solved in acetic anhydride (30 ml.) containing 3% sulfuric acid and the rotation followed using a 1-dm. tube:

Time, hr.	0.25	2	3	4	8	24	94
α_D	+6.19°	+5.05	+4.25	+3.39	+1.10	−1.06	−2.75

After it had reached the constant value −2.75°, the reaction mixture was diluted with chloroform (200 ml.) and then decomposed by the addition of crushed ice. The organic layer was then separated and stirred vigorously with an aqueous solution of sodium bicarbonate. As the neutralization proceeded, more bicarbonate was added until the evolution of carbon dioxide ceased. This procedure was adopted since the pentaacetate appeared to be appreciably soluble in water, and repeated washing of the chloroform layer with dilute aqueous bicarbonate solutions resulted in low yields. The chloroform layer was then separated, washed with a small volume of water and dried with magnesium sulfate. Evaporation afforded a colorless glass of 3-acetamido-1,2,4,6-tetra-*O*-acetyl-3-deoxy-αβ-D-gulose, which after drying over P_2O_5 weighed 2.82 g. (64%) and had $[\alpha]_D$ −8.05° (*c* 7.03, methanol).

Anal. Calcd. for $C_{16}H_{23}O_{10}N$: C, 49.38; H, 5.95; N, 3.60. Found: C, 49.73; H, 5.65; N, 3.75.

3-Acetamido-3-deoxy-D-gulose.—The pentaacetyl derivative (2.16 g.) was dissolved in dry methanol (30 ml.) and 5 ml. of 0.4 *N* barium methoxide added and the solution kept at room temperature for 24 hr. It was then concentrated to a sirup which was dissolved in water and treated with carbon dioxide until a clear solution was obtained, and then evaporated. The residue was extracted with methanol and the extract concentrated to a frothy sirup (1.08 g.) which failed to crystallize. Chromatography revealed that the sugar, which had R_{rh} 0.88 (F.D.) and 0.71 (B.A.W.), was contaminated with smaller amounts of slower moving material. The impure sirup had $[\alpha]_D$ − 8° (*c*1.19, water).

Anal. Calcd. for $C_8H_{15}O_6N$: N, 6.33. Found: N, 6.33.

The sugar (30 − 48 mg.) was treated with 0.01 *M* sodium metaperiodate (100 ml.) at *p*H 4 and under unbuffered conditions:

Time, hr.	0.17	0.5	1	1.5	3.25	24
Uptake at *p*H 4	2.0	2.46	2.64	3.0	..	4.38
Uptake (unbuffered)	1.5	2.02	2.82	..	3.16	>4.4

Preparation of an osazone, a polyol and an anilide failed to yield a crystalline derivative.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, THE FLORIDA STATE UNIVERSITY, TALLAHASSEE, FLA.]

The Sesquiterpene Lactones of *Artemisia tilesii* Ledeb.[1]

BY WERNER HERZ AND KANICHI UEDA

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Three sesquiterpene lactones were isolated from *Artemisia tilesii* Ledeb. The major constituent was identical with matricarin, a minor constituent of *Matricaria chamomilla* L. Its structure was shown to be I. The second lactone was a stereoisomer of I. The third lactone was desacetylmatricarin.

The search for santonin has prompted the chemical investigation of a large number of Artemisia species and has resulted in the discovery of many interesting new sesquiterpene lactones.[2] We now wish to report the isolation of three guaianolides from *Artemisia tilesii* Ledeb., a previously uninvestigated species.

Artemisia tilesii Ledeb. is wide-spread, though scattered, in the Northwest portions of the United States and Canada; large populations occur in central and Northern Alaska. Among mainland Eskimos it enjoys a reputation as a medicinal plant.[3] In 1957, we received a small sample of this plant[4] through the courtesy of Mrs. May Ivanoff of Unalakleet, Alaska, and were able to isolate two crystalline fractions of formulas $C_{17}H_{20}O_5$ and $C_{15}H_{18}O_4 \cdot H_2O$. Material supplied by Mrs. Ivanoff in subsequent years showed that the first fraction was in fact a difficultly separable mixture of two stereoisomeric sesquiterpene lactones of very similar properties which were named artilesin A and B and permitted us to deduce structures for all three compounds.

The mixture of artilesin A and B was obtained in larger yield (0.04–0.06%). Artilesin A, the less soluble component, had m.p. 190–191°, $[\alpha]_D$ 23.5°, and was doubly unsaturated (microhydrogenation). In the infrared ($CHCl_3$) it exhibited bands at 1780 (γ-lactone), 1740, 1690, 1645, and 1622 cm.$^{-1}$, the latter two frequencies being assigned to the two double bonds. The band at 1690 cm.$^{-1}$ was provisionally ascribed to a cyclopentenone carbonyl because tetrahydroartilesin A (IIa) had only two carbonyl bands at 1770 (lactone) and 1730 cm.$^{-1}$ (double strength, combination of cyclopentanone and other carbonyl). The preparation of a thioketal from IIa confirmed the presence of a ketone group.

An acetate group was responsible for the 1745 cm.$^{-1}$ band since the hydrolysis of desoxotetrahydroartilesin A (IIIa, R = Ac) resulted in the formation of desacetyldesoxotetrahydroartilesin A (IIIa, R = H), $C_{15}H_{24}O_4$: The hydroxyl involved

(1) Supported in part by a grant (RG-5814) from the National Institutes of Health, U. S. Public Health Service.

(2) For a survey, see G. Wichmann, *Pharm.*, **13**, 487 (1958). More recent articles dealing with sesquiterpene lactones from *Artemisia* species include M. Sumi, *J. Am. Chem. Soc.*, **80**, 4869 (1958); M. Sumi, W. G. Dauben and W. K. Hayes, *ibid.*, **80**, 5704 (1958); W. G. Dauben, J. S. P. Schwarz, W. K. Hayes and P. D. Hance, *ibid.*, **82**, 2239 (1960); V. Herout and F. Šorm, *Chemistry & Industry*, 1067 (1959).

(3) We are indebted to Dr. Christine Heller, nutritionist, Artic Health Center, Anchorage, Alaska, and to Dr. Margaret Lantis, Anthropologist, U. S. Public Health Service, for this information. Dr. Heller writes that infusions are used internally in the treatment of hemorrhages and severe colds and as an analgesic against rheumatic and ill-defined aches and pains. Poultices or dried leaves applied to the skin (the preferred method) are used as a treatment for impetigo and sores which resist healing or have become infected. However, according to Dr. Heller the plant is not used medicinally on St. Lawrence Island and material collected there in the summer of 1958 did not yield crystalline substances. This could be due to the existence of several subspecies (see footnote 4).

(4) This was identified as *Artemisia tilesii* Ledeb. by Dr. Quentin Jones, New Crops Research Branch, Agricultural Research Service, U. S. Department of Agriculture, Beltsville, Md. The most recent treatment of *A. tilesii* Ledeb. lists four subspecies, *A. tilesii*, *A. tilesii* ssp. *unalaskensis* (Bess.) Hult, ssp. *gormanii* (Rydb.) Hult, and ssp. *elatior* T. and G., but our sample was not specifically assigned to any of these.[5]

(5) J. P. Anderson, "Flora of Alaska," Iowa State University Press, Ames, Iowa, 1959.

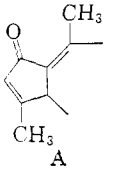
in ester formation was secondary because IIIa (R = H) was easily oxidized to a ketone (IVa).

Fractions rich in artilesin B could not be freed sufficiently from contaminants, principally artilesin A, to permit adequate characterization (m.p., rotation, ultraviolet, infrared and n.m.r. spectra of these fractions were very similar to those of artilesin A), but were hydrogenated to mixtures rich in tetrahydroartilesin B. The latter gave a thioketal different from that of IIa whose conversion to isomers of IIIa and IVa established the presence of the same functional groups.

The infrared spectrum of the third constituent, m.p. 123–125°, had bands at 3500 (hydroxyl), 1780 (lactone), 1690 (cyclopentenone), 1645 and 1620 cm.$^{-1}$. This indicated that it might be a desacetylartilesin (I, R = H), a hypothesis which could be confirmed by direct acetylation with acetic anhydride in pyridine. The product was artilesin A. Hydrogenation furnished a tetrahydro derivative the acetate of which was shown to be IIa.

The ultraviolet spectra of artilesin A (λ_{max} 255 mμ, log ϵ 4.15) and desacetylartilesin (λ_{max} 255 mμ, log ϵ 4.16) exhibited a striking resemblance to the spectrum of lactucin (VII).[6] Evidence for the presence in artilesin A of the cross-conjugated dienone grouping A was the isolation, in poor yield, of dihydroartilesin A (V, R = Ac), λ_{max} 248 mμ, log ϵ 3.98, infrared bands at 1770 (lactone), 1735 (acetate), 1710 (cyclopentenone), 1610 (strong, cisoid enone system).

The n.m.r. spectra were in complete accord with partial structure A. Artilesin A had a complex

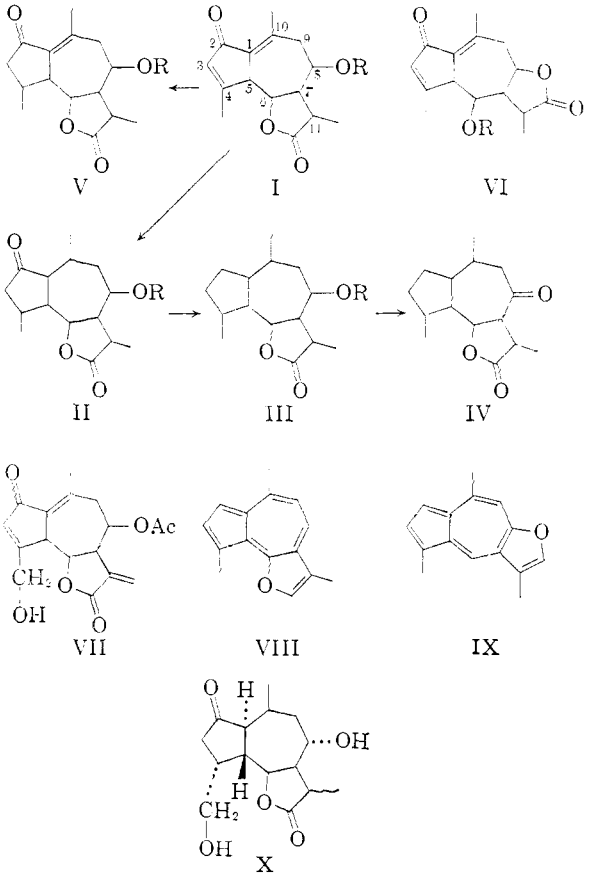


A

multiplet centered at 56.5 c.p.s. relative to chloroform[7] whose intensity corresponded to one proton (—C(=O)—C=C<H) coupled to non-adjacent hydrogens (coupling constant about 1.5 c.p.s.), three —C—CH_3 peaks at 204, 208 and 209 (split) and 215 c.p.s. (two allylic methyls and one acetate methyl) and a fourth split peak at 240.5 and 247 c.p.s. (combined intensity three protons) due to the C-11 methyl group. Tetrahydroartilesin, on the other hand, had one peak at 207 c.p.s. (three protons, acetate methyl) and a complex set of signals at 234, 235.5, 242, 245, 251 and 252 c.p.s. whose combined intensity was equivalent to nine protons.

During this work there appeared a report by Čekan, Procházka, Herout and Šorm[8] on the isolation of matricarin, a minor constituent of *Matricaria chamomilla* L. Although there were some slight discrepancies (see Experimental), the physical properties of matricarin and tetrahydromatricarin were sufficiently close to those of artilesin A and tetrahydroartilesin A to warrant a direct comparison.[9] This showed that artilesin A and matricarin were indeed identical. In view of the prior publication of the Czech workers, we adopt their nomenclature, and reserve the term artilesin for the new isomer of matricarin.

The Czech workers suggested structure I or VI for matricarin (with preference given to I on biogenetic grounds) because of the ultraviolet and infrared spectra and because dehydrogenation furnished a mixture of artemazulene VIII and linderazulene IX. The work described in this paper has furnished proof for the presence of the dienone chromophore A and favors I. Conversion of tetrahydromatricarin to the desoxo derivative IIIa (R = Ac, infrared bands at 1775 and 1735 cm.$^{-1}$) followed by mild hydrolysis under conditions



which have been shown not to involve lactone ring opening[10] gave IIIa (R = H). This substance was oxidized smoothly to dehydrodesoxodesacetyltetrahydromatricarin (IVa) which gave a positive Zimmermann test and exhibited bands in the infrared spectrum at 1780 (γ-lactone) and 1705 cm.$^{-1}$ (cycloheptanone). While this supports formula I in which the acetoxy group is attached to C-8 of the guaianolide skeleton, IVa did not

(6) (a) D. H. R. Barton and C. R. Narayanan, *J. Chem. Soc.*, 963 (1958); (b) L. Dolejš, M. Souček, M. Horák, V. Herout and F. Šorm, *Coll. Czechoslov. Chem. Commun.*, **23**, 2195 (1958).

(7) N.m.r. spectra were run at 40 mc. in deuterlochloroform solution with chloroform or tetramethylsilane as internal standards. Frequencies were determined by the side-band technique.

(8) Z. Čekan, V. Procházka, V. Herout and F. Šorm, *Coll. Czechoslov. Chem. Commun.*, **24**, 1554 (1959).

(9) We are grateful to Dr. V. Herout for comparing samples.

(10) W. A Rohde, Ph.D. dissertation, Florida State University June, 1960. That no isomerization had occurred during this step was shown by reacetylation which regenerated IIIa (R = Ac).

condense with piperonal. The infrared spectrum of IV also contained a band at 1405 cm.$^{-1}$ which, however, could not be attributed to $-CH_2C-$ since it did not disappear on deuteration. The presence in the deuterated material of 56% tri- and 1.2% tetradeuterated product is, however, strong evidence for the formulation of matricarin as I.

Although at the present time there is no dehydrogenative evidence for the carbon skeleton of the compounds derived from artilesin B, the great similarity which extends to the fingerprint region of the infrared spectra rendered it almost certain that it was a guaianolide and that it differed from matricarin only in minor detail. Added to the already-established presence of a cyclopentenone ring, the following reaction sequence, by pointing to the presence of a cycloheptane ring, confirmed this supposition. The thioketal of tetrahydroartilesin was converted to the desoxo derivative (IIIb, R = Ac) which was hydrolyzed without isomerization (reacetylation regenerated starting material) to desacetyldesoxotetrahydroartilesin (IIIb, R = H). Oxidation furnished a ketolactone, dehydrodesacetyldesoxotetrahydroartilesin (IVb), which exhibited infrared bands at 1790 cm.$^{-1}$ (γ-lactone) and 1705 cm.$^{-1}$ (cycloheptanone) and gave a positive Zimmermann test, but again failed to yield a condensation product with piperonal.

The fact that the changes in rotation accompanying the conversions IIIa→IVa and IIIb→IVb are so different suggests that the two series differ in configuration at the carbon atom bearing the acetoxy group, presumably C-8. However, the difference between matricarin and artilesin cannot be attributed solely to stereoisomerism at C-8 since IVa and IVb are not identical.

The optical rotatory dispersion curve of tetrahydromatricarin (IIa) is similar to that of hexahydrolactucin (X)[6] in shape and sign (positive) of Cotton effect, although the amplitude is much smaller (see Fig. 1). At the moment, however, the absence of information as to the nature of the ring junction allows no decision between B and C. If the ring junction be *trans*, analogy to the curve of cholestan-3-β-ol-15-one[11] would permit assignment of absolute configuration B, with the customary reservations about comparing bicyclo[5,3,0]-decanes with bicyclo[4,4,0]decanes,[12] *cis*-hydrogenation of the 1,10-olefinic linkage being assumed. If it be *cis*, the similarity to the curves of 3-keto-A-norcholanic acid[13] and a number of pentacyclic triterpene ketones[14] would suggest absolute configuration C.

It was therefore of considerable interest to observe that tetrahydromatricarin, like hexahydrolactucin, could be isomerized on treatment with

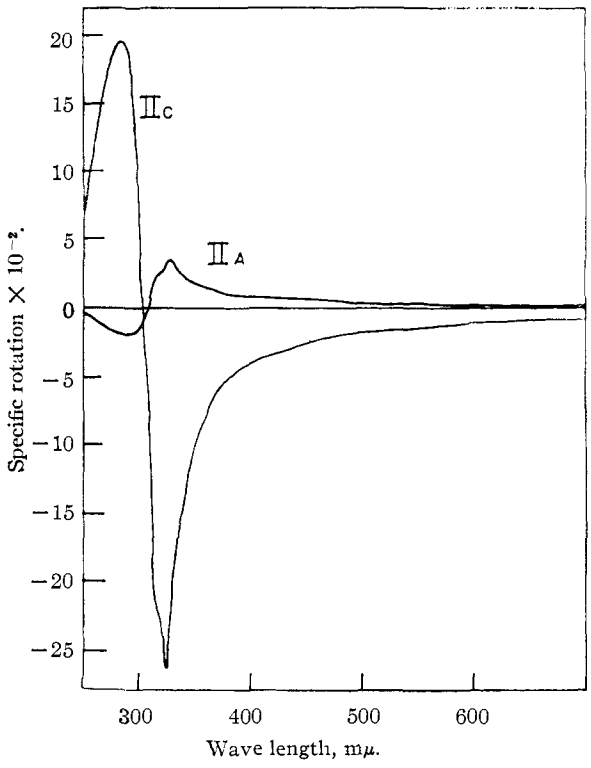
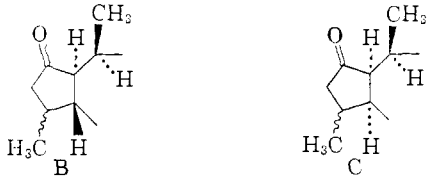


Fig. 1.—Optical rotatory dispersion curves of tetrahydromatricarin (IIA) and isotetrahydromatricarin (IIC).

base. The reaction was accompanied by hydrolysis and furnished an oily desacetylisotetrahydromatricarin (IIc, R = H) which was different from the substance prepared by hydrogenation of naturally-occurring desacetylmatricarin and was characterized by conversion to a crystalline acetate



(IIc, R = Ac). The optical rotatory dispersion curve of the latter, isotetrahydromatricarin, was the mirror image of and, when reflected around the x-axis, practically superimposable on the dispersion curve of 3-keto-A-norcholanic acid[13] (see Fig. 1). If it is assumed, as is most likely, that this isomerization involves inversion at C-1[15] and that, as is perhaps less warranted, a *cis*-bicyclo(5,3,0)decan-1-one ring system is thermodynamically more stable than the corresponding *trans* isomer, partial absolute configuration B could be assigned to tetrahydromatricarin which is the same as that deduced for hexahydrolactucin. However, this conclusion must be treated with reservations since the yield of crystalline IIc was only about 25% and it is possible that the less stable isomer was isolated from an equilibrium mixture.[14c]

(11) C. Djerassi, W. Closson and A. E. Lippman, *J. Am. Chem. Soc.*, **78**, 3164 (1956).

(12) C. Djerassi, J. Osiecki and W. Herz, *J. Org. Chem.*, **22**, 1361 (1957).

(13) C. Djerassi, R. Riniker and B. Riniker, *J. Am. Chem. Soc.*, **28**, 6362 (1956).

(14) (a) C. Djerassi, J. Osiecki and W. Closson, *ibid.*, **81**, 4587 (1959); (b) G. V. Baddeley, T. G. Halsall and E. R. H. Jones, *J. Chem. Soc.*, 1715 (1960); (c) N. L. Allinger, R. B. Hermann and C. Djerassi, *J. Org. Chem.*, **25**, 922 (1960).

(15) Simultaneous epimerization at C-11 cannot be excluded at present.

Acknowledgment.—We wish to thank the following individuals: Mrs. May Ivanoff for collecting the plant material, Dr. Christine Heller for collections on St. Lawrence Island and Noatak and for information concerning the medicinal use of *A. tilesii* Ledeb., Dr. Margaret Lantis for valuable correspondence, Dr. Quentin Jones for botanical identification, Dr. Merle T. Emerson and Mr. G. Caple for the n.m.r. spectra and Dr. Michael O'Dwyer for determining the optical rotatory dispersion curves. We are greatly indebted to Mr. George Young of the R. J. Reynolds Tobacco Company for the mass spectrographic analysis.

Experimental[16]

Isolation of Matricarin and Desacetylmatricarin.—Ground leaves and stems of *Artemisia tilesii* Ledeb., collected by Mrs. Ivanoff near Unalakleet, Alaska, in the fall of 1958 and 1959, wt. 19.5 lb., were extracted in a Lloyd extractor with chloroform for 2 days. The extract was freed of solvents, the residue taken up in hot ethanol and tannins precipitated with lead acetate solution. The usual work-up[17] gave 42 g. of viscous residue which was taken up in 100 ml. of benzene and chromatographed over 280 g. of alumina (Alcoa F-20). The chromatogram was eluted successively with benzene, benzene–ether, ether and methanol, 100-ml. fractions being collected.

Fractions 2 and 3 (benzene) gave 6.6 g. of crystalline material, colorless plates after several crystallizations from benzene–petroleum ether and acetone–petroleum ether; m.p. 190–191°, $[\alpha]^{23}D$ +23.5° (*c* 0.65, $CHCl_3$); lit.[8] m.p. 193–195°, $[\alpha]^{20}D$ + 23°; m.p. undepressed on admixture of matricarin, infrared spectra superimposable, λ_{max} 255 mμ (ε 15 100).

Anal. Calcd. for $C_{17}H_{20}O_5$: C, 67.09; H, 6.62. Found: C, 67.31; H, 6.37.

The mother liquors from the crystallization of matricarin contained a mixture of matricarin and artilesin. Fractional crystallization from benzene–petroleum ether gave more matricarin of slightly lower m.p.; the more soluble artilesin could not be isolated in pure form. Evidence for its presence came from the hydrogenation of the mother liquors. This resulted in isolation of crude tetrahydroartilesin which was converted to the thioketal of m.p. 156–158° (*vide infra*).

Fractions 4–8 (benzene) gave gummy material which did not crystallize. Fractions 9–14 (benzene–ether, 4:1) furnished 0.7 g. of desacetylmatricarin which was recrystallized from benzene–acetone; m.p. 123–125° (foaming), resolidified and then melted at 143–146°.

Anal. Calcd. for $C_{15}H_{18}O_4 \cdot H_2O$: C, 64.27; H, 7.19. Found: C, 64.33; H, 7.02.

Treatment of desacetylmatricarin with acetic anhydride–pyridine at room temperature gave a quantitative yield of matricarin, m.p. 188–190°.

Fractions 15–16 (benzene–ether, 4:1), 17–18 (benzene–ether, 1:1), 19–29 (ether) and 30–35 (methanol) gave gummy residues which did not crystallize.

An attempt to reduce matricarin with zinc dust and acetic anhydride[6a] resulted in 70% recovery of starting material.

Leaves and stems of *Artemisia tilesii* Ledeb., collected by Mr. Bill Pippel in August, 1958, near Palmer, Alaska, yielded an extract which gave somewhat different proportions of artilesin and matricarin. The ground material, wt. 30 lb., was extracted and purified as described previously; the crude extract, wt. 63 g., was dissolved in 250 ml. of benzene and chromatographed over 260 g. of alumina (Alcoa F-20). The chromatogram was eluted successively with benzene and benzene–ether in 100-ml. portions.

Fraction 2 (benzene), gave 4.5 g. of crystalline material, m.p. 170–178°. Fraction 3 (benzene) gave a gum containing some crystals. Fractions 4–11 (benzene) and 12–24 (benzene–ether) did not crystallize. Fractions 3–6, wt. 27 g., were combined, dissolved in benzene and rechromatographed. Elution with benzene gave, in fractions 2 and 3, 3.6 g. of crystalline material; subsequent fractions did not crystallize. Recrystallization of the solid material, wt. 8.1 g., from petroleum ether–benzene gave crude artilesin containing some matricarin; wt. 5.6 g., m.p. 179–184°, $[\alpha]^{25}D$ + 18.8° (*c* 1.49, $CHCl_3$), λ_{max} 255 mμ (ε 13 700).

Systematic fractional crystallization of this material gave comparatively pure matricarin, m.p. 186–189°, which after catalytic hydrogenation could be converted to the thioketal of tetrahydromatricarin, m.p. 139–141° (*vide infra*). Crystalline material from the mother liquors was combined with crystalline material from the original recrystallization, dissolved in benzene and rechromatographed. The first eluate fraction (benzene) gave solid material, mainly artilesin, which was recrystallized from acetone–isopropyl ether; m.p. 183–184°, $[\alpha]^{25}D$ +18.8°, mixed m.p. with matricarin 174–187°. This artilesin was still somewhat impure as shown by the following experiment. Hydrogenation gave solid material which could be converted *in toto* to the thioketal of tetrahydroartilesin, m.p. 152–155°. However, if the hydrogenated material was recrystallized several times from benzene–petroleum ether, there was obtained, in poor yield, slightly impure tetrahydromatricarin, m.p. 173–176°, $[\alpha]^{23}D$ +32.7° which was identified through the thioketal, m.p. 139–135°.

Desacetyltetrahydromatricarin.—A solution of 0.3 g. of desacetylmatricarin in 30 ml. of 95% ethanol was hydrogenated with 22 mg. of prereduced platinum oxide catalyst at atmospheric pressure; hydrogen uptake (23°) observed 53 ml., calcd. for two double bonds 52.4 ml. The solvent was removed and the residue recrystallized repeatedly from petroleum ether–benzene; m.p. 182–185°, yield 0.14 g.

Anal. Calcd. for $C_{15}H_{22}O_4$: C, 67.64; H, 8.33. Found: C, 68.04; H, 8.57.

Acetylation with acetic anhydride–pyridine gave tetrahydromatricarin, no depression on admixture of an authentic sample prepared by reduction of matricarin.

Tetrahydromatricarin.—A solution of 1 g. of matricarin in 150 ml. of 95% ethanol was reduced with 0.25 g. of 5% palladium–charcoal at atmospheric pressure and 23°; calculated hydrogen uptake for two double bonds 160 ml., found 160 ml. The solvent was removed and the residue recrystallized from benzene–petroleum ether; yield 0.79 g. The colorless needles melted at 175–178°, $[\alpha]^{22}D$ + 32.3° (*c* 1.92, $CHCl_3$); lit.[8] m.p. 180–182°, $[\alpha]^{20}D$ +18.6°; rotatory dispersion curve, determined on a recording Rudolph spectropolarimeter in dioxane (*c* 0.90): $(\alpha)_{700}$ + 18°, $(\alpha)_{589}$ + 23°, $(\alpha)_{327}$ + 343°, $(\alpha)_{320}$ +271 (infl.), $[\alpha]_{300}$ − 171° (infl.), $(\alpha)_{292}$ − 218°.

Anal. Calcd. for $C_{17}H_{24}O_5$: C, 66.21; H, 7.85. Found: C, 66.17; H, 7.95.

The ethylene thioketal was prepared as follows: Tetrahydromatricarin, wt. 0.75 g., was mixed with 0.34 g. of ethanedithiol and 4 ml. of boron trifluoride etherate. After 12 hours, the mixture was decomposed with ice, extracted with ether, the ether extract washed, dried and concentrated. The residue solidified on standing and was recrystallized from aqueous methanol; yield 0.75 g., m.p. 139–141°.

Anal. Calcd. for $C_{19}H_{28}O_4S_2$: C, 59.36; H, 7.35. Found: C, 59.21; H, 7.78.

When the hydrogenation of 0.4 g. of matricarin was carried out with 0.1 g. of Lindlar catalyst and interrupted after the absorption of one mole-equivalent of hydrogen, the solvent removed and the residue chromatographed over neutral alumina (activity III, solvent and eluent benzene), the first fractions furnished 42 mg. of crystalline material which was recrystallized from petroleum ether–acetone; m.p. 179–181°, $[\alpha]^{24}D$ − 65.3° (*c* 0.95, $CHCl_3$), λ_{max} 248 and 302 mμ (ε 9500 and 273); infrared bands at 1770, 1735, 1710 and 1610 cm.$^{-1}$.

Anal. Calcd. for $C_{17}H_{22}O_5$: C, 66.65; H, 7.24. Found: C, 67.29; H, 6.83.

In another run using 5% palladium–calcium carbonate, there was obtained, from the first three fractions, 53 mg. of the above and from the fourth fraction, 10 mg. of an isomer which was recrystallized from petroleum ether–benzene;

(16) M.p.'s and b.p.'s are uncorrected. Analyses by Dr. Weiler and Dr. Strauss, Oxford, England. Infrared spectra were run on a Perkin-Elmer Infracord spectrophotometer; ultraviolet spectra were run on a Cary model 14 ultraviolet spectrophotometer in 95% ethanol solution.

(17) W. Herz and R. B. Mitra, *J. Am. Chem. Soc.*, **80**, 4876 (1958); W. Herz, R. B. Mitra and P. Jayaraman, *ibid.*, **81**, 6061 (1959).

m.p. 150–152°, infrared spectrum similar to the above. It is possible that this compound is derived from artilesin.

Anal. Calcd. for $C_{17}H_{22}O_5$: C, 66.65; H, 7.24. Found: C, 66.87; H, 7.27.

Desoxotetrahydromatricarin.—Desulfurization of 0.75 g. of the preceding thioketal with Raney nickel in ethanol yielded a solid which, after several recrystallizations from petroleum ether, gave colorless pillars, m.p. 118°, $[\alpha]^{23}D$ +29.2° (*c* 9.66, $CHCl_3$), yield 0.48 g.

Anal. Calcd. for $C_{17}H_{26}O_4$: C, 69.36; H, 8.90. Found: C, 69.22; H, 8.95.

Desacetyldesoxotetrahydromatricarin.—A solution of 0.34 g. of desoxotetrahydromatricarin in 122 ml. of methanol was mixed with potassium carbonate in 25 ml. of water and allowed to stand at room temperature for 2 days. The solution was acidified with 0.82 ml. of acetic acid, methanol was removed *in vacuo* and the aqueous layer extracted with ether. The ether extract was dried, evaporated and the solid residue recrystallized from petroleum ether–acetone; yield 0.3 g. The silky crystals melted at 138°, $[\alpha]^{23}D$ +38.2° (*c* 1.52, $CHCl_3$), infrared band (CCl_4) at 1780 cm.$^{-1}$ (γ-lactone).

Anal. Calcd. for $C_{15}H_{24}O_3$: C, 71.39; H, 9.59. Found: C, 71.12; H, 9.77.

Reacetylation of 30 mg. of this substance with acetic anhydride and pyridine gave 26 mg. of material, m.p. 119°, mixed m.p. with desoxotetrahydromatricarin m.p. 118–119°. The infrared spectra were completely superimposable.

Dehydrodesacetyldesoxotetrahydromatricarin.—A mixture of 0.22 g. of the preceding compound and 66 mg. of chromic acid in 20 ml. of acetic acid was allowed to stand in the refrigerator for 2 days. The solution was neutralized and the product extracted with ether. Removal of solvent from the washed and dried ether extract yielded 0.12 g. of an oil which was distilled, b.p. 155° (0.4 mm., air-bath). It solidified on standing and was recrystallized from aqueous methanol. The colorless needles melted at 53–55°, $[\alpha]^{25}D$ −24.1° (*c* 1.08, $CHCl_3$); infrared bands at 1780 (γ-lactone), 1705 (ketone) and 1405 cm.$^{-1}$. The substance gave a positive Zimmermann test, but the color disappeared within one minute.

Anal. Calcd. for $C_{15}H_{22}O_3$: C, 71.97; H, 8.86. Found: C, 72.49; H, 9.12.

A mixture of 100 mg. of this substance, 15 ml. of dioxane, 2 ml. of deuterium oxide and 6 drops of deuterium chloride solution was heated on the steam-bath under nitrogen for 31 hours. The solvent was removed and the residue taken up in ether. The residue solidified on standing and was recrystallized from aqueous methanol; yield 41 mg., m.p. 55°, undepressed on admixture of starting material. There were some changes in the fingerprint region of the infrared spectrum, but the band at 1405 cm.$^{-1}$ had not disappeared. Mass spectrographic analysis indicated the presence of 2.47 atoms of deuterium. The material was a mixture of 7.6% mono-, 35.2% di-, 56% tri- and 1.2% tetradeutero derivative.

Tetrahydroartilesin.—A solution of 1.0 g. of crude artilesin (containing also some matricarin) in 150 ml. of 95% ethanol was hydrogenated with 0.25 g. of 5% palladium–charcoal at atmospheric pressure; calculated hydrogen uptake (23°) 160 ml., observed 160.5 ml. The solvent was removed and the residue dissolved in benzene. Dilution gave colorless crystals, yield 0.63 g., m.p. 170–174°, depression on admixture of tetrahydromatricarin.

The thioketal was prepared from 1.0 g. of this material in the same manner as described for tetrahydromatricarin. The oily material solidified on standing and was recrystallized from aqueous methanol; yield 1 g., m.p. 148–150°. Two additional recrystallizations raised the m.p. to 156–158°. There were significant differences in the fingerprint region of the two thioketals.

Anal. Calcd. for $C_{19}H_{28}O_4S_2$: C, 59.36; H, 7.35. Found: C, 59.65; H, 7.65.

Desoxotetrahydroartilesin.—A mixture of 1.0 g. of the preceding thioketal and two and a half teaspoons of Raney nickel in 130 ml. of absolute ethanol was refluxed, with stirring, for 20 hours. The catalyst was removed by filtration and the filtrate and washings evaporated at reduced pressure. The residue crystallized on standing and was recrystallized from petroleum ether–acetone; yield 0.56 g., m.p. 102–104°, $[\alpha]^{25}D$ +91.7° (*c* 5.79, $CHCl_3$).

Anal. Calcd. for $C_{17}H_{26}O_4$: C, 69.36; H, 8.90. Found: C, 68.99; H, 8.87.

Desacetyldesoxotetrahydroartilesin.—A solution of 0.5 g. of desoxotetrahydroartilesin, 180 ml. of methanol, 1.2 g. of potassium carbonate and 36 ml. of water was allowed to stand at room temperature for 2 days. Neutralization with acetic acid followed by removal of methanol at reduced pressure gave a solid which was recrystallized from petroleum ether–acetone; yield 0.24 g., m.p. 138–139°, $[\alpha]^{27}D$ +97.4° (*c* 1.17, $CHCl_3$).

Anal. Calcd. for $C_{15}H_{24}O_3$: C, 71.39; H, 9.59. Found: C, 71.84; H, 9.06.

Reacetylation with acetic anhydride–pyridine gave crystals, m.p. 103°, undepressed on admixture of desoxotetrahydroartilesin, infrared spectra superimposable.

Dehydrodesacetyldesoxotetrahydroartilesin.—A mixture of 0.19 g. of desacetyldesoxotetrahydroartilesin, 56 mg. of chromic oxide and 17 ml. of acetic acid was allowed to stand in the refrigerator for 48 hours, neutralized with dilute sodium hydroxide solution, extracted with ether, the ether extract washed, dried and evaporated. The residue solidified on standing and was recrystallized from aqueous methanol. The product melted at 84–85°, $[\alpha]^{25}D$ +92.3° (*c* 1.22, $CHCl_3$), yield 0.14 g.

Anal. Calcd. for $C_{15}H_{22}O_3$: C, 71.97; H, 8.86. Found: C, 72.06; H, 8.91.

This substance gave a positive Zimmermann test which faded within 1 minute. The infrared spectrum (CCl_4) exhibited bands at 1790 (lactone), 1710 (ketone) and a shoulder at 1400 cm.$^{-1}$. From an attempted condensation with piperonal, 35% of starting material was recovered.

Isomerization of Tetrahydromatricarin.—A mixture of 0.5 g. of tetrahydromatricarin (m.p. 170–175°), 180 ml. of methanol, 1.2 g. of potassium carbonate and 35 ml. of water was allowed to stand at room temperature for 48 hours. The product was isolated in the usual manner. The resulting gum, wt. 0.31 g., could not be induced to crystallize even after chromatography. It exhibited infrared bands at 3600 (OH), 1780 (γ-lactone) and 1740 cm.$^{-1}$ (cyclopentanone). Acetylation with acetic anhydride–pyridine in the usual fashion gave, after crystallization from petroleum ether–acetone, 0.12 g. of colorless pillars, m.p. 173–174°, $[\alpha]^{25}D$ −94.3° (*c* 1.58, $CHCl_3$), infrared bands at 1780 (γ-lactone) and 1735 cm.$^{-1}$ (double-strength, combination of cyclopentanone and acetate); rotatory dispersion curve in dioxane (*c* 0.515): $(\alpha)_{700}$ −78°, $(\alpha)_{589}$ −107°, $(\alpha)_{327}$ −2640°, $(\alpha)_{320}$ −2235° (infl.), $(\alpha)_{282}$ +1945°. The fingerprint region of this material differed distinctly from the fingerprint region of tetrahydromatricarin and tetrahydroartilesin.

Anal. Calcd. for $C_{17}H_{24}O_5$: C, 66.21; H, 7.85. Found: C, 67.05; H, 7.74.