

## 71. Synthesis of the Glycopeptide Partial Sequence A<sup>80</sup>–A<sup>84</sup> of Human Fibroblast Interferon

by Horst Kunz\* und Herbert Waldmann

Institut für Organische Chemie, Johannes-Gutenberg-Universität Mainz, Johann-Joachim-Becher-Weg 18–20,  
D–6500 Mainz

(25.X.84)

---

The glycopeptide H-(GlcNAc $\beta$ 1-)Asn-Glu-Thr-Ile-Val-OH (**10**) representing the partial sequence A<sup>80</sup>–A<sup>84</sup> of human fibroblast interferon was synthesized using the newly developed allyl-ester protection of carboxy functions. The allyl esters, which are stable to acids and to bases, can be cleaved under very mild, neutral conditions using tris(triphenylphosphine)rhodium(I) chloride or tetrakis(triphenylphosphine)palladium(0) as a catalyst. This synthetic method opens up a preparative route to glycopeptide model structures of glycoproteins of high biological interest.

---

Glycoproteins are currently receiving increasing attention, due to their central roles in biological processes, especially in biological recognition [1]. In the field of the glycoproteins, the cell-protecting principle consisting of interferons has been extensively investigated in recent years. Despite of the numerous biochemical, microbiological, and immunological studies concerning interferons, the role of the glycosidation in their production, secretion, antiviral, and antitumor activity remains not fully clarified [2] [3]. Therefore, synthetic glycopeptides which represent partial sequences of the linkage region of natural interferons may be of interest as standards in structural analysis as well as in immunological tests and as model compounds in mechanistic investigations of the activities of glycosidases and glycosyl transferases.

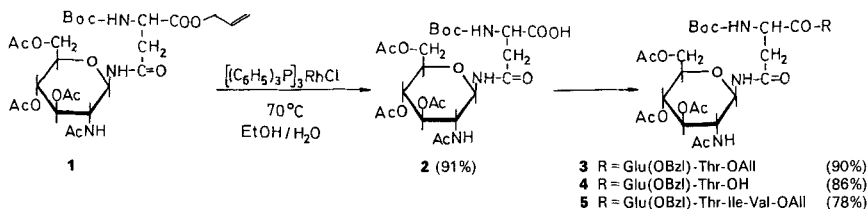
In contrast to peptides, glycopeptides are not directly available by gene-technological procedures. The chemical synthesis of such glycopeptide structures is more difficult than a peptide synthesis, since many different functional groups have to be selectively blocked, and the chemically labile glycoside and saccharide bonds must be conserved during the whole synthesis [4].

The selective deprotection is a central problem in glycopeptide synthesis [5]. A second difficulty arises from the low efficiencies in condensation reactions with this complex compounds. Using our recently developed allyl-ester protection of the carboxy function of amino acids and peptides [6] [7] we now have succeeded in synthesizing the glycopeptide partial sequence A<sup>80</sup>–A<sup>84</sup> of human fibroblast interferon [8].

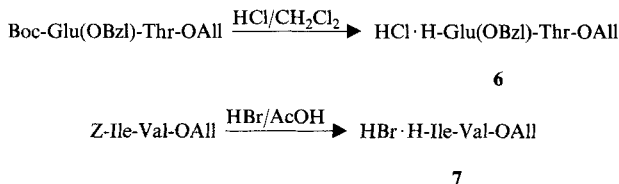
Starting with the fully protected N<sup>4</sup>-glycosylated asparagine allyl ester **1** [6], the selective carboxyl deblocking is achieved by Rh(I)-catalyzed isomerization of the allyl group followed by hydrolysis of the propenyl ester [6] [9] affording **2** nearly quantitatively (*Scheme 1*).

The condensation of **2** with the dipeptide allyl ester **6** using ethyl 2-ethoxy-1,2-dihydroquinoline-1-carboxylate (EEDQ) [10] gives the glycotriptide allyl ester **3** in 90%

Scheme 1



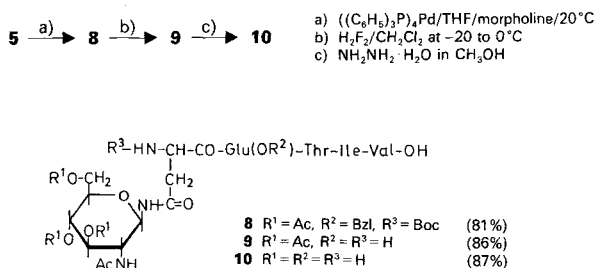
Scheme 2



yield. The dipeptide allyl esters **6** and **7** were obtained from their *N*-Boc and *N*-Z derivatives, respectively, according to the general procedures described earlier [6] (Scheme 2). Rh-catalyzed cleavage of the glycotriptide allyl ester **3** gives the selectively carboxy-deblocked product **4** in high yield, which then is elongated at the C-terminus with **7** by means of the EEDQ method to give the fully protected glycopentapeptide **5**. The high efficiency in both condensation reactions forming the complex products **3** and **5** demonstrates the advantageous properties of the small allyl ester as protecting group, which does not disturb the peptide-bond formation, neither by steric hinderance nor by decreasing the solubility.

Finally, we carried out the successive and selective removal of all protecting groups of glycopeptide **5**. To remove the allyl group, we applied the gentle but highly effective allyl transfer [11] to morpholine in tetrahydrofuran at room temperature. This method has been shown to be successful in the synthesis of *O*-glycopeptides containing the labile glycosyl-serine bond [7]. The selectively C-terminal deprotected product **8** is formed from **5** in high yield. In contrast, the classical hydrogenolytic removal of the  $\gamma$ -benzyl group of the glutamic acid ester turned out to be surprisingly critical. Therefore, we performed the benzyl-ester splitting together with the removal of the Boc group using  $\text{H}_2\text{F}_2$  in  $\text{CH}_2\text{Cl}_2$  at low temperature. Under these conditions, the *N*-glycosidic bond is not attacked and the

Scheme 3



deblocked compound **9** is obtained smoothly. Finally, the carbohydrate ester functions are hydrazinolized according to the procedure tested with *O*-glycosidic serine peptide derivatives [12].

Thus, based on the highly selective removal of the allyl-ester protection, the completely deblocked glycopentapeptide partial sequence A<sup>80</sup>–A<sup>84</sup> **10** of human fibroblast interferon was synthesized in good yield. <sup>1</sup>H- and <sup>13</sup>C-NMR spectra confirm the structures of the synthetic glycopeptides including the end product **10**; **9** and **10** are additionally identified by their FAB mass spectra.

Glycopeptides, *e.g.* **10**, of exactly specified structure are, therefore, now available in preparative amounts *via* these new techniques and may serve as model substances in biochemical and immunological investigations, *e.g.*, in recognition processes on membranes or in investigations exploring the function of carbohydrates in biological processes of glycoproteins such as interferons.

This work was supported by the *Deutsche Forschungsgemeinschaft* and by the *Fonds der Chemischen Industrie*.

### Experimental Part

1. *General*. FAB-MS were obtained on a *Varian-MAT-312* spectrometer. NMR spectra were recorded on *Bruker-WH-90* (90 MHz (<sup>1</sup>H) and 22,63 MHz (<sup>13</sup>C)), *Bruker-WP-80-DS* (20.15 MHz (<sup>13</sup>C)) and *Bruker-AM-400* spectrometer (400 MHz (<sup>1</sup>H) and 100.6 MHz (<sup>13</sup>C)).

2. *N-Acyl-dipeptide Allyl Esters*. To a soln. of amino acid allyl ester *p*-toluene sulfonate (10 mmol), Et<sub>3</sub>N (1 g, 10 mmol), and *N*-(*tert*-butyl)oxycarbonyl- or *N*-benzyloxycarbonyl-amino acid (10 mmol), in CH<sub>2</sub>Cl<sub>2</sub> (20 ml), EEDQ [10] (3 g, 12 mmol) was added. After 12 h at r.t. the mixture was worked up as described elsewhere [6].

*N*-(*tert*-Butyl)oxycarbonyl-O<sup>5</sup>-benzyl-L-glutam-1-yl-L-threonine Allyl Ester (*Boc-Glu(OBzl)-Thr-OAll*): 71% yield, m.p. 99–100°,  $[\alpha]_D^{25} = -10.6^\circ$  (*c* = 1, CH<sub>2</sub>Cl<sub>2</sub>). Anal. calc. for C<sub>24</sub>H<sub>34</sub>N<sub>2</sub>O<sub>8</sub> (478.5): C 60.23, H 7.16, N 5.85; found: C 60.06, H 7.34, N 5.81.

*N*-Benzyloxycarbonyl-L-isoleucyl-L-valine Allyl Ester (*Z-Ile-Val-OAll*): 56% yield, m.p. 96–99°,  $[\alpha]_D^{25} = -4.6^\circ$  (*c* = 1, CH<sub>2</sub>Cl<sub>2</sub>). Anal. calc. for C<sub>22</sub>H<sub>32</sub>N<sub>2</sub>O<sub>5</sub> (404.5): C 65.32, H 7.97, N 6.92; found: C 65.14, H 7.80, N 6.85.

3. *O*<sup>5</sup>-Benzyl-L-glutam-1-yl-L-threonine Allyl Ester Hydrochloride (**6**; *HCl·H-Glu(OBzl)-Thr-OAll*). A soln. of *Boc-Glu(OBzl)-Thr-OAll* (0.48 g, 1 mmol) in dry Et<sub>2</sub>O (5 ml) was stirred with 10 ml of a sat. soln. of HCl in Et<sub>2</sub>O for 2 h at r.t. After evaporation, the residue was extracted with Et<sub>2</sub>O and recrystallized from CH<sub>2</sub>Cl<sub>2</sub>/petroleum ether: 0.42 g (100%) of amorphous **6**,  $[\alpha]_D^{25} = +4.5^\circ$  (*c* = 1, CH<sub>3</sub>OH). Anal. calc. for C<sub>19</sub>H<sub>27</sub>ClN<sub>2</sub>O<sub>6</sub> · 1.5H<sub>2</sub>O (442.5): C 51.58, H 6.83, N 6.34; found: C 51.49, H 6.57, N 6.63.

4. *L-Isoleucyl-L-valine Allyl Ester Hydrobromide* (**7**; *HBr·H-Ile-Val-OAll*). At –10°, *Z*-Ile-Val-OAll (0.81 g, 2 mmol) was stirred in 10 ml of 30% HBr/AcOH for 1 h. The hydrobromide **7** was precipitated by addition of dry Et<sub>2</sub>O (200 ml), filtered off, washed with Et<sub>2</sub>O and dried *in vacuo*: 0.51 g (73%), m.p. 100–105°,  $[\alpha]_D^{25} = +5.4^\circ$  (*c* = 1, CH<sub>3</sub>OH). Anal. calc. for C<sub>14</sub>H<sub>27</sub>BrN<sub>2</sub>O<sub>3</sub> · 2H<sub>2</sub>O (387.3): C 43.41, H 8.07, N 7.23; found: C 43.56, H 8.00, N 7.54.

5. *General Procedure for the Elongation at the C-Terminus of the Glycopeptide Chain*. To a soln. of 1 mmol of *N*<sup>4</sup>-(2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-β-D-glucopyranosyl)-*N*<sup>2</sup>-[(*tert*-butyl)oxycarbonyl]-L-asparagine (**1**) or **4** (see below), of the corresponding dipeptide allyl ester hydrohalogenide (1 mmol) and of Et<sub>3</sub>N (0.1 g, 1 mmol) in CHCl<sub>3</sub> (20 ml), EEDQ (0.4 g, 1.6 mmol) was added. After stirring at r.t. for 5 d, the mixture was extracted with 10 ml of 1N HCl, 1N NaHCO<sub>3</sub> and H<sub>2</sub>O, dried over MgSO<sub>4</sub>, and evaporated *in vacuo*. The residue was recrystallized.

*N*<sup>4</sup>-(2-Acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-β-D-glucopyranosyl)-*N*<sup>2</sup>-[(*tert*-butyl)oxycarbonyl]-L-asparaginyl-O<sup>5</sup>-benzyl-L-glutam-1-yl-L-threonine Allyl Ester (**3**; *Boc-(GlcNAc3,4,6Acβ1)-Asn-Glu(OBzl)-Thr-OAll*): 90% yield, m.p. 222° (dec., from CH<sub>2</sub>Cl<sub>2</sub>/Et<sub>2</sub>O),  $[\alpha]_D^{25} = 10.9^\circ$  (*c* = 1, CH<sub>3</sub>OH). <sup>13</sup>C-NMR (22.63 MHz, (D)<sub>6</sub>DMSO): 172.3–169.2 (9s, 9 C=O); 155.2 (C=O, urethane); 136.2 (*ipso*-C); 132.2 (CH=CH<sub>2</sub>); 128.4–127.8 (3s, *o*-, *m*-, *p*-C); 117.7 (CH=CH<sub>2</sub>); 78.4 ((CH<sub>3</sub>)<sub>3</sub>C); 77.9 (C(1) of Glc); 73.3 (C(5) of Glc); 72.3 (C(3) of Glc); 29.7 (C(3) of Glu); 28.0 ((CH<sub>3</sub>)<sub>3</sub>C); 22.6 (CH<sub>3</sub>CONH); 20.4 (CH<sub>3</sub>COO); 20.1 (C(4) of Thr). Anal. calc. for C<sub>42</sub>H<sub>59</sub>N<sub>5</sub>O<sub>18</sub> (922.0): C 54.67, H 6.45, N 7.60; found: C 54.66, H 6.46, N 7.46.

$N^4$ -(2-Acetamido-3,4,6-tri-O-acetyl-2-deoxy- $\beta$ -D-glucopyranosyl)- $N^2$ -[(tert-butyl)oxycarbonyl]-L-asparaginyl-O<sup>5</sup>-benzyl-L-glutamyl-L-threonyl-L-isoleucyl-L-valine Allyl Ester (**5**; Boc-(GlcNAc3,4,6Ac $\beta$ 1)-Asn-Glu(OBzl)-Thr-Ile-Val-OAll): 78% yield, m.p. 273° (dec., from acetone/Et<sub>2</sub>O),  $[\alpha]_D^{25} = 9.5^\circ$  ( $c = 0.32$ , DMSO). <sup>13</sup>C-NMR (22.63 MHz, (D)<sub>6</sub>DMSO): 171.1–169.0 (C=O); 156.5 (C=O, urethane); 135.2 (*ipso*-C); 131.4 (CH=CH<sub>2</sub>); 128.2, 127.6 (*o*-, *m*-, *p*-C); 119.1 (CH=CH<sub>2</sub>); 78.3 ((CH<sub>3</sub>)<sub>3</sub>C); 78.0 (C(1) of Glc); 73.7 (C(5) of Glc); 72.9 (C(3) of Glc); 27.9 ((CH<sub>3</sub>)<sub>3</sub>C); 22.5 (CH<sub>3</sub>CONH); 20.2 (CH<sub>3</sub>COO); 19.3 (C(4) of Thr); 18.9, 18.3 (C(4), C(4') of Val); 15.7, 11.9 (C(3'), C(5) of Ile). FAB-MS: 1135 ( $(M + 1)^+$ ). Anal. calc. for C<sub>53</sub>H<sub>79</sub>N<sub>7</sub>O<sub>20</sub> · 1.5 H<sub>2</sub>O (1161.3)<sup>1)</sup>: C 54.82, H 7.11, N 8.44; found: C 54.35, H 6.69, N 8.49.

$6. N^4$ -(2-Acetamido-3,4,6-tri-O-acetyl-2-deoxy- $\beta$ -D-glucopyranosyl)- $N^2$ -[(tert-butyl)oxycarbonyl]-L-asparaginyl-O<sup>5</sup>-benzyl-L-glutamyl-L-threonine (**4**; Boc-(GlcNAc3,4,6Ac $\beta$ 1)-Asn-Glu(OBzl)-Thr-OH). At 70°, tris-(triphenylphosphine)rhodium(I) chloride (0.1 g, 0.11 mmol) was added to a soln. of **3** (0.92 g, 1 mmol) in EtOH/H<sub>2</sub>O 9:1 (20 ml). After 2 h stirring, the mixture was filtered, the filtrate evaporated *in vacuo*, and the residue recrystallized from MeOH/Et<sub>2</sub>O: 0.76 g (86%), m.p. 215°,  $[\alpha]_D^{25} = -12.2^\circ$  ( $c = 1$ , CH<sub>3</sub>OH). <sup>13</sup>C-NMR (22.63 MHz, CD<sub>3</sub>OD): 174.5–171.3 (C=O); 157.4 (C=O, urethane); 137.5 (*ipso*-C); 129.5, 129.1 (*o*-, *m*-, *p*-C); 81.1 ((CH<sub>3</sub>)<sub>3</sub>C); 79.5 (C(1) of Gln); 38.3 (C(3) of Asn); 31.2 (C(3) of Glu); 28.7 ((CH<sub>3</sub>)<sub>3</sub>C); 22.9 (CH<sub>3</sub>CONH); 20.6 (CH<sub>3</sub>COO). Anal. calc. for C<sub>39</sub>H<sub>55</sub>N<sub>5</sub>O<sub>18</sub> · 0.5(C<sub>2</sub>H<sub>5</sub>)<sub>2</sub>O (919.0): C 53.58, H 6.58, N 7.62; found: C 53.77, H 6.64, N 7.56.

$7. N^4$ -(2-Acetamido-3,4,6-tri-O-acetyl-2-deoxy- $\beta$ -D-glucopyranosyl)- $N^2$ -[(tert-butyl)oxycarbonyl]-L-asparaginyl-O<sup>5</sup>-benzyl-L-glutamyl-L-threonyl-L-isoleucyl-L-valine (**8**; Boc-(GlcNAc3,4,6Ac $\beta$ 1)-Asn-Glu(OBzl)-Thr-Ile-Val-OH). Under Ar, tetrakis(triphenylphosphine)palladium(0) (0.05 g, 4.4 · 10<sup>-5</sup> mol) was added to a soln. of **5** (0.5 g, 4.4 · 10<sup>-4</sup> mol) in THF/DMSO 10:1 (33 ml) followed by the addition of morpholine (0.44 ml, 4.4 · 10<sup>-3</sup> mol). After 3 h at r.t., the solv. was evaporated *in vacuo*, the residue dissolved in CHCl<sub>3</sub> (100 ml), extracted twice with 50 ml of 2N HCl, dried over MgSO<sub>4</sub>, and evaporated *in vacuo*. The crude **8** was recrystallized from MeOH/Et<sub>2</sub>O: 0.39 g (81%), m.p. 252° (dec.),  $[\alpha]_D^{25} = -21.2^\circ$  ( $c = 0.14$ , CD<sub>3</sub>OD). <sup>13</sup>C-NMR (20.15 MHz, (D)<sub>6</sub>DMSO): 177.3–169.2 (C=O); 155.9 (C=O, urethane); 136.2 (*ipso*-C); 128.6, 128.3 (*o*-, *m*-, *p*-C); 78.4 ((CH<sub>3</sub>)<sub>3</sub>C); 77.9 (C(1) of Glc); 73.3 (C(5) of Glc); 72.3 (C(3) of Glc); 28.0 ((CH<sub>3</sub>)<sub>3</sub>C); 22.5 (CH<sub>3</sub>CONH); 20.3 (CH<sub>3</sub>COO); 19.3 (C(4) of Thr); 19.0, 18.6 (C(4), C(4') of Val); 15.2, 11.0. (C(3'), C(5) of Ile). Anal. calc. for C<sub>50</sub>H<sub>75</sub>N<sub>7</sub>O<sub>20</sub> (1094.2): C 54.88, H 6.91, N 8.96; found: C 54.69, H 6.78, N 8.75.

$8. N^4$ -(2-Acetamido-3,4,6-tri-O-acetyl-2-deoxy- $\beta$ -D-glucopyranosyl)-L-asparaginyl-L-glutamyl-L-threonyl-L-isoleucyl-L-valine (**9**; H-(GlcNAc3,4,6Ac $\beta$ 1)-Asn-Glu-Thr-Ile-Val-OH). At -20°, dry liq. H<sub>2</sub>F<sub>2</sub> (1 ml) was added to **8** (0.18 g, 1.64 · 10<sup>-4</sup> mol) suspended in CH<sub>2</sub>Cl<sub>2</sub> (5 ml). After 30 min at -15° and an additional 30 min at -5°, the solv. was allowed to evaporate in a fume hood. Then, Et<sub>2</sub>O (30 ml) was added, the mixture evaporated *in vacuo* and the crude **9** recrystallized from MeOH/Et<sub>2</sub>O giving 0.13 g (86%) of crystalline solid, m.p. 190–195° (dec.),  $[\alpha]_D^{25} = -6.2^\circ$  ( $c = 0.13$ , DMSO). <sup>1</sup>H-NMR (90 MHz, (D)<sub>6</sub>DMSO): 1.98, 1.96, 1.91, 1.76 (4s, 4 CH<sub>3</sub>CO); 1.2–0.85 (*m*, CH<sub>3</sub>(4) of Thr, 2 CH<sub>3</sub>-C(3) of Val, CH<sub>3</sub>(3') and CH<sub>3</sub>(5) of Ile). FAB-MS: 904 ( $(M + 1)^+$ ).

$9. N^4$ -(2-Acetamido-2-deoxy- $\beta$ -D-glucopyranosyl)-L-asparaginyl-L-glutamyl-L-threonyl-L-isoleucyl-L-valine (**10**; H-(GlcNAc $\beta$ 1)-Asn-Glu-Thr-Ile-Val-OH). At r.t., **9** (0.11 g, 1.19 · 10<sup>-4</sup> mol) suspended in MeOH (15 ml) was stirred with NH<sub>2</sub>NH<sub>2</sub> · H<sub>2</sub>O (3 ml) for 3 h. Acetone (20 ml) was dropped into the mixture (at 0°) and, after a further 30 min, it was evaporated to dryness at r.t. The residue was dissolved in H<sub>2</sub>O (5 ml) and *i*-PrOH (20 ml) and precipitated by AcOEt: 0.082 g (87%), m.p. 210° (dec.),  $[\alpha]_D^{25} = -21.2^\circ$  ( $c = 0.115$ , H<sub>2</sub>O). <sup>1</sup>H-NMR<sup>2)</sup> (400 MHz, D<sub>2</sub>O, (D<sub>6</sub>)acetone as internal standard): 5.05 (*d*,  $J_{1,2} = 9.6$ , H-C(1) of Glc); 4.44 (*dd*,  $J_{2,3a} = 9.5$ ,  $J_{2,3b} = 5.5$ , H-C(2) of Glu); 4.39 (*dd*,  $J_{2,3a} = 4.5$ ,  $J_{2,3b} = 8$ , H-C(2) of Asn); 4.28 (*d*,  $J = 6.5$ , H-C(2) of Thr); 4.20 (*d*,  $J = 9.5$ , H-C(2) of Val); 4.09 (*d*,  $J = 6$ , H-C(2) of Ile); 4.085 (*m*, H-C(3) of Thr); 3.83 (*dd*,  $J_{6a,6b} = 13$ ,  $J_{6a,5} = 2.5$ , H<sub>a</sub>-C(6) of Glc); 3.79 (*dd*,  $J_{2,3} = 10.1$ , H-C(2) of Glc); 3.72 (*dd*,  $J_{6b,5} = 5$ , H<sub>b</sub>-C(6) of Glc); 3.57 (*dd*,  $J_{3,4} = 9$ , H-C(3) of Glc); 3.49–3.41 (*m*, H-C(4) and H-C(5) of Glc); 3.0 (*dd*,  $J_{gem} = 17.5$ , H<sub>a</sub>-C(3) of Asn); 2.87 (*dd*, H<sub>b</sub>-C(3) of Asn); 2.43–2.36 (*m*, 2H-C(4) of Glu); 2.15–2.0 (*m*, 2H-C(3) of Glu); 1.98 (*s*, CH<sub>3</sub>CO); 1.9–1.8 (*m*, H-C(3) of Val); 1.5–1.4 (*m*, H-C(3) of Ile); 1.25–1.15 (*m*, 2H-C(4) of Ile); 1.16 (*d*,  $J = 6.5$ , CH<sub>3</sub>(4) of Thr); 0.92–0.86 (*m*, CH<sub>3</sub>(3') of Ile, 2 CH<sub>3</sub>-C(3) of Val); 0.82 (*t*,  $J = 6$ , CH<sub>3</sub>(5) of Ile). <sup>13</sup>C-NMR<sup>2)</sup> (100.6 MHz, (D<sub>2</sub>O, (D<sub>6</sub>)acetone as internal standard): 175.1–168.8 (C=O); 78.66 (C(1) of Glc); 60.87 (C(6) of Glc); 49.85 (C(2) of Asn); 36.39 (C(3) of Ile); 35.63 (C(3) of Asn); 30.59 (C(3) of Val); 27.04 (C(4) of Ile); 26.9 (C(4) of Glu); 24.75 (C(3) of Glu); 22.43 (CH<sub>3</sub>CO); 19.2 (C(4) of Thr); 18.88, 17.72 (C(4), C(4') of Val); 15.0 (C(3') of Ile); 10.25 (C(5) of Ile). FAB-MSM<sup>2)</sup>: 778 (72,  $M^+$ ), 800 (100,  $M^+ - 1 + Na^+$ ).

<sup>1)</sup> Compound **5** obstinately retained H<sub>2</sub>O and traces of solvs. This causes the deviations in the anal. values.

<sup>2)</sup> The free glycopentapeptide **10** exhibits a remarkable complexation ability indicated by the base peak of the FAB-MS. Since it can be recrystallized only from H<sub>2</sub>O containing solvents, small amounts of inorganic impurities are not removable. The high field NMR spectra show that **10** is free of org. impurities.

## REFERENCES

- [1] K. Olden, B. A. Bernard, S. L. White, J. B. Parent, *J. Cell. Biochem.* **1982**, 18, 313, Cellular Recognition 637.
- [2] e.g., E. Dinolfo, K. C. Chadha, *Microbiol. Immunol.* **1983**, 27, 589.
- [3] E. A. Havell, W. A. Carter, *Virology* **1981**, 108, 80.
- [4] H. Kunz, *Nachr. Chem. Tech. Lab.* **1984**, 32, 11.
- [5] a) H. G. Garg, R. W. Jeanloz, *Carbohydr. Res.* **1972**, 23, 437; b) *ibid.* **1976**, 52, 247.
- [6] H. Waldmann, H. Kunz, *Liebigs Ann. Chem.* **1983**, 1712.
- [7] H. Kunz, H. Waldmann, *Angew. Chem. Int. Ed.* **1984**, 23, 71.
- [8] a) R. Derynck, J. Content, E. De Clercq, G. Volckaert, J. Tavernier, R. Devos, W. Fiers, *Nature (London)* **1980**, 285, 542; b) T. Taniguchi, N. Mantei, M. Schwarzstein, S. Nagata, M. Muramatsu, C. Weissmann, *ibid.* **1980**, 285, 547.
- [9] E. J. Corey, J. W. Suggs, *J. Org. Chem.* **1973**, 38, 3234.
- [10] B. Belleau, G. Malek, *J. Am. Chem. Soc.* **1968**, 90, 1651.
- [11] B. M. Trost, *Acc. Chem. Res.* **1980**, 13, 385.
- [12] P. Schultheiss-Reimann, H. Kunz, *Angew. Chem. Int. Ed.* **1983**, 22, 62.