

Synthesis and Characterization of (-)-Dibornyl Oxalate

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Abstract. (-)-Dibornyl oxalate was synthesized by the reaction of natural (-)-borneol with oxalyl chloride under the optimized reaction conditions: temperature 35 °C, time 1 h and the molar ratio of (-)-borneol and oxalyl chloride 1.0 : 0.6. The reaction underwent in good selectivity as 99 % for target product which can be easily purified to 99.9 % through recrystallization. The structure of (-)-dibornyl oxalate was characterized by GC-MS, FT-IR, ¹H NMR and ¹³C NMR.

Introduction

Dibornyl oxalate (1,2-bis[1,7,7-trimethyl bicyclo[2.2.1] hept-2-yl] ethanedioic acid ester) which has optical activity is one of the main intermediates in the synthetic process of borneol. Because of the significant medicinal value of borneol, dibornyl oxalate possesses important potential prospect in medicinal application. In general, dibornyl oxalate is a symmetrical compound in structure, so there are isomers owning different optical activity, and (±)-dibornyl oxalate are a pair of enantiomers. Efficient selective synthesis of (+)-dibornyl oxalate or (-)-dibornyl oxalate is very important in organic synthesis and catalytic industry, and which may be used to realize the analysis of bornyl esters in the synthetic process of borneol. In recent years, several procedures have been developed to synthesis bornyl esters which main contain fenchyl ester, dibornyl and isobornyl ester. (+)-dibornyl oxalate has been gotten from the esterification of (+)-natural borneol with anhydrous oxalic and meso-diisobornyl oxalate also can be obtained from camphene, tricyclene or isoborneol^[1,2]. However, to the best of our knowledge, researches concerning the synthesis of (-)-dibornyl oxalate has been rare reported.

In most cases, ester compounds could be obtain from the direct esterification of alcohols with carboxylic acids or indirect esterification of alcohols with carboxylic acid derivatives^[3]. For alcohols with high steric hindrance, indirect esterification method is much more suitable than other methods. Because of high steric hindrance of (-)-borneol, indirect esterification of (-)-borneol with oxalyl chloride was found to be the most convenient synthesis method for (-)-dibornyl oxalate^[3-5]. Furthermore, n-hexane was used as solvent because of the low polarity to reduce the influence of hydrogen chloride. From this reaction, high purity dibornyl oxalate was obtained via mild reaction conditions in short reaction time and high purity. All products were purified by recrystallization and characterized by GC-MS, FT-IR, ¹H NMR and ¹³C NMR.

Experimental

Materials

(-)-Borneol was purchased from Nanning Chenkang Biological Technology Co., Ltd at a purity level of 99.29 % (GC, area normalization method), $[\alpha]_D^{20}$: -37.2° (c 5 g/100 mL, EtOH). Oxalyl chloride (CP) and n-hexane (AR) were used as received from Sinopharm Chemical Reagent Co., Ltd. All other reagents and solvents were analytical grade and were used as received without any other treatment.

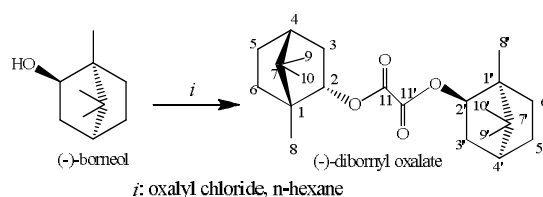
Apparatus and product analysis

The conditions of the reaction were determined by monitoring the concentration of dibornyl oxalate, and the reaction products were analyzed by gas chromatograph (Shimadzu, Model no. GC-2014AF), equipped with a Rtx-5 capillary column (30 m length, 0.25 mm internal diameter, 0.25 μm film thickness) and a FID detector. Nitrogen was used as carrier gas, the detector and injection port temperature were 280 $^{\circ}\text{C}$, the sample was dissolved in n-hexane, and the injection volume was 1.0 μL . Temperature programmed method was used to analysis as follows: the initial temperature was set at 70 $^{\circ}\text{C}$ with the holding time of 2 min, and then increased to 115 $^{\circ}\text{C}$ at 3 $^{\circ}\text{C}/\text{min}$, to 180 $^{\circ}\text{C}$ at 5 $^{\circ}\text{C}/\text{min}$, and to 250 $^{\circ}\text{C}$ at 2 $^{\circ}\text{C}/\text{min}$, finally to 270 $^{\circ}\text{C}$ at 10 $^{\circ}\text{C}/\text{min}$. The component content was detected by the normalization method of peak area.

The purified product was characterized by means of GC-MS, FT-IR, ^1H NMR and ^{13}C NMR. GC-MS from Agilent Technologies consists of 6890N Network GC System Technologies and 5973 mass spectrometer with a HP-5 capillary column (30 m \times 0.32 mm \times 0.25 μm). Infrared spectra is recorded on a Thermo Nicolet IS10 FT-IR spectrophotometer from the company of Thermo in America, the scanning frequency range is 400~4000 cm^{-1} . Nuclear magnetic resonance (NMR) spectrum is obtained on a Bruker AV-300 spectrometer. Chemical shifts are expressed in ppm downfield from TMS, using the middle resonance of CDCl_3 (7.28 ppm for ^1H and 76.97 ppm for ^{13}C) as an internal standard and coupling constants (J) in Hz. The melting point of dibornyl oxalate was measured by a WRS-1B digital melting-point apparatus with the standard capillary (outer diameter 1.4 mm, inner diameter 1.0 mm) which sealed in one end and sample was loaded in 3 mm, the initial temperature was set at 106 $^{\circ}\text{C}$ with the heating rate of 1 $^{\circ}\text{C}/\text{min}$, determined 5 times to get the average. The optical activity was performed with a WZZ-2S digital automatic polarimeter, samples were dissolved in ethanol. Melting-point apparatus and polarimeter are from Shanghai ShenGuang instrument Co., Ltd.

General experimental procedures

A magnetic stirrer with water-bath heater was used to carry out (-)-borneol esterification tests. Firstly, (-)-borneol in a quantity of 1.54 g (0.01 mol) and n-hexane (20 g) were put into the reactor vessel. After (-)-borneol completely dissolved, oxalyl chloride was added dropwise to the vessel in 5 min under continuous stirring, the reaction was conducted for certain time, then the reaction liquid was washed to neutral by 2 % Na_2CO_3 (wt %) and saturated NaCl, finally, dibornyl oxalate can be gotten by means of vacuum distillation and recrystallized with ethanol. The reaction process is displayed in Scheme 1.



Scheme 1. The route of synthetic dibornyl oxalate

Results and discussion

Effect of synthesis conditions on dibornyl oxalate

Effect of reaction temperature on the esterification reaction

The effect of reaction temperature was studied on the conditions that the molar ratio of borneol and oxalyl chloride was 1.0 : 0.6 and the reaction time was 2 h. The content of dibornyl oxalate changed with temperature as shown in Fig. 1. The reaction owns good selectivity so that the ester content is high, and the law of the ester content is increased at first and then decreased because of the influence of temperature on the molecular thermal motion and the increase of side effects. The effective collision between the molecules is relatively low when the temperature below 25 $^{\circ}\text{C}$, and the dibornyl oxalate increases slow between 35 $^{\circ}\text{C}$ and 55 $^{\circ}\text{C}$. what is more, the decrease of ester content is observed when the reaction temperature is further raised. Therefore, 35 $^{\circ}\text{C}$ ~55 $^{\circ}\text{C}$ is better for the reaction, and in order to save electricity, 35 $^{\circ}\text{C}$ is selected as the better temperature for the next step.

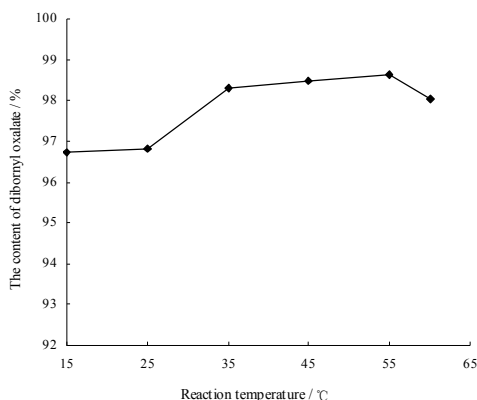


Fig. 1. Effect of reaction temperature on the esterification reaction: $n(\text{borneol}) : n(\text{oxalyl chloride}) = 1 : 0.6$, react for 2 h.

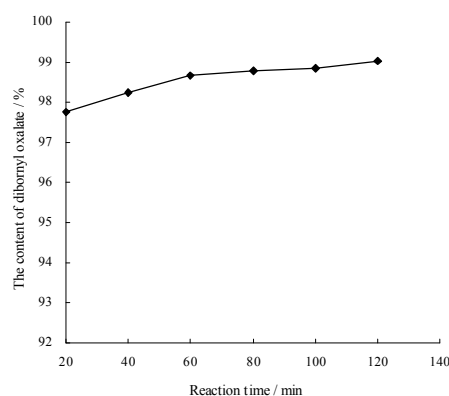


Fig. 2. Effect of reaction time on the esterification reaction: $n(\text{borneol}) : n(\text{oxalyl chloride}) = 1 : 0.6$, react at 35 °C.

Effect of reaction time on the esterification reaction

The effect of reaction time on the esterification reaction is shown in Fig. 2. Samples were removed at regular intervals for GC at the temperature of 35 °C, the reaction time has little influence on the content of dibornyl oxalate own to the activity of oxalyl chloride, the purity has been reached 97% just 20 minutes, and the rate of the ester content is increasing relatively quickly between 20 and 60 min, dibornyl oxalate accounts for 98.7% in the product at 60 min and then increased very slowly. So 60 min is the optimal reaction time.

Effect of molar ratio of (-)-borneol and oxalyl chloride on the esterification reaction

The effect of molar ratio of (-)-borneol and oxalyl chloride on the esterification reaction is given in Fig. 3. As oxalyl chloride increases, the content of dibornyl oxalate reaches a maximum and then shows a little decline. What is more, if oxalyl chloride is too much excess, dibornyl oxalate can not be solid by vacuum distillation, and in order to eliminate redundant oxalyl chloride, the yield will down. The ester content is 99.36% when molar ratio of borneol and oxalyl chloride is 1.0 : 0.6.

Spectral data of the product

The dibornyl oxalate is white crystal with purity of 99.9%, m.p. 107-108 °C (*lit.* mp: 106.5 °C^[6]), and $[\alpha]_D^{20} : -53.1^\circ$ (c 3.62 g/100 mL, EtOH).

MS (m/z): 362.1 [M], 181.1 [M-COOC₁₀H₁₇]⁺, 137.1 [C₁₀H₁₇]⁺, 95.1 [C₇H₁₁]⁺, 81.0 [C₆H₉]⁺, 69.1, 41.0. From the mass spectrum data, 362.1 is the molecular weights, 181.1 comes from the fracture of the two carbonyl ester, 95.1 and 81.0 are base peaks which are from bornyl. These characteristic peak of fragment ions accord with the structure of dibornyl oxalate.

FTIR (ATR, cm⁻¹): 2986 (m, ν_{CH}), 2952 (s, ν_{CH}), 2877 (m, ν_{CH}), 1762 (s, ν_{C=O}), 1477 (m, δ_{asCH}), 1455 (m, δ_{asCH}), 1377 (m, δ_{C(CH₃)₂}), 1315 (s, δ_{C(CH₃)₂}), 1188 and 1158 (s, ν_{asC-O-C}), 1011 and 977 (m, ν_{sC-O-C}). It can be seen from the infrared spectra that the absorption peak of 2986, 2959 and 2877 are the stretching vibration of methyl and methylene, 1762 is the strong absorption peak of carbonyl, 1477 and 1455 are from the asymmetrical deformation vibration of methyl and methylene, 1377 and 1315 are the typical absorption peaks which coming from the flexural vibrations of Thorpe-Ingold effect. 1188, 1158 and 1011, 977 are symmetric and anti-symmetric stretching vibration of ether linkage. So the data are in conformity with the structure of dibornyl oxalate.

¹H NMR (300 MHz, CDCl₃, δ/ppm, J/Hz): 0.91 (s, 6H, CH₃-8, CH₃-8'), 0.92 (s, 6H, CH₃-10, CH₃-10'), 0.95 (s, 6H, CH₃-9, CH₃-9'), 1.10~1.16 (2d, 2H, H_a-3, H_a-3', J=13.92 and 3.36), 1.28~1.32 (m, 2H, H_a-6, H_a-6'), 1.34~1.38 (m, 2H, H_a-5, H_a-5'), 1.74~1.77 (t, 2H, H-4, H-4', J=4.29), 1.78~1.84 (m, 2H, H_e-5, H_e-5'), 1.98~2.06 (m, 2H, H_e-6, H_e-6'), 2.39~2.50 (m, 2H, H_e-3, H_e-3'), 5.02~5.07 (2t, 2H,

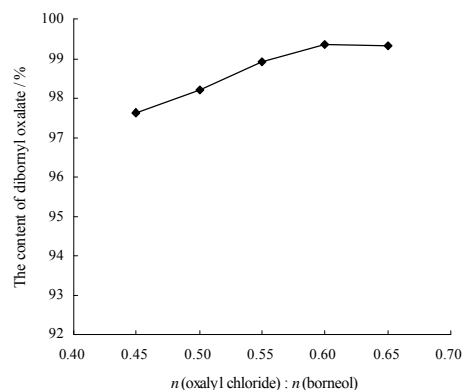


Fig. 3. Effect of molar ratio of borneol and oxalyl chloride on the esterification reaction: react for 1 h at 35 °C.

H-2, H-2', J=9.9 and 2.04). The product was characterized, the chemical shifts and the number of H are introduced in briefly, which can prove that (-)-dibornyl oxalate was successfully synthesized.

¹³C NMR (300 MHz, CDCl₃), and the chemical shift is given in Table 1.

Table 1. Chemical shift of each carbon atom in dibornyl oxalate

Carbon number	δ(ppm)	Carbon number	δ(ppm)
1	48.6	1'	48.6
2	82.5	2'	82.5
3	35.9	3'	35.9
4	44.4	4'	44.4
5	27.4	5'	27.4
6	26.5	6'	26.5
7	47.5	7'	47.5
8	13.0	8'	13.0
9	19.2	9'	19.2
10	18.3	10'	18.3
11	158.0	11'	158.0

The carbon atoms of the left and right dibornyl are in a identical chemical environment which can be seen from Table 1, so the ¹³C NMR data indicated that (-)-dibornyl oxalate has a symmetrical structure.

Conclusion

Pure (-)-dibornyl oxalate was successfully prepared by the reaction of (-)-borneol with oxalyl chloride. The optimum reaction conditions are determined as follows: the molar ratio of borneol and oxalyl chloride is 1.0 : 0.6, reaction time is 1 h and reaction temperature is 35 °C . The optical rotation and melting point of the pure target product is mensurated and the structure is characterized by means of MS, FT-IR, ¹H NMR and ¹³C NMR.

Acknowledgements

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