Towards continuous Rh-hydroformylation of long chain alkenes:
Handling methodology for the long-term stability of Biphephos in a continuous reactor with an attached membrane separation unit

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Supplementary Information

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SI 1: Different decomposition pathways of phosphite ligands

There are several different decomposition pathways that phosphite ligands can undergo. An overview of the most important phosphite decomposition reactions is presented in Figure 1.
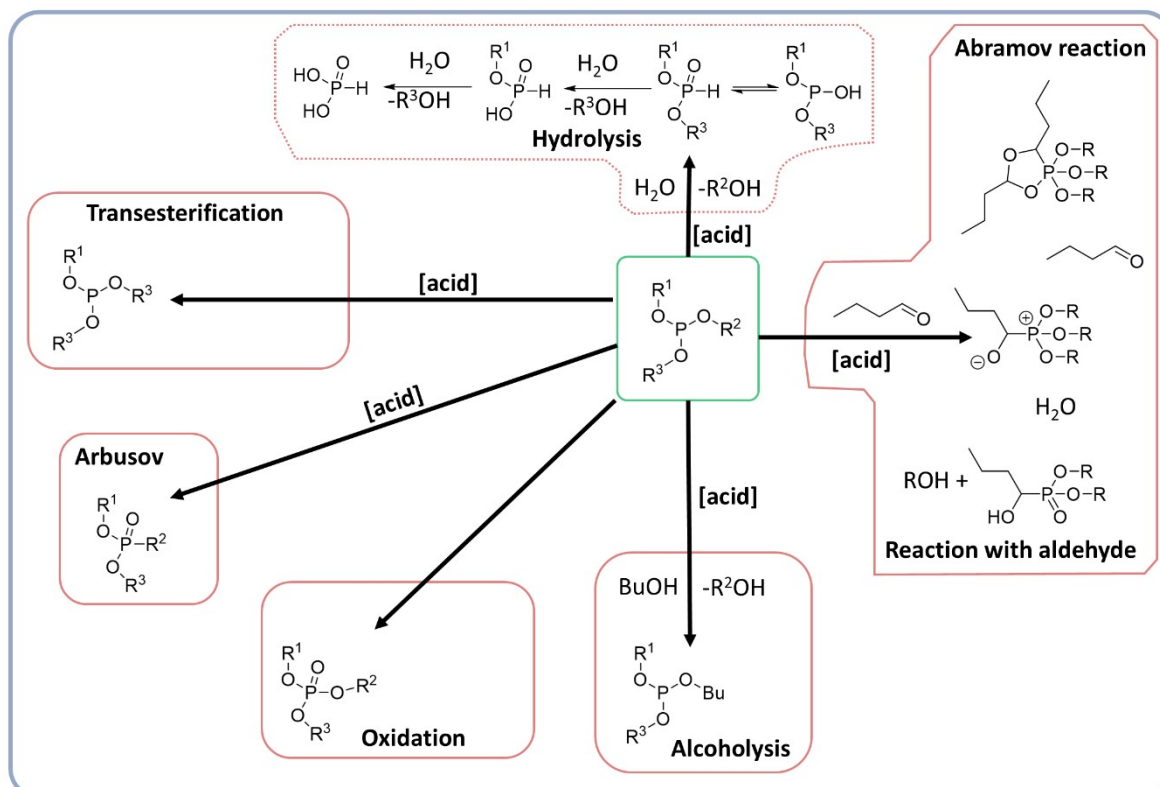

Figure 1: Decomposition pathways of phosphites include hydrolysis, alcoholysis, trans-esterification, Arbusov rearrangement and reaction with aldehydes (Abramov reaction). All these decomposition reactions are catalysed by strong and weak acids.

The decomposition reactions that phosphites can undergo include hydrolysis, alcoholysis, trans-esterification and Arbusov rearrangement.[1] But when phosphites are applied as ligands in hydroformylation their susceptibility to perform nucleophilic attack on aldehydes (Abramov reaction) must also be considered.[2]

SI 2: Catalytically active but unselective ligand decomposition products

The pentavalent phosphorus species formed from the hydrolysis are also known as pentavalent heteroatom-substituted phosphine oxide (HASPO). A HASPO can rearrange and form trivalent phosphoric compounds which have ligating capabilities, see Figure 2. The two type of species exist in a tautomeric equilibrium with each other.
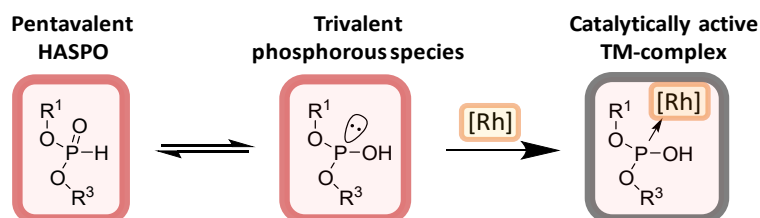

Figure 2: A phosphonic acid diester is a pentavalent phosphoric species, also knowns as a pentavalent heteroatom-substituted phosphine oxide (HASPO). It is in an equilibrium with a trivalent species that has coordinating abilities. This trivalent species can therefore coordinate to a metal, e.g. rhodium.

Trivalent HASPOs have been studied as ligands in various catalytic systems,[3,4,5,6,7,8,9,10,11] including Rh-catalysed hydroformylation.[12,13] They form Rh-complexes that are highly active in hydroformylation, but without any selectivity. Thus, the expectations of the catalyst system based on the initially applied phosphite ligand will become increasingly tainted when HASPOs accumulate in the reaction mixture.

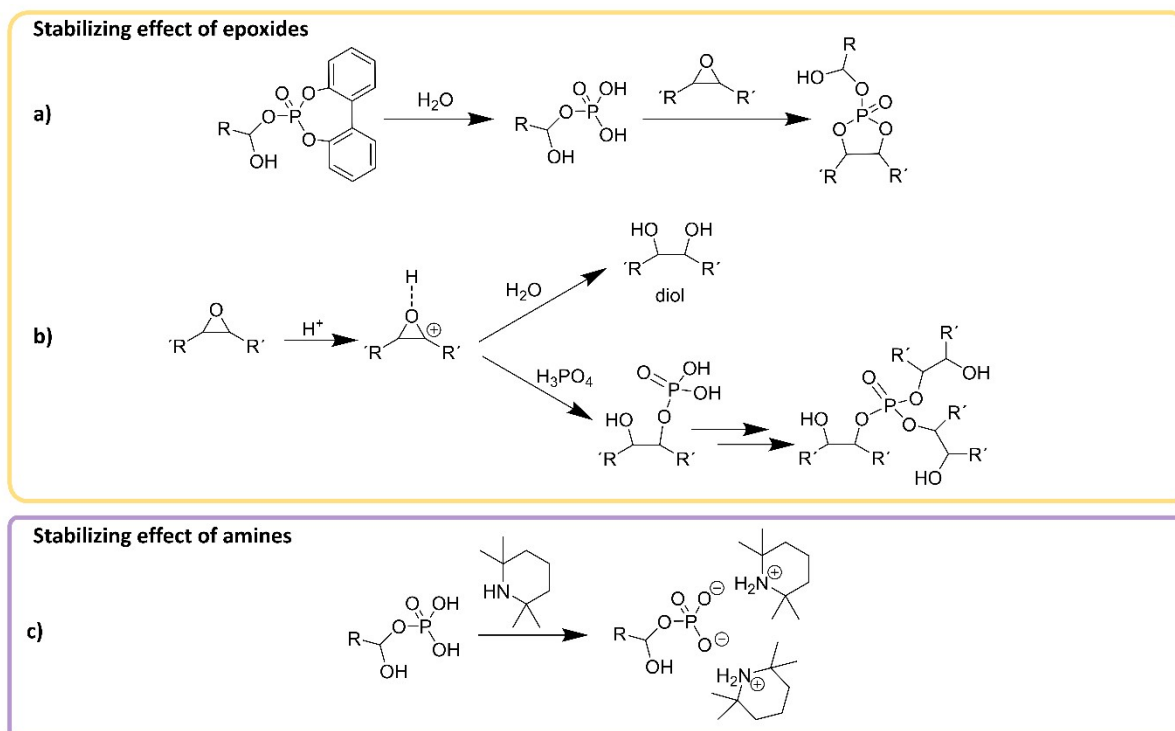## SI 3: Mechanism through which the stabilizers stabilize Biphephos

Figure 3: The mechanism through which the stabilizers stabilize Biphephos by scavenging acids that are formed

The epoxide stabilizers will scavenge any phosphorus acid formed from hydrolysis of Biphephos. This happens either by reacting with the aldehyde acid to form a cyclic adduct according to a) in Figure 3 above.[14] Or reacting with phosphonic acids according to b) in Figure 3 above.[15–17] There were no evidence of the epoxide stabilizer CHO causing any oxidation of the Biphephos during the experiments performed for this paper. Epoxides are known to have the potential to oxidize phosphites.[18] A reason for the lack of reaction can be the sterically bulky groups around the phosphor atoms of the Biphephos, which provide little chance for that epoxide access the phosphor. Only after the Biphephos has been hydrolysed there would be an opening for the epoxide to access the phosphor. Amines like the stabilizer TMP will scavenge acids by forming salts with them according to c) in Figure 3 above.[19]
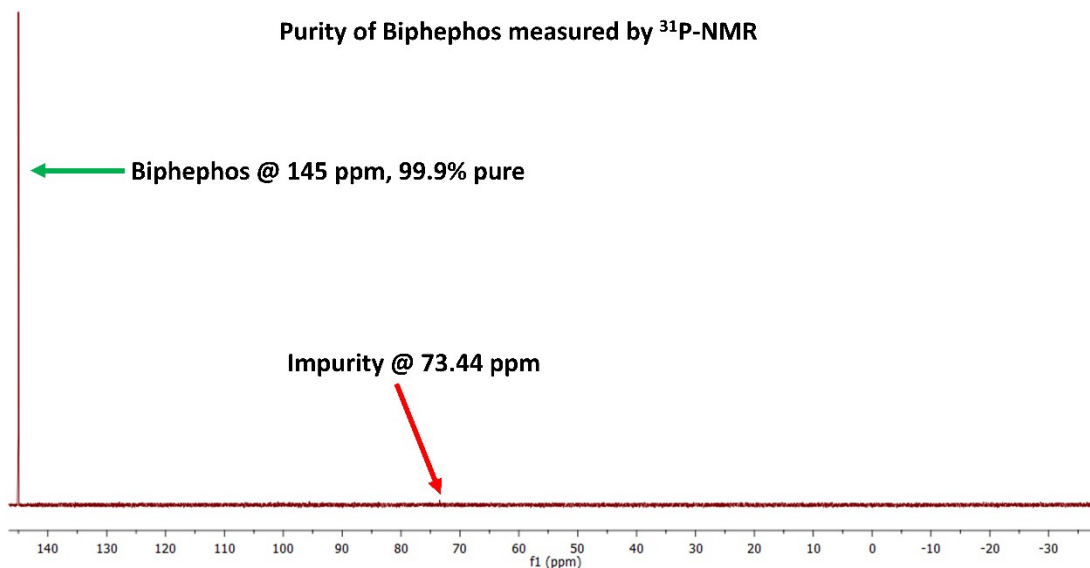
SI 4: The purity of the Biphephos used

Figure 4: The purity of Biphephos was determined to be 99.9% pure according to ^{31}P-NMR measured in d-Toluene.

The purity of Biphephos was measured by ^{31}P-NMR. It is important to prepare the sample using a non-chlorinated deuterated solvent as chlorinated solvents such as $CDCl_3$ has the potential to contain small but significant amounts of HCl due to the solvent decomposition.

SI 5: A collection of selected publications on phosphite ligands used in Rh-catalysed hydroformylation and their various approaches to preparation methodologies

Table 2: Reports on phosphite-based catalytic systems and measures taken during the reaction preparation.

Ligand	Year	Type	Cat. sol. prep method	Purified substrate	Final inert gas flush / PDP-cycles	Stabilizers	Ref.
Monodentate phosphite	1983	Batch	Unknown	Percolation over alumina	No	No	20
Monodentate phosphite	1985	Batch	Unknown	No	Yes, one cycle	No	21
Monodentate phosphite	1985	Cont.	Unknown	No	Yes	No	
Monodentate phosphite	1986	Batch	Unknown	No	No	Tertiary amines	22
Biphephos	1987	Batch	Simultaneous solvation of Rh and ligand	No	Yes, one cycle	No	23
Biphephos	1987	Cont.	Simultaneous solvation of Rh and ligand	No	Yes	No	
Biphephos	1988	Batch	Simultaneous solvation of Rh and ligand	No	Yes, one cycle	No	24
Biphephos	1988	Cont.	Unknown	No	Yes	Amberlyst -A-21	
Polymer bound phosphite	1992	Batch	Unknown	No	No	No	25
Heterogenized bulky phosphite	1993	Batch	Unknown	No	No	No	26
Biphephos	1993	Batch	Simultaneous	No	Yes	No	27

			solvation of Rh and ligand				
Biphephos	1994	Cont.	Unknown	No	Yes	epoxides	[28]
Biphephos	1996	Batch	Simultaneous solvation of Rh and ligand	No	No	No	[29]
Biphephos type	1999	Batch	Separate solvation of Rh and ligand	Freshly distilled	No	No	[30]
Phosphane-phosphite	1999	Batch	Simultaneous solvation of Rh and ligand	No	No	No	[31]
Biphephos	2003	Batch	Simultaneous solvation of Rh and ligand	No	No	No	[32]
Biphephos	2003	Batch	Unknown	Freshly distilled	No	No	[33]
POSSphites	2004	Batch	Separate solvation of Rh and ligand	Percolation over alumina	No	No	[34]
Biphephos	2005	Batch	Simultaneous solvation of Rh and ligand	No	No	No	[35]
Biphephos	2005	Batch	Simultaneous solvation of Rh and ligand	No	No	No	[36]
Biphephos	2005	Batch	Separate solvation of Rh and ligand	No	Yes	No	[37]
POSSphites	2005	Batch	Separate solvation of Rh and ligand	No	No	No	[38]
JanaPhos	2009	Batch	Simultaneous solvation of Rh and ligand	No	No	No	[39]
Biphephos	2009	Batch	Simultaneous solvation of Rh and ligand	No	No	TMP derivatives	[40]
Biphephos	2011	Cont.	Rh dissolved separately	No	Yes	No	[41]
Biphephos	2011	Batch	Unknown	No	No	No	[42]
Sulfonated calix[4]arene	2011	Batch	Separate solvation of Rh and ligand	No	yes, one cycle	No	[43]
JanaPhos	2011	Cont.	Simultaneous solvation of Rh and ligand	Freshly distilled	No	No	[44]
Bulky phosphite	2013	Batch	Simultaneous solvation of Rh and ligand	Percolation over alumina	Yes	No	[45]
Biphephos	2013	Batch	Simultaneous solvation of Rh and ligand	No	No	No	[46]
Bulky phosphite	2014	Batch	Unknown	Percolation over alumina	No	No	[47]
Biphephos	2014	Batch	Simultaneous solvation of Rh and ligand	No	No	No	[48]
Biphephos	2014	Batch	Simultaneous solvation of Rh and ligand	No	No	No	[49]
Biphephos	2015	Batch	Simultaneous solvation of Rh and ligand	No	No	No	[50]
Biphephos	2015	Batch	Simultaneous solvation of Rh and ligand	No	No	No	[51]
Biphephos	2015	Cont.	Rh dissolved	No	No	Tinuvin	[52]

			separately				
Biphephos	2016	Batch	Simultaneous solvation of Rh and ligand	No	No	No	53
Biphephos	2016	Cont.	Unknown	No	No	No	54
Biphephos	2017	Batch	Simultaneous solvation of Rh and ligand	No	Yes	No	55
Biphephos	2017	Batch	Simultaneous solvation of Rh and ligand	No	No	No	56
Biphephos	2018	Batch	Rh dissolved separately	Percolation over alumina + vacuum distilled	No	No	57
Biphephos	2018	Batch	Simultaneous solvation of Rh and ligand	No	No	No	58
Biphephos	2019	Batch	Unknown	No	Yes	No	59
Biphephos	2023	Batch	Unknown	Freshly distilled	Yes, 3 cycles	No	60
Biphephos	2023	Batch	Simultaneous solvation of Rh and ligand	Freshly distilled	Purged 10 min	No	61
Bulky phosphite	2023	Batch	Both simultaneous solvation and separate solvation	No alkenes included in experiments	No[1]	No	62

1   To have fully oxygen free conditions were not decisive for these experiments as there was no hydroformylation performed.

SI 6: Membrane part

SI 6.a: Chemicals used

Table 1: List of chemicals used.

Substance	CAS	Supplier	Purity
1-Octene	111-66-0	Acros Organics	≥ 99%
Toluene	108-88-3	Acros Organics	≥ 95%
Cyclohexene oxide	286-20-4	Acros Organics	98%
$Rh(acac)(CO)_2$	14874-82-9	Alfa Aesar	99%
Biphephos	121627-17-6	Molisa	97%
Syngas	-	Messer	5.0
Argon	7440-37-1	Messer	3.8
Nitrogen	7727-37-9	Messer	2.5

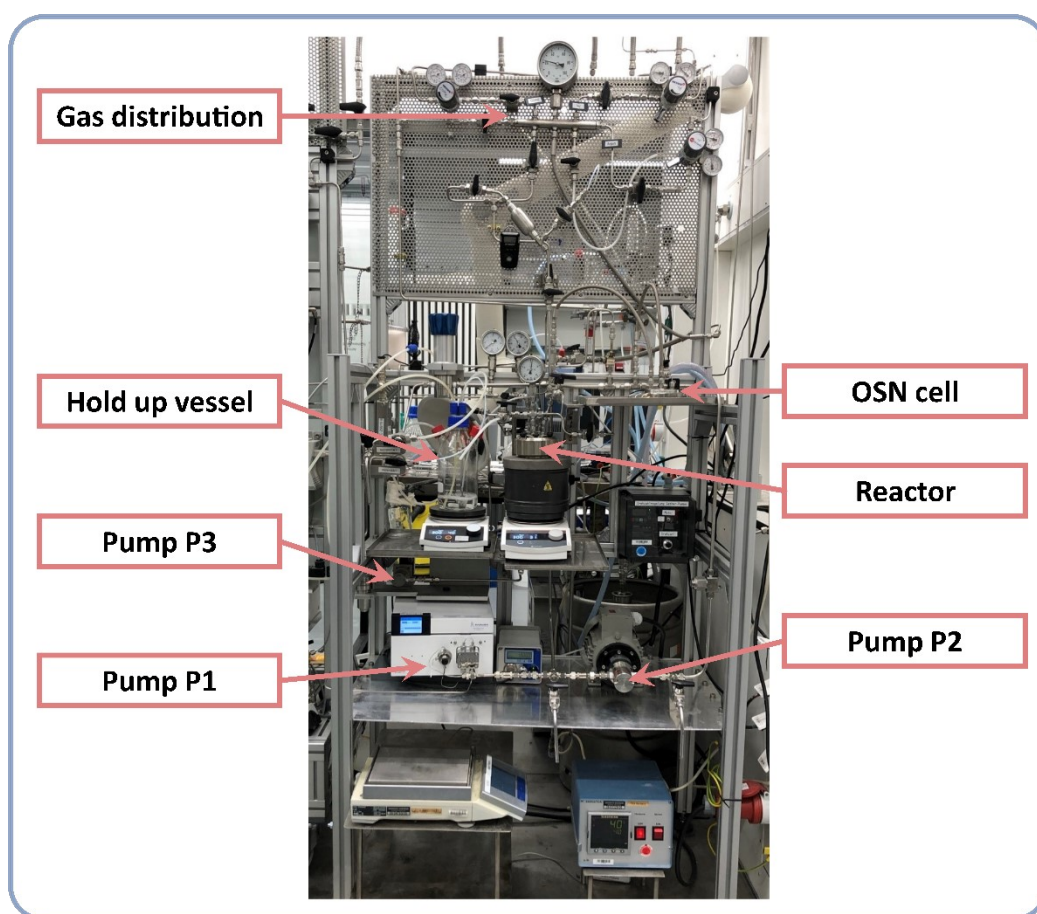## SI 6.b: Membrane miniplant

Figure 5: Photo of miniplant NEMO 2.0 with highlighted main components.
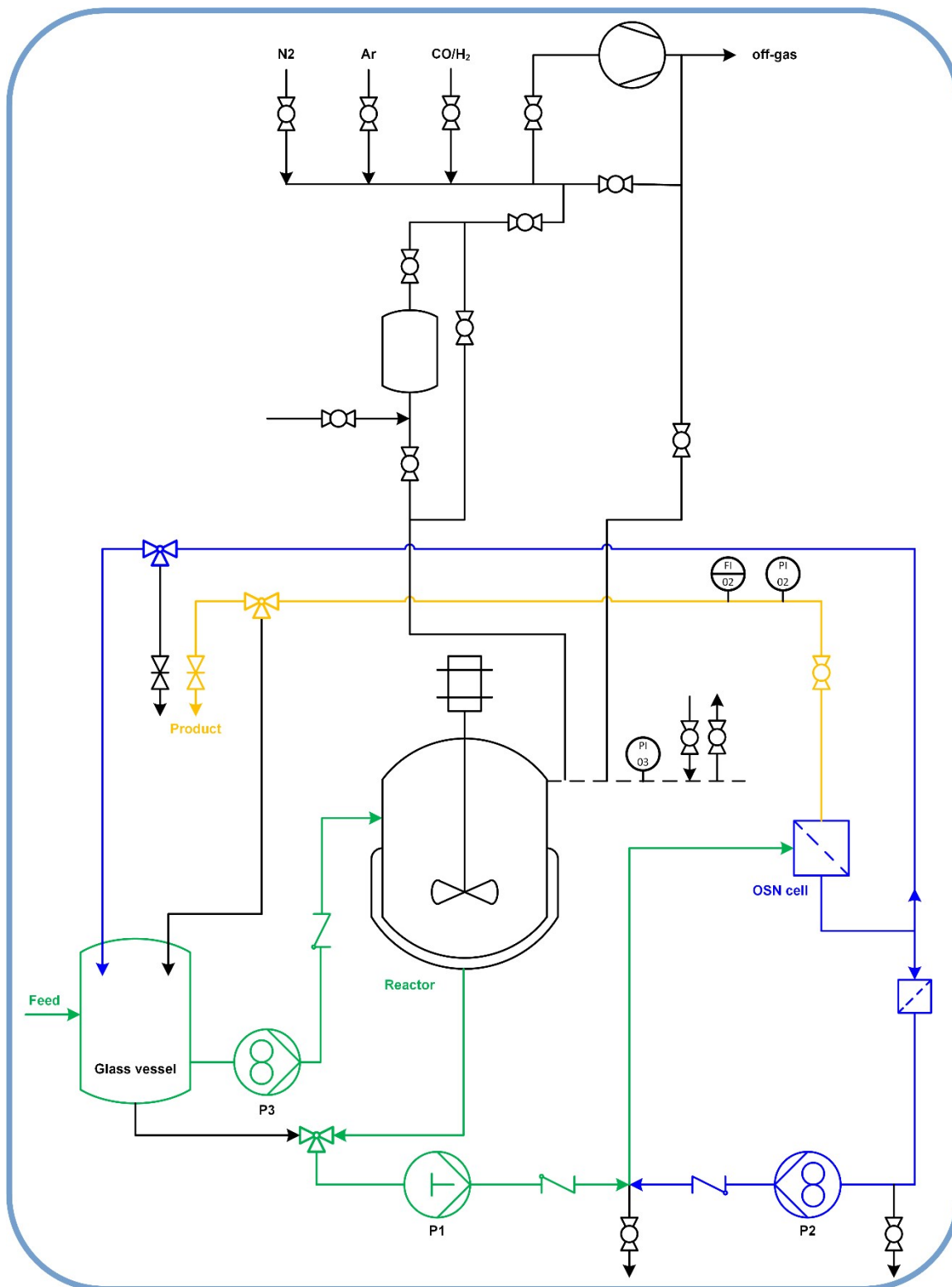
Figure 6: P&ID of NEMO 2.0. Reaction cycle (green), permeate (yellow) and retentate cycle (blue).

SI 6.c: Membrane screening

The most significant outcome parameters for this pre-study were the retention of both the catalyst and the ligand to obtain a maximum of it inside of the reaction system and the flux through the membrane to receive as many exchanged reactor volumes as possible. For this reaction system the membranes in Table 2 were identified as suitable and available in our research group. All membranes are organic solvent nanofiltration membranes with different properties due to their chemical structure. The results indicated, that the membrane *SolSep BV NF030105* was the most suitable one for the long-term experiment due to a higher flux.

Table 2: Comparision of different membranes applied in NEMO 2.0. [Rh] and [P] measured after 2 h and 4 h via ICP-OES. Flux measured via mass flow indicator.

OSN Membrane		Retention [%]		Flux
Supplier	**Model**	**Rh**	**P**	**[g cm^{-2} h^{-1}]**
SolSep BV	NF030105	98	98	10
Evonik	PuraMem S600	84	84	5
Evonik	PuraMem 280	95	94	4
Evonik	PuraMem Selective	99	98	6
GMT	oNF-2	87	81	8

SI 6.d: Experimental for membrane screening

The procedure during the membrane selection was like the latter long-term experiment.

<u>Preparation of the substrates:</u> 1-octene was cleaned over Al_2O_3-column to remove traces of peroxides, toluene was cleaned over Al_2O_3-column to remove traces of water. The substrate solution was prepared by weighing out 1-octene (25 wt%) and toluene (75wt%) as well as CHO.

<u>Preparation of the miniplant:</u> miniplant incl. reactor, valves and glassware was cleansed with acetone to remove any residues in the pipes and afterwards with toluene to remove any acetone. Three PDP-cycles were applied (2x nitrogen (<10 bar), 1x argon, each followed by vacuum to remove any air and low boiling solvents.

<u>Preparation of the membrane:</u> cutting flat-sheet membrane, insertion of membrane in membrane module (2,5" MET-cell), low pressure argon flushing of the module, connection to miniplant. Further flushing of miniplant with nitrogen (<2 bar) and argon (< 2 bar) to remove further air. Filling in toluene and 1-octene for conditioning of membrane (each according to the supplier, around 4 h total; reactor: T = 40 °C, p = 20 bar; membrane part: T = 40 °C, Δp = 40 bar; glass flask: T = 40 °C, p = 1 bar, stripped with argon).

<u>Preparation of Catalyst, BP and CHO:</u> Solving of Biphephos (1,87 g) and CHO (1,86 g) in toluene (50 ml) as well as solving of Rh (112 mg) in toluene (50 ml) in a separate flask in ultrasonic bath under argon stream. Inserting both mixtures into the reactor via gear pump (both flasks are topped with argon). Preforming for 1 h (T = 40 °C, p = 20 bar).

<u>Start-up for screening run:</u> HPLC pump starts to feed the membrane cycle (Time = 0) and the other pump is starting to feed the reactor from the glass flask again. Applying syngas to the reactor (20 bar). Both permeate and retentate were collected in the glass flask and stayed within the system. Samples were taken after 2 and 4 h of experiment and measured via ICP-OES. Flux was measured via mass flow indicator.
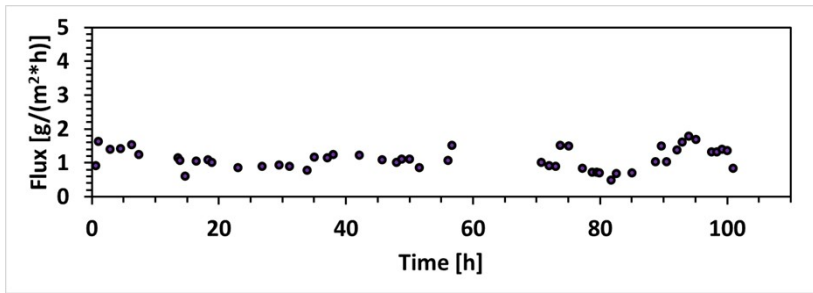
SI 6.e: Long-term experiment

Figure 7: Flux over time during long-term miniplant experiment. Measured via balance.

Table 3: Concentration and retention of rhodium and phosphorus over time and sample measured by ICP-OES.

Sample	Time [h]	c_Rh [ppm]	c_P [ppm]	R_Rh	R_P
Permeate	5	11	46		
Permeate	6	10	47		
Permeate	7	11	47		
Permeate	14	10	43		
Permeate	23	9	40	96%	95%
Retentate	23	203	730		
Permeate	27	12	47		
Permeate	31	11	43		
Permeate	35	10	36	93%	94%
Retentate	35	152	578		
Permeate	42	9	34		
Permeate	46	9	34		
Permeate	50	9	32	94%	94%
Retentate	50	145	542		
Permeate	56	8	31		
Permeate	72	7	27	99%	83%
Retentate	72	721	155		
Permeate	80	7	25		
Permeate	85	7	27		
Permeate	90	4	16	94%	91%
Retentate	90	64	187		
Permeate	95	3	11		
Permeate	100	3	10	93%	91%
Retentate	100	40	110		
Permeate	102	3	6		
Permeate	104	5	5		

SI 6.f: Membrane experiment with TINUVIN 770

The experiment had to be determined, due to a decrease in flux. TINUVIN 770 is prone to precipitation and clogged the filter upstream of the membrane (s. Figure 6).

Figure 8: Clogged filter with precipitated TINUVIN 770 (taken from pre-experiments).

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