ON A NEW SYNTHESIS OF TYROSINE.

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IN THE LANCET of Dec. 16th, 1905, p. 1757, I described a new method for the synthesis of tyrosine from anhydrous prussic acid and *p* oxy-benzaldehyde; a method not only interesting in itself but, as I suggested, affording an explanation of the mode of formation of tyrosine in the animal body—namely, by the combination of adenine with the above-mentioned aldehyde.

In the section on p. 1759, describing the mode of directly transforming *p*-oxy-benzoyl-amino-cinnamic acid into tyrosine, there is an important clerical error with regard to the amount of barium hydrate which was employed and which is there stated to be "about 6·0 grammes." The amount should be 2·25 grammes. On making a number of further experiments with fresh materials I found that if more than 2·25 grammes are employed little or no tyrosine is produced, as an excess of hydrogen is liberated and the reduction of the *p*-oxy-benzoyl-amino-cinnamic acid is carried too far. This error, however, has been turned to good account and has led me to an improved and much more simple method. After making several experiments it occurred to me to dispense altogether with the barium hydrate and to try what action potassium cyanide alone would have upon the oxy-acid. The result was most satisfactory. Not only is the *p* oxy-benzoyl-amino-cinnamic acid reduced by the cyanide to benzoyl tyrosine, but the latter is also simultaneously decomposed into tyrosine and benzoic acid, a result I had not anticipated. The following are the changes:—

$$2KCN + 4H_2O = \underset{\text{Potassium formate.}}{(H.COO)_2K_2} + 2NH_3$$

$$= H_2 + \underset{\text{Potassium oxalate.}}{(COO)_2K_2} + 2NH_3$$

and

$$OH.C_6H_4.CH:C(NH.CO.C_6H_5).COOH + H_2$$

p-oxy-benzoyl-amino-cinnamic acid.

$$= OH.C_6H_4.CH_2.CH(NH.CO.C_6H_5).COOH$$

Benzoyl tyrosine.

which acted upon by the ammonia and water is resolved into

$$\underset{\text{Tyrosine.}}{OH.C_6H_4.CH_2.CH(NH_2)COOH} \text{ and } \underset{\text{Ammonium benzoate.}}{C_6H_5.COONH_4}$$

The process, therefore, is much simplified and the yield of tyrosine is greater than when the barium hydrate is used. The only drawback is that the amount of colouring matter is considerable and necessitates a large dilution of the contents of the combustion tube before decolourising with animal charcoal, as well as two or three re-crystallisations, each involving marked loss in the product.

I have made a number of experiments with different proportions of KCN at various temperatures and with varying results. The following, however, are the details of the experiment which yielded the best result, the proportion of the oxy-acid to the KCN employed being one molecule of the former and three molecules (instead of two) of the latter. 7·1 grammes of *p*-oxy-benzoyl-amino-cinnamic acid together with five grammes of KCN (98 per cent.) were placed in a combustion tube and to this mixture 48 cubic centimetres of hot water were added. The tube was then sealed (the contents occupying about one-half its capacity) and heated for three hours to a temperature gradually rising from 130° to 170° C. The temperature was then raised and maintained for four and a half hours between 175° and 182° C. On opening the tube there was a free escape of ammonia. The contents of the tube were washed out with hot water and well diluted, so that the total amount measured 300 cubic centimetres. The dark solution was filtered and then placed in a water bath (100° C.) with animal charcoal for half an hour, and again filtered and evaporated to dryness at 100°. The residue (still coloured) was then treated with small quantities of *cold* water to dissolve out the potassium oxalate, &c., and the solution aspirated, leaving the impure tyrosine behind. This was now dissolved in dilute aqueous ammonia, filtered, and then evaporated in the water bath to about 36 cubic centimetres when crystals of tyrosine began to form on the margin of the liquid. The solution whilst hot was poured into a watch glass and set aside for 12 hours, when the tyrosine was found to have crystallised out almost completely in the form of beautiful silky colourless sheaves of needles. The mother liquor was then separated by aspiration with a pipette. The yield of tyrosine in this experiment was 0·6 gramme, being 13·2 per cent. of the theoretical amount—that is, 4·54 grammes. Its melting point was found to be 237° C. and Millon's and Piria's tests gave the usual reactions.

Mr. M. M. Pattison Muir, to whose valuable help and encouragement in this investigation I have been greatly indebted, kindly undertook to analyse some of the specimens for me. The following are the details of his analysis. On combustion, 0·1785 gramme yielded 0·3862 gramme CO_2, and 0·1002 gramme H_2O. For the nitrogen determination 0·2055 gramme yielded 13·4 cubic centimetres of nitrogen at 20° C. and 774 millimetres pressure.

	Calculated for $C_9H_{11}NO_3$	Obtained. I.		II.
C	59 67	59 00	.....	—
H	6 08	6 23	.....	—
N	7 74	—	.....	7 72

Cambridge.

A CASE OF EPILEPTIC IDIOCY ASSOCIATED WITH TUBEROSE SCLEROSIS OF THE BRAIN.

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THE patient, a male epileptic idiot, was admitted into the West Riding Asylum, Wakefield, on Feb. 16th, 1901. He died on May 25th, 1906, aged ten years, from pneumonia, accelerated by exhaustion from epilepsy.

Family history.—The mother is of a nervous temperament and the father suffers from a "weak chest." A brother, aged seven years, suffers from epileptic fits and is extremely impulsive and emotional. Two maternal uncles died from convulsions at the age of two years and four months and one year and four months respectively. A paternal uncle was intemperate and died from pulmonary tuberculosis and three paternal aunts died from the same disease. A maternal great-uncle was addicted to alcoholic excess and is now in an asylum suffering from general paralysis of the insane. A maternal great-aunt was an inmate of the West Riding Asylum, Wakefield, in 1886–87, suffering from alcoholic pseudo-paralytic dementia.

Clinical history.—The patient was healthy and well formed at birth. Labour was normal, no forceps being used. He was the eldest of four living children. At the age of three or four weeks "twitching of the face and nodding of the head" was noticed. Convulsions resembling those of idiopathic epilepsy commenced one year after birth. The patient's mental condition on admission to the asylum was as follows. He was a low grade idiot and was unable to do anything for himself. He would grasp and pull to pieces or twist anything that was given to him. He made inarticulate noises and was quite incapable of answering the simplest questions. In his habits he was wet and dirty. As regards his physical condition he was below the average size, the frontal region of the skull was prominent, and his head was of the usual size. The palate was of the low, broad type. The teeth were good. The lobules of the ears were deficient. He suffered from the somewhat rare skin affection known as adenoma sebaceum. Little nodules were noticed on his face, occupying chiefly the cheeks and naso-labial folds; a few were noticed on the forehead. The nodules had a symmetrical distribution on the lower part of the face: their consistence was hard, their surfaces were smooth and dome-shaped, and the skin over them showed no blocked sebaceous duct. Vascular telangiectases around and between these nodules gave the patient a pink flushed look. The heart and lungs were normal. No sensory abnormal symptoms were noticed during life. His gait was peculiar in that he had a tendency to walk on his toes and seemed incapable of walking in a straight line; he would rotate