The products of reduction at the 2- and the 6-positions may absorb less strongly in the 340 mμ region than does the product of reduction at the 4-position. Only the latter product would be expected to show enzymatic activity.[7]

(7) M. E. Pullman, *Federation Proc.*, **12**, 255 (1953).

DEPARTMENTS OF PEDIATRICS AND BIOCHEMISTRY
UNIVERSITY OF CHICAGO
CHICAGO, ILLINOIS

Preparation of Highly Compressed Samples for Adsorption Studies[1]

BY S. V. R. MASTRANGELO,[2] R. J. TYKODI AND J. G. ASTON

RECEIVED JULY 13, 1953

While determining the B.E.T.[3] surface area of a highly compressed sample of TiO_2, it was discovered that equilibrium time for coverages between $0.5V_m$ and saturation was very much greater than usual, 8–10 hours as compared to 1–2 hours in less compact samples. When the B.E.T. surface area plot was made a non-linear curve was obtained as shown by the dotted curve through the circles with a left bar in Fig. 1. The surface area determined

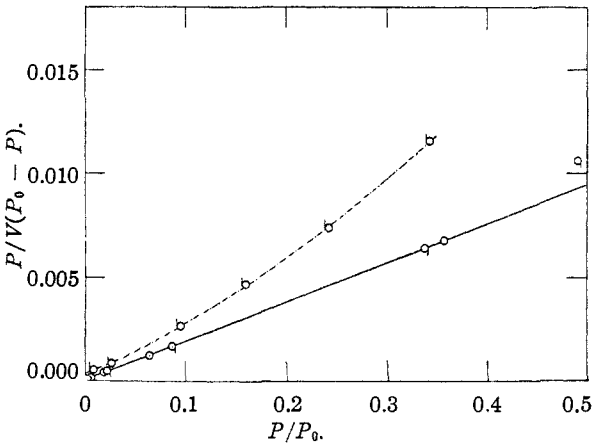


Fig. 1.—B.E.T. plot for nitrogen on TiO_2: o, points for loosely packed test sample; b, points for highly compressed samples; q, points for highly compressed samples after vibration.

by means of a straight line through the low pressure points is 134.5 m.²/g. However, a portion of the same sample had already been run in a small testing chamber, and this sample gave an excellent linear B.E.T. plot as shown by the plain circles in Fig. 1. This test sample was loosely packed relative to the first mentioned sample, and equilibrium was reached in 1–2 hours. The surface area obtained for the test sample is 230.0 m.²/g.

From these results it was concluded that some TiO_2 was not available to the gas in the first sample and that the slow equilibration was caused by gas leaking through solid cakes resulting from high compression. The packed calorimeter was vibrated by means of an ordinary electric vibrating machine. The calorimeter was clamped above the vibrator with a rubber stopper placed between to absorb most of the shock. It was not necessary to use the vibrating mechanism; the vibration of the body of the machine was apparently sufficient to loosen the packing. In order to prevent the machine from getting too hot, the sample was vibrated periodically for about 8 hours.

After the treatment described above the B.E.T. surface area determination was made again with nitrogen. This time, equilibrium was attained in less than 1 hour and in 0.5 hour for some points, all above coverages of $0.5V_m$. The points below $0.5V_m$ were, as usual, slow. The B.E.T. plot obtained for this run is not only linear, but falls on the same plot as for the test sample. These data are shown by the circles with a right bar in Fig. 1.

The authors wish to recommend this technique for preparing highly compressed samples used in adsorption studies at very low temperatures where the dead space corrections are large.

SCHOOL OF CHEMISTRY AND PHYSICS
THE PENNSYLVANIA STATE COLLEGE
STATE COLLEGE, PENNSYLVANIA

The Reactions of *p*-Arsanilic Acid and 4-Hydroxyphenylarsonic Acid with Brominated Fatty Acids[1,2]

BY ROBERT L. MCGEACHIN AND MARVIN GREENWALD

RECEIVED JULY 13, 1953

In the course of a study of the preparation of homologs and analogs of Tryparsamide, the condensations of a number of brominated fatty acids with *p*-arsanilic acid and 4-hydroxyphenylarsonic acid were attempted. Standard conditions known to give satisfactory results in the preparation of N-4-arsonophenylglycine[3] and several variations from these conditions (including the use of sodium iodide as a catalyst) all failed to bring about the condensation of α-bromobutyric, α-bromoisobutyric, α-bromovaleric and α-bromoisovaleric acids with *p*-arsanilic acid. However, condensations of *p*-arsanilic acid with α-bromopropionic and β-bromopropionic acids were successful under the standard conditions[3] giving N-(4-arsonophenyl)-α-aminopropionic acid (I) and N-(4-arsonophenyl)-β-aminopropionic acid (II). These products did not recrystallize from hot water as readily as the lower homolog, N-4-arsonophenylglycine, making their isolations somewhat more difficult and resulting in lower yields.

Preparation of α-(4-arsonophenoxy)-propionic acid (III) and β-(4-arsonophenoxy)-propionic acid (IV) were carried out following conditions outlined[4] for 4-arsonophenoxyacetic acid but the yield for the β-isomer was very low. Here again recrystallization and purification were more difficult than with the lower homolog.

The ethyl esters of I, II and III were prepared using the method given by Jacobs and Heidelberger[5] for the ethyl and methyl esters of N-4-arsonophenylglycine. The amide of I (a higher

(1) This Research was carried out under Contract N6ONR, Task Order X, of the Office of Naval Research.

(2) Postdoctoral Fellow, 1950–1951. Barrett Division of Allied Chemical and Dye Corporation, Genolden, Pa.

(3) S. Brunauer, P. H. Emmett and E. Teller, THIS JOURNAL, **60**, 309 (1938).

(1) This work was aided by a grant to the University of Louisville from the Kentucky State Medical Research Commission.

(2) From the M.S. Thesis of Marvin Greenwald, 1952.

(3) German Patent 204,644.

(4) H. Gilman and A. H. Blatt, "Organic Syntheses," Coll. Vol. I, John Wiley and Sons, Inc., New York, N. Y., 1947, p. 75.

(5) W. A. Jacobs and M. Heidelberger, THIS JOURNAL, **41**, 1950 (1919).

homolog of Tryparsamide) was prepared from its ethyl ester.[5]

Experimental

Preparation of I and II.—These compounds were prepared by the method given for N-4-arsonophenylglycine.[3] One variation in purification that was found necessary to remove final traces of unreacted bromopropionic acids was washing the products several times with ether; yields I (65%), II (41%).

Anal. Calcd. for $C_9H_{12}AsNO_5$: As, 25.99. Found: (I) As, 25.50; (II) As, 25.91.

Preparation of III and IV.—These compounds were prepared by the method given for 4-arsonophenoxyacetic acid[4]; yields III (37%), IV (5%).

Anal. Calcd. for $C_9H_{11}AsO_6$: As, 25.86. Found: (III) As, 25.90; (IV) As, 25.80.

Preparation of Ethyl Esters of I, II and III.—Prepared by the method used for the esterification of N-4-arsonophenylglycine[5]; yields I (45%), II (60%), III (50%).

Anal. Calcd. for $C_{11}H_{16}AsNO_5$: As, 23.69. Found: (I) As, 23.30; (II) As, 23.60. Calcd. for $C_{11}H_{15}AsO_6$: As, 23.63. Found: (III) As, 23.50.

Preparation of the Amide of I.—Prepared by ammonolysis of the ethyl ester using the method given for the amide of N-4-arsonophenylglycine[5]; yield 52%.

Anal. Calcd. for $C_9H_{13}AsN_2O_4$: As, 26.04; N, 9.72. Found: As, 26.0; N, 9.15.

DEPARTMENT OF BIOCHEMISTRY
SCHOOL OF MEDICINE
UNIVERSITY OF LOUISVILLE
LOUISVILLE, KY.

Preparation of 3-(6-Methoxynaphthyl-2)-2-cyclohexen-1-one and Related Compounds

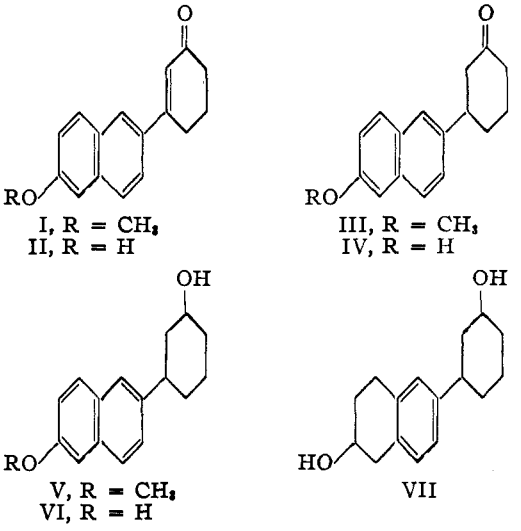
BY FREDERICK C. NOVELLO AND MARCIA E. CHRISTY

RECEIVED JULY 14, 1953

The condensation reaction between aryl β-dialkylamino ketones and acetoacetic ester and related compounds containing an active methylene group offers a convenient method for preparing 3-aryl-2-cyclohexen-1-one derivatives.[1] This procedure was employed to prepare 3-(6-methoxynaphthyl-2)-2-cyclohexen-1-one (I) and the related compounds, II–VII, which were of interest in view of the estrogenic activity of 1-ethyl-2-(4-hydroxyphenyl)-6-hydroxy-1,2,3,4-tetrahydronaphthalene and 1-methyl-2-(4-hydroxyphenyl)-6-methoxy-3,4-dihydronaphthalene.[2]

Synthesis of I was accomplished by condensation between 2-(β-dimethylaminopropionyl)-6-methoxynaphthalene hydrochloride and acetoacetic ester in the presence of alcoholic potassium hydroxide. Demethylation to II was effected by brief treatment with aluminum chloride in boiling xylene.[3] Conversion of I and II to the cyclohexanone and cyclohexanol derivatives, III–VII, was carried out by catalytic hydrogenations. Separation of stereoisomers was not attempted although V and VI were isolated as apparent homogeneous crystalline entities; VII was obtained as a glass. In the course of these hydrogenation studies it was found that vigorous stirring was superior to conventional methods of agitation and in the reduction of 3-(6-methoxynaphthyl-2)-2-cyclohexen-1-one to the cyclohexanone III, a sixfold increase in the reaction rate was realized when vigorous stirring was employed.

Of this series, 3-(6-hydroxynaphthyl-2)-2-cyclohexen-1-one (II) was the most active and gave a positive estrogenic response at a dosage level of 500 μg. in the vaginal cornification assay procedure.[4]



Experimental[5]

2-(β-Dimethylaminopropionyl)-6-methoxynaphthalene Hydrochloride.—A mixture of 37.5 g. (0.19 mole) of 2-acetyl-6-methoxynaphthalene,[6] 16.3 g. of dimethylamine hydrochloride, 8.8 g. of paraformaldehyde in 100 ml. of ethanol and 5 drops of concentrated hydrochloric acid was refluxed for 48 hours and concentrated to dryness *in vacuo*. The residual solid was suspended in ether, collected on a funnel and crystallized from ethanol; yield 39.1 g. (70%) of yellow needles, m.p. 180–184°. After further recrystallizations, pale yellow needles were obtained, m.p. 184–185.5°.

Anal. Calcd. for $C_{16}H_{20}O_2NCl$: C, 65.41; H, 6.86; N, 4.77. Found: C, 65.21; H, 7.04; N, 4.73.

The free base was obtained as colorless plates, m.p. 77–79°, from ether–petroleum ether.

Anal. Calcd. for $C_{16}H_{19}O_2N$: C, 74.68; H, 7.44; N, 5.44. Found: C, 74.47; H, 7.41; N, 5.41.

3-(6-Methoxynaphthyl-2)-2-cyclohexen-1-one (I).—A solution of 11.5 g. of potassium hydroxide in 150 ml. of isopropyl alcohol was added to a well-stirred mixture of 30 g. (0.1 mole) of 2-(β-dimethylaminopropionyl)-6-methoxynaphthalene hydrochloride and 13.1 g. of methyl acetoacetate in 150 ml. of isopropyl alcohol. The mixture was heated to reflux and stirred until the mixture became too viscous to allow further stirring (4–5 hours). After heating for a total of 72 hours, the mixture was poured into 3 l. of water and allowed to cool. The product was collected on a funnel, sucked dry, and then digested on the steam-bath with 200 ml. of benzene. The filtered benzene solution was washed with 10% hydrochloric acid, water and dried over sodium sulfate. After removal of solvent, the residue was distilled at 0.5 mm. and the product crystallized from acetone; yield 18.0 g. (70%) of yellow needles, m.p. 138–141°.

An analytical sample was obtained by repeated recrystallizations from acetone as pale yellow needles, m.p. 142.3–143.3°.

Anal. Calcd. for $C_{17}H_{16}O_2$: C, 80.92; H, 6.39; OCH_3, 12.30. Found: C, 81.00; H, 6.45; OCH_3, 12.24.

The oxime derivative crystallized from alcohol as pale yellow plates, m.p. 171.2–172.5°.

Anal. Calcd. for $C_{17}H_{17}O_2N$: C, 76.38; H, 6.41. Found: C, 76.40; H, 6.45.

(1) F. C. Novello, M. E. Christy and J. M. Sprague, THIS JOURNAL, **75**, 1330 (1953).

(2) W. Salzer, *Z. physiol. Chem.*, **274**, 39 (1942).

(3) K. Fries and K. Schimmelschmidt, *Ber.*, **58**, 2835 (1925).

(4) The authors are indebted to Dr. Roland K. Meyer and Dr. Elva S. Meyer, University of Wisconsin, for the estrogenic assays.

(5) The authors are indebted to Mr. Kermit B. Streeter and his associates, Miss J. L. Pyett and Mr. J. P. Laux for the analytical data.

(6) R. Robinson and H. N. Rydon, *J. Chem. Soc.*, 1399 (1939).