STUDIES OF THE METABOLISM OF TRYPTOPHAN LABELED WITH N\textsuperscript{15} IN THE INDOLE RING* 

BY RICHARD W. SCHAYER† 

(From the Department of Biochemistry, College of Physicians and Surgeons, Columbia University, New York) 

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Recent interest in tryptophan metabolism has been stimulated by evidence that tryptophan is a precursor of nicotinic acid in mammals (1) as well as in Neurospora crassa (2). The formation of kynurenine, kynurenic acid, and xanthurenic acid from tryptophan has been demonstrated by numerous experiments (3–5) and has been confirmed by isotope technique in the case of kynurenine and kynurenic acid (6). Recently it has been shown that indole plus serine can act as a precursor of tryptophan in N. crassa, and there are indications that the same relationship may hold true for certain bacteria (7). In order to study these and other aspects of tryptophan and indole metabolism, indole labeled with N\textsuperscript{15} and tryptophan labeled with N\textsuperscript{16} in the indole ring were synthesized. 

EXPERIMENTAL 

Synthesis of Indole Containing N\textsuperscript{15}—Potassium phthalimide (containing excess N\textsuperscript{16}) was converted successively into anthranilic acid (8), phenylglycine-o-carboxylic acid (9), indoxylic acid, indoxyl, and indole (10). The indole was recrystallized twice from ligroin. It contained 33.1 per cent excess N\textsuperscript{15}; m.p. 52°; calculated N (based on 33.1 per cent N\textsuperscript{16}) 12.11 per cent; found, 12.22. 

Synthesis of Tryptophan Containing N\textsuperscript{16} in Indole Ring—N\textsuperscript{16}-labeled indole was converted by way of gramine to DL-tryptophan by the method of Howe et al. (11). The over-all yield from potassium phthalimide was 

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4.1 per cent of the theoretical amount. It contained 31.2 per cent excess N\textsuperscript{15}; m.p. 286-290\degree; calculated N (based on 31.2 per cent N\textsuperscript{15}) 13.86 per cent; found, 13.86.

The tryptophan was resolved by the method of Shabica and Tishler (12); L-tryptophan, [\alpha]\textsubscript{D} = -31.5\degree; D-tryptophan, [\alpha]\textsubscript{D} = +31.6\degree for 1 per cent aqueous solution.

**Relationship of Tryptophan to Kynurenine, Kynurenic Acid, and Xanthurenic Acid**—The rats and rabbits used in experiments on the conversion of tryptophan to kynurenic acid were fed a stock diet. Those used in experiments on the conversion of tryptophan to kynurenine were fed a polished rice diet for 2 to 3 weeks. Rats for experiments on the conversion of tryptophan to xanthurenic acid were fed a pyridoxine-deficient diet (13) for 4 to 5 weeks and injected with 1.5 mg. of desoxypyridoxine along with the tryptophan. In all cases the N\textsuperscript{15}-tryptophan was injected intraperitoneally in neutral solution. The level of tryptophan injected into rabbits ranged from 0.5 to 0.8 gm. per kilo of body weight, while for rats it ranged from 1.5 to 2.0 gm. per kilo of body weight. In the rabbit experiments, one animal was used; in those with rats, three to six animals were employed.

Kynurenine sulfate was isolated by the method of Kotake and Iwao (3) from the urine of rats and rabbits. Crystallization by addition of alcohol to the concentrated urine produced a substance which after two recrystallizations from 60 per cent alcohol had an N content of 8.48 per cent. While this is in agreement with the value of 8.51 per cent obtained by Kotake and Iwao (3) and of 8.54 per cent reported by Jackson and Jackson (14), it does not conform with the theoretical value of 9.15 per cent required by the revised formula of Butenandt et al. (15). However, when subjected to precipitation with mercuric sulfate in 0.3 N sulfuric acid, the product contained 9.12 per cent N, [\alpha]\textsubscript{D} = +7.4\degree (1 per cent aqueous solution); reported [\alpha]\textsubscript{D} = +7.3\degree. The concentrations of N\textsuperscript{15} in the urinary kynurenine are given in Table I, Experiments 2, 6, and 7.

Kynurenic acid was isolated by the Capaldi method (16) from the urine of rats and rabbits. After two recrystallizations from 50 per cent acetic acid, the isotope content was constant. The melting point of kynurenic acid was 287\degree; reported 290\degree (17); of methyl ester, 224\degree; reported 224\degree (18). Concentrations of N\textsuperscript{15} in the urinary kynurenic acid are given in Experiments 1 to 4 and 7, Table I.

Xanthurenic acid was isolated from the urine of rats. Isolation was accomplished by strongly acidifying the urine with hydrochloric acid, allowing the precipitate to settle for 1 hour, and shaking the entire mixture with three portions of isobutanol. The isobutanol extract was dried, filtered, and evaporated to dryness in vacuo. The residual red-brown tar
was taken up in saturated sodium chloride solution and filtered. The insoluble residue was washed with water and then with acetone, dissolved in warm dilute sodium hydroxide solution, and reprecipitated with hydrochloric acid. The crude xanthurenic acid was purified as the methyl ester.

### Table I

**N\(^{15}\) Excretion after Injection of Tryptophan and Kynurenine**

<table>
<thead>
<tr>
<th>Experiment No.</th>
<th>Animal</th>
<th>Compound Injected</th>
<th>N(^{15}) Concentration of Compound Injected*</th>
<th>Compound Isolated</th>
<th>N(^{15}) Concentration of Compound Isolated*</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Rabbit</td>
<td>66.4 mg. DL-tryptophan + 1.021 gm. normal L-tryptophan</td>
<td>1.071§</td>
<td>Kynurenic acid</td>
<td>0.850</td>
</tr>
<tr>
<td>2</td>
<td>“</td>
<td>201.0 mg. DL-tryptophan + 1.980 gm. normal L-tryptophan</td>
<td>1.507§</td>
<td>Kynurenine sulfate</td>
<td>1.294</td>
</tr>
<tr>
<td></td>
<td>“</td>
<td>L-Tryptophan</td>
<td>0.248</td>
<td>Kynurenic acid</td>
<td>0.219</td>
</tr>
<tr>
<td>4</td>
<td>Rat</td>
<td>“</td>
<td>0.310</td>
<td>Kynurenic acid</td>
<td>0.237</td>
</tr>
<tr>
<td>5</td>
<td>“</td>
<td>“</td>
<td>0.310</td>
<td>Xanthurenic acid methyl ester</td>
<td>0.297</td>
</tr>
<tr>
<td>6</td>
<td>“</td>
<td>“</td>
<td>0.544</td>
<td>Kynurenine sulfate</td>
<td>0.504</td>
</tr>
<tr>
<td>7</td>
<td>“</td>
<td>18.3 mg. DL-tryptophan + 1.192 gm. normal L-tryptophan</td>
<td>0.238§</td>
<td>Kynurenine sulfate</td>
<td>0.486</td>
</tr>
<tr>
<td></td>
<td>“</td>
<td>Kynurenine sulfate, natural isomer</td>
<td>0.472</td>
<td></td>
<td>Kynurenic acid</td>
</tr>
<tr>
<td>8</td>
<td>“</td>
<td>“</td>
<td>0.126</td>
<td>Xanthurenic acid</td>
<td>0.137</td>
</tr>
<tr>
<td>9</td>
<td>Rabbit</td>
<td>“</td>
<td>0.172</td>
<td>Kynurenic acid</td>
<td>0.127</td>
</tr>
</tbody>
</table>

* All N\(^{15}\) values for tryptophan are based on the ring nitrogen only; those for kynurenine are based only on the nitrogen attached to the ring.
† Discrepancies due to isotope content are negligible.
‡ 31.2 per cent excess N\(^{15}\) in the ring.
§ Based on L isomer only.
∥ Based on L + DL.

(19) or recrystallized by dissolving in slightly alkaline 50 per cent alcohol, heating, and acidifying. The xanthurenic acid melted at 288°; m.p. 290° (Lepkovsky et al. (19)). The methyl ester melted at 261–262°; m.p. 260–261° (19). The concentration of N\(^{15}\) in the urinary xanthurenic acid is given in Table I, Experiment 5.

**Relationship of Kynurenine to Kynurenic Acid and Xanthurenic Acid—**
A sample of N\textsuperscript{15}-labeled kynurenine sulfate was prepared from the urine of rats and rabbits which had received isotopic tryptophan, and purified by recrystallization from 60 per cent alcohol. After neutralization it was injected intraperitoneally into a rabbit fed a stock diet. The N\textsuperscript{15} concentration of the urinary kynurenic acid is given in Table I, Experiment 9.

Xanthurenic acid was obtained from the urine of three rats injected intraperitoneally with N\textsuperscript{15}-labeled kyrurenine as given in Table I, Experiment 8.

**Relationship of Tryptophan to Hemin**—Each of three 250 gm. male rats on a tryptophan-deficient diet was injected in two doses with a total of 305 mg. of dL-tryptophan containing 31.2 per cent N\textsuperscript{15}. The rats were killed by exsanguination 17 days after the last dose of tryptophan, and the hemin was isolated (20) and recrystallized. It contained 0.014 per cent N\textsuperscript{18} excess.

**Distribution of N\textsuperscript{15} after Ingestion of Labeled Indole, L-Tryptophan, D-Tryptophan, and dL-Tryptophan**—Four young, mature rats were placed on a protein-free diet for 5 days and then fed the test compound mixed with their food. Rat 1 received 50 mg. of indole containing 33.1 per cent N\textsuperscript{15} excess, plus 400 mg. of dL-serine; Rat 2, 110 mg. of L-tryptophan containing 6.00 per cent N\textsuperscript{15} excess in the indole ring; Rat 3, 200 mg. of d-tryptophan containing 6.08 per cent N\textsuperscript{15} excess in the indole ring; and Rat 4, 140 mg. of dL-tryptophan containing 31.2 per cent N\textsuperscript{15} excess in the indole ring.

Urine and feces were collected during the period of consumption of the test compound (20 to 30 hours) and 24 hours thereafter (Urine 1 and Feces 1). Collection was continued for an additional 24 hours (Urine 2 and Feces 2). The rat was then killed and the carcass used for isolations.

Ammonia and urea were isolated only from Urine 1. Ammonia was isolated by adsorption on permutit. Urea for N\textsuperscript{16} determination was isolated as the xanthydrol derivative. Total urea nitrogen was determined by treating an aliquot of the ammonia-free filtrate from permutit with urease and adsorbing the liberated ammonia on permutit, followed by distillation and titration.

Tryptophan was isolated from the entire rat carcass as acetyl-dL-tryptophan as follows: After removal of the contents of the stomach and intestines, the entire rat carcass was hydrolyzed in 750 ml. of 5 N sodium hydroxide on a steam bath for 20 hours in an atmosphere of nitrogen. After filtration, the filtrate was cooled and made slightly acid with 18 N sulfuric acid. It was again filtered, diluted to 2.5 liters, and made 1 N with sulfuric acid. To this was added a solution of 60 gm. of mercuric sulfate in 1.5 liters of 1 N sulfuric acid. After the mixture had been heated to 60° on a steam bath and allowed to stand for 1 or 2 hours, the supernatant liquid was decanted and the voluminous precipitate recovered by centri-
The precipitate was finely suspended in 4 liters of 0.1 N sulfuric acid, thoroughly stirred, recovered by decantation and centrifugation, suspended in 600 ml. of water, and saturated with hydrogen sulfide 6 hours with vigorous stirring. The mercuric sulfide was removed, the filtrate was adjusted to pH 6, and a solution of 8 gm. of silver lactate in water added with stirring. After a few minutes the precipitate was removed by filtration, washed thoroughly, and discarded. This removed the purines and some dark colored material. Silver was removed as the sulfide and the tryptophan was reprecipitated from a volume of 4 liters with 60 gm. of mercuric sulfate in 1 N sulfuric acid. The lemon-yellow precipitate was washed with 0.1 N sulfuric acid and with water, and the mercury was removed as the sulfide. After filtration, the solution was evaporated to about 50 ml. in vacuo, neutralized with sodium hydroxide, evaporated to about 20 ml., made alkaline to phenolphthalein, and treated with excess of acetic anhydride, the solution being kept alkaline. It was finally made acid to Congo red and chilled. Crystallization, aided by seeding or scratching, was usually complete in 2 or 3 days. The acetyl-DL-tryptophan, after two or three recrystallizations from boiling water, melted at 205–206° (21).

The amino acids tyrosine, leucine, arginine, glutamic acid, and aspartic acid were isolated in the usual manner (22) from the combined liver, plasma, kidneys, and spleen of the rat receiving DL-tryptophan.

The results of the feeding experiments are shown in Tables II and III.

**Discussion**

Relationship of Tryptophan to Kynurenine, Kynurenic Acid, and Xanthurenic Acid (Table I, Experiments 1 to 3)—As can be seen from these experiments, the N16 concentrations of kynurenine and kynurenic acid isolated from rabbit urine are approximately the same after injection of either L- or DL-tryptophan. There is no evidence of the utilization of D-tryptophan by rabbits under the conditions of this experiment for the formation of kynurenine and kynurenic acid. The N15 concentrations of the isolated kynurenine and kynurenic acid indicate that over 80 per cent of these substances originated from the injected tryptophan.

Experiments 4 to 6—The conversion of L-tryptophan to kynurenine, kynurenic acid, and xanthurenic acid in rats occurred with a very slight dilution, indicating that over 90 per cent of these substances originated from the injected tryptophan. The dilution in rats was considerably less than in rabbits; however, the rats received doses of tryptophan per unit of body weight approximately 3 times as high as for the rabbits.

Experiment 7—The results suggest that the rats converted the small amount of D-tryptophan present into L-tryptophan and utilized it in the
production of kynurenine and kynurenic acid. This inversion has been known in rats, since the D isomer is equal to the L isomer in growth promotion (23).

Experiments 8 and 9—N\textsuperscript{15}-Kynurenine injected into rats produced xanthurenic acid without dilution of the isotope (Experiment 8). N\textsuperscript{16}-Kynurenine injected into a rabbit produced kynurenic acid in which the isotope was significantly diluted (Experiment 9). It would therefore appear that kynurenine is normally formed in the rabbit and is not merely a means of getting rid of large excesses of tryptophan.

Relationship of Tryptophan to Hemin—The value of 0.014 per cent N\textsuperscript{15} excess in hemin isolated from rats indicates that there is no significant conversion of the ring structure of tryptophan to hemin in rats.

Distribution of N\textsuperscript{15} after Ingestion of Labeled Indole, L-Tryptophan, D-Tryptophan, and DL-Tryptophan—After ingestion of indole the very high N\textsuperscript{15} values of the whole Urine 1 and the low values of the ammonia and urea fractions indicate that the ring of ingested indole is only slightly disrupted and that the major portion is excreted as a compound in which the indole nucleus is intact, probably indican. The urinary excretion of isotope is almost complete 24 hours after ingestion. Fecal excretion is small, indicating great efficiency of absorption of indole by the gut (Rat 1, Table II).

After ingestion of L-, D-, and DL-tryptophan, the N\textsuperscript{15} values of urinary ammonia and urea are high and indicate that these products account for 11 to 18 per cent of the ingested N\textsuperscript{15} (Rats 2, 3, and 4, Table II).

The fact that in all cases the urinary ammonia has an N\textsuperscript{15} concentration 4 times greater than that of the urinary urea suggests the existence in rat kidney, as well as in liver, of an enzyme system which splits the indole nucleus of tryptophan to ammonia, which is excreted before conversion to urea. This behavior is unlike that of L-α-amino acids, which yield urea and ammonia of approximately equal isotopic concentrations (24), but resembles the behavior of n-leucine (25). In this case, a ratio of ammonia to urea of approximately 4:1 exists and is explained by the presence in rat kidney of a d-amino acid oxidase, which splits off the α-amino nitrogen as ammonia, which is rapidly excreted before conversion to urea.

In the experiment with DL-tryptophan, the rat received tryptophan with sufficiently high isotope concentration to provide a significant N\textsuperscript{15} concentration in the amino acids of the organs whose proteins undergo rapid turnover; i.e., liver, plasma, gut, and spleen (Table III). The N\textsuperscript{15} distribution in these amino acids follows the usual pattern (26), with the amidine group of arginine highest, glutamic and aspartic acids slightly lower, and leucine, ornithine, and tyrosine low. This demonstrates that the indole nitrogen of tryptophan can enter the general nitrogen pool.
### TABLE II

**Distribution of N\textsuperscript{15} after Ingestion of Labeled Indole and Tryptophan**

<table>
<thead>
<tr>
<th>Fraction</th>
<th>N\textsuperscript{15}</th>
<th>Total N</th>
<th>Per cent of isotope*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rat 1, male, 164 gm.; fed 50 mg. indole containing 33.1% N\textsuperscript{15} excess + 400 mg. DL-serine</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Urine 1</strong></td>
<td>per cent excess</td>
<td>mg.</td>
<td></td>
</tr>
<tr>
<td>&quot; 1, ammonia</td>
<td>1.270</td>
<td>101.6</td>
<td>63.5</td>
</tr>
<tr>
<td>&quot; 1, urea</td>
<td>0.026</td>
<td>10.1</td>
<td>1.6</td>
</tr>
<tr>
<td>&quot; 2</td>
<td>0.42</td>
<td>48.0</td>
<td>1.0</td>
</tr>
<tr>
<td><strong>Feces 1</strong></td>
<td>0.87</td>
<td>87.6</td>
<td>0.4</td>
</tr>
<tr>
<td>&quot; 2</td>
<td>0.47</td>
<td>15.0</td>
<td>0.3</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td></td>
<td></td>
<td>68.6</td>
</tr>
<tr>
<td>Rat 2, male, 158 gm.; fed 110 mg. L-tryptophan containing 6.00% N\textsuperscript{15} excess in indole ring</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Urine 1</strong></td>
<td>0.244</td>
<td>103.4</td>
<td>55.5</td>
</tr>
<tr>
<td>&quot; 1, ammonia</td>
<td>0.266</td>
<td>12.2</td>
<td>7.1</td>
</tr>
<tr>
<td>&quot; 1, urea</td>
<td>0.067</td>
<td>65.1</td>
<td>9.6</td>
</tr>
<tr>
<td>&quot; 2</td>
<td>0.036</td>
<td>29.6</td>
<td>2.4</td>
</tr>
<tr>
<td><strong>Feces 1</strong></td>
<td>0.039</td>
<td>38.0</td>
<td>3.3</td>
</tr>
<tr>
<td>&quot; 2</td>
<td>0.025</td>
<td>17.6</td>
<td>1.0</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td></td>
<td></td>
<td>62.2</td>
</tr>
<tr>
<td>Rat 3, female, 160 gm.; fed 200 mg. (\beta)-tryptophan containing 6.08% N\textsuperscript{15} excess in indole ring</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Urine 1</strong></td>
<td>0.251</td>
<td>184.8</td>
<td>55.4</td>
</tr>
<tr>
<td>&quot; 1, ammonia</td>
<td>0.190</td>
<td>24.4</td>
<td>5.5</td>
</tr>
<tr>
<td>&quot; 1, urea</td>
<td>0.046</td>
<td>106.2</td>
<td>5.8</td>
</tr>
<tr>
<td>&quot; 2</td>
<td>0.040</td>
<td>46.3</td>
<td>2.1</td>
</tr>
<tr>
<td><strong>Feces 1</strong></td>
<td>0.082</td>
<td>73.1</td>
<td>7.1</td>
</tr>
<tr>
<td>&quot; 2</td>
<td>0.043</td>
<td>11.3</td>
<td>0.7</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td></td>
<td></td>
<td>65.3</td>
</tr>
<tr>
<td>Rat 4, male, 177 gm.; fed 140 mg. (\alpha)-tryptophan containing 31.2% N\textsuperscript{15} excess in indole ring</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Urine 1</strong></td>
<td>0.850</td>
<td>162.4</td>
<td>45.1</td>
</tr>
<tr>
<td>&quot; 1, ammonia</td>
<td>1.290</td>
<td>15.2</td>
<td>6.4</td>
</tr>
<tr>
<td>&quot; 1, urea</td>
<td>0.323</td>
<td>108.6</td>
<td>11.5</td>
</tr>
<tr>
<td>&quot; 2</td>
<td>0.076</td>
<td>54.7</td>
<td>1.4</td>
</tr>
<tr>
<td><strong>Feces 1</strong></td>
<td>0.474</td>
<td>7.2</td>
<td>1.1</td>
</tr>
<tr>
<td>&quot; 2</td>
<td>0.456</td>
<td>19.4</td>
<td>2.9</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td></td>
<td></td>
<td>50.5</td>
</tr>
</tbody>
</table>

Acetyl \(\alpha\)-tryptophan isolated from carcass, (Rat 1) 0.013, (Rat 2) 0.170, (Rat 3) 0.251 N\textsuperscript{15} per cent excess; m.p. 205-206°.

* The figures in parentheses are excluded from the total.
Following ingestion of D-tryptophan, the finding of excess N\textsuperscript{15} (Rat 3) in the total nitrogen of tryptophan isolated from the carcass is proof of the conversion of D-tryptophan to L-tryptophan in the rat.

Following ingestion of both L- and D-tryptophan, the finding of excess N\textsuperscript{15} (Rats 2 and 3) in the total nitrogen of tryptophan isolated from the carcass demonstrates the incorporation of dietary tryptophan into the body proteins. In both cases it is likely that the N\textsuperscript{15} concentration of the

\begin{table}[h]
\centering
\caption{Amino Acids Isolated from Combined Liver, Spleen, Intestines, and Plasma}
\label{tab:amino-acids}
\begin{tabular}{l|l|l|l}
\hline
Amino acid & Criterion of purity & Values from literature & N\textsuperscript{15} \\
\hline
Tyrosine  & $[\alpha]_D^{25} = -10.9^\circ$ & -10.8 & 0.022 \\
Leucine   & M.p. benzylsulfonylleucine, 128\degree & 129 & 0.032 \\
Glutamic acid & Glutamic acid hydrochloride, $[\alpha]_D^{25} = +25.3^\circ$ & +25.3 & 0.067 \\
Aspartic acid & Recrystallized 3 times as Cu salt & per cent & 0.070 \\
Arginine  & Arginine monoflavianate; found N 17.30\% & 17.21 & 0.057 \\
Ornithine & & & 0.032 \\
Amidine N & & & 0.079 \\
\hline
\end{tabular}
\end{table}

\alpha-amino group is very low, since studies in this laboratory have demonstrated that tryptophan isolated from rats given N\textsuperscript{15}-glycine contains a lower N\textsuperscript{16} concentration than any other amino acid except lysine.\textsuperscript{1}

The finding of 0.013 per cent excess N\textsuperscript{15} in the total nitrogen of tryptophan isolated from the carcass of a rat which had received the isotopic indole indicates that there is no significant conversion of indole to tryptophan.

**SUMMARY**

1. Indole containing N\textsuperscript{15} has been synthesized. DL-Tryptophan containing N\textsuperscript{15} in the indole ring has been synthesized and resolved into the D and L isomers.

2. Studies of the conversion of tryptophan to kynurenine, kynurenic acid, and xanthurenic acid in rats and rabbits are reported. Tryptophan is converted to kynurenine, kynurenic acid, and xanthurenic acid with only slight dilution. D-Tryptophan is utilized by the rat but not by the rabbit.

\textsuperscript{1}Foster, G. L., unpublished data.
Kynurenine is converted to xanthurenic acid in the rat without dilution, and to kynurenic acid in the rabbit with significant dilution.

3. There is no detectable conversion of the pyrrole ring of tryptophan to the tetapyrrole structure of hemin in the rat.

4. N\textsuperscript{16}-Labeled indole fed to rats is mainly excreted in the urine. There is very little rupture of the ring and no detectable conversion to tryptophan.

5. d-Tryptophan is readily converted to L-tryptophan, which is incorporated efficiently into the tissue proteins of rats. Both the d and L isomers showed significant rupture of the indole ring. Urinary ammonia had an isotope concentration 4 times as high as that of urinary urea, indicating that the kidney is probably the principal site of the ring-splitting reaction. Fecal excretion of isotope was small.

6. Amino acids isolated from the internal organs of a rat fed a high isotope concentration of dl-tryptophan contained N\textsuperscript{16}, demonstrating that the ring nitrogen of tryptophan can enter the general nitrogen pool.

The author is indebted to Professor G. L. Foster and Professor David Shemin for their guidance during the course of this research, to Mr. I. Sucher for N\textsuperscript{16} determinations, and to Miss Renata Rother for microanalyses.

BIBLIOGRAPHY

CORRECTION

On page 783, Table II, lines 10 to 12, Vol. 187, No. 2, December, 1950, read 0.042, 0.087, and 0.047 per cent excess of Urine 2, Feces 1, and Feces 2, respectively, for 0.42, 0.87, and 0.47 per cent excess.
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