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ScienceDirect
Tetrahedron
Tetrahedron 63 (2007) 4762–4767

A general method for the synthesis of the most powerful naturally occurring Maillard flavors

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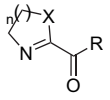
Received 10 November 2006; revised 24 February 2007; accepted 15 March 2007
Available online 18 March 2007

Abstract—The natural flavors 2-acetyl-1-pyrroline **1a**, 2-propionyl-1-pyrroline **1b**, 2-acetyl-3,4,5,6-tetrahydropyridine **1c**, 2-acetyl-2-thiazoline **1d**, 2-propionyl-2-thiazoline **1e**, and the artificial flavor 2-acetyl-5,6-dihydro-4*H*-1,3-thiazine **1f** have been prepared by catalytic SeO_2 oxidation of the corresponding cyclic imines **6a–c** and sulfur cyclic imines **7a–c** using TBHP as co-oxidant. The oxidation of the pyrrolines **1a** and **b** is completely regioselective. Professional olfactory evaluation together with the odor threshold of the new flavor **1f** is reported.

1. Introduction

Historically, the heterocycles 2-acetyl-1-pyrroline **1a** and 2-acetyl-3,4,5,6-tetrahydropyridine **1c** have been identified as the most important flavors of cooked rice and bread, moreover, their flavor significance has been shown in many other foods. They exhibit a pleasant bread like scent with very low odor thresholds. The sulfur containing analogue of **1a** is the 2-acetyl-2-thiazoline **1d**, it exhibits a similar odor, corresponding to that of popcorn, and, it has been detected in the roasted meat and in the beefbroth.[1]

Recently, the 2-propionyl-1-pyrroline **1b** and 2-propionyl-2-thiazoline **1e** have gained interest in the food industry, since have been added to the FEMA-GRAS list of the naturally occurring aromas admitted for the food flavor formulations.[2]



1a, n=1, X=CH_2, R=Me
1b, n=1, X=CH_2, R=Et
1c, n=2, X=CH_2, R=Me
1d, n=1, X=S, R=Me
1e, n=1, X=S, R=Et
1f, n=2, X=S, R=Me

The presence of these compounds in many foods results from the cooking process. The reaction between the amino acids and the sugars present on the surface of foods generates, at high temperatures, these heterocycles (Maillard reaction).[1] However, the reproduction of such a process in laboratory is not suitable for the preparation of single Maillard flavor on large scale. For this reason many chemists have been engaged in the identification of efficient and simple synthetic routes to these compounds. Many syntheses, concerning the preparation of **1a–c**, have been reported. They are distinguishable by two main strategies: (i) modification of commercially available starting materials containing already the heterocyclic unit,[3–9] such as the 2-acetyl-pyrrole[3] or the 2-acetyl-pyridine,[4] the methylester of proline,[5,6] the pyrrolidine,[7] the 2-pyrrolidinone[8,9] or the 2-piperidone,[9] to give the final products in moderate to good overall yields and (ii) preparation of acyclic precursors[10–12] such as **2** or **3**, which are then cyclized to give **1a** or **b** (Scheme 1).

In comparison to the preparation of **1a–c**, little effort has been dedicated to the synthesis of **1d** and **e**. A method of broad synthetic significance is that of Unilever,[13a,b] which consists of condensation of the required cysteamine with nitriles **4a–d** to give the 2-thiazolinic derivatives bearing the carbonyl functionality protected as ketal **5a** and **b** or oxime **5c** and **d**. Then, the carbonyl groups are revealed by acidic hydrolysis of the latter to give **1d** or **e** in an overall yield of 12% or 19%, respectively (Scheme 1). Alternatively, Duñach et al. have shown that the oxidation of the 2-acetylthiazolidine by a catalytic ruthenium complex (10% in weight) in presence of TBHP furnishes **1d** in 70% yield.[14]

However, all these synthetic procedures suffer to some extent from at least one of three following drawbacks: (i) high cost of the reagents; (ii) length of the reaction sequence; and (iii) requirement of acid or base work-up in the final stages, which is incompatible with low chemical stability of these imines. In addition, some of these procedures require the use of dangerous and/or toxic reagents such as NaCN,[11,13a,b] HCN,[7] and *tert*-butyl hypochlorite[7] or *tert*-BuLi,[9] and, finally, none of these synthetic routes is general

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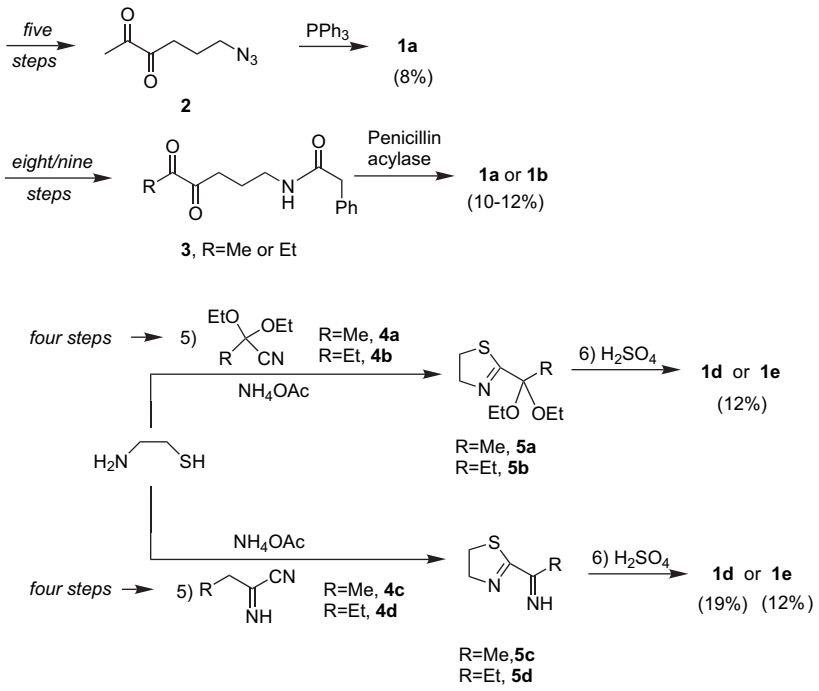
doi:10.1016/j.tet.2007.03.089



Scheme 1. Selected synthetic routes to **1a** and **b** and **1d** and **e**. In brackets are reported the overall yields.

for the preparation of all flavors **1a**–**e**. In the following we report a new and straightforward synthesis of the naturally occurring Maillard flavors **1a**–**e**. In addition we report the synthesis of the new flavor **1f** together with its olfactory description and odor threshold.

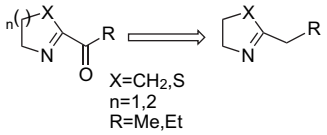
2. Results and discussion

The final acidic or alkaline work-up in the final stage adopted in most of the above cited procedures proved to be detrimental to the overall yield. Keeping this in mind, we designed a new synthetic strategy suited to the preparation of these compounds avoiding such a work-up in the final step. This strategy is based on the regioselective oxidation of cyclic imine precursors with SeO_2 (Scheme 2). To the knowledge of the authors, just one example of SeO_2 oxidation of imines has been reported in literature.[15] Moreover, no study on the regioselectivity has been done. The preparation of the cyclic imine precursors is outlined in Scheme 3. The 2-alkyl pyrrolines **6a** and **b**, and the 2-ethyl-3,4,5,6-tetrahydropyridine **6c** were obtained by addition of the *n*-alkyl Grignard reagent to the *N*-Boc-pyrrolidone[16] or to the *N*-Boc-piperidone in presence of TMEDA[17] (−78 °C in THF) to give the *N*-Boc-ketones that were treated with TFA in CH_2Cl_2 (2:8) to give the cyclic imines in good yields (Scheme 3).

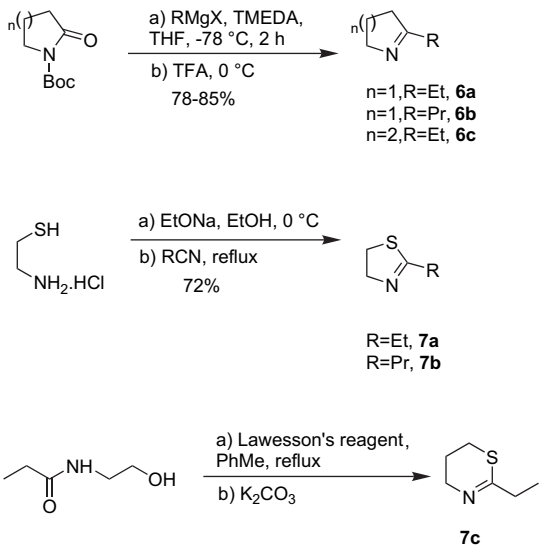
The 2-alkyl-thiazolines **7a** and **b** were obtained by condensation of the cysteamine with the propionitrile or the butyronitrile in presence of NH_4Ac in EtOH to give **7a** or **b** in 72% yield.[13a,18]

The 2-ethyl-5,6-dihydro-4*H*-1,3-thiazine **7c** was prepared in 75% yield by treatment of the *N*-(2-hydroxyethyl)-propionamide with the Lawesson's reagent followed by exposure to a solution of K_2CO_3 to give **7c**.[19a,b]

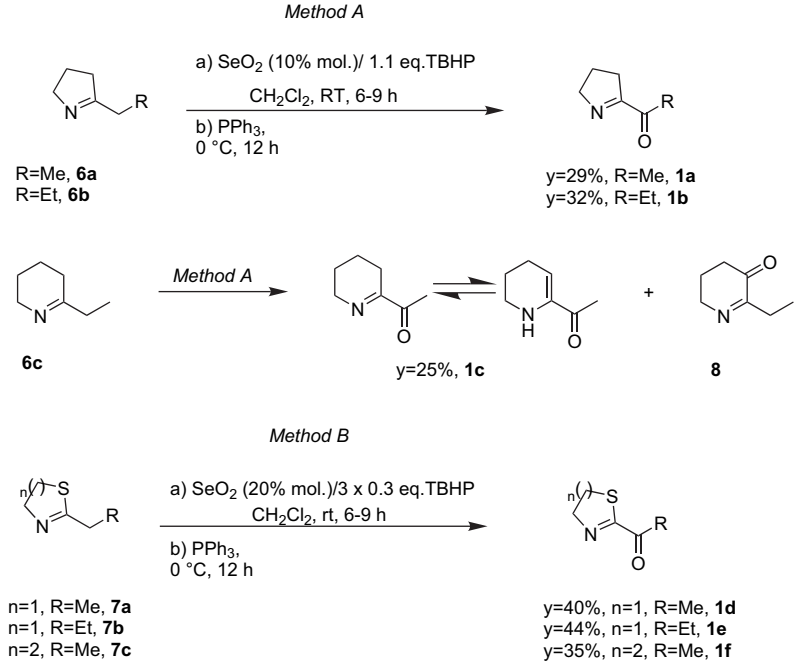
In the first instance, it was observed that when the pyrroline **6a**, was treated with 1 equiv of SeO_2 in Et_2O/EtOH (3:1) at room temperature, there was, within few hours, complete disappearance of the starting material with the formation of **1a** with 80% conversion was obtained (checked by GC–MS). The oxidation of **6a** also proved entirely regioselective (by GC–MS and ^1H NMR). However, the work-up of the reaction



Scheme 2.



Scheme 3.



Scheme 4.

mixture was troublesome; this was likely due to the presence of colloidal Se and to the intrinsic chemical instability of **1a**, which after few hours started to decompose. Thus, the yield of the pure material after column chromatography and bulb-to-bulb distillation was just of 4% with purity around 90%. Instead, the catalytic procedure (Method A) proved to be more efficient [20] (Scheme 4). The latter consisted in adding **6a** to a mixture of 1.1 equiv of TBHP and 0.1 equiv of SeO_2 in CH_2Cl_2. Indeed, using this procedure, even if the conversion of **6a** was lower than in the stoichiometric process (50%–60% by GC–MS and by ^1H NMR, on three different runs), the yield and the purity of **1a** increased substantially, since the work-up was much easier. The product **1a** was isolated by adding sufficient Ph_3P to the reaction mixture to reduce all the residual TBHP, then, the organic phase was stirred with charcoal to aid the elimination of residual colloidal Se, and, after SiO_2 chromatography and bulb-to-bulb vacuum distillation **1a** in 29% yield was obtained (98% purity). The oxidation of **6b** and **c**, following the same procedure, afforded **1b** and **c** in a similar yields (32% and 25%). It's noteworthy that the oxidation of **6c** proved to be non regioselective, thus, together with the formation of **1c**, in equilibrium with its tautomer, was also isolated the regioisomer **8** (in the ratio of 1:1 by GC–MS).

The conversions, during the oxidations, were deliberately kept at around 50%, because longer exposure of the products to the reaction conditions is not beneficial to the final yields, moreover, the products are surprisingly less polar than the reagents, thus, the chromatographic separation easily allowed the recovery of non reacted starting materials.

The procedure adopted for the oxidation of the sulfur cyclic imines **7a**–**c** was slightly modified (Scheme 4, Method B). This consisted of adding the imine to a mixture of 0.3 mol equiv of TBHP and 0.2 equiv of SeO_2 in CH_2Cl_2. Every 3 h was added the remaining stoichiometric TBPH in 0.3 equiv portions. This was done to minimise the formation of the sulfoxide (detected by GC–MS). After the same work-up adopted for the oxidation of **1a**, was followed, **e** and **f**, respectively, were isolated in a 40%, 44%, and 35% yield.

Finally, the professional olfactory evaluation (Givaudan Perfumers) of a sample of **1f** gave the following odor description: bread, rice, moldy, musty, and pirazine-like with an odor threshold of 0.54 ng/L in air. In conclusion this new synthetic route allowed the preparation of these important flavors on multi gram scale and in improved overall yields (20%–30%). The oxidation of the pyrrolines **6a** and **b**, proceeds exclusively at the exocyclic position, such regioselectivity is apparently lost for the oxidation of six-atom member rings such as **6c**. Finally, this synthetic strategy compares favorably with respect to other reported procedures in terms of execution, costs, simplicity, flexibility, and overall yields.

3. Experimental part

3.1. General

GC–MS: HP 6890 gas chromatograph equipped with a 5973 mass-detector, using a HP-5MS column (30 m×0.25× 0.25 μm). The following temperature program was employed: 60 °C (1 min)/6 °C/min–12 °C/min/280 °C (5 min). ^1H and ^{13}C NMR are recorded on a Bruker AMX 400 (400 MHz) or AC 250 (250 MHz); $CDCl_3$ solns at room temperature, chemical shifts δ in parts per million relative to internal TMS, J values in hertz. TLC analyses: Merck Kieselgel 60 F254 plates. All the gravimetric chromatographic columns were carried out using silica. All solvents and reagents were purchased from Fluka and were used without any further purification.

3.1.1. Preparation of cyclic imines 6a–c.

3.1.1.1. Representative synthesis: 2-ethyl-1-pyrroline (6a). A freshly prepared solution of EtMgBr (Mg (5.8 g) in THF (50 mL) plus EtBr (21.2 g, 195.0 mmol) in THF (150 mL)) and TMEDA (30 mL) was added drop-wise to a mechanically stirred solution of *N*-Boc-pyrrolidinone (30.0 g, 162.0 mmol) in THF (300 mL) at −78 °C and under a N_2 atmosphere. After 12 h the reaction was quenched with a solution of 2 M HCl (300 mL) and washed with Et_2O (3×200 mL). The combined organic phases were washed with brine (2×200 mL) and a satd solution of $NaHCO_3$ (200 mL), dried over Na_2SO_4. Evaporation of the solvent under reduced pressure gave the *N*-Boc-4-oxo-hexilamine of sufficient purity for the next step. The latter was dissolved in a mixed solvent system of DCM/TFA (100 mL, 8:2) and cooled to 0 °C. After 24 h at room temperature, the reaction mixture was cooled at 0 °C and treated with sufficient NaOH (2 M) to reach pH=10–11. Then, the aqueous solution was washed with Et_2O (2×200 mL), the combined organic phases were then washed with 1 M HCl (3×200 mL). The combined aqueous solution was washed with Et_2O (100 mL), brought at pH=10–11 with 2 M NaOH and then washed with Et_2O (4×150 mL). The organic phases were washed with brine (2×100 mL), dried over Na_2SO_4, and the solvent was removed by distillation (40 cm Vigreux column). Then, the residual yellowish liquid was distilled (bp 124 °C) to give **6a** (12.0 g, 78%) as colorless liquid; [Found: C, 74.3; H, 11.5. $C_6H_{11}N$ requires C, 74.17; H, 11.41]; Chemical purity 99% by GC–MS (t_R 4.62); *m/z*: 97 (5, $[M]^+$), 83 (100%). The ^1H and ^{13}C data fit well with those reported.[21]

3.1.1.2. 2-Propyl-1-pyrroline (6b). The compound **6b** (15.2 g, 85%) was obtained following the same procedure described above; [Found: C, 75.5; H, 11.9. $C_7H_{13}N$ requires C, 75.62; H, 11.79]; Chemical purity 99% by GC–MS (t_R 6.11); bp 70–80 °C at 100 mmHg; δ_H (400 MHz, $CDCl_3$) 3.78 (2H, tt, *J*=7.3, 1.6 Hz, H-C(5)), 2.43 (2H, br t, *J*=8.0, H-C(3)), 2.29 (2H, br t, *J*=7.7, 2.3 Hz, =CCH_2CH$_2$), 1.83 (2H, m, H–C(4)), 1.60 (2H, m, CH_2CH$_3$), 0.93 (3H, t, *J*=7.4 Hz, CH_3); δ_C (100.6 MHz, $CDCl_3$) 178.2, 60.6, 36.8, 35.7, 22.4, 19.6, 10.5; *m/z*: 111 (95, $[M]^+$), 83(5), 60 (100%).

3.1.1.3. 2-Ethyl-3,4,5,6-tetrahydropyridine (6c). The compound **6c** (14.7 g, 82%) was obtained following the same procedure described above; [Found: C, 75.7; H, 11.9. $C_7H_{13}N$ requires C, 75.62; H, 11.79]; Chemical purity 99% by GC–MS (t_R 6.75); bp 85–90 °C at 100 mmHg; the ^1H and ^{13}C fit well with those reported.[22]

3.1.2. Preparation of sulfur cyclic imines 7a–c.

3.1.2.1. Representative synthesis: 2-ethyl-2-thiazoline (7a). To an ice cooled solution of EtONa (from 10.1 g of Na) in EtOH (200 mL) was added portion wise the cysteamine hydrochloride (50 g, 0.44 mol). Then, to the reaction mixture was added the propionitrile (115.3 mL, 1.32 mol) and NH_4OAc (20 g). After 12 h at reflux the reaction mixture was concentrated, the residue was diluted with Et_2O (400 mL) and washed with brine (2×100 mL), and dried over Na_2SO_4. The solvent was removed under reduced pressure to give **7a** (36.1 g, 72%) as liquid of sufficient purity for the next step; [Found: C, 52.3; H, 7.9. C_5H_9NS requires C, 52.13; H, 7.87]; Chemical purity 98% by GC–MS (t_R 6.11); δ_H (250 MHz, $CDCl_3$) 4.21 (2H, tt, *J*=7.3, 1.6 Hz, H–C(4)), 3.28 (2H, t, *J*=8.0 Hz, H–C(5)), 2.51 (2H, qt, *J*=7.7, 1.6 Hz, CH_2CH$_3$), 1.22 (3H, t, *J*=7.4 Hz, CH_3); δ_C (62.5 MHz, $CDCl_3$) 171.9, 64.4, 36.3, 31.8, 15.8; *m/z*: 115 (95, $[M]^+$), 69 (5), 60 (100%).

3.1.2.2. 2-Propyl-2-thiazoline (7b). The compound **7b** (41 g, 72%) was obtained following the same procedure described above; [Found: C, 55.5; H, 8.8. C_5H_9NS requires C, 55.77; H, 8.58]; Chemical purity 97% by GC–MS (t_R 8.02); δ_H (250 MHz, $CDCl_3$) 4.19 (2H, br t, *J*=7.5 Hz, H–C(4)), 3.25 (2H, t, *J*=8.0 Hz, H–C(5)), 2.47 (2H, br t, *J*=7.7 Hz, =CCH_2CH$_2$), 1.66 (2H, m, CH_2CH$_3$), 0.94 (3H, t, *J*=7.4 Hz, CH_3); δ_C (62.5 MHz, $CDCl_3$) 172.2, 64.4, 36.3, 33.8, 21.1, 13.8; *m/z*: 129 (10, $[M]^+$), 114 (5), 101 (80), 60 (100%).

3.1.2.3. 2-Ethyl-5,6-dihydro-4*H*-1,3-thiazine (7c). A solution of *N*-(2-hydroxyethyl)-propionamide (11.7 g, 100 mmol) and Lawesson's reagent (40.4 g, 100 mmol) in toluene (400 mL) was heated at reflux for 1 h under a nitrogen atmosphere. The reaction mixture was concentrated, stirred with a solution of 2 M K_2CO_3 (200 mL) for 1 h, and extracted with Et_2O (5×200 mL). The organic phase was washed with a solution of 1 M HCl (3×100 mL) and the aqueous solution treated with a solution of 1 M NaOH until pH=7, then, was washed with Et_2O (5×200 mL). The organic phase was dried over Na_2SO_4 and concentrated under reduced pressure. The crude was distilled to give **7c** (9.7 g, 75%) as pale yellow liquid; [Found: C, 55.6; H, 8.7. C_5H_9NS requires C, 55.77; H, 8.58]; Chemical purity 99% by GC–MS (t_R 9.01); δ_H (250 MHz, $CDCl_3$) 3.66 (2H, br t, *J*=7.5 Hz, H–C(4)), 3.00 (2H, t, *J*=8.0 Hz, H–C(6)), 2.32 (2H, q, *J*=7.7 Hz, =CCH_2CH$_3$), 1.79 (2H, m, H–C(5)), 1.17 (3H, t, *J*=7.4 Hz, CH_3); δ_C (62.5 MHz, $CDCl_3$) 162.2, 47.3, 35.1, 26.3, 19.2, 11.8; *m/z*: 129 (10, $[M]^+$), 129 (100), 101 (10), 94 (5), 82 (31%).

3.1.3. Method A: oxidation of 6a–c.

3.1.3.1. Representative synthesis: 2-acetyl-1-pyrroline (1a). To a mixture of SeO_2 (1.5 g, 13.5 mmol) in CH_2Cl_2 (50 mL) was added a solution of 2 M TBHP in CH_2Cl_2 (68 mL). After 30 min a solution of **6a** (13.1 g, 135.1 mol) in CH_2Cl_2 (30 mL) was added dropwise. After 9 h sufficient PPh_3 was added portion wise to the ice cooled reaction mixture, which was kept in the fridge overnight.[23] After that time, the reaction mixture was stirred with charcoal (3 g) and dried over Na_2SO_4. Evaporation of the solvent under reduced pressure (in a cold bath) afforded crude material that was triturated with a cold mixture of 1:1 hexane/Et_2O (50 mL), the solid was then filtered off and the solvent was removed under reduce pressure (in a cold bath), affording a yellow liquid, which was submitted to the column chromatographic purification (hexane/Et_2O, 6:4) to obtain a pale yellow liquid, which after bulb-to-bulb distillation (60 °C, 100 mmHg,) gave **1a** (4.3 g, 29%) as slightly yellow liquid; [Found: C, 64.7; H, 8.2. C_6H_9NO requires C, 64.84; H, 8.16]; R_f (hexane/Et_2O, 6:4) 0.47; Chemical purity 98% by GC–MS (t_R 5.90); *m/z*: 111 (30, $[M]^+$), 97 (100), 69 (80%). The ^1H and ^{13}C data fit well with those reported.[11]

3.1.3.2. 2-Propionyl-1-pyrroline (1b). The compound **1b** (5.4 g, 32%) was obtained following the same procedure

described above; [Found: C, 67.3; H, 8.9. $C_7H_{11}NO$ requires C, 67.17; H, 8.86]; R_f (hexane/Et_2O, 6:4) 0.56; Chemicalpurity 99% by GC–MS (t_R 7.26); bp 115 °C (70 mmHg); δ_H (400 MHz, $CDCl_3$) 4.10 (2H, tt, J=7.5, 2.4 Hz, H–C(5)), 2.92 (2H, q, J=7.3 Hz, CH_2CH$_3$), 2.73 (2H, tt, J=8.4, 2.3 Hz, H–C(3)), 1.93 (2H, m, H–C(4)), 1.12 (3H, t, J=7.4 Hz, CH_3); δ_C (100.6 MHz, $CDCl_3$) 203.4, 177.0, 65.5, 36.4, 36.3, 24.9, 10.5; *m/z*: 125 (30, $[M]^+$), 97 (100), 69 (80%).

3.1.3.3. 2-Acetyl-3,4,5,6-tetrahydropyridine (1c). The compound **1c** (4.2 g, 25%) was obtained following the same procedure described above; [Found: C, 67.2; H, 8.8. $C_7H_{11}NO$ requires C, 67.17; H, 8.86]; R_f (hexane/Et_2O, 6:4) 0.53; Chemical purity 99% by GC–MS (t_R 7.63); bp 90–100 °C (60–70 mmHg); *m/z*: 125 (30, $[M]^+$), 97 (100%). The ^1H and ^{13}C data fit well with those reported.[9]

3.1.3.4. 2-Ethyl-5,6-dihydropyridine-3(4*H*)-one (8). Chemical purity 93% by GC–MS (t_R 7.46); R_f (hexane/Et_2O, 6:4) 0.59; δ_H (400 MHz, $CDCl_3$) 4.11 (2H, tt, J=6.9, 2.3 Hz, H–C(6)), 2.95 (2H, q, J=7.3 Hz, CH_2CH$_3$), 2.74 (2H, tt, J=6.9, 2.3 Hz, H–C(4)), 1.94 (m, 2H, H–C(5)), 1.12 (t, J=7.4 Hz, 3H, CH_3); δ_C (100.6 MHz, $CDCl_3$) 201.1, 174.8, 63.2, 34.1, 32.2, 22.6, 8.2; *m/z*: 125 (30, $[M]^+$), 97 (100%).

3.1.4. Method B: oxidation of 7a–c.

3.1.4.1. Representative synthesis: 2-acetyl-2-thiazoline (1d). To a mixture of SeO_2 (2.6 g, 23.3 mmol) in CH_2Cl_2 (50 mL) was added a solution of TBHP in CH_2Cl_2 (17 mL, 2 M). After 30 min a solution of **7a** (13.3 g, 116.3 mol) in CH_2Cl_2 (30 mL) was added drop wise. After 3 h and 6 h was added drop wise a 2 M solution of TBHP in CH_2Cl_2 (17 mL). After 3 h, sufficient PPh_3 was added portion wise to the ice cooled reaction mixture, which was then kept in the fridge overnight. After that time, the reaction mixture was stirred with charcoal (5 g) and dried over Na_2SO_4. Evaporation of the solvent under reduced pressure in a cold bath afforded a crude solid that was triturated with a cold mixture of 4:1 hexane/Et_2O (50 mL), the solid was filtered off and the solvent was removed under reduce pressure to afford a yellow liquid, which was submitted to the column chromatographic purification (hexane/Et_2O, 8:2) to afford a pale yellow liquid, which after bulb-to-bulb distillation (50 °C, 2 mmHg) gave **5** (6.0 g, 40%); [Found: C, 46.7; H, 5.7. C_5H_7NOS requires C, 46.49; H, 5.46]; R_f (hexane/Et_2O, 6:4) 0.45; Chemical purity 99% by GC–MS (t_R 9.21); δ_H (400 MHz, $CDCl_3$) 4.52 (2H, t, J=8.7 Hz, H–C(4)), 3.33 (2H, t, J=8.7 Hz, H–C(5)), 2.52 (3H, s, CH_3); δ_C (100.6 MHz, $CDCl_3$) 194.2, 171.6, 66.7, 33.4, 26.8; *m/z*: 129 (100, $[M]^+$), 101 (50), 87 (10), 60 (70%). These ^1H NMR data fit well with those reported.[13a]

3.1.4.2. 2-Propionyl-2-thiazoline (1e). The compound **1e** (7.3 g, 44%) was obtained following the same procedure described above; [Found: C, 50.4; H, 6.4. C_6H_9NOS requires C, 50.32; H, 6.33]; R_f (hexane/Et_2O, 6:4) 0.48; Chemicalpurity 99% by GC–MS (t_R 11.63); bp 80–90 °C at 2 mmHg; δ_H (400 MHz, $CDCl_3$) 4.50 (2H, t, J=8.7 Hz, H–C(4)), 3.31 (2H, t, J=8.7 Hz, H–C(5)), 2.92 (2H, q, J=7.3 Hz, CH_2CH$_3$), 1.14 (3H, t, J=7.3 Hz, CH_3); δ_C (100.6 MHz, $CDCl_3$) 196.5, 170.6, 66.2, 23.7, 23.3, 7.7; *m/z*: 143 (50, $[M]^+$), 115 (50), 87 (30), 60 (25), 57 (100%). These ^1H NMR data fit well with those reported.[13a]

3.1.4.3. 2-Acetyl-5,6-dihydro-4*H*-1,3-thiazine (1f). The compound **1f** (4.1 g, 25%) was obtained following the same procedure described above; [Found: C, 50.3; H, 6.4. C_6H_9NOS requires C, 50.32; H, 6.33]; R_f (hexane/Et_2O, 6:4) 0.49; Chemical purity 99% by GC–MS (t_R 13.34); bp 90–100 °C at 2 mmHg; δ_H (400 MHz, $CDCl_3$) 3.89 (2H, t, J=8.5 Hz, H–C(4)), 3.01 (2H, t, J=8.6 Hz, H–C(6)), 2.37 (3H, s, CH_3), 1.82 (2H, m, H–C(6)); δ_C (100.6 MHz, $CDCl_3$) 196.7, 159.5, 48.1, 25.0, 24.2, 18.7; *m/z*: 143 (50, $[M]^+$), 115 (50), 101 (30), 73 (40), 43 (75%).

Acknowledgements

The authors are indebted to Dr. Philip Kraft (Givaudan Schweiz AG, Fragrance research, Switzerland) for the odor descriptions. Cofin-Murst is acknowledged for financial support.

References and notes

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