It is soluble in ether, chloroform, acetone, acetic ester, carbon disulfide, benzene, toluene, or nitrobenzene, forming dark purple solutions; slightly soluble in cold, soluble in hot alcohol, which is the best solvent for it. Strong sulfuric acid gives a greenish black solution, turning brownish on standing, sodium hydroxide does not act in the cold, but on warming forms a red solution from which an acid throws down a black substance probably diiodohydroxyanilinoquinone.

The yellowish brown product separated from the preceding by its slight solubility in hot alcohol was formed in small quantity in the cold, but became the principal product, if the aniline was added to a hot alcoholic solution of diiodoacetoxyethoxyquinone. It was purified by crystallization from toluene.

Subst., 0.1868; AgI, 0.1623. Calc. $C_6I_2(NHC_6H_5)_2O_2$: I, 46.86. Found: I, 46.94.

Properties of Diiododianilinoquinone.—It crystallizes from toluene in dark brown needles decomposing at about 220°. It is slightly soluble in chloroform, acetone, acetic ester, benzene, toluene, nitrobenzene, or aniline, more soluble hot; essentially insoluble in alcohol, ether, carbon disulfide, glacial acetic acid, or naphtha. It is decomposed on warming with sodium hydroxide forming a yellow solution, which with bromine water gives a precipitate of tribromoaniline. The best solvent for it is hot toluene.

Action of Sodium Hydroxide on Bromoanil in Ethyl Alcohol.—Ten grams of bromoanil suspended in 50 cc. of ethyl alcohol were treated with 10 cc. of 50% aqueous sodium hydroxide solution; the solid dissolved at once, and soon deposited purple needles of sodium bromoanilate, recognized by the analysis of the free acid after it had been crystallized several times from toluene ($C_6Br_2(OH)_2O_2$, Br 53.69, found Br 53.65). The experiment was repeated several times under varying conditions, but in every case the product was sodium bromoanilate.

In the hope of getting α or β addition compounds similar to those obtained from tetrabromoorthoquinone iodoanil, or bromoanil was allowed to stand for 5 months with methyl alcohol, but no action was observed.

CAMBRIDGE, MASS.

[CONTRIBUTION FROM THE CHEMICAL LABORATORIES OF COLUMBIA UNIVERSITY, NO. 231.]

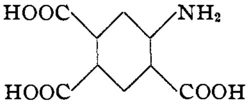
RESEARCHES ON QUINAZOLINES. XXXII. ON SOME QUINAZOLONES, BENZIMIDAZOLES, AND RELATED COMPOUNDS, DERIVED FROM *s*-PSEUDOCUMIDINE.

BY MARSTON TAYLOR BOGERT AND ANDREW BENDER.

Received January 27, 1914.

1. Introduction, and Discussion of Results.

In continuation of the investigations which have been going on for several years in this laboratory on heterocyclic systems obtainable from various o-amino compounds,[1] we have endeavored to prepare for study the 5-amino-1,2,4-benzene tricarboxylic acid(I), since it presents an interesting combination of an anthranilic with an o-phthalic structure, and further because none of the six possible aniline tricarboxylic acids have as yet been described in the literature.



(I)

Two lines of approach have been followed towards this goal: (1) s-pseudocumidine was acetylated and the acetyl derivative oxidized; (2) pseudocumene was converted into the 5-nitro derivative, the nitro pseudocumene oxidized to the nitro tricarboxylic acid, and the latter reduced. Unfortunately, serious obstacles have been encountered on both paths.

On the first route, the chief obstacle proved to be the oxidation of the acetpseudocumidide. Although we tried various oxidizing agents, under varied conditions, only once did we obtain any of the acid sought, and then only in sufficient amount to carry out a few superficial tests. Plenty of the mono- and dibasic acids were separated, but it seemed impossible to oxidize all three methyl groups without simultaneously destroying the entire molecule, irrespective of whether the initial material was pseudocumidide, mono- or dibasic acid. This was decidedly disappointing, in view of the fact that both amino o-phthalic acids are fairly stable compounds,[2] as well as the p-diamino terephthalic and the 4,6-diamino isophthalic acids,[3] and we had no difficulty in preparing this latter acid by oxidation of the corresponding diacetaminoxylene, or in oxidizing 2,4-diacetaminotoluene to the corresponding diacetaminobenzoic acid.[4]

Jannasch and Weiler[5] met with similar difficulties in attempting to oxidize isodurene, $C_6H_2(CH_3)_4$. When the oxidation was conducted in acetic acid solution with chromic anhydride, part of the hydrocarbon was unattacked, and part was burned to carbon dioxide and water. With very dilute potassium permanganate solution, mono- and dibasic acids were produced, but no tetracarboxylic acid. On the other hand, Mills[6] obtained a yield of 85–88% of pyromellitic acid, $C_6H_2(COOH)_4$, when he oxidized durylic acid, $(CH_3)_3C_6H_2COOH$, with dilute alkaline potassium permanganate solution.

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[1] Bogert, *et al.*, THIS JOURNAL, **32**, 784, 1297, 1654 (1910); **33**, 949 (1911); **34**, 183, 516, 524, 683, 1569, 1576 (1912).

[2] Bogert and Renshaw, THIS JOURNAL, 30, 1135 (1908); Bogert and Jouard, *Ibid.*, 31, 483 (1909).

[3] Bogert and Kropff, *Ibid.*, 31, 842 (1909).

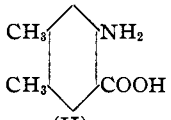
[4] Bogert, Amend and Chambers, *Ibid.*, **32**, 1299 (1910).

[5] *Ber.*, **27**, 3443 (1894).

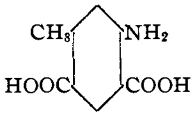
[6] *J. Chem. Soc.*, (*London*) 101, 2193 (1912).

By the second route, we travelled fairly smoothly to the point reached by Schultz and Herzfeld,[1] namely the production of the nitro tricarboxylic acid by oxidation of nitropseudocumene; but there our difficulties began, and we have not yet succeeded in getting any satisfactory reduction of this nitro acid to the amino acid.

Pending further experiments in the production of the tricarboxylic acid, we turned our attention to the mono- (II) and dibasic (III) acids obtained by the partial oxidation of the acetpseudocumidide. The configuration of these acids indicates that in the oxidation of acetpseudocumidide, under the conditions of our experiments, the methyl group in position 4 is first attacked, and then that at 2.

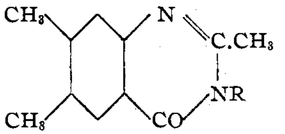


(II)

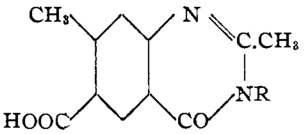


(III)

As both of these are of anthranilic type, they yielded acetyl anthranils and 4-quinazolones of types IV and V:



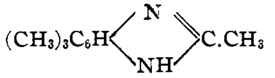
(IV)



(V)

A study of these new compounds disclosed no peculiarities of especial interest.

By nitration of acetpseudocumidide and subsequent reduction of the nitro compound, Edler[2] obtained the 2,4,5,7-tetramethylbenzimidazole (VI):



$$(CH_3)_3C_6H\langle\begin{matrix}N\\NH\end{matrix}\rangle C.CH_3$$

(VI)

We have repeated his work and in addition have prepared a number of new derivatives of this imidazole, including the phthalones.

The propionyl derivative of pseudocumidine is also described in the following pages, together with the benzimidazoles and other compounds obtained from it. By a Friedel-Crafts reaction, the chloroacetyl group was introduced but, unfortunately, as Kunckell[3] has shown in the case of the acetyl derivative, this group enters in position 3, instead of 6, so that the resulting ketone could not be used for the preparation of substituted indigos.

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[1] *Ber.*, **42**, 3607 (1911).

[2] *Ibid.*, **18**, 630 (1885).

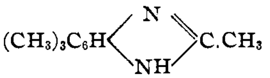
[3] *Ibid.*, **33**, 2652 (1900).

2. Experimental.

s-Pseudocumidine(5-amino-1,2,4-trimethylbenzene) was acetylated by the action of acetic anhydride upon its solution in glacial acetic acid. The crude product (yield, 96%) was purified by recrystallization from 50% acetic acid, and then formed long colorless needles, melting at 164.5° (corr.). Auwers[1] gives the melting point as 164°.

This pseudocumidide was dissolved in glacial acetic acid and nitrated at low temperature with fuming nitric acid, giving the 6-nitro derivative in small colorless glassy needles, which were recrystallized until the melting point remained constant at 199.5° (corr.). Edler[2] gives the melting point as 193–4°, and Auwers[3] as 202–4°.

By reduction of this nitro acetamino compound, the benzimidazole[4]



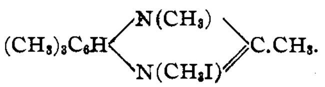
$$(CH_3)_3C_6H \begin{cases} N \\ NH \end{cases} C.CH_3$$

was obtained in minute colorless silky needles, melting at 232° (corr.).

2,4,5,7-Tetramethylbenzimidazole Iodomethylate, $C_{11}H_{14}N_2.CH_3I$.—Four grams of the above imidazole were dissolved in 200 cc. of benzene, 15 cc. of methyl iodide added, and the solution boiled for five hours under a reflux condenser. The crude product was recrystallized from 50% alcohol, giving minute colorless needles, which darken above 330°, but remain unmelted at 350°, and are insoluble in ether.

Subst. 0.2768, 0.2040; 22 cc. N_2 (19° and 750 mm. over H_2O), 0.1526 AgI.
Calculated for $C_{12}H_{17}N_2I$: N, 8.87; I, 40.14. Found: N, 8.97; I, 40.41.

1,2,4,5,7-Pentamethylbenzimidazole Iodomethylate,



$$(CH_3)_3C_6H \begin{cases} N(CH_3) \\ N(CH_3I) \end{cases} C.CH_3.$$

—Five grams of the above tetramethylbenzimidazole, four grams of metallic sodium, 20 cc. of methyl iodide, and 200 cc. of dry xylene, were

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[1] *Ber.*, 18, 2661 (1885).

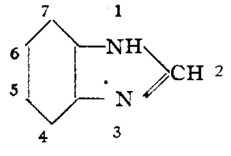
[2] *Ibid.*, 18, 629 (1885).

[3] *Loc. cit.*

[4] Edler, *Loc. cit.*

This compound is not listed in Richter's *Lexikon*, nor in Kuehling's *Handbuch der Stickstoffhaltigen Orthocondensationsproducte.* In Beilstein's *Handbuch*, it is not in its proper place in Vol. IV, but appears merely as an anhydro base under the nitro acetpseudocumidine (II, 552).

For convenience of reference, the positions on the benzimidazole nucleus will be indicated in the following pages according to the system adopted in Richter's *Lexikon*,



boiled together for six hours under a reflux condenser. The iodomethylate separated gradually. After cooling and removal of excess of metallic sodium, the crude iodomethylate was crystallized several times from 50% alcohol, and was thus obtained in minute straw-colored crystals, melting at 274–5° (corr.). Yield, 5 g.

It is soluble in water, alcohol, chloroform, carbon tetrachloride or pyridine; practically insoluble in ether, benzene or ligroin.

Subst. 0.2336, 0.2009; 17.80 cc. N_2 (21° and 749 mm. over H_2O), 14.5 cc. N_2 (18° and 763.4 mm. over H_2O).

Subst. 0.2485; AgI, 0.1801.

Calculated for $C_{13}H_{19}N_2I$: N, 8.48; I, 38.45. Found: N, 8.51, 8.33; I, 38.89.

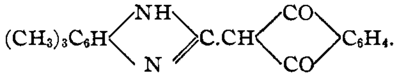
2-Cinnamenyl-4,5,7-trimethylbenzimidazole, $(CH_3)_3C_6H[N_2H]C.CH : CH.C_6H_5$.—An intimate mixture of six grams of 2,4,5,7-tetramethylbenzimidazole and 3.9 grams of benzaldehyde was heated for two hours at 180°. When cold, the crystalline mass was washed carefully with small portions of cold alcohol and then crystallized from the same solvent. It was thus obtained as a colorless crystalline solid, melting at 257.5° (corr.), insoluble in ligroin or ether.

Subst. 0.2077; 19.2 cc. N_2 (13° and 760 mm. over H_2O).

Calculated for $C_{18}H_{18}N_2$: N, 10.70. Found: N. 10.87.

2-p-Nitrocinnamenyl-4,5,7-trimethylbenzimidazole, $(CH_3)_3C_6H[N_2H]C.CH : CH.C_6H_4.NO_2(p)$, was prepared in a similar manner by heating for two hours at 210° an intimate mixture of six grams (one mole) of the tetramethylbenzimidazole with 5.17 grams (one mole) of *p*-nitrobenzaldehyde. The cold crystalline melt was pulverized, washed repeatedly with small portions of cold alcohol, and finally crystallized from hot alcohol. It separated as a yellow powder, darkening at 280°, and melting at 303–5° (uncorr.); easily soluble in isoamyl alcohol, chloroform or acetone; difficultly soluble in ether or benzene; and practically insoluble in ligroin, carbon tetrachloride or carbon disulfide.

2,4,5,7-Tetramethylbenzimidazole Phthalone,



$$(CH_3)_3C_6H\left\langle\begin{matrix}NH\\N\end{matrix}\right\rangle C.CH\left\langle\begin{matrix}CO\\CO\end{matrix}\right\rangle C_6H_4.$$

—Tetramethylbenzimidazole (5.8 g.) and phthalic anhydride (4.36 g.) were intimately mixed and the mixture heated for three hours at 180°. The cooled vitreous melt was extracted with hot 95% alcohol and, as these filtered extracts cooled, the phthalone separated in yellow crystals. The product was recrystallized until its melting point remained constant at 296–7° (corr.). Yield, 2.8 g. This phthalone is readily soluble in isoamyl alcohol or chloroform; slightly soluble in ether, carbon tetrachloride, acetone, ethyl acetate or benzene; and insoluble in ligroin or cold aqueous alkalies.

Subst. 0.1893; 15.3 cc. N_2 (22° and 762 mm. over H_2O).
Calculated for $C_{19}H_{17}O_2N_2$: N, 9.21. Found: N, 9.15.

Propionopseudocumidide, $(CH_3)_3C_6H_2NH.CO.C_2H_5$, was prepared by the direct action of propionic anhydride upon pseudocumidine. The crude product crystallized from 50% acetic acid in colorless needles, melting at 144° (corr.). Yield, 36 grams from 30 grams of the pseudocumidine. It was also prepared by dissolving the pseudocumidine in glacial acetic acid, adding the calculated amount of propionic anhydride, heating the solution to boiling, and diluting with water. On cooling, the propionyl derivative crystallized out practically pure. It is easily soluble in alcohol, acetone, chloroform or carbon tetrachloride; moderately soluble in ligroin, ether or benzene; difficultly soluble in water.

Subst. 0.2246; 14.7 cc. N_2 (20° and 761 mm. over H_2O).
Calculated for $C_{12}H_{17}ON$: N, 7.33. Found: 7.40.

6-Nitro-5-propionamino-1,2,4-trimethylbenzene, $(CH_3)_3C_6H(NO_2)NH.CO.C_2H_5$.—Ten cc. of fuming nitric acid were cooled to —12°, and six grams of the above propionyl derivative added slowly. After standing for a short time, the solution was poured into ice-water, and the precipitated nitro compound crystallized from alcohol. Yield, 6.5 g.

The pure substance forms minute colorless, prismatic crystals, melting at 167° (corr.); easily soluble in isoamyl alcohol, acetone, chloroform, carbon tetrachloride, benzene or pyridine; slightly soluble in ligroin or ether; and practically insoluble in carbon disulfide. Boiled for three hours with 20% hydrochloric acid, under a reflux condenser, it dissolved gradually, but separated unchanged as the solution cooled.

Subst. 0.1576; 16.6 cc. N_2 (20° and 758 mm. over H_2O).
Calculated for $C_{12}H_{16}O_3N_2$: N, 11.88. Found: N. 11.95.

2-Ethyl-4,5,7-trimethylbenzimidazole, $(CH_3)_3C_6H[N_2H]C.C_2H_5$. — Ten grams of the above nitropropionamino compound were mixed with 30 cc. of concentrated hydrochloric acid, and granular tin added in small portions. The reduction proceeded smoothly. At its conclusion, the solution was filtered from excess of tin and the hydrochloride of the base precipitated by adding concentrated hydrochloric acid. Yield, 6.8 g. This salt is soluble in water, but is insoluble in strong hydrochloric acid. It dissolves also in alcohol or pyridine, but not in ether, ligroin, chloroform, carbon tetrachloride, acetone or benzene. It melts with decomposition at 318–20° (corr.).

Subst. 0.2508; 27.4 cc. N_2 (19° and 753.7 mm. over H_2O).
Calculated for $C_{12}H_{17}N_2Cl$: N, 12.39. Found: N, 12.47.

By the action of alkalies upon an aqueous solution of the hydrochloride, the free imidazole was precipitated. Recrystallized from dilute alcohol, it formed minute colorless glassy crystals, melting at 197° (corr.). soluble in isoamyl alcohol, ether, chloroform, carbon tetrachloride, acetone, carbon disulfide, benzene or pyridine, and practically insoluble in ligroin.

Subst. 0.1828; 24.9 cc. N_2 (21° and 756.8 mm. over H_2O).
Calculated for $C_{12}H_{16}N_2$: N, 15.45. Found: N, 15.39.

Chloroplatinate.—Yellowish powder, very slightly soluble in water; decomposes with evolution of hydrogen chloride at 245–6° (corr.).

Subst. 0.1865; Pt, 0.0460.
Calculated for $(C_{12}H_{16}N_2)_2H_2PtCl_6$: Pt, 24.79. Found: Pt, 24.66.

Iodomethylate.—Five grams of the imidazole were dissolved in 200 cc. of benzene, 10 cc. of methyl iodide added, and the solution boiled under a reflux condenser. The iodomethylate separated gradually as a colorless crystalline precipitate. It was purified by recrystallization from 80% alcohol and then appeared in minute colorless needles, which darken above 300°, and melt with decomposition at 345–6° (corr.). The compound is insoluble in benzene, and but slightly soluble in ether.

Subst. 0.2343; 17.8 cc. N_2 (21° and 753 mm. over H_2O).
Subst. 0.2020; AgI, 0.1467.
Calculated for $C_{13}H_{19}N_2I$: N, 8.48; I, 38.44. Found: N, 8.53; I, 39.22.

3-Chloroacetyl-5-propionamino-1,2,4-trimethylbenzene, $(CH_3)_3C_6H(CO.CH_2Cl)NH.CO.C_2H_5$.—Ten grams propionopseudocumidide, 16 grams chloroacetyl chloride, and 200 cc. of carbon disulfide, were mixed in a flask and 60 grams of powdered aluminum chloride added gradually in small portions, shaking the flask well between additions. A copious evolution of hydrogen chloride ensued and the ketone separated as a flocculent solid. After all the aluminum chloride had been added, the mixture was allowed to stand for twelve hours. The carbon disulfide was then removed by decantation, followed by warming and exhausting, ice was added to the residue in the flask, the ketone filtered out and recrystallized from alcohol. Fine silky needles, melting at 181° (corr.), were obtained. Yield, 13.5 g. The substance is easily soluble in chloroform, carbon tetrachloride, isoamyl alcohol, acetone or pyridine, moderately soluble in ether or benzene, and practically insoluble in ligroin.

Subst. 0.2246; AgCl, 11.96.
Calculated for $C_{14}H_{18}O_2NCl$: Cl, 13.25. Found: Cl, 13.16.

Boiling for a few minutes with 20% hydrochloric acid splits off the propionyl group, giving the chloroacetyl pseudocumidine, which has been described already by Kunckell.[1]

Graebe[2] found that the chlorine of ω-chloroacetophenone could be easily converted into the corresponding acetate by boiling with an alcoholic solution of lead acetate, or into the corresponding alcohol by boiling with an aqueous solution of sodium carbonate or with lead hydroxide.

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[1] *Ber.*, **33**, 2652 (1900).

[2] *Ibid.*, **4**, 35 (1871).

The chlorine in the chloroacetyl propionopseudocumidide, we could not displace by similar treatment.

3-Chloroacetyl-5-propionoamino-6-nitro-1,2,4-trimethylbenzene, $(CH_3)_3C_6(NO_2)(COCH_2Cl)NH.CO.C_2H_5$.—Ten cc. of fuming nitric acid were cooled to —12°, and five grams of the chloroacetyl propionopseudocumidide added slowly in small portions.[1] The resulting solution was poured into ice-water, the precipitated nitro compound filtered out and crystallized from dilute alcohol, giving colorless fine silky needles, melting at 193.2° (corr.). Yield, 3.2 g. It is readily soluble in chloroform, isoamyl alcohol, acetic acid, acetone, benzene or pyridine; moderately soluble in ether or carbon tetrachloride; and practically insoluble in ligroin.

Subst. 0.1829; 14.8 cc. N_2 (22° and 754 mm. over H_2O).
Calculated for $C_{14}H_{17}O_4N_2Cl$: N, 8.96. Found: N, 9.04.

3,4-Dimethyl-6-acetoaminobenzoic acid, $(CH_3)_2C_6H_2(NH.COCH_3)COOH$.—In the oxidation of acetopseudocumidide by potassium permanganate described beyond, some of this monobasic acid was usually encountered. It is much more soluble in hot water, or in 50% acetic acid, than the accompanying methylacetoaminoisophthalic acid, and this difference in solubilities was made use of to separate the two acids. The pure monobasic acid forms minute colorless crystals, which melt with decomposition at 248–50° (corr.). It is soluble in alcohol or acetone; practically insoluble in ligroin, chloroform, carbon tetrachloride, ether, carbon disulfide or benzene.

Subst. 0.2100; 12.6 cc. N_2 (20° and 757.4 mm. over H_2O).
Calculated for $C_{11}H_{13}O_3N$: N, 6.77. Found: N, 6.80.
Subst. 0.1469; 3.08 cc. standard NaOH: Theory, 3.10 cc.

By distilling the acid with excess of soda lime, a xylidine was obtained which gave an acetyl derivative melting at 98–9° (corr.). Jacobson[2] gives the melting point of the acetyl derivative of 4-amino-1,2-dimethylbenzene as 99°. As to the other possibilities, the acetyl derivative of *p*-xylidine melts at 180°, and that of *as-m*-xylidine at 120°.

Methyl ester.—Three grams of the acid were dissolved in excess of aqueous acid sodium carbonate solution and three grams of dimethyl sulfate added in small portions, warming after each addition. The ester separated in flocculent form and was crystallized from 50% alcohol until its melting point remained constant at 120° (corr.). Yield, 1.2 g. It forms colorless silky minute needles, easily soluble in ligroin, chloroform, carbon tetrachloride, ether, or benzene.

Subst. 0.1756; 9.6 cc. N_2 (19° and 766 mm. over H_2O).
Calculated for $C_{12}H_{15}O_3N$: N, 6.33. Found: N, 6.31.

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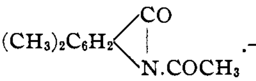
[1] Compare Kunckell, *Loc. cit.*

[2] *Ber.*, 17, 161 (1884).

3,4-Dimethylacetoanthranil, 
$(CH_3)_2C_6H_2\left\langle\begin{matrix}CO\\ |\\ N.COCH_3\end{matrix}\right.$.—Ten grams of the above acetamino acid were dissolved in 25 cc. of acetic anhydride, the solution boiled for 20 minutes and then concentrated. The crude product which separated was purified by repeated crystallization from acetic anhydride. It was thus obtained in nearly colorless minute crystals, melting at 263.5° (corr.), readily soluble in acetic anhydride, but practically insoluble in gasolene, ether or carbon tetrachloride. Yield, poor.

Subst. 0.2617; 16.6 cc. N_2 (18° and 763 mm. over H_2O).
Calculated for $C_{11}H_{11}O_2N$: N, 7.5. Found: N, 7.3.

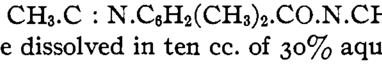
This anthranil is very easily hydrated to the acid. On acting upon it with various amines, there seemed to be a general tendency for the condensation to stop at the intermediate amide stage, instead of continuing to the quinazolone; a difficulty which did not appear in the case of the anthranil from the dibasic acid.

2-Acetoamino-4,5-dimethylbenzamide, $(CH_3)_2C_6H_2(NHCOCH_3)CO.NH_2$.—Three grams of the above acetoanthranil were dissolved in small portions in an excess of concentrated ammonium hydroxide solution; then a little potassium hydroxide was added and the solution boiled for an hour. The clear solution was acidified with hydrochloric acid, and the precipitated amide purified by crystallization from 95% alcohol. It then formed microscopic cream-colored needles, which blacken but do not melt at 340°. The substance is very slightly soluble in ether, and practically insoluble in water, ligroin, carbon tetrachloride or benzene.

Subst. 0.2000; 23.2 cc. N_2 (18° and 762 mm. over H_2O).
Calculated for $C_{11}H_{14}O_2N_2$: N, 13.59. Found: N, 13.36.

2-Acetoamino-4,5-dimethylbenzmethylamide, $(CH_3)_2C_6H_2(NHCOCH_3).CO.NHCH_3$.—Three grams of the acetoanthranil were dissolved in 10 cc. of 33% aqueous methylamine solution, a few cc. of a 10% aqueous solution of potassium hydroxide were added, and the mixture boiled for a few minutes. On acidifying the cooled solution with formic acid, the amide separated instead of the expected quinazolone. Recrystallized from alcohol, this amide was obtained in microscopic colorless needles, which melt with decomposition at 320–2° (corr.), and are soluble in isoamyl alcohol or benzaldehyde, but practically insoluble in ligroin, carbon tetrachloride, ether, acetone or benzene.

Subst. 0.1425; 15.9 cc. N_2 (20° and 766.3 mm. over H_2O).
Calculated for $C_{12}H_{16}O_2N_2$: N, 12.73. Found: N, 12.79.

2,3,6,7-Tetramethyl-4-quinazolone, 
$CH_3.\overline{C : N.C_6H_2(CH_3)_2.CO.N}.CH_3$.—Five grams of the acetoanthranil were dissolved in ten cc. of 30% aqueous methylamine solution, 5 cc. of concentrated (1 : 1) aqueous potassium hydroxide solution added, and the mixture boiled under a reflux condenser

for two hours. The quinazolone separated gradually. Purified by crystallization from 50% alcohol, it formed colorless microscopic needles, melting at 210–2° (corr.), soluble in benzene, but practically insoluble in ether or ligroin. Yield, poor.

Subst. 0.1400; 17.4 cc. N_2 (19° and 756.3 mm. over H_2O).
Calculated for $C_{12}H_{14}ON_2$: N, 13.86. Found: N, 14.15.

2-Acetoamino-4,5-dimethylbenzanilide, $(CH_3)_2C_6H_2(NHCOCH_3)CONHC_6H_5$.—Four grams of the acetoanthranil were dissolved in ten cc. of aniline by warming, five cc. of 10% aqueous potassium hydroxide solution added, and the mixture boiled for 20 minutes, then cooled, acidified with acetic acid, and diluted. The white amorphous precipitate proved to be the anilide and not the quinazolone. Crystallized from dilute alcohol, it was obtained as a cream-colored microcrystalline solid, melting with decomposition at 307° (corr.); soluble in isoamyl alcohol or pyridine, but practically insoluble in ligroin, carbon tetrachloride, ether or benzene.

Subst. 0.1792; 15.4 cc. N_2 (18° and 760.9 mm. over H_2O).
Calculated for $C_{17}H_{18}O_2N_2$: N, 9.94. Found: N, 9.91.

2-Acetoamino-4,5-dimethylbenzhydrazide, $(CH_3)_2C_6H_2(NHCOCH_3)CONHNH_2$.—Three grams of the acetoanthranil were dissolved in an excess of aqueous (50%) hydrazine hydrate solution, a little potassium hydroxide added and the solution warmed for a short time. When cold, it was acidified with formic acid and the yellow precipitate crystallized from 50% alcohol. Colorless microscopic needles resulted, melting with decomposition at 297° (corr.), moderately soluble in ether or pyridine, difficultly in ligroin or 50% alcohol, and practically insoluble in chloroform, carbon tetrachloride, acetone or benzene.

Subst. 0.1637; 26.4 cc. N_2 (18.5° and 762 mm. over H_2O).
Calculated for $C_{11}H_{15}O_2N_3$: N, 19.00. Found: N, 18.60.

3-Amino-2,6,7-trimethyl-4-quinazolone, $CH_3C:N.C_6H_2(CH_3)_2.CO.N.NH_2$.—By boiling the above hydrazide with 10% potassium hydroxide solution and then acidifying with formic acid, this quinazolone was obtained. It crystallized from 50% alcohol in colorless microscopic needles, melting at 215° (uncorr.).

Subst. 0.0938; 17 cc. N_2 (18° and 759 mm. over H_2O).
Calculated for $C_{11}H_{13}ON_3$: N, 20.69. Found, N, 20.81.

4-Methyl-6-acetoaminoisophthalic Acid, $(HOOC)_2C_6H_2(CH_3)NH.COCH_3$.—Oxidation of acetopseudocumidide with potassium permanganate, in neutral or alkaline solution, yielded chiefly this dibasic acid, together with a smaller amount of the monobasic acetoaminodimethylbenzoic acid already described. The best results were secured by oxidizing with the permanganate at 95–100°, in presence of magnesium sulfate, but even then the best yield we could get of the dibasic acid was 25%.

1. A mixture of 20 grams of the acetopseudocumidide, 30 grams magnesium sulfate and five liters of water, was heated in a large evaporating dish at 95–100°, and a solution of 80 grams of potassium permanganate run in slowly, stirring mechanically. The oxidation was completed in three hours. The hot solution was filtered, the filtrate acidified with hydrochloric acid, and the flocculent precipitate crystallized from 50% acetic acid. Colorless microscopic needles were thus obtained, which turned yellow and shrunk at 250–5°, and melted at 278–80° (corr.) with evolution of carbon dioxide and decomposition. Yield, 6 g.

2. Oxidations were also carried out in presence of potassium chloride instead of magnesium sulfate. Eighty grams of potassium chloride were dissolved in two and a half liters of water, four grams of the cumidide added, the solution heated to boiling, stirred mechanically, and a solution of 22 grams of potassium permanganate gradually dropped in. The oxidation was completed in two hours, but on filtering and acidifying the filtrate with hydrochloric acid, nothing precipitated even on long standing.

3. In this experiment the conditions were exactly the same as in the last, except that the oxidation was conducted at 62–4°. After ten hours the oxidation was still uncompleted, so about a third of the mixture was removed, the excess of permanganate reduced by alcohol, the solution filtered and acidified with hydrochloric acid. The precipitate which formed softened at 267–70°, but did not melt completely at 300°, and was not separated in sufficient amount for identification.

The remaining two-thirds of the original mixture were heated five and a half hours longer at 80° with constant stirring. Half of this was then taken, the excess of permanganate reduced by adding alcohol, the solution filtered and acidified with hydrochloric acid. The amorphous precipitate resulting proved to be a mixture of the mono- and dibasic acids.

The final third of the original mixture, after having stood for 24 hours longer at laboratory temperature, was found to have become decolorized. On filtering and acidifying the filtrate, a beautiful crystalline precipitate separated gradually, which proved to be the tribasic acid and is described beyond.

4. In another experiment, the oxidation was conducted at 40–50° for three days, with constant stirring, and gave only mono- and dibasic acids.

The dibasic acid is easily freed from the monobasic by crystallization from water or from 50% acetic acid, in both of which the monobasic acid is much more soluble, as already mentioned in connection with the latter acid.

The pure acid forms colorless microscopic needles, which shrink somewhat at about 250–5°, and melt with decomposition at about 278–80° (corr.), as noted above. It is easily soluble in alcohol, moderately in acetone, and practically insoluble in ligroin, chloroform, ether or benzene.

Calculated for $C_{11}H_{11}O_6N$: C, 55.66; H, 4.68; N, 5.92. Found: C, 55.36, 55.51; H, 4.83, 4.83; N, 6.28, 6.23.

Distilled with excess of soda lime, the acid yielded a toluidine whose acetyl derivative melted at 64.8° (corr.). A sample of aceto-*m*-toluidide, prepared from some Kahlbaum *m*-toluidine, melted at 65.2° (corr.). Aceto-*o*-toluidide melts at 110° and aceto-*p*-toluidide at 153°. The methyl groups of the acetopseudocumidide which have been oxidized by the above treatment are therefore those at positions 2 and 4, thus giving an isophthalic acid.

Dimethyl Ester.—Four grams of the acid were dissolved in a solution of five grams acid sodium carbonate, causing a marked lowering of temperature. The solution was warmed gently, about six grams of dimethyl sulfate added gradually, and the mixture left over night. The ester separated as a flocculent amorphous solid. It was filtered out and crystallized from 50% alcohol. Yield, 3.3 g. The pure ester forms colorless silky hairs; melting at 138° (corr.); easily soluble in chloroform, ether, carbon, disulfide, acetone, ethyl acetate, benzene or pyridine; moderately soluble in ligroin; and practically insoluble in water.

Subst. 0.2513: CO_2, 0.5417; H_2O, 0.1278.
Calculated for $C_{13}H_{15}O_5N$: C, 58.84; H, 5.70. Found: C, 58.75; H, 5.65.

This compound was also prepared by acetylating the aminomethylisophthalic ester.

Diethyl Ester.—Four grams of the aminomethylisophthalic ester were dissolved in excess of acetic anhydride, the solution evaporated to dryness and the final traces of the anhydride removed by leaving the material in a vacuum desiccator over solid potassium hydroxide. The crude product crystallized from 50% alcohol in colorless minute needles, melting at 116.5° (corr.); easily soluble in chloroform, ether, acetone, carbon disulfide, ethyl acetate, benzene or pyridine; moderately soluble in ligroin; and but very slightly soluble in hot water. Yield, 4 g.

Subst. 0.3001; 12.7 cc. N_2 (18° and 760.2 mm. over H_2O).
Calculated for $C_{15}H_{19}O_5N$: N, 4.78. Found: N, 4.83.

4-Methyl-6-aminoisophthalic Acid, $(HOOC)_2C_6H_2(CH_3)NH_2$.—This acid was secured by the hydrolysis of the above acetoamino acid. The hydrolysis was effected more satisfactorily by acid than by alkali.

Four grams of the acetoamino acid were added gradually, with stirring, to a hot solution of 15 cc. of dilute sulfuric acid (9 cc. concentrated acid and 6 cc. water), the clear solution heated quickly to boiling, boiled for about a minute, and then poured into cold water,[1] the amino acid separating as a flocculent precipitate. It crystallized from water in colorless long needles, melting at 305–8° (corr.), which dissolve in alcohol or acetic

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[1] Compare Mayer, *Ber.*, **44**, 2300 (1911).

acid, but are practically insoluble in ligroin, chloroform, ether, ethyl acetate or benzene.

Subst. 0.2132; 14.2 cc. N_2 (22° and 762 mm. over H_2O).
Calculated for $C_9H_9O_4N$: N, 7.17. Found: N, 7.11.

By the action of acetic anhydride, the acetoamino acid is reproduced.

Hydrochloride.—Three grams of the acid were boiled under a reflux condenser with 10 cc. of concentrated hydrochloric acid. After boiling four hours, a clear solution was obtained, and, on cooling, the entire contents of the flask set to a mass of needle crystals. These were recrystallized from concentrated hydrochloric acid and dried over solid potassium hydroxide. They are easily soluble in water, but very difficultly soluble in cold concentrated hydrochloric acid, and melt with decomposition at 196–7° (corr.). Yield, 2.8 g.

Subst. 0.1416; AgCl, 0.0870.
Calculated for $C_9H_{10}O_4NCl$: Cl, 15.3. Found: Cl, 15.1.

Dimethyl ester.—The acetoamino acid was used for the preparation of this ester.

Five grams of the acetamino acid were suspended in 200 cc. of absolute methyl alcohol, the mixture heated under a reflux condenser and saturated with dry hydrogen chloride. The acetoamino acid dissolved gradually, forming a light yellow solution, and the odor of methyl acetate was noted. After passing hydrogen chloride through it for two hours, the hot solution, which had become a deep red, was allowed to cool. The hydrochloride of the ester separated in crystals. These were filtered out and a second crop obtained by concentration of the mother liquor. The amino ester was liberated from this hydrochloride by treatment with sodium carbonate solution in slight excess, and then crystallized from 50% alcohol. Fine colorless silky hairs resulted, melting at 150 °(corr.); easily soluble in chloroform, ether, ethyl acetate, carbon disulfide, benzene or pyridine; slightly soluble in ligroin; and insoluble in water.

Subst. 0.1620; 8.90 cc. N_2 (19° and 760.4 mm. over H_2O).
Calculated for $C_{11}H_{13}O_4N$: N, 6.28. Found: N, 6.29.

After precipitating the free ester from its hydrochloride by the action of excess of sodium carbonate solution, this carbonate mother liquor was acidified and a white flocculent precipitate obtained. Crystallized from dilute alcohol, it formed colorless minute needles, melting at 217° (uncorr.); soluble in aqueous alkalies. It is perhaps an acid ester. Not enough of it was recovered to investigate further.

Diethyl Ester.—This was prepared in an entirely analogous manner, using absolute ethyl alcohol instead of methyl. It crystallized from dilute alcohol in straw-yellow glassy needles, melting at 103.5° (corr.); easily soluble in ligroin, chloroform, ether, ethyl acetate, carbon disulfide, benzene or pyridine; insoluble in water.

Subst. 0.2669; CO_2, 0.6795; H_2O, 0.1866.
Calculated for $C_{13}H_{17}O_4N$: C, 62.15; H, 6.82. Found: C, 62.48; H, 6.98.

Acetoanthranil of 4-Methyl-6-amino Isophthalic Acid,

$HOOC(CH_3)C_6H_2.CO.N.COCH_3$.—Twenty-five grams of the acetoamino acid were dissolved in 40 cc. of acetic anhydride, the solution heated just below its boiling point until its volume was reduced to 20 cc., and then allowed to cool. The acetoanthranil separated in clusters of microscopic yellowish needles, which were recrystallized repeatedly from acetic anhydride, washed with dry benzene and carefully dried. As thus purified, it melts at 285–6° (corr.); it is difficultly soluble in chloroform or ethyl acetate; and apparently insoluble in ligroin, ether, benzene or toluene. Moisture rapidly hydrates it, regenerating the acetoamino acid.

Subst. 0.1857; 10.3 cc. N_2 (24° and 769 mm. over H_2O).
Calculated for $C_{11}H_9O_4N$: N, 6.38. Found: N, 6.30.

It can be prepared in similar manner from the amino acid itself.

2-Methyl-4-acetoamino-5-carbaminobenzoic Acid, $HOOC(CH_3)C_6H_2(NH.CO.CH_3)CONH_2$.—Four grams of the above acetoanthranil were added in small portions to 12 cc. of concentrated ammonium hydroxide solution. The reaction was vigorous, the anthranil dissolving to a clear solution. This solution was boiled for ten minutes, then cooled, filtered, and acidified with hydrochloric acid. The precipitated amide separated from 60% alcohol in nearly colorless microscopic short glassy crystals, which melt to a dark liquid at 303–5° (corr.), and are soluble in acetone, but practically insoluble in ligroin, chloroform, ether or benzene.

Subst. 0.1823; 19.0 cc. N_2 (19° and 768.3 mm. over H_2O).
Calculated for $C_{11}H_{12}O_4N_2$: N, 11.87. Found: N, 11.98.

2,7-Dimethyl-4-quinazolone-6-carboxylic Acid,

$CH_3.C : N.C_6H_2(CH_3)(COOH).CO.NH$.—The acetoanthranil was dissolved in concentrated ammonium hydroxide solution, some potassium hydroxide was added, the solution boiled about an hour, cooled, and acidified with hydrochloric acid. The precipitated quinazolone was extracted with boiling alcohol, to remove any amide, then dissolved in ammonium hydroxide solution, reprecipitated by hydrochloric acid, washed and dried. It is apparently insoluble in water, ligroin, alcohol, ether, acetone or benzene; at 340° (corr.), it chars without melting.

Subst. 0.1834; 20.95 cc. N_2 (21° and 762.6 mm. over H_2O).
Calculated for $C_{11}H_{10}O_3N_2$: N, 12.85. Found: N, 12.98.

2,3,7-Trimethyl-4-quinazolone-6-carboxylic Acid,

$CH_3.C : N.C_6H_2(CH_3)(COOH).CO.N.CH_3$.—Three grams of the acetoanthranil were dissolved in eight cc. of 33% aqueous methylamine solution, a little potassium hydroxide added, the solution boiled for ten minutes and then neutralized with acetic acid. On cooling, the contents of the flask set to a crystalline mass of the quinazolone. These crystals were separated, washed with hot water, and recrystallized from 95% alcohol, until they showed a constant melting point of 299.5° (corr.). Yield, 1.2 g. The purified compound forms colorless microscopic crystals, difficultly soluble or insoluble in water, ligroin, ether, ethyl acetate or benzene. It is easily soluble in aqueous alkalies, and reprecipitates when these solutions are acidified.

Subst. 0.1501; 16.1 cc. N_2 (20° and 761 mm. over H_2O).
Calculated for $C_{12}H_{12}O_3N_2$: N, 12.07. Found: N, 12.22.

2,7-Dimethyl-3-ethyl-4-quinazolone-6-carboxylic Acid, $CH_3.\overline{C : N.C_6H_2(CH_3)(COOH)CO.N}.C_2H_5$, prepared in a similar manner, crystallized from 30% alcohol in colorless silky needles, melting sharply (with decomposition) at 250.8° (uncorr.), and showing much the same solubilities as the above trimethyl compound.

Subst. 0.2170; 21.8 cc. N_2 (22° and 758 mm. over H_2O).
Calculated for $C_{13}H_{14}O_3N_2$: N, 11.38. Found: N, 11.30.

2,7-Dimethyl-3-phenyl-4-quinazolone-6-carboxylic Acid.—Four grams of the acetoanthranil were dissolved in 10 cc. of aniline, the solution boiled ten minutes, cooled, and neutralized with dilute hydrochloric acid. The precipitated quinazolone was crystallized from 80% alcohol, from which it separated in minute pale yellow needles, melting at 300–1° (corr.), practically insoluble in ether or benzene.

Subst. 0.1578; 13.2 cc. N_2 (23° and 765.7 mm. over H_2O).
Calculated for $C_{17}H_{14}O_3N_2$: N, 9.53. Found: N, 9.48.

2,7-Dimethyl-3-amino-4-quinazolone-6-carboxylic Acid.—Three grams of the acetoanthranil were added in small portions to an excess of aqueous hydrazine hydrate solution (50%). The anthranil dissolved with evolution of heat. Dilute potassium hydroxide solution was added, the liquid heated to boiling for a short time, left over night, and then acidified with acetic acid. The quinazolone separated gradually in minute silky needles, which were recrystallized from dilute alcohol. Yield, 2.8 g. It melts with decomposition at 306° (corr.), is difficultly soluble in acetone and apparently insoluble in ligroin, chloroform, ether, carbon disulfide or benzene.

Subst. 0.2521; 40.4 cc. N_2 (20.5° and 765.6 mm. over H_2O).
Calculated for $C_{11}H_{11}O_3N_3$: N, 17.95. Found: N, 18.12.

Acetyl Derivative.—Three grams of the above aminoquinazolone were dissolved in 12 cc. of acetic anhydride, the solution evaporated to small volume and then placed in a vacuum desiccator over solid potassium hydroxide. The crude product was crystallized first from dilute acetic acid and then from alcohol. Transparent glassy minute plates were obtained, melting at 220° (uncorr.); soluble in ethyl acetate, but apparently insoluble in ligroin, ether, carbon disulfide or benzene.

Subst. 0.1475; 19 cc. N_2 (19° and 762 mm. over H_2O).
Calculated for $C_{13}H_{13}O_4N_3$: N, 15.27. Found: N, 14.8.

Evaporation of the amino quinazolone with glacial formic acid failed to yield any formyl derivative.

Benzal derivative.—When a mixture of three grams of the amino quinazolone with excess of benzaldehyde was heated to boiling, water was driven out and, on cooling, needles separated. These were recrystallized from a mixture of benzaldehyde and alcohol (1 : 4), as good crystals could not be secured from other solvents tried. The minute straw-colored needles so obtained were washed with ether, to remove benzaldehyde, and dried. They are soluble in water, ligroin, alcohol or acetic acid, but practically insoluble in ether. At 237.5° (corr.), they melt to a clear liquid which decomposes at 278° (corr.). The substance decolorizes a bromine solution.

Subst. 0.2032; 23.2 cc. N_2 (22° and 760.7 mm. over H_2O).
Calculated for $C_{18}H_{15}O_3N_3$: N, 13.09. Found: N, 13.00.

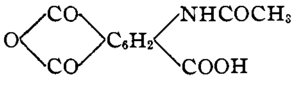
Dimethyl 4-Methyl-6-phenyluraminoisophthalate, $(CH_3OOC)_2C_6H_2(CH_3).NH.CO.NHC_6H_5$.—Four grams (one mole) of dimethylmethylaminoisophthalate were dissolved in 60 cc. of carefully dried benzene, 2.1 grams (one mole) of phenyl isocyanate added, the solution boiled for two hours under a reflux condenser, then concentrated to half its original volume and allowed to cool. The crystals which separated were washed with dry benzene, to remove any unchanged isocyanate, and recrystallized from 95% alcohol. Rosettes of colorless microscopic needles resulted, melting at 192.5° (corr.); easily soluble in alcohol, acetone or pyridine, moderately in chloroform or benzene, difficultly in ether, and apparently insoluble in carbon tetrachloride or carbon disulfide. It was not hydrolyzed by boiling for three hours with dilute hydrochloric acid.

Subst. 0.2509; 18.40 cc. N_2 (21° and 757 mm. over H_2O).
Calculated for $C_{18}H_{18}O_5N_2$: N, 8.19. Found: N, 8.23.

Diethyl Ester.—Prepared in a similar manner, this ester crystallized from 95% alcohol in colorless microscopic needles, melting at 177–8° (corr.); easily soluble in alcohol, chloroform, ether, acetone, benzene or pyridine; slightly soluble in ligroin, carbon tetrachloride or carbon disulfide. Yield, 2.6 g. from 3 g. of the initial compound.

Subst. 0.2005; 13.5 cc. N_2 (20° and 762 mm. over H_2O).
Calculated for $C_{20}H_{22}O_5N_2$: N, 7.57. Found: N, 7.66.

Anhydride of 5-Acetamino-1,2,4-benzenetricarboxylic Acid,



$$O\left\langle\begin{matrix}CO\\CO\end{matrix}\right\rangle C_6H_2\left\langle\begin{matrix}NHCOCH_3\\COOH\end{matrix}\right.$$

—In describing the preparation of the acetoaminomethylisophthalic acid by oxidation of acetopseudocumidide, it is there noted that in one case (No. 3), when the oxidation was conducted at moderate temperature (62–4°), some of this tribasic acid was isolated. It crystallized from water in regular glassy prisms, which fell to powder on drying. This powder melts with decomposition at 240–2° (corr.), and is soluble in alcohol, and apparently insoluble in ether.

Subst. 0.2046; 9.79 cc. N_2 (16° and 772 mm. over H_2O).
Calculated for $C_{11}H_7O_6N$: N, 5.63. Found: N, 5.64.

Subst. 0.1989; 9.80 cc. standard KOH solution. Theory for anhydride of the tribasic acid, 9.80 cc.

The glassy crystals first obtained by crystallization from water were, therefore, probably the acid itself. Unfortunately, the amount of substance isolated was too small for further study, and experiments to secure more of it have so far proven fruitless. An oxidation carried out at laboratory temperature, and lasting 32 days in all, yielded only the mono- and dibasic acids. Attempts to oxidize the dibasic acid in various ways also proved failures, the acid being invariably either unchanged or else wholly destroyed with evolution of carbon dioxide.

3. Summary.

1. A number of new derivatives of 2,4,5,7-tetramethylbenzimidazole are described.
2. Propionopseudocumidide was prepared, and from it the benzimidazole and other new derivatives.
3. Oxidation of acetopseudocumidide gives mono- and dibasic acids. Only in one experiment was a small amount of tribasic acid isolated.
4. The structure of the acids so produced indicates that the methyl group in position 4 is first oxidized, then that at 2.
5. As both the mono- and the dibasic acid so obtained are of anthranilic type, they yield acyl anthranils and 4-quinazolones by the usual methods.

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[Contribution from the Texas Experiment Station.]

UTILIZATION OF THE PROTEINS OF COTTON SEED BY MAN.

By J. B. Rather.[1]

Received January 1, 1914.

Cotton seed meal has been used, to some extent, as a human food, for a number of years in the South. In Texas, at least, it is claimed to be used both by those who are too poor to buy sufficient meat, and by those who use it by preference, mixing it with wheat flour. Since cotton seed meal contains more than twice as much protein as meat, and since it can

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[1] Under the general direction of G. S. Fraps, Chemist. Abstracted by the author from *Bulletin* 163 of the Texas Experiment Station.