.4H), 1.29−1.34 (m, 3.6H), 3.55−3.78 (m, 1.6H), 4.00−4.18 (m, 2.4H), 4.49 (d, *J* = 9.2 Hz, 1H), 5.65 (d, *J* = 9.2 Hz, 0.6H), 5.67 (d, *J* = 9.2 Hz, 0.4H), 7.22−7.40 (m, 10H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.7, 15.8, 15.9, 16.0, 54.9, 55.0, 64.4(64.35), 64.4(64.41), 64.7, 64.8, 67.4(67.36), 67.4(67.42), 116.3, 127.7, 128.0, 128.1, 128.2, 128.3, 128.4(128.38), 128.4(128.40), 128.9, 129.0, 129.9, 137.2, 137.6; HRMS (EI): *m*/*z* [M$^+$] calcd for $C_{19}H_{23}NO_4P$: 360.1365; found: 360.1364.

*[2-(Allyloxy)phenyl]cyanomethyl Diethylphosphate (**12m**: Table 5, entry 11).* According to the general procedure 2, aldehyde **2m** (486 mg, 3 mmol) provided **12m** (980 mg, quant, colorless oil), after purification by silica gel column chromatography (EtOAc:hexane, 1:3). ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.20−1.40 (m, 6H), 4.02−4.32 (m, 4H), 4.64 (d, *J* = 5.1 Hz, 2H), 5.32 (d, *J* = 10.8 Hz, 1H), 5.46 (d, *J* = 17.4 Hz, 1H), 6.06 (ddt, *J* = 17.4, 10.8, 5.1 Hz, 1H), 6.38 (d, *J* = 8.4 Hz, 1H), 6.94 (d, *J* = 8.4 Hz, 1H), 7.04 (t, *J* = 7.8 Hz, 1H), 7.43 (t, *J* = 7.8 Hz, 1H), 7.58 (d, *J* = 7.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.8, 15.9(15.87), 15.9(15.90), 16.0, 61.7, 61.8, 64.5(64.47), 64.5(64.53), 64.6(64.57), 64.6(64.62), 69.2, 112.14, 116.3(116.25), 116.3(116.29), 118.0, 121.0(120.95), 121.0(121.01), 121.1, 128.2, 131.7, 132.3, 155.3; HRMS (EI): *m*/*z* [M$^+$] calcd for $C_{15}H_{20}NO_5P$: 325.1079; found: 325.1079.

*(E)-1-Cyano-3-phenylallyl Diethylphosphate (**12n**: Table 5, entry 12).*[47] According to the general procedure 2, cinnamaldehyde **2n** (133 mg, 1 mmol) was treated at 0 °C to provide, after purification by silica gel column chromatography (EtOAc:hexane, 2:3) to give **12n** (290 mg, 98%) as a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.23−1.50 (m, 6H), 4.08−4.28 (m, 4H), 5.68 (ddd, *J* = 8.4, 7.2, 1.2 Hz, 1H), 6.26 (dd, *J* = 15.9, 7.2 Hz, 1H), 6.98 (d, *J* = 15.9 Hz, 1H), 7.33−7.46 (m, 5H).

*(E)-1-Cyano-3,7-dimethylocta-2,6-dien-1-yl Diethylphosphate (**12o**: Table 5, entry 13).* According to the general procedure 2, (*E*)-citral **2o** (380 mg, 2.5 mmol) was treated at 0 °C to provide **12o** (785 mg, 99%, colorless oil), after purification by silica gel column chromatography (EtOAc:hexane, 1:3). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.32−1.41 (m, 6H), 1.61 (s, 3H), 1.69 (s, 3H), 1.82 (s, 3H), 2.07−2.17 (m, 4H), 4.08−4.24 (m, 4H), 5.03−5.09 (m, 1H), 5.40 (d, 1H, *J* = 8.8 Hz), 5.69 (t, 1H, *J* = 8.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.9(15.91), 15.9(15.93), 16.0(15.97), 16.0(16.00), 17.0, 17.7, 25.6, 25.8, 39.2, 61.4(61.37), 61.4(61.41), 64.4, 64.5, 64.6(64.55), 64.6(64.61), 116.4(116.35), 116.4(116.41), 116.5(116.48), 116.5(116.54), 132.6, 147.5; HRMS (EI): *m*/*z* [M+H] calcd for $C_{15}H_{27}NO_4P$: 316.1678; found: 316.1676.

*(Z)-1-Cyano-3,7-dimethylocta-2,6-dien-1-yl Diethylphosphate (**12p**: Table 5, entry 14).* According to the general procedure 2, (*Z*)-citral **2p** (380 mg, 2.5 mmol) was treated at 0 °C to provide **12p** (781 mg, 99%, colorless oil), after purification by silica gel column chromatography (EtOAc:hexane, 1:3). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.30−1.39 (m, 6H), 1.61(s, 3H), 1.71 (s, 3H), 1.84 (s, 3H), 2.04−2.22 (m, 4H), 4.05−4.25 (m, 4H), 5.04−5.12 (m, 1H), 5.41 (d, 1H, *J* = 9.6 Hz), 5.68 (t, 1H, *J* = 8.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.9(15.88), 15.9(15.91), 16.0(15.95), 16.0(15.98), 17.6, 23.4, 25.7, 26.0, 32.4, 61.1, 61.2, 64.4(64.38), 64.4(64.44), 64.5, 64.6, 116.5, 116.6, 117.2(117.15), 117.2(117.21), 122.4, 133.5, 147.3; HRMS (EI): *m*/*z* [M+H] calcd for $C_{15}H_{27}NO_4P$: 316.1678; found: 316.1679.

*General Procedure 6 (Synthesis of Alkynes **9** from CPs **12**). Method A.* To a solution of CPs **12** (1.0 mmol) in THF (10 mL), NaN_3 (195 mg, 3.0 mmol) and Et_3N·HCl (413 mg, 3.0 mmol) were added. The reaction mixture was refluxed for 16 h. Subsequently, the reaction mixture was diluted with EtOAc and washed twice with H_2O, and brine. The organic phase was dried over Na_2SO_4, filtered, and concentrated. The residue was purified by silica gel column chromatography (EtOAc:hexane) to give the corresponding alkynes **9**.

Method B. To a solution of CPs **12** (1.0 mmol) in toluene (10 mL), $TMSN_3$ (115 mg, 1.0 mmol) and Bu_2SnO (25 mg, 0.1 mmol) were added, and the reaction mixture was refluxed for 2 h. Subsequently, the reaction mixture was concentrated and the residue was purified by silica gel column chromatography (EtOAc:hexane) to give the desired alkynes **9**.

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*1-Ethynyl-4-isobutylbenzene (**9a**: Table 5, entry 10). Method A.* CP **12a** (325 mg, 1.0 mmol) provided **9a** (46 mg, 29%) as a colorless oil after purification by silica gel column chromatography (hexane). Method B: CP **12a** (325 mg, 1.0 mmol) was treated at reflux for 0.5 h to provide **9a** (112 mg, 71%) after purification by silica gel column chromatography (hexane).

*(2R,3R,4S,5S)-3,4-Bis(benzyloxy)-2-[(benzyloxy)methyl]-5-ethynyltetrahydrofuran (**9d**: Table 5, entry 1).*[48] *Method A.* CP **12d** (1600 mg, 2.70 mmol) provided **9d** (786 mg, 68%) as a colorless oil after purification by silica gel column chromatography (EtOAc:hexane, 1:3).

Method B. CP **12d** (240 mg, 0.40 mmol) provided **9d** (80 mg, 47%) after purification by silica gel column chromatography. ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.54 (d, 1H, J = 2.4 Hz), 3.57 (dd, 1H, J = 6.6, 4.5 Hz), 3.61 (dd, 1H, J = 6.6, 4.2 Hz), 4.00−4.08 (m, 2H), 4.22 (quart, 1H, J = 4.5 Hz), 4.48−4.76 (m, 7H), 7.25−7.40 (m, 15H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 70.0, 70.7, 72.2, 72.3, 73.4, 75.0, 77.8, 81.4, 81.5, 81.7, 127.5, 127.6, 127.8, 127.9(127.86), 127.9(127.90), 127.9(127.93), 128.3(128.27), 128.3(128.34), 128.4, 137.4, 137.6, 138.1.

*(2R,3R,4S,5S)-3,4-Bis(benzyloxy)-2-[(benzyloxy)methyl]-5-(prop-2-yn-1-yl)tetrahydrofuran (**9e**: Table 5, entry 2). Method A.* CP **12e** (305 mg, 0.50 mmol) provided **9e** (222 mg, quant) as a colorless oil after purification by silica gel column chromatography (EtOAc:hexane, 1:3).

Method B. CP**12e** (305 mg, 0.50 mmol) provided **9e** (181 mg, 82%) after purification by silica gel column chromatography. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.95 (t, 1H, J = 2.8 Hz), 2.44 (ddd, 1H, J = 17.2, 5.6, 2.8 Hz), 3.52 (dd, 1H, J = 10.8, 4.4 Hz), 3.55 (dd, 1H, J = 10.8, 4.4 Hz), 3.84 (t, 1H, J = 5.6 Hz), 3.93 (t, 1H, J = 5.2 Hz), 4.17 (quart, 1H, J = 5.6 Hz), 4.23 (dd, 1H, J = 9.2, 4.4 Hz), 4.48−4.62 (m, 6H), 7.25−7.35 (m, 15H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 23.1, 70.1, 70.2, 71.8, 71.9, 73.4, 77.1, 79.2, 79.4, 80.4, 71.3, 127.6, 127.8(127.77), 127.8(127.79), 128.0, 128.1(128.06), 128.1(128.13), 128.3(128.31), 128.3(128.33), 128.4(128.35), 128.4(128.40), 137.8(137.77), 137.8(137.78), 138.2; HRMS (FAB, TEOA+NaCl): m/z [M+Na$^+$] calcd for $C_{29}H_{30}O_4Na$: 465.2042; found: 465.2047

*(2R,3R,4S,5S)-3,4-Bis(benzyloxy)-2-[(benzyloxy)methyl]-5-(but-3-yn-1-yl)tetrahydrofuran (**9f**: Table 5, entry 3). Method A.* CP **12f** (312 mg, 0.50 mmol) provided **9f** (228 mg, quant) as a colorless oil after purification by silica gel column chromatography (EtOAc:hexane, 1:3).

Method B. CP **12f** (305 mg, 0.50 mmol) provided **9f** (196 mg, 86%) after purification by silica gel column chromatography. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.63−1.72 (m, 1H), 1.89−1.98 (m, 1H), 1.93 (t, 1H, J = 2.8 Hz), 2.22−2.35 (m, 2H), 3.47 (dd, 1H, J = 6.4, 4.4 Hz), 3.50 (dd, 1H, J = 6.4, 4.4 Hz), 3.60 (dd, 1H, J = 6.4, 5.6 Hz), 3.88 (dd, 1H, J = 5.2, 4.4 Hz), 4.06−4.14 (m, 1H), 4.18 (quart, 1H, J = 4.4 Hz), 4.47−4.61 (m, 6H), 7.24−7.36 (m, 15H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.9, 32.7, 68.5, 70.3, 71.7, 71.9, 73.4, 77.4, 79.4, 80.5, 81.3, 84.0, 127.6(127.56), 127.6(127.59), 127.8, 127.9, 128.1, 128.3, 128.4, 137.8(137.78), 137.8(137.81), 138.11; HRMS (FAB, TEOA+NaCl): m/z [M+Na$^+$] calcd for $C_{30}H_{32}O_4Na$: 479.2198; found: 479.2202.

*(2R,3S,5R)-3-Benzyloxy-2-[(benzyloxy)methyl]-5-ethynyltetrahydrofuran (**9g**: Table 5, entry 4).*[49] *Method A.* CP **12g** (538 mg, 1.10 mmol) provided **9g** (280 mg, 74%) as a colorless oil after purification by silica gel column chromatography (EtOAc:hexane, 1:9). ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.19 (ddd, J = 12.8, 4.8, 4.0 Hz, 1H), 2.43 (dt, J = 12.8, 7.2 Hz, 1H), 2.50 (d, J = 2.4 Hz, 1H), 3.53 (dd, J = 10.4, 4.4 Hz, 1H), 3.57 (dd, J = 10.4, 4.4 Hz, 1H), 4.11 (dt, J = 7.2, 4.0 Hz, 1H), 4.28 (dd, J = 8.4, 4.4 Hz, 1H), 4.49 (d, J = 12.0 Hz, 1H), 4.50 (d, J = 12.4 Hz, 1H), 4.55 (d, J = 12.0 Hz, 1H), 4.56 (d, J = 12.4 Hz, 1H), 4.77−4.58 (m, 1H), 7.25−7.35 (m, 10H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 39.2, 67.6, 70.1, 71.5, 73.3, 73.4, 79.6, 82.8, 83.5, 127.6(127.59), 12.7.6(127.62), 127.8, 128.3, 128.4, 138.0(137.97), 138.0(138.02).

*(S)-4,8-dimethylnon-7-en-1-yne (**9h**: Table 5, entry 5).*[50] *Method A.* CP **12h** (795 mg, 2.50 mmol) provided **9h** (212 mg, 57%) as a colorless oil after purification by silica gel column chromatography (hexane).

Method B. CP **12h** (475 mg, 1.50 mmol) provided **9h** (123 mg, 55%) after purification by silica gel column chromatography. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.00 (d, 3H, J = 6.8 Hz), 1.19−1.29 (m, 1H), 1.40−1.50 (m, 1H), 1.61 (s, 3H), 1.62−1.72 (m, 1H), 1.68 (s, 3H), 1.93−2.03 (m, 2H), 1.95 (t, 1H, J = 2.8 Hz), 2.08 (ddd, 1H, J = 16.8, 6.8, 2.8 Hz), 5.10 (tquint, 1H, J = 7.2, 1.6 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 17.6, 19.3, 25.5, 25.6, 25.7, 31.9, 36.0, 69.0, 83.3, 124.4, 131.4; $[\alpha]_D^{20}$ +6.27 (c 0.80, $CHCl_3$).

*Benzyloxy-prop-1-yne (**9i**: Table 5, entry 6).*[51] *Method A.* CP **12i** (313 mg, 1.0 mmol) provided **9i** (128 mg, 88%) as a colorless oil after purification by silica gel column chromatography (EtOAc:hexane, 1:3).

Method B. CP **12i** (814 mg, 2.6 mmol) provided **9i** (310 mg, 82%) after purification by silica gel column chromatography. ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.47 (t, 1H, J = 2.4 Hz), 4.17 (d, 2H, J = 2.4 Hz), 4.61 (s, 2H), 7.28−7.38 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 57.0, 71.5, 74.7, 79.6, 127.9, 128.1, 128.4, 137.2.

*1-(tert-Butyl)-4-(2-methylbut-3-yn-1-yl)benzene (**9j**: Table 5, entry 7). Method A.* CP **12j** (435 mg, 1.18 mmol) provided **9j** (176 mg, 74%) as a colorless oil after purification by silica gel column chromatography (hexane).

Method B. CP **12j** (800 mg, 2.18 mmol) provide **9j** (295 mg, 68%) after purification by silica gel column chromatography. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.19 (d, J = 6.4 Hz, 1H), 1.31 (s, 9H), 2.07 (d, J = 2.0 Hz, 1H), 2.62−2.74 (m, 2H), 2.84 (dd, J = 11.6, 6.0 Hz, 1H), 7.16 (d, J = 8.0 Hz, 2H), 7.31 (d, J = 8.0 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.4, 27.6, 31.9, 34.4, 42.3, 68.9, 88.7, 125.1, 128.8, 136.3, 149.1; HRMS (EI): m/z [M$^+$] calcd for $C_{15}H_{20}$: 200.1565; found: 200.1563.

*1-Benzyl-4-ethynylpiperidine (**9k**: Table 5, entry 8). Method A.* CP **12k** (140 mg, 0.38 mmol) provided **9k** (54 mg, 71%) as a colorless oil after purification by silica gel column chromatography (EtOAc:hexane, 1:1).

Method B. CP **12k** (650 mg, 1.8 mmol) provided **9k** (217 mg, 61%) after purification by silica gel column chromatography. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.64−1.74 (m, 2H), 1.81−1.89 (m, 2H), 2.06 (d, J = 2.4 Hz, 1H), 2.08−2.22 (brm, 2H), 2.34−2.44 (brm, 1H), 2.66−2.76 (brm, 2H), 3.48 (s, 2H), 7.21−7.32 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 26.8, 31.7, 52.1, 63.4, 68.7, 87.6, 126.9, 128.1, 129.1, 138.4; HRMS (EI): m/z [M$^+$] calcd for $C_{14}H_{16}N$: 198.1283; found: 198.1283.

*3,3-Diphenylpropyne (**9l**: Table 5, entry 9).*[52] *Method A.* CP **12l** (418 mg, 1.2 mmol) provided **9l** (226 mg, quant) after purification by silica gel column chromatography (EtOAc:hexane, 1:9).

Method B. CP **12l** (405 mg, 1.1 mmol) provided **9l** (138 mg, 64%) after purification by silica gel column chromatography (EtOAc:hexane, 1:9). ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.47 (d, J = 2.4 Hz, 1H), 5.00 (d, J = 2.4 Hz, 1H), 7.18−7.40 (m, 10H).

*1-(Allyloxy)-2-ethynylbenzene (**9m**: Table 5, entry 11).*[53] *Method B.* CP **12m** (310 mg, 0.95 mmol) provided **9m** (132 mg, 88%) as a colorless oil after purification by silica gel column chromatography (EtOAc:hexane, 1:4). ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.29 (s, 1H), 4.64 (d, J = 8.1 Hz, 2H), 5.29 (dd, J = 10.8, 3.3 Hz, 1H), 5.46 (dd, J = 17.4, 3.6 Hz, 1H), 6.00−6.14 (m, 1H), 6.85−6.95 (m, 2H), 7.25−7.30 (m, 1H), 7.44−7.48 (m, 1H).

*(E)-1-(But-1-en-3-ynyl)benzene (**9n**: Table 5, entry 12).*[54] *Method A.* CP**12n** (266 mg, 0.90 mmol) provided **9n** (24 mg, 17%) as a colorless oil after purification by silica gel column chromatography (hexane).

Method B. CP **12n** (295 mg, 1.0 mmol) was treated with $TMSN_3$ (345 mg, 3.0 mmol) and Bu_2SnO (25 mg, 0.1 mmol) at reflux 0.5 h to provide **9n** (102 mg, 80%) as a colorless oil after purification by silica gel column chromatography (hexane). ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.05 (d, 1H, J = 2.4 Hz), 6.13 (dd, 1H, J = 16.5, 2.4 Hz), 7.04 (d, 1H, J = 16.5 Hz), 7.29−7.40 (m, 5H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 79.2, 82.7, 106.9, 126.3, 128.7, 128.9, 135.8, 143.1.

*(E)-4,8-Dimethylnona-3,7-dien-1-yne (**9o**: Table 5, entry 13).*[33b] *Method B.* CP **12o** (315 mg, 1.0 mmol) was treated with $TMSN_3$ (345 mg, 3.0 mmol) and Bu_2SnO (25 mg, 0.1 mmol) at reflux for 0.5 h to provide **9o** (101 mg, 68%, E/Z = 15/1) as a colorless oil after purification by silica gel column chromatography (hexane). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.60(s, 3H), 1.69(s, 3H), 1.91(d, 3H, J = 1.2 Hz), 2.07−2.17(m, 4H), 3.01(d, 1H, J = 2.0 Hz), 5.04−5.10(m, 1H), 5.25−5.28(m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 17.7, 19.3, 25.6, 26.1, 38.6, 79.5, 81.8, 103.7, 123.3, 132.2, 154.2.

*(Z)-4,8-Dimethylnona-3,7-dien-1-yne (**9p**: Table 5, entry 14). Method B.* CP**12p** (315 mg, 1.0 mmol) was treated with $TMSN_3$ (345 mg, 3.0 mmol) and Bu_2SnO (25 mg, 0.1 mmol) at reflux for 0.5 h to provide **9p** (78 mg, 53%, E/Z = 1/10) as a colorless oil after purification by silica gel column chromatography (hexane). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.63 (s, 3H), 1.69 (s, 3H), 1.80 (d, 3H, J = 1.2 Hz), 2.13

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(quart, 2H, J = 8.0 Hz), 2.34 (t, 2H, J = 7.2 Hz), 2.97 (d, 1H, J = 2.4 Hz), 5.14 (tquint, 1H, J = 7.2, 1.2 Hz), 5.25−5.28(m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 17.6, 22.6, 25.7, 26.2, 34.8, 79.1, 81.6, 104.4, 123.6, 132.1, 154.4.

*Reactivity of Aldehyde **2e** under Ohira−Bestmann Reaction and Shioiri Method (Scheme 11). Ohira−Bestmann Reaction.* According to the synthetic procedure for **20**, aldehyde **2e** (223 mg, 0.5 mmol) provided a 5:2 mixture (192 mg, 87%) of ***β*-9e** and ***α*-9e**[55] after purification by silica gel column chromatography (EtOAc:hexane, 1:9).

Shioiri Method. By the same procedure as used for the preparation of **21**, aldehyde **2e** (223 mg, 0.5 mmol) provided a 9:1 mixture (138 mg, 62%) of ***β*-9e** and ***α*-9e**[55] after purification by silica gel column chromatography (EtOAc:hexane, 1:9).

*Transformation of **2q** into Alkyne **9q** using the Present Method and Shioiri Procedure (Scheme 12). 1-Cyano-3-(1,3-dioxoisoindolin-2-yl)propyl Diethylphosphate (**12q**).* According to the general procedure 2, aldehyde **2q** (609 mg, 3 mmol) provided **12q** (897 mg, 82%, colorless oil), after purification by silica gel column chromatography (EtOAc:hexane, 3:2). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.33−1.40 (m, 6H), 2.32−2.46 (m, 2H), 3.97 (t, J = 7.2 Hz, 2H), 4.15−4.25 (m, 4H), 5.11 (t, J = 6.4 Hz, 0.5H), 5.13 (t, J = 6.4 Hz, 0.5H), 7.72−7.77 (m, 2H), 7.84−7.90 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.9(15.88), 15.9(15.91), 16.0(15.95), 16.0(15.98), 32.8, 32.9, 33.0, 62.5(62.47), 62.5(62.53), 64.9, 65.0, 116.0, 116.1, 123.4, 131.8, 134.2, 167.9; HRMS (EI): m/z [M$^+$] calcd for $C_{16}H_{20}N_2O_6P$: 367.1059; found: 367.1057.

*2-(But-3-yn-1-yl)isoindoline-1,3-dione (**9q**).*[56] According to the Method A, CP **12q** (312 mg, 0.85 mmol) provided **9q** (115 mg, 68%) as a colorless oil after purification by silica gel column chromatography (EtOAc:hexane, 1:3). ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.97 (t, J = 2.7 Hz, 1H), 2.62 (td, J = 6.9, 2.7 Hz, 2H), 3.89 (t, J = 6.9 Hz, 2H), 7.70−7.80 (m, 2H), 7.80−7.90 (m, 2H).

*Transformation of **2q** under Ohira−Bestmann Reaction (Scheme 12).* According to the synthetic procedure for **20**, a solution of **2q** (203 mg, 1.0 mmol) provided **9q** (200 mg, 10%) as a colorless oil after purification by silica gel column chromatography (EtOAc:hexane, 1:3).

*Reactivity of Cinnamaldehyde (**2n**) under Ohira−Bestmann Reaction (Scheme 13).* According to the synthetic procedure for **20**, cinnamaldehyde (**2n**, 133 mg, 1 mmol) provided **27**[57] (16 mg, 10%) and **28**[58] (120 mg, 67%) after purification by silica gel column chromatography (EtOAc:hexane, 1:3).

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.7b00346.

Differential scanning calorimetry of **14a** and ^{1}H and/or ^{13}C NMR spectral data of compounds **8a−h**, **8j−l**, **8n−z**, **8aa-ee**, **9a**, **9d−q**, **11a−c**, **11e−l**, **11n−z**, **11aa-ee**, **12a−q**, **13i**, **14a−h**, **15a−c**, **16**, **17a−c**, and **23ee** (PDF)

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Notes

The authors declare no competing financial interest.

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