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Ti(O*i*Pr)$_4$-Mediated nucleophilic substitution of propargylic esters

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Abstract—The direct and catalytic displacement reactions of propargylic esters are reported. The reaction is based on the Ti(OR)$_4$/α-hydroxy acid mediated ligand exchange. This methodology enables the inclusion of a broad range of acetylenes and aldehydes into this substitution reaction.

1. Introduction

Interest in the synthesis of chiral propargylic compounds has recently been steadily growing.[1] Specifically, chiral propargylic alcohols are powerful building blocks for asymmetric synthesis as they possess a useful stereodirecting influence for chemical transformations such as reduction or metal assisted addition followed by selective functionalization of the resulting double bond. Only a few methods exist at that time for the synthesis of chiral propargylic compounds and they are listed below.

The very first attempt of an enantioselective Nicholas reaction was carried out by Montana et al. They used chiral propargyl cobalt hexacarbonyl cations in addition reactions to aldehydes.[2]

Carreira et al. published the catalytic and enantioselective addition of metallated alkynilides to aldehydes.[3]

Previously, we have described a nucleophilic displacement reaction of propargylic esters mediated by $TiCl_4$,[4] a suitable approach to chiral propargylic compounds. Attempts in the enantioselective execution of this displacement reaction were not successful.

During that work we developed a new catalytic methodology for this displacement reaction under remarkably mild conditions. The versatility of this process is such that a broad range of both acetylenes and aldehydes participate in this substitution reaction. For the first time, we were successful with nucleophilic substitution of non-activated or so-called non-stabilized propargylic esters by using this protocol.

Herein we describe this new methodology: the Ti(OR)$_4$-mediated substitution reaction of propargylic esters.

2. Results and discussion

As we described earlier, propargylic esters undergo nucleophilic substitution in the presence of Lewis acids. Thus we were able to synthesize propargylic ethers[4a,b] and propargylic amines[4c] in the presence of substoichiometric amounts of $TiCl_4$, the Lewis acid giving the best results concerning to yields in this reaction.[4a] The enantioselective execution of this method by using chiral modified $TiCl_n$-Lewis acids failed. In some cases, no reaction was observed (the titanium complexes were unreactive) while in other cases the determined enantioselectivities were very low (ee$<$25%). These results are comparable with those obtained in $TiCl_4$-mediated direct aldol addition.[5]

Moreover, we observed that substituents promote the substitution which is able to stabilize a propargylic cation[4b] during this reaction (so-called stabilized or activated substrates, R_1/R_3–Ph or *t*Bu). On the other hand, substituents which are not able to stabilize a cation, inhibit the nucleophilic substitution. No reaction was observed using such substrates in the $TiCl_4$-mediated displacement reaction (unstabilized or non-activated substrates: entries 11 and 12; Table 1). A substitution was achieved only under drastic conditions (−78°C, Me_3SiOTf; entry 13, Table 1). Additionally, we observed that the stabilizing effect of substituent R_1 is much more important than that of substituent R_3 (compare entries 10, 11 and 12, Table 1).

In order to overcome these problems and in connection with our ongoing studies in the field of catalytic, enantioselective and direct aldol additions, we tested the Ti(OR)$_4$/α-hydroxy acid ligand exchange mediated methodology.[6]

Propargylic esters were reacted with alcohols in the presence of Ti(O*i*Pr)$_4$/α-hydroxy acid at room temperature.

Keywords: propargylic esters; nucleophilic substitution; ethers; titanium complexes.

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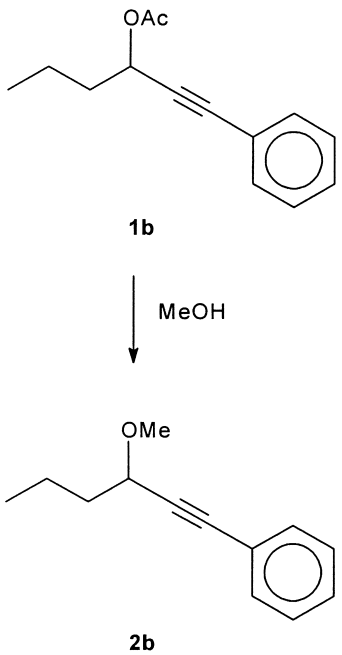
Table 1. Ti(O*i*Pr)$_4$-Mediated nucleophilic substitution of non-activated propargylic esters with methanol

Entry	Substance	R_1	R_2	R_3	Yield (%, method)
1	**2a**	Me	H	Ph	78[a]
2	**2b**	*n*Pr	H	Ph	45[b], 52[a]
3	**2c**	*s*bu	H	Ph	57[a]
4	**2d**	*t*Bu	H	Ph	91[a]
5	**2e**	Et	Me	Ph	74[b]
6	**2f**	Me	Me	Ph	86[b]
7	**2g**	*n*Pr	H	*n*Bu	10[a]
8	**2h**	*s*bu	H	*n*Bu	19[a]
9	**2i**	Et	Me	*n*Bu	51[a]
10		Ph	H	*n*Bu	76[c]
11	**2b**	*n*Pr	H	Ph	–[c]
12		*t*Bu	H	*t*Bu	–[c]
13	**2b**	*n*Pr	H	Ph	38[d]

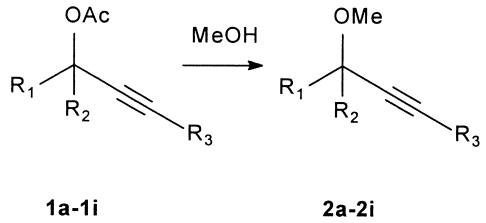
[a] Method B.
[b] Method A.
[c] $TiCl_4$ (see Ref. 4b).
[d] Me_3SiOTf (see Ref. 4b).

A substitution indeed occurred under these conditions but in low yield. Several optimizations led us to the use of hexafluoroisopropanol (HFIP), a valuable solvent of high polarity and low nucleophilicity.[7] It is used in the stabilization of cations[8] and is a preferred solvent for direct substitution of phenol ethers.[9] By using equimolar amounts of HFIP in these reactions, we were able to isolate the corresponding non-activated propargylic ethers **2b** in high yield (Scheme 1).

Two general and useful procedures for this catalytic displacement reaction were developed as a result of our optimization. In those cases where R_3 is the stabilizing substituent (R_3=Ph), method A gave the best results (10 mol% Ti(O*i*Pr)$_4$, mandelic acid, room temperature, Scheme 1). In all other cases (R_1=R_2=R_3=alkyl groups),



Scheme 1. *Method A*: 10 mol% Ti(O*i*Pr)$_4$, (±)-mandelic acid, HFIP, room temperature, yield: 45%. *Method B*: 10 mol% Ti(O*i*Pr)$_4$, camphorsulfonic acid, HFIP, 40–50°C, yield 52%.



Scheme 2.

method B provided the highest yields of isolated propargylic ethers (10 mol% Ti(O*i*Pr)$_4$, camphorsulphonic acid, 40–50°C, Scheme 1). By using these procedures we were able to react even non-activated substrates to give the expected methylethers in good yields (Scheme 2, Table 1). The non-activation on both sides of the propargylic system (R_1 and R_3=alkyl substituents) resulted in lower yields (entries 7 and 8, Table 1). Two alkyl residues on the propargylic carbon atom are able to stabilize a carbocation as well (entry 9, Table 1). Substitution reaction of this substrate with methanol yields the corresponding propargylic methylether **2a**–**2i** in good yields (Scheme 2).

In addition, by the use of activated molecular sieves, one can increase yields of the corresponding ethers **2a**–**2i** by approx. 10%.

Work in our group continues to elucidate details of this process. Attempts in enantioselective execution of this reaction are under way.

3. Experimental

^{1}H and ^{13}C NMR spectra were recorded at 300 and 75 MHz, respectively using a AC-300 spectrometer. Mass spectra were acquired on a HP 5995 (Hewlett-Packard) spectrometer (70 eV). MS spectra were obtained on a HP 5995 (Hewlett-Packard) spectrometer (70 eV). IR spectra were recorded on a Bio-Rad FT-IR 3000 MX machine.

All reactions were carried out under an argon atmosphere in glassware which had been flame-dried under a stream of argon. Solvents were dried and distilled prior to use. $LiClO_4$ was dried i. vac. at 120°C.

3.1. General procedure for the synthesis of propargylic acetates 1a–1i

The synthesis of propargylic acetates **1a**–**1i** were performed according to Ref. 4b.

3.1.1. [(1-Methyl-3-phenyl)-prop-2-ynyl]-acetate (1a).[10] Colourless oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.50–7.30 (5H, m, aromatic), 5.61 (1H, q, J=6.8 Hz, H1), 2.03 (3H, s, $-COCH_3$), 1.51 (3H, d, J=6.8 Hz, $-CH_3$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.0 (C=O), 131.2, 128.6, 128.2, 122.2 (aromatic), 87.4 (C2), 84.5 (C3), 60.8 (C1), 21.5 ($-COCH_3$), 21.2 ($-CH_3$).

3.1.2. [(1-*n*Propyl-3-phenyl)-prop-2-ynyl]-acetate (1b).[4b,11] Colourless oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.40–7.20 (5H, m, aromatic), 5.54 (1H, t, J=6.4 Hz, H1), 2.03 (3H, s,

$-COCH_3$), 1.78 (2H, m, $-CH_2$), 1.45 (2H, m, $-CH_2$), 0.91 (3H, t, J=6.4 Hz, $-CH_3$).

3.1.3. [(1-*s*Butyl-3-phenyl)-prop-2-ynyl]-acetate (1c). Colourless oil; IR (neat) ν_{max} 3467 (br), 2967, 2933, 2879, 2229, 1743, 1646, 1607, 1400, 1230, 1018 cm^{-1}; two stereoisomers with unknown diastereoselectivity were described: ^1H NMR (300 MHz, $CDCl_3$) δ 7.50–7.10 (5H, m, aromatic), 5.49 (1H, d, J=5.3 Hz, H1), 2.05 (3H, s, $-COCH_3$), 1.85–1.70 (1H, m), 1.70–1.45 (1H, m), 1.35–1.15 (1H, m), 1.00 (3H, t, J=7.0 Hz, $-CH_3$), 0.87 (3H, d, J=7.2 Hz, $-CH_3$) and for the minor isomer 7.50–7.10 (5H, m, aromatic), 5.46 (1H, d, J=5.3 Hz, H1), 2.05 (3H, s, $-COCH_3$), 1.85–1.70 (1H, m), 1.70–1.45 (1H, m), 1.35–1.15 (1H, m), 1.00 (3H, t, J=7.0 Hz, $-CH_3$), 0.90 (3H, d, J=6.4 Hz, $-CH_3$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.2 (C=O), 131.9, 128.5, 128.2, 122.4 (aromatic), 86.0 (C2), 85.7 (C3), 68.5 (C1), 39.3 (–CH), 25.6 ($-CH_2$), 21.1 ($-COCH_3$), 15.0 ($-CH_3$), 11.6 ($-CH_3$) and for the minor isomer 170.1 (C=O), 131.9, 128.5, 128.2, 122.4 (aromatic), 85.6 (C2), 85.1 (C3), 68.4 (C1), 38.9 (–CH), 24.9 ($-CH_2$), 21.1 ($-COCH_3$), 14.5 ($-CH_3$), 11.5 ($-CH_3$); MS: *m/z* (relative intensity) 230 (20), 201 (28), 188 (48), 155 (58), 131 (100); HRMS: *m/z* calcd for $C_{15}H_{18}O_2$ 230.1307. Found: 230.1308.

3.1.4. [(1-*t*Butyl-3-phenyl)-prop-2-ynyl]-acetate (1d).[12] Colourless oil; ^1H NMR (300 MHz, $CDCl_3$) δ 7.50–7.10 (5H, m, aromatic), 5.27 (1H, s, H1), 2.06 (3H, s, $-COCH_3$), 1.00 (9H, s, $-CH_3$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.3 (C=O), 131.9, 128.5, 128.2, 122.5 (aromatic), 89.0 (C2), 85.7 (C3), 72.3 (C1), 35.4 (qC), 25.6 ($-CH_3$), 21.0 ($-COCH_3$).

3.1.5. [(1-Ethyl-1-methyl-3-phenyl)-prop-2-ynyl]-acetate (1e). Colourless oil; IR (neat) ν_{max} 3468 (br), 2679, 2938, 2882, 2231, 1744, 1601, 1490, 1366, 1239, 1016 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.50–7.10 (5H, m, aromatic), 2.01 (3H, s, $-COCH_3$), 1.95–1.81 (2H, 2q, J=7.0 Hz, $-CH_2$), 1.72 (3H, s, $-CH_3$), 1.05 (3H, t, J=7.0 Hz, $-CH_3$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.8 (C=O), 132.2, 128.7, 128.5, 123.1 (aromatic), 89.6 (C2), 85.4 (C3), 76.6 (C1), 35.0 ($-CH_2$), 26.5 ($-COCH_3$), 22.4 ($-CH_3$), 9.1 ($-CH_3$); MS: *m/z* (relative intensity) 216 (75), 159 (87), 145 (100); HRMS: *m/z* calcd for $C_{14}H_{16}O_2$ 216.1150. Found: 216.1150.

3.1.6. [(1.1-Dimethyl-3-phenyl)-prop-2-ynyl]-acetate (1f).[13] Colourless oil; ^1H NMR (300 MHz, $CDCl_3$) δ 7.70–7.30 (5H, m, aromatic), 2.23 (3H, s, $-COCH_3$), 1.94 (6H, s, $-CH_3$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.4 (C=O), 131.8, 128.3, 128.1, 122.6 (aromatic), 90.2 (C2), 83.9 (C3), 72.5 (C1), 29.1 ($-CH_3$), 22.1 ($-COCH_3$).

3.1.7. (1-*n*Propyl-hept-2-ynyl)-acetate (1g).[14] Colourless oil; ^1H NMR (300 MHz, $CDCl_3$) δ 5.29 (1H, ddt, J=2.0, 2.0, 6.0 Hz, H1), 2.14 (2H, dt, J=2.0, 6.0 Hz, $-CH_2$), 2.06 (3H, s, $-COCH_3$), 1.65 (2H, m, $-CH_2$), 1.40 (6H, m, $-CH_2$), 0.87 (3H, t, J=7.0 Hz, $-CH_3$), 0.84 (3H, t, J=7.0 Hz, $-CH_3$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.5 (C=O), 86.5 (C2), 77.8 (C3), 64.8 (C1), 37.6 ($-CH_2$), 31.0 ($-CH_2$), 22.3 ($-CH_2$), 21.5 ($-COCH_3$), 18.7 ($-CH_2$), 14.0 ($-CH_3$), 13.9 ($-CH_3$); HRMS: *m/z* calcd for $C_{12}H_{20}O_2$ 196.1463. Found: 196.1477.

3.1.8. (1-*s*Butyl-hept-2-ynyl)-acetate (1h). Colourless oil; IR (neat) ν_{max} 3466, 2964, 2934, 2875, 2236, 1742, 1648, 1461, 1373, 1234, 1017 cm^{-1}; two stereoisomers with unknown diastereoselectivity were described: ^1H NMR (300 MHz, $CDCl_3$) δ 5.46 (1H, dt, J=2.0, 5.0 Hz, H1), 2.35 (2H, dt, J=2.0, 7.0 Hz, $-CH_2$), 2.21 (3H, s, $-COCH_3$), 1.85–1.35 (7H, m), 1.12 (3H, d, J=6.8 Hz, $-CH_3$), 1.05 (3H, t, J=7.2 Hz, $-CH_3$), 1.04 (3H, t, J=7.2 Hz, $-CH_3$) and for the minor isomer 5.42 (1H, dt, J=2.0, 5.0 Hz, H1), 2.34 (2H, dt, J=2.0, 7.0 Hz, $-CH_2$), 2.21 (3H, s, $-COCH_3$), 1.85–1.35 (7H, m), 1.13 (3H, d, J=6.8 Hz, $-CH_3$), 1.06 (3H, t, J=7.2 Hz, $-CH_3$), 1.02 (3H, t, J=7.2 Hz, $-CH_3$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.2 (C=O), 86.9 (C2), 76.5 (C3), 68.5 (C1), 39.3 ($-CH_2$), 30.6 ($-CH_2$), 25.5 ($-CH_2$), 21.9 ($-COCH_3$), 21.1 ($-CH_2$), 14.9 ($-CH_3$), 13.5 ($-CH_3$), 11.5 ($-CH_3$) and for the minor isomer 170.1 (C=O), 86.5 (C2), 75.8 (C3), 68.4 (C1), 38.8 (–CH), 30.6 ($-CH_2$), 24.7 ($-CH_2$), 21.7 ($-COCH_3$), 18.4 ($-CH_2$), 14.4 ($-CH_3$), 13.5 ($-CH_3$), 11.4 ($-CH_3$); MS: *m/z* (relative intensity) 210 (3), 195 (9), 181 (30), 168 (45), 139 (67), 121 (70), 111 (91), 43 (100); HRMS: *m/z* calcd for $C_{13}H_{22}O_2$ 210.1620. Found: 210.1622.

3.1.9. (1-Ethyl-1-methyl-hept-2-ynyl)-acetate (1i). Colourless oil; IR (neat) ν_{max} 3470 (br), 2961, 2934, 2878, 2243, 1744, 1466, 1369, 1244, 1120 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 2.15 (1H, t, J=7.0 Hz, $-CH_2$), 1.94 (3H, s, $-COCH_3$), 1.92–1.82 (1H, m, $-CH_2$), 1.79–1.65 (1H, m, $-CH_2$), 1.55 (3H, s, $-CH_3$), 1.47–1.25 (4H, m, $-CH_2$), 0.93 (3H, t, J=7.5 Hz, $-CH_3$), 0.83 (3H, t, J=7.0 Hz, $-CH_3$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.4 (C=O), 85.6 (C3), 80.2 (C2), 76.3 (C1), 34.7 ($-CH_2$), 30.7 ($-CH_2$), 26.3 ($-CH_2$), 22.1 ($-COCH_3$), 21.9 ($-CH_2$), 18.4 ($-CH_3$), 13.6 ($-CH_3$), 8.6 ($-CH_3$); MS: *m/z* (relative intensity) 196 (0.2), 181 (0.5), 154 (40), 125 (95), 112 (80), 97 (82), 43 (100); HRMS: *m/z* calcd for $C_{12}H_{20}O_2$ 196.1463. Found: 196.1464.

3.2. General procedures for the Ti(O*i*Pr)$_4$-mediated displacement reaction

Method A. $Ti(OiPr)_4$ (30 mg, 0.1 mmol) was carefully added to a stirred suspension of activated molecular sieves and the corresponding propargylic acetate **1a–1i** (1.0 mmol). $LiClO_4$ (dry, 11 mg, 0.1 mmol) was added after 1 h stirring at room temperature. *rac*-Mandelic acid (150 mg, 1.0 mmol) and methanol (320 mg, 10 mmol) were added 1 h later. A few minutes later HFIP (168 mg, 1.0 mmol) was added. The resulting solution (or sometimes suspension) was stirred for further 16 h at room temperature. The reaction mixture was poured into aqueous $NaHCO_3$ solution and extracted several times with diethyl ether. The organic layers were separated, dried (Na_2SO_4), concentrated i. vac. and purified by column chromatography (hexane/ethyl acetate=30/1). *Method B*. $Ti(OiPr)_4$ (30 mg, 0.1 mmol) were carefully added to a suspension of molecular sieves and the corresponding propargylic acetate (1.0 mmol). The solution was stirred for 1 h at room temperature. Camphorsulphonic acid (232 mg, 1.0 mmol) were added and the resulting solution was stirred for further 1 h at room temperature. Methanol (320 mg, 10 mmol) and HFIP (126 mg, 0.75 mmol) was added at that time. The resulting solution was stirred for 16 h at approx. 40–50°C. The reaction mixture was poured into saturated aq. $NaHCO_3$

solution and extracted several times with diethyl ether. The organic layers were separated, dried (Na_2SO_4), concentrated i. vac. and purified by column chromatography (hexane/ethyl acetate=30/1).

3.2.1. Methyl-[(1-methyl-3-phenyl)-prop-2-ynyl]-ether (2a).[15] Colourless oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.10–7.50 (5H, m, aromatic), 4.23 (1H, q, J=7.0 Hz, H1), 3.00 (3H, s, $-OCH_3$), 1.45 (3H, d, J=7.0 Hz, $-CH_3$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 131.7, 128.3, 128.3, 122.7 (aromatic), 88.8 (C2), 85.1 (C3), 67.3 (C1), 56.4 ($-OCH_3$), 14.1 ($-CH_3$).

3.2.2. Methyl-[(1-*n*propyl-3-phenyl)-prop-2-ynyl]-ether (2b).[4b] Colourless oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.10–7.50 (5H, m, aromatic), 4.10 (1H, t, J=7.0 Hz, H1), 3.40 (3H, s, $-OCH_3$), 1.80–1.60 (2H, m, $-CH_2$), 1.60–1.40 (2H, m, $-CH_2$), 0.90 (3H, t, J=7.0 Hz, $-CH_3$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 131.7, 128.3, 122.9 (aromatic), 88.2 (C2), 85.8 (C3), 71.5 (C1), 56.5 ($-OCH_3$), 37.8 ($-CH_2$), 18.6 ($-CH_2$), 13.9 ($-CH_3$).

3.2.3. Methyl-[(1-*s*butyl-3-phenyl)-prop-2-ynyl]-ether (2c). Colourless oil; IR (neat) ν_{max} 3500 (br), 2964, 2930, 2877, 2822, 2227, 1691, 1602, 1489, 1458, 1283, 1094 cm^{-1}; two stereoisomers with unknown diastereoselectivity were described: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.50–7.10 (5H, m, aromatic), 3.98 (1H, d, J=5.3 Hz, H1), 3.40 (3H, s, $-OCH_3$), 1.70–1.50 (3H, m), 0.98 (3H, d, J=6.4 Hz, $-CH_3$), 0.87 (3H, t, J=7.5 Hz, $-CH_3$) and for the minor isomer 7.50–7.10 (5H, m, aromatic), 3.95 (1H, d, J=5.3 Hz, H1), 3.40 (3H, s, $-OCH_3$), 1.70–1.50 (3H, m), 0.97 (3H, d, J=6.8 Hz, $-CH_3$), 0.81 (3H, t, J=6.8 Hz, $-CH_3$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 131.8, 128.2, 123.0 (aromatic), 87.4 (C2), 86.7 (C3), 76.4 (C1), 56.9 ($-OCH_3$), 39.9 ($-CH$), 25.7 ($-CH_2$), 15.1 ($-CH_3$), 11.7 ($-CH_3$) and for the minor isomer 131.7, 128.2, 123.0 (aromatic), 86.8 (C2), 86.4 (C2), 76.3 (C1), 56.9 ($-OCH_3$), 39.6 ($-CH$), 25.0 ($-CH_2$), 14.7 ($-CH_3$), 11.6 ($-CH_3$); MS: m/z (relative intensity) 202 (8), 145 (100); HRMS: m/z calcd for $C_{14}H_{18}O$ 202.1358. Found: 202.1358.

3.2.4. Methyl-[(1-*t*butyl-3-phenyl)-prop-2-ynyl]-ether (2d). Colourless oil; IR (neat) ν_{max} 3450 (br), 2959, 2934, 2869, 2821, 1601, 1487, 1441, 1237, 1177, 1102, 1045 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.50–7.10 (5H, m, aromatic), 3.67 (1H, s, H1), 3.41 (3H, s, $-OCH_3$), 0.98 (9H, s, $-CH_3$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 131.7, 128.2, 128.1, 124.1 (aromatic), 87.2 (C2), 86.5 (C3), 81.6 (C1), 57.6 ($-OCH_3$), 35.8 (qC), 25.9 ($-CH_3$); MS: m/z (relative intensity) 202 (5), 145 (100); HRMS: m/z calcd for $C_{14}H_{18}O$ 202.1358. Found: 202.1358.

3.2.5. Methyl-[(1-ethyl-1-methyl-3-phenyl)-prop-2-ynyl]-ether (2e). Colourless oil; IR (neat) ν_{max} 3060, 2966, 2933, 2878, 2229, 1744, 1480, 1371, 1231, 1018 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.50–7.10 (5H, m, aromatic), 3.35 (3H, s, $-OCH_3$), 1.80–1.60 (2H, dq, J=7.5, 6.0 Hz, $-CH_2$), 1.41 (3H, s, $-CH_3$), 0.78 (3H, t, J=7.5 Hz, $-CH_3$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 131.7, 128.2, 128.1, 123.0 (aromatic), 90.3 (C2), 85.3 (C3), 74.5 (C1), 51.5 ($-OCH_3$), 34.0 ($-CH_2$), 25.1 ($-CH_3$), 8.8 ($-CH_3$); MS: m/z (relative intensity) 156 (100), 141 (65), 128 (28), 115 (53); HRMS: m/z calcd for $C_{12}H_{12}$ [M$-CH_3OH$] 156.0939. Found: 156.0937.

3.2.6. Methyl-[(1.1-dimethyl-3-phenyl)-prop-2-ynyl]-ether (2f).[16] Colourless oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.50–7.10 (5H, m, aromatic), 3.36 (3H, s, $-OCH_3$), 1.47 (6H, s, $-CH_3$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 131.7, 128.2, 128.2, 122.9 (aromatic), 91.0 (C2), 84.2 (C3), 70.9 (C1), 51.7 ($-OCH_3$), 28.4 ($-CH_3$).

3.2.7. Methyl-(1-*n*propyl-hept-2-ynyl)-ether (2g). Colourless oil; IR (neat) ν_{max} 3453 (br), 2862, 2928, 2870, 2234, 1728, 1639, 1462, 1264, 1104, 1072, 1037 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.85 (1H, tt, J=1.9, 7.0 Hz, H1), 3.31 (3H, s, $-OCH_3$), 2.16 (2H, dt, J=1.9, 7.0 Hz, $-CH_2$), 1.70–1.50 (4H, m, $-CH_2$), 1.50–1.30 (4H, m, $-CH_2$), 0.86 (3H, t, J=7.0 Hz $-CH_3$), 0.84 (3H, t, J=7.0 Hz, $-CH_3$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 86.3 (C2), 78.9 (C3), 71.3 (C1), 56.1 ($-OCH_3$), 38.0 ($-CH_2$), 31.9 ($-CH_2$), 29.4 ($-CH_2$), 22.7 ($-CH_2$), 18.6 ($-CH_2$), 13.8 ($-CH_3$), 13.6 ($-CH_3$); MS: m/z (relative intensity) 137 (35), 119 (18), 95 (100), 81 (95); HRMS: m/z calcd for $C_{10}H_{17}$ [M$-CH_3O$] 137.13303. Found: 137.13303.

3.2.8. Methyl-(1-*s*butyl-hept-2-ynyl)-ether (2h). Colourless oil; IR (neat) ν_{max} 3384 (br), 2961, 2934, 2873, 2218, 1667, 1461, 1379, 1034, 1002 cm^{-1}; two diastereoisomers with unknown configuration were described: ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.74 (1H, dt, J=2.3, 5.3 Hz, H1), 3.32 (3H, s, $-OCH_3$), 2.35 (2H, dt, J=2.3, 7.5 Hz, $-CH_2$), 1.85–1.35 (7H, m, $-CH_2$), 0.89 (3H, d, J=7.3 Hz, $-CH_3$), 0.81 (3H, t, J=7.2 Hz, $-CH_3$), 0.84 (3H, t, J=7.2 Hz, $-CH_3$) and for the minor isomer 3.70 (1H, dt, J=1.9, 4.9 Hz, H1), 3.31 (3H, s, $-OCH_3$), 2.34 (2H, dt, J=4.9, 2.1 Hz, $-CH_2$), 1.85–1.35 (7H, m, $-CH_2$), 0.86 (3H, d, J=7.3 Hz, $-CH_3$), 0.82 (3H, t, J=7.2 Hz, $-CH_3$), 0.85 (3H, t, J=7.2 Hz, $-CH_3$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 83.0 (C2), 77.6 (C1), 77.2 (C3), 56.6 ($-OCH_3$), 39.5 ($-CH$), 31.1 ($-CH_2$), 25.7 ($-CH_2$), 21.9 ($-CH_2$), 19.2 ($-CH_2$), 15.0 ($-CH_3$), 14.0 ($-CH_3$), 11.6 ($-CH_3$) and for the minor isomer 83.2 (C2), 76.9 (C1), 76.0 (C3), 56.5 ($-OCH_3$), 39.2 ($-CH$), 30.9 ($-CH_2$), 24.9 ($-CH_2$), 22.1 ($-CH_2$), 18.5 ($-CH_2$), 14.5 ($-CH_3$), 13.6 ($-CH_3$), 11.6 ($-CH_3$); MS: m/z (relative intensity) 167 (11), 137 (25), 111 (56), 95 (84), 81 (100); HRMS: m/z calcd for $C_{10}H_{17}$ [M$-CH_3OCH_2$] 137.1330. Found: 137.1336.

3.2.9. Methyl-(1-ethyl-1-methyl-hept-2-ynyl)-ether (2i). Colourless oil; IR (neat) ν_{max} 3458, 2961, 2934, 2872, 2216, 1723, 1677, 1637, 1461, 1375, 1220, 1070 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.26 (3H, s, $-OCH_3$), 2.15 (3H, t, J=7.0 Hz, $-CH_2$), 1.58 (2H, dq, J=3.1, 7.1 Hz, $-CH_2$), 1.50–1.30 (4H, m, $-CH_2$), 1.27 (3H, s, $-CH_3$), 0.89 (3H, t, J=7.0 Hz, $-CH_3$), 0.84 (3H, t, J=7.0 Hz, $-CH_3$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 85.7 (C2), 81.0 (C3), 74.2 (C1), 51.1 ($-OCH_3$), 34.1 ($-CH_2$), 31.0 ($-CH_2$), 25.3 ($-CH_2$), 21.9 ($-CH_2$), 18.3 ($-CH_3$), 13.6 ($-CH_3$), 8.7 ($-CH_3$); MS: m/z (relative intensity) 153 (13), 139 (100); HRMS: m/z calcd for $C_{10}H_{17}O$ 153.1279. Found: 153.1280.

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