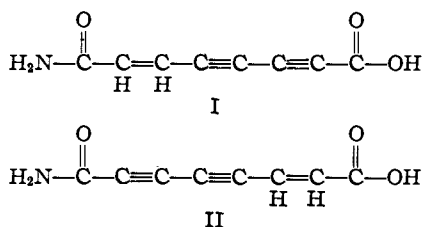


with suberic acid was obtained by alkaline hydrolysis (of the former) to suberic acid, identified by mixed melting point.

Accordingly, the polyacetylene must have the structure I or II.



Choice between these two formulations could probably best be made on the basis of synthetic model compounds or of authentic samples of the compounds themselves.

Acknowledgments.—This investigation was supported in part by a research grant (E-226) from the National Microbiological Institute of the National Institutes of Health, Public Health Service. The author is indebted to Dr. Julian Wolff for the preparation of Figure 1.

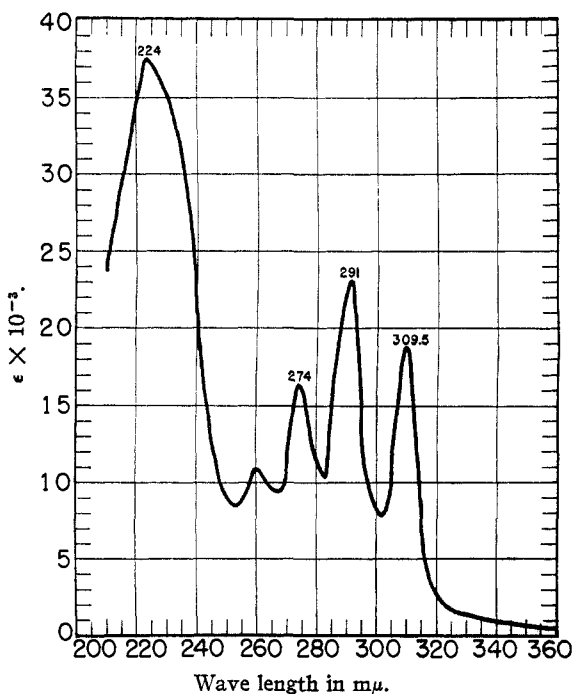


Fig. 1.—Ultraviolet absorption spectrum of the suberic acid ene-diyne, 0.0005% in 95% ethanol. The readings were made on a Beckmann DU spectrophotometer.

THE NEW YORK BOTANICAL GARDEN MARJORIE ANCHEL
BRONX PARK, NEW YORK 58, N. Y.

RECEIVED JULY 6, 1953

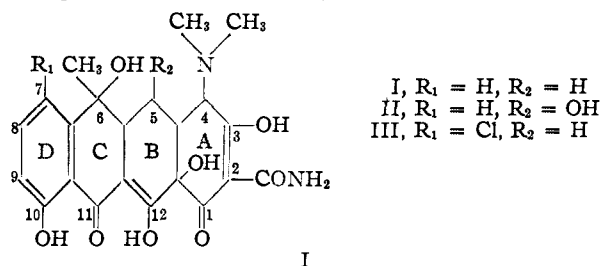
TERRAMYCIN. XI. TETRACYCLINE

Sir:

In a previous communication,¹ it has been indicated that the structure I, designated tetracycline, is common to the broad spectrum anti-

(1) C. R. Stephens, L. H. Conover, F. A. Hochstein, P. P. Regna, F. J. Pilgrim, K. J. Brunings and R. B. Woodward, *THIS JOURNAL*, **74**, 4976 (1952).

biotics, Terramycin (II) and Aureomycin (III).² At this time, we wish to report the preparation and antibiotic activity of tetracycline, I (4-dimethylamino-1,4,4a,5,5a,6,11,12a-octahydro-3,6,10,12,12a-pentahydroxy-6-methyl-1,11-dioxo-2-naphthacene-carboxamide).^{2a}



Treatment of a dioxane-methanol solution of chlorotetracycline with hydrogen in the presence of palladized carbon resulted in the ready hydrogenolysis of the aromatic halogen atom to give the hydrochloride of tetracycline. The latter was converted to the crystalline base, I; m.p. 170–175° dec., $[\alpha]_D^{25} - 239^\circ$ (c 1% in methanol), pK_a 8.3, 10.2 (50% aqueous dimethylformamide). *Anal.* Calcd. for C₂₂H₂₄N₂O₈: C, 59.45; H, 5.44; N, 6.31; mol. wt., 444. Found: C, 59.35; H, 5.41; N, 6.15; equiv. wt. (titration), 227.

On treatment with methanolic hydrogen chloride, tetracycline was readily converted to the previously reported deschloroanhydroaureomycin.³

The ultraviolet absorption spectrum of I exhibits maxima at 268 m μ , log ϵ 4.27, and 363 m μ , log ϵ 4.14, in 0.01 M methanolic hydrogen chloride, and at 246 m μ , log ϵ 4.24, and 372 m μ , log ϵ 4.20, in 0.01 M methanolic sodium hydroxide.

The ultraviolet spectra of tetracycline in acidic and basic solution are nearly identical with the corresponding spectra⁴ for oxytetracycline and provide further confirmation of the structure assigned to tetracycline. The spectra of tetracycline and chlorotetracycline⁵ in acid solution are very similar. A slight hypsochromic shift of the long wave length tetracycline peak is attributed to the removal of the aromatic chlorine.⁶ In contrast to chlorotetracycline,⁷ tetracycline is quite stable in alkaline solution, and its spectrum in this medium is very similar to that of oxytetracycline. This observation demonstrates the profound influence of the aromatic chlorine on the stability of the C ring in chlorotetracycline⁸ and is in agreement with

(2) Terramycin is the registered trade name of Chas. Pfizer and Company for the antibiotic whose generic name is oxytetracycline. Aureomycin is the registered trade name of Lederle Laboratories for the antibiotic whose generic name is chlorotetracycline.

(2a) This name and numbering system follows suggestions kindly made by the Editors of *Chemical Abstracts*.

(3) C. W. Waller, B. L. Hutchings, R. W. Broschard, A. A. Goldman, W. J. Stein, C. F. Wolf and J. H. Williams, *THIS JOURNAL*, **74**, 4981 (1952).

(4) P. P. Regna, I. A. Solomons, K. Murai, A. E. Timreck, K. J. Brunings and W. A. Lazier, *ibid.*, **73**, 4211 (1951).

(5) R. Broschard, A. Dornbush, S. Gordon, B. Hutchings, A. Kohler, G. Krupka, S. Kushner, D. Lefemine and C. Pidacks, *Science*, **109**, 199 (1949).

(6) The ultraviolet spectra of oxytetracycline and chlorotetracycline are discussed in reference 1.

(7) Cf. M. S. Bryer, E. B. Schoenbach, C. A. Chandler, E. A. Bliss and P. H. Long, *J. Am. Med. Assoc.*, **138**, 117 (1948).

(8) C. W. Waller, B. L. Hutchings, C. F. Wolf, A. A. Goldman, R. W. Broschard and J. H. Williams, *THIS JOURNAL*, **74**, 4981 (1952).

observed differences in the course of the alkaline degradation of chlorotetracycline and oxytetracycline.

Although tetracycline lacks both the 5-hydroxyl group of oxytetracycline and the 7-chloro group of chlorotetracycline, it possesses *in vitro* activity (Table I) against a variety of microorganisms which parallels the broad antimicrobial spectra of these two antibiotics.^{9,10}

TABLE I
ACTIVITY¹¹ IN VITRO OF TETRACYCLINE

Species	Minimum inhibitory concentration, mcg./ml.
<i>Aerobacter aerogenes</i>	50.0
<i>Klebsiella pneumoniae</i>	12.5
<i>Escherichia coli</i>	1.56
<i>Salmonella typhosa</i>	0.78
<i>S. paratyphi</i>	0.78
<i>Staphylococcus aureus</i>	<0.19
<i>Proteus sp.</i>	50.0
<i>Pseudomonas sp.</i>	12.5
<i>Brucella bronchisepticae</i>	0.39
<i>Mycobacterium ranae</i>	<0.19
<i>Streptococcus faecalis</i>	<0.19

(9) A. C. Finlay, G. L. Hobby, S. Y. P'an, P. P. Regna, J. B. Routien, D. B. Seeley, G. M. Shull, B. A. Sobin, I. A. Solomons, J. W. Vinson and J. H. Kane, *Science*, **111**, 85 (1950).

(10) T. F. Paine, Jr., H. S. Collins and M. Finland, *J. Bact.*, **56**, 489 (1948).

(11) A serial dilution procedure was employed to determine the minimum concentration of tetracycline at which growth was completely inhibited.

RESEARCH LABORATORIES
CHAS. PFIZER AND CO., INC.
BROOKLYN 6, N. Y.

L. H. CONOVER
W. T. MORELAND
A. R. ENGLISH
C. R. STEPHENS
F. J. PILGRIM

RECEIVED AUGUST 13, 1953

LOW PRESSURE VALIDITY OF THE BET EQUATION Sir:

As a prelude to a systematic study of the adsorption of gases on solids in the micron and sub-micron pressure range, we have determined the adsorption isotherms of heptane on ferric oxide at 29.55, 23.10 and 16.55° and at pressures ranging from 0.01 to 70 microns. We failed to find the first order transition reported for this system by Jura, Loeser, Basford and Harkins¹ and our results are in qualitative agreement with those reported by Smith² and by Young and Beebe.³ Certain experimental difficulties associated with the use of mercury float valves were encountered; it is possible to attribute the apparent first order transition previously reported to an artifact of this sort as well as to the possible lack of equilibrium suggested by Young and Beebe. Equilibrium was attained only after two weeks at one micron pressure when the conventional adsorption bulb was employed; this time was shortened to approxi-

(1) G. Jura, E. H. Loeser, P. R. Basford and W. D. Harkins, *J. Chem. Phys.*, **14**, 117 (1946).

(2) L. N. Smith, *THIS JOURNAL*, **74**, 3477 (1952).

(3) D. M. Young and R. A. Beebe, private communication.

mately two days through use of the tray system described by Jura and Criddle.⁴

The specific surface area of the ferric oxide as calculated from a BET plot of the nitrogen adsorption data at liquid nitrogen temperature is 6.82 sq. meters per gram. The adsorption data for heptane at constant temperature may be fitted by the equation $p/v = k_1p + k_2$ for relative pressures ranging from 3×10^{-4} to the highest measured; a relative pressure of 3×10^{-4} corresponds to a surface coverage, θ , of approximately 0.4 monolayer. In the pressure range investigated the above equation is characteristic of the Langmuir and the Brunauer, Emmett and Teller isotherms. In the BET notation, v_m ranges from 0.367 cc. at 29.55° to 0.401 cc. at 16.55°, while "c" ranges from 2070 to 2470. If the nitrogen surface area be accepted as correct, the area per heptane molecule in the monolayer varies from 63 sq. angstrom at 16.55° to 69 sq. angstroms at 29.55°; these values may be compared with that of 65 sq. angstroms at 25° reported by Loeser and Harkins.⁵ The isosteric heat changes rapidly with θ up to approximately 0.4; for higher values of θ the isosteric heat is roughly constant at 14.5 kcal. per mole. The heat of adsorption calculated from the BET "c" is 13.5 kcal. per mole.

It is customary to state the range over which the BET equation fits the experimental data in terms of relative pressure; the low point of this range is generally given as 0.05. The fact that the low point of this range in our experiments is 0.0003 indicates that this statement is incorrect. In general the BET equation is valid for θ less than unity when the heat of adsorption is roughly independent of surface coverage. It might be expected that the relative pressures corresponding to this portion of the isotherm would become lower as the heat of adsorption increases. Thus it would seem preferable to state the region in which the BET equation fits the data in terms of surface coverage rather than relative pressure.

The data at hand permit the calculation of the full set of thermodynamic functions described by Hill, Emmett and Joyner.⁶ These functions as well as complete details of the experimental procedure will be presented in a future publication.

(4) G. Jura and D. Criddle, *J. Phys. Coll. Chem.*, **55**, 163 (1951).

(5) E. H. Loeser and W. D. Harkins, *THIS JOURNAL*, **72**, 3247 (1950).

(6) T. L. Hill, P. H. Emmett and L. G. Joyner, *ibid.*, **73**, 5102 (1951).

GENERAL ELECTRIC COMPANY
SCHENECTADY, NEW YORK

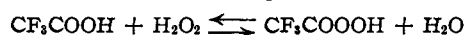
MYRON L. CORRIN

RECEIVED AUGUST 13, 1953

OXIDATION REACTIONS WITH PERTRIFLUOROACETIC ACID

Sir:

We have recently observed that a solution of hydrogen peroxide in trifluoroacetic acid has unique properties as an oxidizing agent presumably due to the *in situ* formation of pertrifluoroacetic acid.



This reagent has been found to oxidize aniline and