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Macrocyclization strategies for cyclic peptides and peptidomimetics

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Supplementary Table S1: Commonly used macrocyclization reactions for peptides. The required reaction partners are listed as well as if they have been reported to work succesfully on-resin, in solution, in a chemoselective way or on unprotected petides, a green tick signfiying it has been reported, a red cross that it has not been reported.

Bond or functional group formed	Required functional groups: Reaction partner I (N-terminus)	Reaction partner II (C-terminus)	Reaction	On-resin	In solution	Chemoselective	Unprotected	Comments
Amide	H_2N-	-COOH	Amide coupling	✓	✓	☐	✓	
	HNCys-	-COSR	NCL	✓	✓	✓	✓	
	HNAla-	-COSR	NCL + desulfurisation	✓	✓	✓	✓	
	H_2N-	-COSR	aminolysis	☐	✓	✓	Lys	Other lysine needs to be protected
	H_2N-	-COO-Sanger	aminolysis	☐	✓	✓	Lys	Other lysine needs to be protected
	H_2N-	-COO-Dbz	aminolysis	✓	✓	✓	☐	
	N_3CH_2NH-	$-COSCH_2PPh_2$	Staudinger	☐	✓	✓	☐	
	2-amino thioamide-	-COOH	Ag-promoted lactamisation	✓	✓	✓	✓	
	HNCys-	-glycolaldehyde	Thiazolidine formation	☐	✓	✓	☐	Or sidechain aldehyde
	RONH-	-Ketoacide	KAHA	☐	✓	✓	☐	Mild conditions
	5-oxaproline-	-Ketoacide	KAHA II	☐	✓	✓	☐	Introduces homoserine, epimerization
	HNSer/Thr-	-COO-salicylaldehyde	Ser/Thr ligation	✓	✓		☐	
	H_2N-	-COOH	Lactam formation, subsequent O-to-N transfer		✓		☐	Depsipeptide mediated
	2-OH-6-NO_2-benzyl-NH-	-COOH	Lacton formation and O-to-N migration		✓			
	H_2N- -COOH	*tert*-butyl-isocyanide and aziridine aldehyde	MCR, disrupted Ugi	✓	✓	☐	☐	
N-substituted amide	COOH, $-NH_2$, -CHO, -NC	-	MCR, Ugi		✓	☐	☐	
Amine	H_2N- nitrotyrosine	-CHO, -NC	MCR, Ugi-Smiles	✓	✓	☐	☐	
	$-NH_2$ (Lys)	Diborono-benzene scaffold	Petasis reachtion stapling	✓	✓	☐	☐	
Imine to amine	H_2N-	-CHO	Trapping imine: CN^- Strecker Reduction with BH_3CN		✓	✓		
	H_2NTrp/His-	-CHO	Trapping imine Pictet-Spengler		✓	✓		
	H_2N-	-CHO	Intramolecular 4-imidazolidinone formation		✓	✓		CyClick
	NH_2-Gly-	Carboxybenzaldehyde on sidechain	Trapping imine with dipolarophiles	✓		✓		
	NH_2 (Lys)	HCHO	Trapping with Trp or Arg		✓	✓		
Imine	H_2N-	-CHO	Trapping imine as iminoboronate		✓	✓		Introduction of non-natural amino acid; reversible upon stimuli (pH, oxidation, small molecules)
Imine to pyrrole	NH_2 (Lys)	Furan to diketoene	Ketoenal formation		✓	✓		
Oxime	hydroxylamine	aldehyde	oxime		✓	✓		E- and Z-isomer
-S-S-	Thiol	Thiol	oxidation	✓	✓	✓		
$-S-CH_2-S-$	Thiol	Thiol	Methylene thioacetal formation	☐	✓	✓	✓	
-S-	Thiol	Bromo/chloroacetate	Attached to Lys-sidechain or N-terminal amino group	✓	✓	✓	✓	Primary amines have to be protected; can be applied on in vitro techniques
	Thiol	alkene	Thiol-ene	✓	✓	✓	✓	Alkene as acryloyl, compatible on phage

	Thiol	alkene	Radical thiol-ene	✓	✓	✓		Alkene as allyloxy PG or non-natural AA
	Thiol	alkyne	Radical thiol-yne		✓	✓		Generates E- and Z- isomer
	Thiol	DHA	Michael-addition	✓	✓	✓		
	Thiol	scaffolds		✓	✓	✓		
C-O	Alcohol	Aryl boronic acid	Evans-Chan-Lam coupling	?	✓	✓	?	Also for aryl amines or aryl thioethers
	Alcohol	Carbonate	Tsuji-Trost reaction	?	✓	✓	✓	
	Alcohol	Aryl bromide	Metal-photoredox-catalsed reactions	?	✓	✓	?	
C-C	Organometal, alkene	Halide	Traditional cross coupling	✓	✓	✓	?	Suzuki couplings on unprotected peptides reported, but usually protected
	Alkene, allyl, aryl	Aryl, aryl halide	CH activation – cross coupling	?	✓	✓	?	
	Acrylate	C-terminal carboxylic acid	Ir-photocatlysed reaction	?	✓	✓	✓	
	Alkyne	Alkyne	Glaser-Hay coupling	✓	✓	✓	?	
C=C	Alkene	Alkene	RCM	✓	✓	✓	✓	Also suitable for DNA-enocded libraries
C≡C	Alkyne	Alkyne	RCAM	✓	✓	✓	?	
1,4-Disubstiuted triazole	Alkyne	Azide	CuAAC	✓	✓	✓	✓	
1,5-Disubstiuted triazole	Alkyne	Azide	RuAAC	✓	✓	✓	?	
1,5-Disubstiuted triazole	Alkyne	Azide	Metal-free Dipolar cycloaddition	✓	?	✓	?	

Supplementary Table S2: Selection of examples in which peptide macorcyclizations were used to improve biological properties of peptides. AT_2 = Angiotensin II receptor type 2, AT_1 = Angiotensin II receptor type 1, OXTR = oxytocin receptor, IR = insulin receptor, pAkt = phosphorylated Akt, eIF4E = eukaryotic translation initiation factor 4E, UTR = urotensin II receptor.

Functional group or bond formed	Reaction	Aim	Change of	Target	Result	Comment	Reference
Lactam	Lactam coupling head-to-tail	β-hairpin as smaller α-helix mimetic	Secondary structure (α-helix)	p53-HDM2	IC_{50} 0.53 µM (8 AA β-hairpin) vs 1.1 µM (15 AA α-helix)		[1]
	Lactam sidechain-to-sidechain	Smallest α-helix (pentapeptide)			Induction of α-helix in water		[2]
	NCL	Improve proteolytic stability	Free N- and C-terminus	α-conotoxin MII derivatives on nicotinic acetylcholine receptor	Improved proteolytic stability (20%)	Preserve full activity (1.3 µM)	[3]
	Aldehyde + N-term. Cys	Synthesis natural compound		Lugdunin	S. aureus MIC 1.5 µg/mL		[4]
	Serine ligation	Synthesis natural compound		Daptomycin	First total synthesis		[5]
	Scaffold	PPI	Linear peptide	TNFα:TNFα receptor	3.1 µM (ELISA) K_D 0.45 µM	scaffold essential for affinity (KD >10 µM)	[6]
Oxime		Affinity and proteolytic stability	Linear peptide	p53 HDM2/X	IC_{50} HDM2 110 nM; HDMX 340 nM (linear: 1.5 µM; 7.5 µM)	10- to 15- fold higher stability, 40% higher helicity	[7]
Disulfide	Oxidation of Cysteines		Linear vs lactam vs disulfide cyclized	ERα	K_i 0.17 µM vs 0.22 µM vs 0.025 µM	Stabilized helicity	[8]
Thioacetal	TBAF-mediated thioacetalization	Selectivity	Linear peptide	AT_2	selectivity over AT_1 increased from 0.5-fold to 10-fold	Change of affinity strongly dependent on linker length;	[9]
	CH_2I_2-mediated thioacetalization		Disulfide	OXTR	6-fold decrease in affinity	only weak decrease in affinity, serum stability increased 2.5-fold	[10]
	CH_2I_2-mediated thioacetalization	Affinity and serum stability	Disulfide	IR	2-fold decrease in pAkt signalling, but strongly increased serum stability		[11]
Thioether	Scaffold	Activity, helicity	Linear vs stapled peptide	Mdm2/Mdmx	Mdm2: IC_{50} 57 nM vs 5.4 nM Mdmx: IC_{50} 1800 nM vs 14 nM	Increased cell permeability of stapled peptides	[12]
	Photo controllable scaffold	Activity, helicity	Linear vs trans vs cis	Bcl-xl	K_D 134 nM vs 825 nM vs 42 nM	Opportunity to activate apoptotic process under light control	[13]
C-C single bond	C(sp^3)–H activation-mediated macrocyclization	Binding, stability	Linear peptide	Integrins	>100-fold increased proteolytic stability	When applied to RGD-containing peptides: binding to αvβ3 integrin-overexpressing cells strongly increased	[14])
Alkene	RCM	Affinity	Linear peptide	eIF4E	6-fold increase in affinity	Affinity dependent on ring size	[15]
	RCM	Activity, stability	Linear peptide	Bcl-xl	K_D 154 nM vs 69 nM; stability 60 fold improved	intramolecular H-bond mimetic	[16]
	RCM	Affinity, helicity	Linear peptide	p53 MDM2/X	K_i (MDM2) 14 nM vs 1 nM, K_i (MDX) 47 nM vs 7 nM		[17]

		Insulin Activity	Disulfide	IR	Cis-Isomer showed increased efficacy in mice compared to native insulin	Binding of trans-isomer to IR (A and B) 50-fold reduced	[18]
Alkyne	RCAM	Affinity	Linear peptide	Rab8a	>10-fold increase in affinity	Affinity strongly dependent on linker lenght	[19]
1,4-substituted 1,2,3-triazole	CuAAC	Affinity, helicity	Linear peptide	BCL9 β-catenin	K_i 0.6 μM vs 0.13 μM; Helicity 44% vs 90%	improved stability	[20]
	CuAAC	Activity	Disulfide		Equipotent as the disulfide in rat model for neuropathic pain	Drastically increased plasma stability	[21]
1,5-substituted 1,2,3-triazole	RuAAC	Affinity	Disulfide	UTR	Maintained affinity	1,4-substituted triazole analogues lost affinity	[22]
	RuAAC	Inhibitory activity, hepatic stability	Disulfide	Set of proteases	Reduced inhibition 5-100-fold compared to disulfide; hepatic stability of triazoles increased >2 - >6-fold		[23]

Supplementary Table S3: Example reaction conditions used for in solution RCM for peptides. stochi. = stochiometric, TCE = 1,1,2-trichloroethane, TFE = 1,1,1-trifluoroethanol, rt = room temperature

Substrate conc.	**Catalyst**	**Catalyst loading**	**Solvent**	**T (°C)**	**other conditions**	**t**	**Yields**	**workup**	**Comment**	**Ref.**
5 mM	Grubbs I	20%	$CHCl_3$	25 °C		3 -4 h	85-90%			[24]
5 mM	Hoveyda-Grubbs I	2.50%	DCM	40 °C		20 h	85%			[25]
10 mM	Hoveyda-Grubbs I	5%	DCM	40 °C (reflux)		24 h	87%			[26]
2.5 mM	Grubbs II	stochi.	TCE/DMF				67%			[27]
7 mM	Grubbs I	20%	DCM	rt	dry, degassed	48 h	40%			[28]
0.6 mM	Grubbs II	10%	DCM	reflux	dry	24 h	9% (overall: SPPS, cleavage, macrolactamizstion, RCM)	Removed solvent	Gave specifically cis alkene	[29]
4 mM	Grubbs II	15-20%	DCM	rt		6-7.5 h	42-52%		Catalyst added in two portions, second portion after 2- 3 h	[30]
10 mM	Hoveyda-Grubbs II	20%	TFE/DCM (4:1)	**rt**		48 h	20-30%	Removed solvent, purified by HPLC		[31]

Supplementary Table S4: Example reaction conditions used for on resin RCM for peptides. † = nominal concentration (resin loading/solvent volume), DCE = 1,2-dichloroethane, TCE = 1,1,2-trichloroethane, rt = room temperature, µW = microwave, * = not specified which generation.

Substrate conc.†	Catalyst	Catalyst loading	Additives (eq)	Solvent	T (°C)	Other conditions	t	Yields	Workup	Comment	Ref.
	Grubbs II	15%		DCM	100 °C		75 min				[32]
82 mM	Hoveyda-Grubbs II	20%		DCM	100 °C	µW (300 W)	1 h	29%		Was essential to change from chlorotritiyl to HMBA resin	[33]
	Hoveyda-Grubbs II	15%		DCM/DMF	100 °C	µW (120 W)	2 h	7 - 16%			[34]
5.5 mM	Grubbs II	18%	2,6-Dichlorotoluene (3.6 eq)	TCE	reflux	N_2	16 h	45		Mixture of E/Z (9%/37%)	[35]
33.3 mM	Hoveyda-Grubbs*	200 g/mol (x2)		TCE	50 °C		overnight				[36]
13 mM	Grubbs I	40%		DCM	rt	Ar	48 h				[37]
24 mM	Grubbs II	20%	LiCl (0.8 eq.)	DCM/DMF (95/5)	100 °C	µW (100 W)	2 h	95%		RCM was unsuccesful on full length peptide, needed to be done on truncated version which was afterwards elongated, 3:1 E:Z	[38]
33.3 mM	Grubbs II	10%	LiCl (4 eq.)	DCM:DMF (4:1)	40 °C, reflux	dry, degassed	48 h	22% (overall: SPPS, RCM, cleavage)	Washed with DMSO for 12 h after RCM, filtration, washed with DCM, MeOH		[29]
	Hoveyda-Grubbs II			DCE	50 °C		8 h		Washed with DMF, DCM		[17]
	Grubbs II	20%	LiCl	DCM	100 °C	µW (60 W)	1 h				[39]
24 mM	Grubbs II	20%	LiCl (0.8)	DCM:DMF (19:1 or 20:1)	100 °C	µW (80 - 100 W)	1 - 2 h	100%			[40]
	Hoveyda-Grubbs II	30%		DCM:DMF (4:1)	100 °C	µW (100 W)	2 h	26% (crude)			[41]
	Hoveyda-Grubbs II	20-35%		TFE:DCM (4:1)	rt		48 h	20-30% (overall, convsersion > 90%)	Wash with DMSO:DMF (1:1) overnight	Reaction on Novapeg resin required only 20% catalyst, on Wang resin 35%	[31]

Supplementary Table S5: Example reaction conditions used for solution CuAAC for peptides. TFE = 1,1,1-trifluoroethanol, TBTA = tris[(1-benzyl-1*H*-1,2,3-triazol-4-yl)methyl]amine, THTPA = tris(3-hydroxypropyltriazolylmethyl)amine, rt = room temperature.

Substrate conc.	Cu salt (eq)	Ascorbate (eq)	Additives (eq)	Solvent	T	Other conditions	time	Yield	Workup	Comment	Ref.
1 mM	$CuSO_4$ x 5 H_2O (3)	6		NH_4CO_3 buffer (0.1 M)	rt	Ar	30 min		pH 2 (TFA), SPE (C18)		42
1.2 M (!)	CuBr (1)	-	DBU (3)	DCM	rt	dry, N_2	12 h		Washed with 3 M HCl, extracted with DCM		43
0.775 mM	$CuSO_4$ x 5 H_2O (14)	Large excess		H_2O:*t*BuOH (2:1)	rt		Overnight		Concentrated, lyophilise, C18 HPLC		44
0.5 mM	$CuSO_4$ x 5 H_2O (14)	13		H_2O:*t*BuOH (2:1)	rt		1 h		HPLC (C12)		45
0.954 mM	$CuSO_4$ x 5 H_2O (8.4)	8.45		H_2O:*t*BuOH (2:1)	rt		overnight		Concentrated, lyophilise, C18 HPLC (SPE)		46
1 mM	CuBr (0.2)	-	DBU (3)	$PhCH_3$	110 °C		16 h	70%		CuI gave substantial iodoatriazole adducts	47
0.15 mM	CuI.$P(OEt)_3$ (0.31)	-	DIPEA (3)	DCM	rt	Protected from light	42 h	83%			48
0.3 mM	$CuSO_4$ x 5 H_2O (4.4)	4.4	-	H_2O:*t*BuOH (2:1)	rt		Overnight				49
1 mM	$Cu(MeCN)_4][PF_6]$ (1.8)	2.1	Tris-tri(methylazolyl)-amine (2.7)	10 mM Na-Phosphate, pH 8	rt	Protected from light	Overnight				50
10 mM	$Cu(MeCN)_4][PF_6]$ (0.05)	-	TBTA (0.05)	DCM	55 °C		12 h	39-79%			51
0.8 mM	$CuSO_4$ x 5 H_2O (4)	6	-	H_2O:*t*BuOH (1:1)	rt		Overnight				36
10 mg/mL	CuBr (0.01)	-	DBU (0.03)	DCM	rt		6 h				52
1 mM	CuI (2)	-	DIPEA (2), 2,6-lutidine (2)	MeCN	rt	Ar, degassed	12 h				53
0.5 mM	$CuSO_4$ (1)	5	THTPA (1)	H_2O:*t*BuOH (1:1) or H_2O:TFE (1:1)	rt		< 1 h	13-51%			54
1 mg/mL	$CuSO_4$ (1)	1	DIPEA (8)	H_2O	rt	Degassed	12 h				22
0.1 mM	$Cu(MeCN)_4][PF_6]$ (0.95)	-		THF:MeOH (1:1)	40 °C	Degassed	20 h	64-83%			55
0.5 mM	$CuSO_4$ (2)	10	THTPA (2)	DMF/H_2O (2:1)	rt		5 min				56,57
0.8 mg/mL	$CuSO_4$ x 5 H_2O (1)	3	THTPA (1)	H_2O:*t*BuOH (1:1)	rt	N_2, degassed		52-92%	Diluted with H_2O, lyophilised, HPLC		58
1.5 mM	$CuSO_4$ (10)	10	TBTA (10)	H_2O:*t*BuOH (1:1)	rt		12 h		HPLC		59
0.91 mg/mL	$CuSO_4$ x 5 H_2O (1)	3	THTPA (1)	H_2O:*t*BuOH (1:1)	rt	N_2	16 h				60
1 mg/mL	$CuSO_4$ x 5 H_2O (1)	3	THTPA (1)	H_2O:*t*BuOH (1:1)	rt	N_2	16 h				61
	$CuSO_4$ x 5 H_2O (1)	3	THTPA (1)	H_2O:*t*BuOH (1:1)	rt	N_2	15 min - 2 h				62

	$CuSO_4$ x 5 H_2O (1)	3	THTPA (1)	H_2O:*t*BuOH (1:1)	rt	N_2, degassed	16 h				[63]
0.01 mM	$CuSO_4$ (4)	4	-	buffer pH 8 (250 mM Na borate, 1M NaCl)	60 °C		30 min				[64]
1 mM	CuBr (0.8)	-	-	$PhCH_3$	Reflux	Ar	Overnight	43%	Celite filtration, DCM wash of filter, flash column chromatography		[65].
1.1 mM	CuI.$P(OEt)_3$ (1.5)	-	-	DCM	rt	Protected from light	5 days	75%	Solvent removal, flash chromatography		[66]
1 mM	$Cu(MeCN)_4][PF_6]$ (1.5)	-		$PhCH_3$/MeOH (4:1)	rt	N_2	24 h	0-46%	Solvent removal, flash chromatography	Yield depended on chain length of employed azide	[67]
0.35 mM	$CuSO_4$ (2)	10	THTPA (10)	H_2O	37 °C	N_2	3 h	45-55%	Monitored by HPLC, purification by HPLC		[23]
1 mg/mL	$CuSO_4$ x 5 H_2O (1)	1	DIPEA (8)	H_2O	rt	Ar, degassed	Overnight	7.5-12.8% (overall)	Lyophilisation, HPLC prufication by HPLC		[68]
	$CuSO_4$ x 5 H_2O (2)	3	THTPA (1) for some	H_2O:*t*BuOH (1:1)	rt	N_2 ,degassed	overnight		SPE, HPLC purification	.	[69]
2 mM	$CuSO_4$ x 10 H_2O (2.5)	10		H_2O:*t*BuOH (1:1.5)			overnight		Removal tBuOH, filtration, HPLC purifcation		[70].
1 mM	CuBr (0.2)	-	DBU (3)	$PhCH_3$	reflux	Ar, degassed	16 h	36-56%	Celite filtration, DCM wash of filter, flash column chromatography	Head-to-tail, tetrapeptide	[71]
0.2 mM	CuI (2)	-	TBTA (2), DIPEA (2), 2,6-lutidine (2)	MeCN	rt	Ar, degassed	48 h		Removed solvent, HPLC purification	Head-to-tail, tetrapeptide	[72]
1 mM	CuI (0.33)	-	DIPEA (3), 2,6-lutidine (2)	MeCN:THF (4:1)	rt	Degassed	14 h	57-92%	Filtration, removal of solvent, HPLC purification	Head-to-tail, pentapeptide	[73]
	CuBr (1)	1	DIPEA (10), 2,6-lutidine (10)	DMF:H_2O	rt		18 h		Washed with DMF, DCM		[74]

Supplementary Table S6: Example reaction conditions used for on-resin CuAAC for peptides. TBTA = tris[(1-benzyl-1*H*-1,2,3-triazol-4-yl)methyl]amine, † = nominal concentration (resin loading/solvent volume), rt = room temperature.

Substrate conc.†	Cu salt (eq)	Ascorbate (eq	Additives (eq)	Solvent	T	Other conditions	Time	Yield	Workup	Ref.
15 µL/mg resin	CuI (2)	-	DIPEA (50 eq)	THF			16 h	76%		[75]
625 mL/mmol	CuI (0.5)	1	2,6-Lutidine (2 eq)	NMP/H_2O (4:1)			48 - 96 h	8.4%		[76]
20 mg/mL	CuBr (1)	1	2,6-Lutidine (10 eq), DIPEA (10 eq)	DMSO	rt	Degassed	16 h			[77]
	CuBr	yes	2,6-Lutidine, DIPEA	DMF/MeCN	rt		8 h	22% (overall)		[78]
	CuBr (1)	3	2,6-Lutidine (10 eq), DIPEA (10 eq)	DMF/MeCN (10/3)	rt	Degassed	6 h	20%-75%		[79]
	CuI (2)	2	DIPEA (3)	DMF	rt		Overnigh t			[36]
	[$Cu(CH_3CN)_4$] [PF_6] (1)	-	TBTA (1), DIPEA (2)	DMF			24 h			[80]
	CuI (1.5)	7 (as ascorbic acid)	Piperidine (20 vol%)	DMF	rt	Light protected	15 h		Wash with 5% sodium diethyldithiocarbaamte, 5% DIEPA in DMF, MeOH, DMF, NMP	[81]

Supplementary Table S7: Example reaction conditions used for in solution RuAAC for peptides. cod = 1,5-cycloocatadien, rt = room temperature.

Substrate conc.	Catalyst	Catalyst loading	Solvent	T	Other conditions	Time	Yield	Workup	Comment	Ref.
1.9 mM	[Cp*RuCl]$_4$	3.75%	DMF	115 °C	µW (200 W)	30 min	10%	Removal of DMF in vacuo, extraction DCM/water, silica column chromatography followed by RP-8	Desired product only minor, major product correct m/z, but no symmetry in NMR --> probably 1,4-analogue	[82]
5 mM	[Cp*RuCl]$_4$	30%	THF/MeOH	50 °C	-	24 h	40%			[83]
5 mM	[Cp*RuCl]$_4$	15%	THF/MeOH (95:5)	50 °C	N_2	24 h	14-68%	Removal of solvent, flash chromatography		[84]
3.1 mM	Cp*RuCl(cod)	50%	DMF	80 °C	dry	18 h	3.4-7.0% (overall: SPPS, RuAAC, deprotection)	Addition of DCM, washed organic phase with H_2O+0.05% TFA, removal of solvent, redissolved in H_2O/MeCN (1:1)+0.05% TFA, lyophilised	Sidechain protected peptide	[85]

Supplementary Table S8: Example reaction conditions used for on-resin solution RuAAC for peptides. † = nominal concentration (resin loading/solvent volume), cod = 1,5-cycloocatadien

Substrate conc.†	Catalyst	Catalyst loading	Solvent	T	Other conditions	Time	Yield	Workup	Ref.
200 mM	Cp*RuCl(cod)	3.75%	DMF	60 °C	Dry, degassed, Ar	6 h		Wash with DMF, MeOH, DCM	[22]
< 12.5 mM	Cp*RuCl(cod)	30%	DMF	60 °C	μW (30 W)	5 h	2.1% (overall)	Wash with MeOH, 0.5% dietyhldithiocarbamate in DMF, DMF, DCM	[68]
25 mM	Cp*RuCl(cod)	15%	DMF	70 °C	Dry, degassed	1 h	8-21%	Monitored by IR, continued with Fmoc-deprotection	[86]
	Cp*RuCl(cod)	50%	DMF	60 °C	μW (30 W), N_2	3 h		Wash with MeOH, 2% dietyhldithiocarbamate in DMF, DMF	[69]
75 mM	Cp*RuCl(PPh_3)$_2$		DMF	65 °C	μW, degassed, Ar	2.5 h		Wash with DMF, Et_2O	[70]

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