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TABLE S4: MS cleavable linkers

Cleavable linker	Structure	Cleavage products	Cleavage Conditions	Advantages	Disadvantages
Di- succinimidyl sulfoxide ¹			CID	Commercial building block available	
Urea ²		$ \underbrace{ \begin{array}{c} H \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ $	CID	Commercial building block available	
Quarternary ammonium ³			CID		
Sulfonium⁴	$\bigvee_{0}^{H} \bigvee_{0}^{Me} \bigvee_{1}^{Me} \bigvee_{0}^{H} \bigvee$	$ \begin{array}{c} & & \\ & & $	CID		
Cyanuric acid derivative ^{5,6}		+ N N HS N S	CID		
Asp-Pro ^{7,8}		$ \begin{array}{c} 0 \\ 0 \\ H \\ 0 \\ 0 \\ 0 \\ H \\ 0 \\ 0 \\ H $	CID	Easy to synthesise from amino acid building blocks	
Rink linker ^{9,10}			CID	Based on SPPS Rink linker; may also be chemically cleaved by TFA (application not yet reported in target ID- ing)	

Ester ^b of secondary alcohol ¹¹	O_O Asp/Glu	+ HO_O Asp/Glu	CID		Not all diazirine is converted to a diazonium species, so this crosslinking phenomenon may vary in its efficiency
TEMPO- based ¹²	VH CON H	\downarrow	CIDª		
Azo ¹³	$(\mathcal{A}_{N} \overset{O}{\underset{N}{\overset{O}}} (\mathcal{A}_{N} \overset{O}{\underset{N}{\overset{O}}} (\mathcal{A}_{N} \overset{O}{\underset{N}{\overset{O}}} (\mathcal{A}_{N} \overset{O}{\underset{O}{\overset{O}}} (\mathcal{A}_{N} \overset{O}{\underset{O}{\overset{O}}} (\mathcal{A}_{N} \overset{O}{\underset{O}{\overset{O}}} (\mathcal{A}_{O} \overset{O}{\underset{O}{\overset{O}}} (\mathcal{A}_{O} \overset{O}{\underset{O}{\overset{O}}} (\mathcal{A}_{O} \overset{O}{\underset{O}{\overset{O}}} (\mathcal{A}_{O} \overset{O}{\underset{O}{\overset{O}}} (\mathcal{A}_{O} \overset{O}{\underset{O}{\overset{O}}} (\mathcal{A}_{O} \overset{O}{\underset{O}{\overset{O}{\overset{O}}} (\mathcal{A}_{O} \overset{O}{\underset{O}{\overset{O}{\overset{O}{\overset{O}}}} (\mathcal{A}_{O} \overset{O}{\underset{O}{\overset{O}}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}}{\overset{O}{\overset{O}{\overset{O}}{\overset{O}{\overset{O}{\overset{O}{\overset{O}}{\overset{O}{\overset{O}{\overset{O}}{\overset{O}{\overset{O}{\overset{O}}{\overset{O}{\overset{O}}}}}}}}}$	$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	CIDª		
Azo-bis- imido ¹⁴	$\bigwedge_{H}^{H_2} \bigvee_{N \geq N} \bigvee_{H_2}^{H_2} H_{N \geq N}$	$\bigwedge_{H}^{+} \underset{H}{\overset{H_2}{}} \underset{N_2}{\overset{N_2}{}} \underset{N_2}{\overset{H_2}{}} \underset{N_2}{\overset{H_2}{}} \underset{N_2}{\overset{H_2}{}} \underset{N_2}{\overset{H_2}{}} \underset{N_2}{\overset{H_2}{}} \underset{N_2}{\overset{H_2}{}} \underset{N_2}{\overset{H_2}{}} \underset{N_2}{\overset{H_2}{}} \underset{N_2}{\overset{H_2}{}} \underset{N_2}{\overset{H_2}{\overset{H_2}{}}} \underset{N_2}{\overset{H_{H_2}{H_{H_{H_{H_{H_{H_{H_{H_{H_{H_{H_{H_{H_{$	CID/HCDª		
Bisaryl- hydrazone ¹⁵	K K K K K K K K K K K K K K K K K K K		ETD	Can also be chemically cleaved (see Table S1)	
Disulfide ¹⁶	/~~s~~/	/~ ^{\$} HS ∕∕	ETD	Can also be chemically cleaved (see Table S1)	
Diformyl ethynyl- benzyene ¹⁷	HZ HZ	H H ₂ N	ETD		
DEST ^c - derived ¹⁸	NH NH NH NH	$ \begin{array}{c} & & \\ & & $	ETD		

^a This CID cleavage is also called FRIPS (for: free radical initiated peptide sequencing)

^b This results from photoactivation of a diazirine, which partially rearranges to a diazonium ion, which then reacts with nucleophilic Asp or Glu side chains, forming an ester bond

^c Resulting from amine crosslinking of diethyl-thiosuberthioimidate

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