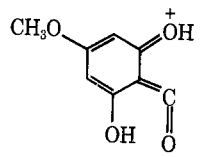
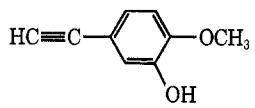
indicating that each aromatic ring contained one methoxyl group.



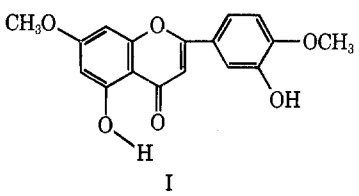
A



B

These spectral findings were supported by converting pilloin to both luteolin and luteolin tetramethyl ether.

Pilloin was shown to be different by direct comparison (ir, tlc, melting point, and mixture melting point) with velutin, luteolin 3′,7-dimethyl ether,[2] and, since the ultraviolet spectral curve with $AlCl_3$ (a bathochronic shift of 24 mμ of band I)[3] and ir (band at 3300 cm^{-1} for a hydrogen-bonded C-5 hydroxyl group) data established the presence of a C-5 hydroxyl group, pilloin must be the previously undescribed luteolin 4′-7-dimethyl ether (I). The ultraviolet spectrum in sodium acetate–ethanol confirmed that the 4′ position was blocked.[3]



I

Experimental Section[4]

Pilloin (3′,5-Dihydroxy-5′,7-dimethoxyflavone).—Leaves and branches of *Ovidia pillo-pillo* were collected in December 1968, in Los Ulmos, about 10 km south of Valdivia, Chile. Dried and ground material (2 kg) was extracted three times with 6 l. of ethanol at 50° for 12 hr. The ethanolic extract was concentrated under vacuum to give a syrup, which was poured into water (2 l.). The precipitate was discarded and the aqueous solution was then extracted with chloroform. On concentration a dark yellow precipitate was obtained, which was recrystallized from a methanol–chloroform mixture (2:1); with a yield of 0.2 g of pilloin: mp 235.5–236.5°; uv max 250, 270, and 330 mμ (log ε 4.13, 4.15, and 4.21); ir (KBr) 3300 (OH), 1660 (C=O), 1605, 1506, and 1455 (C=C), 813 cm^{-1} (two adjacent free hydrogen atoms); nmr (pyridine-d_5) 3.77 (s, OCH_3), 3.81 (s, OCH_3), 4.94 (s, 3′-OH), 6.61 (s, 2, 6 H and 8 H), 7.00 (s, 3 H), 7.08 (d, J = 8 Hz, 5′ H), 7.59 (q, J = 8, 2 Hz, 6′ H), and 7.89 (d, J = 2 Hz, 2′ H); mass spectrum 314 (parent), 285 (M − 29), 271 (M − 43), 167 ($C_8H_7O_4$), 148 ($C_9H_8O_2$), 138 ($C_7H_6O_3$), 133 ($C_8H_5O_2$), and 123 ($C_7H_7O_2$).

Anal. Calcd for $C_{17}H_{14}O_6$: C, 64.96; H, 4.49. Found: C, 64.60; H, 4.76.

3′,5-Diacetoxy-4′,7-dimethoxyflavone.—Treatment of pilloin with acetic anhydride–pyridine formed the diacetate: uv max 232, 260, and 321 mμ (log ε 4.37, 4.17, and 4.46); nmr ($CDCl_3$) 2.35 (s, $OOCCH_3$), 2.42 (s, $OOCH_3$), 3.78 (s, $2OCH_3$), 6.47 (s, 3 H), 6.58 and 6.83 (each d, J = 2 Hz, 6 H and 8 H), 7.02 (d, J = 8.5 Hz, 5′ H), 7.54 (d, J = 2 Hz, 2′ H), 7.69 (q, J = 8.5, 2 Hz, 6′ H).

3′,5-Diethoxy-4′,7-dimethoxyflavone.—Ethylation of pilloin with diethyl sulfate–potassium carbonate gave the diethoxy derivative: mol wt 370 (mass spectrum); nmr ($CDCl_3$) 1.53 (2 t, 6, CH_2CH_3), 4.16 (2 q, 4, CH_2CH_3), 3.88 and 3.93 (each s, OCH_3), 6.33 and 6.51 (each d, J = 2 Hz, 6 H and 8 H), 6.52 (s, 3 H), 6.93 (d, J = 8 Hz, 5′ H), 7.30 (d, J = 2 Hz, 2′ H), 7.46 (q, J = 8, 2 Hz, 6′ H).

3′,4′,5,7-Tetramethoxyflavone.—Methylation of pilloin with dimethyl sulfate–potassium carbonate formed the tetramethoxy derivative, which was crystallized from benzene: mp 190–191° (lit.[5] mp 192–193°); mass spectrum 342 (parent), 341 (M − 1), 313 (M − 29), 312 (M − 30), 162 ($C_{10}H_{10}O_2$), 152 ($C_8H_8O_3$), 147 ($C_9H_7O_2$), 137 ($C_8H_9O_2$).

3′,4′,5,7-Tetrahydroxyflavone, Luteolin.—Demethylation of pilloin with hydrogen iodine gave luteolin. The ultraviolet spectra in ethanol was identical with an authentic sample of luteolin.[6] The ultraviolet shifts with sodium acetate–ethanol were almost identical with those reported for luteolin.[7]

Registry No.—1, 32174-62-2; 1 deacetate, 32174-63-3; 1 diethyl ether, 32174-64-4; 1 tetramethyl ether, 855-97-0.

Acknowledgments.—I wish to express my thanks to Dr. Juan Garbarino, Universidad Católica de Chile, for helpful discussions, and to Mr. Aurelio Reyes for his participation in early phases of this work. Thanks are also due to Professor F. Marcus for his help with the preparation of the manuscript.

(2) K. C. Das, W. J. Farmer, and B. Weinstein, *J. Org. Chem.*, **35**, 3989 (1970). The author thanks Professor B. Weinstein, University of Washington, for a sample of velutin.

(3) L. Jurd in "The Chemistry of Flavonoid Compounds," T. A. Geissman, Ed., Macmillan, New York, N. Y., 1962, p 107.

(4) Melting points are uncorrected. Mass spectrum, nuclear magnetic resonance (internal tetramethylsilane, 100 MHz) and mycroanalysis were generously provided by the University of Zurich, through Dr. Jorge Naranjo, whose cooperation I gratefully thank. Thin layer chromatography employed silica gel G as a support, chloroform as the developer, and iodine for detection.

(5) J. Grinpenberg in "The Chemistry of Flavonoid Compounds," T. A. Geissman, Ed., Macmillan, New York, N. Y., 1962, p 406.

(6) The author thanks Professor C. Galeffi, Instituto Chimico dell'Universitá, Torino, and Professor S. Tira, Instituto Superiore di Sanitá, Roma, for samples of luteolin.

(7) B. Valdes, *Phytochemistry*, **9**, 1253 (1970).

A Directing Effect of Oxygen in Perhydrophthalans

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Pasto's recent evaluation of the directive effects caused by a 3-alkyl group in substituted cyclohexenes[2] prompts us to report our work related to this problem. As part of an investigation directed toward the synthesis of guaianolide sesquiterpenes, we chose as one of our models 7-methyl-*cis*-3a,4,7,7a-tetrahydrophthalan-5-one (2), presumably to be prepared by a sequence as delineated in eq 1.[3] It became apparent during the early phases of our research, however, that we might be able to observe some directive effects caused by the phthalan oxygen during hydration of **1**, and we accordingly attempted an analysis of regiospecific[7] directive effects. Of the several methods available for hydration we chose to investigate hydroboration with diborane and disiamylborane and oxymercuration. In all cases studied, the alcohols resulting from the hy-

(1) NDEA Predoctoral Fellow, 1968–1971.

(2) D. J. Pasto and J. A. Gontarz, *J. Amer. Chem. Soc.*, **92**, 7480 (1970).

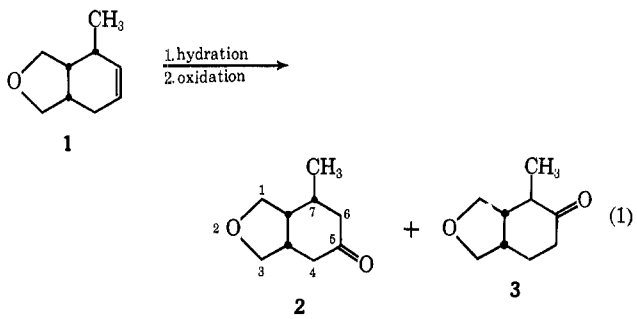
(3) The ease of preparation of phthalan derivatives has resulted in their occasional use as models for the corresponding carbocyclic systems. The various oxygen-containing models have been useful for mechanism studies[4] and synthetic work.[5] The question of whether there are electronic and directive effects associated with the heteroatom has been raised.[6]

(4) E. L. Eliel and C. Pillar, *J. Amer. Chem. Soc.*, **77**, 3600 (1955).

(5) A. P. Krapcho and B. P. Mundy, *J. Org. Chem.*, **32**, 2041 (1967).

(6) B. Rickborn and S. Y. Lwo, *ibid.*, **30**, 2212 (1965).

(7) A. Hassner, *Accounts Chem. Res.*, **4**, 9 (1971).



drations were immediately subjected to Jones oxidation, and the ketones were analyzed.[8]

The results of several experiments are summarized in Table I, along with a parallel study on the conforma-

TABLE I

HYDRATIONS OF 1 AND 3-METHYLCYCLOHEXENE

Expt no.	Hydration method	Ketone ratio— 2	3
	1. hydration 1 ⟶ 2 + 3 2. Jones oxidation		
1	B_2H_6/H_2O_2, OH^-	40	60
2	R_2BH/H_2O_2, OH^-	62	38
3	$Hg(OAc)_2/OH^-$, NaBH	82	18
3-methylcyclohexene ⟶ 3-methylcyclohexanone + 2-methylcyclohexanone		A	B
		A	B
1[a]	B_2H_6/H_2O_2, OH^-	46	54
2[b]	R_2BH/H_2O_2, OH^-	33	67
3	$Hg(OAc)_2/OH^-$, $NaBH_4$	88	12
4	$Hg(O_2CPh)_2/OH^-$, $NaBH_4$	87	13
	R_2BH designates disiamylborane		

[a] See ref 9 and H. C. Brown and G. Zweifel, *J. Amer. Chem. Soc.*, **83**, 2544 (1961). [b] Brown (footnote *a*) has reported that disiamylborane attacks equally at C-2 and C-3. We have repeated our experiments several times and consistently get the results reported in Table I. It is not easy to reconcile these differences, however; a reasonable explanation invoking allylic strain[10] accounts for our results.

tionally less homogeneous 3-methylcyclohexene. The ketones **2** and **3** could be separated by glc for quantitative analysis; however, column chromatography was the method of choice for separation and purification on a preparative scale. Identification and structure assignment of **2** and **3** was accomplished after deuterium exchange of the α hydrogens by examining, *via* nmr, the loss of the methyl doublet for **3**.

From the data in Table I it is evident that directive effects do exist, both for **1** and 3-methylcyclohexene. For 3-methylcyclohexene the directive effects must be due to the methyl group, and there is the possibility of competing inductive and steric effects.[9] The conformationally more rigid **1** can exhibit similar effects due to its methyl group as well as effects associated with the fused tetrahydrofuran system.

(8) We realize that some important stereochemical data was lost in the conversion of the alcohols to the ketones. However, our initial studies were not concerned with any chemistry of the alcohols and we did not try to analyze them. Also, conversion to the ketone greatly reduces the analytical problems associated with the evaluation of gross directive effects.

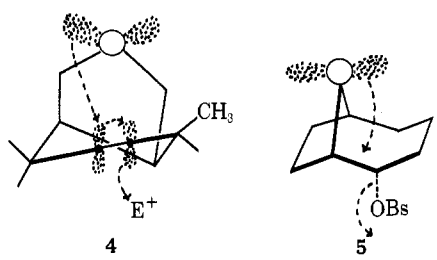
(9) D. J. Pasto and F. M. Kline, *J. Org. Chem.*, **33**, 1468 (1968).

Because of the conformational inhomogeneity of 3-methylcyclohexene, it is difficult to establish the source of directive effects. Diborane, a relatively small and highly reactive molecule, shows little regiospecificity, although there is a stereospecificity of addition trans to the methyl group.[9] Steric effects associated with oxymercuration should be expected to be minimal because of the low *A* values of mercury. However, the sevenfold preference of C-2 as the site of reaction with mercury demonstrates that this is the more nucleophilic carbon. An explanation for this increased nucleophilicity might be to attribute a fairly substantial inductive role to the methyl group. Alternately, the preferential addition may be a reflection of torsional angle effects.[2]

Hydroboration of 3-methylcyclohexene with disiamylborane again demonstrates that C-2 is the more reactive carbon, and the lesser reactivity of the hindered borane allows for the selectivity in reaction sites. The lack of steric interaction with the methyl group might be attributed to the 3-methylcyclohexene molecule adopting a reaction conformation in which the methyl group becomes axial, a condition quite common when considering conformations exhibited by molecules to relieve allylic strain.[10] Thus, the methyl group contributes little steric effect, but can maintain its inductive ability.

Examining the results of the phthalan reactions, it can be noted that *only those results obtained by hydration with disiamylborane are not consistent with the 3-methylcyclohexene data.* Since **1** is conformationally more rigid than 3-methylcyclohexene, it is not unreasonable that an interaction of the methyl group with the bulky hydroborating agent would occur. Why, however, is there not a dramatic steric effect noted?

An examination of several types of molecular models leads to the suggestion that the phthalan oxygen is playing a role in directing the course of reactions for the system. Because of the interaction of the methylene protons of C-3 with the methyl protons, the molecule is twisted in such a way that the ether oxygen orbitals lie directly over C-6. Thus, addition of any electrophilic agent to C-5 of **4** will result in a transition-state stabilization of the incipient positive charge at C-6. Although there would be a methyl steric effect, the increased reactivity of C-5 (due to oxygen participation and methyl induction) would force the boron to preferentially add to C-5.[11] Long range oxygen-



(10) F. Johnson, *Chem. Rev.*, **68**, 375 (1968).

(11) At this time we have no evidence related to the steric course of addition of the various hydrating agents. However, considering that both the hydroboration and oxymercuration reactions are run in excess tetrahydrofuran, we would suggest that there is no particular requirement for the hydrating agents to preferentially coordinate with the phthalan oxygen. We have also established with *cis*-3a,4,7,7a-tetrahydrophthalan that electrophilic addition occurs primarily anti to the phthalan ring. Details regarding the electronic and stereochemical course of addition to *cis*-3a,4,7,7a-tetrahydrophthalan will be presented in another paper.

orbital stabilization has been suggested by Paquette[12] for the solvolysis of **5**.

Experimental Section

The infrared spectra were recorded on a Beckman IR-5 instrument. Nuclear magnetic resonance spectra were recorded on a Varian A-60 spectrometer, using TMS as an internal standard and deuteriochloroform as solvent. Melting and boiling points are not corrected. Gas chromatographic analysis were performed on an F & M Model 400 unit, using a hydrogen flame detector and Disc integrator.

Preparation of 4-Methyl-*cis*-3a,4,7,7a-tetrahydrophthalan (1).—The known *cis*-3-methyl-4-cyclohexene-*cis*-1,2-dicarboxylic acid anhydride[13] (60 g) was dissolved in 600 ml of anhydrous ether and this was added to a refluxing solution prepared from 15.2 g of lithium aluminum hydride in 600 ml of anhydrous ether. After hydrolyzing the reaction mixture, the ethereal layer was separated, dried, and distilled [116–124° (0.5 mm)] to yield 33.0 g (59%) of a crude diol. The diol (21 g) was immediately dissolved in 40 ml of dry pyridine and heated to reflux while 38 g of *p*-toluenesulfonyl chloride in 40 ml of pyridine were added. The reaction mixture was refluxed for 12 hr, cooled, and poured over an ice–sulfuric acid mixture. The product was extracted with pentane and distilled to yield 14 g (73%) of a water-clear liquid, bp 44–48° (0.2 mm). The infrared spectrum exhibited the characteristic ether linkage of tetrahydrofuran derivatives at 9.2 μ (1087 cm^{-1}).

Anal. Calcd for $C_9H_{14}O$: C, 78.21; H, 10.21. Found: C, 78.00; H, 10.14.

Hydration of 1 by Hydroboration.—Sodium borohydride (1.43 g) was added to a solution containing 3.5 g of **1** and 15 ml of anhydrous THF. The reaction mixture was placed under a nitrogen atmosphere at 0° and BF_3 etherate (9.3 g, 0.056 mol) was slowly added. After hydrolysis of the boron complex, the reaction mixture was warmed to room temperature. After about 12 hr, the mixture was extracted with ether to yield a crude alcohol mixture. This was immediately subjected to Jones oxidation, giving the liquid ketones **2** and **3**, bp 76–82° (10 mm). These could be separated on a 6 ft × 6 mm glass column packed with 20M Carbowax on 30/60 firebrick or by column chromatography utilizing a 30 × 60 mm water-cooled column packed with silica gel (14 g silica gel G, 30 ml of H_2O, activated for 45 min) and eluted with solvent [chloroform–ether–pentane (55:28:17)]. The identity of **3** was established by deuterium exchange. No distinguishing features could be noted in the infrared spectrum. The nmr spectra of the ketones were consistent with the assigned structures. The 2,4-dinitrophenylhydrazones of **2** (mp 164–165°) and **3** (mp 176–177°) were prepared.

Anal. Calcd for $C_{15}H_{18}N_4O_5$ (the 2,4-dinitrophenylhydrazone of **2**): C, 53.89; H, 5.43. Found: C, 53.81; H, 5.31. Calcd for $C_{15}H_{18}N_4O_5$ (the 2,4-dinitrophenylhydrazone of **3**): C, 53.89; H, 5.43. Found: C, 53.92; H, 5.55.

Hydration of 1 by Disiamylborane.—The disiamylborane was prepared and used according to the procedure of Brown.[14] Products were worked up and after Jones oxidation the ketones were subjected to analytical glc.

Hydration of 1 by Oxymercuration–Demercuration.—Utilizing the procedure of Brown,[15] the alkene **1** was converted to the alcohol mixture and after Jones oxidation the ketones were analyzed.

Hydrations of 3-Methylcyclohexene.—These reactions were performed as discussed for **1**.

Registry No.—**1**, 31684-77-2; **2**, 31684-78-3; **2** 2,4-DNPH, 31684-79-4; **3**, 31684-80-7; **3** 2,4-DNPH, 31731-95-0; 1-methylcyclohexene, 591-49-1; 3-methylcyclohexene, 591-48-0.

(12) L. A. Paquette and P. C. Storm, *J. Amer. Chem. Soc.*, **91**, 7657 (1969).
(13) R. L. Frank, R. D. Emmick, and R. S. Johnson, *ibid.*, **69**, 2363 (1947).
(14) H. C. Brown, "Hydroboration," W. A. Benjamin, New York, N. Y., 1962, Chapter 13.
(15) H. C. Brown and P. J. Gaoghengan, Jr., *J. Org. Chem.*, **35**, 1844 (1970).

Acknowledgments.—We express our appreciation to the Endowment and Research Foundation of Montana State University for their generous support of this work. Special thanks also to Professor A. Paul Krapcho (University of Vermont, Burlington, Vermont) for analytical data on some of the compounds.

Epoxidation. III. The Relative Reactivities of Some Representative Olefins with Peroxybenzimidic Acid[1]

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We recently reported[3] that the stereochemistry of epoxidation of conformationally biased methylenecyclohexanes with peroxybenzimidic acid (formed *in situ* from benzonitrile and alkaline hydrogen peroxide[4]) differed significantly from the results obtained with a variety of peracids, and these results have been confirmed in an independent study by Sykes.[5] We earlier suggested that the observed difference in stereochemistry resulted from the greater reactivity of the peroxybenzimidic acid. In order to test this hypothesis we have examined the relative reactivities of some representative olefins with peroxybenzimidic acid utilizing the competition technique. The results of these studies are summarized in Table I along with some comparative data for peracid epoxidation[6] and methylenation.[7]

In addition, 4-vinylcyclohexene and *d*-limonene were epoxidized with 0.1 equiv of *m*-chlorperbenzoic acid and 0.1 equiv of peroxybenzimidic acid and the results of these experiments are summarized in Figures 1 and 2.

It is clear from these results that peroxybenzimidic acid is a far less selective reagent for the epoxidation of double bonds than are peracids. Although the reaction of peracids with alkenes is very markedly accelerated by the presence of electron-donating alkyl groups and a trisubstituted double bond is epoxidized approximately 275–300 times as fast as a monosubstituted double bond, the relative rates are greatly attenuated with peroxybenzimidic acid and the trisubstituted double bond is only five times as reactive as a monosubstituted olefin. As in peracid oxidations,[6] however, the cis isomer of a cis–trans pair is oxidized more rapidly. In contrast to a number of other addition reactions,[7] cyclopentene is oxidized less readily than both cyclohexene and cycloheptene.

This study indicates that peroxybenzimidic acid is a relatively indiscriminate reagent and is not the reagent of choice for selective epoxidation of polyunsaturated substrates. The data are consistent with a transition

(1) For part II, see R. G. Carlson and R. Ardon, *J. Org. Chem.*, **36**, 216 (1971).
(2) Alfred P. Sloan Foundation Research Fellow, 1970–1972.
(3) R. G. Carlson and N. S. Behn, *J. Org. Chem.*, **32**, 1363 (1967).
(4) G. B. Payne, *Tetrahedron*, **18**, 763 (1962), and references cited therein.
(5) J. D. Ballantine and P. J. Sykes, *J. Chem. Soc. C*, 731 (1970).
(6) D. Swern, *J. Amer. Chem. Soc.*, **69**, 1692 (1947).
(7) B. Rickborn and J. H. Chan, *J. Org. Chem.*, **32**, 3576 (1967).