SHORT PAPER

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Phase transfer catalysis method of synthesis of benzyl- and benzhydryloxyalkoxyalkynes†

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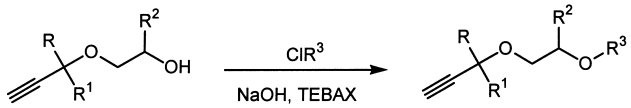
The synthesis of benzyl- and benzhydryloxyalkoxyalkynes and the determination of the influence of phase transfer catalyst, solvent and temperature on this nucleophilic substitution reaction is reported.

Keywords: alkynes, benzyloxyalkynes, benzhydryloxyalkynes, oxyalkynoles, phase transfer

As a continuation of the application of the phase transfer catalysis (PTC) method in the synthesis of oxyalkynes[1] we have synthesised some oxyethoxyalkynes: 3-(2-benzyl oxyethoxy)-1-propyne[2] and 3-(2-benzhydryloxyethoxy)-1-propyne[3]. In this work we analyse the possibility of synthesising new benzyl- and benzhydryloxyethoxyalkynes by reaction of oxyalkynoles with benzyl chloride or chlorodiphenylmethane, under PTC conditions, and using benzyltriethylammonium halide TEBAX (X = Cl, Br) as a phase transfer catalyst. We have established the optimal conditions for the formation of oxyalkoxyalkynes having one or two phenyl groups; we also look at the influence of the catalyst, temperature and solvent on this nucleophilic substitution reaction.

Earlier[2] {[2-(prop-2-ynyloxy)ethoxy]methyl}benzene was synthesised using the PTC method, with benzene as solvent; however, under these conditions the reaction would not go the completion. Therefore acetonitrile was chosen and the ratio of reaction agents was changed. When the reaction was performed in acetonitrile (ratio of 2-(propyn-2-yloxy)ethanol, benzyl chloride and NaOH was 2:1:1) and 10% of TEBAX at 50°C, 80% of benzyl chloride reacted over 1 h; and when the ratio of the reaction agents was 2:1:1.2 or 2:1:1.5, respectively 85% and 90% of benzyl chloride reacted. We also established that even in the absence of a catalyst, at the start of the reaction the speed was almost the same; however, it slows down and no more than 80% of benzyl chloride reacts. If 10% or 5% of TEBAX was added over 2 h at 50°C (or over 1 h at 70°C) all the benzyl chloride reacts. When the reaction was performed in benzene under similar conditions only 50–70% of benzyl chloride reacted. Thus, as a result of the reaction between oxyalkynoles and benzyl chloride, in the presence of alkali and using acetonitrile as a solvent, and when the ratio of the reaction agents was 2:1:1.2, with 5% of TEBAX added, 85–90% of corresponding benzyloxyethoxyalkynes **1**–**4** (Scheme 1) were isolated after 1–2 h of stirring at 50–70°C. The reaction with 1-prop-2-ynyloxypropan-2-ol was performed at 55–60°C; after 14 h of stirring 54% of (1-methyl-2-prop-2-ynyloxy-ethoxymethyl)-benzene **5** (Scheme 1) was isolated. The duration of the reaction was established according to integral intensities of $RO\underline{CH_2}C_6H_5$ and $Cl\underline{CH_2}C_6H_5$ groups in ^{1}H NMR spectra.



Scheme 1 [**1, 5, 6** R = R^1 = H; **2, 7** R = H, R^1 = CH_3; **3, 8** R = R^1 = CH_3; **4, 9** R = CH_3, R^1 = C_2H_5; **1-4, 6-9** R^2 = H, **5** R^2 = CH_3; **1-5**, R^3 = $CH_2C_6H_5$; **6-9** R^3 = $CH(C_6H_5)_2$]

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We found that during the reactions of oxyalkynoles with chlorodiphenylmethane, the hydrolysis of chlorodiphenylmethane took place in the solvent and diphenylmethanol was formed. In acetonitrile 10–25% of diphenylmethanol was formed, depending upon the temperature of the reaction mixture and the duration of the reaction. Therefore, only 37–46% of the corresponding benzhydryloxyethoxyalkynes **6**–**9** was isolated after 5–8 h of heating at ~70°C, as their yields were greatly reduced by the formed diphenylmethanol which was difficult to separate by distillation. During the reaction of 2-(2-propynyloxy)ethanol and chlorodiphenylmethane in benzene, after 15 h of stirring at ~70°C, 20% of {phenyl[2-(prop-2-ynyloxy)ethoxy]methyl}benzene **(6),** with 70% of diphenylmethanol were formed and ~10% of chlorodiphenylmethane did not react. When the reaction was performed in toluene, after 5 h of stirring and at ~100°C – the values were 42%, 48% and 10% respectively; therefore, we synthesised all benzhydryloxyethoxyalkynes according to the method that we suggested earlier,[2] only the ratio of the reactants was changed. When the ratio of oxyalkynol, chlorodiphenylmethane and NaOH was 4:1:1.2 and when 5% of TEBAX was added, after 3 h of stirring at 50–70°C, 65–70% of corresponding benzhydryloxyethoxyalkynes **6**–**9** (Scheme 1) were isolated.

We established the duration of the reaction between oxyalkynoles and chlorodiphenylmethane by performing reactions with similar quantities of chlorodiphenylmethane and NaOH and by heating and stirring the reaction mixture to pH ≈ 6. However, during the synthesis of benzhydryloxyethoxyalkynes, up to 20% of excess NaOH can be cored in order to react off the all chlorodiphenylmethane (which makes the isolation of a product more difficult). We established the ratio of by-products formed in the course of the reaction by noting the integral intensities of $RO\underline{CH}(C_6H_5)_2$ and $Cl\underline{CH}(C_6H_5)_2$ groups in the ^{1}H NMR spectra.

Oxyalkoxyalkynoles used in our work were formed as a result of the reaction between alkynol and oxyrane or 2-methyl-oxyrane.[4] We also tried to use 1-chloro-propan-2-ol in the synthesis of benzyloxypropoxyalkynes. However, even under PTC conditions we did not succeed in getting 1-benzyl oxy-propan-2-ol, as 2-methyl-oxyrane is formed in alkaline media. During the reaction between prop-2-yn-1-ol and 1-chloro-propan-2-ol the dehydrohalogenation of 1-chloro-propan-2-ol takes place as well; also, a small amount of 1-propy-2-ynyloxy-propan-2-ol was formed.

Experimental

^{1}H NMR spectra were recorded on a Tesla BS-567A NMR spectrometer at 80 MHz with *TMS* as internal standard.

Synthesis of benzyloxyethoxyalkynes **(1–4):** 4000 mg (100 mmol) of powdered NaOH and 4 mmol of TEBAX (850 mg of TEBACl or 1030 mg of TEBABr) were added to 100 cm^3 of acetonitrile, and 200 mmol of corresponding oxyalkynole was added while stirring

Table 1 Data of benzyl- and benzhidryloxyalkoxyalkynes **1–9**

Compound no.	Yield/%	B.p.°C/mm	n_D^{20}	Found/required/% C	H	Formula	NMR ^{1}H data/δppm
1	85	137–139/5	1.5106	75.61 75.76	7.49 7.41	$C_{12}H_{14}O_2$	3.05 (1H, t, ^4J = 3 Hz), 3.79 (4H, m), 4.32 (2H, d, ^4J = 3 Hz), 4.66 (2H, s), 7.48 (5H, m).
2	71	145–147/10	1.5027	76.29 76.43	8.01 7.89	$C_{13}H_{16}O_2$	1.51 (3H,d, ^3J = 6 Hz), 3.06 (1H, d, ^4J = 2 Hz), 3.61 – 4.05 (4H, m), 4.37 (1H, q, ^3J = 6 Hz, ^4J = 2 Hz), 4.66 (2H, s), 7.46 (5H, m).
3	80	149–152/12	1.4982	76.85 77.03	8.47 8.31	$C_{14}H_{18}O_2$	1.57 (6H, s), 3.09 (1H, s), 3.81 (4H, m), 4.68 (2H, s), 7.46 (5H, m).
4	75	159–162/12	1.4992	77.46 77.55	8.75 8.67	$C_{15}H_{20}O_2$	1.11 (3H, t, ^3J = 7 Hz), 1.51 (3H, s), 1.79 (2H, q, ^3J = 7 Hz), 3.09 (1H, s), 3.81 (4H, m), 4.68 (2H, s), 7.46 5H, m).
5	54	119–121/3	1.5122	76.31 76.43	7.96 7.89	$C_{13}H_{16}O_2$	1.31 (3H, d, ^3J = 6 Hz), 3.07 (1H, t, ^4J = 3 Hz), 3.70 (2H, d), 3.86 (1H, m), 4.31 (2H, d, ^4J = 3 Hz), 4.73 (2H, s), 7.47 (5H, m).
6	80	165–167/1	1.5595	81.05 81.17	6.91 6.81	$C_{18}H_{18}O_2$	3.02 (1H, t, ^4J = 3 Hz), 3.79 (4H, m), 4.33 (2H, d, ^4J = 3 Hz), 5.63 (1H, s), 7.52 (10H, m).
7	65	175–178/3	1.5461	81.25 81.39	7.26 7.19	$C_{19}H_{20}O_2$	1.55 (3H, d, ^3J = 6 Hz), 3.09 (1H, d, ^4J = 2 Hz), 3.70 – 4.12 (4H, m), 4.41 (1H, q, ^3J = 6.5 Hz, ^4J = 3 Hz), 5.66 (1H, s), 7.49 (10H, m).
8	75	167–170/2	1.5441	81.53 81.60	7.61 7.52	$C_{20}H_{22}O_2$	1.57 (6H, s), 3.08 (1H, s), 3.77 (4H, m), 5.65 (1H, s), 7.5 (10H, m).
9	73	175–180/2	1.5391	81.68 81.78	7.91 7.84	$C_{21}H_{24}O_2$	1.12 (3H, t, ^3J = 7 Hz), 1.51 (3H, s), 1.79 (2H, q, ^3J = 7.5 Hz), 3.08 (1H, s), 3.79 (4H, m), 5.65 (1H, s), 7.51 (10H, m).

vigorously. The reaction mixture was heated to 50°C; over 0.5 h, 10120 mg (80 mmol) of benzyl chloride dissolved in 20 cm^{3}of acetonitrile was added dropwise; then the mixture was stirred for another 2 h at 50°C; or for 1 h at 70°C. The reaction mixture was cooled to room temperature and 200 cm^{3}of benzene and 150 cm^{3}of 0.1N HCl solution were added. The benzene layer was separated, washed with water to pH = 7 and dried with $MgSO_4$. After the solvent was distilled off, the products were re-distilled in vacuum. ^{1}H NMR spectra were recorded in deuterated acetone ($(CD_3)_2CO$) and C and H analyses were carried out. Information about benzyloxyalkoxyalkynes **1**–**4** is given in Table 1.

Synthesis of (1-methyl-2-prop-2-ynyloxy-ethoxymethyl)-benzene **(5)**: 4800 mg (120 mmol) of NaOH, 2560 mg of TEBABr, and 14000 mg (122 mmol) of 1-prop-2-ynyloxypropan-2-ol was added to 100 cm^{3}of acetonitrile, and 12600 mg (100 mmol) of benzyl chloride dissolved in 10 cm^{3}of acetonitrile was added dropwise over 1 h at 55-60°C. Then the mixture was heated for another 14 h at 65°C, cooled, and 100 cm^{3}of water and 100 cm^{3}of benzene were added. The benzene layer was separated, washed with water to pH = 7 and dried with $MgSO_4$. The solvent was distilled off, and the product was re-distilled in vacuum. ^{1}H NMR spectra were recorded in $(CD_3)_2CO$ and C and H analyses were carried out. Information about (1-methyl-2-prop-2-ynyloxy-ethoxymethyl)-benzene **(5)** is given in Table 1.

Synthesis of benzhydryloxyethoxyalkynes **(6–9):** 2000 mg (50 mmol) of powdered NaOH and 2 mmol of TEBAX (420 mg of TEBACl or 640 mg of TEBABr) were added to 200 mmol of corresponding oxyalkynol while stirring vigorously, and 8240 mg (40 mmol) of chlorodiphenylmethane was added dropwise over 0.5 h at ~ 30°C. The mixture was stirred for another 0.5 h at the same temperature; then the temperature was increased to 50°C during the synthesis of benzhydryloxyethoxyalkynes **6, 7**; during the synthesis of benzhydryloxyethoxyalkynes **8, 9** the temperature was increased to 70°C; and in each case stirring continued for another 3 h. After the reaction was complete the mixture was cooled to the room temperature, and 100 cm^3 of benzene and 75 cm^3 of 0.1M HCl solution was added. The benzene layer was separated, washed with water to pH = 7 and dried with $MgSO_4$. After the solvent was distilled off, the products were re-distilled in vacuum. ^{1}H NMR spectra were recorded in $(CD_3)_2CO$ and C and H analyses were carried out. Information about benzhydryloxyethoxyalkynes **(6–9)** is given in Table 1.

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