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SHORT COMMUNICATION

Trimerization of aldehydes with one α-hydrogen catalyzed by sodium hydroxide

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Trimerization of 2-methylpropanal (isobutyraldehyde) is a simple and effective method to synthesize 2,2,4-trimethyl-1,3-pentanediol monoisobutyrate and 2,2,4-trimethyl-1,3-pentanediol-3-monoisobutyrate which are often used as film forming auxiliaries in paints. The use of solid sodium hydroxide as a catalyst provides an excellent yield of above 85 % after the optimization of the reaction time and the catalyst dosage. Furthermore, trimerization of four other aldehydes with one α-hydrogen catalyzed by solid sodium hydroxide can also take place and the yield of 1,3-diol monoesters reaches 50–70 %. Trimerization of aldehydes with one α-hydrogen can be explained by a three-step reaction mechanism: (i) aldol condensation of aldehyde; (ii) crossed Cannizzaro reaction; and (iii) esterification of carboxylic acid and alcohol.

Keywords: trimerization, isobutyraldehyde, aldehydes, sodium hydroxide

Trimerization of aliphatic aldehydes with one α-hydrogen is of fundamental importance in synthetic organic chemistry granting access to 1,3-diol monoesters widely used as coalescing agents in the paint industry (Törmäkangas & Koskinen, 2001; Gallagher et al., 2008). Our work was focused on 2,2,4-trimethyl-1,3-pentanediol monoisobutyrate (*Va*) and its isomers (2,2,4-trimethyl-1,3-pentanediol-3-monoisobutyrate; *VIa*) synthesized by the trimerization of 2-methylpropanal (isobutyraldehyde). Since *Va* is a glycol ester with a high boiling point and it is hardly soluble in water, it has drawn attention as a solvent and plasticizer having remarkable properties such as very good miscibility with resins, low solidifying point, excellent viscosity stability, and low soiling property in latex emulsions and paints (Takasu et al., 1972; Duccini et al., 2007). In recent years, it has been used as a film forming auxiliary in paints (Swan, 2005). *VIa* has the same industrial applications as *Va* and it is not necessary to separate them in industrial scale.

With the field of applications widening, the development of general and efficient methods for the synthesis of *Va* is an active area of research. Self-condensation of isobutyraldehyde catalyzed by various catalysts is a convenient method and the reaction with high atom economy is friendly to the environment. However, the catalysts used to promote the self-condensation of isobutyraldehyde are usually expensive and not easily accessible, $[Al(OC_2H_5)_4]_2Mg$, $[Al(OC_3H_7)_4]_2Mg$, $[Al(OC_4H_9)_4]_2Mg$ (Kulpinski & Nord, 1943; Villani & Nord, 1947), $LiWO_2$ (Villacorta & Filippo, 1983), 1,3-diol monoalcoholates (Törmäkangas & Koskinen, 2001), $Fe_3(CO)_{12}$ (Ito et al., 1983), $Cp^*{}_2Sm(thf)_2$ (Miyano et al., 1998). Preparation of the above-mentioned catalysts is usually complicated and costly which limits their industrial application. Jian et al. (2003a) disclosed a method to obtain *Va*. The reaction was carried out in two steps in the presence of a 45 mass % sodium hydroxide solution. The condensation reaction was conducted at temperatures in the range of 20–30 °C for 3 h, and at 60 °C for 2 h in the second step. After the removal of the aqueous phase by delamination, the organic phase was purified by fractional distillation under reduced pressure. Tic et al. (2012) introduced a method of continuous production of isobutyraldehyde. The reaction

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Table 1. Effect of the catalyst amount and the reaction time on the yield of the isobutyraldehyde[a] trimerization at 60 ℃

Entry	n(NaOH)	Time	x(*Ia*)	x(*IIa*)	x(*IIIa*)	x(*IVa*)	x(*Va*), x(*VIa*)	x(*VIIa*)	Yield[b]
	mol	h	mole %						%
1	0.025	4	84.4	1.9	2.1	2.0	9.5	0.0	23.2
2	0.038	4	55.9	2.7	3.4	3.3	34.6	0.1	59.3
3	0.050	4	40.4	0.0	4.8	4.1	50.0	0.7	72.8
4	0.063	4	17.0	0.0	5.9	5.7	71.1	0.3	86.2
5	0.073	4	16.1	0.0	9.1	8.8	65.7	0.3	82.1
6	0.063[c]	4	41.1	0.0	8.8	7.7	41.2	1.1	63.6
7	0.063	2	61.4	0.0	2.9	2.6	32.9	0.2	58.8
8	0.063	3	41.0	0.0	5.0	4.1	49.0	0.9	71.9
9	0.063	5	16.8	0.0	6.3	5.7	70.5	0.6	85.4

a) Amount of isobutyraldehyde was 120 mL (1.3 mol); *b*) yield of *Va* and *VIa* determined by GC; *c*) 6.25 g of 40 mass % sodium hydroxide solution was used.

was carried out in the presence of a mixture of sodium hydroxide and sodium isobutyrate in the mass ratio of 3 : 1 as the catalyst, first at temperatures in the range of 58–62 ℃ for 8–12 min and then at temperatures in the range of 88–92 ℃ for 3–7 min. After the removal of the catalyst, the organic phase was purified by fractional distillation under reduced pressure. However, in either case, the yield obtained was unsatisfactory.

As it is well known, the sodium hydroxide solution destroys esters via hydrolysis, thus, water is supposed to have a negative effect on the reaction yield. To achieve higher yields, the use of water should be avoided and solid sodium hydroxide was used as the catalyst instead of the sodium hydroxide solution. Although the sodium hydroxide solution is broadly used as a catalyst for the self-condensation of *Ia*, this is the first time sodium hydroxide has been used directly as the catalyst.

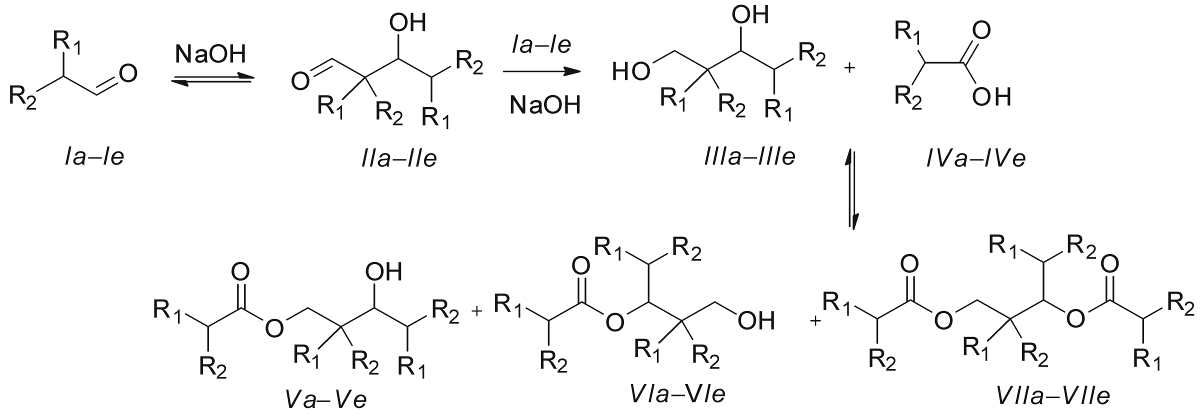
This paper provides a detailed study of the trimerization of isobutyraldehyde, *Va*, and *VIa* catalyzed by sodium hydroxide with excellent yield and proposes a three-step reaction mechanism for the first time. Trimerization of other aldehydes with one α-hydrogen was also studied.

Starting materials and reagents were of reagent grade (> 98 %) and used as received. GC (Agilent 1705A; Agilent, USA) and GC-MS (TRACE G2000/TRACE MS, ThermoQuest, USA) were used to analyze the reaction mixtures. ^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra were recorded on a Bruker AC-P400 spectrometer (USA). The spectra were measured in $CDCl_3$, relative to TMS as an internal standard. All reactions were accomplished in pre-dried glassware (150 ℃, 4 h).

To a 250 mL three-necked flask with a reflux condenser, thermometer, and a mechanic stirrer *Ia* (120 mL, 1.3 mol) was added. Then, flake sodium hydroxide (2.5 g, 0.063 mol) was added in batches over 2 h because of the exotermicity of the reaction. Dry and pure sodium hydroxide was protected from air in a desiccator before being added to the reaction. The reaction was carried out at 60 ℃. The reaction was stopped after 4 h by removing the heat source and the reaction mixture was cooled to room temperature. Gaseous HCl (0.074 mol) was introduced into the reaction vessel at the rate of 60 mL min^{-1} for 30 min to transform sodium hydroxide and sodium isobutyrate into sodium chloride. After sodium chloride was removed by filtration, the reaction mixtures were analyzed using gas chromatopraphy and GC-MS. Relative contents of the components were determined by the area normalization method. The yield of *Va* and *VIa* was determined by an external standard method as described below. First, standard samples of nine different concentrations around the probable concentration of the analyte were analyzed by GC at the same injection volume to obtain a scatter diagram with a regression line, with the abscissa representing the concentration of the standard sample and its ordinate the peak area. Then, the reaction mixture was analyzed by GC at the same injection volume as the standard samples and the concentration was calculated considering the peak area.

The filtrate was purified using a fractional column of 10 cm with corrugated wire gauze packing in four steps. Unreacted *Ia* was collected in the range of 63–65 ℃ at atmospheric pressure. Isobutyric acid (*IVa*) was collected in the range of 146–149 ℃ at atmospheric pressure. 2,2,4-Trimethyl-1,3-pentanediol (*IIIa*) was collected in the range of 120–122 ℃ at 1.33 kPa (absolute pressure). *Va* and *VIa* were collected in the range of 127–129 ℃ at 1.33 kPa (absolute pressure). The remainder was 2,2,4-trimethyl-1,3-pentanediol diisobutyrate (*VIIa*). *Va* and *VIIa* were separated by column chromatography (EA/Hex; $\varphi_\mathrm{r} = 1 : 4$).

In the experiments, the amount of sodium hydroxide was varied from 1.0 g (0.025 mol) to 3.0 g (0.073 mol) to study its effect on the reaction (Table 1). Formation of 3-hydroxy-2,2,4-trimethylpentanal (*IIa*) and *IIIa* was observed and the conversion of *Ia* was poor when the amount of sodium hydroxide was below 1.5 g (0.038 mol). When the amount of sodium hydroxide was increased, *IIa* disappeared and the amount of



I–VII	R_1	R_2
a	CH_3	CH_3
b	CH_3	CH_3CH_2
c	CH_3	$CH_3CH_2CH_2$
d	CH_3	Ph
e	CH_3CH_2	CH_3CH_2

Fig. 1. Trimerization of *Ia* and aldehydes with α-hydrogen catalyzed by sodium hydroxide.

IIIa increased considerably (Table 1). In addition, formation of *IVa* was observed after a sufficient amount of gaseous HCl, originally intended to be used to achieve complete transformation of sodium hydroxide into sodium chloride, was added. Furthermore, when the reaction mixtures were analyzed with GC at 15 min intervals during the reaction, it was observed that the amount of *IIIa* showed an increasing and then a decreasing trend, indicating that the formation of the desired product, *Va* and *VIa*, can be explained by a three-step reaction mechanism (Fig. 1): (i) aldol condensation (Han et al., 2000; Mahrwald et al., 1998) of *Ia* providing *IIa*; (ii) *IIa* not containing α-hydrogen reaction with the original aldehyde (*Ia*) to give *IIIa* and *IVa* via a crossed Cannizzaro reaction (Swain et al., 1979; Bikbaeva et al., 1975). It is necessary to state that in some cases, the Cannizzaro and Tishchenko reactions (Fouquet et al., 1979) are competitive with each other. The balance between them can be controlled by the proper choice of catalyst, reaction temperature and solvents. Experimental results showed that *IIa* reacted with the original aldehyde to give *IIIa* and *IVa* via a Cannizzaro reaction when catalyzed by flake sodium hydroxide at 60 ℃. The crossed Cannizzaro reaction did not proceed to completion unless enough sodium hydroxide was added into the reaction, thus, *IIa* could not be transformed into *IIIa* completely and the conversion of *Ia* was poor when the amount of sodium hydroxide was below 1.5 g (0.038 mol); (iii) esterification of *IIIa* and *IVa* producing *Va* or *VIa*. At the same time, *VIIa* was prepared as a side product by esterification at the 1 : 2 mole ratio of *IIIa* to *IVa*. Because of the reversibility of the esterification reaction, the conversion of *IIIa* and *IVa* was incomplete. Unreacted *IVa* was turned into sodium isobutyrate by sodium hydroxide, so it could not be observed unless a sufficient amount of HCl was added into the reaction. More *IVa* was turned into sodium isobutyrate when the amount of sodium hydroxide increased, which led to the shortage of *IVa* when the esterification of *IIIa* and *IVa* took place. The amount of *IIIa* which was not transformed to *Va* or *VIa* increased, as shown above. Spectral data of the corresponding compounds are summarized in Table 2.

Experimental data are shown in Table 1. The yield of *Va* and *VIa* increased with the increasing amount of sodium hydroxide (up to 0.063 mol). When the amount of sodium hydroxide was above 0.063 mol, the yield did not increase obviously. Therefore, the value of 0.063 mol was chosen for further experiments. In case of a very short reaction time, the yield was not high, the period of 4 h was found to be optimal to achieve a good yield. As predicted, water had a negative effect on the yield. When sodium hydroxide solution was used as the catalyst instead of solid sodium hydroxide, the yield was lower and the content of *IIIa* was high.

The effect of *IVa* present in the starting materials on the reaction was also studied. *IVa* consumes sodium hydroxide and the reaction needs enough sodium hydroxide, therefore, more sodium hydroxide had to be added when the amount of *IVa* in *Ia* increased.

On basis of the above results, many aldehydes with one α-hydrogen such as 2-methyl-butyraldehyde (Jian et al., 2003b) (*Ib*), 2-methyl-pentanal (*Ic*), D,L-2-phenylpropionaldehyde (*Id*), 2-ethyl-butyraldehyde (*Ie*) can to react in the presence of sodium hydroxide at 60 ℃ (Table 3).

Table 2. Spectral data of the corresponding compounds

Compound	Spectral data
IIIa	^{1}H NMR (CDCl$_3$), δ: 3.47 (m, 2H, $J = 10.6$ Hz), 3.39 (d, 1H), 2.81 (s, 2H), 1.94 (m, 1H), 1.04 (d, 3H), 0.98 (d, 3H), 0.93 (s, 6H) ^{13}C NMR (CDCl$_3$), δ: 82.7, 73.2, 39.2, 29.1, 23.5, 20.0, 17.0
IVa	^{1}H NMR(CDCl$_3$), δ: 2.59 (m, 1H), 1.17 (d, 6H) ^{13}C NMR (CDCl$_3$), δ: 183.2, 33.6, 18.4
Va	^{1}H NMR (CDCl$_3$), δ: 3.94 (m, 2H, $J = 10.9$ Hz), 3.22 (d, 1H), 2.54 (m, 1H), 1.85 (m, 1H), 1.15 (d, 6H), 0.97 (d, 3H), 0.93 (s, 3H), 0.91 (s, 3H), 0.87 (d, 3H) ^{13}C NMR (CDCl$_3$), δ: 177.4, 79.3, 71.5, 39.3, 34.0, 28.9, 23.4, 22.0, 20.5, 19.2, 19.2, 16.6
VIa	^{1}H NMR (CDCl$_3$), δ: 4.79 (d, 1H), 3.11 (m, 2H, $J = 11.6$ Hz), 2.64 (m, 1H), 2.09 (m, 1H), 1.21 (d, 6H), 1.01 (s, 3H), 0.97 (d, 3H), 0.94 (d, 3H), 0.88 (s, 3H) ^{13}C NMR (CDCl$_3$), δ: 178.2, 79.4, 69.8, 40.0, 34.8, 28.2, 22.7, 22.3, 19.6, 19.5, 17.6
VIIa	^{1}H NMR (CDCl$_3$), δ: 4.74 (d, 1H), 3.86 (m, 2H, $J = 11.0$ Hz), 2.61 (m, 1H), 2.57 (m, 1H), 2.01 (m, 1H), 1.21 (d, 3H), 1.19 (d, 3H), 1.16 (d, 6H), 0.98 (s, 3H), 0.96 (d, 3H), 0.93 (s, 3H), 0.91 (d, 3H) ^{13}C NMR (CDCl$_3$), δ: 176.8, 176.7, 79.3, 69.8, 38.7, 34.6, 34.0, 28.5, 23.3, 21.9, 21.4, 19.3, 19.3, 19.2, 18.8, 17.9

Table 3. Trimerization of aldehydes with one α-hydrogen catalyzed by NaOH^{a}

Aldehyde	Time/h	Products	Yield^{b}/%
Ib	7	*Vb*, *VIb*	63.3
Ic	7	*Vc*, *VIc*	59.7
Id	7	*Vd*, *VId*	58.2
Ie	8	*Ve*, *VIe*	51.8

a) Mole ratio of aldehyde/NaOH was 20 : 1 and reaction temperature was 60 °C; *b*) yield determined by GC.

The reaction is similar to the trimerization of *Ia* (Fig. 1). It can also be explained by a three-step reaction mechanism: (i) aldol condensation of aldehyde; (ii) crossed Cannizzaro reaction; and (iii) esterification of carboxylic acid and alcohol. In general, the longer is the carbon chain of an aldehyde, the more difficult is the reaction and the longer reaction time is needed (Table 3).

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