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Synthesis of 3-Oxo-α-ionol Ethyl Carbonate and its Conversion to Megastigmatrienones in Tobacco Smoke*

by

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SUMMARY

3-Oxo-α-ionol ethyl carbonate, a precursor of megastigmatrienones was prepared by reduction of α-ionone to α-ionol, followed by esterification with ethyl chloroformate and then by oxidation with *t*-butyl chromate. The total yield was about 23%. Infrared (IR) and mass spectra of this compound were determined. Upon smoking, cigarettes to which 0.002% by weight of the titled compound was added had an improved and more harmonious flavor. The smoke was sweeter and had a cleaner after taste. Experimental results suggest that the title compound added to the tobacco pyrolyzes to form megastigmatrienones during smoking. [Beitr. Tabakforsch. Int. 19 (2001) 339–343]

ZUSAMMENFASSUNG

3-Oxo-α-ionol-ethylcarbonat, eine Vorläufersubstanz der Megastigmatrienone, wurde durch Reduktion von α-Ionon zu α-Ionol und nachfolgender Veresterung mit Ethylchloroform und anschließender Oxidation mit *t*-Butylchromat hergestellt. Die Gesamtausbeute lag bei 23%. IR- und Massenspektren dieser Substanz wurden aufgenommen. Cigaretten, denen bezogen auf das Gewicht 0,002% 3-Oxo-α-ionol-ethylcarbonat zugesetzt wurden, hatten einen verbesserten und ausgewogeneren Geschmack. Der Rauch war milder und hatte einen reineren Nachgeschmack. Experimentelle Ergebnisse lassen darauf schließen, dass 3-Oxo-α-ionol-ethylcarbonat bei Zugabe zum Tabak während des Rauchens zu Megastigmatrienonen pyrolysiert wird. [Beitr. Tabakforsch. Int. 19 (2001) 339–343]

RESUME

3-Oxo-α-ionol éthyl carbonate, un précurseur du mégastigmatriénone, a été synthétisé par réduction de α-ionone en α-ionol, suivie d'une estérification par l'éthyl chloroformate et d'une oxydation par *t*-butylchromate. Le rendement total était de 23%. Les caractéristiques infrarouges (IR) et de spectrophotométrie de masse de ce composé ont été déterminées. Les cigarettes, auxquelles était apporté 0,002% de 3-oxo-α-ionol éthyl carbonate, avaient un arôme amélioré et plus harmonieux. La fumée était plus douce et l'arrière-goût plus franc. Les résultats expérimentaux suggèrent que le 3-oxo-α-ionol éthyl carbonate apporté au tabac est pyrolysé en mégastigmatriénone au cours du fumage. [Beitr. Tabakforsch. Int. 19 (2001) 339–343]

INTRODUCTION

Megastigmatrienones are known to make an important contribution to the overall flavor character of tobacco and its smoke (1–5). However, because of the four highly conjugated double bonds of their molecular structure, megastigmatrienones have a tendency to polymerize making it difficult to store and formulate. The use of a megastigmatrienone precursor may be one means of solving this tobacco-flavoring problem. U.S. Patent 4,827,012 (4) discloses the synthesis of 3-oxo-α-ionol ethyl carbonate by esterifying 3-oxo-α-ionol, but the starting material is very expensive and not easily prepared or purchased (6). To overcome this deficiency in the preparation of the megastigmatrienone precursor, 3-oxo-α-ionol ethyl carbonate was prepared by reduction of α-ionone to α-ionol, followed by esterification with ethyl

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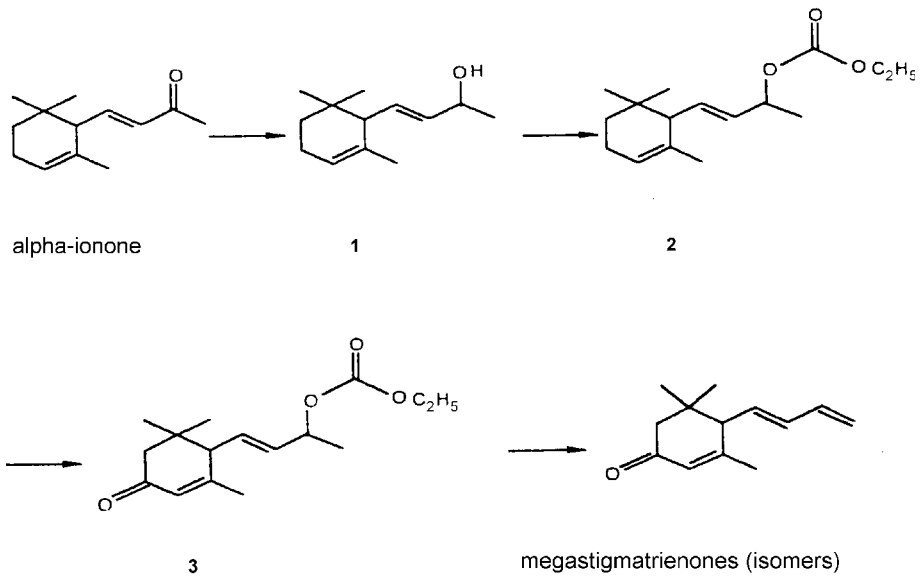

Figure 1.
Synthesis of 3-oxo-α-ionol ethyl carbonate, a precursor of megastigmatrienones

chloroformate and then oxidation with *t*-butyl chromate. The total yield of this synthesis is about 23% and the starting material α-ionone is rather cheap and easy to obtain.

EXPERIMENTAL

Sodium borohydride (96%) was purchased from MERCK-Schuchardt. α-Ionone (CP), ethyl chloroformate (CP), chromium trioxide (AR) and tertiary-butyl alcohol (AR) were obtained from domestic sources.

Infrared (IR) spectra were recorded on a Magna-IR Nicolet 750 spectrometer. Gas chromatography-mass spectrometry (GC-MS) data were obtained with a HP6890/HP5973 GC-MS spectrometer equipped with a HP-Ultra 2 capillary gas chromatographic column (5% phenyl methyl siloxane, 0.33 μm, 0.20 mm × 25 m). Compounds **1**, **2** and **3** (*see* Figure 1) were dissolved in ethanol at a concentration of about 1% by weight for the GC-MS analysis. The injection and auxiliary temperatures were 240 and 250 °C, respectively. For the chromatography, the column temperature program included an initial 2-min hold at 80 °C followed by an increase of 5 °C/min until the final temperature of 230 °C was reached and maintained for 15 min. The column helium gas flow was 28.6 mL/min, the injection volume was 1 μL with a split ratio of 20:1. For the MS, the electron energy was 70 eV, the temperature of the ion source and MS quadrupole were 230 and 150 °C, respectively, and the electron multiplier voltage (EMV) was 1,635 volts.

3-Oxo-α-ionol ethyl carbonate (**3**) was dissolved in ethanol and was added at a rate of 0.002% by weight to a portion of unflavored blended tobacco from Changsha Cigarette Factory, which consists of 45% of Virginia tobacco, 30% of burley tobacco, 10% of stem, 5% of aromatic tobacco, and 10% of expanded cut tobacco. Experimental cigarettes were made from the treated tobacco. Control cigarettes for comparison were made from the original untreated tobacco blend. All the cigarettes have a length of 84 mm, a weight of 0.9 g/cig and a pressure drop of 1150 Pa in average. Both the control and compound **3**-treated cigarettes were evaluated for smoking characteristics.

With a portion of Virginia tobacco instead of blended tobacco, two other types of cigarettes were prepared. One was a control with no 3-oxo-α-ionol ethyl carbonate (**3**) added and the second had 3% by weight of **3** added to the Virginia tobacco. The control and test Virginia-type cigarettes were each smoked on a Filtrona COA 200 smoking machine. Twenty cigarettes of each type were smoked and the smoke particulate matter from four cigarettes was collected on separate Cambridge filter pads, i.e., five pads were used to collect the smoke from 20 cigarettes. A non-standard smoking regime was used with a puff taken every 20 sec, puff volume of 35 mL and puff duration of 2 sec, smoking to a butt length of 28 mm.

The Cambridge filters with the collected smoke condensate were extracted twice each with a mixture of 25 mL diethyl ether and 2 mL dibutyl phthalate. The combined extract was filtered, concentrated to a volume of 5 mL, and analyzed by GC-MS. The column oven temperature program used for these analyses included an initial 1-min hold at 80 °C, then increasing at a rate of 10 °C/min to an intermediate temperature of 180 °C where it was held for 8 min, then increasing at a rate of 2 °C/min to a final temperature of 230 °C where it was maintained for 1 min. The carrier gas was helium at a flow rate of 34.2 mL/min, and the injection volume was 1 μL splitless. The MS conditions were the same as described earlier.

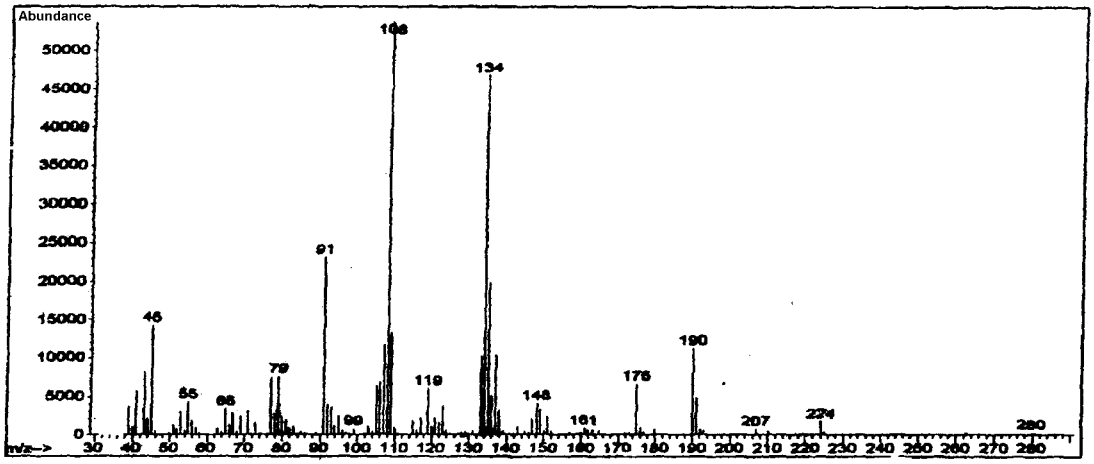

Figure 2.
Mass spectrum of compound 3

Preparation of α-ionol (**1**)

One hundred grams of α-ionone was dissolved in 500 mL of absolute ethanol followed by 5.8 g of sodium borohydride added slowly with stirring. The resulting mixture was stirred for 4 h. Five hundred milliliters of water was added to make the resulting boric acid ester hydrolyze. Following this step, most of the ethanol was evaporated under reduced pressure and the residue was extracted 4 times with 100-mL portions of diethyl ether. The ether solution was washed twice with 100 mL of water, dried over anhydrous magnesium sulfate, filtered and evaporated to yield 99 g of a yellow oily liquid.

Preparation of α-ionol ethyl carbonate (**2**)

19.4 g of α-ionol prepared as described above was dissolved in 300 mL of dichloromethane and then 15.8 g of pyridine was added to the solution. To this mixture under stirring and cooling, 21.7 g of ethyl chloroformate was added dropwise over a 30-min period. Stirring was continued for 18 h at 25 °C after which 200 mL of dichloromethane was added. This mixture was then washed sequentially with 5% phosphoric acid solution three times, saturated sodium bicarbonate solution, and twice with water. After drying over anhydrous magnesium sulfate, the solvent was removed on a warm water bath and 25 g of light yellow oily liquid was produced.

Preparation of 3-oxo-α-ionol ethyl carbonate (**3**)

To a stirred solution of 16.8 g of α-ionol ethyl carbonate, prepared as described above and dissolved in 100 mL of carbon tetrachloride, was added 50 mL of acetic acid and 4 mL of acetic anhydride. To this mixture was added *t*-butyl chromate that was prepared previously by the reaction of 40 g of CrO_3 with 100 mL of *t*-butyl alcohol and 100 mL of carbon tetrachloride. The reaction mixture was stirred for 1 h at 40 °C, and then allowed to stand at room temperature for four days. After standing, 100 g of oxalic acid dissolved in 500 mL of water was added to the reaction mixture. This solution was stirred for 2 h and then the aqueous layer was extracted with diethyl ether. The carbon tetrachloride layer and ether extract from the chromate reaction were washed independently several times with saturated sodium bicarbonate solution, combined, dried, filtered and evaporated to yield a crude product. The crude material was purified by column chromatography with silica gel as solid adsorbent and 1 : 1 mixture of cyclohexane and diethyl ether as eluting solvent to yield 4.8 g of compound **3**.

RESULTS AND DISCUSSION

The synthesized compounds **1**, **2** and **3** were analyzed independently by GC and according to the total peak area were 92%, 90% and 93% pure, respectively.

Absorption peaks ν_{max} 2960, 1748, 1672, 1631, 1470, 1448, 1369, 1370 and 1264 cm^{-1} were observed in the IR spectrum of **3** and these are consistent with literature values for 3-oxo-α-ionol ethyl carbonate (4).

Figure 2 is the mass spectrum of **3**, and MS data of the compounds prepared were as follows: compound **1**: *m/e* 194 (M^+, 3), 176 (2), 161 (4), 138 (44), 123 (20), 105 (100), 79 (18); compound **2**: *m/e* 266 (M^+, <1), 210 (16), 176 (50), 161 (26), 138 (15), 120 (49), 105 (100), 95 (77), 79 (27), 43 (33); and compound **3**: *m/e* 280 (M^+, <1), 224 (4), 190 (18), 175 (12), 134 (83), 108 (100), 91 (45), 77 (16), and 45 (25). The number in parenthesis is the relative abundance of the ion.

The *m/e* values of the molecular ion peaks in the mass spectra of **1**, **2** and **3** correspond to the molecular weights of the individual compounds. The remaining major peaks in the mass spectra can be reasonably assigned to the

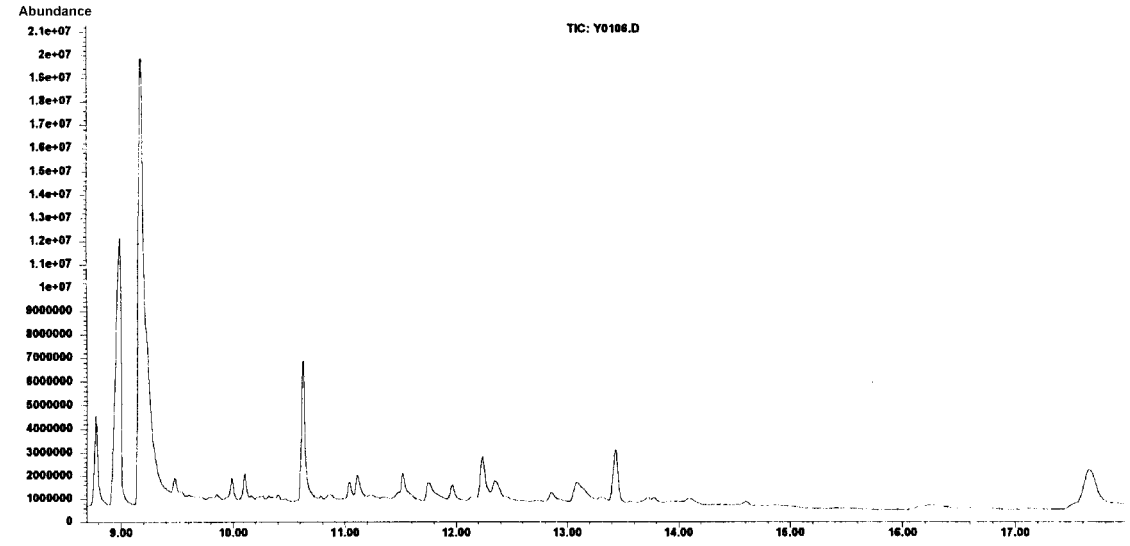

Figure 3.
Gas chromatogram of smoke particulate matter of test cigarettes

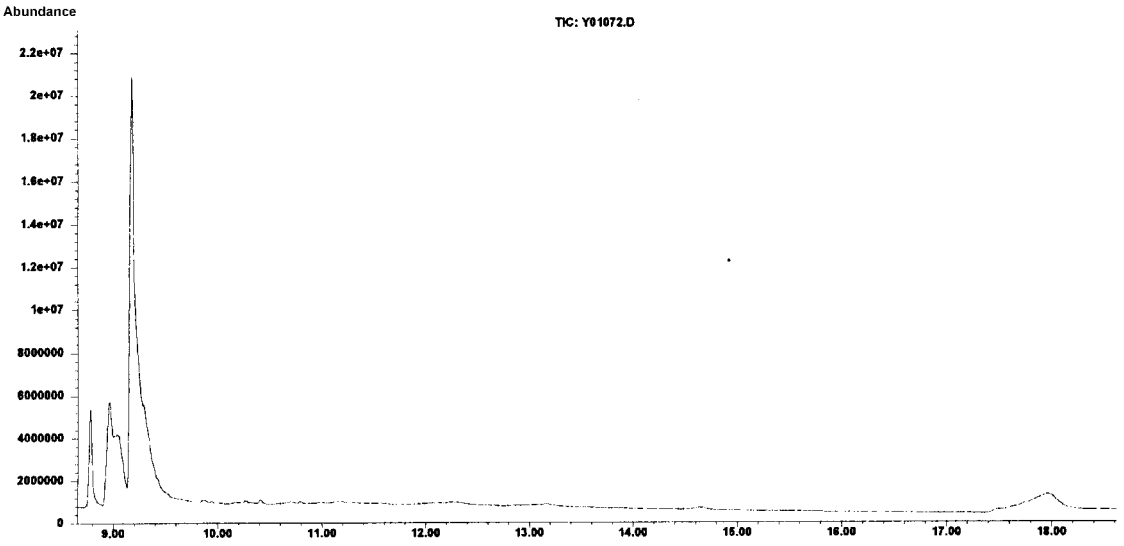

Figure 4.
Gas chromatogram of smoke particulate matter of control cigarettes

fragmentation mechanism expected from these compounds. The mass spectral data of **3** were consistent with those of 3-oxo-α-ionol ethyl carbonate published in the literature (4).

Smoking sensory evaluation of the control and test blended tobacco cigarettes showed that the cigarettes with the 0.002% by weight added compound **3** had an improved and more harmonious flavor with a sweeter and cleaner after taste. This indicates that **3** functions as an efficient flavor enhancer and modifier for blended tobacco cigarette smoke.

The gas chromatograms of the smoke particulate matter extract from the test and control Virginia-type cigarettes are shown in Figures 3 and 4, respectively.

For the control Virginia blend cigarette containing no added compound **3** (Figure 4), there are no significant peaks found in the chromatogram between retention times of 9.4 and 17.4 min while many peaks are found during this time frame for the test cigarette (*see* Figure 3). The mass spectra of peaks corresponding to retention times of 11.6, 12.2, 12.9 and 13.1 min were very similar and the mass spectral library search of the instrumentation indicated that all of these peaks had a quality index >90 for megastigmatrienones. The mass spectral data of the chromatographic peak at a retention time of 13.1 min (Figure 5) were as follows: *m/e* (190 M^+, 97), 175 (90), 148 (80), 147 (88), 133 (100), 122 (37), 119 (68), 105 (60), 91 (72), 77 (45). These data are consistent with those of one

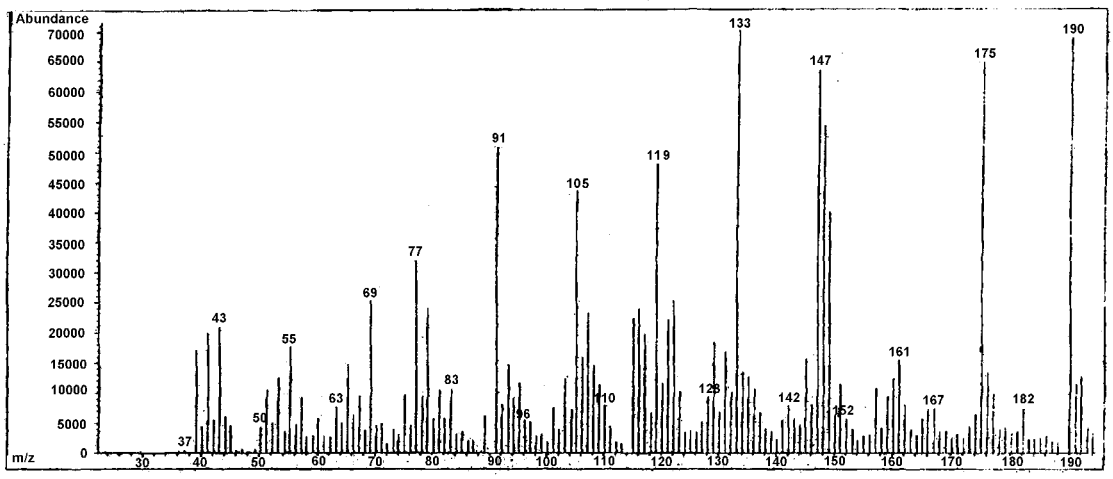

Figure 5.
Mass spectrum of the chromatographic peak at a retention time of 13.1 min

megastigmatrienone (NIST no. 109824) found in the NIST/EPA/NIH Mass Spectra Library (version 1.1a) and those of a megastigmatrienone found in literature (5). From these results, we concluded that 3-oxo-α-ionol ethyl carbonate, the compound whose synthesis is described herein, can undergo a thermal degradation to produce megastigmatrienones in treated tobacco smoke.

CONCLUSION

The preparation of 3-oxo-α-ionol ethyl carbonate from α-ionone, a cheap and readily available starting material is described. The yield of this synthesis is approximately 23%. When applied to tobacco and smoked, the carbonate undergoes a thermal elimination reaction producing megastigmatrienones in the smoke. The carbonate appears to be stable on tobacco and is shown by our study to be an efficient precursor of flavorful megastigmatrienones in smoke.

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