Phosphine-Catalyzed Reaction of Cyanohydrins with Activated Alkynes

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Abstract: A new method for preparing α-cyanoacrylates and α-cyanoenones is described. The procedure uses a phosphine-catalyzed α-C addition of cyanide ion, generated in situ from cyanohydrins, to activated alkynes. An unexpected tandem reaction producing benzylidenecyclopentanones is also described.

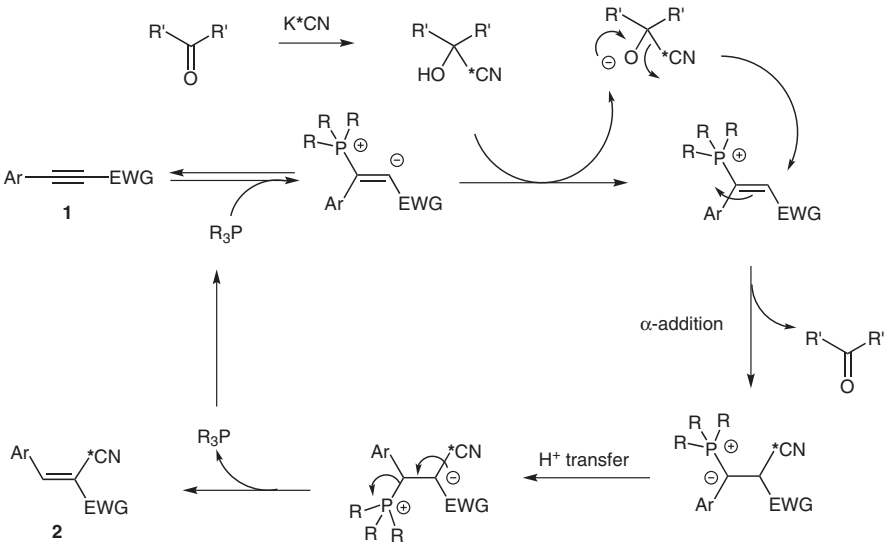
Key words: cyanoacrylates, alkynes, catalysis, phosphines

α-Cyanoacrylates and α-cyanoenones are common building blocks for the synthesis of numerous heterocycles; their use as monomers in polymer synthesis is also well established. These products have been mostly synthesized by the Knoevenagel condensation using active methylene compounds such as cyanoacetates and α-cyanoketones.[1] However, α-cyanoenones may be reactive or unstable to base, so that classical Knoevenagel conditions are not always suitable for the preparation of these compounds.[2] Only few alternative synthetic approaches to α-cyanoenones such as isoxazoline oxidation,[3] ring opening of isoxazoles by bases,[4] and α-cyanoacylation of aldehydes[5] have been described in literature.

During the course of our work on the preparation of ^{14}C-labeled cyanoacrylates and their polymer derivatives,[6] we have been interested in developing a mild procedure based on previous work described by our group using labeled KCN as starting material for the synthesis of α-cyanoenones. We have described a series of phosphine-catalyzed α-addition reactions of pronucleophiles on activated alkynes that allows the formation of polyfunctionalized activated alkenes.[7] We contemplated using this type of chemistry for the formation of α-cyanoacrylates and α-cyanoenones through α-C-addition of cyanide ion to activated alkynes **1** (Scheme 1). We designed cyanohydrins, easily prepared from reaction of KCN with aldehydes or ketones, as cyanide sources.[8]

Cyanohydrines may indeed react as an indirect pronucleophile upon reaction with the zwitterion intermediate generated by Michael addition of the phosphine catalyst on the activated alkyne. H-abstraction of the cyanohydrin by this intermediate should release cyanide ion that may then add onto the vinyl phosphonium intermediate. Elimination of the phosphine after H^+ transfer should then afford the desired acrylonitrile **2**. To test the feasibility of this reaction, various cyanohydrins were reacted with ethyl phenylpropiolate (**1a**) in the presence of several phosphines (Table 1).

To our delight, the reaction was found to work through the desired pathway and afforded ethyl *trans*-α-cyanocinnamate (**2a**) at room temperature in acceptable yield (Table 1, entry 1). Higher yields and shorter reaction times are obtained upon heating and by using $MePh_2P$,



Scheme 1 Proposed route to labeled acrylonitrile **2**

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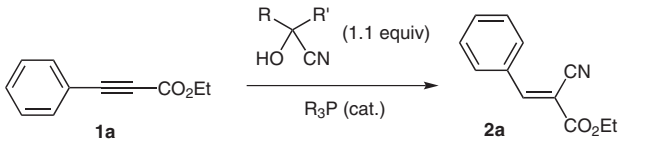
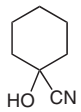
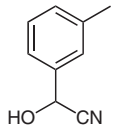
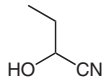
Table 1 Optimization of the Reaction of Cyanohydrins with Alkyne **1a**



1a **2a**

Entry	R, R', HO, CN	R_3P (mol%)	Conditions	Yield of **2a** (%)[a]
1		Bu_3P (20%)	toluene, r.t., 20 h	66
2		Bu_3P (20%)	toluene, 110 °C, 1 h	63
3		$MePh_2P$ (20%)	toluene, 110 °C, 1 h	**72**
4		Ph_3P (20%)	toluene, 110 °C, 1 h	30
5		$MePh_2P$ (5%)	toluene, 110 °C, 6 h	72
6		$MePh_2P$ (20%)	*i*-PrOH, 90 °C, 7 h	40
7		$MePh_2P$ (20%)	CH_2Cl_2, 40 °C, 24 h	72
8		$MePh_2P$ (20%)	toluene, 110 °C, 7 h	73
9		$MePh_2P$ (20%)	toluene, 110 °C, 5 h	61
10		$MePh_2P$ (20%)	toluene, 110 °C, 4 h	74[b]

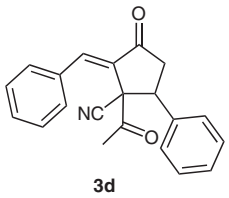
[a] Isolated yields.
[b] A by-product in 17% yield resulting from the α-O-addition of the cyanohydrin was isolated in this case.

which was found the most active catalyst (compare entry 3 with 2 and 4, Table 1). Among the tested cyanohydrins, acetone cyanohydrin was found the most efficient (compare entries 8, 9, and 10 with 3, Table 1). The other cyanohydrins required longer reaction times; in each cases the formation of the corresponding ketone or aldehyde by-products were observed in the crude reaction mixture.

We then looked at the scope and limitations of this reaction by employing a panel of activated alkynes starting materials. As illustrated in Table 2, the presented methodology appeared to be amenable on a variety of substrates affording a straightforward route to polyfunctionalized acrylonitriles.

The reaction proceeded smoothly on a panel of activated alkynes affording the desired α-cyanoacrylates **2a–c** and α-cyanoenones **2d–g** products in moderate to good yields. In the case of alkynes activated by a ketone function, the reaction requires room temperature conditions due to the thermal instability of the resulting products.

Compounds **2** were fully characterized and their structure established by NMR and MS experiments as well as by comparison with published analytical data. By-product **3d** (26% isolated yield) has also been observed when enolizable yne-one starting material **1d** was used. The structure of this by-product (Figure 1) was determined by extensive spectral analysis. The *E*-form of the double bound was assigned by comparison with the published NMR data.[9]



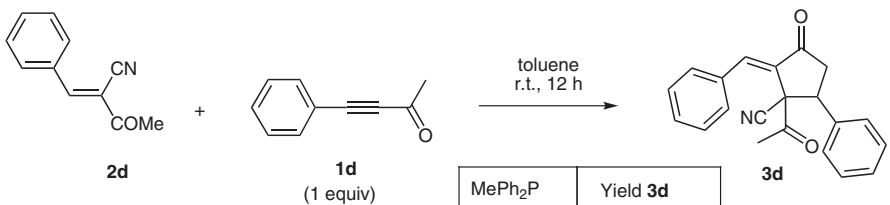
3d

Figure 1 Structure of by-product **3d**

Control experiments proved that this cyclopentanone product resulted from a phosphine-catalyzed condensation of alkyne **1d** on cyanoenone **2d** (Scheme 2).

One possible reaction pathway yielding product **3d** from **1d** and **2d** is shown in Scheme 3.

The zwitterionic intermediate **4** produced by conjugate addition of the phosphine catalyst undergoes an intramolecular proton migration (1,3-proton shift) from the methyl group. A nucleophilic attack of the resulting enolate **5** to cyanoacrylate **2d** produces the carbanionic intermediate **6**, which then undergoes intramolecular α-C-addition on the α,β-unsaturated ketone moiety generating ylide **7**. Proton transfer followed by phosphine elimination then produces **3d**.

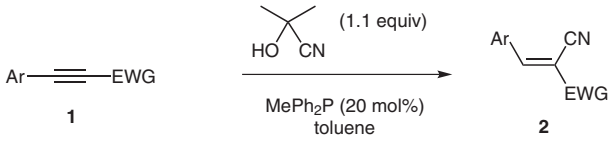


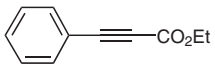
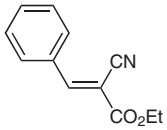
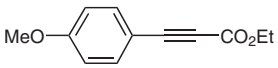
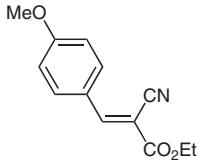
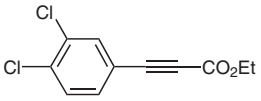
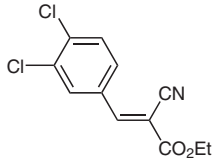
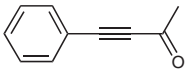
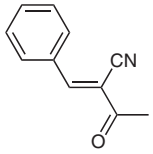
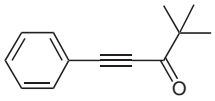
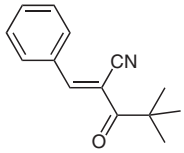
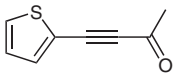
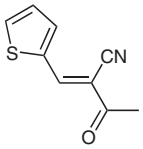
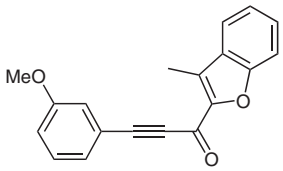
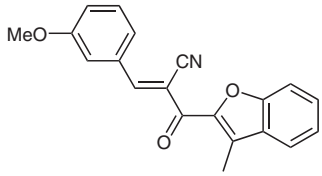
2d **1d** (1 equiv) **3d**

$MePh_2P$	Yield **3d**
none	no reaction
20 mol%	40%

Scheme 2 Control experiment yielding product **3d**

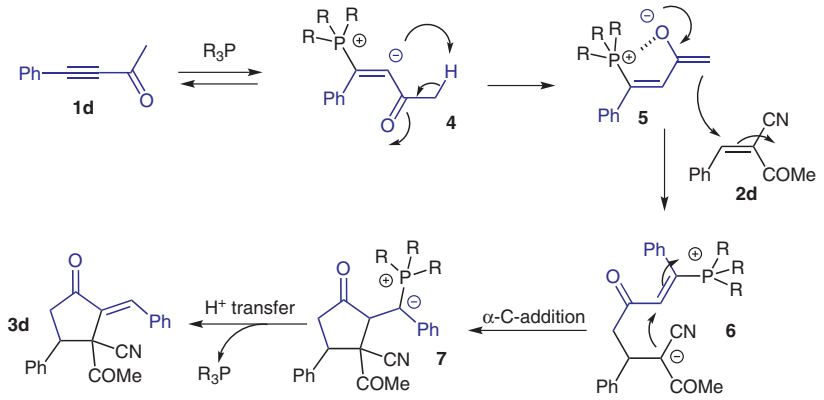
Table 2 Phosphine-Catalyzed Reaction of Acetone Cyanohydrin with Activated Alkynes[a]



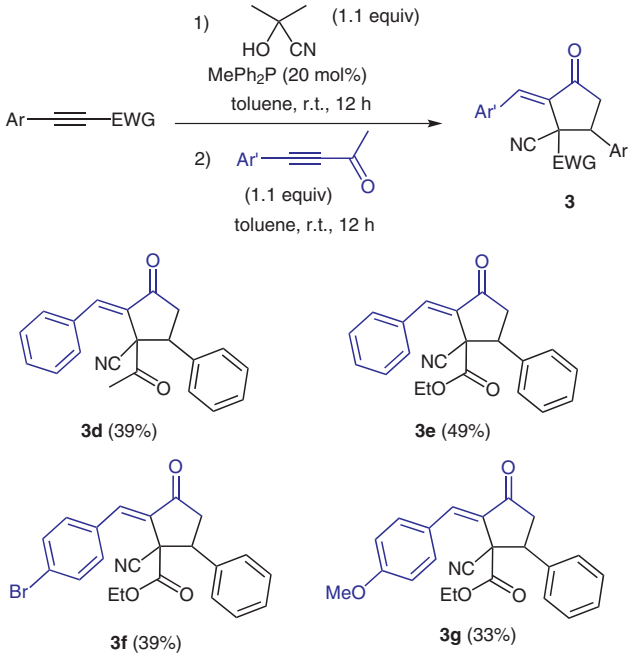
Entry	Ar—≡—EWG	Conditions	Product **2**, Yield (%)[a]
1	 **1a**	110 °C, 1 h	 **2a** (72)
2	 **1b**	110 °C, 5 h	 **2b** (81)
3	 **1c**	110 °C, 2 h	 **2c** (66)
4	 **1d**	r.t., 20 h	 **2d** (66)
5	 **1e**	r.t., 20 h	 **2e** (66)
6	 **1f**	r.t., 2 h	 **2f** (71)
7	 **1g**	r.t., 5 h	 **2g** (54)

[a] Isolated yields.

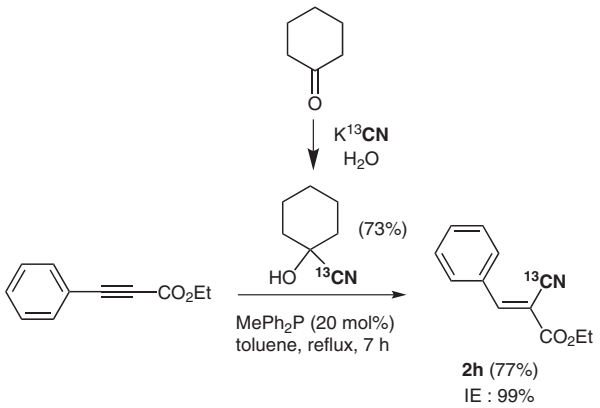
We therefore decided to take advantage of this new reaction for the straightforward synthesis of poly-functionalized benzylidenecyclopentanones. After several attempts, we developed a two-step, one-pot process that worked in reasonable yields (Scheme 4). The process is based on sequential addition of 1) cyanohydrin to generate α-cyanoacrylonitrile derivative, and 2) the alkyne-one to produce cyclopentatones **3** as a mixture of diastereoisomers.



Scheme 3 Proposed route to cyclopentanone **3d**



Scheme 4 Phosphine-catalyzed reaction yielding benzylidenecyclopentanones **3**



Scheme 5 Synthesis of ^{13}C-labeled cyanoacrylate **2h**

In conclusion, we have developed a simple and practical method for the preparation of α-cyanoacrylates and α-cyanoenones starting from activated alkynes and cyanohydrins. Besides the practical advantages of the method, this reaction is interesting for the preparation of labeled acrylonitriles. Preliminary investigations conducted in our laboratory proved that this reaction is highly suitable for the synthesis of labeled α-cyanoacrylates: reaction of ethyl phenylpropiolate (**1a**) with ^{13}C-labeled cyclohexanone cyanohydrin, obtained as previously described,[10] afforded product **2h** in high yield and isotopic enrichment (IE) (Scheme 5).

During the course of this work a new construction of benzylidenecyclopentanone from a phosphine-catalyzed cycloaddition of α-cyanoacrylates and α-cyanoenones with 4-arylbut-3-yn-2-ones has also been highlighted. This allowed us to optimize a tandem phosphine-catalyzed one-pot process that afforded polyfunctionalized cyclopentanones in moderate yields.

All reagents were used directly as obtained commercially, unless otherwise noted. Melting points were determined on a Büchi 535 capillary melting point apparatus and are uncorrected. Flash chromatography was carried out on Merck silica gel (40–63 μm). IR spectra were obtained on a PerkinElmer system 2000 FT-IR spectrophotometer. ^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) were measured on a Bruker Avance 400 MHz spectrometer. Electrospray mass spectra were obtained using an ESI/TOF Mariner Mass Spectrometer.

$MePh_2P$-Catalyzed Synthesis of α-Cyanoacrylates and α-Cyanoenones; General Procedure

To a solution of ethyl arylpriopiolate **1** (1 mmol) and acetone cyanohydrin (100 μL, 1.1 mmol) in anhyd toluene (5 mL) was added diphenylmethylphosphine (37.3 μL, 0.2 mmol) under argon. The mixture was heated at reflux and then evaporated under reduced pressure. The residue was purified by flash chromatography on a silica gel column to give α-cyanoacrylates as the final product (Table 2). Identical procedure, but at r.t., was applied to 4-arylbut-3-yn-2-one for the preparation of α-cyanoenones (Table 2).

(*E*)-2-Cyano-3-phenylacrylic Acid Ethyl Ester (2a)

Purified by column chromatography (CH_2Cl_2–hexane, 50:50); beige solid; mp 50–51 °C.

IR (KBr): 3030, 2981, 2223, 1727, 1607, 1572, 1496, 1465, 1444, 1386, 1367, 1301, 1258, 1202, 1089, 1010, 970, 887, 849, 768, 683, 579, 524 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 8.25 (s, 1 H), 8 (d, *J* = 7.2 Hz, 2 H), 7.55 (m, 3 H), 4.4 (q, *J* = 7.1 Hz, 2 H), 1.4 (t, *J* = 7.1 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 162.4, 154.9, 133.2, 131.4, 131.0, 129.2, 115.4, 102.9, 62.6, 14.1.

MS (ESI): *m*/*z* = 202 $[M + H]^+$.

(*E*)-2-Cyano-3-(4-methoxyphenyl)acrylic Acid Ethyl Ester (2b)
Purified by column chromatography (CH_2Cl_2–hexane, 70:30); yellow solid; mp 81–82 °C.

IR (KBr): 3415, 3084, 3025, 2993, 2943, 2844, 2577, 2215, 1968, 1912, 1748, 1586, 1562, 1513, 1461, 1431, 1364, 1320, 1263, 1211, 1182, 1127, 1089, 1018, 984, 894, 837, 817, 763, 737, 723, 625, 586 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 8.2 (s, 1 H), 8 (d, *J* = 8.9 Hz, 2 H), 7 (d, *J* = 8.9 Hz, 2 H), 4.4 (q, *J* = 7.1 Hz, 2 H), 3.9 (s, 3 H), 1.4 (t, *J* = 7.1 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 163.7, 163.0, 154.3, 133.6, 124.3, 116.1, 55.5, 14.1.

MS (EI, 70 eV): *m*/*z* (%) = 231 (100, $[M^+]$), 216 (7), 203 (37), 186 (53), 158 (22), 143 (9), 115 (11), 77 (8), 29 (9).

(*E*)-3-(3,4-Dichlorophenyl)-2-cyanoacrylic Acid Ethyl Ester (2c)
Purified by column chromatography (CH_2Cl_2–hexane, 70:30); beige solid; mp 118–120 °C.

IR (KBr): 3424, 3087, 3065, 3037, 2985, 2938, 2905, 2225, 1921, 1804, 1720, 1611, 1585, 1548, 1473, 1445, 1396, 1366, 1354, 1281, 1261, 1209, 1136, 1094, 1029, 1014, 973, 904, 826 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 8.15 (s, 1 H), 8 (d, *J* = 2.0 Hz, 1 H), 7.9 (dd, *J* = 2.0, 8.4 Hz, 1 H), 7.7 (d, *J* = 8.4 Hz, 1 H), 4.4 (q, *J* = 7.1 Hz, 2 H), 1.4 (t, *J* = 7.1 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 162.7, 151.8, 137.5, 133.7, 132.6, 131.3, 131.1, 129.2, 114.7, 104.8, 62.9, 14.0.

MS (EI, 70 eV): *m*/*z* (%) = 273 (12, $[M (2\ ^{37}Cl)]^+$), 271 (68, $[M (^{37}Cl, ^{35}Cl)]^+$), 269 (100, $[M (2\ ^{35}Cl)]^+$), 245 (9), 243 (50) 241 (75), 228 (7), 226 (41), 224 (63), 196 (39), 161 (63), 124 (20), 75 (18), 50 (9), 29 (56).

HRMS: *m*/*z* calcd for $C_{12}H_9{}^{35}Cl_2O_2$ + Na: 291.9908; found: 291.9901; *m*/*z* calcd for $C_{12}H_9{}^{35}Cl^{37}ClO_2$ + Na: 293.9879; found: 293.9885.

3-Oxo-2-[1-phenylmeth-(*E*)-ylidene]butyronitrile (2d)
Purified by column chromatography (CH_2Cl_2–hexane, 70:30); white solid; mp 81–82 °C.

IR (KBr): 3380, 3030, 3008, 2216, 1697, 1586, 1567, 1494, 1450, 1419, 1363, 1317, 1294, 1243, 1200, 1186, 1081, 1026, 980, 960, 761, 687, 637, 561, 547, 522 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 8.25 (s, 1 H), 8 (d, *J* = 7.3 Hz, 2 H), 7.55 (m, 3 H), 2.66 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 191.11, 153.1, 133.48, 131.39, 131.26, 129.28, 117.18, 109.64, 27.81.

MS (ESI): *m*/*z* = 172 $[M + H]^+$.

4,4-Dimethyl-3-oxo-2-[1-phenylmeth-(*E*)-ylidene]pentanenitrile (2e)
Purified by column chromatography (CH_2Cl_2–hexane, 50:50); yellow solid; mp 69–72 °C.

IR (KBr): 3360, 3064, 3020, 2973, 2935, 2876, 2210, 1968, 1897, 1689, 1583, 1565, 1497, 1478, 1446, 1396, 1367, 1343, 1321, 1294, 1214, 1134, 1075, 1035, 1035, 1002, 984, 956, 939, 834, 795, 761, 733, 685, 625, 600, 570, 523 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 8.23 (s, 1 H), 8.0 (d, *J* = 7.2 Hz, 2 H), 7.5 (m, 3 H), 1.4 (s, 9 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 198.9, 156.1, 132.9, 131.9, 131.1, 129.1, 113.2, 107.31, 44.54, 26.4.

MS (EI, 70 eV): *m*/*z* (%) = 213 (30, $[M^+]$), 185 (34), 170 (12), 157 (63), 129 (98), 102 (41), 77 (21), 57 (100), 41 (47), 29 (23).

3-Oxo-2-[1-thiophen-2-ylmeth-(*E*)-ylidene]butyronitrile (2f)
Purified by column chromatography (CH_2Cl_2–heptane, 80:20); yellow solid; mp 79–81 °C.

IR (KBr): 3443, 3082, 3046, 2364, 2330, 2212, 1833, 1717, 1695, 1676, 1579, 1504, 1413, 1360, 1268, 1243, 1201, 1054, 976, 948, 858, 786, 742, 635, 600, 567, 518 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 8.3 (s, 1 H), 7.8 (dd, *J* = 3.7, 15.8 Hz, 2 H), 7.3 (q, *J* = 4.1 Hz, 1 H), 2.6 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 190.9, 144.8, 137.9, 136.2, 135.7, 128.8, 117.5, 106.1, 27.9.

MS (EI, 70 eV): *m*/*z* (%) = 177 (100, $[M]^+$), 162 (65), 135 (42), 108 (18), 90 (13), 63 (14), 43 (99).

HRMS: *m*/*z* calcd for C_9H_7NOS + Na: 200.0146; found: 200.0150.

(*E*)-3-(4-Methoxyphenyl)-2-(3-methylbenzofuran-2-carbonyl)acrylonitrile (2g)
Purified by column chromatography (CH_2Cl_2–heptane, 80:20); orange solid; mp 102.7–104.6 °C.

IR (KBr): 2958, 2838, 2219, 1726, 1650, 1567, 1488, 1465, 1434, 1385, 1363, 1339, 1292, 1260, 1221, 1196, 1176, 1150, 1098, 1048, 977, 940, 902, 872, 787, 746, 725, 683 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 8.3 (s, 1 H), 7.7 (m, 3 H), 7.5 (m, 3 H), 7.4 (t, *J* = 8.1 Hz, 1 H), 7.3 (t, *J* = 7.1 Hz, 1 H), 7.1 (dd, *J* = 1.98, 8.2 Hz, 1 H), 3.9 (s, 3 H), 2.6 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 177.6, 159.9, 155, 154.3, 146.6, 133.2, 130.1, 129.1, 120.0, 116.2, 114.5, 112.5, 110.2, 55.4, 9.9.

MS (EI, 70 eV): *m*/*z* (%) = 317 (100, $[M^+]$), 302 (19), 286 (69), 274 (10), 251 (11), 210 (18), 159 (57), 103 (29), 77 (37).

HRMS: *m*/*z* calcd for $C_{20}H_{15}NO_3$ + Na: 340.0950; found: 340.0943.

(*E*)-2-^{13}C-Cyano-3-phenylacrylic Acid Ethyl Ester (2h)
^1H NMR (400 MHz, $CDCl_3$): δ = 8.3 (d, *J* = 13.9 Hz, 1 H), 8 (d, *J* = 7.4 Hz, 2 H), 7.5 (m, 3 H), 4.4 (q, *J* = 7.1 Hz, 2 H), 1.5 (t, *J* = 7.1 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 162.4, 155, 133.2, 131.4, 131, 129.2, 115.4, 102.9 (d, *J* = 84 Hz), 62.7, 14.1.

MS (ESI): *m*/*z* = 203 $[M + H]^+$.

$MePh_2P$-Catalyzed Construction of Polyfunctionalized Cyclopentanones; General Procedure
To a solution of the activated alkyne (1 mmol) and acetone cyanohydrin (100 μL, 1.1 mmol) in anhyd toluene (5 mL) was added diphenylmethylphosphine (37.3 μL, 0.2 mmol) under argon. The mixture was stirred at r.t. for 12 h, then 4-arylbut-3-yn-2-one (1 mmol, 1 equiv) dissolved in anhyd toluene (5 mL) was added dropwise over 5 h (syringe pump, 0.2 equiv/h). After the complete addition, the mixture was further stirred overnight at r.t. and then concentrated under reduced pressure. The residue was purified by flash chromatography on a silica gel column to give the final product.

1-Acetyl-2-benzylidene-3-oxo-5-phenylcyclopentanecarbonitrile (3d)
Purified by column chromatography (CH_2Cl_2–hexane, 70:30); colorless oil.

IR (film): 3428, 3062, 3032, 2925, 2855, 2240, 1963, 1720, 1619, 1575, 1494, 1450, 1410, 1360, 1312, 1287, 1234, 1180, 1146, 1108, 1080, 1029, 1001, 966, 927, 827, 759, 736, 698, 662, 619, 606 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.9 (s, 1 H), 7.4 (m, 9 H), 7.3 (dd, *J* = 1.8, 5.2 Hz, 2 H), 3.7 (dd, *J* = 7.2, 12.9 Hz, 1 H), 3.1 (dd, *J* = 12.9, 17.6 Hz, 1 H), 2.9 (dd, *J* = 7.3, 17.6 Hz, 1 H), 2.05 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 199, 198.5, 140.12, 134, 132.99, 131.0, 129.9, 129.03, 129.15, 128.07, 107, 62.04, 50.11.

MS (EI, 70 eV): *m*/*z* (%) = 315 (13, $[M]^+$), 273 (100), 244 (22), 230 (15), 196 (13), 167 (6), 140 (9), 103 (8), 77 (10), 43 (73).

HRMS: *m*/*z* calcd for $C_{21}H_{17}NO_2$ + Na: 338.1157; found: 338.1158.

2-Benzylidene-1-cyano-3-oxo-5-phenylcyclopentanecarboxylic Acid Ethyl Ester (3e)
Purified by column chromatography (EtOAc–heptane, 75:25), yellow oil.

IR (film): 3446, 3082, 3003, 2935, 1744, 1729, 1625, 1575, 1493, 1469, 1452, 1404, 1367, 1316, 1264, 1230, 1177, 1108, 933, 909, 853, 779, 762, 694, 649, 623, 604, 546, 524 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.9 (s, 1 H), 7.2–7.6 (m, 10 H), 3.9 (m, 3 H), 3.1 (dd, *J* = 13.6, 17.6 Hz, 1 H), 2.9 (dd, *J* = 7, 17.6 Hz, 1 H), 1 (t, *J* = 7.15 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 199.2, 166.05, 139.9, 143.3, 132.84, 132.6, 130.83, 130.15, 129.0, 128.9, 128.7, 127.93, 115.7, 63.2, 56.4, 50.4, 40.2, 13.6.

MS (EI, 70 eV): *m*/*z* (%) = 345 (36, $[M]^+$), 299 (12), 272 (35), 241 (91), 213 (100), 195 (35), 168 (24), 141 (46), 114 (16), 103 (17), 91 (9), 77 (20), 29 (35).

HRMS: *m*/*z* calcd for $C_{22}H_{19}NO_3$ +Na: 368.1263; found: 368.1259.

2-(4-Bromobenzylidene)-1-cyano-3-oxo-5-phenylcyclopentanecarboxylic Acid Ethyl Ester (3f)
Purified by column chromatography (CH_2Cl_2–heptane, 80:20), yellow oil.

IR (film): 3417, 3091, 3033, 2985, 2930, 2363, 2242, 1888, 1736, 1719, 1618, 1582, 1562, 1543, 1487, 1455, 1402, 1363, 1305, 1264, 1226, 1178, 1152, 1108, 1072, 1050, 1025, 1007, 946, 922, 852, 820, 769, 727, 697, 672, 631, 606, 562, 521 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.8 (s, 1 H), 7.6 (d, *J* = 8.4 Hz, 2 H), 7.4 (m, 5 H), 7.3 (m, 2 H), 3.9 (m, 3 H), 3.1 (dd, *J* = 13.4, 17.2 Hz, 1 H), 2.9 (dd, *J* = 7.2, 17.2 Hz, 1 H), 1.1 (t, *J* = 7.2 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 199, 166, 134.5, 134.2, 133.3, 132, 131.6, 131.5, 129.1, 128.9, 127.9, 125.5, 115.4, 63.4, 56.3, 50.4, 13.6.

MS (EI, 70 eV): *m*/*z* (%) = 425 (33, $[M\ (^{81}Br)]^+$), 423 (34, $[M\ (^{79}Br)]^+$), 379 (17), 377 (16), 352 (35), 350 (35), 321 (77), 319 (77), 293 (60), 291 (60), 270 (13), 243 (11), 229 (41), 212 (100), 202 (16), 167 (13), 139 (24), 104 (37), 78 (27), 29 (55).

1-Cyano-2-(4-methoxybenzylidene)-3-oxo-5-phenylcyclopentanecarboxylic Acid Ethyl Ester (3g)
Purified by column chromatography (CH_2Cl_2–heptane, 80:20); yellow oil.

IR (film): 3548, 3059, 2961, 2934, 2872, 2840, 2242, 2099, 1889, 1728, 1664, 1621, 1577, 1516, 1494, 1463, 1448, 1391, 1367, 1293, 1256, 1229, 1179, 1155, 1108, 1077, 1031, 953, 930, 902, 852, 834, 759, 738, 696, 653, 620, 604, 571 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.9 (s, 1 H), 7.6 (m, 2 H), 7.5 (m, 3 H), 7.3 (d, *J* = 8.7 Hz, 2 H), 6.9 (d, *J* = 8.7 Hz, 2 H), 3.9 (m, 6 H), 3.1 (dd, *J* = 3.7, 17.5 Hz, 1 H), 2.9 (dd, *J* = 7.1, 17.5 Hz, 1 H), 1 (t, *J* = 7.2 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 199.3, 166.1, 160, 139.8, 132.9, 132.7, 130.8, 130.1, 129.1, 128.7, 126.2, 115.8, 114.2, 63.1, 56.6, 55.2, 50, 40.4, 13.6.

MS (EI, 70 eV): *m*/*z* (%) = 375 (61, $[M]^+$), 329 (36), 302 (21), 241 (19), 213 (48), 195 (23), 134 (100), 119 (13), 91 (15).

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