[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE UNIVERSITY OF RICHMOND]

Creatinine Derivatives. II

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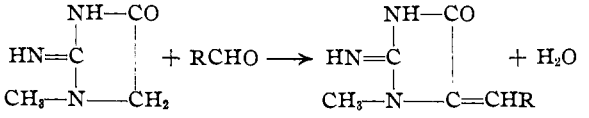
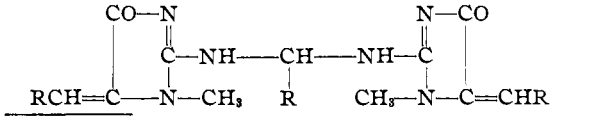
This paper is a continuation of the work of Cornthwaite and Jordan[1] on the condensation of aldehydes with creatinine. The methylene group is the most active in these condensations which take place according to the equation



This reaction goes most favorably when the reactants are mixed and heated to a temperature of 160–180° in an oil-bath. It was found also that acetamide could be used as a solvent and the condensation effected smoothly in this medium.

In the condensations of *p*-methylbenzaldehyde, *o*-methoxybenzaldehyde, *o*-ethoxybenzaldehyde, piperonal and *o*-chlorobenzaldehyde with creatinine, residues were obtained after complete extraction of the main product with water which were characterized by their insolubility in water, benzene, hydrochloric acid, potassium hydroxide, acetone and alcohol. They are soluble in boiling glacial acetic acid, hot aniline and hot nitrobenzene from which they may be recrystallized. Twenty hours boiling with concentrated hydrochloric acid or with 20% potassium hydroxide apparently has no effect on the *o*-ethoxybenzaldehyde derivative. A similar residue from a condensation with benzaldehyde was unchanged after twenty hours of heating with saturated barium hydroxide. Heating the *o*-ethoxybenzaldehyde derivative for a short time with 40% potassium hydroxide in a nickel crucible effected a decomposition. The odor of the free aldehyde was observed as well as ammonia. Some solid which floated on the surface was skimmed off and identified as 5-*o*-ethoxybenzalcreatinine by its melting point, mixed melting point and picrate. From a consideration of the nitrogen analyses of these substances it would seem that two moles of the normal condensation product had reacted further with one mole of aldehyde to form a compound whose possible structure is given below.



(1) Cornthwaite and Jordan, THIS JOURNAL, **56**, 2733 (1934).

To test this, pure 5-*o*-ethoxybenzalcreatinine was heated for one hour at 175° with excess *o*-ethoxybenzaldehyde. The reaction mixture yielded material agreeing in melting point and solubility with that obtained from the condensation of creatinine with *o*-ethoxybenzaldehyde.

Condensation with *p*-Hydroxybenzaldehyde.—While this work was in progress an article by Deulofeu and Mendivelzua[2] appeared describing the condensation of *p*-hydroxybenzaldehyde with creatinine. Their analyses indicated that the condensation took place between two moles of the aldehyde and one of creatinine and they give a suggested formula on that basis. We also had carried out this condensation in a similar manner, using purified aldehyde, and had subjected the product to repeated crystallizations from water and from glacial acetic acid. Consistent analyses could not be obtained when the product was dried in the oven at 105°. It was found, however, that the product if crystallized from water lost weight corresponding to two moles of water when heated for one hour at 140° and if crystallized from glacial acetic acid lost weight corresponding to one mole of acetic acid when heated to constant weight at 165° (two hours). These values were calculated from thoroughly air-dried samples which remained in a desiccator overnight before being placed in the oven. Although this compound retains its solvent of crystallization rather tenaciously it is not unusual for hydroxy compounds to separate with solvent of crystallization. Our results are in accord with the fact that the condensation took place normally, *i. e.*, mole for mole and in no experiment were we able to isolate a compound of more complex nature.

Experimental Part

General Procedure.—Three to ten grams of creatinine and an excess of the aldehyde were heated in an oil-bath at temperatures ranging from 150 to 180° until reaction ceased. The mixtures were allowed to cool, ground up and extracted with ether, with alcohol and finally with a small amount of hot water. The residues were then crystallized from water or alcohol. All

(2) Deulofeu and Mendivelzua, *Ber.*, **68**, 786 (1935).

samples for analysis were dried at 105° except 5-*p*-hydroxybenzalcreatinine which was heated at 165° for one hour. The condensation with hydrocinnamaldehyde was carried out in melted acetamide.

TABLE I

ALDEHYDE CONDENSATION PRODUCTS OF CREATININE

Compound, -creatinine	Color	M. p.,[a] °C.	Solvent for crystallization	Yield, %
5-*p*-Methoxybenzal-	Yellow	248–249[b]	Water	63
5-*o*-Methoxybenzal-	Cream	241	Water	31
5-*o*-Ethoxybenzal-	Yellow	236[b]	Water	34
5-*p*-Hydroxybenzal-	Yellow	289	Water	32
5-Hydrocinnamal-	Yellow	225–230	Ethanol	25
5-*p*-Methylbenzal-	Yellow	285[b]	Ethanol	28
5-Piperonal-	Yellow	274[b,c]	Water	29
5-*o*-Chlorobenzal-	Yellow	242[b,c]	Pptd. from dil. HCl with NH_3	57

Formula	Nitrogen, % Calcd.	Found	M. p.,[a] °C. of picrate	M. p.,[a] °C. of hydrochloride
$C_{12}H_{13}O_2N_3$	18.18	18.01	244[b]	247–248[b]
$C_{12}H_{13}O_2N_3$	18.18	17.49	255–270[b]	258–259[b]
$C_{13}H_{15}O_2N_3$	17.14	17.01	244–246[b]	214[b]
$C_{11}H_{11}O_2N_3$	19.27	19.23	252–257[b]	...
$C_{13}H_{16}ON_3$	18.29	18.22	221	...
$C_{12}H_{13}ON_3$	19.53	19.45	256[b]	256[b]
$C_{12}H_{11}O_3N_3$	17.14	16.55	255	...
$C_{11}H_{10}ON_3Cl$	17.84	17.31	260	241

[a] Melting points are uncorrected. [b] Melts with decomposition. [c] Melting point taken in closed tube.

TABLE II

RESIDUES FROM ALDEHYDE CONDENSATIONS SUGGESTED AS TRIALDEHYDE-DI-CREATININE DERIVATIVES

Aldehyde from which product is derived	Solvent for crystallization	Color
o-Methoxybenzaldehyde	Acetic acid	Yellow
o-Ethoxybenzaldehyde	Nitrobenzene	Red
p-Methylbenzaldehyde	Acetic acid	Yellow
o-Chlorobenzaldehyde	Acetic acid	Yellow
Piperonal	Aniline	Red-orange

M. p.,[a] °C.	Formula	Nitrogen, % Calcd.	Found
292	$C_{32}H_{33}O_5N_6$	14.45	14.62
297	$C_{35}H_{39}O_5N_6$	13.47	13.94
309	$C_{31}H_{32}O_2N_6$	16.14	16.18
270	$C_{29}H_{23}O_2N_6Cl_3$	14.17	14.26
327	$C_{32}H_{26}O_8N_6$	13.50	13.88

[a] Melting points are uncorrected.

The experimental data are summarized in Tables I and II.

We wish to express our appreciation to the Valentine Meat Juice Company for the creatine from which the creatinine used in these experiments was prepared and to the Virginia Academy of Science for a grant with which to purchase chemicals.

Summary

1. *p*-Methoxybenzaldehyde, *o*-methoxybenzaldehyde, *o*-ethoxybenzaldehyde, *p*-hydroxybenzaldehyde, hydrocinnamaldehyde, *p*-methylbenzaldehyde, piperonal and *o*-chlorobenzaldehyde have been condensed with creatinine.

2. The picrates of the above condensation products and the hydrochlorides of all except piperonalcreatinine, *p*-hydroxybenzalcreatinine and hydrocinnamalcreatinine have been prepared and described.

3. The nitrogen content and apparent purity of products isolated from the condensations of creatinine with certain of the above-named aldehydes suggest that two moles of the primary condensation product condense further with one mole of aldehyde.

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[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY OF THE UNIVERSITY OF MINNESOTA]

The Reaction between Quinones and Sodium Enolates. IV. Pseudocumoquinone, Sodium Acetoacetic Ester and Sodium Malonic Ester[1]

BY LEE IRVIN SMITH AND C. W. MACMULLEN

Previous papers in this series[2] have dealt with the reaction between a fully substituted quinone, duroquinone and sodium malonic ester. In this case the reaction was unlike any of the other addition reactions of quinones, for the product was a coumarin derivative (I) and one of the methyl groups of the quinone was involved in the reaction. In order to explore the limits of this reaction, it was desired to study the addition of sodium enolates to pseudocumoquinone (trimethylquinone) (II).

This quinone has three methyl groups attached to the nucleus, and therefore offers the possibility of undergoing the same type of reaction with sodium enolates as was shown by duroquinone. In addi-

(1) Abstracted from a thesis by C. W. MacMullen, presented to the Graduate Faculty of the University of Minnesota, in partial fulfilment of the requirements for the degree of Doctor of Philosophy, July, 1935.

(2) (a) Smith and Dobrovolny, THIS JOURNAL, **48**, 1693 (1926); (b) Smith, *ibid.*, **56**, 472 (1934); (c) Smith and Denyes, *ibid.*, **58**, 304 (1936).