New Pyridine Derivatives from Essential Oils

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Abstract. Four new pyridines 1-4 have been isolated from jonquil absolute and their structures confirmed by synthesis. These pyridines also occur in other essential oils.

Introduction

For many decades, the Geneva-based perfume and flavour company Firmenich has invested considerable research effort into the chemical analysis of essential oils and other perfume and flavour materials of natural origin. The discovery of many organoleptically interesting compounds, today important chemicals widely used by the flavour and perfume industry, can be traced back to the analysis of natural products. Well-known examples are Hedione®, Furaneol®, Damascenone and the Damascenones.

Continuing this tradition, we have analyzed the basic fractions extracted from several commercial essential oils and absolutes: jonquil abs. (Narcissus jonquilla L.), narcissus abs. (Narcissus poeticus L.), cardamom oil (Elettaria cardamomum MATON), petitgrain oil (Citrus aurantium, sp. amara ENGL.), and patchouli oil (Pogostemon patchouli PELLETT.). We were intrigued by the fact that analysis by GC/MS of the aforementioned basic fractions revealed the presence of the same unknown compound in each of the five samples. The mass spectrum (Fig. 1) indicated a molecular weight of 133.

Two samples (jonquil and patchouli) contained a second unknown of longer retention time whose mass spectrum (Fig. 2) suggested a molecular weight of 175. This second compound was probably a higher homologue of the first, although no intermediate members of the series were detected.

Results and Discussion

Both compounds, 1 and 3, were most abundant in the basic fraction of jonquil abs. and were, therefore, isolated from this source by prep. GC.

The 1H-NMR spectrum of the first compound confirmed the empirical formula C₉H₁₅N (11 H-atoms) and suggested the structure 1: the 3-substituted pyidine ring was indicated by four signals (1 H each) at 7.25, 7.57, 8.44, and 8.53 ppm, whereas the remaining signals were in good agreement with a (Z)-but-1-enyl side chain (coupling between the olefinic protons 11.5 Hz).

The structure was confirmed by synthesis (Scheme 1). The Wittig reaction of 3-pyridinecarbaldehyde (5) with tri...
phenyl(propyldene)phosphorane gave a mixture of the (Z)- and the (E)-isomer, 1 and 2, resp. (ratio 8:2), which were isolated pure by GC (silicone, 140°C). The synthetic (Z)-isomer was identical (GC, 1H-NMR, MS) to the natural compound 1; traces of the (E)-isomer 2 were detected (GC, MS) in the basic fraction of jonquil abs. and patchouli oil. The concentrations of these pyridines in jonquil abs. can be estimated at 10 ppm for 1 and 1 ppm for 2.

The 1H-NMR spectrum of the second unknown confirmed the empirical formula C12H17N(17 protons) and suggested the presence of a 3,4-disubstituted pyridine with a (Z)-but-1-enyl and a Pr side chain. It seemed reasonable, in analogy to compound 1, to leave the C5-substituent at C(3) and to place the Pr group at C(4). Structure 3 for the second unknown was confirmed by synthesis (Scheme 2).

The Grignard reaction of PrMgBr with the known nitrile 6 [1] in toluene gave, after acidic hydrolysis of the imine intermediate, the ketone 7 in 77% yield. Reduction of 7, followed by acetylation, led to the acetate 9 which upon thermolysis at 60-80°C gave a 1:1 mixture (72% from 9) of the (Z)- and (E)-isomers 3 and 4, resp. The pure isomers were isolated by GC. The (Z)-isomer 3 was identical (GC, 1H-NMR, MS) with the unknown isolated from jonquil abs. (concentration ca. 20 ppm) and was also identified in trace amounts in the basic fraction of patchouli oil. The (E)-isomer 4 was also present in jonquil (GC, MS) at a level of ca. 10 ppm.

To our surprise, none of the four pyridines 1–4 had a GC-material collected in the cooling trap at ~180°C. The 1H-NMR spectra were obtained in CDCl3 at r.t., and the aq. phase was washed with Et2O. The alkaline soln. was continuously extracted with Et2O for 30 h, and the red soln. was filtered. The aq. phase was basified with NaOH, saturated with NaCl and extracted with Et2O. Evaporation of the Et2O soln. gave a crude product which, after distillation (90-94°C/1 Torr) through a Vigreux column, gave 10% (71%) of a mixture 1/2 (8:2). Distillation through a Fischer Spaltrohr column allowed partial separation of the isomers, which were isolated pure by GC (silicone, 140°C). Both, the lower-boiling 1 and the higher-boiling 2 were identical (MS, GC, NMR) to the natural compounds.

Practically 1 was obtained in 92% yield, when the Wittig reaction was carried out under "salt-free" conditions, cf. [4].

Data of 1. Colourless oil. IR (film): 1635w, 1575w, 1555w, 1510s, 1410s, 1285s, 1095s, 1035w, 900w, 835w, 755w, 695w. MS: f. t. 1H-NMR (360 MHz, CDCl3): 1.08 (t, J = 7.5, H-C(2'); 3.20 (m, H-C(5')); 5.80 (dd, J = 7.5, 11.5, H-C(2)); 6.34 (br. d, J = 11.5, H-C(1)'); 7.25 (dd, J = 8, 9, H-C(3)); 7.57 (dd, J = 2, 8, H-C(4)); 8.44 (dd, J = 6, 2, H-C(6)); 8.53 (dd, J = 2, H-C(2)); 9.00 (s, 1H, H-C(1)).

Data of 2. Colourless oil. IR (film): 1640m, 1575w, 1560s, 1405s, 1115s, 955s, 835m, 785m, 695s. MS: identical with (Z)-isomer. 1H-NMR (360 MHz, CDCl3): 1.11 (t, J = 7.5, CH3); 2.26 (m, CH2); 6.35 (m, H-C(1)'); H-C(2)'; 7.21 (dd, J = 8, 5, H-C(3)); 7.55 (dd, J = 2, 8, H-C(4)); 8.42 (dd, J = 6, 2, H-C(6)); 8.55 (dd, J = 2, H-C(2)).

Isolation From Jonquil Absolute. Distillation of commercial jonquil abs. (500 g, Chauvet, Grass) in a short-path distillation apparatus (Leybold) gave a distillate (365 g, 73%), including the

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**Scheme 1**

![Scheme 1](image)

**Scheme 2**

![Scheme 2](image)

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Acetoxymaleic Anhydride as Ketene Equivalent in the Diels-Alder Reaction

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Abstract. Acetoxymaleic anhydride (AMA, 1) [2] as ketene equivalent in the Diels-Alder reaction (Scheme 1).

Six-membered ring compounds cannot be obtained from simple ketenes and 1,3-dienes via a [4+2] cycloaddition reaction, since ketenes undergo exclusively [2+2] cycloaddition leading to four-membered ring structures instead. Therefore, synthons which are equivalent to ketenes but react in a [4+2] mode with 1,3-dienes are most useful building blocks [1].

In this publication, we describe the use of acetoxymaleic anhydride (AMA, 1) [2] as ketene equivalent in the Diels-Alder reaction (Scheme 1).

The known reaction of AMA (1) with cyclopentadiene 2 gave the adduct 3 (82%) [3]. It was assumed that acetoxyglutaric anhydride 3 or its dihydro derivative 4 would undergo hydrolytic decarboxylation in analogy to the behavior of α-oxyacids, which lose CO upon acid treatment forming carbonyl compounds [4] (Scheme 2). When the saturated acetoxyglutaric anhydride 4 [5] was treated with 96% H₂SO₄ between 5 and 20°C, a 42:58 mixture (57%) of 5a and 5b, was obtained (Scheme 1). Acid-catalyzed decarboxylation of the

![Scheme 1](image-url)

Reagents: a) 24 h/25°C, benzene; b) H₂/Pd-C; c) 96% H₂SO₄/55°C -> 25°C; d) AcOH, 2 h reflux.

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