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Synthesis of 12-Methoxyabietic Acid Methylester, a Feeding Deterrent of the Larch Sawfly *Pristiphora erichsonii* (Hartig)

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The diastereomeric methylesters of 12-methoxyabietic acid, an antifeedant for the larch sawfly *Pristiphora erichsonii* (Hartig) have been synthesised from abietic acid methylester (**2**). The unknown configuration at C-12 of the natural product has been determined by comparing the spectral and analytical data of the synthesised compounds with data given in the literature for the natural product as being (*S*).

Synthese von 12-Methoxyabietinsäuremethylester

12-Methoxyabietinsäuremethylester spielt eine Rolle als Repellent beim Freßverhalten der Larven von *Pristiphora erichsonii* (Hartig). Es wird die erstmalige Synthese (ausgehend) von Abietinsäuremethylester (**2**, in zwei Stufen) beschrieben. Beide Diastereomere wurden erhalten. Aufgrund von Vergleichen der spektroskopischen und analytischen Daten der Produkte mit den Literaturdaten des Naturproduktes konnte die Konfiguration an C-12 für den Naturstoff mit (*S*) festgelegt werden.

[Keywords: 12-Methoxyabieticacidmethylester, η^4*-{[1R-(1α,4aβ,4bα,10aα)]-1,2,3,4,4a,4b,5,9,10,10a-Decahydro-1,4a-dimethyl-7-(-1-methylethyl)-1-phenanthrencarboxylic acid methylester}-tricarbonyliron,* ^{1}H-, ^{13}C-, *2D-NMR]*

Introduction

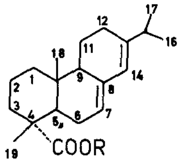
The feeding of defoliating insects is sometimes strongly affected by chemical substances occurring in the leaves, thus giving rise to chemically associated defenses by the plants. A very interesting example of differential feeding behavior has recently been investigated [1]. The larvae of the larch sawfly *Pristiphora erichsonii* (Hartig) are refusing single needles of the new shoot of tamarack [*Larix laricina* (Du Roi) K. Koch] in favour of tufted needles from short shoots on older wood. Three biological active compounds have been isolated from the single needles: One of them was, after esterification, tentatively identified as 12-methoxyabietic acid methylester. The quantity of the isolated material was, however, too small to obtain information on the configuration at C-12. We have synthesized both diastereomers of 12-methoxyabietic acid methylester (**4**, **5**) and determined the configuration of C-12.

Results and Discussion

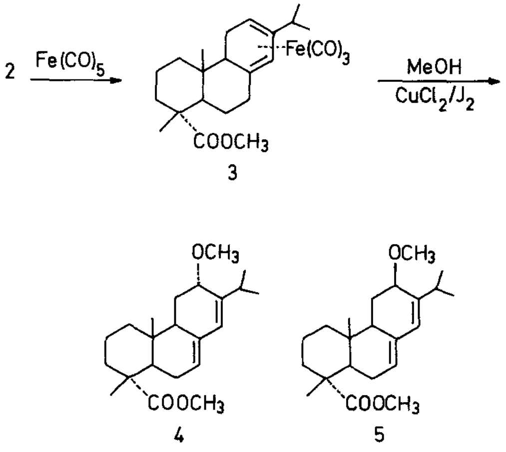
Synthesis of 12-Methoxyabietic Acid Methylester (**4**, **5**)

Unfortunately the most abundant resin acid, abietic acid (**1**) is not a good starting material, because the direct introduction of an oxygen function in position 12 of **1** is not possible. A product obtained by SeO_2 oxidation of **1** was later demonstrated to be 9-hydroxyabietic acid [2], not 12-hydroxyabietic acid as originally proposed [3]. 12-Hydroxyabietic acid has been prepared so far only from levopimaric acid by reaction with hypochlorous acid [4]. It has been also obtained during a study of the oxidation of levopimaric acid with $KMnO_4$ [5].

In the course of our investigation on double bond isomerisation in tricyclic diterpenes we had prepared the levopimaric acid methylester iron carbonyl complex (**3**) by reaction of **2** with $Fe(CO)_5$. **3** is a stable crystalline



1 R = H
2 R = CH_3



material, from which by decomplexation under various conditions [6] levopimaric acid may be obtained. We found, however, that direct addition of methanol *in situ*, during the decomplexation is possible and leads directly to the desired products **4** and **5**. They were obtained in good yields, and could be separated and isolated in crystalline from.

Determination of the Configuration at C-12 in 4 *and* 5 *by NMR-measurements*

The ^{1}H-NMR-signal of H-12 is easily recognized in **4** and **5** and the splitting pattern in both cases is slightly different. But since the cyclohexene ring system with an additional exocyclic double bond is very strained, different conformational equilibria may exist in **4** and **5**. Therefore it is not possible to determine the relative configuration at C-12 from the coupling constants of H-12. To get the desired information we had

Table 1. *^{1}H- and ^{13}C-resonances in ppm for* **4** *and* **5** *in C_6D_6 obtained from COSY and ^{1}H-^{13}C-shift correlation experiments.* The assignment for carbons 16 and 17 may be interchanged

	4			**5**		
	^{1}H		^{13}C	^{1}H		^{13}C
Pos.	ax	eq		ax	eq	
1	0.9–1.0	1.6–1.7	38.1	0.8–0.9	1.5–1.6	38.3
2	1.3–1.5		18.4	1.3–1.4		18.3
3	1.5–1.6	1.8–1.9	37.1	1.5–1.6	1.7–1.8	37.6
4	—		46.7	—		46.6
5	2.2–2.3	—	45.4	2.1–2.2		44.8
6	1.8–1.9	2.0–2.1	26.2	2.0–2.1		26.0
7	5.4–5.5		123.6	5.4		122.1
8	—		135.4	—		135.3
9	2.4–2.5		44.3	1.7–1.8		48.5
10	—		34.2	—		34.8
11	0.9–1.1	1.8–1.9	25.2	1.2–1.3	2.0–2.1	27.8
12	3.6–3.7		75.7	3.8–3.9		78.4
13	—		142.9	—		146.9
14	5.8–5.9		126.4	5.9		124.1
15	2.3–2.5		33.3	2.9–3.0		28.6
16	1.1		21.9	1.1		20.9
17	1.1		22.5	1.1		22.9
18	0.7		14.6	0.7		14.2
19	1.3		17.3	1.3		17.3
20	—		178.1	—		178.3
21	3.3		51.5	3.3		51.5
22	3.2		56.1	3.1		56.0

to assign all resonances in the ^{1}H- and ^{13}C-spectra of compound **4** and **5**. It was necessary for this purpose to run COSY and ^{1}H-^{13}C-shift correlation experiments [7, 8]. These lead to the assignment of all proton and carbon resonances (Table 1). Having isolated the resonance of H-9 from the overlapping lines, it was easy to analyse an NOE-experiment performed by saturating the resonance of H-12 in **4** and **5**. Only the latter gave a positive NOE at H-9 and at the same time a negative NOE at H-5. This proves that these three protons are at the same side of the ring system and occupy a linear arragment [9]. From these results we conclude that the configuration of C-12 in **4** is (*S*) and in **5** (*R*), resp.

Conclusion

The R_f-value of **4** in hexane-ethylacetete (10:1) is 0.41 which corresponds with the R_f-value given in the literature. The R_f of **5** in the same solvent is 0.52. The ^{1}H-NMR spectra of **4** and **5** in $CDCl_3$ are significantly different, but only the spectrum of **4** corresponds exactly to the published NMR data [1]. We therefore propose that the biological active compound isolated from the single needles of the new shoot of *Larix laricina* (Du Roi) K. Koch has the structure **4**. Whether **5** is also biological active remains to be determined.

Acknowledgments

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Experimental Part

Melting points were obtained on a Reichert Thermovar apparatus and are uncorrected. The NMR spectra were run on a Bruker AC 300 spectrometer in C_6D_6 or $CDCl_3$ as stated (δ was determined relative to the solvent resonance). 2D-NMR experiments were performed using Bruker standard software. Sample concentration was usually 200 m*M*/l.

IR spectra were obtained on a Pye Unicam SP3 spectrometer (Philips) in solution (CCl_4) and mass spectra on a Varian-MAT-312-Spectrometer. Elemental analysis were performed by Dr. *G. Zak* at the Microanalytical Laboratory of the Department of Physical Chemistry of the University of Vienna.

TLC was performed with "Kieselgel-Fertigplatten" from Machery-Nagel. The starting material was a resin acid fraction obtained by destillation of talloil available from Krems Chemie Ges.m.b.H. (Krems, Austria), containing 40% abietic acid.

{η^4-[1R-(1α,4aβ,4bα,10aα)]-1,2,3,4,4a,4b,5,9,10,10a-Decahydro-1,4a-dimethyl-7-(1-methylethl)-1-phenantrenecarboxylic Acid Methylester}-Tricarbonyliron (**3**)

33.5 g (0.1 mol) **2** were dissolved in 700 ml dry, peroxide-free dibutylether in an argon atmosphere. This mixture was refluxed under argon and 100 g (0.51 mol) $Fe(CO)_3$ was added dropwise during 12 h. This mixture was heated until no further CO evolution took place (usually 2 or 3 days).

Yield 28 g (60%) pale yellow crystals; R_f, 0.70 (petrolether-ethyl acetate = 14: 1); m.p. 135–137 °C; IR 2033, 1960, 1715, 1634, 1470 cm^{-1}; ^{1}H NMR (C_6D_6) δ 0.3 (s, 3 H), 0.6–0.8 (m, 1 H), 0.9–1.3 (m), 1.4–1.5 (m, 1 H), 1.02 (d, 3 H), 1.05 (d, 3 H), 1.2 (s, 3 H), 1.5–1.6 (m, 1 H), 1.6–2.1 (m), 2.5 (m, 1 H), 3.35 (s, 3 H), 4.75 (s, 1 H); ^{13}C NMR (C_6D_6) δ (multiplicity) 14.0 (q), 16.9 (q), 18.2 (t), 19.7 (q), 25.1 (q), 27.4 (t), 27.7 (t), 33.4 (d), 37.0 (s), 38.4 (t), 39.1 (t), 39.9 (s), 47.3 (s), 49.6 (q), 51.5 (d), 55.9 (d), 60.2 (d), 78.8 (s), 84.5 (d), 108.0 (s), 178.1 (s), 213.3 (s); mass spectrum, m/z (relative intensity) 428 (18), 399 (16), 398 (52), 370 (28), 368 (100), 308 (30). Anal. calcd for $C_{24}H_{32}O_5Fe$: C 63.16, H 7.07; found: C 63.21, H 7.02.

[1R-(1α,4aβ,4bα,6α,10aα)]-1,2,3,4,4a,4b,5,6,10,10a-Decahydro-1,4a-dimethyl-6-methoxy-7-(1-methylethyl)-phenanthrenecarboxylic Acid Methylester (**4**)

and

[1R-(1α,4aβ,4bα,6β,10aα)]-1,2,3,4,4a,4b,5,6,10,10a-Decahydro-1,4a-dimethyl-6-methoxy-7-(1-methylethyl)-phenanthrenecarboxylic Acid Methylester (**5**)

1.3 g (2.8 mmol) **3** were dissolved in 10 ml dry methanol and 60 ml dry diethylether. 1.9 g (14 mmol) dry $CuCl_2$ and 2.2 g (8.5 mmol) I_2 were added at once. This mixture was stirred for 2 h at RT and then filtered through silica (30 g). The silica was washed with 30 ml ether. The combined filtrates were extracted two times with 2 *N* aqueous solution of $Na_2S_2O_3$ and then dried over Na_2SO_4. After evaporation of the solvent a pale yellow oil was obtained which was purified by column chromatography on silica (petrolether-ethyl acetate = 14: 1).

Yield: 14 mg (1.5%) levopimaric acid methylester, 682 mg (69%) **4**, and 30 mg (3%) **5**.

4: R_f 0.68 (petrolether-ethyl acetate = 5: 1), 0.38 (petrolether-ethyl acetate = 14: 1), 0.41 (hexane-ethyl acetate = 10: 1); m.p. 110.5–112 °C; IR 2940, 2920, 2860, 1730, 1460, 1250, 1085, 1110 cm^{-1}; UV (acetonitril) λ_{max} 234 nm (ε = 12100), 241 nm (ε = 13700), 250 nm (ε = 9700); mass spectrum, m/z (relative intensity) 346 (8), 303 (100), 121 (66), 146 (46), 109 (14), 131 (14), 43 (18). Anal. calcd. for $C_{22}H_{34}O_3$: C 76.26, H, 9.89; found: C 76.17, H 9.95.

5: R_f 0.76 (petrolether-ethyl acetate = 5: 1), 0.52 (petrolether-ethyl acetate = 14: 1), 0.52 (hexane-ethyl acetate = 10: 1); m.p. 101–103 °C; IR 2920, 2945, 2860, 1745, 1100 cm^{-1}; mass spectrum, m/z (relative intensity) 346 (32), 304 (88), 303 (100), 121 (56). Anal. calcd. for $C_{22}H_{34}O_3$: C 76.26, H 9.89; found: C 76.14, H 9.64.

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