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Characterisation of a by-product formed in the industrial production of γ-nonalactone

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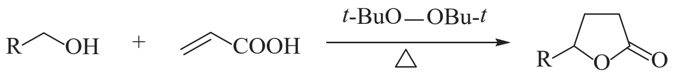
Distillation residues from the industrial production of γ-nonalactone, which is accomplished by reaction of hexanol with methyl acrylate initiated by t-butyl peroxide, yielded a by-product which we deduced to be 4-(methoxycarbonylethyl)-γ-nonalactone. The possible pathway of formation of this by-product is discussed.

Keywords: 4-(methoxycarbonylethyl)-γ-nonalactone, γ-nonalactone, identification, industrial production

γ-Lactones are well known naturally-occurring flavour compounds and many are present as important aroma components of various foods such as dairy products, fruits, nuts and vegetables. Several representative compounds, such as γ-octalactone, γ-nonalactone, γ-decalactone, and γ-undecalactone, are widely used in various fragrance and flavour formulations due to their low odour threshold values and pleasant sweet, creamy and fruity aromas.[1] Among the commercialised γ-lactones, synthetic products still account for most of the market share due to their lower cost compared to natural lactones, although natural products are preferred by the more discerning consumers. Many synthetic routes for γ-lactones have been developed, such as lactonisation of olefinic fatty acids catalysed by various Lewis or protonic acids.[2–6] However, the methods suitable for industrial production are very limited. In addition to hemi-synthesis of γ-undecalactone from undecylenic acid obtained by degradation of natural ricinoleic acid, which is catalysed by acid usually with a relatively low yield,[7] the method developed by Nikishin and Vorob′ev[8] is still the commonest one for the industrial production of γ-lactones, which involves peroxide-catalysed addition of an aliphatic alcohol to acrylic acid (or its ester) (Scheme 1).

The Anhui Hyea Aromas Company is one of the top 10 flavour and fragrance companies in China, and it focuses on the production of lactones, including γ- and δ-lactones. The production of γ-lactones is based on the synthetic route shown in Scheme 1. The average yields of these lactones are about 65% based on the amounts of the unrecovered alcohols, which are not satisfying to the manufacturer. High costs confront the manufacturer with strong competitive pressure in the market and lowering costs becomes most urgent. Undoubtedly, one of the most efficient ways to lower costs is by the analysis and identification of by-products so that methods to avoid their formation can be developed. Alternatively, a by-product can sometimes have commercial value.

We recently analysed and identified one by-product provided by the manufacturer derived from the production of γ-nonalactone (so-called ‘aldehyde C_{18}’). It was from the distillation residue derived from the production of γ-nonalactone, in which the manufacturer replaced usually-used acrylic acid in its production of γ-lactones with methyl acrylate. The major unknown component was found to account for about 51% of the residue after γ-nonalactone had been distilled off. Herein, we will report the characterisation of this by-product and discuss its possible route of formation.



Scheme 1

Results and discussion

Structure determination of the by-product isolated from distillation residues

The mass data of the by-product obtained by GC/EIMS did not match with any data in the NIST library. Its molecular formula was determined to be $C_{13}H_{22}O_4$ by HR-ESI-MS, from which the number of double-bond equivalents (DBE) in this molecule was calculated to be three. 1D NMR spectra, including ^{1}H NMR, ^{13}C NMR and dept135 indicated that there were 2 ester carbonyl groups (2 × DBE), 2 methyl groups (one was the end methyl of a long-chain alkyl group and the other should be from a methyl ester), 8 methylene groups and 1 quaternary carbon in this compound. So the remaining double-bond equivalent must be accounted for by a ring. Based on all these data, one possible structure was postulated to be 4-(methoxycarbonylethyl)-γ-nonalactone as shown in Fig. 1.

In order to confirm this structure, this by-product was analysed further with 2D NMR methods, including H,H- and H,C-correlation, and HMBC. All of the 2D NMR data agreed well with the structure. All peaks in the ^{1}H and ^{13}C NMR spectra were assigned as shown in Table 1 based on the information obtained from 2D NMR spectra. Two ester carbonyl groups were easily assigned based on the cross peak corresponding to the methyl peak of δ 51.7 in the HMBC spectrum, which led to the identification of the two similar spin systems attached to the ester carbonyl groups.

The possible route of formation of the by-product

It is well known that the reaction mechanism for the industrial production of γ-nonalactone is as shown in Scheme 2. In the initiation step, abstraction of an α-hydrogen from hexanol by

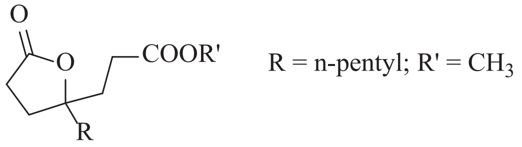


Fig. 1 The possible structure of the by-product.

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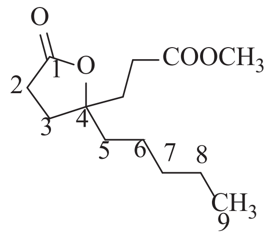
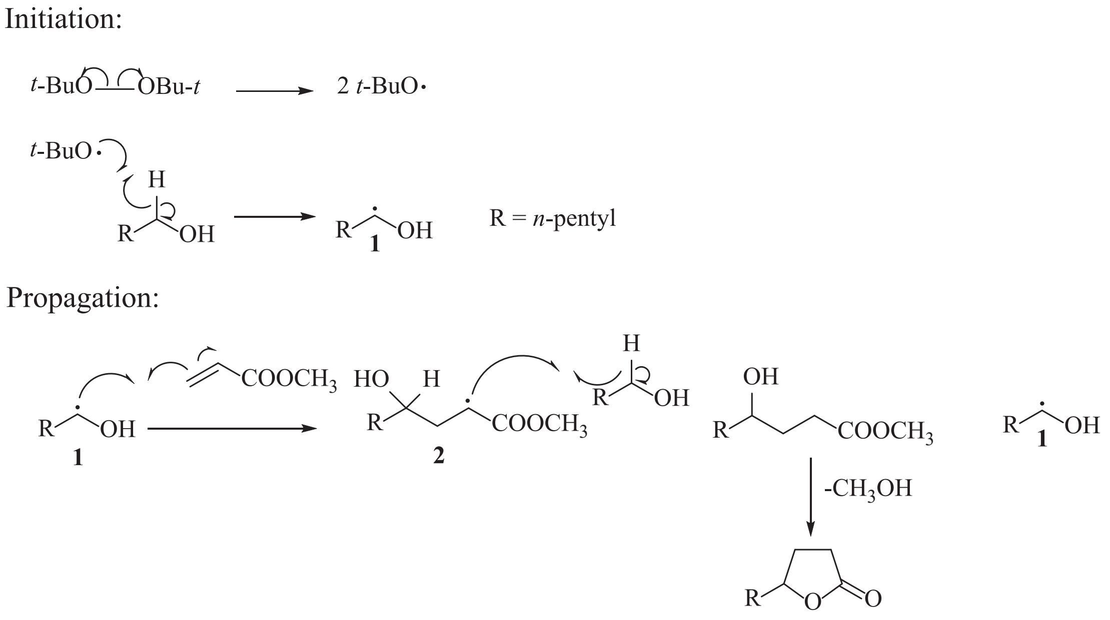
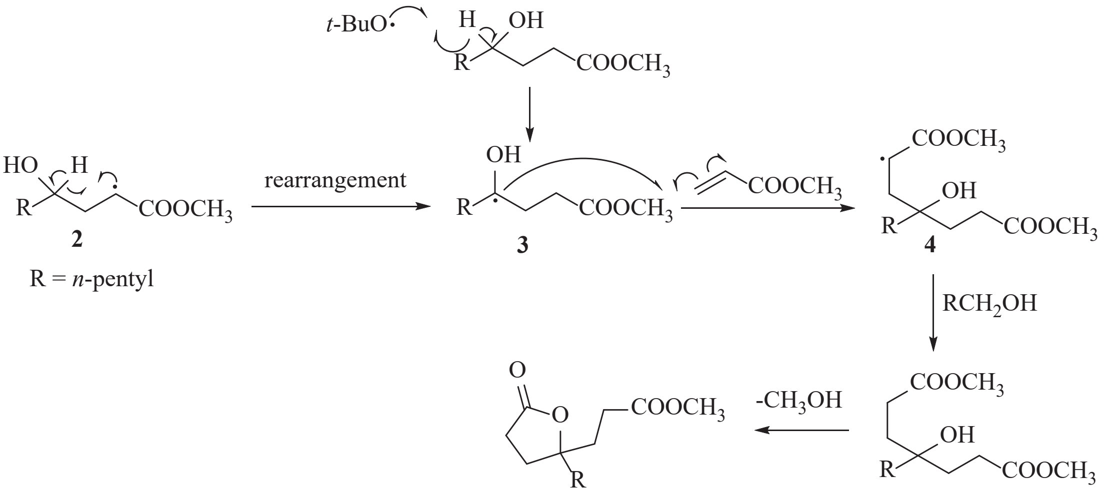
Table 1 The assignment of peaks in ^{1}H and ^{13}C NMR spectra of the by-product

Compound	Assignment	Chemical shift δ	
		^{13}C NMR	^{1}H NMR
	H–C9	13.8	0.93
	H–C8	22.3	1.27–1.40
	H–C7	22.9	1.27–1.40
	$-CH_2\underline{CH_2}COOCH_3$	28.3	2.38–2.50
	H–C2	28.7	2.63
	H–C3	30.6	2.08–2.15, 2.00–2.08
	H–C6	31.8	1.27–1.40
	$-\underline{CH_2}CH_2COOCH_3$	33.2	2.00–2.08
	H–C5	38.1	1.60–1.74
	$-CH_2CH_2COO\underline{CH_3}$	51.7	3.72
	C4	87.6	
	$-CH_2CH_2\underline{C}OOCH_3$	173.2	
	C1	176.3	



Scheme 2



Scheme 3

t-BuO• produces radical intermediate **1**. In the propagation step, the addition of radical intermediate **1** to methyl acrylate gives a new radical intermediate **2**, which then abstracts an α-hydrogen from the starting material, hexanol to give methyl 4-hydroxy-nonanoate and regenerates a radical intermediate **1** (Scheme 2).

The proposed pathway of formation of the by-product is as shown in Scheme 3. This postulation involved a radical intermediate **3**, which could be formed *via* a rearrangement of the radical intermediate **2** and/or α-hydrogen abstraction of the intermediate methyl 4-hydroxynonanoate by a butyloxy radical. The addition of the radical intermediate **3** to methyl acrylate gave a new radical intermediate **4** which abstracted an α-hydrogen from hexanol to produce methyl 4-hydroxy-4-methoxycarbonylethyl nonanoate, intramolecular esterification of which, gave 4-(methoxycarbonylethyl)-γ-nonalactone.

This by-product was found to occur in the distillation residues in the production of γ-nonalactone when methyl acrylate replaced acrylic acid. Earlier we had tried to help the manufacturer characterise the components of the residue derived from the industrial production of γ-undecalactone through the reaction of octanol with acrylic acid. However, the separation of the residue by column chromatography failed to give any useful results. A component similar to 4-methoxycarbonylethyl γ-nonalactone might, by analogy, also occur in the distillation residue as an acid form (as shown in Fig. 1, R = *n*-heptyl, R′ = H). The reason that we did not find this component was due to the strong polarity of the acid which would have been retained by the silica column. It is important to the manufacturer to characterise the components of such residues since they are usually produced in a relatively large amounts equal to about 25% of the γ-lactone products. This work is under way in our laboratory.

Experimental

The reagents were purchased from the Beijing Huaxue Shiji Company. NMR spectra were obtained on a Bruker AV 300 spectrometer (^{1}H NMR at 300 MHz, ^{13}C NMR at 75 MHz) or an AV 600 spectrometer (^{1}H NMR at 600 MHz, ^{13}C NMR at 150 MHz) in $CDCl_3$ using TMS as an internal standard. Chemical shifts (δ) are given in ppm and coupling constants (*J*) in Hz. The high resolution mass spectrum was obtained on a Bruker Apex IV FTMS.

A sample provided by the Anhui Hyea Aromas Company was the residue derived from the production of γ-nonalactone, in which the major component to be analysed was isolated.

GC-MS chromatography

An Agilent 6890N-5973i (Agilent, Santa Clara, CA, USA) was used under the following conditions: capillary column HP-INNOWAX (30 m × 0.25 mm × 0.25 μm); the oven temperature was programmed from 40 °C to 250 °C at a rate of 15 °C min^{-1}; carrier gas, helium; flow rate, 0.8 mL min^{-1}; electron ionisation, 70 eV; ion source temperature, 230 °C.

Industrial production of γ-nonalactone

A mixture of hexanol (2 equiv.), methyl acrylate (1 equiv.) and *t*-butyl peroxide (0.1 equiv.) was added dropwise to hexanol (4 equiv.) at 160–170 °C for 8 h while distilling off *t*-BuOH and methanol which were produced during the reaction. After the addition, the reaction mixture was kept stirring at 160–170 °C for 1 h. The reaction mixture was submitted to a distillation process, in which the first cut was the excess hexanol for recycling and the second cut contained the crude product which was purified for further fractionation. Some residues usually remained after γ-nonalactone was distilled out in the second cut.

Purification of the sample

The sample was subjected to silica-gel column chromatography (silica gel, petroleum ether-diethyl ether, 4:1) to separate a major component, which was obtained as a light yellow oil in about 20% yield.

Spectroscopic data of the by-product: ^{1}H NMR ($CDCl_3$) δ 0.93 (t, *J* = 6.6 Hz, 3H), 1.27–1.40 (m, 6H), 1.60–1.74 (m, 2H), 2.00–2.08 (m, 3H), 2.08–2.15 (m, 1H), 2.38–2.50 (m, 2H), 2.63 (t, *J* = 9 Hz, 2H), 3.72 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 13.8, 22.3, 22.9, 28.3, 28.7, 30.6, 31.8, 33.2, 38.1, 51.7, 87.6, 173.2, 176.3; GC/MS (EI) m/z (%) 41 (17), 43 (22), 55 (36), 56 (11), 95 (17), 111 (100), 143 (75), 155 (94), 171 (94), 211 (14); HR-ESI-MS, m/z 265.14065 [M + Na^+] (calcd. for $C_{13}H_{22}NaO_4$, 265.14103).

Electronic Supplementary Information

The NMR spectra of the by-product are available through: stl.publisher.ingentaconnect.com/content/stl/jcr/supp-data

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