

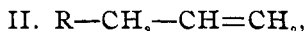
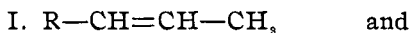
[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE PENNSYLVANIA STATE COLLEGE.]

DERIVATIVES OF EUGENOL.

BY F. J. POND AND F. T. BEERS.

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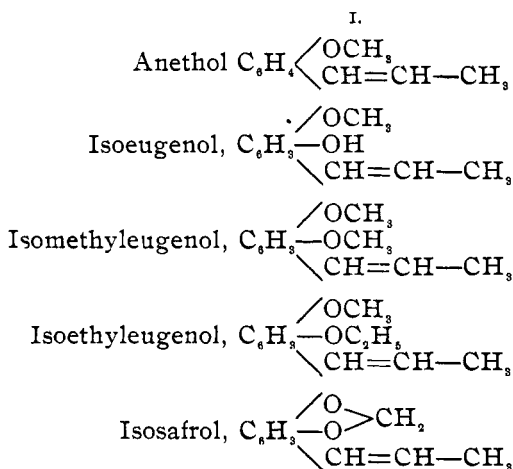
THE two classes of unsaturated benzene derivatives having the general formulas,



contain the unsaturated group C_3H_5 joined to a benzene nucleus. In the first class of compounds the C_3H_5 group has a propenyl, in the second an allyl structure.

The study of these bodies has been especially directed towards finding a suitable reaction by means of which the character of the unsaturated group might be definitely determined.

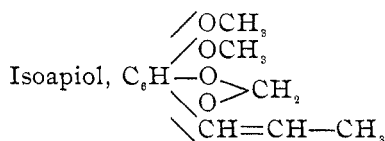
The results obtained by the action of nitrogen trioxide on anethol, described by P. Toennies,¹ and those of A. Angeli,² embracing the action of the same reagent on eugenol, isoeugenol, safrol, isosafrol, apiol, and isoapiol, led Angeli to give the following classification to these bodies :³



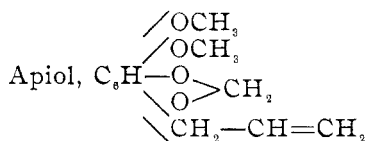
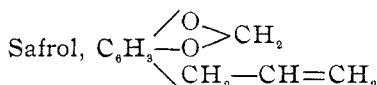
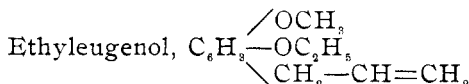
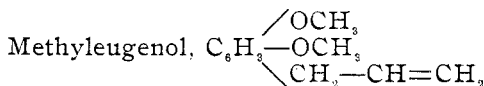
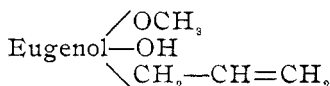
¹ *Ber. d. chem. Ges.*, 11, 1511; 13, 1845; 18, 850; 20, 2982.

² *Gazz. chim. ital.*, 22 (II), 445; *Ber. d. chem. Ges.*, 24, 3996.

³ *Ber. d. chem. Ges.*, 24, 3994.



II.



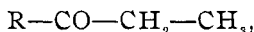
All members of the first group were said to give nitrosites when treated with nitrous anhydride, while those in the second class did not. Hence it was assumed that one of the properties which the compounds with a propenyl side chain possessed was to form these addition-products with nitrogen trioxide, which could not be obtained from the allyl side chain bodies.

Later, however, Angeli¹ was able to prepare similar addition-products from the compounds containing the allyl group, and the reaction therefore could not be called characteristic for the propenyl series.

During the study of the action of sodium alcoholate on the bromine addition-products of these two classes of compounds, Wallach and Pond² found that some of the propenyl series gave dibromides, which, on treatment with sodium alcoholate, yielded ketones having the general formula

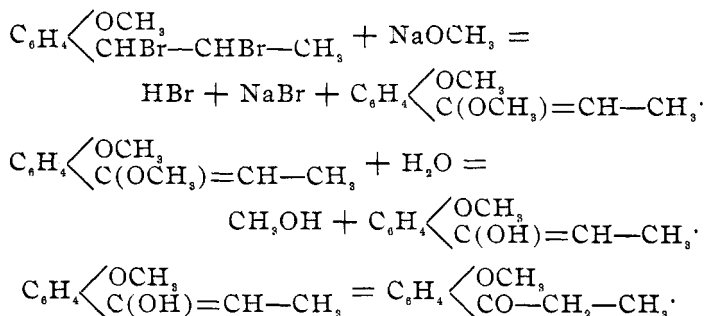
¹ *Ber. d. chem. Ges.*, **26**, Ref. 195.

² *Ber. d. chem. Ges.*, **28**, 2714; also Pond, Inaug. Diss., Goettingen, 1896.



while the bromine products of the corresponding allyl series, treated in precisely the same manner, gave no ketones, but were, partially at least, changed back into the original compounds. This reaction, which was carried out with anethol, safrol, and isosafrol, eugenol and isoethyleugenol, seemed to give reasonable ground for the belief that it might prove a characteristic reaction, by means of which the nature of the side chain in these two classes of unsaturated bodies could be determined.

The formulation of the reaction of sodium methylate on anethol dibromide (anethol being taken as an example of the propenyl compounds) is the following :

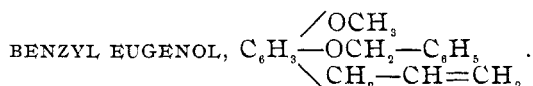


The alcoholate splits off one molecule of hydrobromic acid from the dibromide in the normal manner, while the second bromine atom suffers replacement by the OCH_3 group. The latter is easily saponified and the resulting unsaturated alcohol, following the Erlenmeyer hypothesis, changes into the more stable saturated ketone.

Eugenol, which was taken as a fair illustration of the allyl series, gave a liquid dibromide, which, on treatment with sodium alcoholate, simply parted with the two bromine atoms, yielding no characteristic body. Safrol acted in much the same manner, while anethol, isosafrol, and isoethyleugenol dibromides gave well defined ketones. It has seemed to us, therefore, of interest to examine this reaction with some other members of the propenyl series, in order, if possible, to give further support to the results already obtained.

Some ester of isoeugenol seemed to promise well for this pur-

pose, and as ethyl and methyl isoeugenol have both shown themselves to conform to the reaction, the question arose whether an aromatic ester of isoeugenol, as for example, benzyl isoeugenol, would not also form a dibromide which could be changed into a ketone. Our results have fully substantiated the belief that such is the case.

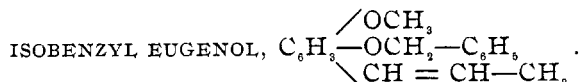


The general rule for preparing esters of eugenol is to treat the potassium or sodium salt of eugenol with an alkyl bromide or chloride.

In such a manner Cahours¹ obtained the benzoyl, toluyl, and ethyl ester, and Wassermann² the methyl and some other esters.

Our method was similar to this and consisted in dissolving thirty grams potassium hydroxide in seventy-five cc. alcohol, in a round-bottomed flask with an upright condenser. Seventy cc. eugenol were added and the whole heated on a water-bath. Fifty-three cc. benzyl chloride were introduced, drop by drop, and the heating continued about three hours, until end of the reaction. The potassium chloride formed was dissolved in water and the heavy oil thrown out separated. An attempt to purify by steam distillation proved of no avail, since the oil is almost non-volatile with steam.

The benzyl eugenol is a dark-colored oil, heavier than water, and after drying over calcium chloride boils at about 235° with decomposition. It also suffers decomposition by vacuum distillation.



This propenyl compound was easily prepared from the benzyl eugenol according to the general method of Eykman³ and Angeli⁴ by heating with an alcoholic potassium hydroxide solution.

One hundred and fifty grams potassium hydroxide, 300 cc. alcohol, and seventy-five grams benzyl eugenol were heated on

¹ *Ann. Chem.* (Liebig), **46**, 220; **108**, 320.

² *Ann. Chem.* (Liebig), **179**, 375.

³ *Ber. d. chem. Ges.*, **23**, 855.

⁴ *Gazz. chim. ital.*, **22**, (2) 101.

a water-bath for about twenty-four hours. After distilling off most of the alcohol the remaining solution was poured into a liter of water, a heavy oil separating, which, after twelve hours standing, solidified. This was filtered, dried on a porous plate, and crystallized from alcohol. The product is at first rather dark-colored and quite impure, hence repeated treatment with animal charcoal is advisable. The substance has the habit of separating from a saturated alcoholic solution as an oil, which slowly solidifies.

When finally crystallized from alcohol, it is perfectly white and in the form of long, fine needles, melting at 48° .

The analyses gave the following results :

I. 0.1858 gram gave 0.5429 gram carbon dioxide and 0.1138 gram water.

II. 0.1804 gram gave 0.5289 gram carbon dioxide and 0.1113 gram water.

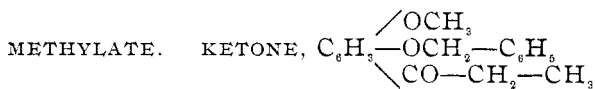
	Calculated for $\text{C}_6\text{H}_5-\begin{matrix} \diagup \text{OCH}_3 \\ \text{OCH}_2-\text{C}_6\text{H}_5 \\ \diagdown \text{CH}=\text{CH}-\text{CH}_3 \end{matrix}$	I.	Found.	II.
Carbon.....	80.31	80.13		79.94
Hydrogen.....	7.08	6.80		6.85

ISOBENZYL EUGENOL DIBROMIDE, $\text{C}_6\text{H}_5-\begin{matrix} \diagup \text{OCH}_3 \\ \text{OCH}_2-\text{C}_6\text{H}_5 \\ \diagdown \text{CHBr}-\text{CHBr}-\text{CH}_3 \end{matrix}$

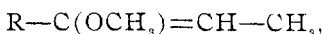
Twenty-five grams isobenzyl eugenol was dissolved in 100 cc. dry ether and after cooling with a mixture of ice and salt, five and four-tenths cc. bromine (one molecule) were added very slowly. The last drops gave the liquid a permanent yellow color, and at the same time a mass of fine white crystals appeared. These were filtered, washed with cold ether to remove excess of bromine, dried, and crystallized from alcohol. A second crop may be obtained from the ether filtrate by washing with a solution of sulphur dioxide to remove bromine, and evaporating the ether. It crystallizes in white needles melting at 122° , easily soluble in alcohol, more difficultly soluble in ether.

No evolution of hydrobromic acid was noticed either during the addition of bromine or on crystallization.

TREATMENT OF ISOBENZYL EUGENOL DIBROMIDE WITH SODIUM



To a solution of sodium methylate, formed by dissolving five grams of sodium in 100 cc. methyl alcohol, twenty-six grams of isobenzyl eugenol dibromide were added. A violent reaction at once took place with formation of considerable sodium bromide. The solution was heated with an upright cooler, in a water-bath for about three hours. On addition of water a dark-colored, heavy oil separated, which, owing to being difficultly driven over with steam, was removed by a separating funnel. The oil was then boiled for a short time with a dilute solution of potassium hydroxide to insure a complete saponification of the unsaturated ester, *viz.* :



and then allowed to stand twenty-four hours. At the end of this time a solid appeared, and after three days nearly all the oil had changed into the white solid. The latter was filtered by suction, pressed on a plate to remove any adhering oil, and crystallized from ether in small, white needles melting at 93° .

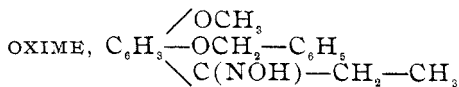
The analyses gave the figures :

I. 0.2282 gram substance gave 0.6306 gram carbon dioxide and 0.1389 gram water.

II. 0.2251 gram substance gave 0.6216 gram carbon dioxide and 0.1354 gram water.

	Calculated for $\text{C}_6\text{H}_5-\begin{array}{l} \diagup \text{OCH}_3 \\ \text{OCH}_2-\text{C}_6\text{H}_5 \\ \diagdown \text{CO}-\text{CH}_2-\text{CH}_3 \end{array}$	Found.	
		I.	II.
Carbon.....	75.55	75.32	75.31
Hydrogen	6.66	6.85	6.68

If the substance actually is a ketone it should naturally be converted into an oxime by treatment with hydroxylamine.



Fifteen grams of the ketone were dissolved in fifty cc. alcohol, heated to boiling, and a hot solution of fifteen grams hydroxylamine hydrochloride in thirty cc. water added. To this solution fifteen grams potassium hydroxide in fifteen cc. water were

slowly added, care being taken to shake well after each addition. On cooling, the whole was poured into ice water, a white, crystalline precipitate being thrown out. After filtering and drying it crystallized from alcohol, yielding beautiful white needles which melt at 118.5° .

Analyses gave the following :

I. 0.1529 gram gave 0.4024 gram carbon dioxide and 0.0886 gram water.

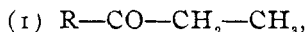
II. 0.1946 gram gave 0.5116 gram carbon dioxide and 0.1120 gram water.

		Calculated for	
		$\begin{array}{c} \text{C}_6\text{H}_5 \begin{array}{l} \nearrow \text{OCH}_3 \\ \searrow \text{OCH}_2-\text{C}_6\text{H}_5 \\ \text{C}(\text{NOH})-\text{CH}_2-\text{CH}_3 \end{array} \end{array}$	
		I.	Found. II.
Carbon.....	71.58	71.77	71.69
Hydrogen.....	6.66	6.43	6.39

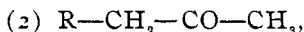
There can therefore be no doubt but that the substance obtained from isobenzyl eugenol dibromide by the action of sodium methylate, consists of a ketone mixed with some unsaturated alcohol or ether, the latter being saponified and changed into the ketone structure on heating with potassium hydroxide or with a dilute mineral acid, as was later found to be the case.

The oxime is easily changed back into the ketone melting at 93° , by heating with dilute sulphuric acid.

That the carbonyl group in the ketone occupies the α -position to the benzene nucleus,



and not β -



has been proved in all this series of ketones by the action of concentrated sulphuric acid on both the ketone and the corresponding oxime, by which propionic acid and not acetic acid results, thus allowing only formula 1.

Isobenzyl eugenol acts thus in a very similar manner to isoeethyl eugenol, and adds one more to the list of bodies containing the unsaturated propenyl side chain, whose bromine addition-products may be used as a starting-point for the formation of ketones. It further supports the belief that this reaction may be used to characterize the atomic grouping in the side chain.

Experiments are now under way in this laboratory on eugenol acetic acid and isoeugenol acetic acid, apiol and isoapiol, from which we hope to secure some satisfactory results.