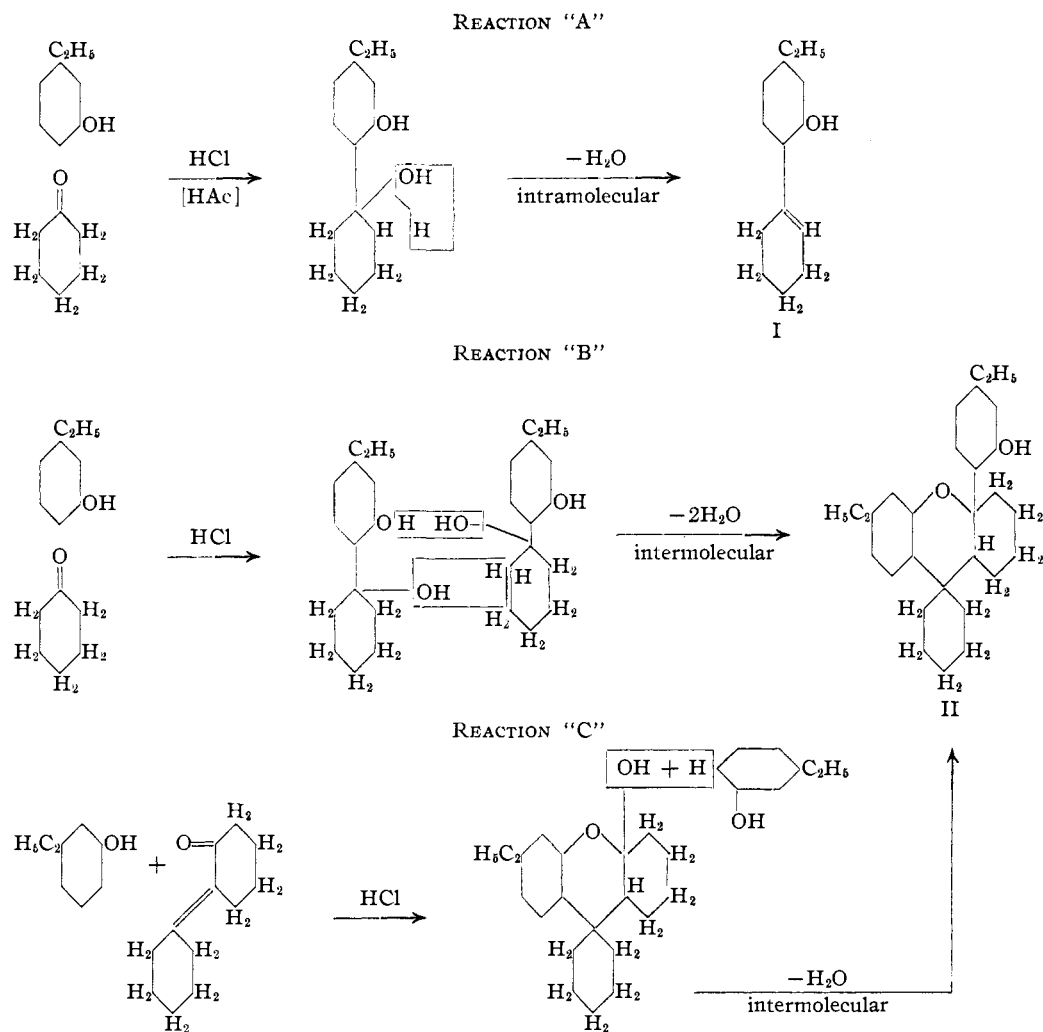


[CONTRIBUTION FROM THE CHEMICAL LABORATORIES OF NEW YORK UNIVERSITY]

## Flavans

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The condensation of cyclohexanone and *m*-flavan (II). Thus the probable mechanisms of ethylphenol to a cyclohexenylphenol (I)<sup>1</sup> takes these condensations can be represented as follows:



place in glacial acetic acid, hydrogen chloride being used as the catalyst. It has now been found that, if the reaction is run without a solvent, the product is entirely different. The new compound is saturated and has twice the molecular weight of the cyclohexenylphenol (I). It has been assigned structure II, 2'-hydroxy-4',7-diethyl-2,3-tetra-4,4-pentamethylene-flavan.

That this structure is correct was shown by an independent synthesis. *m*-Ethylphenol condensed with cyclohexylidencyclohexanone gave the same

This reaction scheme would first of all suggest condensation of the cyclohexanone in the ortho position to the phenolic hydroxyl group, an assumption which is now well substantiated by spirochroman formation of the *m*-ethylphenol<sup>2</sup> and by coumaran formation of the same phenol when condensed with the alpha methylcyclohexanone.<sup>1</sup> That the cyclohexenyl radical is in the ortho position in the condensation product obtained in reaction "A" can be further inferred by the fact that its aryloxyacetic acid derivative,

(1) J. B. Niederl and co-workers, *THIS JOURNAL*, **61**, 1785 (1939).(2) J. B. Niederl and co-workers, *ibid.*, **62**, 324 (1940).

despite being unsaturated, upon bromination gives a saturated monobromo derivative, while under the same condition the isomeric *o*-ethylphenol compound yields a dibromo derivative,<sup>1</sup> a fact which suggests cyclization in the former, yielding the respective coumaran compound (6-ethyl-2-carboxy-3,3-(2'-bromo)-pentamethylene-coumaran).

Thus in the last analysis the difference between condensation "A," involving the formation of the unsaturated phenol, and condensation "B" is that in the first case dehydration of the intermediate "phenol-hydrin" takes place "intramolecularly," whereas the second case, which involves the loss of two molecules of water from two molecules of the "phenol-hydrin," points to "intermolecular" dehydration.<sup>3</sup>

## Experimental

### Condensation Methods

**Cyclohexanone and *m*-Ethylphenol.**—One mol of *m*-ethylphenol was added to 1 mol of cyclohexanone in a 3-necked flask into which was inserted a thermometer, reflux condenser, and a gas inlet tube reaching to the bottom of the flask. A stream of dry hydrogen chloride gas was passed into the mixture for six hours. The temperature rose to 50° and was kept at that level for one hour. The flask was stoppered and set aside for five days, after which time crystals had formed. The mixture was filtered through a fritted glass filter, the crystals washed with benzene and recrystallized repeatedly from alcohol until colorless crystals were obtained; yield, 15% (five days condensation time).

**Cyclohexylidene-cyclohexanone and *m*-Ethylphenol.**—Eighteen grams, 0.1 mol, of cyclohexylidene-cyclohexanone (b. p. 143–146° at 15 mm.) prepared according to C. Mannich<sup>4</sup> was added to 24.6 g. (0.20 mol) of *m*-ethylphenol in a 3-necked flask equipped with a thermometer, reflux condenser, and a gas inlet tube. Hydrogen chloride gas was passed in for six hours, at the end of which time the flask was stoppered and let stand for a week. The crystals were washed with benzene and crystallized from alcohol; yield, 9% (one week condensation time).

**2'-Hydroxy-4',7'-diethyl-2,3-tetra-4,4-pentamethylene-flavan.**—Soluble in organic solvents, but insoluble in Claisen solution; diazotization reactions positive. M. p., 195–196° (uncor.).

(3) M. E. McGreal and J. B. Niederl, "Abstracts of Papers, 97th meeting Am. Chem. Soc.," Baltimore, Md., 1939, pp. M 5–7.

(4) C. Mannich, *Ber.*, **40**, 157 (1907).

*Anal.* Calcd. for C<sub>28</sub>H<sub>38</sub>O<sub>2</sub>: C, 83.17; H, 8.91; mol. wt., 404. Found: C, 82.77; H, 8.92; mol. wt., 404, 409.

### Derivatives

**Di-bromo Derivative.**—One-half gram of the flavan compound was dissolved in 30 cc. of carbon tetrachloride and 0.4 g. of bromine in 10 cc. of the same solvent added drop by drop. The solvent was evaporated at room temperature and the crystals were recrystallized from alcohol; m. p. 180–181° (uncor.).

*Anal.* Calcd. for C<sub>28</sub>H<sub>34</sub>O<sub>2</sub>Br<sub>2</sub>: C, 59.78; H, 6.05; Br, 28.43. Found: C, 59.45; H, 6.25; Br, 28.47.

**Benzoate.**—One-half gram of the flavan was dissolved in 7 cc. of pyridine and 0.5 cc. of benzoyl chloride added. After the mixture had refluxed for one hour, it was poured with stirring into 20 cc. of water. The precipitate formed was taken up in ether and the solution washed with 3 cc. of 5% sodium carbonate solution and then with 5 cc. of water. After drying over calcium chloride and filtering, the ether was allowed to evaporate and colorless crystals of the benzoate remained; m. p. 169–170° (uncor.).

*Anal.* Calcd. for C<sub>38</sub>H<sub>40</sub>O<sub>3</sub>: C, 82.68; H, 7.87. Found: C, 82.81; H, 8.18.

**3,5-Dinitrobenzoate.**—The procedure employed was the same as for the benzoate except that 3,5-dinitrobenzoyl chloride was used. The pale yellow crystals were recrystallized from alcohol; m. p. 176° (uncor.).

*Anal.* Calcd. for C<sub>36</sub>H<sub>38</sub>O<sub>7</sub>N<sub>2</sub>: C, 70.23; H, 6.35. Found: C, 70.20; H, 6.01.

**Acetate.**—One-half gram of the flavan was added to 20 cc. of acetic anhydride and the mixture refluxed for three hours. On pouring the cooled solution into water an oil separated which on standing solidified. The acetate was recrystallized from alcohol; m. p. 118–119° (uncor.).

*Anal.* Calcd. for C<sub>30</sub>H<sub>38</sub>O<sub>3</sub>: C, 80.72; H, 8.52. Found: C, 80.90; H, 8.28.

### Summary

Formation of a "flavan" type of crystalline condensation product from a cyclic ketone and a meta alkylated phenol was observed. The structure of the compound was proved by its synthesis from a cyclic alkylidene ketone and the same phenol. This as well as previous investigations seem to indicate that in condensations with ketones meta alkylated phenols appear to undergo alkylation in the *ortho* position to the phenolic hydroxyl group.

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