COMMUNICATIONS TO THE EDITOR

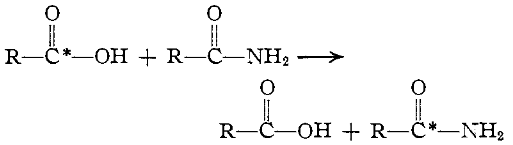
THE WILLGERODT REACTION[1,2]

Sir:

The following sequence of reactions has been carried out using C^{14}. The asterisk (*) denotes a labeled carbon atom and the percentage is that of the initial *specific activity* found in that carbon atom.[3]

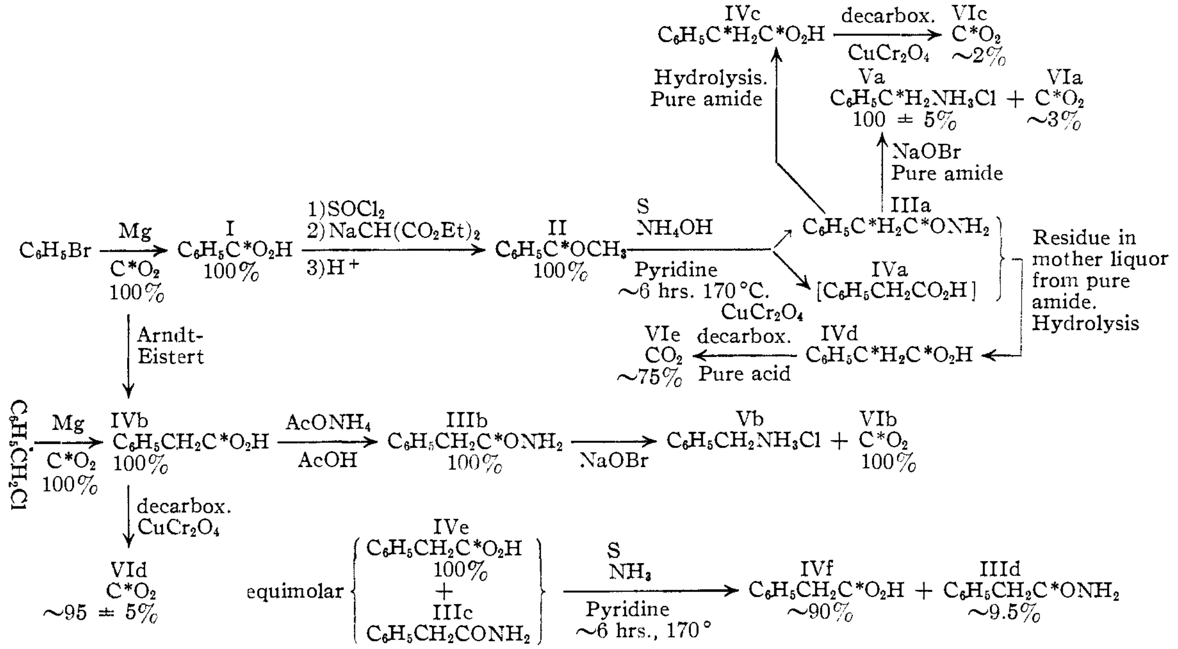
The acetophenone (II) was put through the Willgerodt reaction using sulfur, concentrated ammonia and pyridine.[2b] From the reaction mixture an ~65% yield of phenylacetamide (IIIa), m. p. 156.5–157.5°, was isolated by extraction with hot water and crystallization. From the mother liquors of the amide was obtained a crude acid (IVa) in ~14% yield, containing amide. After hydrolysis of this crude mixture, phenylacetic acid (IVd) was obtained, m. p. 75–76°.

The amide formed in the Willgerodt reaction is clearly formed by oxidation–reduction along the chain and does not involve a migration of carbon atoms. The phenylacetic acid, however, appears to be formed by a different mechanism involving migration of a carbon atom. The appearance of only 75% of the initial specific activity in the carboxyl group of phenylacetic acid (IVd) is clearly due to contamination by phenylacetic acid from some of the amide (IIIa) which was not removed before the hydrolysis. The co-existence, in the original reaction mixture, of acid and amide having different distributions of radiocarbon implies that the exchange reaction (1) goes only slowly



$$R-\overset{\overset{\displaystyle O}{\|}}{C}{}^*-OH + R-\overset{\overset{\displaystyle O}{\|}}{C}-NH_2 \longrightarrow R-\overset{\overset{\displaystyle O}{\|}}{C}-OH + R-\overset{\overset{\displaystyle O}{\|}}{C}{}^*-NH_2 \quad (1)$$

under the conditions of the Willgerodt reaction. This was specifically tested with the results shown in the last reaction scheme. The indication is that only about 20% exchange has taken place during the six-hour heating at 170° and that no appreciable net conversion of acid to amide or amide to acid has taken place. This amount of exchange accounts almost quantitatively for the small amount of activity found in the carboxyl group of the amide, (VIa) and (VIc), when it is remembered that the ratio of amide to acid formed in this reaction is about four.



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[2] (a) C. Willgerodt, *Ber.*, **21**, 534 (1888); (b) Spielman and Carmack, "Organic Reactions," Vol. 3 (in press), J. Wiley and Sons, Inc., New York, N. Y.

[3] All activities are subject to a counting error of ±2% of the value indicated, unless otherwise stated.