Cyanoethyl-*N,N*-diisopropylaminomethoxy phosphine.[18] To a mixture containing 0.17 mL (136 mg, 4.23 mmol) of anhydrous MeOH and 1.47 mL (1.09 g, 8.46 mmol) of ethyl diisopropylamine in 10 mL of dry CH_2Cl_2 was added 1.0 g (4.23 mmol) of cyanoethyl-*N,N*-diisopropylchlorophosphoramidite at 0 °C. The reaction mixture was stirred at room temperature for 1h. The reaction mixture was quenched by the addition of 10 mL of saturated aqueous $NaHCO_3$ and the resulting solution was partitioned against EtOAc. The organic layer was washed with brine and dried over $MgSO_4$. Concentration under diminished pressure gave the desired phosphine as a colorless liquid: yield 969 mg (99%); ^{1}H NMR ($CDCl_3$) δ 1.19 (d, 12H, J = 7 Hz), 2.64 (t, 2H, J = 7 Hz), 3.42 (d, 3H, J = 13 Hz), 3.54 - 3.63 (m, 2H) and 3.75 - 3.90 (m, 2H). The product was used for the next reaction without further purification.

2,5-Dimethoxy-2,5-dihydrofurfuryl cyanoethyl methyl phosphate. Samples containing 1.01 g (6.36 mmol) 2,5-dimethoxy-2,5-dihydrofurfuryl alcohol (**7a**)[17] and 889 mg (12.7 mmol) of tetrazole were added to a round bottom flask equipped with a magnetic stir bar and co-evaporated twice with portions of toluene. The mixture was then suspended in 15 mL of dry CH_3CN and cooled to 0 °C. A solution of 966 mg (4.16 mmol) of the foregoing phosphine in 5 mL of dry CH_3CN was added dropwise over a period of 5 min. The reaction mixture was stirred at 0 °C for 30 min and then at room temperature for 1 h. The reaction mixture was concentrated under diminished pressure and the residue was dissolved in 14 mL of a solution containing 0.6 g of I_2 in a mixture of 13:1:0.2 THF-water-pyridine. The reaction mixture was stirred at room temperature for 20 min and then concentrated under diminished pressure. The residue was dissolved in 10 mL of $CHCl_3$ and washed with 10 mL of 1% aqueous sodium bisulfite. The aqueous layer was extracted with $CHCl_3$, washed with brine and dried ($MgSO_4$). After concentration of the organic phase, the residue was purified on a 20-g silica gel column; elution with 1:4 and then with 2:1 AcOEt-*n*-hexane gave the desired product as a colorless liquid: yield

548 mg (42%); silica gel TLC R_f 0.08 (1:1 AcOEt-*n*-hexane); ^{1}H NMR ($CDCl_3$) δ 2.77 (d, 2H, *J* = 6 Hz), 3.24 (s, 3H), 3.52 (s, 3H), 3.81 (d, 3H, *J* = 11 Hz), 4.00 - 4.32 (m, 4H), 5.53 (s, 1H), 5.98 (d, 1H, *J* = 6 Hz) and 6.16 (d, 1H, *J* = 6 Hz); mass spectrum (FAB), *m/z* 306.0753 $(M-H)^+$ ($C_{11}H_{17}NO_7P$ requires 306.0743).

2,2-Dimethoxypropionyl cyanoethyl methyl phosphate. In analogy with the synthesis of 2,5-dimethoxy-2.5-dihydrofurfuryl cyanoethyl methyl phosphate, 480 mg (4.0 mmol) of 2, 2-dimethoxypropionyl alcohol (**7c**) was treated with 500 mg (2.0 mmol) of cyanoethyl-*N,N*-diisopropylamino methoxy phosphine in the presence of 560 mg (8.0 mmol) of tetrazole to give the desired product as a colorless liquid: yield 131 mg (25%); silica gel TLC R_f 0.08 (1:1 AcOEt-*n*-hexane); ^{1}H NMR ($CDCl_3$) δ 1.37 (s, 3H), 2.78 (t, 1H, *J* = 6 Hz), 2.79 (t, 1H, *J* = 6 Hz), 3.24 (s, 6H), 3.83 (d, 3H, *J* = 11 Hz), 3.99 (d, 1H, *J* = 6 Hz), 4.00 (d, 1H, *J* = 6 Hz) and 4.27 (dt, 2H, *J* = 8, 6 Hz); mass spectrum (FAB), *m/z* 266.2799 $(M-H)^+$ ($C_9H_{17}NO_6P$ requires 266.2794).

2,5-Dimethoxy-2,5-dihydrofurfuryl methyl phosphate (13a). A reaction mixture containing 485 mg (1.58 mmol) of 2,5-dimethoxy-2,5-dihydrofurfuryl cyanomethyl methyl phosphate in 5 mL of pyridine and 5 mL of NH_4OH was stirred at room temperature for 2 h. The solvent was concentrated under diminished pressure and the residue was co-evaporated twice with portions of EtOH. The residue was purified on a Dowex 50W X2 column (100 - 200 mesh, Na^+ form); elution with H_2O gave **13a** as a pale yellow liquid: yield 401 mg (92%); ^{1}H NMR (D_2O) δ 3.08, 3.14, 3.36 and 3.43 (each s, 6H), 3.43 - 3.49 (m, 3H), 3.68 - 3.89 (m, 2H), 5.58 and 5.88 (each br, 1H), 6.06 (m, 1H) and 6.17 (m, 1H); mass spectrum (FAB), *m/z* 253.0456 $(M-H)^-$ ($C_8H_{14}O_7P$ requires 253.0477).

2,2-Dimethoxypropionyl methyl phosphate (13c). A reaction mixture containing 100

mg (0.38 mmol) of 2,2-dimethoxypropionyl cyanoethyl methyl phosphate in 1 mL of pyridine and 1 mL of NH_4OH was stirred at room temperature for 2 h. The solvent was concentrated under diminished pressure and co-evaporated twice with portions of EtOH. The residue was purified on a Dowex 50W X2 column (100 - 200 mesh, Na^+ form); elution with H_2O gave **13c** as a pale yellow liquid: yield 88 mg (92%); ^1H NMR (D_2O) δ 1.27 (s, 3H), 3.14 (s, 6H), 3.46 (d, 3H, J = 11 Hz), 3.66 (d, 2H, J = 5 Hz); mass spectrum (FAB), *m/z* 237.0530 $(M+Na)^+$ ($C_6H_{14}O_6PNa$ requires 237.0504).

Reference

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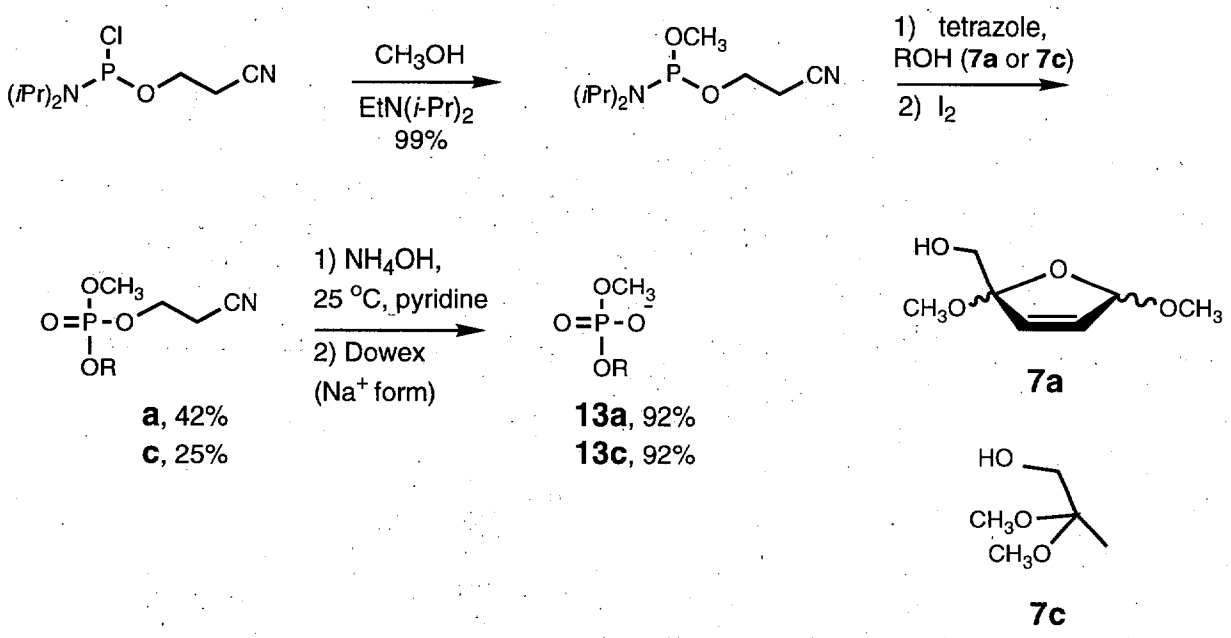
Cl
(iPr)2N
P
O
CN
CH3OH
EtN(i-Pr)2
99%
OCH3
1) tetrazole,
ROH (7a or 7c)
2) I2
OCH3
O=P-O
OR
CN
a, 42%
c, 25%
1) NH4OH,
25 °C, pyridine
2) Dowex
(Na+ form)
13a, 92%
13c, 92%
HO
CH3O
OCH3
7a
7c