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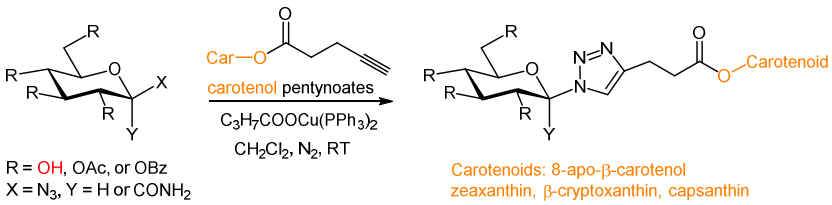

Graphical Abstract

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Synthesis of carotenoid-monosaccharide conjugates via azide–alkyne click-reaction

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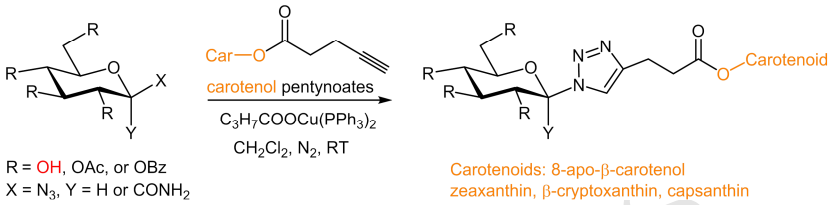

R = OH, OAc, or OBz
X = N_3, Y = H or $CONH_2$

Carotenoids: 8-apo-β-carotenol
zeaxanthin, β-cryptoxanthin, capsanthin

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ABSTRACT

Carotenoid pentynoates were coupled to protected and unprotected sugar azides via an azide-alkyne click-reaction using bis-triphenylphosphano-copper(I)-butyrate ($C_3H_7COOCu(PPh_3)_2$) complex. Protected sugars delivered the conjugates with excellent yields, whereas with unprotected ones amphipathic carotenoid-sugar derivatives were obtained in good or moderate yields in a simple way.

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1. Introduction

Glycosides and glycosyl esters of carotenoids have been described as naturally occurring amphipathic molecules. Many of them were found in extremophile microorganisms, and they are believed to be partially responsible for the resistance of these creatures against heat and/or high osmotic pressure.[1] Thermoxanthins, carotenoid glycoside-branched fatty acid esters of diverse structures, were investigated thoroughly as main pigments of *Thermus* bacteria. The polar sugar moieties and the length of these carotenoid derivatives facilitate their lateral arrangement in cell membranes.[2] Once incorporated in the membrane they could change its fluidity and can act as antioxidants, as well. Carotenoids are known as good antioxidants, whilst hydrophilic carotenoids are even more so,[3] therefore carotenoid glycosides in the cell membrane can play a role in the inhibition of oxidative stress. Since carotenoid glycosides and esters are of limited availability from natural sources, their effect on oxidative stress has not been studied yet.

For the chemical synthesis of carotenoid glycosides only a few examples were described. A classical Königs-Knorr reaction with zeaxanthin resulted in a complex mixture containing mono- and diglucosides in low yields.[4] The total synthesis of thermoxanthins via selective glucosidation of hydroxy-β-ionone has also been reported, and their effect on the stability of cellular phospholipid membrane was examined.[5] Glycosides of astaxanthin and adonixanthin have been prepared by recombinant DNA techniques using modified *E. coli*.[6] The target compounds in the above procedures were obtained in very low overall yields (2-8%) and/or required complicated isolation.

A new tentative approach for the synthesis of carotenoid thioglucosides has been reported using β-carotene and isozeaxanthin as starting materials.[7] The products contained the sugar moieties in position 4 and 4' of the carotenoid ring, and after deprotection, could be regarded as mimetics of naturally occurring thermoxanthins. Some protected 3-*O*-glycosyl-carotenoids have also been prepared in good or moderate yields by modern glycosylation methods.[8] These methods surpassed the previous procedures in terms of yields, but cannot be considered as a general methodology for all kind of carotenoids. Another problem arose during deprotection of the acetyl/benzoyl protected sugar moieties, the unprotected glycosides could be obtained only in low yields.

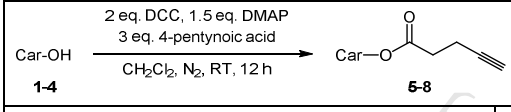
In order to couple monosaccharides to carotenoids with good yields, a new approximation was chosen, which would include unprotected sugars and would give similar amphipathic compounds in one single step. Therefore, we planned to use the copper(I) catalyzed (3+2) azide-alkyne cycloaddition reaction (CuAAC) for the coupling of sugar azides to carotenoid pentynoates. Click chemistry, requiring mild reaction conditions and providing a high yield of products,[9] proved to be an appropriate choice for the very sensitive carotenoids, which have previously been coupled with polyethyleneglycol azides in click reactions.[10]

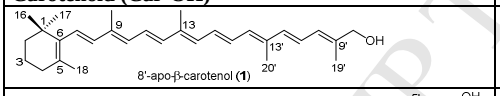
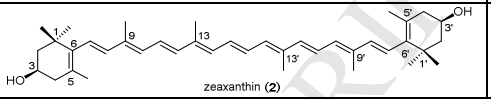
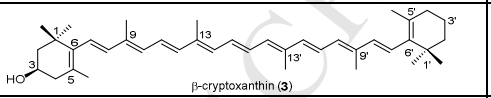
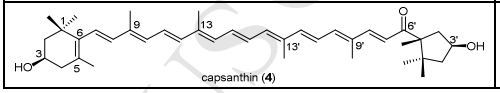
Recently, the use of bis-triphenylphosphano-copper(I)-butyrate ($C_3H_7COOCu(PPh_3)_2$) complex[11] has been reported as an efficient catalyst for the synthesis of 1-glycopyranosyl-4-substituted-1,2,3-triazoles.[12] This paper presents our studies on the coupling of protected and free glycosyl azides with carotenoid pentynoates using $C_3H_7COOCu(PPh_3)_2$ as a catalyst.

2. Results and discussion

Acetyl/benzoyl protected and free glycosyl azides were prepared according to known procedures.[13-15] Hydroxy carotenoids were treated with NaH and propargyl chloride in DMF to give propargyl ethers, but no reaction was detected. The hydroxy carotenoids were planned to be esterified with propiolic acid according to Steglich's method,[16] however, in these reactions unstable products formed in low yields. Hence, 4-pentynoic acid was the reagent of choice, which, in the presence of DCC and DMAP, gave crystalline carotenoid pentynoates in acceptable yields (Table 1).

Table 1. Preparation of 4-pentynoate esters of hydroxy carotenoids



Carotenoid (Car-OH)	Product (yield)
 8'-apo-β-carotenol (**1**)	**5** mono-pentynoate (75%)[a]
 zeaxanthin (**2**)	**6** dipentynoate (53%)
 β-cryptoxanthin (**3**)	**7** mono-pentynoate (90%)
 capsanthin (**4**)	**8** dipentynoate (59%)

[a] Yield calculated for two steps starting from 8'-apo-β-carotenal.

8'-Apo-β-carotenol pentynoate (**5**) was chosen as a model compound for the preliminary experiments. Coupling with peracetyl glycosyl azide (**9**) in the presence of CuI as catalyst was not observed in dichloromethane, toluene/*i*-propanol or DMF, even with triethylamine or ethyl-diisopropylamine (EDIPA).[10] The use of bis-triphenylphosphano-copper(I)-butyrate in dichloromethane, however, resulted in the formation of the triazole **15** (Table 2). Under the same conditions other protected and unprotected sugar azides (**10**-**14**) were reacted with 8'-apo-β-carotenol pentynoate (**5**) giving the target triazoles (**16**-**20**). With the exception of peracetylated 6-deoxy-6-triazolyl-glucose derivative (**18**), the acyl protected glycosyl triazoles formed in excellent yields.

Keeping the reactants in solution was described to be a crucial requirement for a successful click-reaction.[9,17] However, in our experiments dichloromethane was found to be a suitable solvent even in reactions with unprotected sugars that are insoluble in this solvent, they delivered the products in lower but still acceptable yields. These conditions allow the direct synthesis of unprotected glycosyl triazoles, otherwise selective deacylation of the sugar would be hard to achieve.

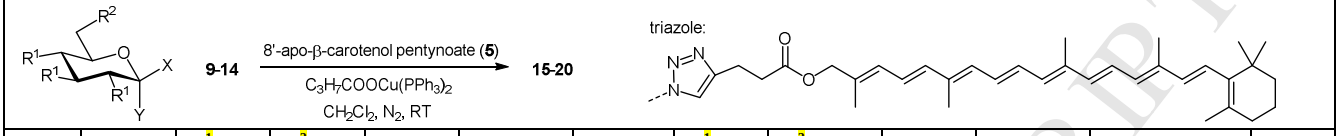
With 1-carboxamido-β-D-glucopyranosyl azide (**14**) the conversion of 8'-apo-β-carotenol pentynoate (**5**) was not complete (~70%). Further experiments on coupling deprotected sugar azides (**13**, **14**) with other hydroxy carotenoid pentynoates (**6**-**8**) were performed under the same conditions (Table 3). All studied carotenoid pentynoates gave good yields with β-D-glucopyranosyl azide (**13**). Starting from a more hydrophilic unprotected sugar was expected to improve the hydrophilicity of the product. To achieve this, 1-carboxamido-β-D-glucopyranosyl azide (**14**) was reacted under the same conditions, but unfortunately yielded complex mixtures with only traces of the triazoles. The low yields in the case of unprotected 1-carboxamido-1-azido-D-glucose can be explained by its even worse solubility in dichloromethane, in addition to the steric hindrance of the azido group as well as the hydrogen bond between the azide and the $CONH_2$.[18,19] To optimize the conditions for 1-carboxamido-1-azido-D-glucose (**14**) acetonitrile was applied as a solvent in the presence or absence of

triethylamine, but no improvements were observed. We also tried to couple capsanthin dipentynoate (**8**) to **14** using CuI as a catalyst in dichloromethane with EDIPA, however, transformation of the starting materials was not detected.

3. Conclusion

Carotenoid pentynoates were synthesized by the Steglich method, and coupled with protected and unprotected sugar azides in a CuAAC reaction using bis-triphenylphosphano-copper(I)-butyrate ($C_3H_7COOCu(PPh_3)_2$) catalyst in dichloromethane. No other reaction conditions were found to be suitable for the coupling of carotenoid pentynoates to sugar azides. In spite of the low solubility, unprotected β-D-glucopyranosyl azide can be used in these reactions, however, 1-carboxamido-β-D-glucopyranosyl azide is less suitable. This way unprotected carotenyloxy-3-oxopropyl-1,2,3-triazol-1-yl glucosides were prepared directly in a single coupling step. Our method provides an easy and general way for the synthesis of these biologically interesting molecules. The new sugar derivatives of capsanthin are especially promising, because capsanthin is one of the best antioxidants among carotenoids.[20]

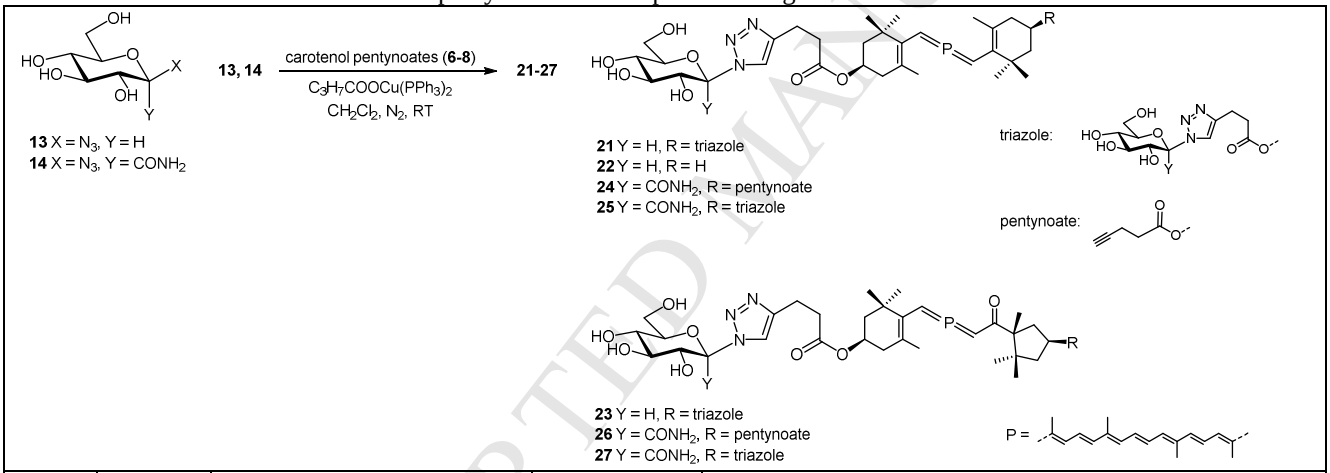
Table 2. CuAAC reaction of 8'-apo-β-carotenol-pentynoate with sugar azides



entry	sugar	R^1	R^2	X	Y	product	R^1	R^2	X	Y	reaction time	yield
1	**9**	OAc	OAc	N_3	H	**15**	OAc	OAc	triazole	H	1.5 h	92%
2	**10**	OAc	OAc	H	N_3	**16**	OAc	OAc	H	triazole	2 h	95%
3	**11**	OBz	OBz	N_3	$CONH_2$	**17**	OBz	OBz	triazole	$CONH_2$	7 h	93%
4	**12**	OAc	N_3	H	OAc	**18**	OAc	triazole	H	OAc	8 h	63%
5	**13**	OH	OH	N_3	H	**19**	OH	OH	triazole	H	1 day	72%
6	**14**	OH	OH	N_3	$CONH_2$	**20**	OH	OH	triazole	$CONH_2$	2 days	49% [a]

[a] Conversion of **5** was ~70%

Table 3. CuAAC reaction of carotenol pentynoates with unprotected sugar azides



entry	sugar	carotenol pentynoate	reaction time	products (yields)
1	**13**	zeaxanthin dipentynoate (**6**)	12 h	**21** ditriazole (65%)
2	**13**	β-cryptoxanthin pentynoate (**7**)	12 h	**22** (76%)
3	**13**	capsanthin dipentynoate (**8**)	12 h	**23** ditriazole (71%)
4	**14**	zeaxanthin dipentynoate (**6**)	2 days	**24** mono-triazole (traces[a]) and **25** ditriazole (traces[a])
5	**14**	β-cryptoxanthin pentynoate (**7**)	2 days	no reaction
6	**14**	capsanthin dipentynoate (**8**)	2 days	**26** mono-triazole (traces[a]) and **27** ditriazole (15%)

[a] detected by MS in the worked-up reaction mixture.

4. Experimental section

Melting points were measured on an HMK hot-stage (Franz Küstner Nacht KG) and are uncorrected. NMR spectra were recorded with a Bruker Avance III Ascend 500 spectrometer (500/125 MHz for $^1H/^{13}C$). The ^{13}C and ^1H NMR assignments for **5**, **6**, **7**, **8** and **21** were made on the basis of 1D (^1H, ^{13}C APT) and 2D (COSY, HSQC) experiments, the assignments for the other compounds were based on structural similarities with the above molecules. Chemical shifts are referenced to the residual solvent signals, or to Me_4Si (^1H). The IR spectra were run on an Impact 400 (Nicolet) FT-IR spectrophotometer in KBr pellets using a KBr pellet as the background reference spectrum. Molar masses were obtained by an Autoflex II MALDI instrument (Bruker Daltonics). 2,5-Dihydroxy-benzoic acid (DHB) was used for the ionization of the samples. Mass spectra were monitored either in positive or in negative mode (depending on the chemical structure) with pulsed ionization (λ = 337 nm; nitrogen laser). Spectra were measured in reflectron mode using a delayed extraction of 120 nsec. The elemental analysis measurements were performed on a Fisons EA 1110 CHNS apparatus.

Thin layer chromatography was performed on TLC Silica gel 60 F_{254} on Al sheets (Merck), and the spots were visualized under UV light and by gentle heating. Preparative layer chromatography was executed on PLC Silica gel 60 F_{254} 1 mm on glass plate (Merck). For column chromatography Kieselgel 60 (Merck, particle size 0.063-0.200 mm) was used. All reagents used for synthesis were commercial and of analytically pure quality and all organic solvents were of HPLC grade. Organic solutions were dried over anhydrous Na_2SO_4 and concentrated

under reduced pressure at 40 ºC (bath temperature). Sugar azides were prepared by published methods;[13-15] the carotenoids were isolated from red pepper *Capsicuum anuum* by standard procedure.[21] Crude 8'-apo-β-carotenol was freshly prepared from commercially available 8'-apo-β-carotenal (Fluka), because the alcohol is susceptible to oxidation.

*4.1. 8'-Apo-β-carotenol pentynoate (**5**)*

8'-Apo-β-carotenal (300 mg, 0.72 mmol, UV (hexane) λ_{max}, nm: 480, 454) was dissolved in toluene (200 mL) and 96% ethanol (100 mL), $NaBH_4$ (300 mg, 7.9 mmol) was added and the mixture was vigorously stirred under nitrogen for 1 h. After the solution became brighter and TLC showed complete conversion to the more polar carotenol, KOH (1 g) was added to the solution. Five minutes later the solution was washed with water (5 x 100 mL), dried (Na_2SO_4) and the solvent was evaporated under reduced pressure. The residue (300 mg, UV (hexane) λ_{max}, nm: 450, 425, 402) was immediately dissolved in dry dichloromethane (150 mL). To the stirred solution 4-pentynoic acid (140 mg, 1.43 mmol), dimethylaminopyridine (DMAP, 175 mg, 1.43 mmol) and dicyclohexyl carbodiimide (DCC, 296 mg, 1.43 mmol) were added. The mixture was stirred for 12 h under nitrogen atmosphere, in darkness, at room temperature. Some drops of water (~0.5 mL) and 10 minutes later hexane (150 mL) were added to the reaction mixture, the obtained precipitate was filtered out, the mother liquor was dried (Na_2SO_4) and evaporated under reduced pressure. The product **5** was crystallized from methanol/toluene mixture by the addition of some water. The formed crystals were filtered off, dried in vacuum and stored in closed ampoules under argon. Yield: 268 mg (75%) red plates; mp: 108-109 °C; R_f = 0.60 (hexane–acetone, 4:1); IR (KBr, cm^{-1}): 1720 *s* (ν C=O, ester), 2119 *w* (ν C≡C), 3279 *w* (ν ≡CH); ^{1}H-NMR (500 MHz, $CDCl_3$): δ = 0.93 (s, 6H, 16, 17-Me), 1.36-1.38 (m, 2H, H-2), 1.51-1.53 (m, 2H, H-3), 1.62 (s, 3H, 18-Me), 1.75 (s, 3H, 20'-Me), 1.85 (s, 1H, HC≡C), 1.87 (brs, 9H, 19, 19', 20-Me), 1.92 (t, 2H, *J* = 6.1 Hz, H-4), 2.41-2.44 (m, 2H, CH_2 pentynoate), 2.48-2.51 (m, 2H, CH_2 pentynoate), 4.50 (s, 2H, H-8'), 6.01-6.58 (m, 12H, H-7, 8, 10, 10', 11, 11', 12, 12', 14, 14', 15, 15'). ^{13}C-NMR (125 MHz, $CDCl_3$): δ = 12.8, 12.8 (19, 19', 20-Me), 14.4 (CH_2-C≡C), 14.8 (20'-Me), 19.3 (C-3), 21.8 (18-Me), 29.0 (16, 17-Me), 33.1, 33.4, 34.3 (C-1, C-4, CH_2-CO), 39.7 (C-2), 69.1 (C≡CH), 70.2 (C-8'), 82.5 (C≡CH), 123.3, 125.3, 126.8, 129.3, 129.7, 130.5, 130.8, 132.3, 133.0, 137.1, 137.7, 138.6 (C-7, 8, 10, 10', 11, 11', 12, 12', 14, 14', 15, 15'), 129.4, 131.6, 135.7, 136.2, 136.8, 137.9 (C-5, 6, 9, 9',13, 13'), 171.56 (C=O). MS (MALDI-TOF, positive mode, with DHB matrix) m/z = 498.4 (M^+). Anal. calcd. for $C_{35}H_{46}O_2$: C 84.29, H 9.30, found C 84.36, H 9.24.

General procedure for carotenoid pentynoates

The hydroxy carotenoids were dissolved in dry dichloromethane (20 mg/mL). To the stirred solution 4-pentynoic acid (2 equiv), DMAP (2 equiv) and DCC (2 equiv) were added. The mixture was stirred for 12 h under nitrogen atmosphere, in darkness, at room temperature. Some drops of water (~0.5 mL) and 10 minutes later hexane (0.5 mL/mg carotenol) were added to the reaction mixture, the obtained precipitate was filtered out, the mother liquor was dried (Na_2SO_4) and evaporated under reduced pressure. The products were crystallized from methanol/toluene mixture by the addition of some water. The formed crystals were filtered off, dried in vacuum and stored in closed ampoules under argon.

*4.2. Zeaxanthin dipentynoate (**6**)*

Following the general procedure, zeaxanthin (**2**, 200 mg, 0.35 mmol) was dissolved in dry dichloromethane (10 mL). To the stirred solution 4-pentynoic acid (69 mg, 0.7 mmol), DMAP (85 mg, 0.7 mmol) and DCC (145 mg, 0.7 mmol) were added. The reaction was worked up, after stirring for 12 h, by addition of some drops of water and 10 minutes later hexane (100 mL). After filtration, drying and evaporation the product was crystallized. Yield: 136 mg (53%); orange crystals; mp: 138 °C; R_f = 0.55 (hexane–acetone, 4:1). IR (KBr, cm^{-1}): 1727 *s* (ν C=O, ester), 2120 *w* (ν C≡C), 3308 *w* (ν ≡CH). ^{1}H-NMR (500 MHz, $CDCl_3$): δ = 1.08, 1.11 (2s, 12H, 16, 16', 17, 17'-Me), 1.57-1.61 (m, 2H, H-2_{ax}, H-$2'_{ax}$), 1.72 (s, 6H, 18, 18'-Me), 1.79 (ddd, 2H, *J* = 1.7 Hz, *J* = 3.3 Hz, *J* = 12.1 Hz, H-2_{eq}, H-$2'_{eq}$), 1.97, 1.98, 1.99 (3s, 14H, 19, 19', 20, 20'-Me, 2 HC≡C), 2.13 (dd, 2H, *J* = 9.4 Hz, *J* = 16.9 Hz, H-4_{ax}, H-$4'_{ax}$), 2.44 (dd, 2H, *J* = 5.7 Hz, *J* = 17.1 Hz, H-4_{eq}, H-$4'_{eq}$), 2.49-2.57 (m, 8H, 4 CH_2 pentynoate), 5.07-5.13 (m, 2H, H-3, H-3'), 6.07-6.12 (m, 4H, H-7, 7', 8, 8'), 6.16 (d, 2H, *J* = 11.7 Hz, H-10, 10'), 6.26 (d, 2H, *J* = 9.7 Hz, H-14, 14'), 6.37 (d, 2H, *J* = 14.9 Hz, H-12, 12'), 6.61-6.67 (m, 4H, H-11, 11', 15, 15'). ^{13}C-NMR (125 MHz, $CDCl_3$): δ = 12.7, 12.8 (19, 19', 20, 20'-Me), 14.4 (2 CH_2-C≡C), 21.5 (18, 18'-Me), 28.5, 30.0 (16, 16', 17, 17'-Me), 33.7 (2 CH_2-CO), 36.7, 38.4, 44.0 (C-1, 1', 2, 2', 4, 4'), 68.9 (C-3, 3'), 69.0 (2 C≡CH), 82.6 (2 C≡CH), 124.9 (C-11, 11'), 125.2 (C-7, 7'), 125.5 (C-5, 5'), 130.1, 131.5, 132.6 (C-10, 10', 14, 14', 15, 15'), 136.5 (C-9, 9'), 137.7 (C-13, 13'), 137.7 (C-12, 12'), 137.9 (C-6, 6'), 138.7 (C-8, 8'), 171.4 (2 C=O). MS (MALDI-TOF, positive mode, with DHB matrix) m/z = 728.3 (M^+). Anal. calcd. for $C_{50}H_{64}O_4$: C 82.37, H 8.85, found C 82.32, H 8.47.

*4.3. β-Cryptoxanthin pentynoate (**7**)*

Following the general procedure, β-cryptoxanthin (**3**, 70 mg, 0.13 mmol) was dissolved in dry dichloromethane (3.5 mL). To the stirred solution 4-pentynoic acid (25 mg, 0.25 mmol), DMAP (31 mg, 0.25 mmol) and DCC (52 mg, 0.25 mmol) were added. The reaction was worked up, after stirring for 12 h, by addition of some drops of water and 10 minutes later hexane (35 mL). After filtration, drying and evaporation the product was crystallized. Yield: 72 mg (90%); red crystals; mp: 139-140 °C; R_f = 0.65 (hexane–acetone, 4:1). IR (KBr, cm^{-1}): 1728 *vs* (ν C=O, ester), 2121 *w* (ν C≡C), 3305 *w* (ν ≡CH). ^{1}H-NMR (500 MHz, $CDCl_3$): δ = 1.03, 1.07, 1.11 (3s, 12H, 16, 16', 17, 17'-Me), 1.45-1.48 (m, 2H, H-2'), 1.59-1.63 (m, 2H, H-2_{ax}, H-3'), 1.72 (2s, 6H, 18, 18'-Me), 1.79 (d, 1H, *J* = 12.0 Hz, H-2_{eq}), 1.97 (brs, 13H, 19, 19', 20, 20'-Me, HC≡C), 2.02 (t, 2H, *J* = 6.3 Hz, H-4'), 2.13 (dd, 1H, *J* = 9.4 Hz, *J* = 16.9 Hz, H-4_{ax}), 2.44 (dd, 1H, *J* = 5.7 Hz, *J* = 17.1 Hz, H-4_{eq}), 2.50-2.54 (m, 4H, 2 CH_2 pentynoate), 5.07-5.13 (m, 1H, H-3), 6.06-6.19 (m, 6H, H-7, 7', 8, 8', 10, 10'), 6.24-6.25 (m, 2H, H-14, 14'), 6.36 (dd, 2H, *J* = 7.1 Hz, *J* = 14.9 Hz, H-12, 12'), 6.57-6.68 (m, 4 H, H-11, 11', 15, 15'). ^{13}C-NMR (125 MHz, $CDCl_3$): δ = 12.8 (19, 19', 20, 20'-Me), 14.4 (CH_2-C≡C), 19.3 (C-3'), 21.5, 21.8 (18, 18'-Me), 28.5, 29.0, 30.0 (16, 16', 17, 17'-Me), 33.2 (C-4'), 33.7, 34.3 (C-1,1'), 36.7 (CH_2-C=O), 38.4 (C-4), 39.7 (C-2'), 44.1 (C-2), 68.9 (C-3), 69.0 (HC≡C), 82.6 (HC≡C), 124.8, 125.1, 125.2, 126.7 (C-7, 7', 11, 11'), 129.9, 130.2, 130.8, 131.5, 132.4, 132.7 (C-10, 10', 14, 14', 15, 15'), 125.5, 129.4, 135.5, 136.1, 136.3, 136.6, 138.0 (C-5, 5', 6, 6', 9, 9', 13, 13'), 137.2, 137.7, 137.8, 138.7 (C-8, 8', 12, 12'), 171.44 (C=O). MS (MALDI-TOF, positive mode, with DHB matrix) m/z = 632.6 (M^+). Anal. calcd. for $C_{45}H_{60}O_2$: C 85.39, H 9.55, found C 85.80, H 9.54.

*4.4. Capsanthin dipentynoate (**8**)*

Following the general procedure, capsanthin (**4**, 200 mg, 0.34 mmol) was dissolved in dry dichloromethane (10 mL). To the stirred solution 4-pentynoic acid (67 mg, 0.68 mmol), DMAP (84 mg, 0.68 mmol) and DCC (141 mg, 0.68 mmol) were added. The reaction was worked up, after stirring for 12 h, by addition of some drops of water and 10 minutes later hexane (100 mL). After filtration, drying and evaporation the product was crystallized. Yield: 150 mg (59%); red crystals; mp: 128-129 °C; R_f = 0.52 (hexane–acetone, 4:1). IR (KBr, cm^{-1}): 1686 *m* (ν C=O, ketone), 1728 *vs* (ν C=O, ester), 2120 *w* (ν C≡C), 3298 *w* (ν ≡CH). ^{1}H-NMR (500 MHz, $CDCl_3$): δ = 0.86, 1.70, 1.10, 1.17 (4s, 12H, 16, 16', 17, 17'-Me), 1.32 (s, 3H, 18'-Me), 1.57-1.62 (m, 2H, H-2_{ax}, H-4'β), 1.72 (s, 3H, 18-Me), 1.73-1.80 (m, 2H, H-2_{eq}, H-2'β), 1.95, 1.97, 1.99 (3s, 14H, 19, 19', 20, 20'-Me, 2 HC≡C), 2.06-2.16 (m, 2H, H-4_{ax}, H-2'α), 2.44 (dd, 1H, *J* = 5.6 Hz, *J* = 17.2 Hz, H-4_{eq}), 2.51-2.55 (m, 8H, 4 CH_2 pentynoate), 2.98 (dd, 1H, *J* = 8.8 Hz, *J* = 14.9 Hz, H-4'α), 5.07-5.13 (m, 1H, H-3), 5.26-5.30 (m, 1H, H-3'), 6.08-6.12 (m, 2H, H-7, H-8), 6.16 (d, 1H, *J* = 11.3 Hz, H-10), 6.26 (d, 1H, *J* = 11.3 Hz, H-14), 6.35-6.38 (m, 2H, H-12, H-14'), 6.42 (d, 1H, *J* = 15.1 Hz, H-7'), 6.50-6.73 (m, 6H, H-10', 11, 11', 12', 15, 15'), 7.33 (d, 1H, *J* = 15.0 Hz, H-8'). ^{13}C-NMR (125 MHz, $CDCl_3$): δ = 12.7, 12.8, 12.9 (19, 19', 20, 20'-Me), 14.4, 14.5 (2 CH_2-C≡C), 20.*8*, 21.*5* (18, 18'-Me), 24.8, 25.6 (17, 17'-Me), 28.5, 30.0 (16, 16'-Me), 33.6, 33.7 (2 CH_2-CO), 36.7, 38.4, 42.2, 43.7, 44.0, 47.6 (C-1, 1', 2, 2', 4, 4'), 68.9 (C-3), 68.9, 69.0 (2 C≡CH), 74.0 (C-3'), 82.5 (2 C≡CH), 120.6, 124.1, 125.5 (C-7, 7', 11, 11'), 129.7, 131.4, 131.7, 132.4 (C-10, 10', 15, 15'), 125.6, 133.6, 135.9, 136.0, 137.6, 137.9 (C-5, 5', 6, 9, 9', 13, 13'), 135.3, 137.5, 138.6, 140.9, 142.1, 147.1 (C-8, 8', 12, 12', 14, 14'), 171.4, 171.4 (2 C=O), 202.4 (C-6'). MS (MALDI-TOF, positive mode, with DHB matrix) m/z = 744.3 (M^+). Anal. calcd. for $C_{50}H_{64}O_5$: C 80.60, H 8.66, found C 80.11, H 8.43.

General procedure for CuAAC reactions

The carotenoid pentynoates were dissolved in dry dichloromethane (0.06 mmol/mL) with sugar azide (1 equiv) and bis-triphenylphosphano-copper(I)-butyrate ($C_3H_7COOCu(PPh_3)_2$) (5 mol%). The reaction mixture was stirred under nitrogen atmosphere in darkness. When TLC showed the disappearance of the starting materials, the solvent was evaporated in vacuum, and the residue was purified by chromatography.

*4.5. 8'-(1-(2",3",4",6"-tetra-O-acetyl-β-d-glucopyranosyl)-1,2,3-triazol-4-yl)-propanoyloxy)-8'-apo-β-carotene (**15**)*

Following the general procedure, 8'-apo-β-carotenol pentynoate (**5**, 45 mg, 0.09 mmol) was dissolved in dry dichloromethane (1.5 mL) with 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl azide (**9**, 34 mg, 0.09 mmol) and $C_3H_7COOCu(PPh_3)_2$ (3 mg, 0.004 mmol). After stirring for 1.5 h under nitrogen atmosphere in darkness, the solvent was evaporated under reduced pressure, and the residue was purified by column chromatography (SiO_2, EtOAc–hexane, 2:3). Yield: 73 mg (92%); red syrup; R_f = 0.45 (EtOAc–hexane, 1:1). ^{1}H-NMR (500 MHz, $CDCl_3$): δ = 1.05 (s, 6H, 16, 17-Me), 1.43-1.46 (m, 2H, H-2), 1.57-1.62 (m, 2H, H-3), 1.69 (s, 3H, Me-18), 1.80, 1.84 (2s, 6H, Me-20,20'), 1.92, 1.95, 2.04 (3s, overlayed), 1.98-2.02 (m) (20H, H-4, 19, 19'-Me, 4 Ac-Me), 2.75 (t, 2H, *J* = 7.3 Hz, CH_2 propanoyl), 3.04 (t, 2H, *J* = 7.4 Hz, CH_2 propanoyl), 3.96-4.00 (m, 1H, H-5"), 4.07-4.13 (m, 1H, H-6"), 4.28 (dd, 1H, *J* = 4.9 Hz, *J* = 12.7 Hz, H-6"), 4.56 (s, 2H, H-8'), 5.22 (t, 1H, *J* = 9.7 Hz, H-4"), 5.36-5.44 (m, 2H, H-2", H-3"), 5.83 (d, 1H, *J* = 8.8 Hz, H-1"), 6.08-6.67 (m, 12H, H-7, 8, 10, 10', 11, 11', 12, 12', 14, 14', 15, 15'), 7.58 (s, 1H, triazole). ^{13}C-NMR (125 MHz, $CDCl_3$): δ = 12.7, 12.8 (19, 19', 20-Me), 14.7 (20'-Me), 19.2 (C-3), 20.1, 20. 5, 20.6, 21.7 (4 Ac-Me, C-18), 20.9 (CH_2-C=C propanoyl), 28.9 (16, 17-Me), 33.0, 33.4, 34.2 (C-1, C-4, CH_2-CO), 39.6 (C-2), 61. 5 (C-6"), 67.6 (C-2"), 70.0 (C-8'), 70.1 (C-3"), 72.6 (C-4"), 75.0 (C-5"), 85.5 (C-1"), 119.5 (CH triazole), 123.3, 125.1, 126.6, 129.1, 129.6, 130.4, 130.7, 132.1, 132.9, 137.1, 137.7, 138.4 (C-7, 8', 10, 10', 11, 11', 12, 12', 14, 14', 15, 15'), 129.3, 131.7, 135.6, 136.0, 136.7, 137.8 (C-5, 6, 9, 9', 13, 13'), 147.0 (C=CH triazole), 168.8, 169.3, 169.8, 170.4 (4 Ac C=O), 172.2 (C=O, propanoyl). MS (MALDI-TOF, positive mode, with DHB matrix) m/z = 871.3 (M^+). Anal. calcd. for $C_{49}H_{65}N_3O_{11}$: C 67.49, H 7.51, N 4.82, found C 67.51, H 7.52, N 4.90.

*4.6. 8'-(1-(2",3",4",6"-tetra-O-acetyl-α-d-glucopyranosyl)-1,2,3-triazol-4-yl)-propanoyloxy)-8'-apo-β-carotene (**16**)*

Following the general procedure, 8'-apo-β-carotenol pentynoate (**5**, 45 mg, 0.09 mmol) was dissolved in dry dichloromethane (1.5 mL) with 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl azide (**10**, 34 mg, 0.09 mmol) and $C_3H_7COOCu(PPh_3)_2$ (3 mg, 0.004 mmol). After stirring for 2 h under nitrogen atmosphere in darkness, the solvent was evaporated under reduced pressure, and the residue was purified by column chromatography (SiO_2, EtOAc–hexane, 1:2). Yield: 75 mg (95%); red syrup; R_f = 0.49 (EtOAc–hexane, 1:1). ^{1}H-NMR (500 MHz, $CDCl_3$): δ = 1.00 (s, 6H, 16, 17-Me), 1.42-1.46 (m, 2H, H-2), 1.57-1.61 (m, 2H, H-3), 1.69 (s, 3H, Me-18), 1.80, 18.5 (2s, 6H, Me-20, 20'), 1.92, 1.95 (2s, overlayed), 1.98-2.05 (m) (20H, H-4, Me-19, 19'-Me, 4 Ac-Me), 2.77 (t, 2H, *J* = 7.1 Hz, CH_2 propanoyl), 3.07 (t, 2H, *J* = 7.1 Hz, CH_2 propanoyl), 3.99 (dd, 1H, *J* = 1.9 Hz, *J* = 12.6 Hz, H-6"), 4.23 (dd, 1H, *J* = 3.7 Hz, *J* = 12.7 Hz, H-6"), 4.32-4.36 (m, 1H, H-5"), 4.55 (s, 2H, H-8'), 5.21-5.28 (m, 2H, H-2", H-4"), 6.08-6.67 (m, 14H, H-1", H-3", H-7, 8, 10, 10', 11, 11', 12, 12', 14, 14', 15, 15'), 7.43 (s, 1H, triazole). ^{13}C-NMR (125 MHz, $CDCl_3$): δ = 12.7, 12.8, 14.1, 14.7 (19, 19', 20, 20'-Me), 19.2 (C-3), 20.2, 20.5, 20.6, 21.7 (4 Ac-Me, C-18), 20.7 (CH_2-C=C propanoyl), 28.9 (16, 17-Me), 33.0, 33.3, 34.2 (C-1, C-4, CH_2-CO), 39.6 (C-2), 61.2 (C-6"), 67.9, 69.8, 70.4, 71.0 (C-2", C-3", C-4", C-5"), 70.1 (C-8'), 81.1 (C-1"), 123.2, 123.5, 125.2, 126.7, 129.2, 129.6, 130.5, 130.7, 132.1, 133.0, 137.1, 137.7, 138.6 (C-7, 8', 10, 10', 11, 11', 12, 12', 14, 14', 15, 15'), 129.3, 131.5, 135.6, 136.1, 136.6, 137.8 (C-7, 8', 10, 10', 11, 11', 12, 12', 14, 14', 15, 15'), 145.8 (C=CH triazole), 169.5, 169.6, 170.1, 170.4 (4 Ac C=O), 172.2 (C=O, propanoyl). MS (MALDI-TOF, positive mode, with DHB matrix) m/z = 871.2 (M^+). Anal. calcd. for $C_{49}H_{65}N_3O_{11}$: C 67.49, H 7.51, N 4.82, found C 67.81, H 7.25, N 4.80.

*4.7. 8'-(1-(2",3",4",6"-tetra-O-benzoyl-1"-carboxamido-β-d-glucopyranosyl)-1,2,3-triazol-4-yl)-propanoyloxy)-8'-apo-β-carotene (**17**)*

Following the general procedure, 8'-apo-β-carotenol pentynoate (**5**, 45 mg, 0.09 mmol) was dissolved in dry dichloromethane (2 mL) with 2,3,4,6-tetra-*O*-benzoyl-1-carboxamido-β-D-glucopyranosyl azide (**11**, 60 mg, 0.09 mmol) and $C_3H_7COOCu(PPh_3)_2$ (3 mg, 0.004 mmol). After stirring for 7 h under nitrogen atmosphere in darkness, the solvent was evaporated under reduced pressure, and the residue was purified by column chromatography (SiO_2, EtOAc–hexane, 2:3). Yield: 98 mg (93%); red syrup; R_f = 0.51 (EtOAc–hexane, 1:1). ^{1}H-NMR (500 MHz, $CDCl_3$): δ = 1.03 (s, 6H, 16, 17-Me), 1.47 (ps, 2H, H-2), 1.61 (ps, 2H, H-3), 1.72, 1.80 (2s, 6H, Me-18, 20'), 1.95-2.03 (m, 11H, H-4, Me-19, 19', 20-Me), 2.67 (ps, 2H, CH_2 propanoyl), 2.97 (ps, 2H, CH_2 propanoyl), 4.55 (s, 3H, 2 H-8', H-6"), 4.89 (d, 1H, *J* = 11.4 Hz, H-6"), 5.26 (pd, 1H, *J* = 8.5 Hz, H-5"), 5.88 (t, 1H, *J* = 8.3 Hz, H-4"), 6.16-6.70 (m, 15H, H-2", H-3", CONH, H-7, 8, 10, 10', 11, 11', 12, 12', 14, 14', 15, 15'),

6.95 (s, 1H, CONH$_2$), 7.26-8.11 (m, 21H, triazole, 4 Bz aromatics). ^{13}C-NMR (125 MHz, $CDCl_3$): δ = 12.7, 12.8 (19, 19', 20-Me), 14.7 (20'-Me), 19.2 (C-3), 20.8 (CH$_2$-C=C propanoyl), 21.7 (C-18), 28.9 (16, 17-Me), 33.0, 33.2, 34.2 (C-1, C-4, CH$_2$-CO), 39.6 (C-2), 62.4 (C-6"), 70.0 (C-8'), 68.2, 71.1, 72.3, 73.9 (C-2"-C-5"), 89.2 (C-1"), 120.2, 123.3, 125.1, 126.6, 137.1 (CH triazole, C-7, 8', 10, 10', 11, 11', 12, 12', 14, 14', 15, 15'), 128.2-133.6 (Bz aromatics), 129.3, 131.6, 135.7, 136.0, 136.7, 137.8 (C-5, 6, 9, 9', 13, 13'), 146.4 (C=CH triazole), 164.2, 164.9, 165.0, 166.0, 166.4 (4 Bz C=O, CONH$_2$), 172.1 (C=O, propanoyl). MS (MALDI-TOF, negative mode, without matrix) m/z = 1161.6 (M^+-1). Anal. calcd. for $C_{70}H_{74}N_4O_{12}$: C 72.27, H 6.41, N 4.82, found C 72.48, H 6.59, N 4.66.

*4.8. 6"-deoxy-6"-(4-(3-(8'-apo-β-caroten-8'-yloxy)-3-oxopropyl)-1,2,3-triazol-1-yl)-1",2",3",4"-tetra-O-acetyl-α-d-glucopyranose (**18**)*

Following the general procedure, 8'-apo-β-carotenol pentynoate (**5**, 45 mg, 0.09 mmol) was dissolved in dry dichloromethane (2 mL) with 6-deoxy-6-azido-1,2,3,4-tetra-*O*-acetyl-α-D-glucopyranose (**12**, 34 mg, 0.09 mmol) and $C_3H_7COOCu(PPh_3)_2$ (3 mg, 0.004 mmol). After stirring for 8 h under nitrogen atmosphere in darkness, the solvent was evaporated under reduced pressure, and the residue was purified by column chromatography (SiO_2, EtOAc–hexane, 1:1). Yield: 50 mg (63%); orange amorphous product; R_f = 0.19 (EtOAc–hexane, 1:1). ^{1}H-NMR (500 MHz, $CDCl_3$): δ = 1.01 (s, 6H, 16, 17-Me), 1.43-4.47 (m, 2H, H-2), 1.58-1.62 (m, 2H, H-3), 1.70, 1.81 (2s, 6H, Me-18, 20'), 1.93-2.10 (m, 23H, H-4, Me-19, 19', 20-Me, 4 Ac-Me), 2.76 (t, 2H, *J* = 7.4 Hz, CH$_2$ propanoyl), 3.04 (t, 2H, *J* = 7.3 Hz, CH$_2$ propanoyl), 4.23-4.37 (m, 2H, H-5", H-6"), 4.50-4.55 (m, 3H, H-8', H-6"), 4.81 (t, 1H, *J* = 9.6 Hz, H-2"/4"), 5.01 (dd, 1H, *J* = 3.7 Hz, *J* = 10.3 Hz, H-4"/2"), 5.45 (t, 1H, *J* = 9.8 Hz, H-3"), 6.09-6.68 (m, 13H, H-1", H-7, 8, 10, 10', 11, 11', 12, 12', 14, 14', 15, 15'), 7.41 (s, 1H, triazole). ^{13}C-NMR (125 MHz, $CDCl_3$): δ = 12.7, 12.8 (19, 19', 20-Me), 14.7 (20'-Me), 19.2 (C-3), 20.4, 20.6, 20.6, 20.7, 21.7 (4 Ac-Me, C-18), 21.0 (CH$_2$-C=C propanoyl), 28.9 (16, 17-Me), 33.06, 33.52, 34.22 (C-1, C-4, CH$_2$-CO), 39.59 (C-2), 50.26 (C-6"), 69.0, 69.2, 69.5, 70.3 (C-2"-C-5"), 69.9 (C-8'), 88.6 (C-1"), 122.7, 123.3, 125.1, 126.7, 129.0, 129.6, 130.4, 130.7, 132.2, 132.9, 137.1, 137.7, 138.4 (CH triazole, C-7, 8', 10, 10', 11, 11', 12, 12', 14, 14', 15, 15'), 129.3, 131.8, 135.7, 136.1, 136.7, 137.8 (C-5, 6, 9, 9', 13, 13'), 146.6 (C=CH triazole), 168.6, 169.4, 169.6, 170.0 (4 Ac C=O), 172.3 (C=O, propanoyl). MS (MALDI-TOF, positive mode, with DHB matrix) m/z = 871.4 (M^+). Anal. calcd. for $C_{49}H_{65}N_3O_{11}$: C 67.49, H 7.51, N 4.82, found C 67.71, H 7.50, N 4.93.

*4.9. 8'-(1-(β-d-glucopyranosyl)-1,2,3-triazol-4-yl)-propanoyloxy)-8'-apo-β-carotene (**19**)*

Following the general procedure, 8'-apo-β-carotenol pentynoate (**5**, 30 mg, 0.06 mmol) was dissolved in dry dichloromethane (1 mL) with β-D-glucopyranosyl azide (**13**, 12 mg, 0.06 mmol) and $C_3H_7COOCu(PPh_3)_2$ (2 mg, 0.003 mmol). After stirring for 1 day under nitrogen atmosphere in darkness, the solvent was evaporated under reduced pressure, and the residue was purified by column chromatography (SiO_2, CH_2Cl_2–MeOH, 95:5). Yield: 30 mg (72%); orange plate crystals; mp: 147-148 °C; R_f = 0.75 (CH_2Cl_2–MeOH, 4:1). ^{1}H-NMR (500 MHz, CD_3OD): δ = 1.04 (s, 6H, 16, 17-Me), 1.48-1.51 (m, 2H, H-2), 1.62-1.66 (m, 2H, H-3), 1.71 (s, 3H, Me-18), 1.82 (s, 3H, Me-20'), 1.96, 1.97, 1.98 (3s, 6H, Me-19, 19', 20-Me), 2.04 (t, 2H, *J* = 6.1 Hz, H-4), 2.78 (t, 2H, *J* = 7.4 Hz, CH$_2$ propanoyl), 3.05 (t, 2H, *J* = 7.4 Hz, CH$_2$ propanoyl), 3.48-3.57 (m, 3H, H-3", H-4", H-5"), 3.71 (dd, 1H, *J* = 5.4 Hz, *J* = 12.1 Hz, H-6"), 3.85-3.89 (m, 2H, H-2", H-6"), 4.58 (s, 2H, H-8'), 5.55 (t, 1H, *J* = 9.2 Hz, H-1"), 6.10-6.73 (m, 12H, H-7, 8, 10, 10', 11, 11', 12, 12', 14, 14', 15, 15'), 7.97 (s, 1H, triazole). ^{13}C-NMR (125 MHz, CD_3OD + $CDCl_3$): δ = 13.0 (19, 19', 20-Me), 14.9 (20'-Me), 20.1 (C-3), 21.6 (CH$_2$-C=C propanoyl), 22.0 (18-Me), 29.4 (16, 17-Me), 33.8, 34.2, 35.0 (C-1, C-4, CH$_2$-CO), 40.5 (C-2), 62.2 (C-6"), 71.0 (C-8'), 70.5, 73.7, 78.1, 80.6 (C-2", 3", 4", 5"), 89.2 (C-1"), 122.3, 124.2, 126.0, 127.4, 130.1, 130.7, 131.4, 131.8, 133.2, 133.9, 138.2, 138.9, 139.4 (CH triazole, C-7, 8', 10, 10', 11, 11', 12, 12', 14, 14', 15, 15'), 132.5, 136.6, 137.5 (C-5, 6, 9, 9', 13, 13'), 147.1 (C=CH triazole), 173.7 (C=O, propanoyl). MS (MALDI-TOF, positive mode, with DHB matrix) m/z = 703.52 (M^+). Anal. calcd. for $C_{41}H_{57}N_3O_7$: C 69.96, H 8.16, N 5.97, found C 69.73, H 7.93, N 5.72.

*4.10. 8'-(1-(1"-carboxamido-β-d-glucopyranosyl)-1,2,3-triazol-4-yl)-propanoyloxy)-8'-apo-β-carotene (**20**)*

Following the general procedure, 8'-apo-β-carotenol pentynoate (**5**, 30 mg, 0.06 mmol) was dissolved in dry dichloromethane (1 mL) with 1-carboxamido-β-D-glucopyranosyl azide (**14**, 15 mg, 0.06 mmol) and $C_3H_7COOCu(PPh_3)_2$ (2 mg, 0.003 mmol). After stirring for 2 days under nitrogen atmosphere in darkness, the solvent was evaporated under reduced pressure, and the residue was purified by preparative thin layer chromatography (SiO_2, CH_2Cl_2–MeOH, 9:1). Yield: 22 mg (49%); red syrup; R_f = 0.70 (CH_2Cl_2–MeOH, 4:1). ^{1}H-NMR (500 MHz, CD_3OD): δ = 1.03 (s, 6H, 16, 17-Me), 1.48-1.50 (m, 2H, H-2), 1.63-1.65 (m, 2H, H-3), 1.71, 1.82 (2s, 6H, Me-18,20'), 1.95, 1.96, 1.97 (3s, 9H, 19, 19', 20-Me), 2.04 (t, 2H, *J* = 6.1 Hz, H-4), 2.78 (t, 2H, *J* = 7.4 Hz, CH$_2$ propanoyl), 3.04 (t, 2H, *J* = 7.4 Hz, CH$_2$ propanoyl), 3.48-3.79 (m, 4H, H-3", 4", 5", 6"), 3.91 (dd, 1H, *J* = 1.5 Hz, *J* = 12.2 Hz, H-6"), 4.00 (d, 1H, *J* = 9.8 Hz, H-2"), 4.58 (s, 2H, H-8), 6.09-6.72 (m, 12H, H-7, 8, 10, 10', 11, 11', 12, 12', 14, 14', 15, 15'), 8.07 (s, 1H, triazole). ^{13}C-NMR (125 MHz, CD_3OD): δ = 12.8, 12.9, 14.8 (19, 19', 20, 20'-Me), 20.4 (C-3), 21.9 (CH$_2$-C=C propanoyl), 22.0 (C-18), 29.5 (16, 17-Me), 34.0, 34.4, 35.3 (C-1, C-4, CH$_2$-CO), 40.9 (C-2), 62.3 (C-6"), 71.2 (C-8'), 70.5, 76.0, 77.2, 79.5 (C-2"-C-5"), 90.6 (C-1"), 122.3, 124.6, 126.2, 127.6, 130.3, 131.7, 132.3, 133.7, 134.2, 137.8, 138.7, 139.5, 139.7 (CH triazole, C-7, 8', 10, 10', 11, 11', 12, 12', 14, 14', 15, 15'), 130.1, 133.1, 136.8, 137.0, 139.3 (C-5, 6, 9, 9', 13, 13'), 147.5 (C=CH triazole), 169.4 (CONH$_2$), 174.0 (C=O, propanoyl). MS (MALDI-TOF, positive mode, with DHB matrix) m/z = 747.1 (M^+). Anal. calcd. for $C_{42}H_{58}N_4O_8$: C 67.54, H 7.83, N 7.50, found C 67.86, H 8.09, N 7.36.

*4.11. 3,3'-bis(1-(β-d-glucopyranosyl)-1,2,3-triazol-4-yl)-propanoyloxy)-β,β-carotene (**21**)*

Following the general procedure, zeaxanthin dipentynoate (**6**, 30 mg, 0.04 mmol) was dissolved in dry dichloromethane (1 mL) with β-D-glucopyranosyl azide (**13**, 8.5 mg, 0.04 mmol) and $C_3H_7COOCu(PPh_3)_2$ (1.4 mg, 0.002 mmol). After stirring for 12 h under nitrogen atmosphere in darkness, the solvent was evaporated under reduced pressure, and the residue was purified by preparative thin layer chromatography (SiO_2, CH_2Cl_2–MeOH, 9:1). Yield: 30 mg (65%); orange plate crystals; mp: 198-199 °C; R_f = 0.34 (CH_2Cl_2–MeOH, 4:1). ^{1}H-NMR (500 MHz, $(CD_3)_2SO$): δ = 1.06, 1.08 (2s, 12H, 16, 16', 17, 17'-Me), 1.53 (t, 2H, *J* = 11.4 Hz, H-2, 2'$_{ax}$), 1.71 (s, 6H, 18, 18'-Me), 1.75-1.78 (m, 2H, H-2, 2'$_{eq}$), 1.94 (s, 12H, Me-19, 19', 20, 20'-Me), 2.10-2.15 (m, 2H, H-4, 4'$_{ax}$), 2.37-2.41 (m, 2H, H-4, 4'$_{eq}$), 2.68 (brs, 4H, CH$_2$ propanoyl), 2.90 (brs, 4H, CH$_2$ propanoyl), 3.20-3.71 (m, 12H, H-2", 3", 4", 5", 2x6"), 4.65 (brs, 2H, OH), 4.98 (brs, 2H, H-3, 3'), 5.24 (brs, 2H, OH), 5.41 (brs, 2H, OH), 5.47 (d, 2H, *J* = 9.0 Hz, H-1"), 6.10-6.26 (m, 6H, H-7, 7', 8, 8', 10, 10'), 6.33-6.42 (m, 4H, H-12, 12', 14, 14'), 6.64-6.72 (m, 4H, 11, 11', 15, 15'),

8.05 (s, 1H, triazole). ^{13}C-NMR (125 MHz, $(CD_3)_2SO$): δ = 12.4, 12.5 (19, 19', 20, 20'-Me), 20.5 CH_2-C=C propanoyl), 21.1 (C-18, 18'), 28.2, 29.7 (16, 16', 17, 17'-Me), 33.0 (CH_2-CO propanoyl), 36.1 (C-4, 4'), 37.9 (C-1, 1'), 43.5 (C-2, 2'), 60.6 (C-6"), 67.6 (C-3), 69.5, 72.0, 76.8, 79.8 (C-2"-C-5"), 87.3 (C-1"), 121.0 (triazole), 124.9, 125.0 (C-7, 7', 11, 11'), 125.5 (C-5,5'), 130.3, 131.5, 132.6 (C-10, 10', 14, 14', 15, 15'), 135.2, 136.1, 137.2 (C-6, 6', 9, 9', 13, 13'), 137.4, 137.9 (C-8, 8', 12, 12'), 145.1 (C=CH triazole), 171.6 (C=O, propanoyl). MS (MALDI-TOF, positive mode, with DHB matrix) m/z = 1161.6 (M^++Na^+). Anal. calcd. for $C_{62}H_{86}N_6O_{14}$: C 65.36, H 7.61, N 7.38, found C 65.07, H 7.75, N 7.58.

*4.12. 3-(1-(β-d-glucopyranosyl)-1,2,3-triazol-4-yl)-propanoyloxy)-β,β-carotene (**22**)*

Following the general procedure, β-cryptoxanthin pentynoate (**7**, 30 mg, 0.047 mmol) was dissolved in dry dichloromethane (1 mL) with β-D-glucopyranosyl azide (**13**, 9.7 mg, 0.047 mmol) and $C_3H_7COOCu(PPh_3)_2$ (1.6 mg, 0.0024 mmol). After stirring for 12 h under nitrogen atmosphere in darkness, the solvent was evaporated under reduced pressure, and the residue was purified by preparative thin layer chromatography (SiO_2, CH_2Cl_2–MeOH, 9:1). Yield: 30 mg (76%); red plate crystals; mp: 178-179°C; R_f = 0.57 (CH_2Cl_2–MeOH, 4:1). ^{1}H-NMR (500 MHz, $CDCl_3$): δ = 1.02, 1.05, 1.09 (3s, 12H, 16, 16', 17, 17'-Me), 1.24 (s, 3H, 18'-Me), 1.47, 1.61 (2brs, 5H, 2 H-2, 2', H-3'), 1.71 (s, 3H, 18-Me), 1.95-2.08 (m, 15H, Me-19, 19', 20, 20'-Me, 2 H-4', H-4_{ax}), 2.39-2.42 (m, 1H, H-4_{eq}), 2.63, 2.93 (2brs, 4H, 2 CH_2 propanoyl), 3.65-4.13 (m, 6H, H-2", 3", 4", 5", 2x6"), 5.04 (brs, 2H, H-3, OH), 5.56 (brs, 4H, H-1", 3OH), 6.07-6.35 (m, 10H, H-7, 7', 8, 8', 10, 10', 14, 14', 12, 12'), 6.60 (brs, 4H, H-11, 11', 15, 15'), 7.71 (brs, 1H, triazole). MS (MALDI-TOF, positive mode, with DHB matrix) m/z = 837.4 (M^+), 860.4 (M^++Na^+). Analysis calc. for $C_{51}H_{71}N_3O_7$: C 73.09, H 8.54, N 5.01, found C 73.37, H 8.75, N 4.75.

*4.13. 3,3'-bis(1-(β-d-glucopyranosyl)-1,2,3-triazol-4-yl)-propanoyloxy)-β,κ-carotene (**23**)*

Following the general procedure, capsanthin dipentynoate (**8**, 30 mg, 0.04 mmol) was dissolved in dry dichloromethane (1 mL) with β-D-glucopyranosyl azide (**13**, 8.5 mg, 0.04 mmol) and $C_3H_7COOCu(PPh_3)_2$ (1.4 mg, 0.002 mmol). After stirring for 12 h under nitrogen atmosphere in darkness, the solvent was evaporated under reduced pressure, and the residue was purified by preparative thin layer chromatography (SiO_2, CH_2Cl_2–MeOH, 4:1). Yield: 33 mg (71%); red syrup; R_f = 0.57 (CH_2Cl_2–MeOH, 4:1). ^{1}H-NMR (500 MHz, CD_3OD): δ = 0.87, 1.08, 1.11, 1.18 (4s, 12H, 16, 16', 17, 17'-Me), 1.33 (s, 3H, 18'-Me), 1.57 (t, 2H, *J* = 11.8 Hz, H-2_{ax}, H-4'$_β$), 1.74 (s, 3H, 18-Me), 1.78-1.80 (m, 2H, H-2_{eq}, H-2'β), 1.97, 1.99, 2.00 (3s, 12H, 19, 19', 20, 20'-Me), 2.03-2.16 (2m, 2H, H-4_{ax}, H-2'$_α$), 2.41 (dd, 1H, *J* = 5.8 Hz, *J* = 17.0 Hz, H-4_{eq}), 2.70-2.74 (m, 4H, 2 CH_2 pentynoate), 2.89 (dd, 1H, *J* = 8.5 Hz, *J* = 14.7 Hz, H-4'α), 3.01-3.03 (m, 4H, 2 CH_2 pentynoate), 3.45-3.65, 3.85-3.88 (2m, 10H, H-2", 3", 4", 5", 6"), 3.71 (dd, 2H, *J* = 5.4 Hz, *J* = 11.9 Hz, H-6"), 5.04-5.10 (m, 1H, H-3), 5.21-5.25 (m, 1H, H-3'), 5.55, 5.56 (2d, overlayed, 2H, *J* = 9.2 Hz, 2xH-1"), 6.15 (ps, 2H, H-7, H-8), 6.18 (d, 1H, *J* = 11.8 Hz, H-10), 6.32 (d, 1H, *J* = 11.2 Hz, H-14), 6.40-6.44 (m, 2H, H-12, H-14'), 6.55 (d, 1H, *J* = 15.1 Hz, H-7'), 6.61-6.65 (m, 2H, H-10', 12'), 6.68-6.81 (m, 4H, 11, 11', 15, 15'), 7.31 (d, 1H, *J* = 15.1 Hz, H-8'), 7.97, 7.98 (2s, 2H, triazoles). ^{13}C-NMR (125 MHz, CD_3OD): δ = 12.8, 12.8, 12.9 (19, 19', 20, 20'-Me), 21.0, 21.8 (18, 18'-Me), 21.91 (2 CH_2-C≡C), 25.3, 26.0 (17, 17'-Me), 29.0, 30.6 (16, 16'-Me), 34.7, 34.8 (2 CH_2-CO), 37.8, 39.3, 43.5, 44.8, 45.2 (C-1, 1', 2, 2', 4, 4'), 62.5 (C-6"), 70.0 (C-3), 75.3 (C-3'), 71.0, 74.1, 78.6, 81.2 (C-2"-C-5"), 89.6 (C-1"), 120.6, 124.1, 125.5 (C-11, 11', 7, 7'), 125.6 (C-5, 5'), 122.0, 122.8, 122.8, 125.3, 126.5, 126.6, 131.2, 132.9, 133.1, 136.8, 138.9, 140.3, 142.6, 143.8 (CH triazole, C-7, 7', 8, 10, 10', 11, 11', 12, 12', 14, 14', 15, 15'), 126.8, 135.0, 136.8, 137.3, 138.8, 139.3 (C-5, 5', 6, 9, 9', 13, 13'), 147.6 (C=CH triazole), 148.6 (C-8'), 173.9, 174.0 (2 C=O propanoyl), 205.1 (C-6'). MS (MALDI-TOF, positive mode, with DHB matrix) m/z = 1177.4 (M^++Na^+), 1193.4 (M^++K^+). Analysis calc. for $C_{62}H_{86}N_6O_{15}$: C 64.45, H 7.50, N 7.27, found C 64.23, H 7.51, N 7.38.

*4.14. 3-(1-(1"-carboxamido-β-d-glucopyranosyl)-1,2,3-triazol-4-yl)-propanoyloxy)-3'-hydroxy-β,β-carotene (**24**) and 3,3'-bis(1-(1"-carboxamido-β-d-glucopyranosyl)-1,2,3-triazol-4-yl)-propanoyloxy)-β,β-carotene (**25**)*

Following the general procedure, zeaxanthin dipentynoate (**6**, 30 mg, 0.04 mmol) was dissolved in dry dichloromethane (1 mL) with 1-carboxamido-β-D-glucopyranosyl azide (**14**, 10 mg, 0.04 mmol) and $C_3H_7COOCu(PPh_3)_2$ (1.4 mg, 0.002 mmol). After stirring for 2 days under nitrogen atmosphere in darkness, the solvent was evaporated under reduced pressure. Compounds **24** and **25** were detected in the worked up reaction mixture by MS. Compound **24**: R_f = 0.65 (CH_2Cl_2–MeOH, 4:1); MS (MALDI-TOF, positive mode, with DHB matrix) m/z = 976.4 (M^+). Compound **25**: R_f = 0.15 (CH_2Cl_2–MeOH, 4:1); MS (MALDI-TOF, positive mode, with DHB matrix) m/z = 1247.2 (M^++Na^+).

*4.15. 3,3'-bis(1-(1"-carboxamido-β-d-glucopyranosyl)-1,2,3-triazol-4-yl)-propanoyloxy)-β,κ-carotene (**27**)*

Following the general procedure, capsanthin dipentynoate (**8**, 30 mg, 0.04 mmol) was dissolved in dry dichloromethane (1 mL) with 1-carboxamido-β-D-glucopyranosyl azide (**14**, 10 mg, 0.04 mmol) and $C_3H_7COOCu(PPh_3)_2$ (1.4 mg, 0.002 mmol). After stirring for 2 days under nitrogen atmosphere in darkness, the solvent was evaporated under reduced pressure, and the residue was purified by preparative thin layer chromatography (SiO_2, CH_2Cl_2–MeOH, 4:1). Yield: 7.5 mg of compound **27** (15%); red syrup; R_f = 0.14 (CH_2Cl_2–MeOH, 4:1). ^{1}H-NMR (500 MHz, CD_3OD): δ = 0.87, 1.09, 1.11, 1.33 (5s, 15H, 16, 16', 17, 17',18'-Me), 1.55-1.60 (m, 2H, H-2_{ax}, H-4'$_β$), 1.74 (s, 3H, 18-Me), 1.76-1.80 (m, 2H, H-2_{eq}, H-2'$_β$), 1.90, 1.98, 1.99 (3s, 12H, 19, 19', 20, 20'-Me), 2.03-2.16 (m, 2H, H-4_{ax}, H-2'$_α$), 2.41 (dd, 1H, *J* = 6.0 Hz, *J* = 14.8 Hz, H-4_{eq}), 2.71-2.73 (m, 4H, 2 CH_2 pentynoate), 2.89 (dd, 1H, *J* = 8.7 Hz, *J* = 14.7 Hz, H-4'α), 3.01-3.05 (m, 4H, 2 CH_2 pentynoate), 3.46-4.02 (m, 12H, H-2", 3", 4", 5", 2x6"), 5.04-5.10 (m, 1H, H-3), 5.21-5.25 (m, 1H, H-3'), 6.15 (ps, 2H, H-7, H-8), 6.19 (d, 1H, *J* = 11.1 Hz, H-10), 6.32 (d, 1H, *J* = 11.4 Hz, H-14), 6.40-6.44 (m, 2H, H-12, H-14'), 6.55 (d, 1H, *J* = 15.1 Hz, H-7'), 6.61-6.64 (m, 2H, H-10', 12'), 6.69-6.81 (m, 4H, 11, 11', 15, 15'), 7.31 (d, 1H, *J* = 14.9 Hz, H-8'), 8.05, 8.07 (2s, 2H, triazoles), 8.55 (s, 2H, CONH$_2$). MS (MALDI-TOF, positive mode, with DHB matrix) m/z = 1263.4 (M^++Na^+). Analysis calc. for $C_{64}H_{88}N_8O_{17}$: C 61.92, H 7.15, N 9.03, found C 61.66, H 7.26, N 8.84. Compound **26** was detected in the worked up reaction mixture by MS. R_f = 0.57 (CH_2Cl_2–MeOH, 4:1); MS (MALDI-TOF, positive mode, with DHB matrix) m/z = 1015.4 (M^++Na^+).

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Supplementary Material

The NMR spectra of the prepared compounds are available.

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