Of the radicals HO, HO_2 and HO_3, rapid exchange seems possible only for HO.

More complete experimental results will be presented in a later report, containing also data on related systems.

JONES HERBERT JONES LABORATORY
UNIVERSITY OF CHICAGO OTTO L. FORCHHEIMER
CHICAGO 37, ILLINOIS HENRY TAUBE

RECEIVED JUNE 7, 1952

TRACER STUDIES ON SOME REACTIONS OF THIOSULFATE AND TETRATHIONATE

Sir:

The oxidation of thiosulfate to tetrathionate with iodine, the reduction of tetrathionate to thiosulfate with sulfide, and the decomposition of both thiosulfate and tetrathionate with mercuric chloride in presence of bisulfite and excess formaldehyde have been studied with the aid of S^{35}.

In order to separate the products of the reactions with mercuric chloride, three successive precipitations were made: $HgCl_2 \cdot 2HgS$ (from thiosulfate) and $HgCl_2 \cdot 2HgS + S$ (from tetrathionate) were precipitated in the cold by means of a large excess of concentrated buffered mercuric chloride and addition of some ammonia after one hour (I), sulfate was precipitated, also in the cold, with acetic acid and barium chloride (II), finally the protected bisulfite was oxidized with potassium hypobromite and precipitated as barium sulfate (III). Radioactive contamination of III was excluded by an intermediate scavenging operation which consisted of the addition of inactive thiosulfate or tetrathionate, mercuric chloride and barium chloride. These intermediate precipitates were checked to be practically inactive.

If thiosulfate labeled at the central S-atom was treated in this way the activity distribution was: 1% in I, 95% in II, none in III.

If the same thiosulfate was titrated to tetrathionate with iodine, and analyzed in the same manner, again 1% was found in I, and 95% in II, but this time 2–3% entered into III.

Save for the infrequent side-reaction which caused the formation of radioactive sulfite during the decomposition of tetrathionate, the reactions may be assumed to proceed according to

$$2SS^*O_3^- + 3HgCl_2 + 2H_2O \longrightarrow HgCl_2 \cdot 2HgS + 2S^*O_4^- + 4Cl^- + 4H^+$$

$$2SS^*O_3^- \longrightarrow O_3S^*SSS^*O_3^- + 2e^-$$

$$2O_3S^*SSS^*O_3^- + 3HgCl_2 + 4H_2O \longrightarrow HgCl_2 \cdot 2HgS + 4S^*O_4^- + 4Cl^- + 8H^+ + 2S$$

If tetrathionate, obtained by titration of the same thiosulfate with iodine, was reduced immediately with inactive sulfide (in presence of inactive bisulfite and excess formaldehyde), the sulfur formed was inactive. The filtrates from this reaction were analyzed with mercuric chloride both directly, and after they had been titrated back to tetrathionate. In the first case the activity distribution was found to be: 1% in I, 96% in II, 1–2% in III; in the second case: 1% in I, 95% in II and 3% in III.

The activities found in all fractions I may well be introduced into the thio-S of the thiosulfate by side-reactions during its formation.

If tetrathionate was prepared from thiosulfate labeled at the thio-S, 2–3% of the total activity was always found in the solid sulfur; if inactive tetrathionate was reduced with active sulfide, 97% was found in the sulfur.

The results indicate that, save for a minor side-reaction, the reduction of tetrathionate with sulfide proceeds according to

$$O_3S^*S\dagger S\dagger S^*O_3^- + S^- \longrightarrow 2S\dagger S^*O_3^- + S$$

This investigation represents part of the research program of the Foundation for Fundamental Research of Matter (F. O. M.). It was performed with the financial aid of the Netherlands Organization for pure Research (Z. W. O.).

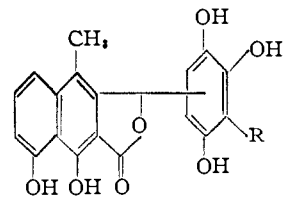
INSTITUUT VOOR KERNPHYSISCH ONDERZOEK
18 OOSTERRINGDIJK, AMSTERDAM HERMAN B. V. D. HEIJDE
THE NETHERLANDS A. H. W. ATEN, JR.

RECEIVED JUNE 9, 1952

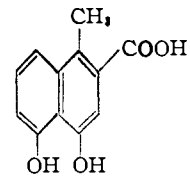
TERRAMYCIN. V. STRUCTURE OF TERRINOLIDE. AN ACID DEGRADATION PRODUCT OF TERRAMYCIN

Sir:

Among the products formed by the degradation of terramycin[1] in dilute hydrochloric acid at elevated temperatures is terrinolide (I), $pK_{a_1} = 4.6$, $pK_{a_2} = 7.5$ (dimethylformamide–water); $[\alpha]_D$ −16.0° (*c* 1% in 1:1 methanol–0.1 *N* hydrochloric acid). *Anal.* Calcd. for $C_{20}H_{15}NO_8$: C, 60.45; H, 3.81; N, 3.53. Found: C, 60.46; H, 4.10; N, 3.52. On hydrolysis in hot 12 *N* sulfuric acid, terrinolide loses ammonia and carbon dioxide to yield a nitrogen-free, optically-inactive compound, decarboxamidoterrinolide (II),[2] $pK_{a_1} = 4.7$, $pK_{a_2} = 10.2$ (dimethylformamide–water). *Anal.* Calcd. for $C_{19}H_{14}O_7$: C, 64.41; H, 3.98; C-methyl, 4.25. Found: C, 64.10; H, 4.41; C-methyl, 3.82. Pentamethyldecarboxamidoterrinolide: m.p. 152–153°, *Anal.* Calcd. for $C_{24}H_{24}O_7$: C, 67.91; H, 5.70; CH_3O, 36.55. Found: C, 67.85; H, 5.74; CH_3O, 35.95. Terrinolide and decarboxamidoterrinolide have been assigned structures I and II, respectively.



I, R = $CONH_2$
II, R = H



III

Alkali fusion of II yields 1,8-dihydroxy-4-methyl-3-naphthoic acid (III).[3] I, II and III enhance the

(1) P. P. Regna, I. A. Solomons, K. Murai, A. E. Timreck, K. J. Brunings and W. A. Lazier, THIS JOURNAL, 73, 4211 (1951).

(2) Terrinolide and decarboxamidoterrinolide were originally assigned the formulas $C_{18}H_{17}NO_8$ and $C_{18}H_{12}O_6$, respectively, in our first Communication (R. Pasternack, P. Regna, R. Wagner, A. Bavley, F. Hochstein, P. Gordon and K. Brunings, THIS JOURNAL, 73, 2400 (1951)). The formation of stable solvates and a tendency of these compounds to decompose under conditions of molecular weight determination complicated the assignment of the molecular formulas.

(3) F. A. Hochstein, *et al.*, to be published.

acidity of boric acid to the marked degree characteristic of 1,8-naphthalenediols.[4]

Lithium aluminum hydride reduction of pentamethyldecarboxamidoterrinolide consumes 0.5 mole of hydride and yields no hydrogen; the reaction product is a dialcohol (IV), m.p. 114–115°, *anal.* Calcd. for $C_{24}H_{28}O_7$: C, 67.27; H, 6.59. Found: C, 67.09; H, 6.69, which is readily dehydrated in dilute mineral acid to an ether, m.p. 141–142°. *Anal.* Calcd. for $C_{24}H_{26}O_6$: C, 70.23; H, 6.38. Found: C, 70.06; H, 6.06. That the lactone structure shown by this reduction is a phthalide is indicated by the extreme resistance of decarboxamidoterrinolide to hydrolysis. This assignment is in agreement with the carbonyl band at 5.73 μ (dioxane) in the infrared absorption spectra of I and II. The marked similarity of the ultraviolet spectra of I, II and 1,8-dihydroxynaphthalene-2-carboxylic acid[3] determines the orientation of the phthalide ring on the naphthalenediol system. Further, the acidity of terrinolide, $pK_{a_1} = 4.5$, is in good agreement with the acidity of 1,8-dihydroxy-2-naphthaldehyde, $pK_a = 4.5$ (dimethylformamide–water).

The presence of five phenolic hydroxyl groups in I and II is shown by the formation of pentamethyl and pentaacetyl derivatives. The stability of II in strong acid, and the marked susceptibility of I and II to air oxidation suggest that the $C_6H_5O_3$ moiety not accounted for by the dihydroxybenzophthalide system is a trihydroxybenzene. Comparison of the ultraviolet spectrum of the dialcohol (IV) to the composite curves derived from 3-hydroxymethyl-4-methyl-1,8-naphthalenediol[3] and the three isomeric trihydroxybenzenes indicates that the $C_6H_5O_3$ group is hydroxyhydroquinone.

The presence in terrinolide of a carboxamide group which is lost by hydrolysis in sulfuric acid is supported by the infrared absorption spectra of I, II and their derivatives. The second acid constant of I, $pK_{a_2} = 7.5$ (compare $pK_{a_1} = 10.2$ for II) requires that the carboxamide group in terrinolide (I) be attached to the hydroxyhydroquinone ring between two phenolic groups.

(4) J. Böeseken, J. de Bruin and W. van Rijswijk de Jong, *Rec. trav. chim.*, **58**, 3 (1939).

RESEARCH LABORATORIES F. A. HOCHSTEIN
CHAS. PFIZER AND CO., INC. P. P. REGNA
BROOKLYN 6, N. Y. K. J. BRUNINGS
CONVERSE LABORATORY
HARVARD UNIVERSITY R. B. WOODWARD
CAMBRIDGE, MASSACHUSETTS

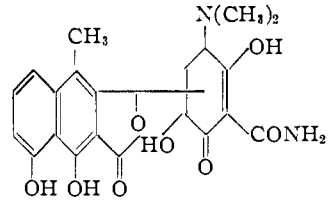
RECEIVED JUNE 25, 1952

TERRAMYCIN. VI. THE STRUCTURE OF α- AND β-APOTERRAMYCIN, ACID REARRANGEMENT PRODUCTS OF TERRAMYCIN

Sir:

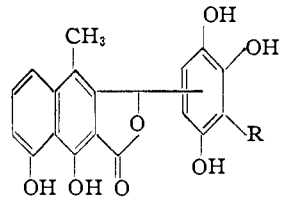
In 1.5 *N* aqueous hydrochloric acid at 60°, terramycin[1] loses a molecule of water and rearranges to form two closely related optically active compounds: α-Apoterramycin hydrochloride (I), $[\alpha]^{25}D$ +123° (*c* 1% in ethanol), $pK_{a_1} = 4.0$, $pK_{a_2} = 5.1$, $pK_{a_3} = 8.4$ (dimethylformamide–water). *Anal.* Calcd. for $C_{22}H_{22}N_2O_8 \cdot HCl$: C, 55.17; H, 4.84; N, 5.85; Cl, 7.40. Found: C, 54.85; H, 5.13; N, 5.97; Cl, 7.19. β-Apoterramycin hydrochloride (I)[2], $[\alpha]^{25}D$ −28° (*c*, 1% in ethanol), $pK_{a_1} = 3.6$, $pK_{a_2} = 5.2$, $pK_{a_3} = 7.8$ (dimethylformamide–water). *Anal.* Calcd. for $C_{22}H_{22}N_2O_8 \cdot HCl \cdot H_2O$: C, 53.17; H, 5.07; N, 5.64; Cl, 7.14. Found: C, 52.90; H, 4.76; N, 5.65; Cl, 6.90.

We consider α- and β-apoterramycin to be stereoisomers of structure I. The two compounds are interconvertible in acid and alkaline solution, and their ultraviolet spectra are virtually identical.



I

Alkali fusion of the apoterramycins yields 1,8-dihydroxy-4-methylnaphthalene-3-carboxylic acid[3] and 2,5-dihydroxybenzoquinone. Both isomers lose carbon dioxide, ammonia and dimethylamine in hot concentrated hydrochloric acid, and are converted to decarboxamidoterrinolide (II).[4] Pentamethylterrinolide is formed by treatment of α-apoterramycin with methyl iodide and potassium carbonate in acetone. The presence of the dihydroxybenzophthalide system in the apoterramycins and terrinolide (III) is evident since the absorption spectra of these compounds are practically superimposable in the 330–420 mμ region of the ultraviolet spectrum, and all three compounds show the strong enhancement of the acidity of boric acid characteristic of 1,8-naphthalenediols.[5] Thus, the apoterramycins differ from terrinolide (III) only in the structure of the isolated six-membered ring.



II, R = H
III, R = $CONH_2$

The isolation of 2,5-dihydroxybenzoquinone from α-apoterramycin suggests the relative positions of two carbonyl groups, a hydroxyl and a dimethylamine group in the isolated ring. The stability of the apoterramycins under the conditions of their formation from terramycin excludes α- or γ-diketone structures within the carbocyclic ring since

(1) P. P. Regna, I. A. Solomons, K. Murai, A. B. Timreck, K. J. Brunings and W. A. Lazier, THIS JOURNAL, **73**, 4211 (1951).

(2) This compound was described by R. Pasternack, P. P. Regna, R. L. Wagner, A. Bavley, F. A. Hochstein, P. N. Gordon and K. J. Brunings, *ibid.*, **73**, 2400 (1951), as $C_{22}H_{24}N_2O_8 \cdot HCl$. It has since been found that Karl Fischer reagent shows the presence of one molecule of water, and that recrystallization from methanol displaces the water with a molecule of methanol.

(3) F. A. Hochstein, *et al.*, to be published.

(4) F. A. Hochstein, P. P. Regna, K. J. Brunings and R. B. Woodward, THIS JOURNAL, **74**, 3706 (1952).

(5) J. Böeseken, J. de Bruin and W. van Rijswijk de Jong, *Rec. trav. chim.*, **58**, 3 (1939).