Overview over solvent consumption and runtime of Synple reaction sequences:

Wash sequences:

SEQUENCE RUNTIME	
Reaction Sequence	**Time**
DCM Wash	15 min
MeOH Wash	15 min

SOLVENT COMSUMPTION FOR DCM WASH	
For Reaction Setup	**Amount**
no solvent	-
Machine Solvents	
Dichloromethane (CH_2Cl_2)	110 mL

SOLVENT COMSUMPTION FOR MEOH WASH	
For Reaction Setup	**Amount**
no solvent	-
Machine Solvents	
Methanol (MeOH)	110 mL

Heterocycle formation:

SEQUENCE RUNTIME	
Reaction Sequence	**Time**
Full Heterocycle sequence (*available for Morpholine, Oxazepane, Piperazine, Diazepane*)	11 h 50 min
Short Heterocycle sequence (*available for Morpholine, Oxazepane, Piperazine, Diazepane*)	5 h 36 min
3-Methylmorpholine	21 h 50 min
2-Methylmorpholine	14 h 50 min
Morpholine-2-spiro-(3-Pyr)	15 h 52 min
Morpholine-2-spiro-(4-Pip)	15 h 52 min
Benzoxazepane	15 h 52 min
9-OMe-Benzoxazepane	14 h 50 min
7-Br-9-OMe-Benzoxazepane	14 h 50 min

SOLVENT COMSUMPTION FOR ALL HETEROCYCLE REACTIONS	
For Reaction Setup	**Amount**
no solvent	
Machine Solvents	
Dichloromethane (CH_2Cl_2)	102 mL
Hexafluoroisopropanol (HFIP)	4 mL
Methanol (MeOH)	87 mL
Diisopropylamine (DIPA) – Tetrahydrofuran (THF) mixture (13:7)	26 mL

Additional notes: The use of dry Dichloromethane and Hexafluoroisopropanol is very important for the reaction conditions and to obtain a good yield.

Fluorination

SEQUENCE RUNTIME	
Reaction Sequence	**Time**
Fluorination	3 h 24 min

SOLVENT COMSUMPTION FOR DEOXYFLUORINATION	
For Reaction Setup	**Amount**
no solvent	-
Machine Solvents	
Methanol (MeOH)	20 mL
Acetonitrile (ACN)	17 mL

PROTAC formation:

SEQUENCE RUNTIME	
Reaction Sequence	**Time**
PROTAC formation amine (via reductive amination)	15 h 49 min
PROTAC formation amide (via amide formation)	5 h 14 min

SOLVENT COMSUMPTION FOR PROTAC AMINE	
For Reaction Setup	**Amount**
Dichloromethane (CH_2Cl_2)	3 mL
Hexafluoroisopropanol (HFIP)	1 mL
Machine Solvents	
Dichloromethane (CH_2Cl_2)	39 mL
Methanol (MeOH)	30 mL
Diisopropylamine (DIPA) – Isopropanol mixture (13:7)	19 mL

SOLVENT COMSUMPTION FOR PROTAC AMIDE	
For Reaction Setup	**Amount**
Dichloromethane (CH_2Cl_2)	3 mL
Hexafluoroisopropanol (HFIP)	1 mL
Machine Solvents	
Dichloromethane (CH_2Cl_2)	10 mL
Methanol (MeOH)	11 mL

Reductive amination:

SEQUENCE RUNTIME	
Reaction Sequence	**Time**
A Aldehyde + primary amine	4 h 43 min
B Aldehyde + secondary amine	4 h 21 min
C Ketone + primary amine	4h 21 min
D Ketone + secondary amine	5 h 29 min

SOLVENT COMSUMPTION FOR SEQUENCES A, B, C	
For Reaction Setup	**Amount**
Dichloromethane (CH_2Cl_2)	3 mL
Hexafluoroisopropanol (HFIP)	1 mL
Machine Solvents	
Dichloromethane (CH_2Cl_2)	37 mL
Methanol (MeOH)	40 mL
Diisopropylamine (DIPA) – Methanol (MeOH) mixture (13:7)	19 mL

SOLVENT COMSUMPTION FOR SEQUENCE D	
For Reaction Setup	**Amount**
Toluene	5 mL
Machine Solvents	
Dichloromethane (CH_2Cl_2)	37 mL
Methanol (MeOH)	40 mL
Diisopropylamine (DIPA) – Methanol (MeOH) mixture (13:7)	19 mL

Mitsunobu

SEQUENCE RUNTIME	
Reaction Sequence	**Time**
Mitsunobu standard sequence	6 h 42 min
Mitsunobu sequence for basic compounds	5 h 18 min

SOLVENT COMSUMPTION FOR MITSUNOBU STANDARD	
For Reaction Setup	**Amount**
no solvent	-
Machine Solvents	
Dichloromethane (CH_2Cl_2)	29 mL

SOLVENT COMSUMPTION FOR MITSUNOBU BASIC	
For Reaction Setup	**Amount**
no solvent	-
Machine Solvents	
Dichloromethane (CH_2Cl_2)	34 mL
Ethanol (EtOH)	30 mL
Diisopropylamine (DIPA) – Ethanol (EtOH) mixture (13:7)	15 mL

Biotin tag formation

SEQUENCE RUNTIME	
Reaction Sequence	**Time**
Biotin tag formation amine (via reductive amination)	13 h 47 min
Biotin tag formation amide (via amide formation)	4 h 36 min

SOLVENT COMSUMPTION FOR BIOTIN AMINE	
For Reaction Setup	**Amount**
Hexafluoroisopropanol (HFIP) or Trifluoroethanol (TFE)	4 mL
Machine Solvents	
Dichloromethane (CH_2Cl_2)	74 mL
Methanol (MeOH)	74 mL
Diisopropylamine – MeOH mixture (13:7)	22 mL

SOLVENT COMSUMPTION FOR BIOTIN AMIDE	
For Reaction Setup	**Amount**
Dimethylformamide (DMF)	2.5 mL
Machine Solvents	
Dichloromethane (CH_2Cl_2)	20 mL
MeOH	20 mL

Azide formation

SEQUENCE RUNTIME	
Reaction Sequence	**Time**
Azide formation	3 h 46 min

SOLVENT COMSUMPTION FOR AZIDE FORMATION	
For Reaction Setup	**Amount**
Acetonitrile (ACN)	0.5 mL
Water (H_2O)	0.5 mL
Machine Solvents	
Acetonitrile (ACN) – water (H_2O) mixture (1:1)	41 mL

Boc protection

SEQUENCE RUNTIME	
Reaction Sequence	**Time**
Boc protection 0.5 mmol (free amine)	5 h 30 min
Boc protection 1.2 mmol (free amine)	5 h 30 min
Boc protection 0.5 mmol (amine salt)	5 h 54 min
Boc protection 1.2 mmol (amine salt)	5 h 55 min

SOLVENT COMSUMPTION FOR BOC (FREE AMINE)	
For Reaction Setup	**Amount**
no solvent	-
Machine Solvents	
Dichloromethane (CH_2Cl_2)	10 mL
Methanol (MeOH)	45 mL

SOLVENT COMSUMPTION FOR BOC (AMINE SALT)	
For Reaction Setup	**Amount**
no solvent	-
Machine Solvents	
Dichloromethane (CH_2Cl_2)	10 mL
Methanol (MeOH)	47 mL

Boc deprotection

SEQUENCE RUNTIME	
Reaction Sequence	**Time**
Boc deprotection	4 h 39 min

SOLVENT COMSUMPTION FOR BOC DEPROTECTION	
For Reaction Setup	**Amount**
no solvent	-
Machine Solvents	
Dichloromethane (CH_2Cl_2)	10 mL
Methanol (MeOH)	47 mL
Dimethoxyethane (DME)	7 mL

Amide formation

SEQUENCE RUNTIME	
Reaction Sequence	**Time**
Amide formation	3 h 50 min

SOLVENT COMSUMPTION FOR AMIDE FORMATION	
For Reaction Setup	**Amount**
Dichloromethane (CH_2Cl_2)	2 mL
Ethanol (EtOH)	2 mL
Machine Solvents	
Dichloromethane (CH_2Cl_2)	16 mL
Methanol (MeOH)	12 mL

Silyl deprotection

SEQUENCE RUNTIME	
Reaction Sequence	**Time**
Silyl deprotection	3 h 8 min

SOLVENT COMSUMPTION FOR SILYL DEPROTECTION	
For Reaction Setup	**Amount**
Methanol (MeOH)	2 mL
Machine Solvents:	
Dichloromethane (CH_2Cl_2)	23 mL
Methanol (MeOH)	6 mL

Nosyl protection

SEQUENCE RUNTIME	
Reaction Sequence	**Time**
Nosyl protection	4 h 44 min

SOLVENT COMSUMPTION FOR NOSYL PROTECTION	
For Reaction Setup	**Amount**
Dichloromethane (CH_2Cl_2)	2 mL-
iso-Propanol (*i*-PrOH)	2 mL
Machine Solvents	
Dichloromethane (CH_2Cl_2)	20 mL
Acetonitrile (ACN)	31 mL

Cbz protection

SEQUENCE RUNTIME	
Reaction Sequence	**Time**
Nosyl protection	4 h 45 min

SOLVENT COMSUMPTION FOR CBZ PROTECTION	
For Reaction Setup	**Amount**
Tetrahydrofuran (THF)	2 mL-
Ethanol (EtOH)	2 mL
Machine Solvents	
Dichloromethane (CH_2Cl_2)	31 mL

Suzuki coupling

SEQUENCE RUNTIME	
Reaction Sequence	**Time**
Suzuki-Miyaura	7 h 07 min

SOLVENT COMSUMPTION FOR SUZUKI COUPLING	
For Reaction Setup	**Amount**
1,2-Dimethoxyethane (DME)	2 mL-
Ethanol (EtOH)	2 mL
Water (H_2O)	
Machine Solvents	
Dichloromethane (CH_2Cl_2)	20 mL
Ethylacetate (EtOAc)	57 mL