Electronic Supplementary Material (ESI) for RSC Advances.

Supporting information

Isopropenyl phosphate as an atom efficient phosphorylation reagent of alcohols with catalytic base.

Jens Wéry[a], Igor Beckers[a] & Dirk E. De Vos[a,]*

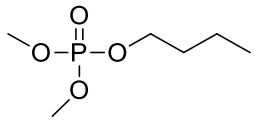
[a]Centre for Membrane separations, Adsorption, Catalysis and Spectroscopy for Sustainable Solutions (cMACS), Department of Microbial and Molecular Systems (M2S); KU Leuven, Celestijnenlaan 200F, post box 2454, 3001 Leuven (Belgium).

1. Reaction procedure

Under the standard reaction conditions, 1.68 mg (0.015 mmol) of *t*-BuOK was dissolved in a solution of 0.4 mL dry THF with 5 equivalents of alcohol and 29 µl (0.2 mmol) of dimethyl isopropenyl phosphate. All reactions were performed at room temperature under argon atmosphere. After reaction, a solution of triphenyl phosphate in DMSO-d_6 was added as an external standard for NMR analysis.

2. NMR data

Dimethylbutyl phosphate (1a)

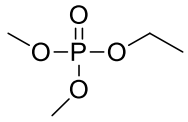


^{1}H NMR (400 MHz, DMSO-d_6): δ 4.04 (dt, J = 7.2 Hz, 2H), 3.71 (d, J = 11.0 Hz, 6H), 1.66 (quintet, 2H), 1.36 (sextet, 2H), 0.90 (t, J = 7.3 Hz, 3H).

^{31}P NMR (400 MHz, DMSO-d_6): δ 1.30.

^{13}C NMR (400 MHz, DMSO-d_6): δ 66.9 (d, J = 5.9 Hz), 53.9 (d, J = 6.0 Hz, 2C), 32.3 (d, J = 6.7 Hz), 18.6, 12.9.

Dimethylethyl phosphate (1b)

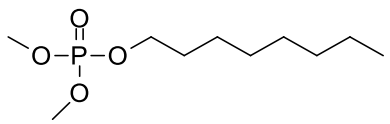


^{1}H NMR (400 MHz, DMSO-d_6): δ 3.71 (dq, J = 7.2 Hz, 2H), 3.35 (d, J = 11.1 Hz, 6H), 0.95 (t, J = 7.0 Hz, 3H).

^{31}P NMR (400 MHz, DMSO-d_6): δ 1.23.

^{13}C NMR (400 MHz, DMSO-d_6): δ 63.5 (d, J = 5.8 Hz), 53.4 (d, J = 6.0 Hz, 2C), 15.4 (d, J = 6.44 Hz).

Dimethyloctyl phosphate (1c)

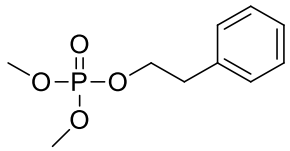


^{1}H NMR (400 MHz, DMSO-d_6): δ 4.01 (dt, J = 7.2 Hz, 2H), 3.70 (d, J = 11.1 Hz, 6H), 1.68 (quintet, 2H), 1.49 (quintet, 2H), 1.44-1.26 (m, 8H), 0.92 (t, J = 7.0 Hz, 3H).

^{31}P NMR (400 MHz, DMSO-d_6): δ 1.52.

^{13}C NMR (400 MHz, DMSO-d_6): δ 67.2 (d, J = 5.9 Hz), 53.2 (d, J = 5.7 Hz, 2C), 31.8 (d, J = 6.9 Hz), 31.3, 29.2, 29.1, 25.4, 22.6, 13.5.

Dimethylphenethyl phosphate (1d)

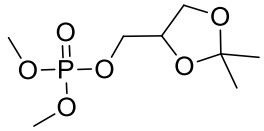


^{1}H NMR (400 MHz, DMSO-d_6): δ 7.32-7.2 (m, 5H), 4.23 (dt, J = 7.1 Hz, 2H), 3.64 (d, J = 11.1 Hz, 6H), 3.00 (t, J = 6.8 Hz, 2H).

^{31}P NMR (400 MHz, DMSO-d_6): δ 1.09.

^{13}C NMR (400 MHz, DMSO-d_6): δ 137.7, 128.9 (s, 2C), 128.2 (s, 2C), 126.3, 67.6 (d, J = 5.8 Hz), 53.2 (d, J = 6.2 Hz, 2C) 36.6 (d, J = 7.2 Hz).

Dimethyl (2,2-dimethyl-1,3-dioxolan-4-yl)methyl phosphate (1e)

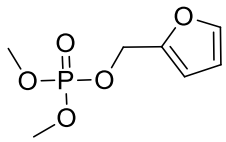


^{1}H NMR (400 MHz, DMSO-d_6): δ 4.28 (m, 2H), 4.10-3.98 (m, 2H), 3.72 (m, 1H) 3.64 (d, J = 11.0 Hz, 6H), 2.08 (s, 6H).

^{31}P NMR (400 MHz, DMSO-d_6): δ 1.19.

^{13}C NMR (400 MHz, DMSO-d_6): δ 120.2, 74.3 (d, J = 7.2 Hz), 67.6 (d, J = 5.6 Hz), 62.7, 54.1 (d, J = 6.2 Hz, 2C), 26.5, 25.2.

Dimethyl 2-furanylmethyl phosphate (1f)

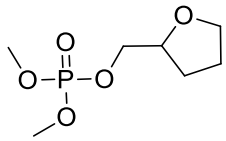


^{1}H NMR (400 MHz, DMSO-d_6): δ 7.3 (m, 1H), 6.37 (m, 1H), 6.27 (m, 1H), 5.0 (d, J = 8.5 Hz, 2H), 3.61 (d, J = 11.0 Hz, 6H).

^{31}P NMR (400 MHz, DMSO-d_6): δ 1.17.

^{13}C NMR (400 MHz, DMSO-d_6): δ 150.5 (d, J = 7.4 Hz), 144.3, 111.3, 110.9, 60.8 (d, J = 5.2 Hz), 54.1 (d, J = 5.9 Hz, 2C).

Dimethyl (tetrahydro-2-furanyl)methyl phosphate (1g)

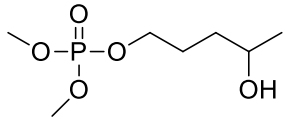


^{1}H NMR (400 MHz, DMSO-d_6): δ 4.28 (m, 1H), 4.01 (m, 1H), 3.84 (m, 1H), 3.76 (m, 1H), 3.62 (d, J = 11.0 Hz, 6H), 1.82 (m, 4H).

^{31}P NMR (400 MHz, DMSO-d_6): δ 1.24.

^{13}C NMR (400 MHz, DMSO-d_6): δ 77.1 (d, J = 7.2 Hz), 69.2 (d, J = 6.1 Hz), 67.9, 54.1 (d, J = 5.7 Hz, 2C), 27.4, 25.6.

Dimethyl (4-hydroxy)pentyl phosphate (1i)

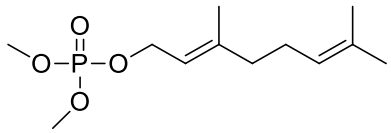


^{1}H NMR (400 MHz, DMSO-d_6): δ 4.40 (s, 1H), 4.03 (dt, J = 7.1 Hz, 2H), 3.71 (d, J = 11.1 Hz, 6H), 3.43 (m, 1H), 1.45 (m, 2H), 1.34 (m, 2H) , 1.07 (d, J = 6.0 Hz, 3H).

^{31}P NMR (400 MHz, DMSO-d_6): δ 1.25.

^{13}C NMR (400 MHz, DMSO-d_6): δ 67.9 (d, J = 6.0 Hz), 65.2, 54.0 (d, J = 6.3 Hz, 2C), 35.1, 26.9 (d, J = 6.8 Hz), 20.9.

Dimethyl (2*E*)-3,7-dimethyl-2,6-octadien-1-yl phosphate (1l)

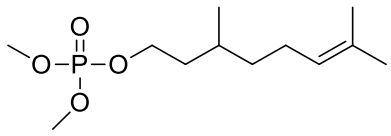


^{1}H NMR (400 MHz, DMSO-d_6): δ 5.34 (m, 1H), 5.13 (m, 1H), 4.54 (m, 2H), 3.68 (d, J = 11.1 Hz, 6H), 2.06 (m, 2H), 1.98 (m,2H), 1.65 (s, 3H), 1.60 (s, 6H).

^{31}P NMR (400 MHz, DMSO-d_6): δ 1.63.

^{13}C NMR (400 MHz, DMSO-d_6): δ 135.4, 130.2, 124.4, 120.0 (d, J = 5.0 Hz), 53.8 (d, J = 6.0 Hz, 2C), 52.0 (d, J = 6.0 Hz), 39.6, 26.5, 25.6, 17.3, 15.9.

Dimethyl 3,7-dimethyl-6-octen-1-yl phosphate (1m)

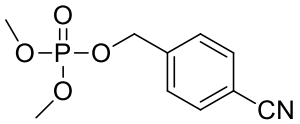


^{1}H NMR (400 MHz, DMSO-d_6): δ 5.11 (m, 1H), 4.05 (dt, J = 7.2 Hz, 2H), 3.75 (d, J = 11.1 Hz, 6H), 1.98 (m, 2H), 1.70 (s, 3H), 1.60 (s, 3H), 1.60-1.12 (m, 5H), 0.92 (d, J = 6.6 Hz, 3H).

^{31}P NMR (400 MHz, DMSO-d_6): δ 1.31.

^{13}C NMR (400 MHz, DMSO-d_6): δ 130.5, 125.9, 65.8 (d, J = 5.6 Hz), 53.9 (d, J = 5.6 Hz, 2C), 37.5, 37.1 (d, J = 6.3 Hz), 29.3, 25.6, 25.5, 19.5, 17.4.

(4-cyanophenyl)ethenyl dimethyl phosphate (1n)

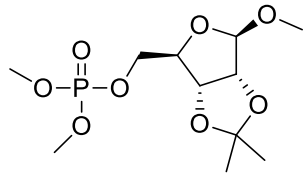


^{1}H NMR (400 MHz, DMSO-d_6): δ 7.84 (d, J = 8.3 Hz, 2H), 7.65 (d, J = 8.3 Hz, 2H), 5.18 (d, J = 8.0 Hz, 2H), 3.73 (d, J = 11.1 Hz, 6H).

^{31}P NMR (400 MHz, DMSO-d_6): δ 1.37.

^{13}C NMR (400 MHz, DMSO-d_6): δ 142.2, 132.6 (s, 2C), 128.3 (s, 2C), 118.6, 111.7, 67.6 (d, J = 5.1 Hz), 54.2 (d, J = 6.1 Hz, 2C).

(6-methoxy-2,2-dimethyltetrahydrofuro[3,4-d][1,3]dioxol-4-yl)methyl dimethyl phosphate (1o)

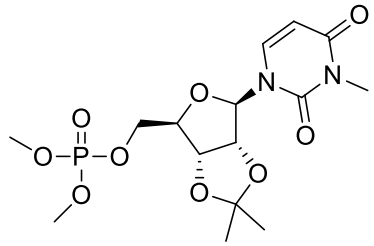


^{1}H NMR (400 MHz, DMSO-d_6): δ 4.76 (s, 1H), 4.61 (d, J = 6.0 Hz, 1H), 4.55 (d, J = 6.0 Hz, 1H), 4.15 (m, 2H), 4.01 (m, 1H), 3.73 (d, J = 11.1 Hz, 6H), 3.17 (s, 3H), 1.41 (s, 3H), 1.28 (s, 3H).

^{31}P NMR (400 MHz, DMSO-d_6): δ 1.11.

^{13}C NMR (400 MHz, DMSO-d_6): δ 126.0, 120.2, 87.4, 84.8 (d, J = 7.7 Hz), 81.4, 67.5 (d, J = 5.8 Hz), 54.3 (d, J = 5.9 Hz, 2C), 54.2, 26.4.

5'-uridylic-3-methyl-2',3'-*o*-(1-methylethylidene) dimethyl phosphate (1p)



^{1}H NMR (600 MHz, THF-d_8): δ 7.47 (d, J = 8.3 Hz, 1H), 5.70 (d, J = 2.0 Hz, 1H), 5.61 (d , J = 8.3 Hz, 1H), 4.99-4.82 (m, 2H), 4.21 (m, 1H), 4.14 (m, 2H), 3.62 (dd, J = 11.0 Hz, 6H), 3.15 (s, 3H), 1.47 (s, 3H), 1.27 (s, 3H).

^{31}P NMR (600 MHz, THF-d_8): δ 1.14.

^{13}C NMR (600 MHz, THF-d_8): δ 161.7, 150.9, 140.5, 113.5, 101.1, 95.3, 86.0 (d, J = 7.5 Hz), 84.5, 81.4, 66.7 (d, J = 5.8 Hz), 53.3 (d, J = 5.8 Hz, 2C), 26.4 (s, 2H), 24.6.

Procedure: To a THF solution (0.8 ml) of iPP (0.2 mmol) and nucleoside (0.2 mmol) *t*-BuOK (0.015 mmol) was added. After stirring for 3 hours at room temperature, the reaction was quenched with acetic acid (0.015 mmol). Next, phosphate buffer of pH 7 was added. This solution was three times extracted with ethylacetate. The extracted layers were dried with magnesium sulphate and concentrated in vacuo. The residue was purified with column chromatography on silica (1:4 heptane/ethylacetate). Compound **1p** was isolated as a colorless oil (48.8 mg, 60%).

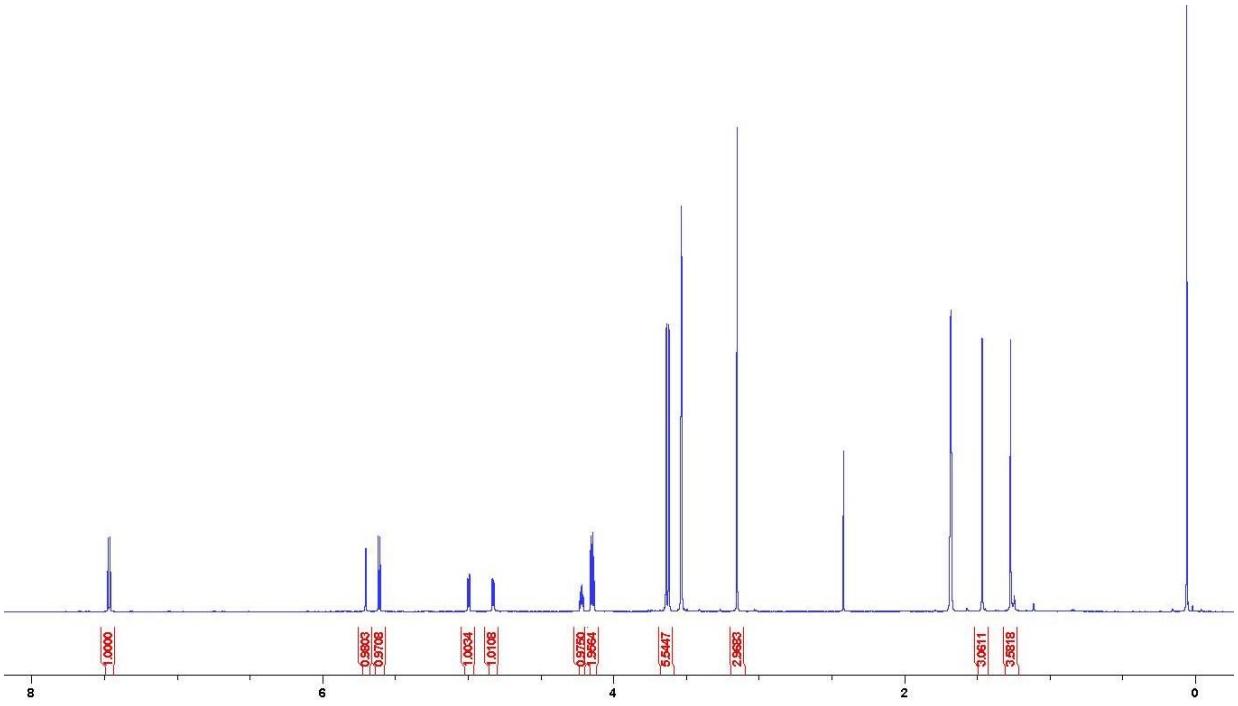


Figure S 1. ^{1}H-NMR spectrum of compound 1p.

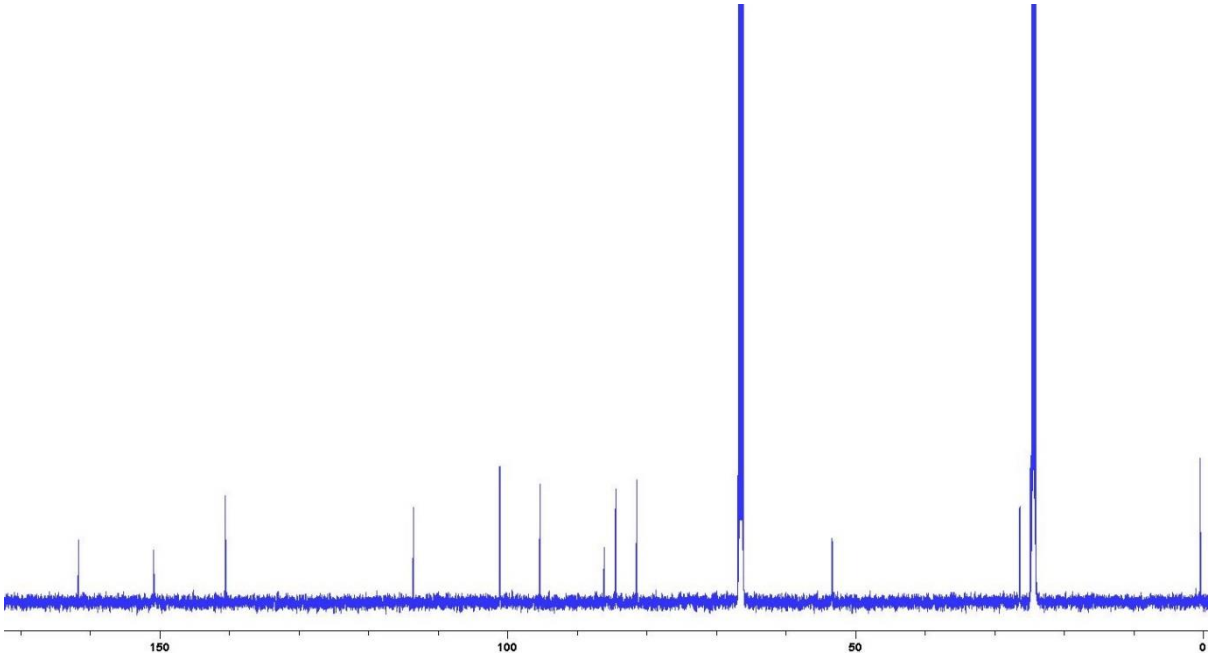
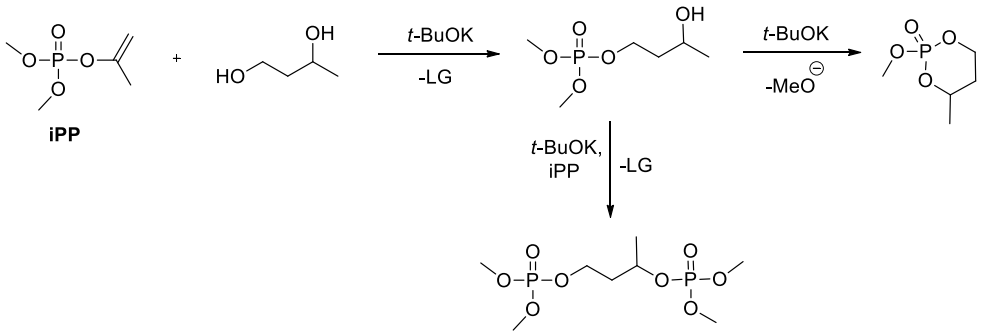


Figure S 2. ^{13}C-NMR spectrum of compound 1p.



Scheme S 1. Phosphorylation of 1,3-butanediol with iPP.

3. Kinetic data

All kinetic measurements were executed on a Bruker Avance II+ 600 MHz NMR spectrometer using Topspin. Therefore, *in operando* inverse gated ^{31}P (zgig30) measurements were performed by obtaining a spectrum every 2 minutes in the first hour followed by every 10 minutes for 3 hours. In these kinetic experiments the concentrations of alcohol and catalyst were varied. To investigate the influence of alcohol concentration, the catalyst and iPP were kept at a constant initial concentration. To do so, the total volume remained constant while the ratio THF:1-BuOH was changed. For a standard kinetic experiment, *t*-BuOK was dissolved in a solution of dry THF and dry 1-BuOH. The reaction started when iPP was added to the solution and loaded into an NMR tube. This NMR tube is fitted with a diptube filled with a solution of DMSO-d_6 and triphenyl phosphate as external standard. Rate constants (*k*) are determined from the plot of the logarithm of the dimethyl isopropenyl phosphate concentration as a function of time:

Rate constant determination:

$$\frac{-d[iPP]}{\mathrm{dt}} = k[tBuOK]^x[BuOH]^y[iPP]$$

With k' = $k[tBuOK]^x[BuOH]^y$:

$$\frac{-d[iPP]}{\mathrm{dt}} = k'[iPP]$$

After integration:

$$ln[iPP] = ln[iPP]_0 - k't$$

Thus, plotting ln[iPP] as a function of time will give *k*' as the slope of the curve at each reaction condition.

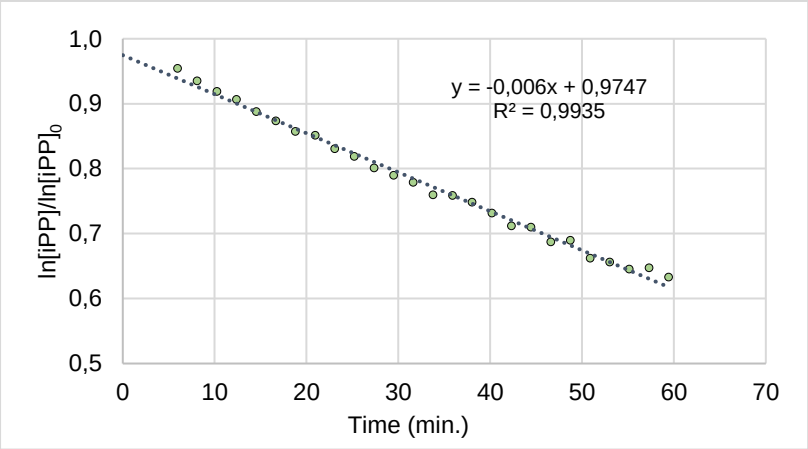


Figure S 3. ln[iPP]/ln[iPP]0 as a function of time.

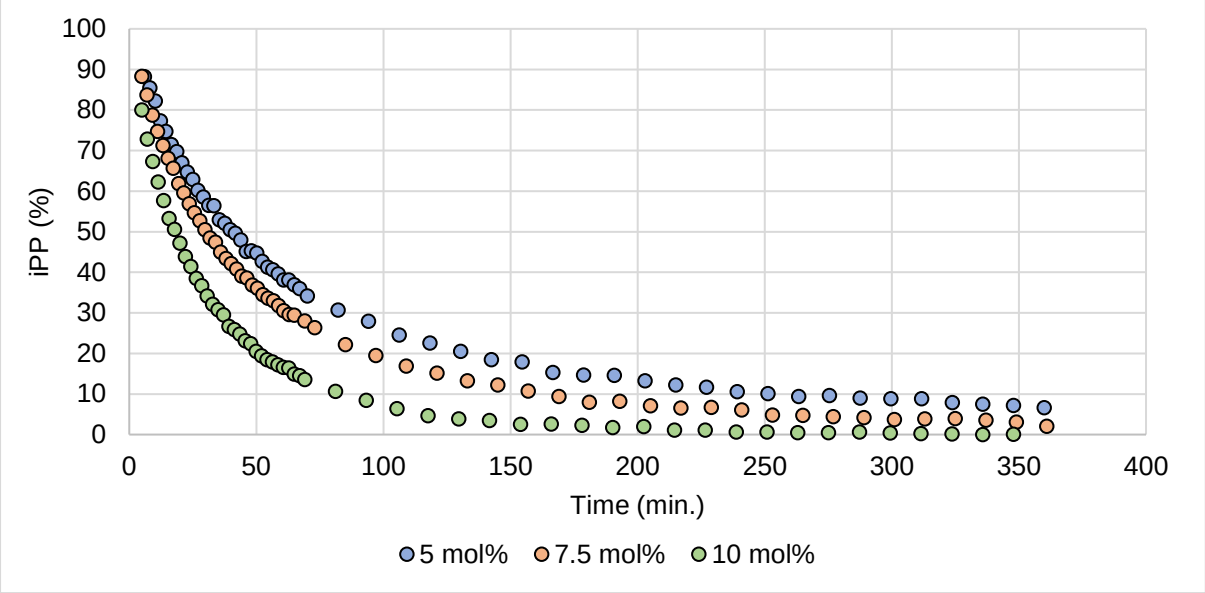


Figure S 4. Conversion of iPP at different concentrations of t-BuOK.

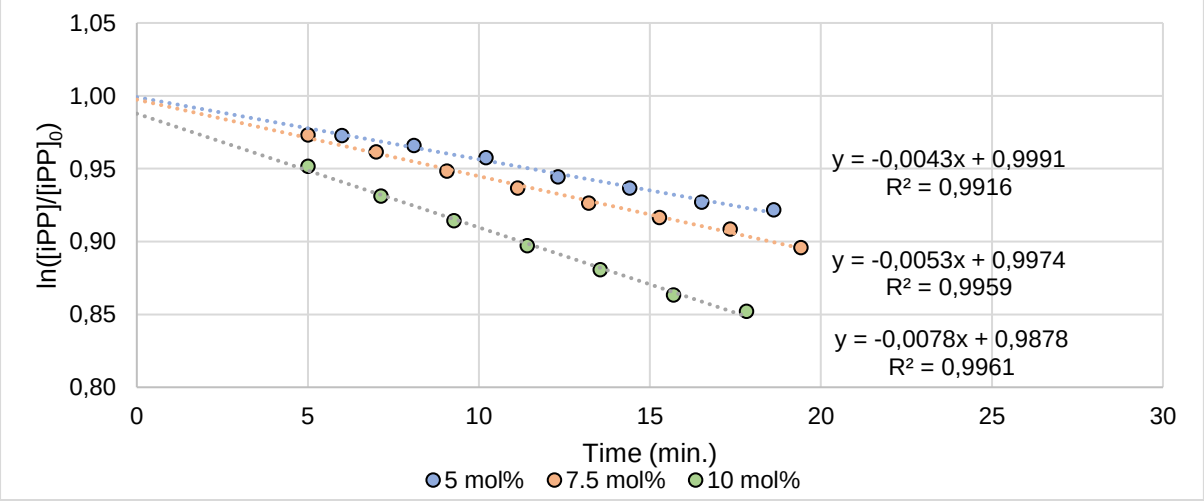


Figure S 5. ln([iPP]/[iPP]$_0$) as a function of time at different t-BuOK concentrations.

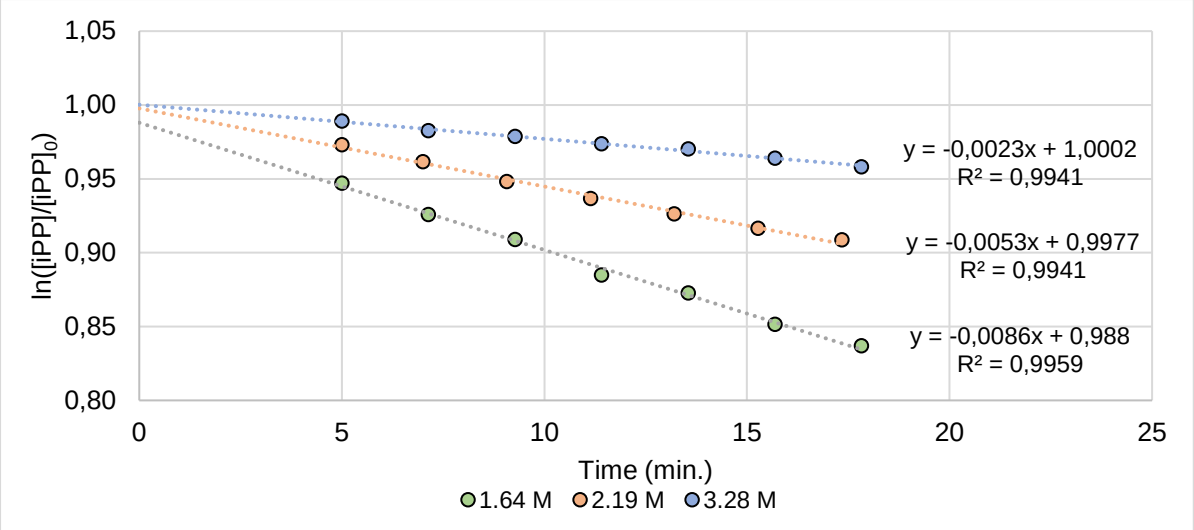


Figure S 6. ln([iPP]/[iPP]$_0$) as a function of time at different 1-butanol concentrations.

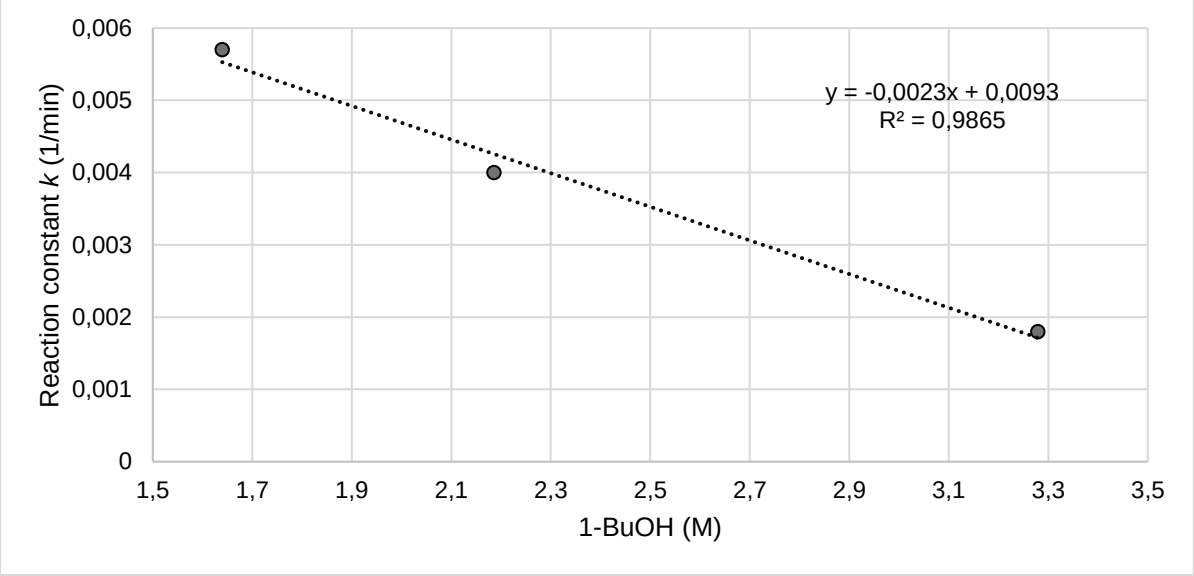


Figure S 7. Reaction constant *k* as a function of 1-butanol concentration.