

$\beta$  are as expected from the known composition of the equilibrium mixture.

$C_1$  is the only carbon atom in the molecule which is linked to two oxygen atoms. The proton at  $C_1$ ,  $H_1$ , is therefore shifted away from the band where the rest of the carbon-linked protons contribute. The  $\beta$ -doublet is shifted to 0.58 ppm at high field relative to the  $\alpha$ -doublet. It is generally accepted that an axial proton will absorb at about 0.50 ppm higher field than its equatorial counterpart<sup>9</sup>. Hence, the bond  $C_1-H_1$  is axial in  $\beta$ -glucose and equatorial in  $\alpha$ -glucose, in accordance with the assignment.

The signal from  $H_1$  is split to a doublet due to the spin-spin coupling with the proton at  $C_2$ . The  $\beta$ -doublet separation is measured to 7c/sec and the  $\alpha$ -doublet splitting to 3c/sec. It is well known that the proton arrangement *aa* gives a larger splitting than *ea* (about 8c/sec for *aa* and 3c/sec for *ea*)<sup>9</sup>. Thus the magnitude of splitting also shows that the current assignment is correct.

The spectra of the unsubstituted anomers discussed in the present paper are in good agreement with results obtained for the pentaacetates dissolved in chloroform<sup>10</sup>.

In conclusion, the structures of the anomers of glucose have been established beyond doubt in the solid state and in aqueous solution by direct physical methods. The structures of a number of other sugars have also been determined by these methods. Attempts, therefore, to explain the properties of sugars should take the results of these investigations into account.

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Received February 26, 1963.

## Constituents of the Umbelliferous Plants

### I. Constituents of the Root of *Angelica archangelica* L.

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The original aim of the present work was to investigate the distribution of lignans in the plant family Umbelliferae. The investigation was prompted by the isolation of desoxypodophyllotoxin from *Anthriscus silvestris* L.<sup>1</sup> and from *Cicuta maculata* L.<sup>2</sup>.

So far we have only been able to detect desoxypodophyllotoxin in Danish material of *Anthriscus* while the other Umbelliferae investigated do not seem to contain lignans.

The analytical method was the paper-chromatographic procedure previously described by one of us<sup>3</sup>.

During the work we have isolated 15 different substances which are not lignans and we found it worth-while to focus our interest on these constituents.

In the present paper preliminary results from the work on *Angelica archangelica* L. are to be discussed.

The identity of the plant material (commercial drug) was established by microscopic comparison with authentic material. (*Angelica archangelica* L. subspecies *eu-archangelica* Thell., varietas *sativa* (Mill.) Rikle).

A new substance,  $C_{49}H_{88}O_2$ , m.p. 77.5°, considered to be  $\beta$ -sitosteryl arachinate, was obtained. The root also afforded  $\beta$ -sitosteryl palmitate, which has not previously been isolated from the family Umbelliferae. Furthermore, angelic acid, palmitic acid and behenic acid were obtained.

*Extraction.* Percolation with diethyl ether of *Angelica* root (5000 g) afforded 12 l of extract. The extract was concentrated to a volume of about  $\frac{3}{4}$  l and stored at  $-10^\circ$ . After 8 days of standing a pale yellow precipitate (P) was formed and collected on a filter.

The mother liquor was worked up according to Hata and Nitta<sup>4</sup>. The obtained fractions A, B and C were examined separately.

*Examination of P.* P (2.3 g) was soluble in boiling ethanol, very soluble in benzene and chloroform. Repeated crystallisations from ethanol gave about 1 g of crystalline material, m.p. 77.5°,  $[\alpha]_D^{22} - 11^\circ$  (c 1.15,  $\text{CHCl}_3$ ). The compound gave analytical data concordant with the composition  $\text{C}_{49}\text{H}_{88}\text{O}_2$ ,  $1\frac{1}{2}\text{H}_2\text{O}$  (Found: C 80.10; H 12.48;  $\text{H}_2\text{O}$  3.24 (dried over  $\text{P}_2\text{O}_5$  at 50° for 48 h). Calc.: 79.95; H 12.45;  $\text{H}_2\text{O}$  3.67).

Upon thin-layer chromatography in toluene-methyl formate-formic acid (5:4:1) and in benzene-ethyl formate-formic acid (7:2:1) P appears to be homogeneous. Chlorosulfonic acid (20%) in acetic acid was used as a spray reagent.

The clue to its identification was found in the IR-spectrum, which contained a conspicuous band at  $1735\text{ cm}^{-1}$  suggesting an ester or a strain-free lactone.

The compound was saponified for 10 h with 0.5 N potassium hydroxide and thus afforded an alcohol, m.p. 134–135°. The alcohol was positive to the Liebermann-Burchard test and was finally identified as  $\beta$ -sitosterol by comparison of the IR-spectrum with the spectrum of authentic material.

From the saponification mixture a carboxylic acid, m.p. 69–71°, was obtained. The IR-spectrum compared with that of authentic material indicated that the acid was arachinic acid with traces of another fatty acid. Accordingly P was considered to be  $\beta$ -sitosteryl arachinate ( $\text{C}_{49}\text{H}_{88}\text{O}_2$ ).

*Examination of A.* The fraction was purified by column chromatography on alumina (Alcoa, acid washed). Benzene was used as the mobile phase. 50-ml fractions were collected. Fraction 2 was pale yellow coloured and afforded 80 mg of a white crystalline substance, m.p. 89.0°,  $[\alpha]_D^{21} - 16.5^\circ$  (c 1.77,  $\text{CHCl}_3$ ). The compound gave analytical data concordant with the composition  $\text{C}_{45}\text{H}_{80}\text{O}_2$ .

The IR-spectrum very closely resembled that of  $\beta$ -sitosteryl arachinate and the substance was also positive to the Liebermann-Burchard test. After saponification  $\beta$ -sitosterol and a carboxylic acid, m.p. 62–63°, was isolated. By means of the IR-spectrum the acid was identified as palmitic acid.

Accordingly, the compound is considered to be  $\beta$ -sitosteryl palmitate. Lit. value<sup>5</sup>: m.p. 84°,  $[\alpha]_D^{16} - 15.8^\circ$  ( $\text{CHCl}_3$ ).

*Examination of B.* The fraction (3 g) consisted of a brown, partly crystalline powder, soluble in acetone, ethanol, ben-

zene, chloroform and in aqueous sodium hydroxide, but only sparingly soluble in diethyl ether and insoluble in pentane. M.p. 180–186° (decomp.).

Thin-layer chromatography according to Stahl and Schorn<sup>6</sup> indicated that B was a mixture of 8 components which in short-wave UV-light fluoresced with different colours. Sprayed with ethanolic potassium hydroxide some of the spots changed in colour and are apparently to be considered as coumarines.

Fractionation of B was attempted by microsublimation *in vacuo*. With a bath temperature at 80° long needle-shaped crystals, m.p. 44°, were obtained.

The IR-spectrum proved the compound to be angelic acid. So far, chromatographically pure coumarines have not been obtained.

*Examination of C.* The fraction (6 g) appeared as a nearly colourless mass, insoluble in water, soluble in diethyl ether and aqueous sodium hydroxide.

By distillation *in vacuo* (2 mm Hg) the following fractions were collected:

Below 60° yellow-brown oil (0.8 g)	I
165–185° white mass, m.p. 45–47° (1.1 g)	II
200–217° white mass, m.p. 60–70° (1.3 g)	III

- I. The examination of I is not finished, but a preliminary gas-chromatographic investigation indicates that among other compounds, I consists of petroselinic-, linolic-, linoleic-, and a  $\text{C}_{16}$ -unsaturated acid. The results from this investigation will be published elsewhere.
- II. Five recrystallisations from glacial acetic acid and washing with water afforded a compound with m.p. 58.2°. The compound gave analytical data concordant with the composition  $\text{C}_{16}\text{H}_{32}\text{O}_2$ . The IR-spectrum indicated the compound to be palmitic acid.
- III. The fraction was recrystallised in the same manner as II. The m.p. of the isolated compound was found to be 73.8°. The analytical data are concordant with the composition  $\text{C}_{22}\text{H}_{44}\text{O}_2$ . The IR-spectrum indicated the compound to be behenic acid.

All melting points are determined in capillary tubes in an electrically heated silicone bath. Rate of heating near the melting point 1°/min. The IR-spectra were recorded in KBr on a

Perkin Elmer Spectrophotometer, Model 21. Microanalyses have been performed by Dr. A. Bernhardt, Mülheim.

*Acknowledgements.* The authors are grateful to Dr. Mogens Wellendorf (Pharmacognostic Laboratory, The Royal Danish School of Pharmacy, Copenhagen, Denmark) for assistance with the microscopic examination of the plant material.

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Received February 28, 1963.

## On an Isomerization in the Reaction of Aromatic Grignard Reagents with Alkyl *p*-Toluenesulphonates

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Alkyl sulphonates have been used as alkylating agents for aromatic compounds, either by thermal decomposition of the ester in the aromatic compound as solvent,<sup>1</sup> or by the reaction with an aromatic Grignard reagent<sup>2</sup>. In the first mentioned type of reaction the substitution follows the general rules of electrophilic substitution although the selectivity appears to be lower than in Friedel-Crafts alkylations, as is evident by the large extent of *meta* substitution<sup>1</sup>. The Grignard reagents on the other hand often give low yields due to side-reactions which may lead to alkyl bromides or reduction of the Grignard reagent<sup>2</sup>. In any case it appears to be generally assumed that, in the alkylation, substitution occurs at the C-Mg bond<sup>2</sup>. However, in attempts to prepare 2-isopropylthiophene from

2-thiophenemagnesium bromide and isopropyl *p*-toluenesulphonate we observed an isomerization and obtained mixtures of the isomeric isopropylthiophenes containing about 55 % of the 2-isomer and 45 % of the 3-isomer. The analyses were carried out using NMR-spectroscopy and measuring the methyl group bands of the two isomers. On metalation with *n*-butyllithium, followed by carbonation, the isomeric mixture gave the same proportions of 2-isopropyl-5-thiophenecarboxylic acid and 3-isopropyl-5-thiophenecarboxylic acid, which were identified by the characteristic coupling constants of disubstituted thiophenes<sup>3</sup>. This verifies the original analysis of the isopropylthiophene mixture. The reaction of 3-thiophenemagnesium bromide with isopropyl *p*-toluenesulphonates also proceeds with isomerization leading to a mixture of about 50 % of 3-isopropylthiophene and 50 % of 2-isopropylthiophene. Heating isopropyl *p*-toluenesulphonate in thiophene as solvent did not lead to alkylation.

Isomeric mixtures are also obtained in the reaction of 2-thiophenemagnesium bromide with ethyl *p*-toluenesulphonate and propyl *p*-toluenesulphonate (70 % 2-isomer and 30 % 3-isomer). No rearrangement of the alkyl chain in the latter case was observed.

It has also been found that, in contrast to earlier statements<sup>4</sup>, a mixture of *t*-butylthiophenes is obtained in the reaction of 2-thiophenemagnesium bromide and *t*-butyl bromide<sup>5</sup>.

Preliminary experiments indicate that the observed isomerization is not limited to the thiophene series. Reaction of *p*-methoxyphenylmagnesium bromide with isopropyl *p*-toluenesulphonate gives a mixture of isomeric isopropylanisols. We are studying the scope and mechanisms of these rearrangements, which in some way may be analogous to the rearrangements occurring in the reaction of certain aromatic zinc, mercury and cadmium compounds with acid chlorides<sup>6-8</sup>, which most probably proceed by a cyclic mechanism<sup>9</sup>.

It is clear that the isomeric purity of many compounds prepared by the reaction of unsymmetrical aromatic Grignard reagents with *p*-toluenesulphonates can be seriously doubted.

*Experimental. 2- and 3-Isopropylthiophene.* The Grignard reagent was prepared in the usual way from 48.9 g (0.3 mole) 2-bromothio-