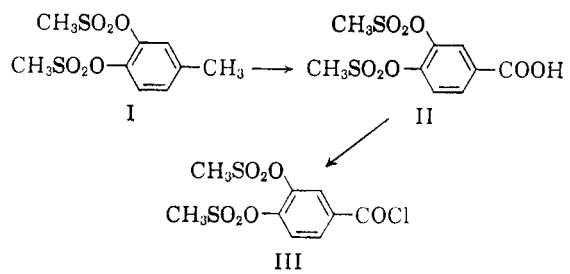
viously described.[1] Direct mesylation of protocatechuic acid can not be employed, since it and other phenolic acids give complex products containing ester linkages upon mesylation in pyridine.[1,4] Although synthesis of II from dimesyl protocatechualdehyde gives a satisfactory yield, it is not readily adaptable to large-scale preparations. Very pure protocatechualdehyde is required in the mesylation step, and in our hands, purification of large quantities of this aldehyde has proved inconvenient. The present note describes a synthesis of II from 4-methylcatechol, in which the remarkable stability of the mesyloxy group under acidic, oxidizing conditions is further demonstrated.

4-Methylcatechol was mesylated in pyridine in the usual manner, except that a somewhat higher temperature (*ca.* 80°) was employed. Oxidation of the dimethanesulfonate I under the previously described oxidizing conditions,[5] which consist of chromic acid in 88% sulfuric acid at temperatures as high as 110°, gave II in approximately 60% yield. The acid II has been converted to III with thionyl chloride. The intermediate III is of interest in the synthesis of natural products containing the catechol moiety.



EXPERIMENTAL

4-Methylcatechol dimethanesulfonate (I). To a 62 g. (0.5 mole) quantity of 4-methylcatechol in 100 ml. of reagent grade pyridine was added, dropwise, 90 ml. (1.1 moles) of methanesulfonyl chloride. The temperature rose to approximately 80°, and the reaction mixture became viscous and dark in color. After standing at room temperature for 90 min., 150 ml. of methanol was added. The resulting solution was poured slowly *without* stirring onto 200 ml. of concentrated hydrochloric acid and 800 g. of ice. The mixture was shaken gently until precipitation began, and then was stirred vigorously. Initial rapid stirring caused the product to precipitate in a very crude state which resisted ready purification. After standing overnight, the precipitate was collected, washed well with water, and air-dried; yield, 116 g. (83%), m.p. 80–86°. Recrystallization from methanol (charcoal) gave the colorless 4-methylcatechol dimethanesulfonate, m.p. 88–90°.

Anal. Calcd. for $C_9H_{12}O_6S_2$: C, 38.56; H, 4.32; S, 22.87. Found: C, 38.60; H, 4.35; S, 22.83.

Dimesyl protocatechuic acid (II). A 28-g. (0.1 mole) quantity of 4-methylcatechol dimethanesulfonate was dissolved in 160 ml. of 88% sulfuric acid. Chromium trioxide (20 g. of chromium trioxide in 80 ml. of water) was added over 20 min. The temperature rose rapidly and was kept below 110° by controlling rate of addition of chromic acid and cooling with water. The reaction mixture was poured immediately into ice water. After standing overnight, the separated solid was collected, washed well with water, and air-dried; yield, 26 g. The crude product was suspended in 500 ml. of 5% sodium bicarbonate and then covered with 150 ml. of ethyl acetate with vigorous stirring. After phase separation, the ethyl acetate layer was extracted three times with 50-ml. portions of 5% sodium bicarbonate. The combined bicarbonate solution and extracts were acidified with concentrated hydrochloric acid, cooled in ice for 3 hr., and the dimesyl protocatechuic acid collected and air-dried; yield, 18 g. (58%), m.p. 207–209°. Recrystallization from ethanol-ethyl acetate (charcoal) gave a white solid, m.p. 208–209° (lit.[1] m.p. 208–210°).

Dimesyl protocatechuyl chloride (III). A 15.8-g. (0.051 mole) quantity of dimesyl protocatechuic acid, m.p. 206–209°, was heated under reflux with 50 ml. of thionyl chloride for 1 hr. After excess thionyl chloride was removed, petroleum ether (b.p. 30–60°) was added. After cooling 2 hr., the solid present was collected and washed with petroleum ether; yield, 16.5 g. (98.5%), m.p. 138–143°. Recrystallization from toluene gave 14 g. of the crystalline acid chloride, m.p. 140–141°.

Anal. Calcd. for $C_9H_9ClO_7S_2$: C, 32.89; H, 2.76; S, 19.51; Cl, 10.79. Found: C, 33.45; H, 3.23; S, 19.11; Cl, 10.59.

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(3) Mesyl (methanesulfonyl or methylsulfonyl) denotes the CH_3SO_2— group; mesyloxy (methane- or methylsulfonoxy, or methane- or methylsulfonyloxy), the CH_3SO_3 group; and mesylation, a reaction with mesyl (methanesulfonyl) chloride. For more detailed nomenclature, see R. S. Tipson, *Advances in Carbohydrate Chem.*, 8, 109 (1953).

(4) J. H. Looker, C. H. Hayes, and D. N. Thatcher, *J. Am. Chem. Soc.*, 79, 741 (1957).

(5) J. H. Looker and D. N. Thatcher, *J. Org. Chem.*, 19, 784 (1954).

The Action of Alkali on 4-Methyl-4-dichloromethyl-2,5-cyclohexadien-1-one

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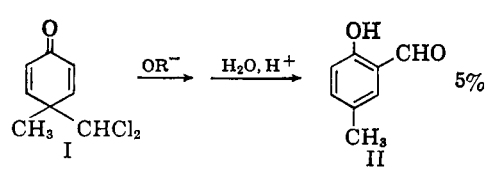
In connection with the work of Dodson *et al.*[1] on the transformations of 1-methyl-1-dichloromethyl-2(1*H*)-naphthalenone in basic medium, it may be of interest to note the corresponding behavior of 4-methyl-4-dichloromethyl-2,5-cyclohexadien-1-one (I), well known by-product of the Reimer-Tiemann synthesis when applied to *p*-cresol.[2] I, when treated with aqueous or alcoholic potassium hydroxide or sodium methoxide in methanol, gives, along with large amounts of dark tars, small yields of 2-hydroxy-5-methylbenzaldehyde (II).



(1) R. M. Dodson, J. R. Lewis, W. P. Webb, E. Wenkert, and R. D. Youssefyeh, *J. Am. Chem. Soc.*, 83, 938 (1961).

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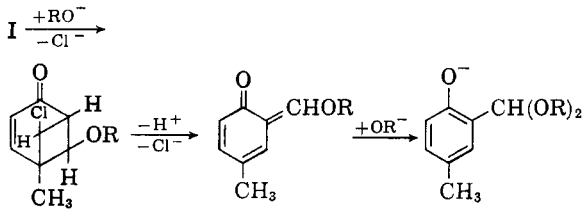
The best yield of II (5%, based on unrecovered dienone) was obtained with sodium methoxide in the cold and subsequent acidification and steam distillation, the other methods giving only traces. Care had been taken to make sure that the dienone used was a pure crystallized sample in which no II could be detected.

The formation of II from I can be best explained by assuming a bicyclic cyclobutane intermediate



This mechanism corresponds exactly to the results of Dodson and coworkers, who found an analogous bicyclic cyclobutane derivative to be an intermediate in their conversion of 1-methyl-1-dichloromethyl-2(1*H*)-naphthalenone to 1-methyl-3-naphthoic acid.

An alternative mechanism for the formation of II involving the primary formation of dichlorocarbene and *p*-cresoxide ion by deprotonation of I (retro-Reimer-Tiemann process)[3] followed by reattachment of carbene to the ortho position of the *p*-cresoxide ion thus leading to II is unlikely on the following grounds: (a) An attempt to trap any intermediate dichlorocarbene by reacting I with sodium *t*-butoxide suspended in cyclohexene[4] was unsuccessful, as no dichloronorcarane could be isolated, tars being the only products. (b) No *p*-cresol could be detected in the reaction mixtures, while it would have been expected to arise as a by-product under these assumptions.

EXPERIMENTAL

Reaction of I *with sodium methoxide in methanol.* A solution of 1.1 g. of I (0.0058 mole, m.p. 54–55°) in 15 ml. of absolute methanol containing 1.17 g. (0.217 mole) of sodium methoxide was left standing at room temperature for 20 hr. The solvent was then removed in vacuo and the residue, after the addition of 200 ml. of water, steam distilled. Thus 0.6 g. of I was recovered. After all distillable material had passed over the contents of the flask were acidified with dilute sulfuric acid and again steam distilled. The distillate now possessed the strong smell of II and gave its color reactions. It was extracted with ether, the ether layer evaporated, and the residue dissolved in ethanol. Upon addition of 2,4-dinitrophenylhydrazine reagent the derivative of II precipitated (0.040 g.—*i.e.* 5% of the theoretical amount based on unrecovered dienone, m.p. 261–264°, undepressed when mixed with an authentic sample showing the same m.p.).

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Conformational Analysis. XXIV. The Dipole Moment of 4-Fluorocoprostan-3-one[1]

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The increasing interest in fluorinated steroids prompted us to study the conformation of the fluorine atom in compounds containing a fluorine on a carbon adjacent to a carbonyl group. It has been shown that the fluorine atom of α-fluorocyclohexanone prefers an equatorial conformation,[3,4] and it was found earlier that the fluorine atom in the only known 2-fluorocholestan-3-one exists in the α (equatorial) configuration.[5] In the present work the dipole moment of the only known 4-fluorocoprostan-3-one has been determined and allows an unambiguous assignment of the configuration at C-4 to be made.

Upon inspection of a model of 4-fluorocoprostan-3-one, it appeared that the α (equatorial) configuration of the fluorine would be the more stable, since an axial fluorine would interfere with one of the hydrogens of the C-7 methylene group. The nearest hydrogen is 1.7 Å from the axial fluorine as measured with Dreiding models. The repulsion energy was calculated according to the method of Hill,[6] using the quantities $\alpha = 0.665$, and $\epsilon = 0.068$ kcal./mole (the geometric mean of the F—F repulsion, obtained from fluorine gas (0.109 kcal./mole) and the H—H value). This repulsion energy was found to destabilize the axial configuration by 5.1 kcal./mole. For an equatorial fluorine the only interaction which does not occur in equatorial fluorocyclohexanone is that between the β-fluorine on C-4 and the equatorial hydrogen on C-6. As these atoms are 2.5 Å apart, the energy of this interaction is negligible. Only one isomer of 4-fluorocoprostanone has been prepared, and from the energy considerations outlined, it seemed likely that it had the 4β-configuration. An unequivocal assignment of the configuration at C-4 was, however, made from the dipole moment.

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(2) Predoctoral National Institutes of Health Fellow, 1960–1962.

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