V_1 is the volume of the total acetone extract, ml;

V_2 is the volume of extract deposited on the plate, ml;

P is the weight of the raw material, g; and

h is the loss in weight on the drying of raw material, %.

SUMMARY

A procedure has been developed for the selective quantitative determination of the triterpene saponins in hawthorn fruit (haws) with the aid of chromato-photodensitometry. The relative error does not exceed ±5.1%.

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TOTAL SYNTHESIS OF THE RACEMIC ALKALOID DIPTOCARPAMINE

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A route for the synthesis of racemic diptocarpamine from hex-5-enoic acid has been developed.

Continuing work on the total synthesis of the alkaloid of Dipthychocarpus strictus [1-3], we have developed a short method of obtaining diptocarpamine (VIII) [4]. Our main attention was devoted to the synthesis of the key 7-thiaoctylamine (VI), which we had used previously in the preparation of the racemic alkaloids diptocarpidine and diptocarpiline [5].

Starting from hex-5-enoic acid,* 7-thiaoctanoic acid (I) was prepared with quantitative yield by the thiylation reaction with methyl mercaptan. Its methyl ester (II) was converted under the action of lithium tetrahydroaluminate into the corresponding alcohol (III). The

*The hex-5-enoic acid was supplied by E. K. Starostin.

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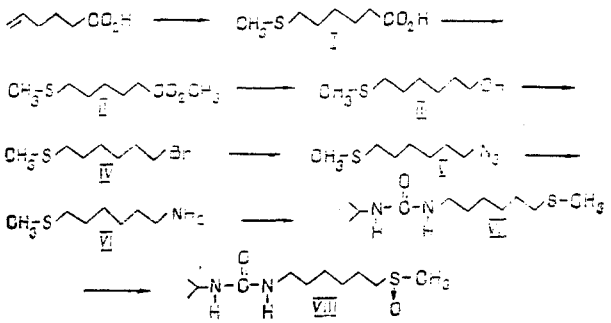
reaction of the latter with phosphorus tribromide in the presence of pyridine gives 7-thiaoctyl bromide (IV). When compound (IV) was heated with sodium azide, 7-thiaoctyl azide (V) was obtained and the reduction of this led to the key amine (VI). Isopropyl isocyanate was prepared from isobutyryl chloride via the corresponding azide [6], and the reaction of this with the amine (VI) gave the sulfide precursor (VII). Its oxidation completed the synthesis of racemic diptocarpamine (VIII).



In the electron-impact mass spectra of compounds (VII) and (VIII) the peaks of molecular ions were recorded with mass numbers corresponding to the empirical formulas $C_{11}H_{24}N_2OS$ (measured 232.1610; calculated 232.1609) and $C_{11}H_{24}N_2O_2S$ (measured 248.1582; calculated 248.1559). The characteristic ions $M - CH_3]^+$, $M - CH_3S(O)]^+$, $M - CH_3S(O)CH_2]^+$, $M - CH_3SOCH_2CH_2]^+$, and $M - CONH\text{-}iC_3H_7]^+$ in the mass spectra of (VII) and (VIII) are formed, according to [7] by simple bond cleavage. For example, the origin of the peak of the $M - 100]^+$ ions is due to the successive splitting out of a methyl radical and isopropyl isocyanate:

VII: *m/z* 132(30%), measured 132.0862, calculated 132.0847

VIII: *m/z* 148(10%), measured 148.0764, calculated 148.0796

$$M^+ \xrightarrow[*]{-C_3H_7\cdot} M-CH_3]^+ \xrightarrow[*]{-CON-iC_3H_7\cdot} S(O)C_6H_{12}NH_2]^+.$$

In the resonance electron capture (REC) mass spectra of compounds (VII) and (VIII) the peaks of the negative ions formed by simple cleavages were observed (see the Experimental part). The compositions of these ions confirmed the sequence of the carbon atoms and functional groups in the molecules considered. In addition, the presence of peaks of rearrangement ions with m/z 171 in (VII) and (VIII) and 107 and 64 in (VIII) permitted the conclusion that the HNCO- and SO-groups interact intermolecularly because of their spatial propinquity as a consequence of the existence of the molecules of (VII) and (VIII) in a folded conformation [5].

EXPERIMENTAL

IR spectra were taken on a UR-20 instrument in Nujol or in a thin layer. PMR spectra were obtained on a Tesla BS-567B instrument with a working frequency of 100 MHz, and ^{13}C NMR spectra were recorded on a JEOL FX-90 Q instrument with a working frequency of 22.5 MHz. TMS was used as internal standard, and $CDCl_3$ as solvent. The positive-ion mass spectra were obtained on a MKh-1320 instrument with a temperature of the ionization chamber of 30-50°C and energies of the ionizing electrons of 70 and 16 eV, using a SVP-5 direct-introduction system. Accurate values of the mass numbers of the ions were measured on a Varian MAT CH-5 instrument with an energy of the ionizing electrons of 70 eV and an ionization chamber temperature of 250°C. Negative-ion mass spectra were obtained on a MI-1201 mass spectrometer reequipped for recording negative ions [8]. The electron energy of the scale was calibrated from the curves of the effective yields of SF_6^- from SF_6 and of NH_2^- from ammonia. The products of synthesis were separated by column chromatography on silica gels L40/100 and L 100/160 (Czechoslovakia). Commercial isobutyryl chloride with a purity of not less than 99.9% was used in the synthesis.

7-Thiaoctanoic Acid (I). A quartz-glass flask was charged with 3.65 g ($3.2\cdot10^{-2}$ mole) of hex-5-enoic acid and 0.03 g of azoisobutyronitrile and was cooled to −10°C. Then 3.54 ml ($6.4\cdot10^{-2}$ mole) of methyl mercaptan was added carefully in one portion. The flask was tightly sealed and, with stirring and cooling (−20°C), the reaction mixture was illuminated

with a UV lamp (PRK-4) for 6 h. After the elimination of the excess of methyl mercaptan, the acid (I) was purified via the sodium salts. The yield was quantitative (5.06 g).

IR spectrum (cm^{-1}): ν_{max} 1715 (CO), 2450-3520 (C(=O)—OH). PMR spectrum (ppm): 2.12 (3 H, s, CH_3—S), 2.30 (2 H, t, J = 7.2 Hz), 2.48 (2 H, t, J = 7 Hz, —CH_2—CO_2H), 10.81 (H, br.s. —C(=O)—OH).

Methyl 7-Thiaoctanoate (II). To 5 g ($3.1 \cdot 10^{-2}$ mole) of the acid (I) was added 50 ml of a 5% solution of gaseous HCl in methanol. After 12 h, the methanol was distilled off, 30 ml of ether was added to the residue, and the resulting solution was washed with 5% $NaHCO_3$ solution (3 × 20 ml), with water (2 × 10 ml), and with saturated NaCl solution. The organic layer was dried with Na_2SO_4, the solvent was evaporated off, and compound (II) was purified by vacuum distillation. The yield was 5.25 g (95%), bp 113°C (10 mm). IR spectrum (cm^{-1}): ν_{max} 1325 (C—S); 1745 (CO). PMR spectrum (ppm): 1.52 (6 H, m, $3CH_2$), 2.08 (3 H, s, CH_3—S), 2.32 (2 H, t, J = 7 Hz, CH_2—S), 2.49 (2 H, t, J = 7 Hz, CH_2—CO_2CH_3), 3.66 (3 H, s, CO_2CH_3).

7-Thiaoctanol (III). At room temperature, with stirring, a solution of 5.23 g ($3 \cdot 10^{-2}$ mole) of compound (II) in 5 ml of ether was added dropwise to 2.26 g ($6 \cdot 10^{-2}$ mole) of $LiAlH_4$ in 50 ml of dry ether, after 20 min the reaction mixture was diluted with 20 ml of moist ether, and 5 ml of a 5% solution of KOH was carefully added, after which the precipitate was filtered off, and the filtrate was washed with 5% HCl solution (2 × 25 ml) and with saturated NaCl solution. The organic layer was dried with $MgSO_4$ and the solvent was evaporated off. Product (III) was purified by column chromatography. The yield was 4.2 g (95%).

IR spectrum (cm^{-1}): ν_{max} 3400 (OH). PMR spectrum (ppm): 1.38 (8 H, m, $4CH_2$), 2.02 (3 H, s, CH_3—S), 2.40 (2 H, t, J = 7 Hz, CH_2—S), 3.47 (2 H, t, CH_2—OH), 4.03 (br.s, OH). The results of elementary analysis corresponded to the calculated figures.

7-Thiaoctyl Bromide (IV). In a current of argon, 0.72 ml ($9 \cdot 10^{-3}$ mole) of pyridine was added to a solution of 4 g ($2.7 \cdot 10^{-2}$ mole) of the alcohol (III) in 50 ml of dry ether. The temperature of the mixture was lowered to −30°C, and 0.85 ml ($9 \cdot 10^{-3}$ mole) of freshly distilled PBr_3 was added. After 3 h, the temperature was raised to that of the room and the mixture was left for 12 h (25°C). Then it was diluted with moist ether (50 ml) and was washed with water (3 × 20 ml), the organic layer was dried with Na_2SO_4, and the solvent was distilled off. The bromide (IV) was isolated by column chromatography. The yield was 3.2 g (65%). PMR spectrum (ppm): 1.42 (8 H, m, CH_2), 2.01 (3 H, s, CH_3—S), 2.38 (2 H, t, J = 7 Hz, CH_2—S), 3.34 (2 H, t, J = 7 Hz, CH_2—Br). The results of elementary analysis corresponded to the calculated figures.

7-Thiaoctyl Azide (V). A mixture of 3.14 g ($1.75 \cdot 10^{-2}$ mole) of the bromide (IV), 1.7 g ($2.6 \cdot 10^{-2}$ mole) of dry sodium azide, 25 ml of the monoethyl ether of ethylene glycol, and 4 ml of water was heated at 90°C for 24 h. Then 30 ml of cold (5°C) water was added, the aqueous layer was separated off and was extracted with ether (3 × 10 ml), the extract was dried with Na_2SO_4, the solvent was evaporated off, and the azide (V) was purified by column chromatography. The yield was 1.7 g (56%). IR spectrum (cm^{-1}): ν_{max} 2110-2170 (—N_3). The results of analysis corresponded to the calculated figures.

7-Thiaoctylamine (VI) [4]. At room temperature, a solution of 1.66 g ($9.6 \cdot 10^{-3}$ mole) of the azide in 3 ml of dry ether was added dropwise to 0.36 g ($9.6 \cdot 10^{-3}$ mole) of lithium tetrahydroaluminate in 20 ml of dry ether. After 20 min, 10 ml of moist ether and 1 ml of 5% KOH solution were added to the mixture. The precipitate was filtered off and the filtrate was washed with saturated NaCl solution and dried with Na_2SO_4, and the solvent was evaporated off. This gave 1.33 g (95%) of the amide (VI).

N-Isopropyl-N'-(7-thiaoctyl)urea (VII). At 25°C, 0.7 g ($9 \cdot 10^{-3}$ mole) of isopropyl isocyanate was added in one portion to a solution of 1.33 g ($9 \cdot 10^{-3}$ mole) of the amine (VI) in 5 ml of dry benzene. After 10 min, the benzene was distilled off, and the compound (VII) was purified by column chromatography. The yield was 1.88 g (90%), mp 68-70°C. IR spectrum (cm^{-1}): ν_{max} 1580, 1620 (CO); 3340-3368 (NH). PMR spectrum (ppm): 1.12 (6 H, d, J = 6.2 Hz, —$C(CH_3)_2$), 1.38 (8 H, m, $4CH_2$), 2.08 (3 H, s, CH_3—S), 2.47 (2 H, t, J = 7 Hz, —CH_2—S), 3.16 (2 H, t, J = 7 Hz, CH_2—N), 3.87 (1 H, m, —CH—N), 4.61 (2 H, m, 2H). ^{13}C

NMR spectrum (ppm): 15.55 q (CH_3–S), 23.51 q ((CH_3)$_2$–C), 26.55 t, 28.44 t, 29.04 t, 30.18 t (4CH_2), 34.19 t (CH_2–S), 40.22 t (CH_2–N), 42.15 d (–CH–N), 158.20 s (C=O). Mass spectrum, m/z (%): M^+ 232 (19.7), 217 (33), 185 (100), 171 (12), 146 (9), 132 (30), 115 (23), 103 (14), 100 (24), 61 (30), 58 (47), 44 (97), 30 (77). REC mass spectrum*: 231 $(M - H)^-$ – 23 (0.4), 16 (2.4); 189 $(M - C_3H_7)^-$ – 5 (1.9), 21 (8.5); 171 $(M - CH_2SNH)^-$ – 11 (0.5), 24 (1.8), 3 (4.4), 5 (8.4); 101 ($C_3H_7NHCONH^-$) –5 (5.1), 23 (8.2); 86 ($C_3H_7NHCO^-$) – 6 (4.9), 4 (8.4); 58 ($C_3H_7NH^-$) – 4 (0.9), 5 (5.5), 3 (7.8); 47 (CH_3S^-) – 3 (0.8), 5 (5.5), 38 (7.8); 42 (OCN^-) – 32 (1.2), 11 (2.4); 26 (NC^-) – 100 (0.9), 68 (1.8). The results of analysis corresponded to the calculated figures.

N-Isopropyl-N'-(6-methylsulfinylhexyl)urea – (±)-Diptocarpamine (VIII). At 25°C, 0.9 g ($8 \cdot 10^{-3}$ mole) of 30% H_2O_2 was added to a stirred solution of 1.88 g ($8 \cdot 10^{-3}$ mole) of the urea (VII) in 5 ml of glacial acetic acid. After 2 h, the reaction mixture was diluted with 10 ml of chloroform and was washed with saturated $NaHCO_3$ solution to remove traces of acid, the organic layer was dried with $MgSO_4$, and the solvent was evaporated off. Product (VIII) was purified by column chromatography. The yield was 1.8 g (91%), mp 98°C. The IR and PMR spectra of compound (VIII) were identical with those given in the literature [4].

^{13}C NMR spectrum (ppm): 23.51 q ((CH_3)$_2$C), 22.49 t, 26.39 t, 28.29 t, 29.96 t, (4CH_2), 38.58 q (CH_3–S), 39.88 t (CH_2–N), 41.83 d (CH–N), 54.45 t (CH_2–S), 158.15 s (CO). Mass spectrum, m/z (%): M^+ 248 (14.0), 233 (33), 218 (1), 190 (57), 185 (58), 171 (19), 162 (18), 148 (10), 117 (53), 100 (30), 61 (13), 58 (67), 44 (100), 30 (83). REC mass spectrum: 247 $(M - H)^-$ – 11 (0.6), 21 (2.1), 10 (3.1); 233 $(M - CH_3)^-$ – 18 (1.0); 205 $(M - C_3H_7)^-$ – 9 (0.5), 3 (8.0); 171 $(M - CH_2SONH)^-$ – 12 (0.5), 26 (1.6); 107 ($H_2NCONHSO^-$) – 50 (0.5); 101 ($C_3H_7NHCONH^-$) – 3 (0.3), 3 (4.9), 11 (8.4); 86 ($C_3H_7NHCO^-$) – 4 (1.0), 3 (4.5), 3 (8.4); 64 (H_2NSO^-) –12 (0.3), 7 (2.3), 5 (4.0), 4 (6.2); 63 (CH_3SO^-) – 10 (1.6), 4 (4.9), 17 (7.9), 7 (9.2); 58 ($C_3H_7NH^-$) – 15 (4.9); 48 (SO^-) – 13 (4.5), 3 (7.2); 42 (OCN^-) – 24 (1.0), 59 (2.2); 26 (NC^-) – 100 (1.6), 5 (4.9), 9 (6.4).

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SUMMARY

A convenient method for the synthesis of racemic diptocarpamine from hex-5-enoic acid has been developed.

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*Here and below, in the REC mass spectra: mass number, composition of the ions, intensities of the peaks in percentages of the maximum, and, in parentheses, the energy of the resonance maximum of the appearance of the ions in electron-volts.