τ_1 in terms of β_1 and β, the half width at half height of the broadened line.

$$1/\tau_1 = \beta - \beta_1 \quad (4)$$

Application.—Raman spectra of sodium trifluoroacetate ion in the presence of excess sodium hydroxide show an intense peak at 1433 cm.$^{-1}$ (probably the symmetrical C=O stretching frequency)[5] with a width at half height of 15.0 cm.$^{-1}$. In the presence of excess base the width is independent of trifluoroacetate concentration. Trifluoroacetate also has a fairly intense peak at 843 cm.$^{-1}$, with a width of 16.2 cm.$^{-1}$. Trifluoroacetic acid in the presence of excess HCl gives a strong peak at 816 cm.$^{-1}$ with a width of 28.8 cm.$^{-1}$. The latter two are presumably the C–C stretching frequencies.[5] In solutions containing trifluoroacetic acid, its conjugate base, and hydronium ion, the trifluoroacetate peak at 1433 cm.$^{-1}$ is broadened by as much as 7.2 cm.$^{-1}$, and the two peaks around 830 cm.$^{-1}$ both broaden and tend to merge. Both the 1433 cm.$^{-1}$ peak and the 816 cm.$^{-1}$ peak also tend to shift toward higher frequency by 2–5 cm.$^{-1}$ in mixed solutions. Spectra were measured on a Cary model 81 photoelectric Raman spectrophotometer, equipped with two Toronto-type mercury arc lamps. Solution temperatures were around 40°. The lines are roughly Lorentzian in shape.

The broadening of the 1433 cm.$^{-1}$ peak was used to obtain k_1 for trifluoroacetate ion by means of eq. (4). These results are shown in Table I. Solutions were made up simply by mixing trifluoroacetic acid and water. Concentrations were obtained by interpolation, using the degree of dissociation results of Redlich and co-workers.[6,7] Concentrations could also be inferred from the intensity of the 1433 cm.$^{-1}$ line in the Raman spectra. The average difference between the two estimates of the trifluoroacetate concentration was 10%. This strongly suggests that the intensity of the 1433 cm.$^{-1}$ band is proportional to the trifluoroacetate concentration and otherwise independent of the composition of the solution. Table I also gives the rate constant k_{-1} for the conversion of trifluoroacetic acid, as determined from the requirement that equilibrium be maintained.

TABLE I

AVERAGE LIFETIME OF TRIFLUOROACETATE ION IN VARIOUS SOLUTIONS

Molar			$10^{-11}\,k_1$	$10^{-11}\,k_{-1}$
$CF_3CO_2^-$	CF_3CO_2H	H^+	sec.$^{-1}$	sec.$^{-1}$
1.8	3.5	1.8	6.9	3.5
1.5	1.5	1.5	4.7	4.7
0.81	0.24	0.81	1.6	5.4

The rate constants cited above were used to calculate the shape of the doublet centering around 830 cm.$^{-1}$. The general shape of the band is moderately well reproduced. The band shape calculated by adding the unbroadened lines is worse, but the difference is not great. This evidence supports the interpretation that the broadening is due to exchange.

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(8) Alfred P. Sloan Foundation Fellow, 1960–1964.

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RECEIVED SEPTEMBER 4, 1962

GLYCEROL AS A PRECURSOR OF RICININE[1]

Sir:

By means of tracer experiments with young *Ricinus communis* L. we have recently established[2,3] that succinic acid, or a closely related four-carbon dicarboxylic acid found in the Krebs tricarboxylic acid cycle, is a specific precursor of carbon atoms 2, 3, and 7 in the biosynthesis of ricinine I.

Since an origin outside of the Krebs cycle was indicated for carbon atoms 4, 5, and 6, glycerol-1-^{14}C and glycerol-2-^{14}C were fed in separate experiments to young *Ricinus* plants. The percentages of the incorporated radioactivity located at the O-methyl, N-methyl, and nitrile carbon atoms of the isolated ricinine have been reported already.[2]

We now wish to describe degradative procedures to isolate the carbon atoms at positions 4, 5, and 6 of the ricinine molecule, and applications of these procedures to the ricinine obtained from both glycerol-1-^{14}C and glycerol-2-^{14}C, as well as, in part, to ricinine from the previously reported succinic acid-2,3-^{14}C and sodium acetate-2-^{14}C feeding experiments.[2,3]

Ricinine I was converted to 4-methoxy-1-methyl-2-pyridone II, m.p. 114–116°,[4] which was reduced with lithium aluminum hydride to 1-methyl-4-piperidone III, b.p. 55–60° (12 mm.),[5] identified by comparison with an authentic sample. Reaction of III with phenyllithium provided the known 4-hydroxy-1-methyl-4-phenylpiperidine[6] IV, m.p. 115–116°, which was oxidized with potassium permanganate to benzoic acid V, m.p. 121–122°, with the carboxyl carbon atom originating from carbon 4 of ricinine.

Nitration of ricinine I afforded the 5-nitro derivative VI, m.p. 163–164° (*anal.* Calcd. for $C_8H_7O_4N_3$: C, 45.94; H, 3.37; N, 20.09. Found: C, 45.94; H, 3.39; N, 20.19) which on treatment with calcium hypobromite yielded tribromonitromethane (bromopicrin) VII, with the carbon atom originating from position 5 of ricinine. The bromopicrin was identified by comparison with an authentic sample prepared from picric acid.[7]

Catalytic reduction of the pyridone II yielded 1-methyl-2-piperidone VIII, b.p. 110–105° (12 mm.) (mercuric chloride derivative, m.p. 117–120°[8]) which was hydrolyzed with hydrochloric acid,

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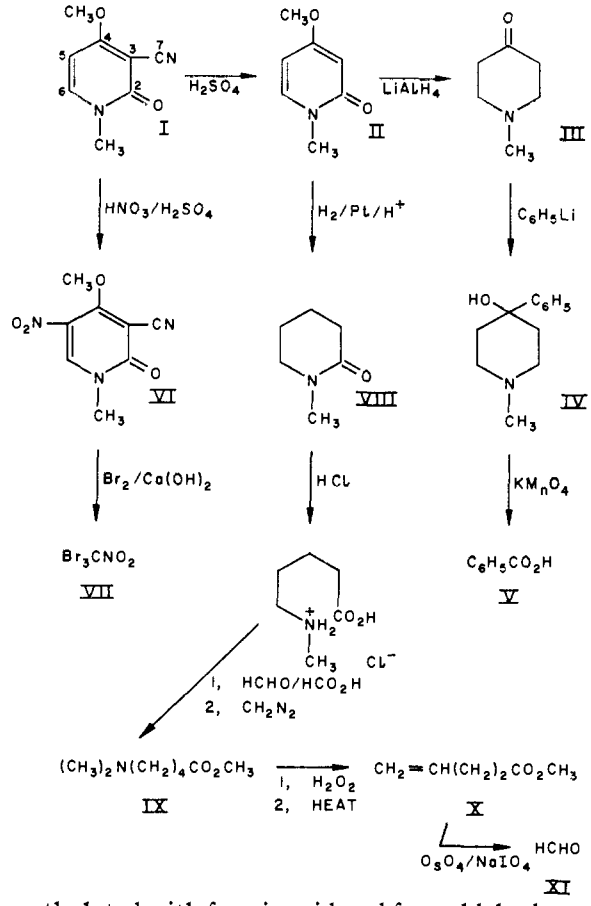

methylated with formic acid and formaldehyde and esterified with diazomethane to methyl 5-dimethylaminovalerate IX, b.p. 90° (20 mm.),[9] characterized as its methiodide (*anal.* Calcd. for $C_9H_{20}O_2NI$: C, 35.88; H, 6.69; N, 4.65; I, 42.13. Found: C, 35.89; H, 6.81; N, 4.77; I, 42.02). The N-oxide of IX when pyrolyzed yielded the methyl ester of allylacetic acid X, identified by comparison of its infrared spectrum with that of an authentic synthetic sample, b.p. 127–128° (760 mm.) (*anal.* Calcd. for $C_6H_{10}O_2$: C, 63.13; H, 8.83. Found: C, 63.3; H, 8.86). The olefin was cleaved using sodium periodate and osmium tetroxide[10] and the liberated formaldehyde XI, containing carbon 6 of ricinine, isolated as the dimedon derivative, m.p. 191–192°.[11]

The results obtained with the use of the procedures outlined above are recorded in Table I.

TABLE I

LOCATION OF RADIOACTIVITY IN RICININE

Precursor	% of activity of ricinine C-4	C-5	C-6
Acetate-2-^{14}C	0.0	0.3	Not detd.
Succinic acid-2,3-^{14}C	0.0	0.0	Not detd.
Glycerol-1-^{14}C	25.8	2.2	19.7
Glycerol-2-^{14}C	2.2	38.8	0.0

As expected[3] there is virtually no activity associated with carbons 4 and 5 of ricinine after feeding acetate-2-^{14}C and succinic acid-2,3-^{14}C. From results reported previously[2] it is clear that at least part of the glycerol is broken down to simpler units prior to incorporation. However, the fact that carbon 5 of ricinine from the glycerol-2-^{14}C experiment contains an appreciable percentage of the incorporated activity while carbon 4 and carbon 6 contain little or no activity suggests that part of the glycerol was incorporated intact into ricinine at positions 4, 5, and 6. The high activity at carbon 4 and carbon 6, and low activity at carbon 5 after the feeding of glycerol-1-^{14}C lends support to this suggestion.

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THE CORRECTED STRUCTURE OF A KETOAMIDE ARISING FROM THE METABOLISM OF (−)-NICOTINE

Sir:

During the course of studies[1] on the metabolism of (−)-nicotine, a ketonic metabolite $C_{10}H_{12}N_2O_2$ was isolated from the urine of dogs, and later from rats.[2] This compound, which has amphoteric properties, as exhibited in its behavior toward ion exchange resins, was ostensibly obtained in pure form and then hydrolyzed to a keto acid $C_9H_9NO_3$ and methylamine. The oxime of the keto acid then was subjected to a Beckmann rearrangement. The isolation of 3-pyridylacetic acid from the reaction products of this rearrangement was a crucial point in the conclusion[1] that the ketoamide had the structure of γ-(3-pyridyl)-β-oxo-N-methylbutyramide. On the basis of current data, which include both a degradation and a synthesis, the foregoing structure which arose through technical errors of a yet undetermined nature is incorrect. Since the ketoamide, now shown to be γ-(3-pyridyl)-γ-oxo-N-methylbutyramide, appears to occupy a key role as an intermediate in the mammalian degradation of the pyrrolidine ring of (−)-nicotine to γ-(3-pyridyl)-γ-oxobutyric acid,[3] γ-(3-pyridyl)-γ-hydroxybutyric acid,[4] 3-pyridylacetic acid,[5] and other substances, a summary of data necessary to the immediate correction of the erroneous formula is presented.

By a procedure patterned after the original,[1] the ketoamide was isolated from the urine of dogs after oral administration of (−)-cotinine. The colorless crystals, R_f 0.74 upon paper chromatography in the ammonia system,[6] were obtained

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