Specialty Products & Technologies

CLEAR™

Cross-Linked Ethoxylate Acrylate Resins

PEPTIDES INTERNATIONAL

RESINS FOR SOLID-PHASE SYNTHESIS

The Future is CLEAR™

Cross-Linked Ethoxylate Acrylate Resin

Are you using CLEAR (*C*ross-*L*inked *E*thoxylate *A*crylate *R*esin) as your preferred support for solid-phase synthesis? Do you need improved synthetic results? If you have encountered a difficult peptide or need to synthesize a longer sequence, then CLEAR may be a solution for you. CLEAR polymers were introduced by Kempe and Barany [1, 2] and further developed as a commercial product in 1997.[3, 4]

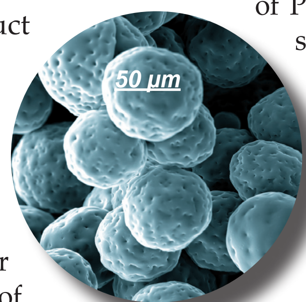


Figure 1. SEM (Scanning Electron Micrograph) of CLEAR resin particles: The structure is nearly 100% cross-linked. The polyethylene glycol backbone makes the resin fully accessible to a wide range of solvents and reagents including aqueous solutions. Unlike liquid phase PEG resins, CLEAR particles are easy to filter and resistant to all but the most harsh acid or base solutions.

The degree of synthetic difficulty for a peptide sequence depends on several factors: known sequence dependent motifs, incomplete coupling reactions, and limited improvement resulting from recoupling or acetylation ("capping"). This is the result of aggregation of the growing peptide chain due to secondary structure formation during synthesis (*i.e.*, β-sheet formation), interchain or intrachain peptide association via hydrogen bonding or hydrophobic interactions, and peptide-polymer matrix association. This leads to a hindered amino terminus, which results in reduced coupling and deprotection efficiencies. In more ideal reaction conditions, a well-solvated peptide-polymer matrix results in faster and more complete coupling reactions. Traditionally, solid-phase peptide synthesis (SPPS) has been carried out employing cross-linked polystyrene (PS) solid supports. Some of the newer solid supports combine a polyethylene glycol (PEG) appendage with a polymer backbone suitable for manipulation during SPPS, such as PEG-PS™ or TentaGel™ resins. The addition of polyethylene glycol linkers to polystyrene supports led to improved synthesis of known difficult sequences. This was attributed to the disruption of aggregation of the growing peptide chain. While our CLEAR resins are highly cross-linked and contain polyethylene glycol, CLEAR does not possess a polystyrene core. The entire cross-linked matrix of CLEAR is PEG-like in character and thus, hydrophilic. CLEAR resin products retain the highly desirable solvation properties of PEG-grafted PS supports and aid disruption of secondary structure formation during synthesis. Also, CLEAR resins offer better swelling properties than PS-based resins in a wider variety of solvents (*i.e.*, DCM, DMF, and water), leading to better coupling efficiencies and improved yields and purities. Importantly, CLEAR resins swell in aqueous systems, which has proven to be useful for on-resin disulfide oxidations (*e.g.* $K_3Fe(CN)_6$)[5] or bio-chemical applications.

"Our customers have told us that they are getting positive results with these products where other resins have failed"

Clearly, your own imagination should lead to many other uses for a product as exciting as CLEAR. Organic Synthesis?[5,6,7] Affinity Chromatography? Enzyme Immobilization? Microwave-Assisted SPPS?[8] Trace Analysis? Remote Sensor Applications? *Isn't it CLEAR what your next solid-phase support choice should be?*

We invite you to try these superior resins. Please contact our technical specialists today.

WHAT CHARACTERISTICS WOULD A **PERFECT** SUPPORT FOR **ALL** SOLID PHASE SYNTHESIS NEEDS POSSESS?

1. Inert matrix
2. Easily filtered
3. Deters aggregation
4. Good swelling properties
5. Promotes rapid reaction rates
6. Suitable for batch or continuous flow synthesis
7. Compatible with water for protein affinity matrix applications

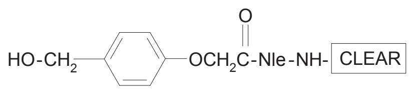
CLEAR™ VS Polystyrene-Based Resins:

- Improved Coupling Efficiencies
- Higher Purities and Yields
- Superior for Difficult Sequences
- Swells in Water! and
- Swells in Organic Solvents
- Suitable for Continuous Flow and Batch Applications

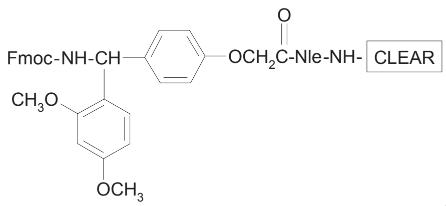
CLEAR-Base Resin

$HCl \bullet NH_2$- CLEAR

CLEAR-Acid Resin
Hydroxymethylphenoxyacetyl-norleucyl-CLEAR Resin



CLEAR-Amide Resin
Rink-Amide-CLEAR Resin
4-(2,4-dimethoxyphenyl-Fmoc-Aminomethyl) phenoxyacetyl-norleucyl-CLEAR Resin



Swelling Properties of CLEAR-Base Resin	
Solvent	Bed Volume (ml) of 1 g of resin
CH_2Cl_2	7.0
DMF	6.5
THF	7.0
MeOH	6.0
H_2O	5.5

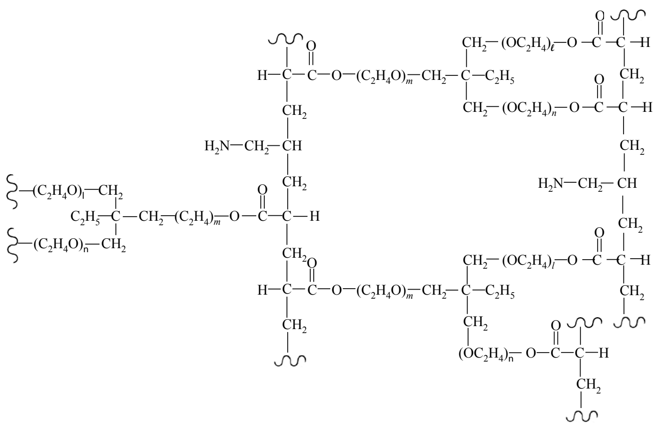


Figure 2. The structure of the polymeric network of CLEAR supports, where l + m + n ~ 14

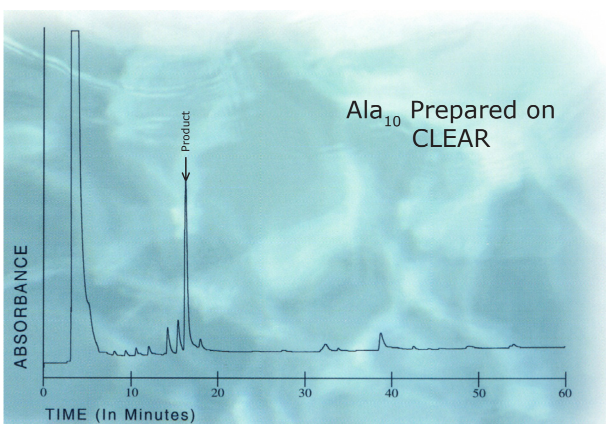


Figure 3a. Analytical HPLC chromatogram of crude H-$(Ala)_{10}$-Val-NH_2 prepared by batch-wise automated synthesis (Rainin, PS-3) on CLEAR-Amide resin. Synthesis performed using HBTU as coupling agent, four fold excess of Fmoc-Ala for 30 + 90 minutes (double coupling). HPLC performed on Vydac C_{18} column (4.6 x 250 mm), gradient 5% →65% ACN/0.05% TFA in 60 minutes, 1 ml/min, 220 nm.

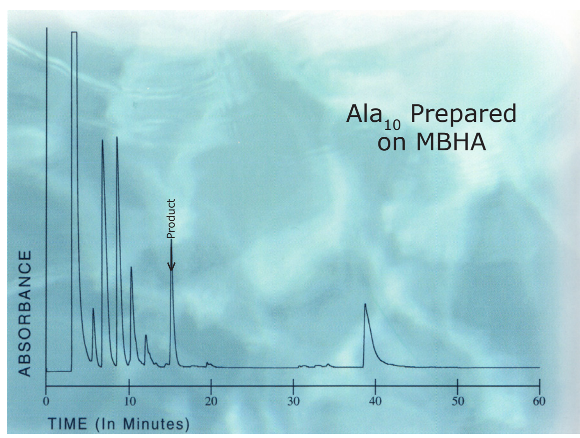


Figure 3b. Analytical HPLC chromatogram of crude H-$(Ala)_{10}$-Val-NH_2 prepared by batch-wise automated synthesis (Rainin, PS-3) on 1% cross-linked polystyrene. Synthesis performed using HBTU as coupling agent, four fold excess of Fmoc-Ala for 30 + 90 minutes (double coupling). HPLC performed on Vydac C_{18} column (4.6 x 250 mm), gradient 5% →65% ACN/0.05% TFA in 60 minutes, 1 ml/min, 220 nm.

1. M. Kempe and G. Barany, "CLEAR: A Novel Family of Highly Cross-Linked Polymeric Supports for Solid Phase Synthesis", *J. Am. Chem. Soc.,* **118**, 7083-7093, (1996).
2. M. Kempe and G. Barany, "Novel Highly Cross-Linked Polymeric Supports for Solid Phase Applications", in *Solid Phase Synthesis* (Fourth International Symposium, Edinburg Scotland) R. Epton, Ed., Mayflower (London) 1996, pp. 191-194.
3. CLEAR products are protected under US Patents 5,910,554 and 5,656,707 granted to the Regents of the University of Minnesota.
4. K. Darlak, I. Romanovska, A.F. Spatola, G. Barany, and M. Kempe, "A New Solid Support for Peptide and Organic Synthesis", Fifteenth American Peptide Symposium; Nashville, Tennessee, USA; June 1997.
5. K. Darlak, D. Wiegandt Long, A. Czerwinski, M. Darlak, F. Valenzuela, A.F. Spatola, and G. Barrany, "Facile preparation of disulfide-bridged peptides using the polymer supported oxidant CLEAR-OX™" *J. Peptide Res.*, **63**, 303-312 (2004).
6. N. Chatla, K. Darlak, and A.F. Spatola, "Applications of CLEAR Resin for Solid Phase Organic Synthesis Comparison with Polystyrene Based Resin" *Innovation and Perspectives in Solid Phase Synthesis and Combinatorial Libraries* (Fifth International Symposium, London, England) R. Epton, Ed., Mayflower (London) 1998, pp. 275-276.
7. K. Darlak, M. Darlak, and A.F. Spatola, "Disulfide Oxidation in Water: Investigation of CLEAR Supports for On-Resin Cyclization" *Peptide Science - Present and Future* (Proceedings of the 1st International Peptide Symposium, Kyoto, Japan) Y. Shimonishi, Ed., Kluwer Academic Publishers (Dordrecht) 1997, pp. 584-586.
8. A. Carenbauer, M. Cecil, A. Czerwinski, K. Darlak, M. Darlak, D. Wiegandt Long, F. Valenzuela, and G. Barany, "Microwave-Assisted Solid-Phase Peptide Synthesis (MW-SPPS) on CLEAR Supports", Nineteenth American Peptide Symposium, San Diego, California, USA; June, 2005.

CODE	PRODUCT	QTY
RCB-1210-PI	**CLEAR-Base Resin (HCl)** HCl • NH_2– CLEAR	5g 25g 100g
RCX-1213-PI	**CLEAR-Acid Resin** Hydroxymethylphenoxyacetyl-Norleucyl-CLEAR-Resin	5g 25g
RCY-1250-PI	**CLEAR-Amide Resin** Rink-Amide-Nle-CLEAR Resin	5g 25g
CFA-1220-PI	**Fmoc-Ala-CLEAR-Acid Resin**	1g 5g
CFX-1221-PI	**Fmoc-ß-Ala-CLEAR-Acid Resin**	1g 5g
CFR-1222-PI	**Fmoc-Arg(Pbf)-CLEAR-Acid Resin**	1g 5g
CFN-1223-PI	**Fmoc-Asn(Trt)-CLEAR-Acid Resin**	1g 5g
CFD-1224-PI	**Fmoc-Asp(OtBu)-CLEAR-Acid Resin**	1g 5g
CFD-1225-PI	**Fmoc-Cys(tBu)-CLEAR-Acid Resin**	1g 5g
CFD-1226-PI	**Fmoc-Cys(Acm)-CLEAR-Acid Resin**	1g 5g
CFD-1227-PI	**Fmoc-Cys(Trt)-CLEAR-Acid Resin**	1g 5g
CFD-1228-PI	**Fmoc-Cys(Xan)-CLEAR-Acid Resin**	1g 5g
CFE-1229-PI	**Fmoc-Glu(OtBu)-CLEAR-Acid Resin**	1g 5g
CFQ-1231-PI	**Fmoc-Gln(Trt)-CLEAR-Acid Resin**	1g 5g
CFG-1233-PI	**Fmoc-Gly-CLEAR-Acid Resin**	1g 5g

CODE	PRODUCT	QTY
CFH-1234-PI	**Fmoc-His(Trt)-CLEAR-Acid Resin**	1g 5g
CFI-1236-PI	**Fmoc-Ile-CLEAR-Acid Resin**	1g 5g
CFL-1237-PI	**Fmoc-Leu-CLEAR-Acid Resin**	1g 5g
CFK-1238-PI	**Fmoc-Lys(Boc)-CLEAR-Acid Resin**	1g 5g
CFM-1240-PI	**Fmoc-Met-CLEAR-Acid Resin**	1g 5g
CFF-1241-PI	**Fmoc-Phe-CLEAR-Acid Resin**	1g 5g
CFP-1242-P	**Fmoc-Pro-CLEAR-Acid Resin**	1g 5g
CFS-1243-PI	**Fmoc-Ser(tBu)-CLEAR-Acid Resin**	1g 5g
CFT-1245-PI	**Fmoc-Thr(tBu)-CLEAR-Acid Resin**	1g 5g
CFW-1246-PI	**Fmoc-Trp-CLEAR-Acid Resin**	1g 5g
CFW-1247-PI	**Fmoc-Trp(Boc)-CLEAR-Acid Resin**	1g 5g
CFY-1248-PI	**Fmoc-Tyr(tBu)-CLEAR-Acid Resin**	1g 5g
CFV-1249-PI	**Fmoc-Val-CLEAR-Acid Resin**	1g 5g
	Multiple Antigenic Peptide Systems (MAPs) Resins	
CFM-1214-PI	**$Fmoc_4$-Lys_2-Lys-β-Ala-CLEAR Acid Resin**	1g
CFM-1218-PI	**$Fmoc_8$-Lys_4-Lys_2-Lys-β-Ala-CLEAR Acid Resin**	1g

All CLEAR products are 100-200 mesh with 0.2-0.6 meq/g substitution range.
Please consult our web site (PEPNET.COM) for technical information and product updates.

CLEAR resins are available with several choices of functional groups and linkers. The base resin has a non-cleavable amine functionality. The Rink-type linker is attached through a norleucine (Nle) spacer, allowing for facile quantitation using amino acid analysis. All CLEAR products are 100-200 mesh, with a substitution level of 0.2-0.6 meq/gram.

CLEAR resins are produced exclusively by Peptides International, Inc., under license from the University of Minnesota and are protected under US Patents 5,656,707 and 5,910,554.

CLEAR™

- Is the solid support with all the advantages of liquid phase synthesis but in a bead form.
- Insures that reactions work rapidly and avoid aggregation but do not require a polystyrene matrix.
- Is the support that swells in water but is also compatible with all your favorite organic solvents.
- Is the support that does all that but costs far less than PEG-PS™ or TentaGel™.

PEPTIDES INTERNATIONAL

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