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SHORT COMMUNICATION

ONE-POT SYNTHESIS OF SPIROGLYCOL

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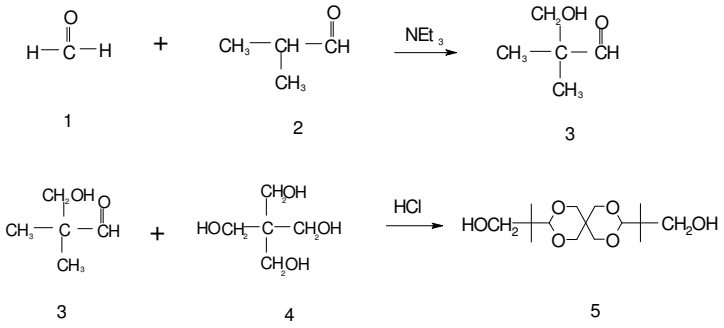
ABSTRACT. The synthesis of spiroglycol by one-pot reaction was studied using pentaerythritol, isobutyraldehyde and formaldehyde as starting materials. Under the optimum reacting conditions, the yield and purity of product were 93.6 % and 99.0 %, respectively. Compared to the synthesis methods reported in literatures, not only was the yield of product improved, but also two operating units were omitted. The product was characterized by ^{1}H NMR and IR.

KEY WORDS: One-pot synthesis, Spiroglycol, Pentaerythritol

INTRODUCTION

Spiroglycol was an important intermediate in organic synthesis. They can be used as starting materials for the synthesis of fine chemicals such as antioxidant [1-3] and functional polymers [4-8]. Although methods for the synthesis of spiroglycol have been reported, they were multistep with poor yield [7-12]. Tanaka Shinya [11] reported that spiroglycol (**5**) could be synthesized by reaction of pentaerythritol (**4**) with hydroxypivalaldehyde (**3**) in the presence of H_2SO_4 in xylene-H_2O at 60 ^oC for 12 h to give 89.7 % spiroglycol. Ninomiya Akiyuki [12] provided a method for producing spiroglycol using pentaerythritol, isobutyraldehyde (**2**) and formaldehyde (**1**) as starting materials. The method included four operating units: reaction of **1** and **2** to produce hydroxypivalaldehyde through aldol addition, separation of **3**, reaction of **3** and **4** to produce **5** and recrystallization of **5**. The synthetic sequences for the preparation of spiroglycol are shown in Scheme 1.



Scheme 1. Synthesis of **5**.

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We tried to use above method to prepare **5** and found that **3** could only be dried at room temperature for its sublimation property. This methodology was time consuming. Moreover, recrystallization was usually used for purification of **5** in reported literatures [4-10]. Kondo Osamu [9] used a mixture of N,N-dimethylformamide and toluene as solvent to purify the product **5** by recrystallization. Obviously this purification method has the drawbacks such as loss of product and recovery of solvent. In the present work, we attempted to provide a convenient and efficient synthesis of spiroglycol by one-pot and the detailed procedures for preparation of spiroglycol were studied. Compared to the synthesis methods reported in literatures, not only was the yield of product **5** improved, but also two operating units were omitted. To our knowledge, there is no report about this method in the literature.

EXPERIMENTAL

General

The materials used were of technical grade. All melting points were determined using a XT4A melting point apparatus and were uncorrected. IR (KBr) spectra (ν_{max} in cm^{-1}) were obtained on a Bruker spectrophotometer. ^1H NMR spectra were recorded in $CDCl_3$ on Bruker AV-400 spectrometer operating at 400 MHz.

*One-pot synthesis procedures of **5***

To a three-necked flask equipped with a mechanical stirrer, a condenser, a thermometer were charged 2.9 mol of **1**, 2.7 mol of **2**, 0.07 mol of triethylamine, and the mixture was heated at 70 ^oC for 6 h. After completion of the aldol addition, the mixture was neutralized by hydrochloric acid to pH = 7. Then 1 mol of **4** and 0.06 mol of hydrochloric acid were added, the mixture was heated at 60 ^oC for 10 h. After completion of the reaction, the formed white powder was filtered and washed by 5 mol of water at 70 ^oC and dried to obtain **5**. The yield of **5** was 93.6 % with the purity 99.0 %.

RESULTS AND DISCUSSION

*Synthesis of **5***

When compound **3** was put in an oven and heated at 70 ^oC for a while, it was surprisingly found that the weight of **3** was decreased dramatically. It is suggested that compound **3** has sublimation property that has not been reported in literature. The effect of drying time on weight loss and melting point of **3** was shown in Table 1. The results indicated that with increasing of drying time the weight loss of **3** increased, but the melting point was not changed. Therefore, the reason for the weight loss of **3** was owing to its sublimation property.

Table 1. Influence of drying time on weight loss and melting point of **3**.

Drying time (h)	Percentage of weight loss (%)	Melting point (^oC)
6	32	90-92
12	41	91-93
24	50	91-93
48	60	92-93
72	75	91-93

Due to its sublimation property, **3** could not be dried by traditional method at higher temperature. In order to avoid the loss of **3**, we tried to explore whether the preparation of compound **5** could be carried out in the same reaction vessel by one-pot method. That is to say, after finishing of the reaction of **1** and **2**, hydrochloric acid and **4** were added directly to the reactor to produce compound **5**. The optimum reaction conditions were examined and the obtained results are given in Table 2 and Table 3.

Table 2. Effects of different catalysts on one-pot synthesis of **5.**

Catalyst 1[a]	Catalyst 2[b]	Yield (%)	m.p. (°C)
Et_3N	HCl	93.6	200-201
Sodium hydroxide	HCl	88.5	197-200
Potassium carbonate	HCl	65.6	196-199
Pyridine	HCl	N.R.	
Et_3N	*p*-Toluene sulfonic acid	90.5	199-201
Et_3N	Sulfuric acid	93.0	200-201
Et_3N	Nitric acid	75.6	197-201
Et_3N	Phosphoric acid	63.5	196-198
Et_3N	Acetic acid	N.R.	

[a] Catalyst 1: the catalyst used in reaction of **1** and **2**. [b] Catalyst 2: the catalyst used in reaction of **3** and **4**. All the catalysts were used in the same mole amount.

From Table 2, it can be seen that the suitable catalyst for the reaction of compounds **1** and **2** is Et_3N. And for the reaction of compounds **3** and **4,** the suitable catalyst is HCl.

Table 3. One-pot synthesis results of **5** under different reaction conditions.

n_1/n_2[a]	Reaction time (h)	Reaction temp (°C)	n(Et_3N) (mol)	n_3 (mol)[b]	Reaction time (h)	Reaction temp (°C)	n(HCl) (mol)	Yield (%)	m.p. (°C)
2.8:2.6	5	60	0.05	1	8	50	0.04	80.5	198-200
2.8:2.6	5	70	0.05	1	8	50	0.04	83.4	199-201
2.8:2.6	5	80	0.05	1	8	50	0.04	81.5	198-200
2.8:2.6	6	70	0.05	1	8	50	0.04	85.7	198-201
2.8:2.6	6	70	0.07	1	8	50	0.04	86.5	199-200
2.8:2.6	6	70	0.09	1	8	50	0.04	83.3	198-200
2.8:2.6	7	70	0.07	1	8	50	0.04	85.3	199-201
2.9:2.7	6	70	0.07	1	8	50	0.04	90.5	200-201
3.2:2.7	6	70	0.07	1	8	50	0.04	89.5	200-201
3.0:2.8	6	70	0.07	1	8	50	0.04	90.1	199-201
2.9:2.7	6	70	0.07	1	8	50	0.04	90.6	200-201
2.9:2.7	6	70	0.07	1	8	60	0.04	91.5	200-201
2.9:2.7	6	70	0.07	1	8	70	0.04	91.7	199-201
2.9:2.7	6	70	0.07	1	10	60	0.04	91.3	200-201
2.9:2.7	6	70	0.07	1	10	60	0.06	93.6	200-201
2.9:2.7	6	70	0.07	1	10	60	0.08	93.4	200-201
2.9:2.7	6	70	0.07	1	12	60	0.06	93.7	200-201

[a] n1/n2: mole ratio of **1** and **2**. [b] n3: mole of **4**.

From the results of Table 3, the optimum reaction conditions for one-pot synthesis of **5** are as follows:

(1) For the reaction of compounds **1** and **2**, n(**1**):n(**2**):n(Et_3N) = 2.9:2.7:0.07, reaction time 6 h, reaction temperature 70 °C.

(2) For the reaction of compounds **3** and **4**, n(**1**):n(**2**):n(**4**) = 2.9:2.7:1, reaction time 10 h, reaction temperature 60 °C.

Purification of spiroglycol

Purification of **5** could be carried out by recrystallization according to literatures [4-10]. However, recrystallization process often caused the problems such as loss of product and recovery of solvent. During the experiment, we found out that all reactants were water-soluble and product **5** was not water-soluble. Therefore, by filtering and washing with water at 70 ^{o}C, it was possible to obtain the product **5** in good yield and purity which were higher than those reported in literatures.

Characterization of product

IR, v/cm^{-1}: 3255 (-OH), 2971 (-CH_3), 2950, 2870 (-CH_2-), 1087 (C-O). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 0.82 (s, 12H, 4-CH_3), 3.26-3.29 (s, 8H, 4-CH_2-), 3.45- 3.50 (w, 4H, 2-CH_2 -OH); 4.22 (m, 2H, 2-O-CH-O-); 4.40-4.42 (w, 2H, -OH).

CONCLUSIONS

A convenient and efficient synthesis of **5** by one-pot method was described. Under the optimum reacting conditions, the yield and purity of product were 93.6 % and 99.0 %, respectively. Compared to the synthesis methods reported in literatures, two operating units were omitted as well as the yield of product was improved.

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