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Microwave-Mediated Cycloaddition of Azides to Propargylic Ethers in PEG-200

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Microwave-Mediated Cycloaddition of Azides to Propargylic Ethers in PEG-200

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The copper(I) catalyzed azide-alkyne cycloaddition (CuAAC) is the most celebrated click reaction owing to several desirable features such as atom economy, high yields, terminal alkyne chemo-selectivity, regio-selectivity in azide addition, true catalytic power of the Cu(I) species, tolerance to plethora of functional groups and reaction conditions. (*Scheme 1*).^{1,2} The reaction is generally conducted with catalytic amount of inexpensive and readily available copper(II) sulfate and sodium ascorbate.^{3,4} Sodium ascorbate acts as the reducing agent to generate reactive Cu(I) species within the reaction medium.



Scheme 1

Even though several improvements in the reaction conditions such as variations in the copper(I) species,^{5,6} microwave heating,^{7–9} acid additives¹⁰ have been introduced, there is still room for fine tuning to improve efficiency particularly with respect to the solvent used. It occurred to us that polyethylene glycol-200 (PEG-200), an environmentally benign solvent, could be employed as the solvent in CuAAC particularly when conducted under microwave irradiation.¹¹ PEG-200 is a water soluble, bio-compatible liquid which efficiently absorbs microwave radiation of 2.45 GHz, the frequency used in microwave synthesizers. PEG-200 is practically insoluble in non-polar solvents such as *tert*-butyl methyl ether and this property can be used for the recovery of many organic compounds from solutions, thus leaving behind the solvent and the inorganic catalysts.¹² Herein we describe optimal conditions for CuAAC reaction of azides with propargylic ethers towards facile synthesis of several triazole-natural product conjugates.

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The reaction of cholesteryl propargyl ether **1a** with benzyl azide **2a** to give cycloadduct **3a** was selected to evaluate the efficiency of different solvents with 0.1 mol% of copper(II) sulfate and 0.2 mol% of sodium ascorbate (Scheme 1 and Figure 1). Although neither cholesteryl propargyl ether **1a** and benzyl azide **2a** were completely miscible in a 30-fold excess of 1:1 aqueous methanol, stirring the non-homogenous reaction mixture at rt for 48 h led to complete reaction in 92% yield as evidenced by the absence of cholesteryl propargyl ether 1a in TLC; the reaction required only a 5-fold excess of PEG-200 and 2 min for completion when conducted under microwave (MW) irradiation in a sealed vessel at 110°C to provide 99% yield of the cycloadduct 3a. Although the reaction proceeds in better than 90% yield in various solvents such as t-BuOH/H₂O(1:1), THF/H₂O(1:1), 1.4-dioxane/H₂O (1:1), DMF, ethylene glycol, diethylene glycol, triethylene glycol and tetraethylene glycol, PEG 200 was selected as the ideal solvent because of the ease of work-up and microwave absorption capacity. Other polyether solvents investigated, e. g., PEG 400, PEG 4000, mono methyl ethers of ethylene glycol, diethylene glycol, triethylene glycol or tetraehtylene glycol and *bis*-methyl ethers of ethylene glycol, diethylene glycol, triethylene glycol or tetraehtylene glycol were less effective or gave lower yields. It was determined that the use of 0.1 mol% of copper(II) sulfate and 0.2 mole% sodium ascorbate was sufficient to provide the product in less than 3 min. The fact that PEG-200 is practically immiscible with tert-butyl methyl ether was used in the recovery of the product and to recycle both the catalyst and the solvent for six runs. After each reaction, 10 mL tert-butyl methyl ether was added to mixture which was swirled and the solution of the adduct in tert-butyl methyl ether (upper layer) was separated. This operation was conducted two more times to recover the product completely. Although the catalytic activity remained excellent for three runs (97%–99%), on further use of the solvent and the catalyst the yield started to decrease (85%–94%) with a concurrent increase in the time required to complete the reaction. A study to determine optimal temperature required in the microwave-mediated reaction revealed that 110°C is ideal for high yield and purity of the product. At higher temperatures still, the yield was lower with considerable charring and at lower temperatures the reaction took longer time. The microwave-mediated conditions were equally applicable to the reaction conducted at 4.7 mmol (2 g) scale of 1a to provide nearly quantitative yield of 3a in 5 min.

This MW-mediated CuAAC to provide alcohol-containing natural product triazole conjugates such as **3a** under optimized conditions proved to be general. Treatment of five propargyl ethers, cholesteryl propargyl ether (**1a**), menthyl propargyl ether (**1b**), glucose diacetonide propargyl ether (**1c**), thymol propargyl ether (**1d**) and eugenol propargyl ether (**1e**) with benzyl azide **2a**, phenyl azide **2b** and hexyl azide **2c** furnished a library of fifteen alcohol-triazole conjugates **3a–o** (*Figure 1*). In each case, the products were isolated by simple dilution of the reaction mixture with excess water. Except for **3a**, **3d** and **3g** the products are unknown.^{13,14} The products were characterized by spectroscopic data (¹H NMR, ¹³C NMR, DEPT), HRMS, combustion analysis and by optical rotation in case of **3a–i**. The HRMS and combustion analysis data for unknown samples is given in *Table 1*. Similarly, ¹H NMR, ¹³C NMR spectral data and optical rotation data is given in *Table 2*. This reaction, however, does not work with acyl and sulfonyl azides since these azides are not stable under microwave irradiation.



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3a, yield 99%, mp 112-115 °C, lit mp 110-113 °C



3c, yield 98%, mp 93 °C



3e, yield 98%, mp 89 °C



3g, yield 99%, mp 121 °C



3i, yield 98%



3k, yield 99%, mp 74 °C



3m, yield 99%, mp 92 °C



3o, yield 99%, mp 53 °C



3b, yield 99%, mp 151-152 °C



3d, yield 98%, mp 48-50 °C, lit mp 46-48 °C



3f, yield 97%



3h, yield 97%, mp 124-125 °C



3j, yield 99%, mp 65 °C



3I, yield 98%



3n, yield 99%, mp 81 °C

Figure 1 Structures of Cycloadducts **3a–o**. Adduct **3g** was reported to be viscous liquid, see Ref. 14.

	Combustio			
Cmpd.	C	Н	N	HRMS (m/z) Calculated (Found)
3b	79.51 (79.73)	9.82 (9.84)	7.73 (7.74)	566.4086 (566.4090)
3c	78.35 (78.36)	11.14(11.17)	7.61 (7.59)	574.4712 (574.4711)
3e	72.81 (73.01)	8.68 (8.69)	13.41 (13.43)	336.2052 (336.2055)
3f	70.98 (70.78)	10.97 (10.98)	13.07 (13.06)	344.2678 (344.2675)
3g	61.24 (61.41)	6.77 (6.76)	9.74 (9.72)	454.1954 (454.1954)
3h	60.41 (60.59)	6.52(6.53)	10.07 (10.10)	440.1798 (440.1795)
3i	59.27 (59.34)	8.29 (8.27)	9.88 (9.86)	448.2424 (448.2412)
3j	74.74 (74.95)	7.21 (7.22)	13.07 (13.09)	344.1735 (344.1739)
3k	74.24 (74.45)	6.89(6.91)	13.67 (13.71)	330.1582 (330.1580)
31	72.34 (72.34)	9.27 (9.27)	13.32(13.34)	338.2208 (338.2208)
3m	71.62(71.65)	6.31 (6.30)	12.53 (12.50)	358.1531 (358.1529)
3n	71.01 (71.06)	5.96 (5.95)	13.08 (13.09)	344.1375 (344.1373)
30	69.27 (69.31)	8.26(8.24)	12.76(12.73)	330.2176 (330.2374)

 Table 1

 Combustion Analysis and HRMS of New Compounds

In conclusion, we have shown that the CuAAC Click reaction works well in PEG-200 under MW irradiation at 110°C to provide alcohol-triazole conjugates close to quantitative yield. It is possible to reuse solvent and catalyst at least for two additional runs.

Experimental Section

Analytical thin-layer chromatography (TLC) was performed on silica gel coated on glass plates (0.25 mm, silica gel G, LOBA Chemicals, UV silica gel GF 254). TLC spots were visualized under UV light and iodine. Column chromatography was carried out using silica gel 100–200 mesh (LOBA Chemicals) using a hexanes-ethyl acetate eluent mixture. ¹H and ¹³C NMR spectra were recorded on a Bruker Avance 400 spectrometer in CDCl₃:CCl₄ (1:1) and chemical shifts values (δ) are relative to the residual solvent peak (δ 7.26 for ¹H, δ 77.0 for 13 C) where possible or alternatively to TMS (δ 0.00) as internal standard. Coupling constants (J) are given in Hz and multiplicities are designated as s (singlet), d (doublet), dd (doublet of doublet), t (triplet), q (quartet), m (multiplet) or broad (br). DEPT-135 NMR spectra were recorded for all the samples to determine the number of hydrogen atoms present on each carbon. Samples for melting point determination were recrystallized from hexane and ethyl acetate (9:1). Melting points were determined using open-ended capillary tubes on VEEGO VMP-DS instrument and are uncorrected. The propargyl ethers were prepared according to literature procedure from the corresponding alcohol or phenols.^{15–17} Phenyl, benzyl and hexyl azides were obtained by literature procedures.^{18,19} CuAAC reactions were carried out in mono-mode CEM Microwave Synthesizer of the model Discover System generating 2.45 GHz and using 30 mL thick walled glass tubes sealed with a

 Table 2

 Optical Rotation, ¹H NMR and ¹³C NMR Spectral Data of Compounds 3a–3o

Cmpd.	$[\alpha]_D^{25}$	¹ H NMR (δ)	¹³ C NMR (δ)
3 a	−16.0°	7.40 (s, 1H),7.35–7.32 (m, 3H), 7.26–7.24 (m, 2H), 5.49 (s, 2H), 5.30–5.29 (m, 1H), 4.62 (s, 2H), 3.31–3.22 (m, 1H), 2.38–2.31 (m, 1H), 2.23–2.14 (m, 1H), 2.04–1.78 (m, 6H), 1.59–1.31 (m, 8H), 1.25 (s, 3H), 1.19–1.01 (m, 6H), 0.98 (s, 3H), 0.92–0.85 (m, 12H), 0.67 (s, 3H).	146.3 (C), 140.4 (C), 134.6 (C), 128.9 (CH), 128.5 (CH), 127.9 (CH), 121.7 (CH), 121.6 (CH), 78.7 (CH), 61.6 (CH ₂), 56.6 (CH), 56.0 (CH), 53.9 (CH ₂), 50.0 (CH), 42.2 (C), 39.6 (CH ₂), 39.4 (CH ₂), 38.9 (CH ₂), 37.0 (CH ₂), 36.7 (CH ₂), 36.1 (CH ₂), 35.6 (CH), 31.8 (CH ₂), 31.7 (CH), 29.5 (CH), 28.19 (CH ₂), 28.15 (CH), 27.9 (CH ₂), 24.2 (CH ₃), 23.7 (CH ₃), 22.7 (CH ₂), 22.5 (CH ₃), 20.9 (CH ₂), 19.3 (CH), 18.7 (CH ₃).
3b	-18.0°	7.95 (s, 1H),7.75–7.72 (m, 2H), 7.54–7.50 (m, 2H), 7.49–7.41 (m, 1H), 5.34 (d, J = 5.2 Hz, 2H), 4.75 (s, 2H), 4.62 (s, 2H), 3.39–3.31 (m, 1H), 2.46–2.39 (m, 1H), 2.30–2.21(m, 1H), 2.04–1.81 (m, 3H), 1.91–1.79 (m, 2H), 1.62–1.42 (m, 7H), 1.41–1.30 (m, 4H), 1.25 (s, 3H), 1.16–1.09 (m, 6H), 1.01 (s, 3H), 0.92–0.85 (m, 7H), 0.68 (s, 3H).	$\begin{array}{c} 147.7 \ (C), 140.7 \ (C), 137.4 \ (C), 129.8 \\ (CH), 128.7 \ (CH), 122.1 \ (C), \\ 120.6 \ (CH), 120.3 \ (CH), 79.1 \\ (CH), 61.8 \ (CH_2), 57.0 \ (CH), 56.4 \\ (CH), 50.4 \ (CH), 42.6 \ (C), 40.0 \\ (CH_2), 39.8 \ (CH_2), 39.3 \ (CH_2), \\ 37.4 \ (CH_2), 37.1 \ (CH_2), 36.4 \\ (CH_2), 36.0 \ (CH), 32.19 \ (CH_2), \\ 32.15 \ (CH), 28.6 \ (CH_2), 28.2 \\ (CH), 24.5 \ (CH_2), 24.1 \ (CH_2), \\ 23.1 \ (CH_3), 22.8 \ (CH_2), 21.3 \\ (CH_3), 20.9 \ (CH_2), 19.6 \ (CH), \\ 19.0 \ (CH_3), 12.1 \ (CH_3). \end{array}$
3c	-16.0°	7.46 (s, 1H), 5.32 (d, $J =$ 4.2 Hz, 1H), 4.66 (s, 2H), 4.32 (t, $J =$ 7.2 Hz, 2H), 3.32–3.26 (m, 1H), 2.41–2.34 (m, 1H), 2.03–2.28 (m, 1H), 2.03–2.78 (m, 7H), 1.68–0.81 (m, 42H), 0.68 (s, 3H).	$\begin{aligned} &145.9\ (\text{C}),\ 140.5\ (\text{C}),\ 121.7\ (\text{CH}),\\ &121.6\ (\text{CH}),\ 78.7\ (\text{CH}_2),\\ &61.7(\text{CH}_2),\ 56.7\ (\text{CH}),\ 56.1\ (\text{CH}),\\ &50.1\ (\text{CH}_2),\ 42.3\ (\text{C}),\ 39.8\ (\text{CH}_2),\\ &39.5\ (\text{CH}_2),\ 39.0\ (\text{CH}_2),\ 37.1\ (\text{CH}_2),\ 36.2\ (\text{CH}_2),\ 35.7\ (\text{CH}),\\ &31.9\ (\text{CH}_2),\ 31.8\ (\text{CH}),\ 31.1\ (\text{CH}_2),\ 30.2\ (\text{CH}_2),\ 28.3\ (\text{CH}_2),\\ &28.2\ (\text{CH}),\ 28.0\ (\text{CH}),\ 26.1\ (\text{CH}_2),\\ &24.3\ (\text{CH}_2),\ 23.8\ (\text{CH}_2),\ 22.8\ (\text{CH}_3),\ 22.6\ (\text{CH}_2),\ 22.4\ (\text{CH}_2),\\ &21.0\ (\text{CH}_2),\ 19.3\ (\text{CH}_3),\ 18.7\ (\text{CH}_3),\ 13.9\ (\text{CH}_2),\ 11.9\ (\text{CH}_3).\end{aligned}$

Cmpd.	$[\alpha]_D^{25}$	¹ H NMR (δ)	¹³ C NMR (δ)
3 d	-83.3°	7.39 (s, 1H), 7.34–7.31 (m, 3H), 7.31–7.23 (m, 2H), 5.48 (s, 2H), 4.71 (d, $J =$ 12.0 Hz, 1H), 4.53 (d, $J =$ 12.0 Hz, 1H), 3.13 (td, $J =$ 10.5, 4.0 Hz, 1H), 2.15–2.07 (m, 3H), 1.64–1.56 (m, 3H), 1.39–1.29 (m, 1H), 1.23–1.13 (m, 1H), 0.91 (d, J = 6.5 Hz, 3H), 0.83 (d, $J =7.0 Hz, 4H), 0.59 (d,J = 7.0$ Hz, 3H).	146.5 (C), 134.7 (C), 128.9 (CH), 128.5 (CH), 127.9 (CH), 121.9 (CH), 78.5 (CH), 61.8 (CH ₂), 53.9 (CH ₂), 48.1 (CH), 40.2 (CH ₂), 34.5 (CH ₂), 31.4 (CH), 25.4 (CH), 23.3 (CH ₂), 22.3 (CH ₃), 20.9 (CH ₃), 16.1 (CH ₃).
3e	-83.8°	7.91 (s, 1H), 7.74–7.72 (m, 2H), 7.52–7.48 (m, 2H), 7.43–7.39 (m, 1H), 4.85 (d, J = 12.4 Hz, 1H), 4.63 (d, $J =12.0, 4.0 Hz, 1H), 2.24–2.18(m, 3H), 1.64–1.59 (m, 3H),1.44–1.34 (m, 1H),1.29–1.21 (m, 1H), 0.94 (d,J = 8.0$ Hz, 3H), 0.88 (d, $J =7.2 Hz, 4H), 0.70 (d, J =8.0 Hz, 3H).$	147.0 (C), 137.2 (C), 129.6 (CH), 128.4 (CH), 120.4 (CH), 120.0 (CH), 78.9 (CH), 61.9 (CH ₂), 48.2 (CH), 40.2 (CH ₂), 34.5 (CH ₂), 31.5 (CH), 25.6 (CH), 23.3 (CH ₂), 22.4 (CH ₃), 21.0 (CH ₃), 16.2 (CH ₃).
3f	-83.5°	7.42 (s, 1H), 4.70 (d, $J =$ 12.2 Hz, 1H), 4.52 (d, $J =$ 12.2 Hz, 1H), 4.29 (t, $J =$ 7.2 Hz, 2H), 3.15 (td, $J =$ 10.5, 4.1 Hz, 1H), 2.17–2.11 (m, 3H), 1.87 (t, $J =$ 7.0 Hz, 3H), 1.64–1.26 (m, 3H), 1.33–1.19 (m, 2H), 0.91 (d, J = 6.5 Hz, 9H), 0.86(d, $J =2.7 Hz, 6H), 0.62 (d, J =6.9 Hz, 3H).$	$\begin{array}{c} 146.3 \ (C), \ 121.8 \ (CH), \ 78.7 \ (CH), \\ 62.1 \ (CH_2), \ 50.3 \ (CH_2), \ 48.4 \ (CH), \\ 40.4 \ (CH_2), \ 34.7 \ (CH_2), \ 31.6 \ (CH), \\ 31.3 \ (CH_2), \ 30.5 \ (CH_2), \ 29.3 \\ (CH_2), \ 25.7 \ (CH_2), \ 23.5 \ (CH_2), \\ 22.6 \ (CH_2), \ 22.5 \ (CH_3) \ 21.2 \\ (CH_3), \ 16.4 \ (CH_3), \ 14.1 \ (CH_3). \end{array}$
3g	<i>−</i> 84.5°	7.51 (s, 1H), 7.38–7.33 (m, 3H), 7.26–7.23 (m, 2H), 5.80 (d, $J = 4.0$ Hz, 1H), 5.50 (s, 2H), 4.78 (q, $J = 10.7$ Hz, 2H), 4.53 (d, $J = 3.6$ Hz, 1H), 4.25–4.20 (m, 1H), 4.04–4.00 (m, 3H), 3.99–3.91 (m, 1H), 1.46 (s, 3H), 1.34 (s, 3H), 1.28 (s, 3H), 1.25 (s, 3H).	134.6 (C), 129.1 (CH), 128.7 (CH), 127.9 (CH), 111.6 (C), 108.9 (C), 105.1 (C), 82.5 (CH), 81.6 (CH), 81.0 (CH), 72.2 (CH), 67.4 (CH ₂), 64.0 (CH ₂), 54.1 (CH ₂), 26.8 (2 x CH ₃), 26.2 (CH ₃), 25.4 (CH ₃).

 Table 2

 Optical Rotation ¹H NMR and ¹³C NMR Spectral Data of Compounds **3a-30** (Continued)

	Table	2	
Optical Rotation,	¹ H NMR and ¹³ C NMR	Spectral Data of	Compounds 3a-30

Cmpd.	$[\alpha]_D^{25}$	¹ H NMR (δ)	¹³ C NMR (δ)
3h	-84.8°	8.10 (s, 1H), 7.72–7.69 (m, 2H), 7.50–7.46 (m, 2H), 7.41–7.39 (m, 1H), 5.81 (d, J = 3.6 Hz, 1H), 4.85 (q, $J =15.9 Hz, 2H), 4.85 (q, J =3.6 Hz, 1H), 4.33–4.28 (m,1H), 4.08–4.00 (m, 3H),3.97–3.94 (m, 1H), 1.44 (s,3H), 1.36 (s, 3H), 1.31 (s, 3H),1.27 (s, 3H).$	145.8 (C), 137.3 (C), 129.8 (CH), 128.7 (CH), 120.5 (CH), 120.4 (CH), 111.9 (C), 109.2 (C), 105.3 (CH), 82.7 (CH), 81.6 (CH), 81.2 (CH), 72.3 (CH), 67.6 (CH ₂), 64.0 (CH ₂), 27.1 (CH ₃), 27.0 (CH ₃), 26.4 (CH ₃), 25.7 (CH ₃).
3i	-85.9°	7.59 (s, 1H), 5.88 (d, $J = 4.0$ Hz, 2H), 4.70 (q, $J = 12.0$ Hz, 2H), 4.53 (d, $J = 3.6$ Hz, 1H), 4.33 (t, $J = 8.0$ Hz, 1H), 4.12–4.07 (m, 4H), 4.05–4.00 (m, 3H), 1.90 (s, 2H), 1.67(s, 2H), 1.49 (s, 3H), 1.42 (s, 3H), 1.36 (s, 3H), 1.34 (s, 3H), 1.31–1.29 (m, 3H), 0.88 (t, $J = 8.0$ Hz, 3H).	144.8 (C), 122.1 (CH), 111.8 (C), 109.0 (C), 105.2 (CH), 82.6 (CH), 81.6 (CH), 81.1 (CH), 72.4 (CH), 67.4 (CH ₂), 64.4 (CH ₂), 50.4 (CH ₂), 31.1 (CH ₂), 30.2 (CH ₂), 29.7 (CH ₂), 26.8 (CH ₃), 26.8 (CH ₃), 26.2 (CH ₃), 26.1 (CH ₃), 25.5 (CH ₂), 22.4 (CH ₂), 13.9 (CH ₃).
3j	_	7.47 (s, 1H), 7.38–7.33 (m, 3H), 7.25–7.23 (m, 2H), 7.06 (d, $J = 7.5$ Hz, 1H), 6.74 (s, 1H), 6.72 (s, 1H), 5.51 (s, 2H), 5.17 (s, 2H), 3.23 (m, 1H), 2.30 (s, 3H), 1.17 (s, 3H), 1.15 (s, 3H).	155.4 (C), 145.3 (C), 136.3 (C), 134.8 (C), 134.2 (C), 129.2 (CH), 128.8 (CH), 128.0 (CH), 126.1 (CH), 122.1 (CH), 122.0 (CH), 113.0 (CH), 62.6 (CH ₂), 54.2 (CH ₂), 26.6 (CH), 22.9 (2xCH ₃), 21.5 (CH ₃).
3k		7.98 (s, 1H), 7.76–7.74 (m, 2H), 7.52 (m, 2H), 7.45–7.40 (m, 1H), 7.07 (d, <i>J</i> = 7.6 Hz, 1H), 6.80 (s, 1H), 6.76 (d, <i>J</i> = 7.7 Hz, 1H), 5.29 (s, 2H), 3.31 (m, 1H), 2.34 (s, 3H), 1.23 (s, 3H), 1.21 (s, 3H).	155.4 (C), 145.8 (C), 137.4 (C), 136.5 (C), 134.3 (C), 129.9 (CH), 128.8 (CH), 126.2 (CH), 122.2 (CH), 120.7 (CH), 120.2 (CH), 112.9 (CH), 62.6 (CH ₂), 26.8 (CH), 23.1 (2xCH ₃), 21.6 (CH ₃).
31	_	7.53 (s, 1H), 7.05 (d, $J = 7.6$ Hz, 1H), 6.74 (s, 1H), 6.72 (d, $J =$ 7.7 Hz, 1H), 5.17 (s, 2H), 4.31 (t, $J = 7.2$ Hz, 2H,), 3.29–3.22 (m, 1H), 2.29 (s, 3H), 1.89 (t, $J =$ 6.9 Hz, 2H), 1.32–1.29 (m, 6H), 1.27 (s, 3H), 1.26 (s, 3H), 1.18 (t, $J = 7.2$ Hz, 3H).	155.3 (C), 144.6 (C), 136.1 (C), 134.0 (C), 125.9 (CH), 121.9 (CH), 121.7 (CH), 112.7 (CH), 62.5 (CH ₂), 50.2 (CH ₂), 31.1 (CH ₂), 30.2 (CH ₂), 26.6 (CH ₂), 26.1 (CH ₂), 22.8 (2xCH ₃), 22.4 (CH ₃), 21.3 (CH ₂),13.9 (CH ₃).

(Continued on next page)

Cmpd.	$[\alpha]_D^{25}$	¹ H NMR (δ)	13 C NMR (δ)
3m		7.50 (s, 1H), 7.68–7.66 (m, 2H), 7.45–7.41 (m, 2H), 7.37–7.33 (m, 1H), 6.89 (d, J = 8.0 Hz, 1H), 6.64–6.62 (m, 2H), 5.94–5.86 (m, 1H), 5.43 (s, 2H), 5.15 (s, 2H), 5.06–5.01 (m, 2H), 3.75 (s, 3H), 3.29 (d, J = 8.0 Hz, 2H).	148.5 (C), 144.9 (C), 143.6, (C), 136.3 (C), 133.6 (C), 132.5 (C), 127.9 (CH), 127.4 (CH), 126.9 (CH), 121.6 (CH), 119.4 (CH),114.6 (CH), 113.6 (CH), 111.2 (CH), 62.3 (CH ₂), 54.5 (CH ₃), 52.8 (CH ₂), 38.7 (CH ₂).
3n	_	8.03 (s, 1H), 7.68–7.66 (m, 2H), 7.45–7.41 (m, 2H), 7.37–7.33 (m, 1H), 6.93 (d, J = 7.9 Hz, 1H), 6.66–6.63 (m, 2H), 5.94–5.86 (m, 1H), 5.85 (s, 2H), 5.26–5.00 (m, 2H), 3.81 (s, 3H), 3.28–3.27 (d, $J =$ 6.6 Hz, 2H).	149.6 (C), 146.0 (C), 145.2 (C), 137.5 (C), 137.1 (C), 133.7 (CH), 129.6 (CH), 128.6 (CH), 120.8 (CH), 120.7 (CH), 120.4 (CH), 115.8 (CH ₂), 114.5 (CH), 112.4 (CH), 63.3 (CH ₂), 55.7 (CH ₃), 39.9 (CH ₂).
30	_	7.56 (s, 1H), 6.91 (d, $J = 7.9$ Hz, 1H), 6.67–6.64 (m, 2H), 5.94–5.86 (m, 1H), 5.23 (s, 1H), 5.07–5.02 (m, 2H), 4.31 (t, $J = 7.2$ Hz, 2H), 3.84 (s, 3H), 3.30 (d, $J = 6.6$ Hz, 2H), 1.88–1.86 (m, 2H), 1.33–1.25 (m, 6H), 0.89–0.86 (m, 3H).	149.5 (C), 146.0 (C), 144.4 (C), 137.4 (CH), 133.4 (C), 122.2 (CH), 120.6 (CH), 115.7 (CH ₂), 114.5 (CH), 112.3 (CH), 63.4 (CH ₂), 55.7 (OCH ₃), 50.2 (CH ₂), 39.8 (CH ₂), 31.1 (CH ₂), 30.2 (CH ₂), 26.1 (CH ₂), 22.4 (CH ₂), 13.9 (CH ₃).

 Table 2

 Optical Rotation, ¹H NMR and ¹³C NMR Spectral Data of Compounds 3a–3o (Continued)

rubber septum. The contents of the reaction vessel were stirred while the temperature was maintained at 110°C. At this temperature internal pressure of the reaction vessel did not exceed 1 bar (750 mm Hg).

1-Benzyl-4-[(cholesteryloxy)methyl]-1H-1,2,3-triazole (3a). Typical Procedure. A heterogeneous mixture of cholesterol propargyl ether (**1a**, 2 g, 4.7 mmol), benzyl azide (**2a**, 629 mg, 4.7 mmol), CuSO₄·5H₂O (5.1 mg, 0.001 mmol), sodium ascorbate (9.9 mg, 0.002 mmol) and PEG 200 (4.71 g, 5 equiv) in a 30 ml thick walled glass tube fitted with a rubber septum was irradiated at 110°C for 5 min, by which time reaction was complete (TLC). The reaction mixture was diluted with ice-cold distilled water (20 mL) to afford a solid suspension which was collected (2.62 g, 99%). Although this sample was sufficiently pure (TLC) for IR and NMR spectra, for the purposes of mp determination, HRMS and combustion analysis a part of the sample was recrystallized from a mixture of hexanes and ethyl acetate (9:1).

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