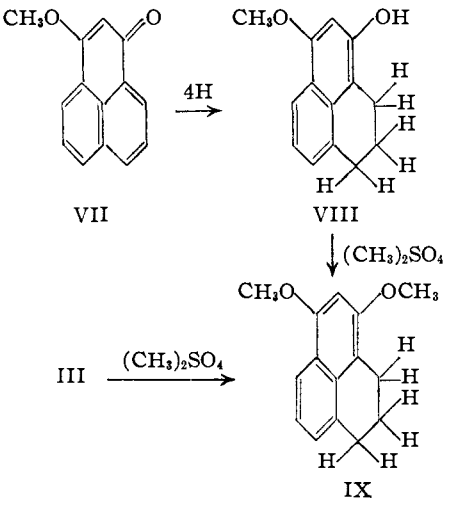

9-Methoxyperinaphthenone (VII).—7,9-Diketoperinaphthane was alkylated by means of dimethyl sulfate in aqueous sodium hydroxide solution. The product was recrystallized with difficulty from a benzene–heptane solution in the form of brown crystals, m.p. 142–146° (lit.[7] 144°).

Reduction of 7,9-Diketoperinaphthane.—Several attempts to reduce the diketone by means of lithium aluminum hydride in ether or in tetrahydrofuran were carried out by refluxing the hydride solution under a Soxhlet extractor containing the ketone. The only solid isolated from the reaction mixture was the starting material. Similarly, sodium borohydride in aqueous sodium hydroxide appeared to be without action on the diketone.

A suspension of 3 g. of 7,9-diketoperinaphthane in 250 ml. of ethanol was hydrogenated in the presence of Raney nickel at 40 lb. pressure and at room temperature for two hours. The catalyst was removed by filtration, the solution was concentrated over a steam-bath *in vacuo* and diluted with water which precipitated 1.6 g. of tan crystals, m.p. 163–166°. The aqueous filtrate was extracted with ether and the latter solution was concentrated to a small volume and extracted with sodium hydroxide solution. The alkaline solution was cooled in an ice-bath and acidified to yield an additional 1.0 g. of crude product. Recrystallization of the product from benzene–heptane solution (Darco) and finally from a small volume of benzene afforded very light orange crystals, m.p. 167–168.5°. The compound tended to darken and became less pure on further recrystallization. It was insoluble in 10% sodium carbonate solution, but dissolved readily in 10% sodium hydroxide solution.

The same reduction can be effected with Adams catalyst under the same conditions.

Anal. Calcd. for $C_{13}H_{12}O_2$: C, 77.98; H, 6.04. Found: C, 78.64; H, 6.03.

Reduction of 9-Methoxyperinaphthenone.—The use of lithium aluminum hydride in refluxing ether–dioxane or ether–benzene solution failed to effect the reduction of 9-methoxyperinaphthenone.

One-half gram of VII in 35 ml. of methanol absorbed 2 molar equivalents of hydrogen at room temperature and at atmospheric pressure in the presence of 100 mg. of Adams catalyst, the solution was filtered and the filtrate diluted with water. There was obtained 0.4 g. of orange needles, m.p. 115–119°. Two recrystallizations of the solid from cyclohexane–hexane solution yielded pale yellow needles, m.p. 118–120°. Repeated crystallizations using decolorizng agents did not effect any further purification. The compound was insoluble in 10% sodium carbonate solution but soluble in 10% sodium hydroxide solution.

The identical product was obtained when 1 g. of VII in the presence of 0.1 g. of copper chromite catalyst suspended in 10 ml. of methanol was hydrogenated at 100° and at 1300 lb./sq. in. for 1 hour.

Anal. Calcd. for $C_{14}H_{14}O_2$: C, 78.48; H, 6.59; CH_3O, 14.48. Found: C, 78.80; H, 6.73; CH_3O, 14.00.

Methylation of 1-Hydroxy-3-methoxyperinaphthane.—A solution of 1.2 g. of VIII in 10% sodium hydroxide was treated dropwise with 15 ml. of dimethyl sulfate at room temperature. The solution was maintained alkaline by the addition of more base as required. The insoluble product was filtered and recrystallized several times from aqueous methanol which afforded white crystals, m.p. 69–70°. A polymorphic modification was obtained which melted at 81–84°, and was readily converted to the lower melting form.

Anal. Calcd. for $C_{15}H_{16}O_2$: C, 78.92; H, 7.07; CH_3O, 27.19. Found: C, 78.77; H, 7.20; CH_3O, 26.96.

Methylation of 1,3-Dihydroxyperinaphthane.—The methylation was carried out as described above for VIII. The product was recrystallized from aqueous methanol and melted at 67–69°. There occurred no depression of the melting point on admixture of this compound with a sample obtained in the preceding experiment. The same polymorphic modifications were obtained in this instance.

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Steric Control of Asymmetric Induction in the *ortho*-Claisen Rearrangement

BY HAROLD HART

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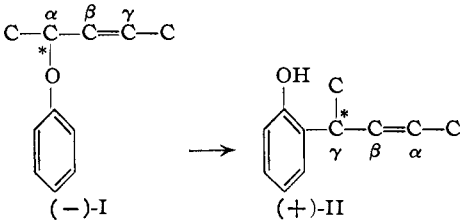
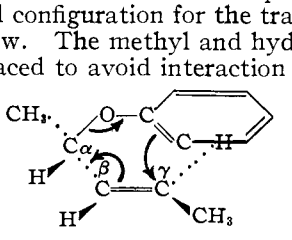
Alexander and Kluiber[1] showed that the Claisen rearrangement of (−)-α,γ-dimethylallyl phenyl ether gave (+)-2-(α,γ-dimethylallyl)-phenol. In



this rearrangement, asymmetry was destroyed at C_α and created at C_γ. But, because of the symmetry of the α,γ-dimethylallyl group, similar moieties are attached to the asymmetric carbon in both the ether and its rearrangement group, *i.e.*, hydrogen, methyl, propenyl and an aromatic group. Alexander and Kluiber suggested that retention of activity was consistent with the established cyclic mechanism proposed for this rearrangement,[2] and that one form of the transition state is preferred over the other because of steric interaction between the methyl on C_α and the hydrogen on C_β. This leads to an asymmetric synthesis.

It is the purpose of this note to make more explicit the explanation of Alexander and Kluiber, and to show that the configuration at C_γ in II will be identical with the configuration at C_α in I. This prediction, based on steric requirements in the transition state, is then substantiated by data taken from Alexander and Kluiber's paper.

A preferred configuration for the transition state is shown below. The methyl and hydrogen on C_α have been placed to avoid interaction between the



(1) E. R. Alexander and R. W. Kluiber, THIS JOURNAL, **73**, 4304 (1951).

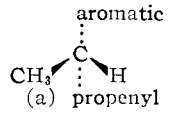
(2) See, for example, J. P. Ryan and P. R. O'Connor, *ibid.*, **74**, 5866 (1952).

methyl and the hydrogen on C_β. Approach of the aromatic ring to C_γ is then from above the plane of the C_β–C_γ double bond. If the C_α–C_β bond were rotated so as to allow approach of the phenyl from below the plane of the double bond, there would be steric interaction between the C_α-methyl and the C_β-hydrogen. Reversal of the positions of the methyl and hydrogen on C_α would favor the transition state in which the aromatic ring approaches from below the plane of the double bond. In either case, if steric interaction between the C_α-methyl and the C_β-hydrogen is to be minimized, then one must predict that the configuration at C_γ in the alkylated phenol will be the same as that at C_α in the ether.[3]

We have recently demonstrated[4] that both Claisen O- and C-alkylation proceed with inversion. The products from the O- and C-alkylation of a phenol by an asymmetric alkyl halide will then have identical configurations. In the preparation of (−)-I by the Claisen procedure, Alexander and Kluiber also isolated some C-alkylate (II) which had a (+) rotation. Presumably, then, (−)-I and (+)-II have the same configurations. Claisen rearrangement of (−)-I gave (+)-II. These facts are clearly consistent with the proposal outlined above that the control of asymmetric induction in the transition state has steric origins.

para-Claisen rearrangement is more difficult to interpret. The *ortho* methyl groups become sterically involved, both in the first stage of the rearrangement (to the 2,2,6-trialkyldienone[5]) and in the second stage (to the 2,4,6-trialkyldienone). Examination of the models shows no clear-cut preferred orientation. Alexander and Kluiber's results indicate that (−)-α,γ-dimethylallyl 2,6-xylyl ether and (+)-4-(α,γ-dimethylallyl)-2,6-xylenol are configurationally related (based on O- and C-alkylation results). Rearrangement of the ether gave product of very low rotation (−0.08°) which indicates only slight stereospecificity in the *para* rearrangement.

(3) For the case shown, this would be (a). The C_β–C_γ bond is represented as *trans* because Alexander and Kluiber used *trans*-crotonaldehyde in their synthesis.



(a) propenyl

(4) H. Hart and H. S. Eleuterio, THIS JOURNAL, **76**, 516, 519 (1954).

(5) H. Conroy and R. A. Firestone, *ibid.*, **75**, 2530 (1953); K. Schmid, *et al.*, *Experientia*, **9**, 414 (1953); D. Y. Curtin and H. W. Johnson, Jr., THIS JOURNAL, **76**, 2276 (1954).

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Relationship of Anthricin, Hernandion and Cicutin to Desoxypodophyllotoxin

BY JONATHAN L. HARTWELL AND ANTHONY W. SCHRECKER

RECEIVED APRIL 1, 1954

Since our last paper on silicicolin,[1] new findings have been made which have enabled us to settle the structure and identity of the isomeric lactonic lignans anthricin, hernandion and cicutin. Anthricin and hernandion are shown to be identical with silicicolin (desoxypodophyllotoxin, DPT), while cicutin is essentially desoxypicropodophyllin (DPP), the C_3-epimer. The new data and their significance form the subject of this communication.

Anthricin.—This compound, isolated[2] from the roots of *Anthriscus sylvestris* Hoffm. (Fam. *Umbelliferae*) (wild chervil) had the physical constants given in Table I. It was believed[1] to consist essentially of DPT.

TABLE I

PHYSICAL CONSTANTS OF LACTONES, $C_{22}H_{22}O_7$

Substance	M.p., °C.	$[\alpha]_D$, degrees Chloroform	Pyridine
Desoxypodophyllotoxin (DPT) (Silicicolin)[1]	168–169	−115	−181
Desoxypicropodophyllin (DPP) (Silicicolin-B)[1]	170.5–172	+ 32	+ 43
Anthricin[2]	168	.....	−142.54
Anthricin[a]	167–169	−112	−171
Isoanthricin[2,b]	170	.....	−127.87
Isoanthricin[a]	170.5–171.5	.....	+ 45.5
Hernandion[3]	167–168	−112.4	.....
Isohernandion[3]	169–170	+ 36.6	.....
Cicutin[4]	171	.....	.....
Cicutin[1,a]	168.7–169.4	+ 15.2	− 14.4
Cicutin[c]	171–172	.....	+ 49
Desoxypodophyllic acid[1,d]	171–173(efferv.)	.....	−165

[a] Determined by us on a sample kindly provided by the original investigator. [b] Formulated as a monohydrate. [c] Purified compound, this paper. [d] Hydroxy acid, $C_{22}H_{24}O_8$.

An authentic specimen, recently received from Dr. Kawanami, gave no mixed melting point depression with DPT, the infrared spectra were identical, and the optical rotations in chloroform and pyridine showed a close correspondence with those of DPT, thus demonstrating the identity.

Isoanthricin.—This substance, prepared by base-catalyzed epimerization of anthricin, should be identical with DPP. A mixed melting point determination of a sample, provided by Dr. Kawanami, with DPP showed no depression, and the infrared spectrum and optical rotation in pyridine were confirmatory. However, our value for the specific rotation (+45.5°) differs remarkably from the value reported[2] by the authors (−127.87°). Our explanation for this discrepancy is that the Japanese investigators originally did not have the pure lactone but the hydroxy acid containing some lactone, and that the compound spontaneously lactonized during the twelve or more years since its isolation. We prepared this hydroxy acid[1] and called it desoxypodophyllic acid; its physical constants are given in Table I. This explanation is borne out by the original analysis of isoanthricin[2] which indicated one additional molecule of water, and the comparison of its original[2] optical rotation (−127.87°) with those of desoxy-

(1) J. L. Hartwell, A. W. Schrecker and J. M. Johnson, THIS JOURNAL, **75**, 2138 (1953).

(2) K. Noguchi and M. Kawanami, *J. Pharm. Soc. Japan*, **60**, 629 (1940). This paper had never been abstracted by the usual abstract journals. Prof. W. J. Gensler of Boston University kindly notified us of its existence, and one of us (J.L.H.) arranged for its abstracting [*C. A.*, **47**, 6386a (1953)].