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乙基麦芽酚丁二酸双酯的合成、热解及抗氧化研究

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摘要 为了开发具有稳定性的焦甜香韵化合物, 以丁二酸酐、香味醇和乙基麦芽酚为原料, 两步法得到 9 种乙基麦芽酚丁二酸双酯类化合物 2-乙基-4-氧代-4*H*-吡喃-3-基苯乙基丁二酸酯(**5a**)～2-乙基-4-氧代-4*H*-吡喃-3-基(2-甲基烯丙基)丁二酸酯(**5i**), 并对其进行结构鉴定、热稳定性和体外抗氧化性研究. 结果表明, 化合物 **5a**～**5i** 具有焦甜香韵, 同时还兼具其它香韵. 化合物 **5a** 和 2-乙基-4-氧代-4*H*-吡喃-3-基丁二酸肉桂酯(**5b**)最大失重率的温度高于原料的温度, 热解时能产生大量乙基麦芽酚和香味醇等物质. 化合物 **5a** 的 1,1-二苯基-2-三硝基苯肼(DPPH)和•OH 清除能力高于化合物 **5b**～**5i** 和乙基麦芽酚. 综上所述, 化合物 **5a** 具有焦甜香韵, 且表现出较高的热稳定性和体外抗氧化能力, 为提高香料的稳定性和拓展其多功能应用开辟了新的途径.

关键词 乙基麦芽酚; 酯化; 热裂解; 抗氧化; 香料香精

Study on Synthesis, Pyrolysis and Antioxidation of Ethyl Maltol Succinate Diester

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Abstract In order to develop burnt sweet fragrance compounds with stability. In this paper, nine ethyl maltol succinate diester compounds 2-ethyl-4-oxo-4*H*-pyran-3-yl phenethyl succinate (**5a**)～2-ethyl-4-oxo-4*H*-pyran-3-yl (2-methylallyl) succinate (**5i**) were obtained by a two-step method using succinic anhydride, flavor alcohols and ethyl maltol as raw materials, and were subjected to structural characterization, thermal stability and *in vitro* antioxidant studies. The results showed that compounds **5a**～**5i** possessed a burnt sweet fragrance as well as other fragrances. Compounds **5a** and cinnamyl (2-ethyl-4-oxo-4*H*-pyran-3-yl) succinate (**5b**) had a highest weight loss at a temperature higher than that of raw materials, and a large amount of substances such as ethyl maltol and flavor alcohols were produced during pyrolysis. The 1,1-diphenyl-2-picrylhydrazyl (DPPH) and •OH scavenging abilities of compound **5a** are higher than those of compounds **5b**～**5i** and ethyl maltol. In summary, compound **5a** has a burnt sweet fragrance, and exhibits high thermal stability and *in vitro* antioxidant capacity. This work may provide a new method to improve the stability of spices and expand their multifunctional application.

Keywords ethyl maltol; esterification; pyrolysis; antioxidant; flavors and fragrances

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1 Introduction

Ethyl maltol is a kind of six-membered oxygen-containing heterocyclic compound with enol ketone structure, which has a distinctive burnt sweet fragrance. Ethyl maltol has been found extensive application in the food industry as a flavoring agent, as well as in the production of cigarette flavors. At the same time, the structure is also widely present in natural products and shows antibacteria[1-2] and antioxidant properties[3-4]. Sun *et al.*[5] have prepared ethyl maltol from ethyl furfuryl alcohol by electrolysis, acidification, glycosylation, oxidation and acidolysis, with the highest yield of 66.8%. Xue *et al.*[6] improved the traditional synthesis method with furfural and chlorine as raw materials, and synthesized ethyl maltol by closed hydrolysis. According to different types of use, ethyl maltol can be roughly divided into three types: A1, A2 and A3 type. A1 type ethyl maltol significantly enhances the sweet and fruity flavour, A2 type ethyl maltol has a very strong burnt sweet fragrance, and A3 type ethyl maltol has a mellow and rich burnt sweet fragrance with a longer lasting fragrance. Flavoring in meat products, cans, candy, chocolate, cocoa and other foods can make its flavor more prominent. Adding ethyl maltol to minced pork can improve color, delay fat oxidation and improve meat flavor[7].

As a kind of fragrance, the application of ethyl maltol is limited for several defects as heavy smell, low threshold, strong volatility and poor stability. In order to solve these problems, the flavor and fragrance industry generally takes measures, such as preparing latent fragrance substances, making capsules or cyclodextrin inclusion[8], so that the fragrance raw materials can play a long-term role. Zou *et al.*[9] synthesized the metal complex of ethyl maltol. It was found that the thermal stability of the complex could be improved, and the release temperature of flavor substances could be effectively adjusted. Megdi *et al.*[10] prepared ethyl maltol into nanoparticles by electrospray method, and the encapsulation efficiency was up to 88%, which effectively slowed down the volatilization of ethyl maltol.

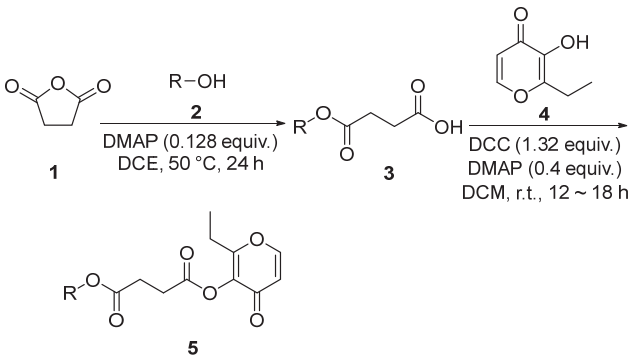
As a kind of γ-pyrone compounds, ethyl maltol also has certain antibacteria and antioxidant properties, but its inhibitory effect is insignificant[11]. Saud *et al.*[1] found that the compound reacting chitosan with ethyl maltol was active against *Escherichia coli bacteria*. Zhang *et al.*[2] found that the ethyl maltolate ligand coordinated to V through the carbonyl and hydroxyl oxygen, and the complexes showed effective antibacterial activity against *B. subtilis*, *S. aureus* and *P. aeruginosa*.

Up to now, there are few reports on the synthesis of ethyl maltol esters, and the research on their antioxidation has not been reported. We intend to use dicyclohexylcarbodiimide (DCC) and 4-dimethylaminopyridine (DMAP) methods to synthesize ethyl maltol compounds **5a**～**5i**. This method is green and environmentally friendly, and has the basis of previous research[12], which can quickly prepare the required ethyl maltol esters. This method combined the caramel flavor of ethyl maltol with the characteristic flavor of aroma alcohols to prepare latent flavor compounds with both flavors. The aroma characteristics of compounds **5a**～**5i** were evaluated by gas chromatography-mass spectrometry-olfactory method (GC-MS-O), and the thermal stability and pyrolysis products of compounds **5a**～**5b** were analyzed by thermogravimetric-differential thermogravimetry (TG-DTG) and pyrolysis gas chromatography/mass spectrometry (Py-GC/MS). At the same time, the antioxidant capacity of ethyl maltol esters was determined by quenching 1,1-diphenyl-2-picrylhydrazyl (DPPH)[13] and •OH[14-15], and the best antioxidant concentration were screened, so as to provide more choices for the development of the fragrance industry and other fields.

2 Results and discussion

2.1 Preparation of ethyl maltol succinate diester

As shown in Scheme 1, the succinic monoester derivatives were obtained by the reaction of alcohol with succinic anhydride in the presence of DMAP, followed by the reaction with ethyl maltol in the presence of DCC and DMAP to give the ethyl maltol succinate diester derivatives (Scheme 1). The pure products were obtained by preparative thin layer chromatography using ethyl acetate/dichloromethane as the eluent. The rates were given in Table 1, the structures of compounds **5a**～**5i** were novel firstly reported and charactered by ^{1}H NMR, ^{13}C NMR, IR, and HRMS.

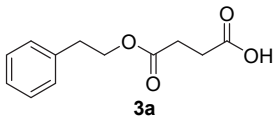
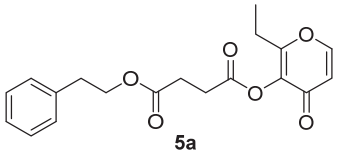
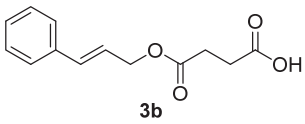
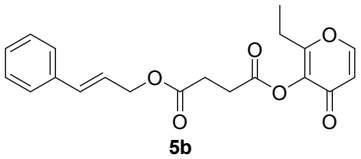
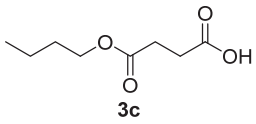
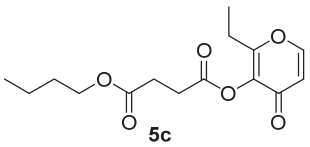
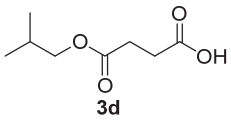
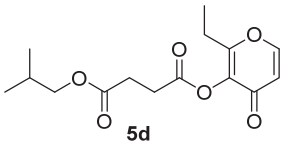
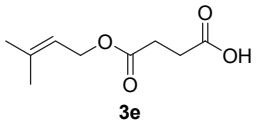
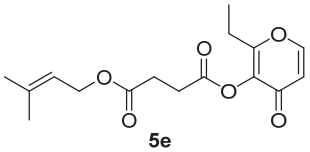
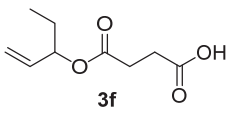
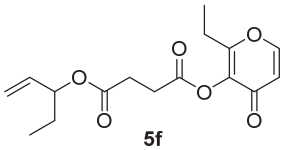
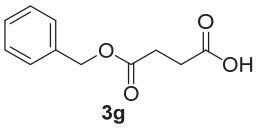
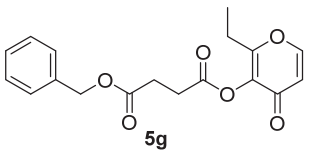
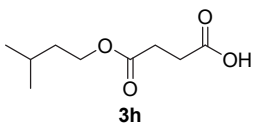
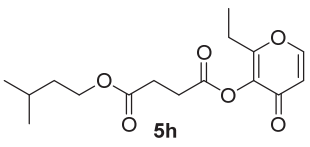
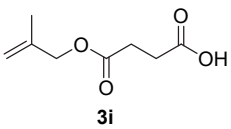
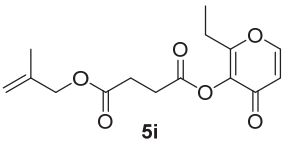


Scheme 1 Synthesis of **5a**～**5i**

2.2 Determination of odor properties

In this study, the odor characteristics of ethyl maltol succinate diester derivatives were evaluated using GC-MS-O. The obtained results are summarized in Table 1. It was observed that all nine ethyl maltol succinate diesters exhibited a burnt sweet fragrance, which can be attributed to the enol structure of ethyl maltol. Notably, the rose fragrance of **5a** may be attributed to phenethyl alcohol, while the herbal aroma of **5b** may originate from cinnamyl alcohol. Isomers **5c** and **5d** displayed similar fragrances of burnt sweet, fruity, and nutty. In contrast, **5e** and **5f**, despite having the same molecular weight, exhibited different fragrances with **5e** displaying burnt sweet, fruity, and alcohol notes, while **5f** had burnt sweet, sour, and spicy tones.

Table 1 The yields of **3**, **5**, and the odor description of **5a**～**5i**

Products of **3**	Yield/% of **3**	Products of **5**	Yield/% of **5**	Odor description of **5**
 **3a**	83	 **5a**	46	Burnt sweet fragrance, rose fragrance, herb fragrance
 **3b**	80	 **5b**	55	Burnt sweet fragrance, alcohol fragrance, bean aroma, herb fragrance
 **3c**	85	 **5c**	56	Burnt sweet fragrance, fruity flavour, nut fragrance
 **3d**	81	 **5d**	44	Burnt sweet fragrance, fruity flavour, nut fragrance
 **3e**	87	 **5e**	57	Burnt sweet fragrance, alcohol fragrance, fruity flavour
 **3f**	87	 **5f**	62	Sour flavor, burnt sweet fragrance, spicy fragrance
 **3g**	86	 **5g**	46	Burnt sweet fragrance, sour flavor, fat wax fragrance
 **3h**	82	 **5h**	50	Burnt sweet fragrance, baked fragrance, spicy fragrance, fat wax fragrance
 **3i**	85	 **5i**	49	Burnt sweet fragrance, grass fragrance, fruity flavour, sour flavor

2.3 TG analysis

To further investigate the flavor intensity of the diesters, TG detection was performed on **5a** and **5b**, which exhibited good flavor intensity. The obtained data was analyzed using TG and DTG, and the results are presented in Figure 1. From Figure 1, it can be seen that the decreasing trend of TG and DTG curves and the highest mass loss rate of compounds **5a** and **5b** are basically the same. The weight loss of compounds **5a** and **5b** was mainly divided into two stages. The first stage of **5a** is 30～206.9 ℃ and the sec-

ond stage is 206.9～450 ℃ with a total weight loss rate of 95.56%. The first stage of **5b** is 30～201.5 ℃, and the second stage is 201.5～450 ℃ with a total weight loss rate of 99.11%. Among them, the highest mass loss rate of compound **5a** is 239.6 ℃, and the highest mass loss rate of compound **5b** occurs at 225.7 ℃, which are both higher than the highest mass loss rate of ethyl maltol (193.04 ℃),[16] cinnamyl alcohol (206.53 ℃),[17] phenethyl alcohol (154.5 ℃) and succinic anhydride (176.5 ℃). This difference in thermal behavior could be attributed to the presence of an additional double bond structure in compound **5b**, which required more heat at the same temperature and resulted in a greater variation in mass loss rate.

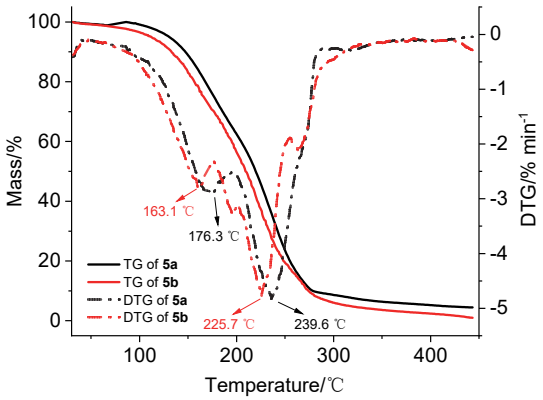
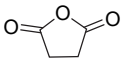
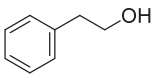
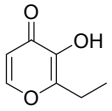
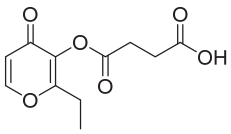
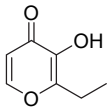
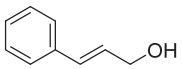
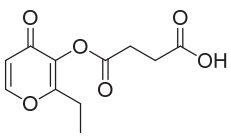
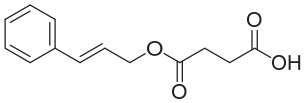


Figure 1 TG and DTG curves of compound **5a** and **5b**

2.4 Thermal degradation products analysis

Based on the results of GC-MS-O and TG-DTG, two uniquely fragrance synthetic products **5a** and **5b** were selected for Py-GC/MS detection, and three temperature conditions (300, 350 and 400 ℃) were set to monitor the pyrolysis of compounds **5a** and **5b** in air atmosphere.[18] Approximately 1 mg of sample was placed into the quartz tube between two quartz wool threads at a time. The pyrolysis products of compounds **5a** and **5b** were analyzed qualitatively and semi-quantitatively by the NIST17 mass spectrometry database using area normalization method. The results of this analysis are presented in Table 2.

Table 2 Pyrolysis analysis of target compounds **5a** and **5b**

Peak	Retention time/min	Pyrolysis product	Structure	Match	Relative content/%		
					300 ℃	350 ℃	400 ℃
Compound **5a**							
1	9.12	Succinic anhydride		91	0.10	0.56	2.15
2	11.78	Phenethyl alcohol		94	6.64	10.42	12.40
3	15.23	Ethyl maltol		94	79.88	82.98	83.47
4	31.58	4-((2-Ethyl-4-oxo-4*H*-pyran-3-yl)oxy)-4-oxobutanoic acid		90	1.53	0.32	—
Compound **5b**							
1	16.36	Ethyl maltol		94	77.81	79.98	81.41
2	19.39	Cinnamyl alcohol		96	11.10	12.30	15.11
3	31.51	4-((2-Ethyl-4-oxo-4*H*-pyran-3-yl)oxy)-4-oxobutanoic acid		91	1.17	0.92	0.09
4	36.15	4-(Cinnamyloxy)-4-oxobutanoic acid		98	2.97	0.09	—

In Table 2, compound **5a** was pyrolyzed to obtain four products. At 300 ℃, the content of succinic anhydride accounted for 0.10% of the total, phenethyl alcohol accounted for 6.64%, ethyl maltol accounted for 80.88%, 4-((2-ethyl-4-oxo-4*H*-pyran-3-yl)oxy)-4-oxobutanoic acid accounted for 0.53%. At 350 ℃, the content of succinic anhydride accounted for 0.56% of the total, phenethyl alcohol accounted for 10.42%, ethyl maltol accounted for 82.98%, 4-((2-ethyl-4-oxo-4*H*-pyran-3-yl)oxy)-4-oxo-butanoic acid accounted for 0.32%. At 400 ℃, the content of succinic anhydride accounted for 2.15% of the total, phenethyl alcohol accounted for 12.40%, ethyl maltol accounted for 83.47%. Four products were also obtained by pyrolysis of compound **5b**. At 300 ℃, the major product obtained was ethyl maltol, accounting for 77.81% of the total, followed by cinnamyl alcohol (11.10%), 4-((2-ethyl-4-oxo-4*H*-pyran-3-yl)oxy)-4-oxobutanoic acid (1.17%), and 4-(cinnamyloxy)-4-oxobutanoic acid (2.97%). At 350 ℃, the content of ethyl maltol and cinnamyl alcohol increased to 79.98% and 12.30%, while the content of 4-((2-ethyl-4-oxo-4*H*-pyran-3-yl)oxy)-4-oxobutanoic acid and 4-(cinnamyloxy)-4-oxobutanoic acid decreased to 0.92% and 0.09%. At 400 ℃, the content of ethyl maltol and cinnamyl alcohol further increased to 81.41% and 15.11%, while the content of 4-((2-ethyl-4-oxo-4*H*-pyran-3-yl)oxy)-4-oxobutanoic acid decreased to 0.09%.

The pyrolysis results of compounds **5a** and **5b** showed that ethyl maltol was the most pyrolyzed, followed by the used aromatic alcohol. At high temperatures, the ester bonds were more prone to break[19], leading to the formation of 4-((2-ethyl-4-oxo-4*H*-pyran-3-yl)oxy)-4-oxobutanoic acid and 4-(cinnamyloxy)-4-oxobutanoic acid, which played a certain role in the slow release of flavors. With the continuous increase of temperature, the other ester bond continued to break, the content of ethyl maltol increased, and the contents of phenethyl alcohol, cinnamyl alcohol and succinic anhydride also increased. Among them, phenethyl alcohol and cinnamyl alcohol are allowed to be used as flavors, and phenethyl alcohol is an edible flavor with rose-like aroma, which can be widely used in various edible flavors and tobacco flavors[20]. Cinnamyl alcohol is a crucial component of floral fragrances due to its hyacinth-like and ointment-like aroma[21].

2.5 Analysis of antioxidant ability

The target compounds **5a**～**5i** were selected, and ethyl maltol was used as a control for antioxidant assays, including DPPH scavenging ability and •OH scavenging ability. The results obtained are shown in Figure 2.

2.5.1 Analysis of DPPH scavenging ability

DPPH radical is a stable free radical with the conjugation and steric hindrance of benzene ring and electron absorption of nitro group. The free radical scavenger can make the single electron of DPPH radical pair, reduce the absorbance of the solution, and quantitatively respond to the free radical scavenging effect of the sample. The DPPH scavenging ability of compounds **5a**～**5i** is shown in Figure 2a. With the increase of concentration, the DPPH scavenging ability of compounds **5a**～**5i** showed an increasing trend, and the scavenging ability of ethyl maltol also showed an increasing trend, but it was significantly lower than that of compounds **5a**～**5i**. The concentrations of compound **5a** were 0.125, 0.25, 0.5, 1.0, 2.0 and 4.0 mg/mL, and the corresponding clearance rates were 20.94%, 19.35%, 23.74%, 30.57%, 42.60% and 64.63%, respectively. At the same concentration, the clearance rates of ethyl maltol were 6.86%, 10.28%, 11.25%, 19.80%, 21.46% and 30.39%, respectively. At 0.25 and 0.5 mg/mL, the scavenging ability of compound **5a** was slightly lower than that of compounds **5f** and **5h**. As can be seen from Figure 2(c), there was no significant difference among compounds **5b**, **5f** and **5h**, which showed better clearance, second only to compound **5a**. Among them, the IC_{50} of DPPH scavenging ability of compound **5a** was 2.48 mg/mL, the IC_{50} of compound **5b** was 7.11 mg/mL, the IC_{50} of compound **5f** was 8.43 mg/mL, the IC_{50} of compound **5h** was 8.61 mg/mL, and the IC_{50} of ethyl maltol was 21.67 mg/mL. On the whole, the scavenging ability of compound **5a** for DPPH was slightly better than that of compounds **5b**～**5i** and ethyl maltol.

2.5.2 Analysis of •OH scavenging ability

The •OH scavenging ability of compounds **5a**～**5i** is shown in Figure 2b. As the concentration increased, the scavenging ability of compounds **5a**～**5i** for •OH showed a slow rising trend, while the scavenging ability of ethyl maltol showed an increasing and then decreasing trend, reaching the maximum at 0.5 mg/mL with a scavenging rate of 87.55%. The concentrations of compound **5a** were 0.125, 0.25, 0.5, 1.0, 2.0 and 4.0 mg/mL, the corresponding clearance rates were 33.8%, 41.43%, 48.74%, 53.49%, 60.81% and 56.59%, respectively. At the same concentration, the clearance rates of ethyl maltol were 38.29%, 57.03%, 87.55%, 69.33%, 44.28% and 7.08%, respectively. At 2 mg/mL, the scavenging ability of ethyl maltol started to be lower than that of compounds **5a**. As can be seen from Figure 2d, the IC_{50} values of compound **5a** and ethyl maltol were relatively similar, and there was no obvious difference. Among them, the IC_{50} of compound **5a** was 0.79 mg/mL, and that of ethyl maltol was 0.84 mg/mL. Except for the higher IC_{50} value of compound **5d** (5.23 mg/mL), the IC_{50} values of other compounds were not much different. Taken together, the •OH scavenging ability of compound **5a** was slightly better than that of compounds **5b**～**5i**.

To sum up, the DPPH scavenging ability of compounds **5a**～**5i** was enhanced compared to ethyl maltol, probably because of the introduced structure of succinic acid and alcohols play a role in the DPPH scavenging ability. The •OH scavenging ability of compound **5a** was slightly higher than that of ethyl maltol, and the rest were lower than that of ethyl maltol. Therefore, compound **5a** showed excellent antioxidant performance.

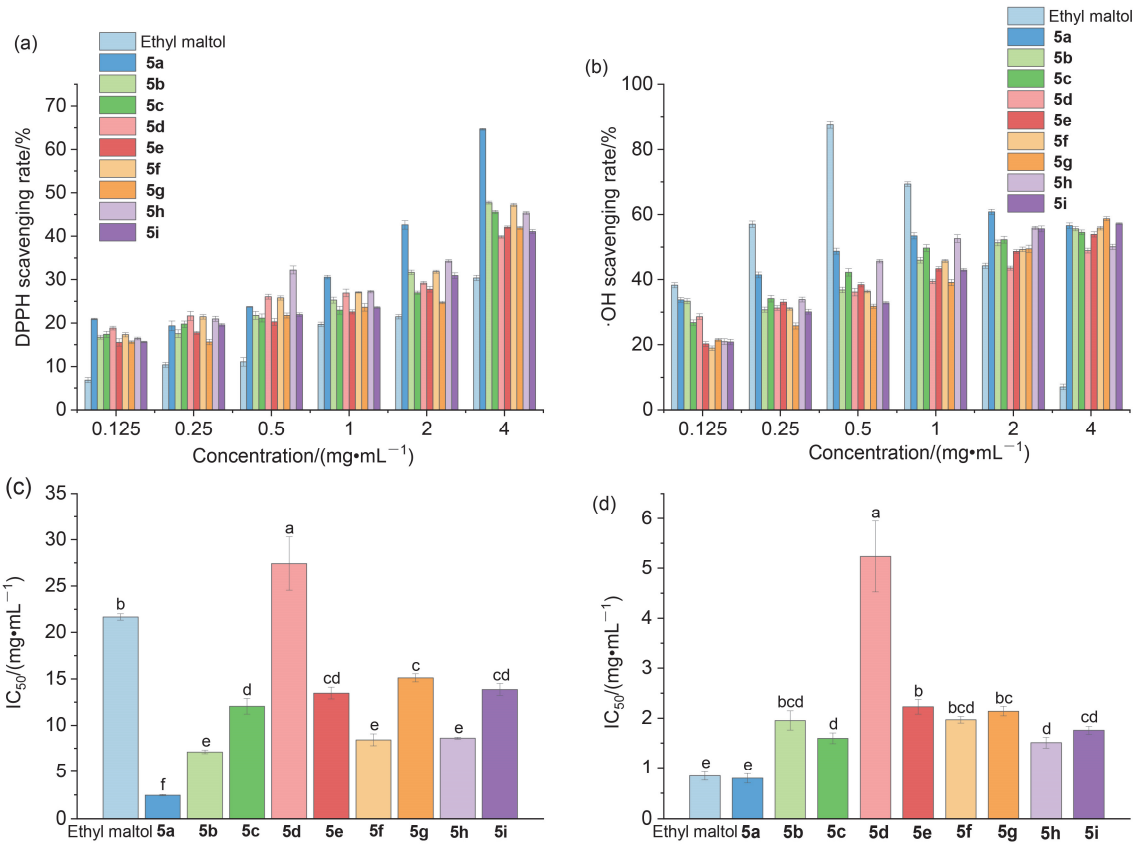


Figure 2 (a) DPPH scavenging ability of compounds **5a**～**5i**, (b) •OH scavenging ability of compounds **5a**～**5i**, (c) IC_{50} of DPPH scavenging ability of compounds **5a**～**5i**, and (d) IC_{50} of •OH scavenging ability of compounds **5a**～**5i**

3 Conclusions

In conclusion, nine novel ethyl maltol succinic diester derivatives were successfully designed and synthesized from succinic anhydride, ethyl maltol and various flavored alcohols. The synthesized compounds were characterized using ^{1}H NMR, ^{13}C NMR, IR, and HRMS. The TG-DTG results showed that the largest weight loss temperature of compounds **5a** and **5b** were above 220 ℃, which was higher than that of ethyl maltol, and improved the thermal stability of the target compounds. The Py-GC/MS results showed that the pyrolysis of compounds **5a** and **5b** at the set temperature produced a large amount of aroma substances, such as ethyl maltol and the used flavor alcohols, which is of great significance to enhance the aroma and increase the selectivity of flavors. The scavenging results of DPPH and •OH showed that the antioxidant ability of compound **5a** was superior to that of compounds **5b**～**5i** and ethyl maltol, and the rest of the compounds was also superior to ethyl maltol to some extent. The research results indicate that the synthesis of ethyl maltol succinate diester compounds can slow down the volatilization of ethyl maltol and flavor alcohols, and also enhance their antioxidant ability, which is potentially applicable in the formulation design of flavor products. Next, the safety of these synthesized ethyl maltol diesters would be evaluated, and their applications in tobacco or other flavor fields also need further exploration.

4 Experimental section

4.1 General information

The ^{1}H NMR and ^{13}C NMR data were acquired on an AVANCE NEO-400 superconducting nuclear magnetic resonance spectrometer (400 MHz, TMS as internal standard), Bruker Company, Switzerland. The functional group of the compounds were observed by a Thermo Nicolet iS50 Fourier transform infrared spectrophotometer, Waltham company, USA. High-resolution mass spectrometry was recorded on a Waters Micromass Q-TOF Micro high resolution mass spectrometry, Agilent, USA. TG-DTG data were obtained by a Q600 Synchronous Thermal Analyzer, TA Company, USA. The pyrolysis data were obtained by a Model 8890-5977 GC-MS, Agilent Company, USA and a Pyrobe 5250T pyrolysis instrument, American CDS company. The antioxidant ability data were obtained by UV-1900 UV-Vis spectrophotometer, Shanghai Jinghua Technology Instrument Co., Ltd., China.

Dicyclohexylcarbodiimide (DCC, $w \geqslant 99.0\%$) and 4-dimethylaminopyridine (DMAP, $w \geqslant 99.0\%$) were purchased from Shanghai Macklin Biochemical Technology Co., Ltd. Succinic anhydride ($w \geqslant 98.0\%$) was purchased from Tianjin Guangfu Institute of Fine Chemical Industry. DPPH ($w \geqslant 98.0\%$) was purchased from Shanghai yuanye

Bio-Technology Co., Ltd. Ferrous sulfate (AR) and salicylic acid (AR) were purchased from Sinopharm Chemical Reagent Co., Ltd. Ethyl maltol and perfume alcohol were provided by Henan province Xinzheng Jinye perfume Co., Ltd. Petroleum ether (AR), ethyl acetate (AR), dichloromethane (AR), chloroform (AR) and dichloroethane (AR) were purchased from Tianjin Damao Chemical Reagent Factory. Unless otherwise specified, all chemicals can be used without further purification. Compounds **3a**～**3i** were synthesized according to the previously published article.[12] Sensory panel was prepared according to the previously published article.[22]

4.2 Synthesis procedure and structure identification of compounds **5a**～**5i**

Compounds **3a**～**3i** (0.55 mmol, 1.1 equiv.) and DCC (0.66 mmol, 1.32 equiv.) were added into a 25 mL round-bottomed flask filled with 4 mL of dichloromethane, and after magnetic stirring for 2 h at room temperature, ethyl maltol (0.5 mmol, 1 equiv.) and DMAP (0.2 mmol, 0.4 equiv.) were added. After 16 h, excess glacial acetic acid was added, and the reaction continued for 2 h. The solvent was evaporated and ice water was added to terminate the reaction. Then, the obtained solution was filtered, extracted twice with 15 mL of ethyl acetate, combined with the ester layer, and washed three times with 10 mL of saturated $NaHCO_3$ water solution, saturated NaCl water and ice water, respectively. The obtained organic phase was dried with anhydrous Na_2SO_4 overnight. The filtrate was filtered, concentrated under reduced pressure, and the compounds **5a**～**5i** were obtained by silica gel thin layer chromatography separation.

2-Ethyl-4-oxo-4*H*-pyran-3-yl phenethyl succinate (**5a**): Orange-yellow oily liquid, eluent: DCM/EA (*V*∶*V*=1∶1). ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 7.61 (d, *J*=5.7 Hz, 1H), 7.23～7.18 (m, 2H), 7.12 (d, *J*=7.8 Hz, 3H), 6.28 (d, *J*=5.7 Hz, 1H), 4.22 (t, *J*=7.1 Hz, 2H), 2.84 (q, *J*=7.2 Hz, 4H), 2.64 (t, *J*=6.7 Hz, 2H), 2.50 (q, *J*=7.6 Hz, 2H), 1.11 (t, *J*=7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ*: 172.2, 172.0, 169.4, 163.5, 154.6, 137.7, 128.9, 128.5, 126.6, 116.6, 65.3, 35.0, 29.0, 28.6, 22.2, 10.8; IR (KBr) *ν*: 3032, 2923, 2850, 1724, 1609, 1559, 1438, 1236, 1163, 834, 696 cm^{-1}; HRMS (ESI) calcd for $C_{19}H_{21}O_6$ $[M+H]^+$ 345.1333, found 345.1320.

Cinnamyl (2-ethyl-4-oxo-4*H*-pyran-3-yl) succinate (**5b**): Light yellow oily liquid, eluent: DCM/EA (*V*∶*V*=1∶1). ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 7.69 (d, *J*=5.7 Hz, 1H), 7.38 (d, *J*=6.9 Hz, 2H), 7.32 (t, *J*=7.3 Hz, 2H), 7.26 (d, *J*=2.8 Hz, 1H), 6.65 (d, *J*=15.9 Hz, 1H), 6.40 (d, *J*=5.7 Hz, 1H), 6.28 (dt, *J*=15.9, 6.4 Hz, 1H), 4.77 (dd, *J*=6.4, 1.4 Hz, 2H), 2.97 (t, *J*=6.7 Hz, 2H), 2.81 (t, *J*=6.7 Hz, 2H), 2.60 (q, *J*=7.6 Hz, 2H), 1.20 (t, *J*=7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ*: 172.2, 171.9, 169.4, 163.5, 154.3, 137.8, 136.1, 134.3, 128.6, 128.1, 126.6, 122.9, 116.7, 65.5, 29.1, 28.6, 22.2, 10.8; IR (KBr) *ν*: 3089, 3030, 2921, 1728, 1604, 1548, 1440, 1262, 1160, 831, 745 cm^{-1}; HRMS (ESI) calcd for $C_{20}H_{21}O_6$ $[M+H]^+$ 357.1333, found 357.1315.

Butyl (2-ethyl-4-oxo-4*H*-pyran-3-yl) succinate (**5c**): Orange-red oily liquid, eluent: DCM/EA (*V*∶*V*=1∶1). ^{1}H NMR (400 MHz, $CDCl_3$), 7.66 (d, *J*=5.7 Hz, 1H), 6.32 (d, *J*=5.7 Hz, 1H), 4.03 (t, *J*=6.7 Hz, 2H), 2.87 (t, *J*=6.8 Hz, 2H), 2.67 (t, *J*=6.8 Hz, 2H), 2.55 (q, *J*=7.6 Hz, 2H), 1.58～1.51 (m, 2H), 1.35～1.25 (m, 2H), 1.15 (t, *J*=7.6 Hz, 3H), 0.85 (t, *J*=7.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ*: 172.2, 172.2, 169.5, 163.5, 154.5, 137.7, 116.7, 64.7, 30.6, 29.0, 28.6, 22.1, 19.1, 13.7, 10.7; IR (KBr) *ν*: 3079, 2961, 2924, 1719, 1606, 1460, 1263, 1170, 834 cm^{-1}; HRMS (ESI) calcd for $C_{15}H_{21}O_6$ $[M+H]^+$ 297.1333, found 297.1321.

2-Ethyl-4-oxo-4*H*-pyran-3-yl isobutyl succinate (**5d**): Orange oily liquid, eluent: DCM/EA (*V*∶*V*=1∶1). ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 7.71 (d, *J*=5.7 Hz, 1H), 6.41 (d, *J*=5.7 Hz, 1H), 3.89 (d, *J*=6.6 Hz, 2H), 2.95 (t, *J*=6.8 Hz, 2H), 2.77 (t, *J*=6.9 Hz, 2H), 2.62 (q, *J*=7.7 Hz, 2H), 1.94 (dt, *J*=13.4, 6.7 Hz, 1H), 1.23 (t, *J*=7.6 Hz, 3H), 0.93 (d, *J*=6.7 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ*: 172.2, 172.2, 169.4, 163.5, 154.3, 137.8, 116.8, 71.0, 29.7, 29.0, 28.6, 27.7, 22.2, 19.1, 10.8; IR (KBr) *ν*: 3082, 2959, 2926, 2881, 1712, 1606, 1460, 1262, 1160, 834 cm^{-1}; HRMS (ESI) calcd for $C_{15}H_{21}O_6$ $[M+H]^+$ 297.1333, found 297.1321.

2-Ethyl-4-oxo-4*H*-pyran-3-yl (3-methylbut-2-en-1-yl) succinate (**5e**): Orange viscous solid, eluent: DCM/EA (*V*∶*V*=5∶1). ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 7.72 (d, *J*=5.7 Hz, 1H), 6.42 (d, *J*=5.7 Hz, 1H), 5.36～5.31 (m, 1H), 4.60 (d, *J*=7.2 Hz, 2H), 2.94 (t, *J*=6.8 Hz, 2H), 2.75 (t, *J*=7.0 Hz, 2H), 2.64～2.60 (m, 2H), 1.76 (s, 3H), 1.71 (s, 3H), 1.26～1.21 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ*: 176.3, 172.1, 169.4, 163.6, 154.4, 139.3, 137.7, 118.4, 116.7, 61.8, 33.7, 28.63, 25.8, 22.2, 18.0, 10.8; IR (KBr) *ν*: 3082, 2982, 2921, 1719, 1606, 1382, 1263, 1161, 935, 834 cm^{-1}; HRMS (ESI) calcd for $C_{16}H_{21}O_6$ $[M+H]^+$ 309.1333, found 309.1320.

2-Ethyl-4-oxo-4*H*-pyran-3-yl pent-1-en-3-yl succinate (**5f**): Orange-red viscous solid, eluent: DCM/EA (*V*∶*V*=5∶1). ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 7.73 (d, *J*=5.7 Hz, 1H), 6.44 (d, *J*=5.7 Hz, 1H), 5.81～5.72 (m, 1H), 5.26 (s, 1H), 5.17 (d, *J*=11.8 Hz, 2H), 2.95 (t, *J*=6.7 Hz, 1H), 2.78 (t, *J*=7.0 Hz, 2H), 2.68～2.66 (m, 1H), 2.66～2.56 (m, 2H), 1.69～1.62 (m, 2H), 1.27～1.20 (m, 3H), 0.90 (t, *J*=7.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ*: 176.3, 171.4, 169.4, 163.7, 154.5, 137.7, 136.1, 116.8, 113.1, 29.2, 28.6, 27.2, 22.2, 21.7, 10.7, 9.4; IR (KBr) *ν*: 3082, 2974, 2923, 1721, 1608,1426, 1263, 1167, 834 cm^{-1}; HRMS (ESI) calcd for $C_{16}H_{21}O_6$ $[M+H]^+$ 309.1333, found 309.1319.

Benzyl (2-ethyl-4-oxo-4*H*-pyran-3-yl) succinate (**5g**): Orange viscous solid, eluent: DCM/EA (*V*∶*V*=1∶1). ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 7.73 (d, *J*=5.6 Hz, 1H), 7.39～7.30 (m, 5H), 6.44 (d, *J*=5.6 Hz, 1H), 5.15 (s, 2H), 2.97 (t, *J*=7.1 Hz, 1H), 2.84～2.73 (m, 2H), 2.69 (s, 2H), 2.58 (q, *J*=6.9, 6.2 Hz, 1H), 1.27～1.18 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ*: 176.6, 172.0, 169.4, 163.6,

154.4, 135.8, 128.6, 128.3, 128.3, 128.2, 116.7, 66.6, 29.1, 28.6, 22.2, 10.8; IR (KBr) ν: 3033, 2924, 2847, 1728, 1611, 1556, 1435, 1264, 1160, 832, 745, 695 cm^{-1}; HRMS (ESI) calcd for $C_{18}H_{19}O_6$ $[M+H]^+$ 331.1176, found 331.1166.

2-Ethyl-4-oxo-4*H*-pyran-3-yl isopentyl succinate (**5h**): Orange viscous solid, eluent: DCM/EA (V∶V=1∶1). ^1H NMR (400 MHz, $CDCl_3$) δ: 7.74 (d, J=5.7 Hz, 1H), 6.42 (d, J=5.7 Hz, 1H), 4.14 (d, J=6.9 Hz, 1H), 2.94 (t, J=6.8 Hz, 2H), 2.75 (t, J=6.9 Hz, 2H), 2.62 (q, J=7.7 Hz, 2H), 1.76～1.62 (m, 2H), 1.52 (q, J=6.9 Hz, 2H), 1.26～1.21 (m, 3H), 0.92 (d, J=6.6 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 172.4, 172.2, 169.4, 163.5, 154.4, 137.7, 116.7, 63.6, 37.3, 29.0, 28.6, 25.0, 22.4, 22.2, 10.8; IR (KBr) ν: 3080, 2956, 2923, 1729, 1611, 1555, 1262, 1161, 832 cm^{-1}; HRMS (ESI) calcd for $C_{16}H_{23}O_6$ $[M+H]^+$ 311.1489, found 311.1477.

2-Ethyl-4-oxo-4*H*-pyran-3-yl (2-methylallyl) succinate (**5i**): Orange viscous solid, eluent: DCM/EA (V∶V=1∶1). ^1H NMR (400 MHz, $CDCl_3$) δ: 7.71 (d, J=5.7 Hz, 1H), 6.42 (d, J=5.7 Hz, 1H), 4.95 (d, J=18.9 Hz, 2H), 4.53 (s, 2H), 2.97 (d, J=13.5 Hz, 2H), 2.81 (t, J=6.8 Hz, 2H), 2.62 (q, J=7.6 Hz, 2H), 1.75 (s, 3H), 1.22 (t, J=7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 172.2, 171.8, 169.4, 163.6, 154.4, 139.7, 137.7, 116.7, 113.1, 68.1, 29.0, 28.6, 22.2, 19.5, 10.8; IR (KBr) ν: 3082, 2923, 2853, 1734, 1608, 1430, 1262, 1160, 832 cm^{-1}; HRMS (ESI) calcd for $C_{15}H_{19}O_6$ $[M+H]^+$ 295.1176, found 295.1166.

4.3 TG analysis

The TG analysis were observed by a simultaneous thermal analyzer (TA Q600, TA, USA). The mass of target compounds was kept around 3～5 mg at a time. Purified air was used as carrier gas, and the flow rate for degradation was 60 mL•min^{-1}. The sample was heated up from 30 ℃ to 450 ℃ at a rate of 10 ℃•min^{-1}.

4.4 Pyrolysis analysis

The pyrolysis temperature was heated to 300, 350, and 400 ℃ at 30 ℃•ms^{-1} with a hold time of 15 s, while the initial temperature of the pyrolysis interface was set to 40 ℃ with a hold time of 0 s. The pyrolysis products were observed by the GC/MS under the air atmosphere. GC-MS test conditions were determined according to the previous literature[12,22].

4.5 Antioxidant analysis

4.5.1 DPPH clearance ability

The scavenging power of DPPH radicals was referred to method by Joubert[13] with slight modifications. The samples were prepared with dry re-steamed acetonitrile at different concentrations (0.125～4 mg/mL). Take 1.0 mL of compound samples with different concentrations, and add 2.0 mL of 0.1 mmol/L DPPH-acetonitrile solution to shake well, and shake rapidly to mix the mixture well. Keep it away from light for 30 min at room temperature, and measure the absorbance at 517 nm by UV-1900 UV-Vis spectrophotometer, and ethyl maltol was used as positive control. The scavenging rate of DPPH radicals by the compound samples was calculated using the following Eq. (1):

$$\text{Scavenging activity}(\%)=1-(A_2-A_1)/A_0\times100\% \quad (1)$$

A_2 is absorbance of 1 mL of compound sample solution+2 mL of DPPH solution, A_1 is absorbance of 1 mL of compound sample solution+2 mL of acetonitrile, and A_0 is absorbance of 1 mL of acetonitrile+2 mL DPPH solution.

4.5.2 •OH clearance ability

•OH scavenging ability was measured according to Zhang's method[14]. 1.0 mL of $FeSO_4$, H_2O_2 and salicylic acid solutions of 9 mmol/L were added to 1.0 mL of different concentrations of compound samples and mixed well, and the reaction was carried out at 37 ℃ for 30 min. The absorbance values were measured at 562 nm using UV-1900 UV-Vis spectrophotometer. Taking ethyl maltol as the positive control, the •OH scavenging rate was calculated by the following Eq. (2):

$$\text{Scavenging activity}(\%)=1-(A_i-A_j)/A_0\times100\% \quad (2)$$

A_i is absorbance of 1.0 mL of compound sample solution+1.0 mL $FeSO_4$ solution+1.0 mL H_2O_2 solution+1.0 mL salicylic acid solution, A_j is absorbance of 1.0 mL of compound sample solution+1.0 mL of $FeSO_4$ solution+1.0 mL of distilled water+1.0 mL of salicylic acid solution, and A_0 is absorbance of 1.0 mL of distilled water+1.0 mL of $FeSO_4$ solution+1.0 mL of H_2O_2 solution+1.0 mL of salicylic acid solution.

Supporting Information ^1H NMR, ^{13}C NMR, IR and HRMS spectra of compounds **5a**～**5i**, and ion chromatogram of the pyrolysis products from **5a** and **5b**. The Supporting Information is available free of charge via the Internet at http://sioc-journal.cn/.

References

[1] Saud, R.; Pokhrel, S.; Yadav, P. N. *J. Macromol. Sci. A* **2019**, *56*, 375.

[2] Zhang, C.-L.; Qiu, X.-Y.; Liu, S.-J. *J. Coord. Chem.* **2019**, *72*, 3248.

[3] Anouar, E. H.; Shah, S. A. A.; Hassan, N. B.; Moussaoui, N. E.; Ahmad, R.; Zulkefeli, M.; Weber, J.-F. *Molecules* **2014**, *19*, 3489.

[4] Ren, C.-X.; Jin, X.; Xie, D.-P.; Guo, X.-Y.; Yu, L.-Y.; Cui, Y.-D.; Kwon, T.; Sun, H.-N. *Appl. Biol. Chem.* **2021**, *64*, 74.

[5] Sun, J.-J.; Hao, M.; Wang, L.; Cui, L.-H. *Appl. Mech. Mater.* **2013**, *284～287*, 380.

[6] Xue, L.-H. *Fine Chem.* **2012**, *29*, 588 (in Chinese).
(薛连海, 精细化工, **2012**, *29*, 588.)

[7] Zhao, M.; Tang, H.-G.; Meng, X.-H.; Chen, L.-H.; Xiao, C.-G. *Sci. Technol. Food Ind.* **2016**, *37*, 273 (in Chinese).
(赵敏, 唐宏刚, 孟祥河, 陈黎洪, 肖朝耿, 食品工业科技, **2016**, *37*, 273.)

[8] Sam, R.; Nico, B. *Macromol. Rapid Commun.* **2023**, 2300120.

[9] Zou, P.; Zhang, S.-Y.; Jia, L.-Y.; He, Z.-Y.; Shu, J.-S.; Liu, C.-H.; Zhu, Y.-Y. *Thermochim. Acta* **2022**, *716*, 179323.

[10] Megdi, E. *Mater. Sci. Forum* **2021**, *1042*, 131.

[11] Chen, Y.-W.; Gao, C.; Yang, Z.-Y.; Wang, J.-Q.; Liu, C.; Hao, Z.-H. *Prog. Vet. Med.* **2022**, *43*, 80 (in Chinese).
(陈宇微, 高琛, 杨志远, 王金泉, 刘畅, 郝智慧, 动物医学进展, **2022**, *43*, 80.)

[12] Yu, Z.-J.; Pan, T.-T.; Lai, M.; Ji, Y.-H.; Yang, X.-P.; Dong, A.-J.; Ji, X.-M. *Flavour Fragrance J.* **2023**, *38*, 301.
[13] Joubert, E.; Winterton, P.; Britz, T. J.; Ferreira, D. *Food Res. Int.* **2004**, *37*, 133.
[14] Zhang, T.; Xiang, J.-L.; Zheng, G.-B.; Yan, R.-Q.; Min, X. *J. Funct. Foods* **2018**, *41*, 19.
[15] Dong, H.-M.; Zhang, Q.; Li, L.; Liu, J.; Shen, L.-W.; Li, H.-Y.; Qin, W. *Ind. Crops Prod.* **2015**, *76*, 290.
[16] Liang, M.; Shen, X.-C.; Wu, J.; Xu, R.-Y.; Wang, R.; Pan, G.-W.; Rao, X.-L.; Shi, H.-B.; Zhang, J.-S.; Zheng, X.-Y. *Acta Tab. Sin.* **2023**, *29*, 12 (in Chinese).
(梁淼, 沈晓晨, 吴佳, 徐如彦, 王瑞, 潘高伟, 饶先立, 石怀斌, 张峻松, 郑晓云, 中国烟草学报, **2023**, *29*, 12.)
[17] Tatyana, V. S.; David, D.; Kenneth, S. A. *Thermochim. Acta* **2002**, *392*～*393*, 315.
[18] Fan, W.-P.; Chu, W.-J.; Li, Y.-G.; Han, L.; Li, P.-Y.; Tian, H.-Y.; Lai, M.; Ji, X.-M. *ChemistrySelect* **2022**, *7*, e20220372.
[19] Fan, W.-P.; Chu, W.-J.; Tian, H.-Y.; Zhang, Z.; Feng, Y.-J.; Gao, Z.-T.; Cheng, B.; Ji, X.-M.; Lai, M. *J. Heterocycl. Chem.* **2022**, *59*, 1397.
[20] Izawa, M.; Kobashi, Y.; Sakaguchi, S. *J. Agric. Chem. Soc. Jpn.* **2014**, *21*, 364.
[21] Bickers, D.; Calow, P.; Greim, H.; Hanifin, J. M.; Rogers, A. E.; Saurat, J. H.; Sipes, I. G.; Smith, R. L.; Tagami, H. *Food Chem. Toxicol*. **2004**, *43*, 799.
[22] Dong, A.-J.; Yu, Z.-J.; Pan, T.-T.; Rong, L.; Lai, M.; Cheng, B.; Ji, X.-M.; Yang, X.-P.; Wang, B. *Flavour Fragrance J.* **2023**, *38*, 416.

(Cheng, F.)

