Supporting Information
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Supporting information

Synthesis of CF₃ Containing 1,2,3,4-Tetrahydroisoquinoline-3-Phosphonates

via Regioselective Ru-Catalyzed Co-cyclotrimerization of 1,7-Azadiynes

Maria A. Zotova, a Daria V. Vorobyeva,a Pierre H. Dixneuf,b Christian Bruneau, b Sergey N. Osipov*a

a A.N. Nesmeyanov Institute of Organoelement compounds, Russian Academy of Sciences, 119991, Vavilov str. 28, Moscow, Russia.
b Centre of Catalysis and Green Chemistry UMR 6226 CNRS-Université de Rennes 1 Campus de Beaulieu, 35042 Rennes Cedex, France.

E-mail: osipov@ineos.ac.ru
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General remarks
All solvents used in reactions were freshly distilled from appropriate drying agents before use. All other reagents were recrystallized or distilled as necessary. Reactions were performed under an atmosphere of dry argon. Analytical TLC was performed with Merck silica gel 60 F254 plates; visualization was accomplished with UV light or spraying with Ce(SO4)2 solution in 5% H2SO4. Flash chromatography was carried out using Merck silica gel 60 (230–400 mesh ASTM) and ethyl acetate/methylene chloride as eluent. NMR spectra were obtained with Bruker AV-300, AV-400, or AV-600 spectrometers operating at 300, 400, or 600 MHz, respectively, for 1H (TMS reference), at 75, 100, or 150 MHz for 13C, and at 288 MHz for 19F (CF3COOH reference) and at 161 MHz for 31P (H3PO4 reference).

Typical procedure for propargylation
To a suspension of sodium hydride (2.16 mmol, 2.5 equiv) in dry DMF (2.5 mL) was added a solution of α-alkynyl-aminophosphonate (0.87 mmol) in dry DMF (2.5 mL) at 0°C dropwise. The reaction mixture was warmed to room temperature and stirred for 2 h. Then propargyl bromide (4.32 mmol, 5 equiv) was added dropwise to the solution and the reaction mixture was stirred at room temperature for 12 h. A resulting mixture was treated with aqueous hydrochloric acid and extracted twice with diethyl ether. The organic layer was separated and dried over MgSO4. The solvent and excess of propargyl bromide was removed under reduced pressure to give a crude product that was used for the next step without additional purification. The yield and purity of product determined by 19F NMR spectroscopy.

Benzyl (2-(diethoxyphosphoryl)-1,1,1-trifluoropent-4-yn-2-yl)(prop-2-yn-1-yl)carbamate (2a): Yield: 89%, purity – 90%; 1H NMR (300 MHz, CDCl3) δ 1.41 (t, J = 6.9 Hz, 6H; 2CH3), 2.15 (t, J = 2.3 Hz, 1H; ≡CH), 2.27 (t, J = 2.0 Hz, 1H; ≡CH), 3.40-3.81 (m, 2H; CH2), 4.17-4.41 (m, 4H; 2OCH2), 4.43-4.63 (m, 2H; NCH2), 5.25 (d, J = 12.4 Hz, 1H; OCH2), 5.32 (d, J = 12.4 Hz, 1H; OCH2), 7.34-7.55 (m, 5H; ArH); 19F NMR (282 MHz, CDCl3) δ 9.43 (s, 3F; CF3).

Benzyl (2-(diethoxyphosphoryl)-1,1,1-trifluoro-5-phenylpent-4-yn-2-yl)(prop-2-yn-1-yl)carbamate (5a): Yield: 87%, purity – 91%; 1H NMR (300 MHz, CDCl3) δ 1.64 (m, 6H; 2CH3), 2.38 (br s, 1H; ≡CH), 3.33-3.51 (m, 2H; CH2), 3.75-3.97 (m, 4H; 2OCH2), 4.21-4.49 (m, 2H; NCH2), 5.27 (m, 2H; OCH2), 7.19-7.60 (m, 10H; ArH); 19F NMR (282 MHz, CDCl3) δ 9.96 (br s, 3F; CF3).

Benzyl (2-(diethoxyphosphoryl)-1,1,1-trifluoro-5-(4-methoxyphenyl)pent-4-yn-2-yl)(prop-2-yn-1-yl)carbamate (5b): Yield: 90%, purity – 91%; 1H NMR (300 MHz, CDCl3) δ 1.32-1.37 (m, 6H; 2CH3), 2.27 (m, 1H; ≡CH), 3.39-3.77 (m, 2H; CH2), 3.84 (s, 3H; OCH3), 4.22-4.40 (m,
4H; 2OCH2), 4.57 (m, 2H; NCH2), 5.20-5.38 (m, 2H; OCH2), 6.84 (d, J = 8.3 Hz, 2H; ArH), 7.35-7.46 (m, 7H; ArH); 19F NMR (282 MHz, CDCl3) δ 9.30 (s, 3F; CF3).

Preparation of 3a
A mixture of dyine (0.82 mmol) and RuClCp*COD (0.07 mmol, 3 mol%) in dry dichloromethane (20 mL) was degassed three times under cooling. The resulting solution was stirred at room temperature under acetylene atmosphere overnight. After the reaction completion (monitoring by TLC and 19F NMR spectroscopy), the solvent was removed under reduced pressure and crude product was purified by column chromatography on silica gel (eluent − dichloromethane/ethylacetate) to afford the titled compound as yellow oil.

Benzyl 3-(diethoxyphosphoryl)-3-(trifluoromethyl)-3,4-dihydroisoquinoline-2(1H)-carboxylate (3a): Yield: 62%; oil; 1H NMR (300 MHz, CDCl3) δ 1.13 (m, 3H; CH3), 1.28 (m, 3H; CH3), 3.34-3.45 (m, 2H; CH2), 3.70-3.78 (m, 2H; CH2), 3.91-4.14 (m, 4H; OCH2), 4.54 (d, J = 14.3 Hz, 2H; NCH2), 4.92 (d, J = 14.0 Hz, 2H; NCH2), 5.17 (d, J = 12.2 Hz, 1H; OCH2), 5.33 (d, J = 12.2 Hz, 1H; OCH2), 7.23-7.47 (m, 9H; ArH); 19F NMR (300 MHz, CDCl3) δ 9.55 (br s, 3F; CF3); 31P NMR (161 MHz, CDCl3) δ 17.64 (m); 13C NMR (151 MHz, CDCl3) δ 16.1 (dd, J = 6.2, 16.8 Hz), 34.5, 46.8, 63.1 (d, J = 7.4 Hz), 63.5 (m), 65.1 (dq, J = 29.3, 154.2 Hz), 67.9, 125.10, 125.11 (qd, J = 13.2, 288.4 Hz), 127.2, 127.6, 127.9, 128.1, 128.3, 128.4, 132.7 (d, J = 5.5 Hz), 135.4, 136.1, 155.7 (m); Anal. Calcd for C22H25F3NO5P: C, 56.05, H, 5.35, N, 2.97; found: C, 56.46, H, 5.40, N, 2.91.

Typical procedure for the Ru-catalyzed cyclotrimerization

Method A: A solution of dyine-containing aminophosphonate (0.67 mmol) and alkyne (2.67 mmol, 4 equiv) in dry dichloromethane (10 mL) was degassed three times under cooling. A catalyst RuClCp*COD (0.02 mmol, 3 mol%) was added to this solution and the resulting mixture was degassed one more time. The reaction mixture was heated at 80°C for 3 h. After cooling to room temperature, the solvent was removed under reduced pressure and the crude product was purified by column chromatography on silica gel (eluent − dichloromethane/ethylacetate) to afford the product.

Method B: A solution of dyine-containing aminophosphonate (0.39 mmol) and alkyne (1.55 mmol, 4 equiv) in dry dichloromethane (7 mL) was degassed three times under cooling. A catalyst Grubbs –II (0.02 mmol, 5 mol%) was added to this solution and the resulting mixture was degassed one more time. The reaction mixture was stirred under heating at 60°C for 3 h. After cooling to room temperature, the solvent was removed under reduced pressure and the crude product was purified by column chromatography on silica gel (eluent − dichloromethane/ethylacetate) to afford the product.
Benzy1 6(7)-butyl-3-(diethoxyphosphoryl)-3-(trifluoromethyl)-3,4-dihydroisoquinoline-2(1H)-carboxylate (3b): Mixture of 6,7-regioisomers (1:1). Yield: 61%; oil; \(^1\)H NMR (300 MHz, d\(_6\)-DMSO) \(\delta\) 0.94 (t, \(J = 7.3\) Hz, 3H; CH\(_3\)), 1.12-1.15 (m, 3H; CH\(_3\)), 1.22-1.24 (m, 3H; CH\(_3\)), 1.31-1.40 (m, 2H; CH\(_2\)), 1.56-1.66 (m, 2H; CH\(_2\)), 2.63 (t, \(J = 5.9\) Hz, 2H; CH\(_2\)), 3.31-3.37 (m, 1H; CH\(_2\)), 3.54-3.62 (m, 1H; CH\(_2\)), 3.84-4.08 (m, 4H; OCH\(_2\)), 4.56 (d, \(J = 14.8\) Hz, 1H; NCH\(_2\)), 4.76 (d, \(J = 14.7\) Hz, 1H; NCH\(_2\)), 5.13 (d, \(J = 12.6\) Hz, 1H; OCH\(_2\)), 5.29 (d, \(J = 12.6\) Hz, 1H; OCH\(_2\)), 7.10-7.27 (m, 3H; Ar\(H\)), 7.36-7.44 (m, 5H; Ar\(H\)); 19F NMR (282 MHz, CDCl\(_3\)) \(\delta\) 11.82 (m, 3F; CF\(_3\)); 31P NMR (161 MHz, CDCl\(_3\)) \(\delta\) 16.87 (m); 13C NMR (151 MHz, d\(_6\)-DMSO) \(\delta\) 14.2, 16.4 (dd, \(J = 5.6, 11.3\) Hz), 22.0 (d, \(J = 17.6\) Hz), 33.6, 33.9, 34.3, 35.0 (d, \(J = 3.2\) Hz), 46.6, 46.9, 63.0, 63.6, 65.0 (dq, \(J = 30.2, 151.7\) Hz), 67.5, 125.4 (d, \(J = 7.8\) Hz), 125.5 (dq, \(J = 13.5, 288.2\) Hz), 127.3, 127.6 (d, \(J = 12.6\) Hz), 128.0, 128.2, 128.3, 128.7, 130.3 (d, \(J = 5.8\) Hz), 132.9 (d, \(J = 5.8\) Hz), 136.7, 141.7, 142.3, 155.5; Anal. Calcd for C\(_{26}\)H\(_{33}\)F\(_3\)NO\(_5\)P: C, 59.20, H, 6.31, N, 2.66; found: C 59.49, H 6.14, N, 3.21.

Benzy1 3-(diethoxyphosphoryl)-6(7)-hexyl-3-(trifluoromethyl)-3,4-dihydroisoquinoline-2(1H)-carboxylate (3c): Mixture of 6,7-regioisomers (1:1); Yield: 65%; oil; \(^1\)H NMR (300 MHz, d\(_6\)-DMSO) \(\delta\) 0.99 (m, 3H; CH\(_3\)), 1.20-1.22 (m, 3H; CH\(_3\)), 1.30-1.32 (m, 3H; CH\(_3\)), 1.41-1.42 (m, 8H; 4CH\(_2\)), 1.70 (br s, 2H; CH\(_2\)), 2.70 (m, 2H; CH\(_2\)), 3.41-3.50 (m, 1H; CH\(_2\)), 3.61-3.70 (m, 1H; CH\(_2\)), 4.64 (d, \(J = 14.4\) Hz, 1H; NCH\(_2\)), 4.84 (d, \(J = 13.6\) Hz, 1H; NCH\(_2\)), 5.21 (d, \(J = 12.6\) Hz, 1H; OCH\(_2\)), 5.37 (d, \(J = 12.5\) Hz, 1H; OCH\(_2\)), 7.22-7.52 (m, 8H; Ar\(H\)); 19F NMR (282 MHz, CDCl\(_3\)) \(\delta\) 11.97 (d, \(J = 4.2\) Hz, 3F; CF\(_3\)); 31P NMR (161 MHz, CDCl\(_3\)) \(\delta\) 17.84 (m); 13C NMR (151 MHz, CDCl\(_3\)) \(\delta\) 14.0, 16.1 (d, \(J = 16.0\) Hz), 22.5, 28.9 (d, \(J = 6.9\) Hz), 31.6 (d, \(J = 15.7\) Hz), 34.2, 34.6, 35.7, 46.6, 46.9, 63.1 (d, \(J = 7.5\) Hz), 63.5 (m), 65.2 (dq, \(J = 13.1, 144.1\) Hz), 67.9, 124.96, 125.1 (qd, \(J = 13.1, 288.2\) Hz), 125.15, 127.2, 127.6, 127.9, 128.1, 128.4, 129.8, 132.5 (d, \(J = 5.6\) Hz), 136.1, 142.1, 142.9, 155.7; Anal. Calcd for C\(_{28}\)H\(_{37}\)F\(_3\)NO\(_5\)P: C, 60.53, H, 6.71, N, 2.52; found: C, 60.11, H, 6.93, N, 2.31.

Benzy1 7-butyl-3-(diethoxyphosphoryl)-5-phenyl-3-(trifluoromethyl)-3,4-dihydroisoquinoline-2(1H)-carboxylate (6a): Yield: 60% (Method A); 77% (Method B) oil; \(^1\)H NMR (300 MHz, CDCl\(_3\)) \(\delta\) 0.98 (t, \(J = 7.3\) Hz, 3H; CH\(_3\)), 1.07 (t, \(J = 7.1\) Hz, 3H; CH\(_3\)), 1.17 (t, \(J = 6.5\) Hz, 3H; CH\(_3\)), 1.32-1.45 (m, 2H; CH\(_2\)), 1.61-1.71 (m, 2H; CH\(_2\)), 2.68 (t, \(J = 7.6\) Hz, 2H; CH\(_2\)), 3.52-3.56 (m, 2H; CH\(_2\)), 3.89-4.20 (m, 4H; OCH\(_2\)), 4.76 (br s, 2H; CH\(_2\)), 5.21 (d, \(J = 12.2\) Hz, 1H; OCH\(_2\)), 5.35 (d, \(J = 12.2\) Hz, 1H; OCH\(_2\)), 7.08-7.21 (m, 2H; Ar\(H\)), 7.32-7.52 (m, 10H; Ar\(H\)); 19F NMR (282 MHz, CDCl\(_3\)) \(\delta\) 9.81 (s, 3F; CF\(_3\)); 31P NMR (161 MHz, CDCl\(_3\)) \(\delta\) 16.63 (q, \(J = 3.3\) Hz); 13C NMR (151 MHz, CDCl\(_3\)) \(\delta\) 13.9, 15.8 (d, \(J = 6.6\) Hz), 16.2 (d, \(J = 5.5\) Hz), 22.4, 33.6, 35.3, 43.4, 47.3, 62.7 (d, \(J = 8.8\) Hz), 64.0 (m), 64.8 (dq, \(J = 28.7, 154.8\) Hz), 67.9, 124.7, 125.9 (dq, \(J = 12.8, 288.9\) Hz), 127.1, 127.2 (d, \(J = 6.6\) Hz), 128.1, 128.2, 128.3, 128.4, 129.2, 129.4,
Benzyl 3-(diethoxyphosphoryl)-7-hexyl-5-phenyl-3-(trifluoromethyl)-3,4-dihydroisoquinoline-2(1H)-carboxylate (6b): Yield: 57% (Method A); 68% (Method B); oil; $^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 0.94 (t, $J$ = 6.5 Hz, 3H; CH$_3$), 1.07 (t, $J$ = 7.1 Hz, 3H; CH$_3$), 1.15-1.25 (m, 3H; CH$_3$), 1.32-1.44 (m, 6H; CH$_2$), 1.62-1.67 (m, 2H; CH$_2$), 2.67 (t, $J$ = 7.0 Hz, 2H; CH$_2$), 3.52-3.57 (m, 2H; CH$_2$), 3.89-4.29 (m, 4H; OCH$_2$), 4.76 (br s, 2H; CH$_2$), 5.22 (d, $J$ = 12.2 Hz, 1H; OCH$_2$), 5.35 (d, $J$ = 12.2 Hz, 1H; OCH$_2$), 7.08-7.23 (m, 2H; ArH), 7.37-7.53 (m, 10H; ArH); $^{19}$F NMR (282 MHz, CDCl$_3$) $\delta$ 9.79 (br s, 3F; CF$_3$); $^{31}$P NMR (161 MHz, CDCl$_3$) $\delta$ 16.64 (d, $J$ = 3.1 Hz); $^{13}$C NMR (151 MHz, CDCl$_3$) $\delta$ 14.1, 15.8 (d, $J$ = 6.6 Hz), 16.2 (d, $J$ = 5.5 Hz), 22.5, 29.0, 31.4, 31.7, 35.6, 47.3, 62.7 (d, $J$ = 7.7 Hz), 64.0 (m), 64.8 (dq, $J$ = 28.7, 154.8 Hz), 68.0, 124.6, 124.9 (qd, $J$ = 12.9, 288.8 Hz), 127.1, 127.2 (d, $J$ = 7.4 Hz), 128.1, 128.2, 128.3, 128.4, 129.2, 129.4, 136.2, 140.2, 140.6, 141.7, 155.7, 167.7; Anal. Calcd for C$_{34}$H$_{41}$F$_3$NO$_5$P: C, 64.65, H, 6.54, N, 2.22; found: C, 64.23, H, 6.32, N, 2.59.

Benzyl 3-(diethoxyphosphoryl)-5,7-diphenyl-3-(trifluoromethyl)-3,4-dihydroisoquinoline-2(1H)-carboxylate (6c): Yield: 51% (Method A); 63% (Method B); oil; $^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 1.08 (t, $J$ = 7.1 Hz, 3H; CH$_3$), 1.19 (t, $J$ = 6.7 Hz, 3H; CH$_3$), 3.59-3.63 (m, 2H; CH$_2$), 3.94-4.20 (m, 4H; OCH$_2$), 4.85 (br s, 2H; CH$_2$), 5.23 (d, $J$ = 12.4 Hz, 1H; OCH$_2$), 5.36 (d, $J$ = 12.2 Hz, 1H; OCH$_2$), 7.42-7.67 (m, 17H; ArH); $^{19}$F NMR (282 MHz, CDCl$_3$) $\delta$ 9.82 (d, $J$ = 2.1 Hz, 3F; CF$_3$); $^{31}$P NMR (161 MHz, CDCl$_3$) $\delta$ 16.49 (d, $J$ = 3.1 Hz); $^{13}$C NMR (151 MHz, CDCl$_3$) $\delta$ 15.8 (d, $J$ = 6.6 Hz), 16.2 (d, $J$ = 5.5 Hz), 31.6, 47.5, 62.8 (m), 64.2 (m), 65.6 (q, $J$ = 28.2 Hz), 68.2, 123.3, 126.3 (d, $J$ = 2.5 Hz), 127.1, 127.4, 127.5, 128.1, 128.2, 128.3, 128.4, 128.5, 128.8, 129.3, 129.8, 135.7, 136.2, 139.9, 140.0, 140.4, 141.4, 155.8; Anal. Calcd for C$_{34}$H$_{33}$F$_3$NO$_5$P: C, 65.49, H, 5.53, N, 2.25; found: C, 65.87, H, 5.19, N, 2.11.

Benzyl 7-butyl-3-(diethoxyphosphoryl)-5-(4-methoxyphenyl)-3-(trifluoromethyl)-3,4-dihydroisoquinoline-2(1H)-carboxylate (6d): Yield: 42% (Method A); 72% (Method B); oil; $^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 0.93 (t, $J$ = 7.3 Hz, 3H; CH$_3$), 1.10 (t, $J$ = 7.1 Hz, 3H; CH$_3$), 1.19 (t, $J$ = 6.8 Hz, 3H; CH$_3$), 1.32-1.42 (m, 2H; CH$_2$), 1.63-1.68 (m, 2H; CH$_2$), 2.66 (t, $J$ = 7.5 Hz, 2H; CH$_2$), 3.53-3.57 (m, 2H; CH$_2$), 3.92 (s, 3H; OCH$_3$), 3.96 (m, 4H; OCH$_2$), 4.75 (br s, 2H; CH$_2$), 5.20 (d, $J$ = 12.2 Hz, 1H; OCH$_2$), 5.34 (d, $J$ = 12.2 Hz, 1H; OCH$_2$), 7.02-7.13 (m, 4H; ArH), 7.29-7.51 (m, 7H; ArH); $^{19}$F NMR (282 MHz, CDCl$_3$) $\delta$ 9.87 (s, 3F; CF$_3$); $^{31}$P NMR (161 MHz, CDCl$_3$) $\delta$ 16.88 (d, $J$ = 2.9 Hz); $^{13}$C NMR (151 MHz, CDCl$_3$) $\delta$ 13.9, 15.9 (d, $J$ = 6.6 Hz), 16.2 (d, $J$ = 5.5 Hz), 22.4, 31.5, 33.6, 35.4, 47.5, 55.4, 62.8 (d, $J$ = 7.7 Hz), 64.0 (d, $J$ = 6.4 Hz), 67.1 (dq, $J$ = 28.9, 136.6 Hz), 68.0, 113.7, 124.4, 125.03 (qd, $J$ = 12.8, 288.7 Hz), 127.40,
127.47, 128.1, 128.5, 129.5, 130.4, 132.8, 136.0, 140.4, 141.6, 155.8, 158.9; Anal. Calcd for C_{33}H_{39}F_{3}NO_{6}P: C, 62.55, H, 6.20, N, 2.21; found: C, 62.08, H, 6.46, N, 2.39.

Benzyl 3-(diethoxyphosphoryl)-7-hexyl-5-(4-methoxyphenyl)-3-(trifluoromethyl)-3,4-dihydroisoquinoline-2(1H)-carboxylate (6e): Yield: 39% (Method A); 75% (Method B); oil; 

^1^H NMR (300 MHz, CDCl_3) δ 0.94 (t, J = 6.5 Hz, 3H; CH_3), 1.11 (t, J = 6.9 Hz, 3H; CH_3), 1.19 (t, J = 6.4 Hz, 3H; CH_3), 1.36-1.39 (m, 6H; 3CH_2), 1.64-1.69 (m, 2H; CH_2), 2.66 (t, J = 8.0 Hz, 2H; CH_2), 3.54-3.58 (m, 2H; CH_2), 3.92 (s, 3H; OCH_3), 3.95-4.18 (m, 4H; OCH_2), 4.75 (br s, 2H; CH_2), 5.22 (d, J = 12.2 Hz, 1H; OCH_2), 5.35 (d, J = 12.2 Hz, 1H; OCH_2), 7.02-7.13 (m, 4H; ArH), 7.30-7.51 (m, 7H; ArH); 19F NMR (282 MHz, CDCl_3) δ 9.90 (s, 3F; CF_3); 31P NMR (161 MHz, CDCl_3) δ 16.88 (d, J = 2.9 Hz); 13C NMR (151 MHz, CDCl_3) δ 14.1, 15.9 (d, J = 6.6 Hz), 16.2 (d, J = 5.5 Hz), 22.5, 29.0, 31.4, 31.5, 31.7, 35.6, 47.4, 55.3, 62.8 (d, J = 7.7 Hz), 63.9 (m), 64.8 (d, J = 8.6 Hz, 2H; ArH), 7.02 (d, J = 8.6 Hz, 2H; ArH), 7.19-7.28 (m, 3H; ArH); Anal. Calcd for C_{35}H_{43}F_{3}NO_{6}P: C, 63.53, H, 6.55, N, 2.12; found: C, 63.91, H, 6.34, N, 1.82.

Benzyl 3-(diethoxyphosphoryl)-5-(4-methoxyphenyl)-7-phenyl-3-(trifluoromethyl)-3,4-dihydroisoquinoline-2(1H)-carboxylate (6f): Yield: 41% (Method A); 60% (Method B); oil; 

^1^H NMR (400 MHz, CDCl_3) δ 1.06-1.36 (m, 6H; 2CH_3), 3.58 (d, J = 11.3 Hz, 2H; OCH_2), 3.89 (s, 3H; OCH_3), 3.79-4.18 (m, 2H; CH_2), 4.80 (br s, 2H; CH_2), 5.19 (d, J = 12.2 Hz, 1H; OCH_2), 5.32 (d, J = 12.2 Hz, 1H; OCH_2), 7.02 (d, J = 8.6 Hz, 2H; ArH), 7.25-7.62 (m, 14H; ArH); ^19^F NMR (282 MHz, CDCl_3) δ 9.93 (s, 3F; CF_3); ^31^P NMR (161 MHz, CDCl_3) δ 16.73 (d, J = 2.9 Hz); ^13^C NMR (151 MHz, CDCl_3) δ 16.1 (dd, J = 6.0, 24.1 Hz), 29.7, 31.6, 47.5, 55.4, 62.9 (d, J = 7.7 Hz), 64.1 (d, J = 7.3 Hz), 67.1 (d, J = 31.2, 140.0 Hz), 68.1, 113.8, 123.0, 124.9 (qd, J = 12.8, 276.2 Hz), 127.1, 127.5, 128.2, 128.4, 128.5, 128.8, 129.4 (d, J = 7.6 Hz), 129.8, 130.4, 132.4, 135.7, 136.2, 139.9, 140.5, 141.1, 155.8, 159.1; Anal. Calcd for C_{35}H_{35}F_{3}NO_{6}P: C, 64.31, H, 5.40, N, 2.14; found: C, 63.94, H, 5.67, N, 2.31.

Typical procedure for removal of Cbz-protecting group

A mixture of alkynyl-containing amino ester (0.26 mmol) and palladium on carbon (0.02 mmol, 10%mol) in methanol (10 mL) was degassed twice and then stirred under hydrogen atmosphere for 3 h. The catalyst was filtered off through a Celite plug and the solvent was removed under reduced pressure to give the pure product.

Diethyl [3-(trifluoromethyl)-1,2,3,4-tetrahydroisoquinolin-3-yl]phosphonate (7): Yield: 94%; oil; ^1^H NMR (600 MHz, CDCl_3) δ 1.22 (t, J = 7.1 Hz, 3H; CH_3), 1.28 (t, J = 7.1 Hz, 3H; CH_3), 2.47 (br s, 1H; ArH), 3.08-3.13 (m, 1H; CH_2), 3.37 (t, J = 15.8 Hz, 1H; CH_2), 4.02-4.04 (m, 2H; NCH_2), 4.15-4.20 (m, 4H; OCH_2), 7.08 (d, J = 6.6 Hz, 1H; ArH), 7.17-7.28 (m, 3H; ArH);
¹⁹F NMR (282 MHz, CDCl₃) δ 5.39 (d, J = 5.8 Hz, 3F; CF₃); ³¹P NMR (121 MHz, CDCl₃) δ 19.03 (q, J = 5.8 Hz); ¹³C NMR (151 MHz, CDCl₃) δ 16.2, 28.3, 44.3 (d, J = 7.8 Hz), 59.6 (dq, J = 26.2, 79.1 Hz), 63.5 (d, J = 7.3 Hz), 64.0 (d, J = 7.0 Hz), 125.4, 126.1 (qd, J = 11.0, 286.7 Hz), 126.2, 126.8, 128.1, 131.4 (d, J = 5.9 Hz), 135.4; Anal. Calcd for C₁₄H₁₉F₃NO₃P: C, 49.86, H, 5.68, N, 4.15; found: C, 50.21, H, 5.47, N, 3.87.

**Diethyl [7-butyl-5-phenyl-3-(trifluoromethyl)-1,2,3,4-tetrahydroisoquinolin-3-yl]phosphonate (8):** Yield: 85%; oil; ¹H NMR (300 MHz, CDCl₃) δ 0.94 (t, J = 7.4 Hz, 3H; CH₃), 1.12 (t, J = 7.0 Hz, 3H; CH₃), 1.20-1.21 (m, 3H; CH₃), 1.36-1.40 (m, 2H; CH₂), 1.60-1.65 (m, 2H; CH₂), 2.49 (br s, 1H; NH), 2.63 (t, J = 7.6 Hz, 2H; CH₂), 2.97-3.02 (m, 1H; CH₂), 3.27-3.32 (m, 1H; CH₂), 3.89-3.92 (m, 1H; NCH₂), 4.03-4.12 (m, 4H; OCH₂), 4.06 (br s, 1H; NCH₂), 6.96 (s, 1H; Ar H), 7.03 (s, 1H; Ar H), 7.28-7.46 (m, 5H; Ar H); ¹⁹F NMR (282 MHz, CDCl₃) δ 4.81 (d, J = 4.8 Hz, 3F; CF₃); ³¹P NMR (161 MHz, CDCl₃) δ 18.58 (d, J = 4.2 Hz); ¹³C NMR (151 MHz, CDCl₃) δ 13.9, 16.1 (dd, J = 3.0, 5.6 Hz), 22.3, 25.6, 33.6, 35.2, 45.1, 60.0 (dq, J = 26.5, 157.9 Hz), 63.3 (d, J = 7.7 Hz), 64.13 (d, J = 7.7 Hz), 124.6, 125.1 (d, J = 12.1 Hz), 126.5 (d, J = 4.4 Hz), 127.0, 128.2, 128.7, 129.1, 136.3, 140.6, 140.7, 141.2; Anal. Calcd for C₂₄H₃₁F₃NO₃P: C, 61.40, H, 6.66, N, 2.98; found: C, 61.69, H, 6.35, N, 2.75.

**Typical procedure for removal of ether group**

To a solution of aminophosphonate 5 (0.20 mmol) in dry chloroform (5 mL) was added Me₃SiBr (0.80 mmol). The reaction mixture was stirred at room temperature for 72 h. Then, the volatiles were removed under reduced pressure. The residue was re-dissolved in ethanol (10 mL) and after stirring for 20 min at room temperature the solvent was evaporated under reduced pressure. This manipulation was repeated three times, and then the residue was treated with ether to afford a solid product.

**7-Butyl-5-phenyl-3-(trifluoromethyl)-1,2,3,4-tetrahydroisoquinolin-3-yl-phosphonate hydrobromide (9):** Yield: 80%; oil; ¹H NMR (600 MHz, d₆-DMSO) δ 0.90 (t, J = 7.4 Hz, 3H; CH₃), 1.27-1.39 (m, 2H; CH₂), 1.57-1.59 (m, 2H; CH₂), 2.60 (t, J = 7.2 Hz, 2H; CH₂), 3.06-2.95 (m, 1H; CH₂), 3.00-3.09 (m, 1H; CH₂), 3.21-3.25 (m, 1H; CH₂), 4.06 (d, J = 14.9 Hz, 1H; NCH₂), 4.15 (d, J = 14.9 Hz, 1H; NCH₂), 7.10 (s, 1H; Ar H), 7.20 (s, 1H; Ar H), 7.35-7.56 (m, 6H; Ar H), 9.13 (br s, 3H; NH, 2OH); ¹⁹F NMR (282 MHz, d₆-DMSO) δ 9.16 (d, J = 3.0 Hz, 3F; CF₃); ³¹P NMR (161 MHz, d₆-DMSO) δ 7.64 (m); ¹³C NMR (151 MHz, d₆-DMSO) δ 14.2, 22.2, 26.5, 33.4, 34.7, 44.7, 59.6 (dq, J = 26.5, 134.9 Hz), 124.3, 126.0, 126.4, 126.8, 127.8, 129.0, 129.3, 129.8, 131.4, 140.1, 141.1 (d, J = 5.7 Hz); Anal. Calcd for C₂₂H₂₃BrF₃NO₃P: C, 48.60, H, 4.89, N, 2.83; found: C, 48.26, H, 5.17, N, 2.61.
$^1$H and $^{13}$C NMR spectra of new compounds

$^1$H NMR spectra of compound 3a

$^{13}$C NMR spectra of compound 3a
$^1$H NMR spectra of compound 3b

$^{13}$C NMR spectra of compound 3b
$^1$H NMR spectra of compound 3e

$^{13}$C NMR spectra of compound 3e
$^1$H NMR spectra of compound 6a

$^{13}$C NMR spectra of compound 6a
$^1$H NMR for compound 6b

$^{13}$C NMR for compound 6b
$^1$H NMR for compound 6d

$^1$C NMR for compound 6d
$^1$H NMR for compound 6e

$^1$C NMR for compound 6e
1H NMR for compound 6f

13C NMR for compound 6f
$^1$H NMR for compound 7

$^{13}$C NMR for compound 7
$^1$H NMR for compound 8

$^{13}$C NMR for compound 8
$^1$H NMR for compound 9

$^{13}$C NMR for compound 9