



# Grundlagen der organischen Chemie II

## Peptide 2

Tim Clark

Computer-Chemie-Centrum

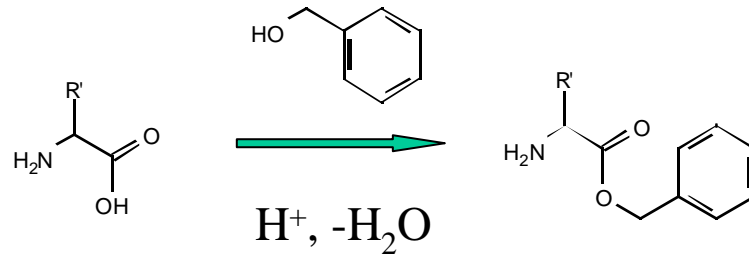
Universität Erlangen-Nürnberg

[clark@chemie.uni-erlangen.de](mailto:clark@chemie.uni-erlangen.de)

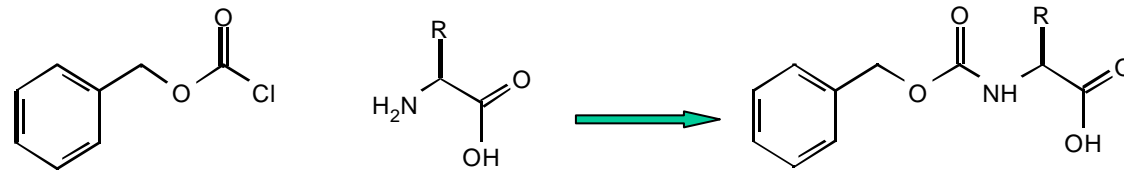


# Eine Dipeptid-Synthese

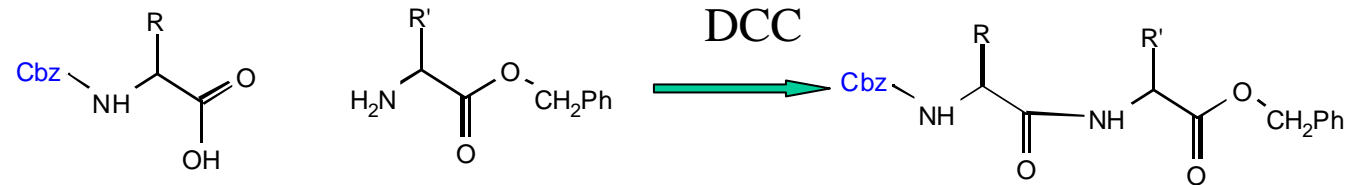
1. COOH-Schutzgruppe



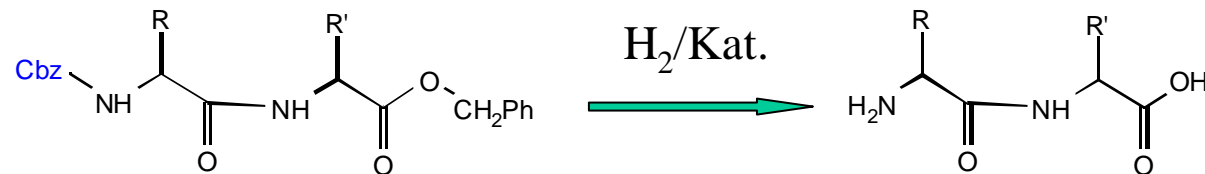
2. NH<sub>2</sub>-Schutzgruppe



3. Kopplung



4. Schutzgruppen entfernen





# Peptid-Synthese

- Schritte:
  - Schutzgruppen anbringen
  - Koppeln
  - Schutzgruppen abspalten
- Ausbeute:
  - „gute“ Ausbeute ? 90%
  - Für eine  $n$ -Schritt-Synthese erwarten wir  $0.9^n$  ? 100 %  
Ausbeute
    - $n = 20$  ? 12%
    - $n = 50$  ? **0.5%**
    - $n = 100$  ? **0.003 %**



# Peptid-Synthese

- Geringe Ausbeute durch:
  - Unvollständige Reaktion (benutze DCC)
  - Trennungsvorgänge
    - Destillieren
    - Auskristallisieren
    - Chromatographie
    - Extrahieren
    - **Filtrieren und waschen**



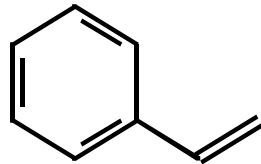
# Nobel-Preis für Chemie 1984



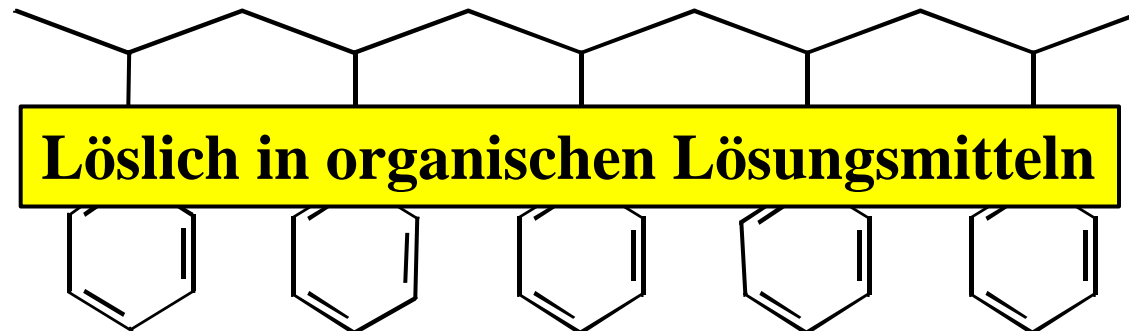
Robert Bruce Merrifield  
15.07.1921 -  
Rockefeller University,  
New York



# Polystyrol

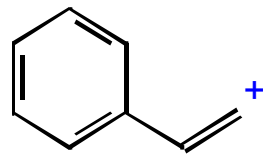


Radikalische polymerisation

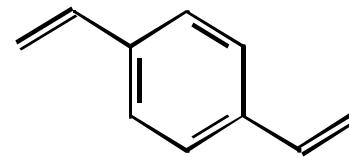




# Vernetztes Polystyrol

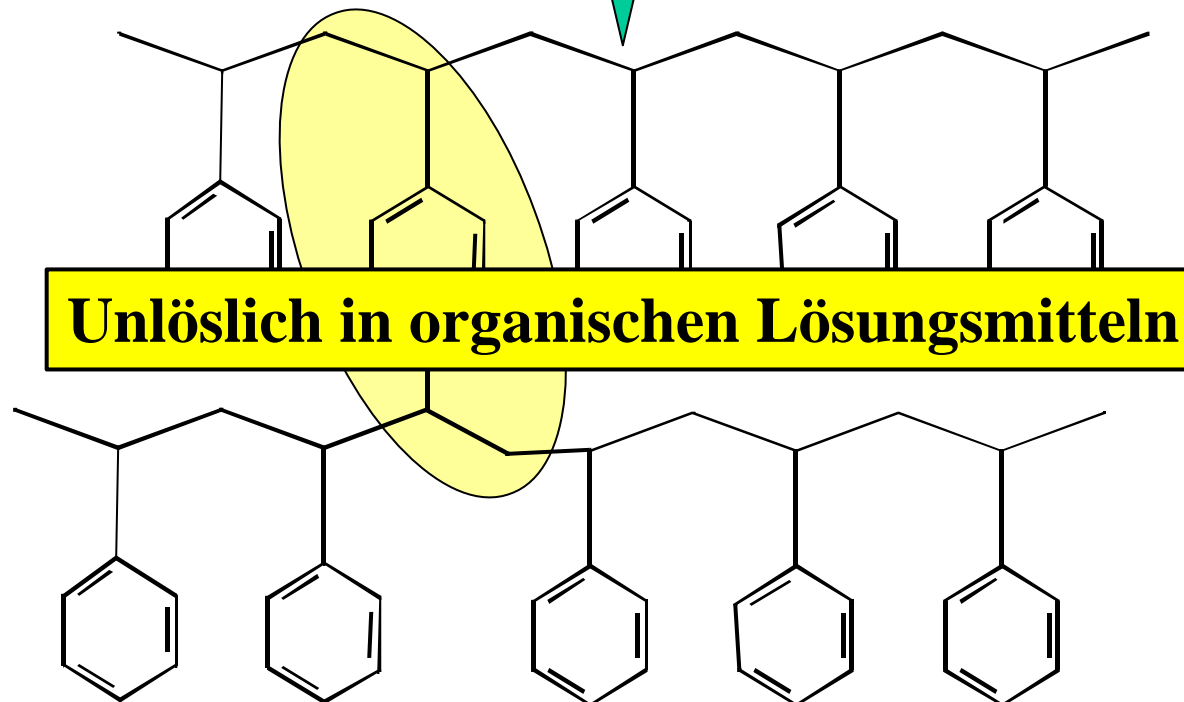


+



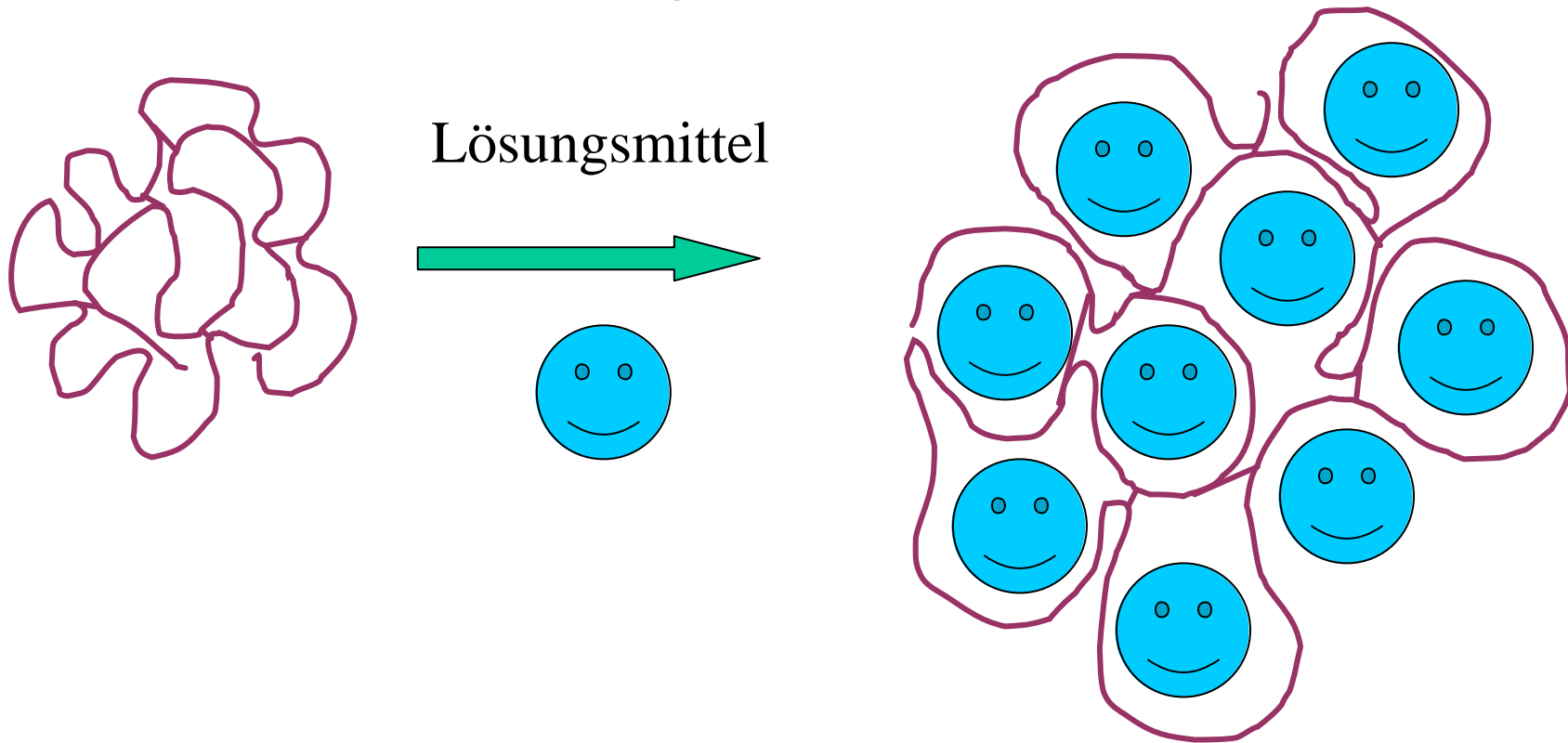
(ca. 2%)

Radikalische Polymerisation



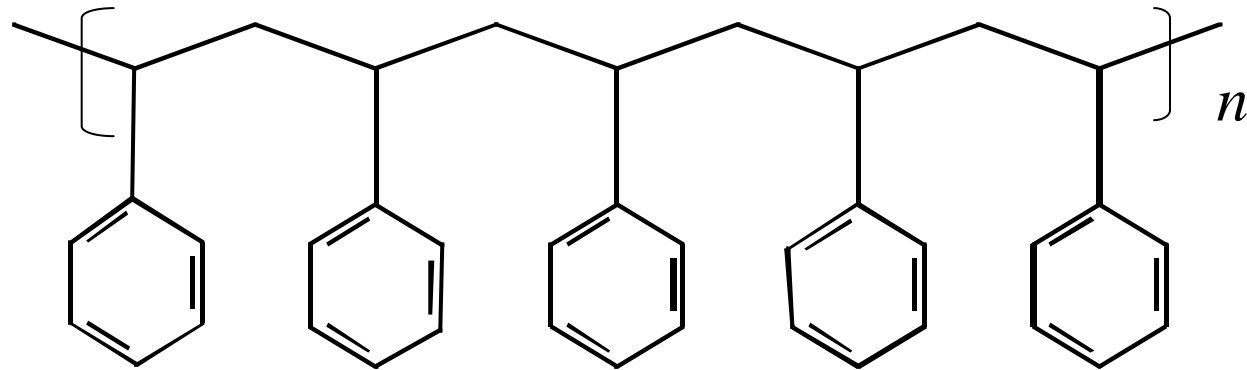


# Verhalten im Lösungsmittel

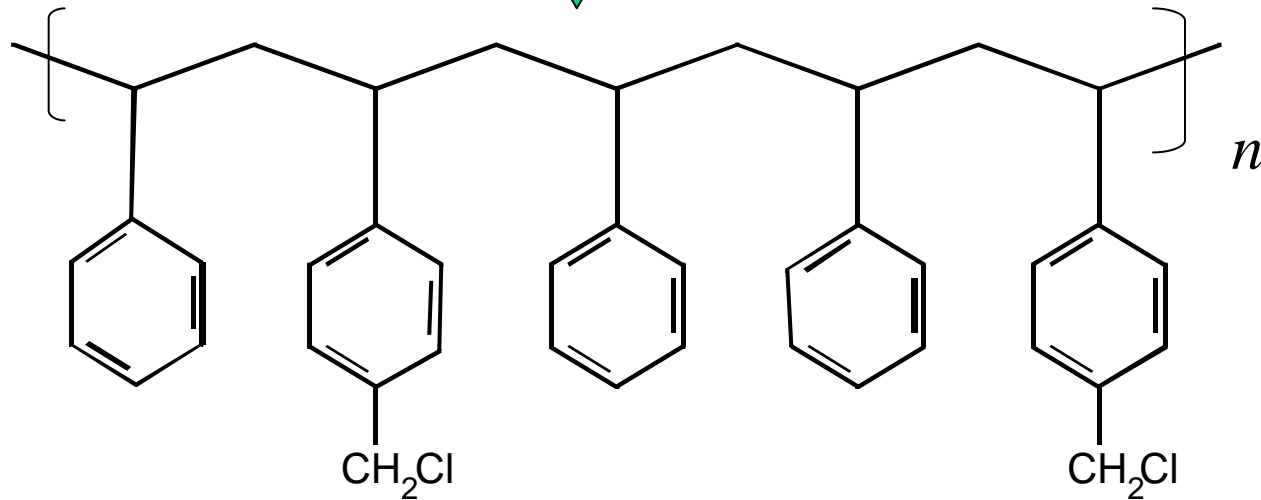
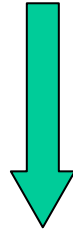




# Funktionalisierung

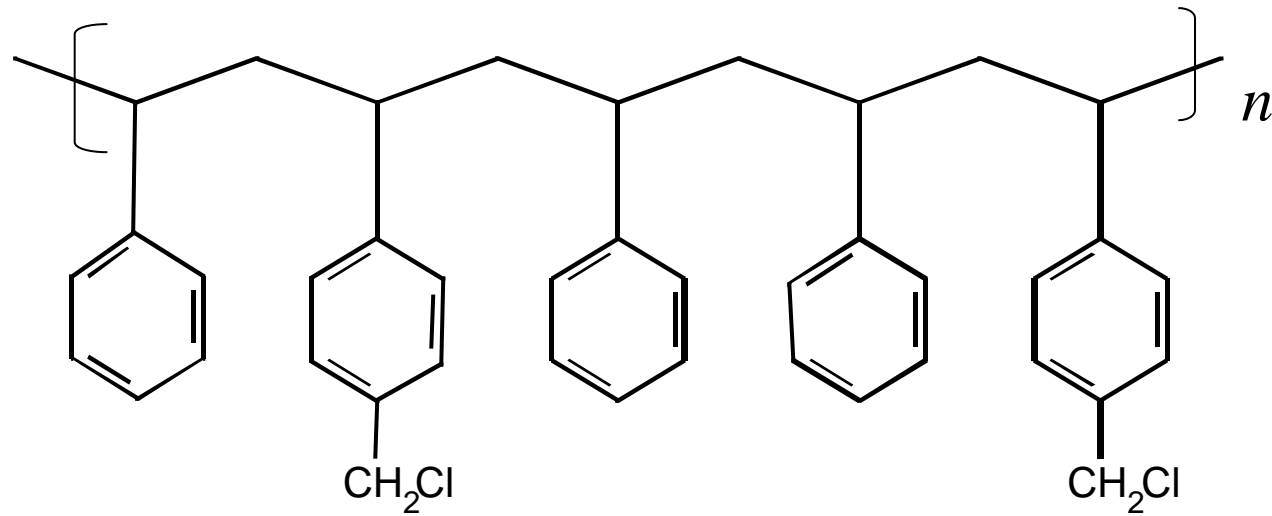


$\text{CH}_3\text{OCH}_2\text{Cl}$ , Lewis-Säure

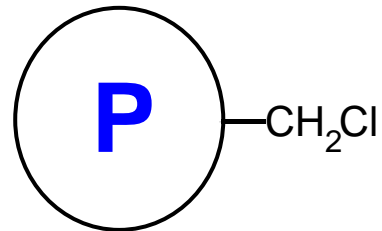




# Synthese

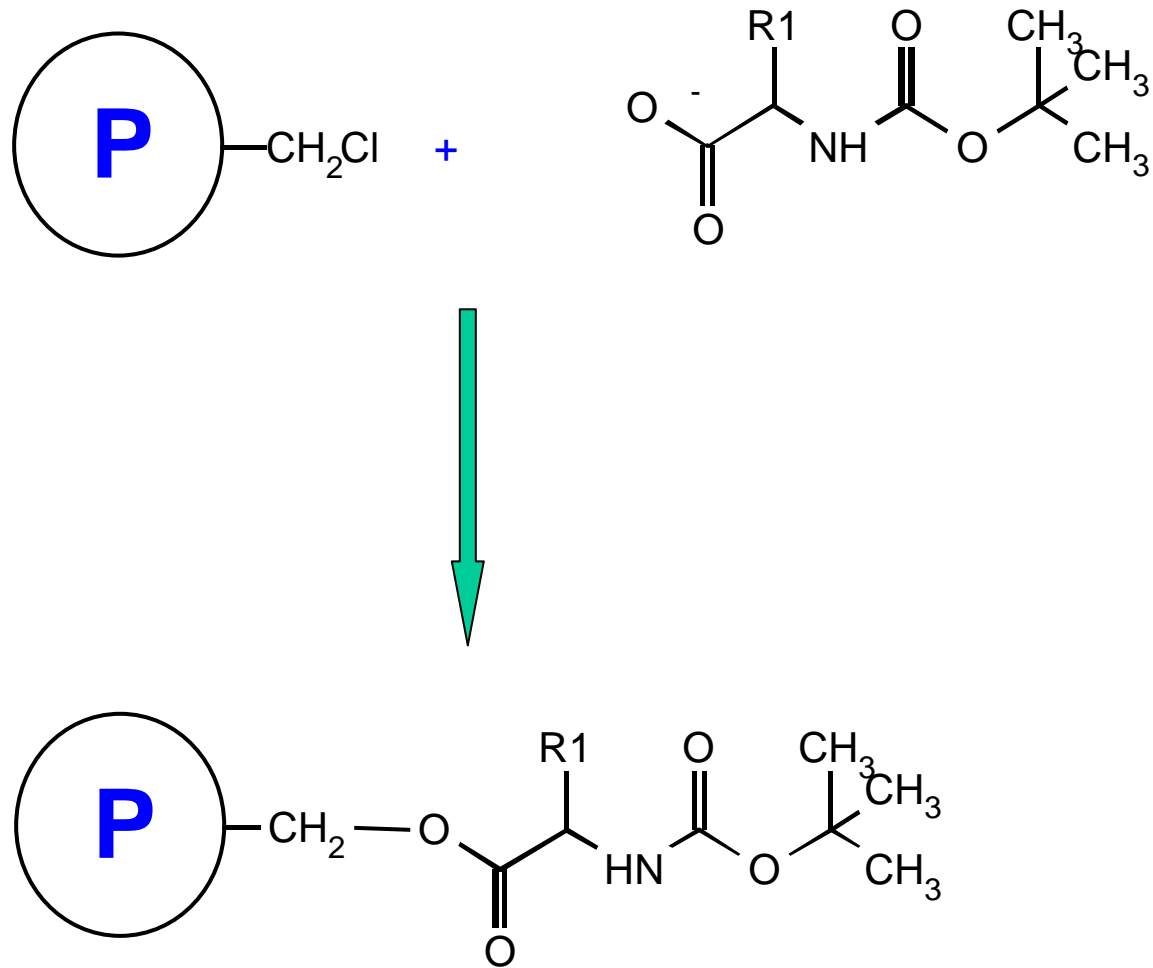


?



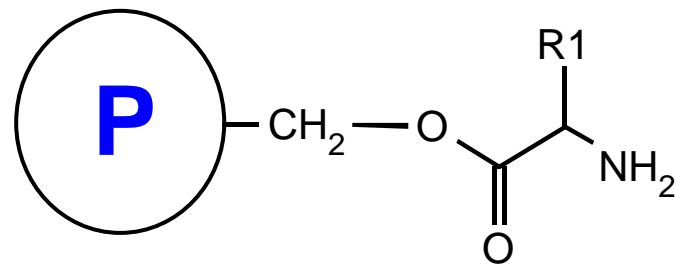
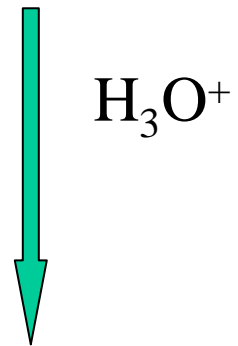
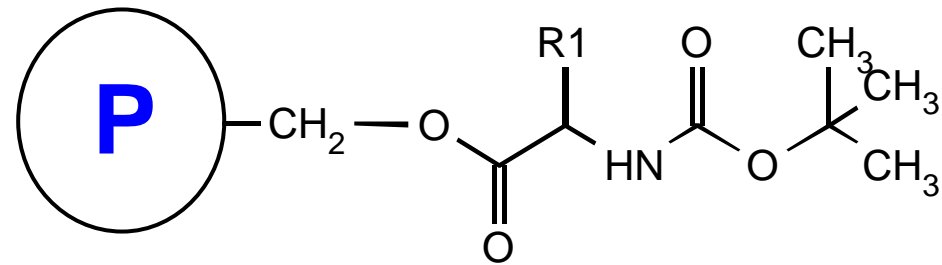


# Synthese



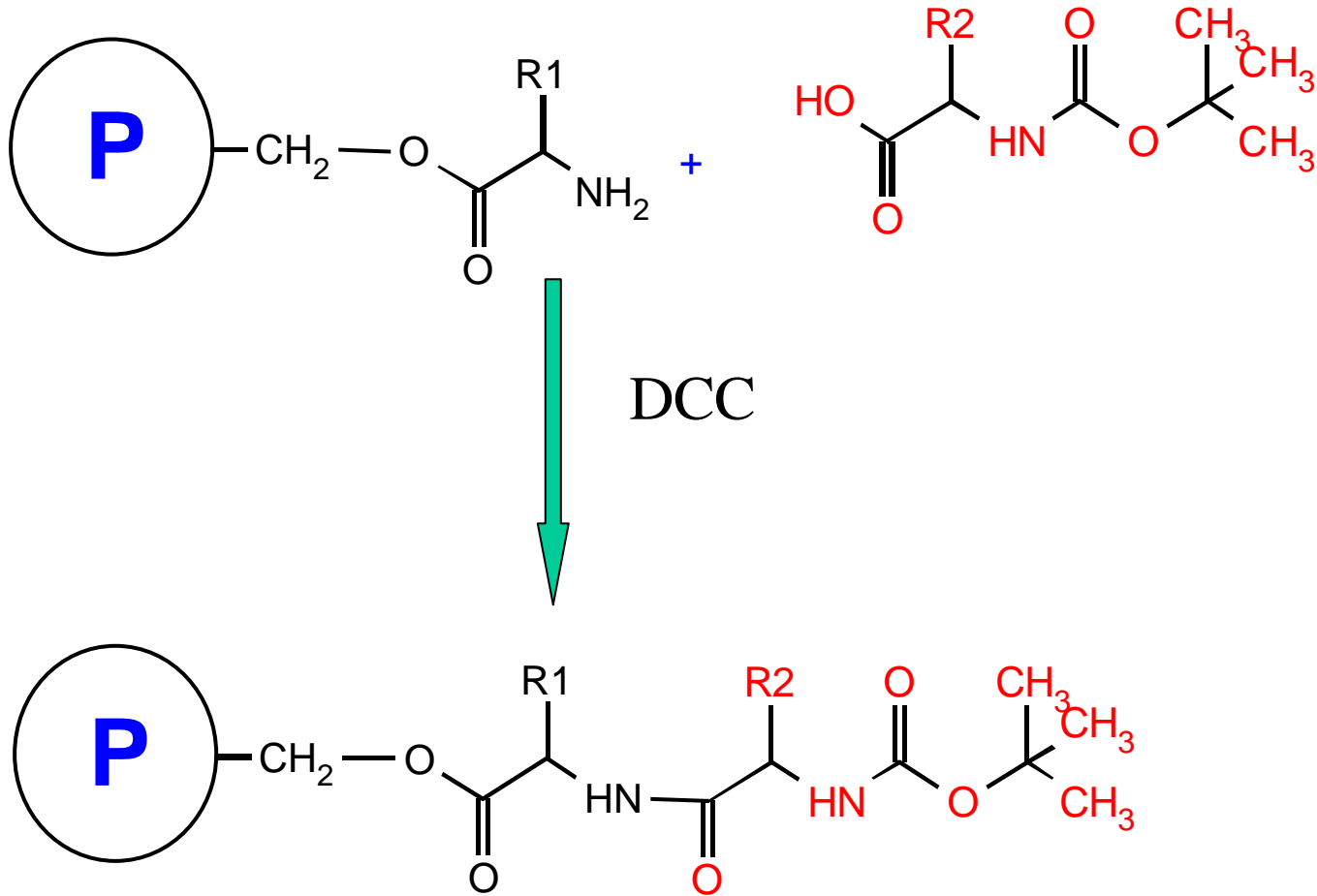


# Synthese



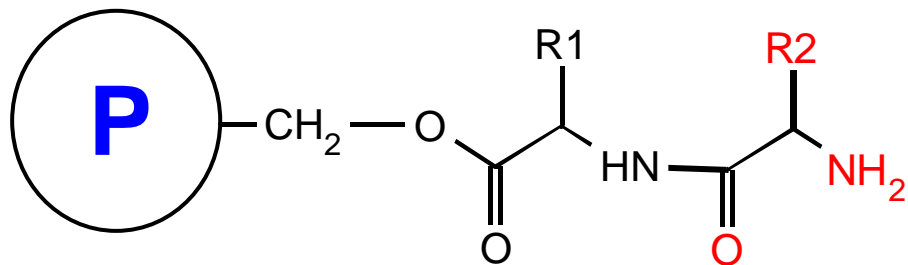
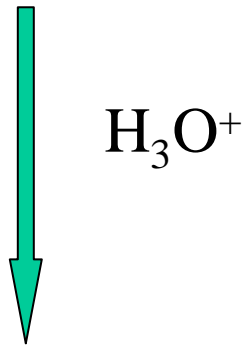
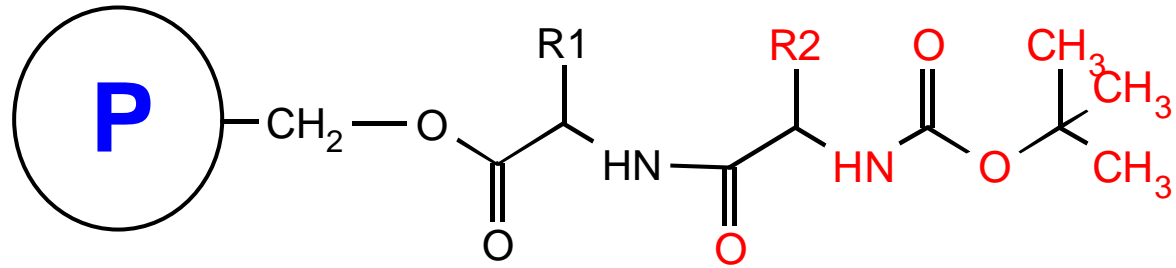


# Synthese



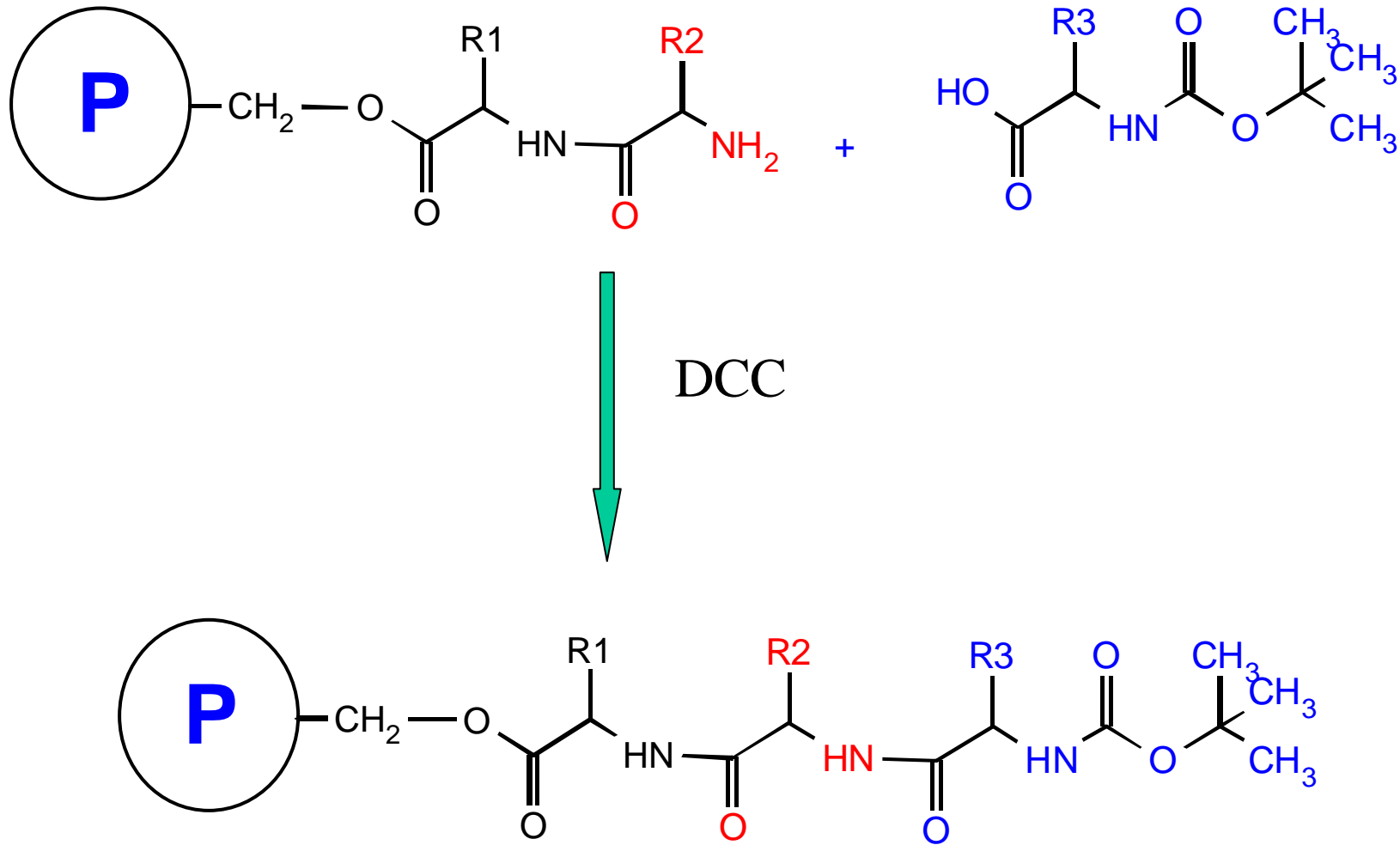


# Synthese



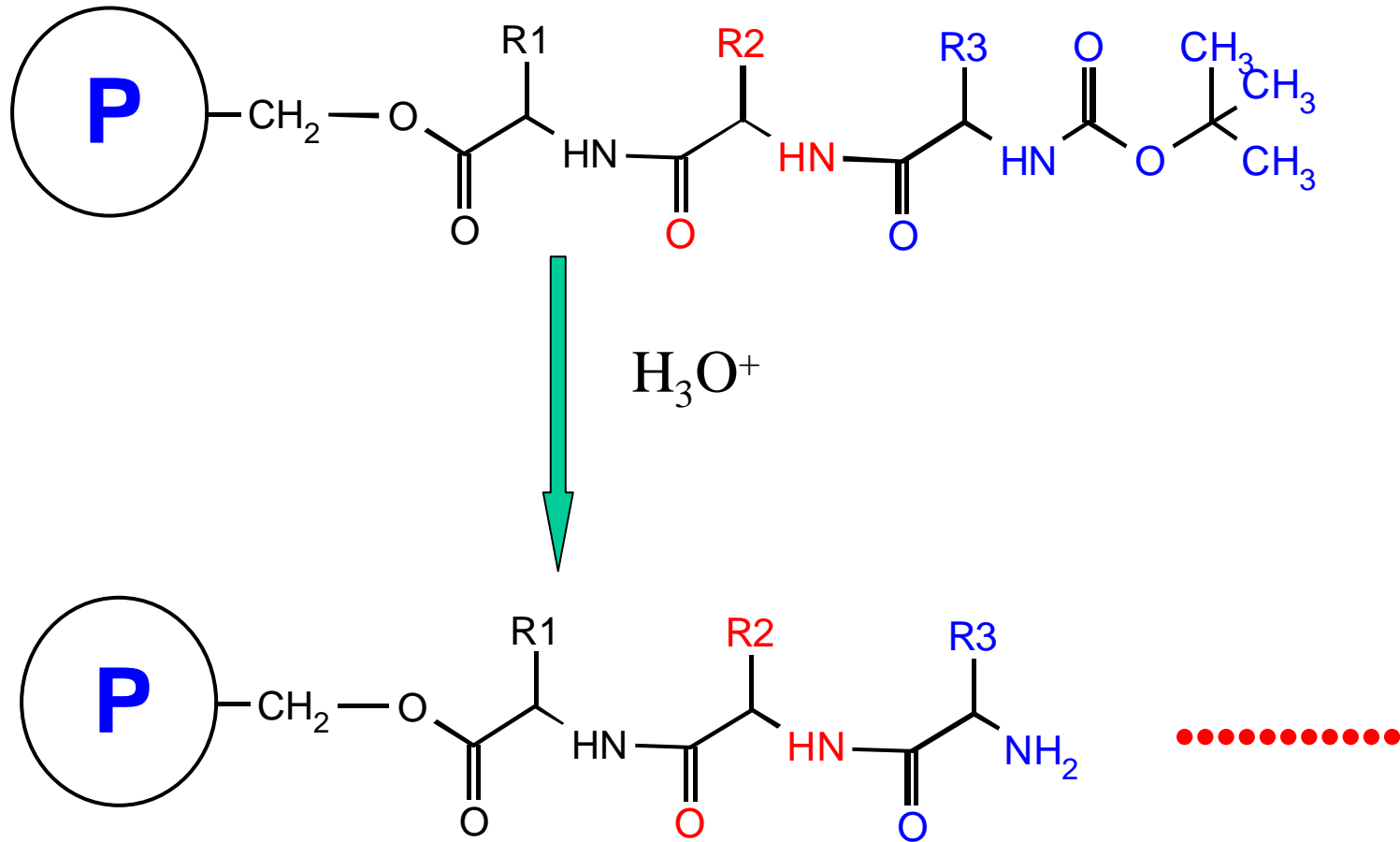


# Synthese



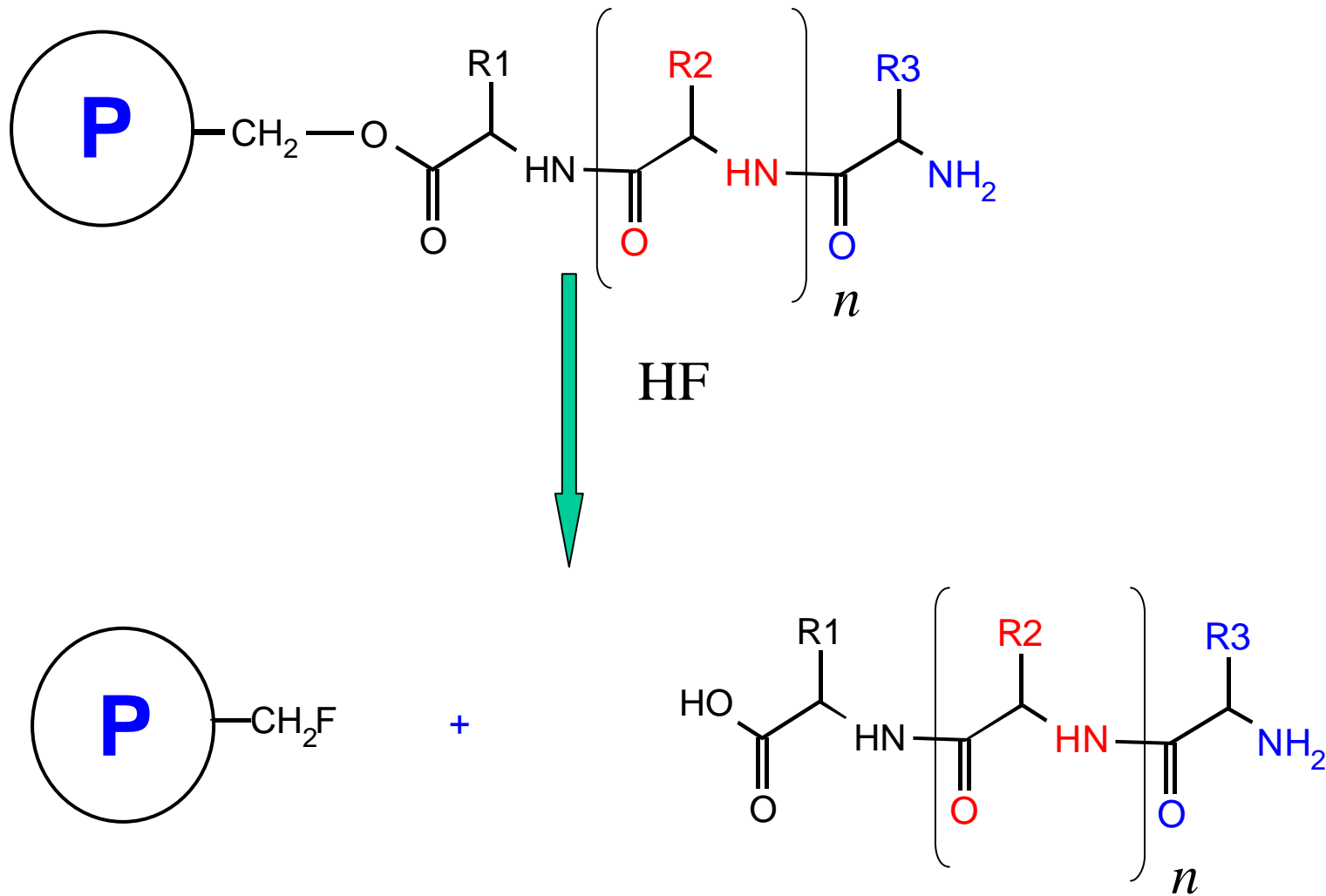


# Synthese





# Abspaltung



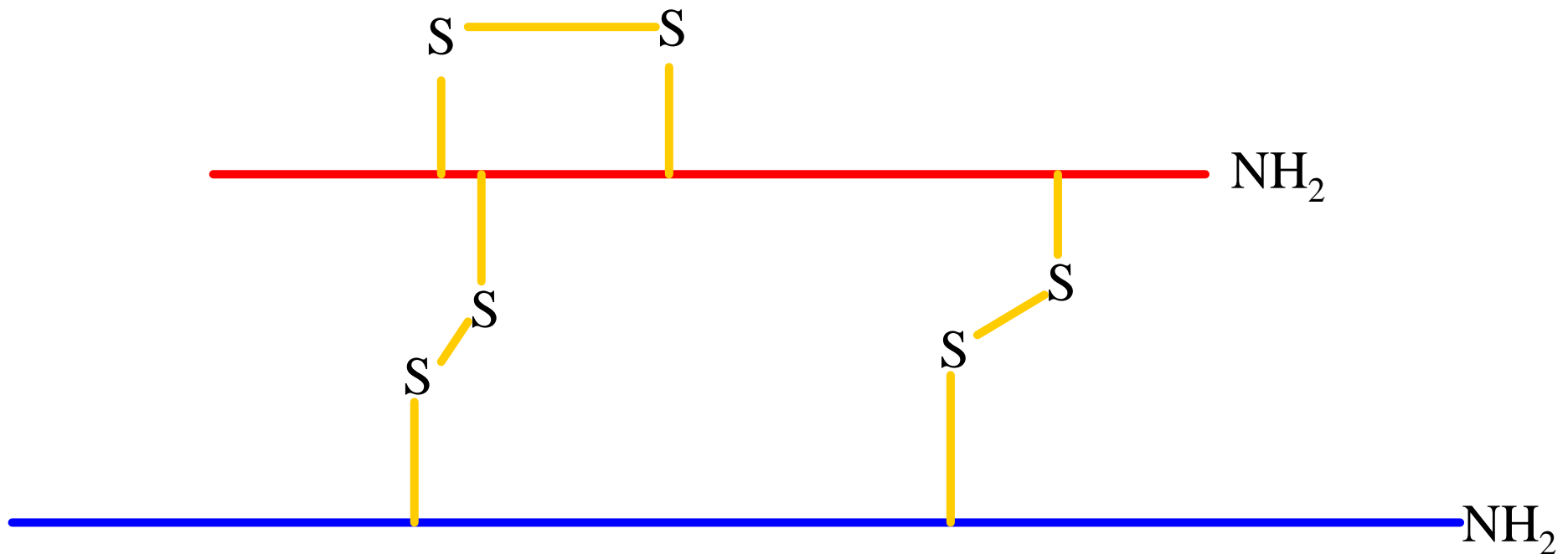


# Synthesen (Merrifield)

- **Bradykinin** – Nonapeptid
  - 85% Ausbeute in 27 Stunden (45-Schritte)
  - Ausbeute pro Schritt > 99.5% !
- **Ribonuclease** – 124 Residuen
  - 18 % Ausbeute, 369 chemische Reaktionen
  - Ausbeute pro Reaktion = 99.54%
- **Insulin**



# Insulin



- A-Kette, 21 Residuen, 8 Tage
- B-Kette, 30 Residuen, 11 Tage
- Disulfid-Brücken



# Synthese-Maschinen





# Probleme der Feststoffsynthese

- Aminosäuren wie Cystein stören (Nebenreaktionen)
- Kurze Peptide als Nebenprodukt
- Relativ kleine Mengen da die Polymere nicht sehr hoch funktionalisiert werden können



## Custom Peptide Synthesis Price Chart

Quantity	Price Per Residue (US\$)					Delivery Time (Weeks)
	5 mg	10 mg	20 mg	50 mg	100 mg	
Unpurified	25	25	25	35	40	1
Purity						
>70%	30	35	40	50	60	2
>80%	34	40	50	60	90	2
>90%	38	50	65	80	110	2
>95%	40	60	75	90	130	2
>98%	50	70	90	110	150	3
MAPS	30	40	45	50	55	2

Please note the following exceptions and guidelines to the pricing given above.

1. These prices and delivery times are limited to 6–20 mer peptides. For 21–30 mer peptides, please add an additional \$5.00 per residue and two days for delivery.
2. Add an additional week on the delivery time for peptides >50 mg and requiring >70% purity in order to accommodate the purification set up time.
3. For peptides >30 mer, >100 mg, or containing special amino acids, please ask for a quotation.
4. Mass Spec and/or Amino Acid Analysis is \$75.00 each per peptide.
5. There is no set up charge for unpurified peptides. There is a \$125 set up charge for either purification or a MAPS peptide.
6. There is a minimum order of \$250.00 per peptide.
7. Delivery time is based on the date purchase order is received.
8. We reserve the right to make exceptions on pricing for unusual peptides and difficult sequences.

### Sample Calculations:

1. <u>10mer peptide, 20mg, unpurified</u>	= \$250.00 (\$25/ residue x 10)	
	= total charge of	\$250.00
2. <u>10mer peptide, 20mg, &gt;70% purity</u>	= \$400.00 (\$40/ residue x 10)	\$400.00
	+ \$125 (set up charge)	\$125.00
	+ \$75 (mass spec)	\$75.00
	= total charge of	\$600.00
2. <u>15mer peptide, 50mg, &gt;90% purity</u>	= \$1200.00 (\$80/ residue x 15)	\$1,200.00
	+ \$125 (set up charge)	\$125.00
	+ \$75 (mass spec)	\$75.00
	= total charge of	\$1,400.00