attached to the central methyl group, the question arises whether these two types of hydrogen atoms are necessary for the facile rupture of the C–C bond. In the case of the phenolic hydrogen, the answer is in the negative as 1,1′-benzal-bis-1-(2-methoxynaphthalene)—the dimethyl ether of II—yielded benzaldehyde and 2-methoxynaphthalene.[2]

To determine whether the hydrogen in the methyl group is essential, we investigated the hydrolysis of 1-triphenylmethyl-2-naphthol (IV)[4] which was prepared by the action of phenylmagnesium bromide on *o*-naphthofuchsone. When IV was heated with hydrochloric acid, it behaved like II, yielding β-naphthol and triphenylcarbinol. IV was acylated with *p*-nitrobenzoyl chloride; this and the fact that it gives the Platkovskaya test[5] for hindered phenols indicates that IV exists in the phenolic form, although it is practically insoluble in aqueous alkali. It is similar, therefore, to 2,4-dimethyl-6-*t*-butylphenol[6] which is also insoluble in alkali (10%), unstable in acid, and gives a positive Platkovskaya test[6]; both substances are soluble in Claisen solution.[6]

Experimental

1-Triphenylmethyl-2-naphthol (IV).—To an ethereal solution of phenylmagnesium bromide (prepared from 0.9 g. of magnesium, 8 g. of bromobenzene and 40 ml. of dry ether) was added a suspension of 1 g. of *o*-naphthofuchsone[7] in 30 ml. of benzene. The reaction mixture was refluxed (steam-bath) for three hours, set aside at room temperature and then decomposed with cold, saturated aqueous ammonium chloride solution containing a few ml. of hydrochloric acid. The reaction mixture was extracted with ether; the ethereal layer was dried (Na_2SO_4) and allowed to evaporate slowly. The solid residue was washed with 25 ml. of cold ethyl alcohol and crystallized from petroleum ether (b.p. 100–120°).

Compound IV (m.p. 155°) is soluble in hot benzene; its alcoholic solution gives no color when treated with alcoholic ferric chloride solution. It is almost insoluble in aqueous sodium hydroxide solution (10%) and gives no color when treated with sulfuric acid.

Anal. Calcd. for $C_{29}H_{22}O$: C, 90.1; H, 5.7; active H, 0.26. Found: C, 90.1; H, 6.1; active H, 0.28.

Compound IV was recovered unchanged from a mixture of 0.2 g. of IV, 0.1 g. of hydroxylamine hydrochloride, 0.2 g. of sodium acetate and 20 ml. of ethyl alcohol which had been refluxed for 6 hours.

Acylation.—To a solution of 0.5 g. of IV in 20 ml. of pyridine was added 0.5 g. of *p*-nitrobenzoyl chloride. The reaction mixture was heated (steam-bath) for 4 hr., then cooled and poured into ice-water. The resulting solid was washed with aqueous sodium carbonate solution and crystallized from acetic acid, m.p. 200°.

Anal. Calcd. for $C_{36}H_{25}NO_4$: C, 80.7; H, 4.7. Found: C, 80.3; H, 4.6.

Hydrolysis.—A stream of hydrogen chloride gas was passed intermittently into a heated mixture of 1 g. of IV and 25 ml. of concentrated hydrochloric acid. After a heating period of 16 hr., IV, which had been suspended, was transformed into an oily substance. After cooling, the oily layer was decanted and set aside overnight at room temperature; colorless crystals (A) separated leaving an oily residue (B). After crystallization from petroleum ether (b.p. 50–60°) (A) (0.2 g., m.p. 121°) were identified as β-naphthol (m.p., mixed m.p. and ready solubility in aqueous sodium hydroxide solution).

(B), which solidified on standing and cooling, was dissolved in ether; the ethereal solution was washed with cold aqueous sodium hydroxide solution (10%) followed by water, and dried. The ether was evaporated and the solid residue, upon crystallization from carbon tetrachloride (0.4 g., m.p. 160°), was identified as triphenylcarbinol.

DEPARTMENT OF CHEMISTRY
FACULTY OF SCIENCE
CAIRO UNIVERSITY
GIZA, CAIRO, EGYPT

(4) D. V. N. Hardy's (*J. Chem. Soc.*, 1000 (1929)) syntheses of this substance (m.p. 228°) has been disproved by the fact that his compound couples with the anti-diazotate of 2,5-dichloroaniline (see ref. 2), and by our results.

(5) V. M. Platkovskaya and S. G. Vatkina, *J. App. Chem.* (*U.S.S.R.*), **10**, 202 (1937), *C. A.*, **31**, 4232 (1937).

(6) G. H. Stillson, D. W. Sawyer and C. K. Hunt, THIS JOURNAL, **67**, 303 (1945).

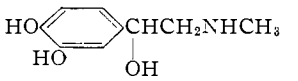
(7) M. Gomberg and F. W. Sullivan, *ibid.*, **42**, 1864 (1920).

Synthesis of Compounds Related to Epinephrine

BY JAMES R. VAUGHAN, JR., AND JACK BLODINGER[1]

RECEIVED JULY 5, 1955

In a program designed to develop more active bronchodilators for the treatment of asthma, several modifications of the structure of the natural product, epinephrine, were synthesized and tested.



The synthetic scheme followed is illustrated in the diagrams on the following page.

1-(3,4-Dimethoxyphenyl)-2-methylaminoethanol hydrochloride (II) was prepared by causing α-bromo-3,4-dimethoxyacetophenone to react with benzylmethylamine, followed by hydrogenation of this compound I using palladium catalyst, to yield the desired product II plus a minor amount of III. The observations of Suter and Ruddy[2] concerning the difficulties encountered in using ammonia or primary aliphatic amines in this condensation were substantiated. Use of their modified procedure in this and the following examples, however, gave excellent results.

1-(3,4-Ureidophenyl)-2-methylaminoethanol (VI) was synthesized by the following scheme. 5-Acetylbenzimidazolone-2 (IV) was prepared both by the Friedel–Crafts reaction between benzimidazolone-2 and acetyl chloride and by the action of phosgene on 3,4-diaminoacetophenone. Both products were identical. This product was then brominated in the side chain and caused to react with benzylmethylamine to give V. This on catalytic reduction, using palladium catalyst in aqueous solution, gave the desired product VI. In ethanol solution, however, the reduction stopped after the hydrogenolysis step and the product isolated was the corresponding ketone VII.

The analog 1-(3,4-ureidophenyl)-2-amino-1-butanol (X) was prepared as follows: benzimidazolone-2 was caused to react with butyryl chloride by the Friedel–Crafts reaction to give VIII. This was side-chain brominated and caused to react with benzohydrylamine to give IX. Catalytic hydrogenation of this in the presence of palladium in ethanol solution led to the preparation of X. This product was further characterized by conversion to the diacetyl derivative XI.

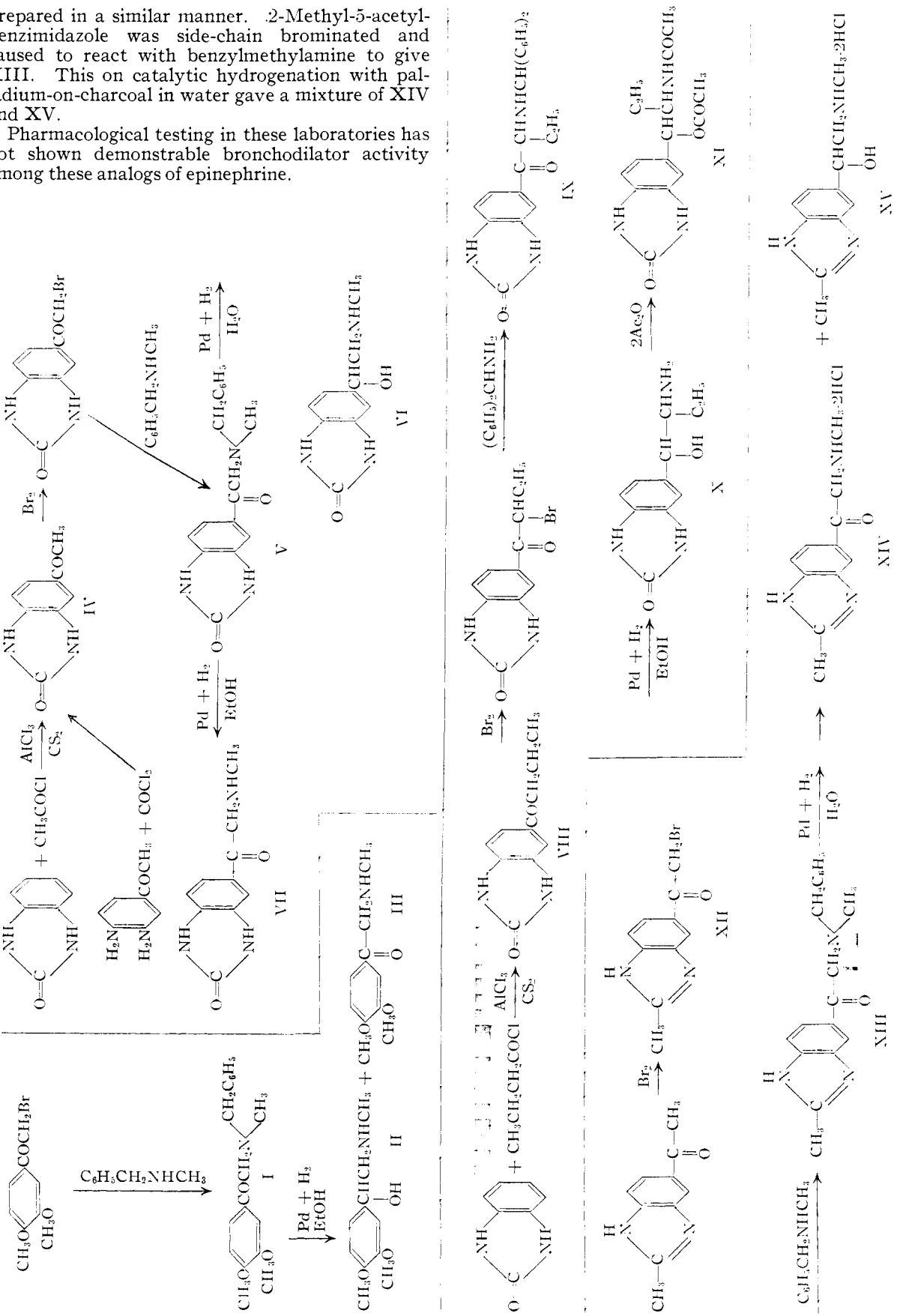
The analog 1-(2-methyl-5-benzimidazolyl)-2-methylaminoethanol dihydrochloride (XV) was

(1) Pharmaceutical Product Development Section, Research Division, American Cyanamid Co., Pearl River, N. Y.

(2) C. M. Suter and A. W. Ruddy, THIS JOURNAL, **66**, 747 (1944).

prepared in a similar manner. 2-Methyl-5-acetylbenzimidazole was side-chain brominated and caused to react with benzylmethylamine to give XIII. This on catalytic hydrogenation with palladium-on-charcoal in water gave a mixture of XIV and XV.

Pharmacological testing in these laboratories has not shown demonstrable bronchodilator activity among these analogs of epinephrine.



Experimental[3]

3,4-Dimethoxy-α-(N-benzyl-N-methyl)-aminoacetophenone Hydrochloride (I).—A solution of 21.0 g. (0.18 mole) of benzylmethylamine in 100 cc. of ether was added to 22.6 g. (0.088 mole) of α-bromo-3,4-dimethoxyacetophenone[4] in 1 liter of dry ether and the mixture allowed to stand overnight. The benzylmethylamine hydrobromide which crystallized was filtered off (wt. 16.8 g., 96%) and the filtrate was washed with two 300-cc. portions of water and dried over potassium carbonate. The ether solution was then saturated with dry hydrogen chloride to precipitate the desired material as a gummy solid. This was recrystallized from 200 cc. of methyl ethyl ketone to give the product as colorless needles, yield 12.5 g. (43%), m.p. 179–184°. Two additional crystallizations from methyl ethyl ketone by Soxhlet extraction gave 11.6 g. (40%) of product melting at 184–186°.

Anal. Calcd. for $C_{18}H_{21}NO_3 \cdot HCl$: C, 64.4; H, 6.61; N, 4.17. Found: C, 64.1; H, 6.68; N, 4.32.

3,4-Dimethoxy-α-methylaminoacetophenone Hydrochloride (III) and 1-(3,4-Dimethoxyphenyl)-2-methylaminoethanol Hydrochloride (II).—A 3.35-g. (0.01 mole) sample of I was placed in 30 cc. of ethanol with 0.2–0.3 g. of 10% palladium-on-charcoal catalyst[5] and shaken at room temperature and under 50 lb./in.^{2} of hydrogen pressure for 10 hours. The mixture was then warmed and filtered hot to remove the catalyst. On cooling the filtrate, colorless crystals separated, wt. 0.60 g. (24%), m.p. 203–210° dec. with darkening above 175°. After two recrystallizations from 20-cc. portions of alcohol, this product melted constantly at 217–220° dec. with softening above 211°. An analysis identified the product as III.

Anal. Calcd. for $C_{11}H_{15}NO_3 \cdot HCl$: C, 53.8; H, 6.57; N, 5.70. Found: C, 54.0; H, 6.57; N, 5.69.

On addition of 10 cc. of ether to the original filtrate from the above product, a second product separated rapidly as colorless crystals, yield 1.15 g. (46.5%), m.p. 112–114°. After two additional crystallizations from alcohol–ether (1:1) the material melted constantly at 114–115° and was identified by analysis as II.

Anal. Calcd. for $C_{11}H_{17}NO_3 \cdot HCl$: C, 53.3; H, 7.32; N, 5.66. Found: C, 53.8; H, 7.49; N, 5.63.

5-Acetylbenzimidazolone-2 (IV). A. Friedel–Crafts Reaction.—To a mixture of 36 g. (0.27 mole) of benzimidazolone-2 and 47 g. (0.60 mole) of acetyl chloride in 183 g. (0.40 mole) of carbon disulfide was added 160 g. (1.2 moles) of anhydrous aluminum chloride with good stirring during a 15-minute period. The reaction mixture was then heated on the steam-bath with stirring for 2 hours to form a brown, tarry mass. This was poured onto 250 g. of cracked ice and hydrolyzed by the dropwise addition of 15 cc. of concentrated hydrochloric acid. The resulting brown solid was filtered off, washed with water and recrystallized (Darco) from 1.5 l. of 95% ethanol to give 30 g. (63%) of crude product, m.p. 280–285°. Four additional crystallizations (Darco) of this product from 95% ethanol gave 15 g. (32%) of material melting at 294–295°.

Anal. Calcd. for $C_9H_8N_2O_2$: C, 61.4; H, 4.58; N, 15.9. Found: C, 61.5; H, 4.34; N, 16.0.

B. **From 3,4-Diaminoacetophenone.**—A 2.4-g. (0.016 mole) sample of 3,4-diaminoacetophenone[6] was dissolved in 50 cc. of dilute hydrochloric acid and the solution cooled while phosgene was bubbled into it during 10–15 minutes. The product separated rapidly as a light tan solid, yield 2.1 g. (76%), m.p. about 280°. This was recrystallized (Darco) from two 100-cc. portions of 95% ethanol to give 1.1 g. (40%) of product as colorless plates, m.p. 294–295°. A mixed melting point with the material prepared by the Friedel–Crafts reaction was not depressed.

5-Bromoacetylbenzimidazolone-2.—A 23.5-g. (0.13 mole) sample of IV was dissolved with warming in 250 cc. of glacial acetic acid and treated dropwise with stirring with a solution of 21.4 g. (0.13 mole) of bromine in 50 cc. of glacial acetic acid over a 30-minute period. The reaction mixture was then heated to boiling, diluted with 250 cc. of water, treated with Darco and filtered. On cooling, the product separated as a colorless solid, yield 25.5 g. (75%). Two recrystallizations from 500-cc. portions of 50% acetic acid gave 16.0 g. (47%) of product as colorless crystals, m.p. 264–266° dec.

Anal. Calcd. for $C_9H_7BrN_2O_2$: C, 42.8; H, 2.77; N, 11.0. Found: C, 42.5; H, 2.86; N, 11.2.

5-(N-Benzyl-N-methylaminoacetyl)-benzimidazolone-2-Hydrochloride (V).—A solution of 4.7 g. (0.018 mole) of 5-bromoacetylbenzimidazolone-2 and 4.4 g. (0.37 mole) of N-benzylmethylamine[7] in 50 cc. of alcohol was heated at reflux for 2 hours. The solution was then diluted with 100 cc. of water and stirred and cooled until the oily product set to a light tan solid, wt. 5.1 g. (95%). This was purified by dissolving it in 75 cc. of dilute hydrochloric acid, clarifying the solution with Darco and basifying with excess sodium hydroxide. On cooling, the product crystallized slowly as its sodium salt. Two additional crystallizations from 3% sodium hydroxide gave a completely colorless salt. This product was redissolved in ethanol and the solution treated with excess ethanolic hydrogen chloride and filtered to remove sodium chloride. On addition of ether to the filtrate the hydrochloride of the product precipitated as a gummy, colorless solid. Two additional crystallizations from 75-cc. portions of ethanol gave 1.5 g. (28%) of material as colorless crystals melting at 252–254° dec.

Anal. Calcd. for $C_{17}H_{17}N_3O_2 \cdot HCl$: C, 61.5; H, 5.47; N, 12.7. Found: C, 60.3[8]; H, 5.47; N, 12.7.

5-(N-Methylaminoacetyl)-benzimidazolone-2 Hydrochloride (VII).—A 2.0-g. (0.006 mole) sample of V and 0.3 g. of 10% palladium-on-charcoal catalyst[5] was placed in 30 cc. of ethanol and shaken at room temperature under 50 lb./in.^{2} of hydrogen pressure for 18 hours. The theoretical hydrogen absorption was observed. The insoluble reaction product was filtered off, dissolved in water and filtered to remove the catalyst. Concentration of the filtrate to dryness yielded 1.15 g. (80%) of crude product as a yellow solid. This was dissolved in 100 cc. of 50% ethanol, treated with Darco, filtered and diluted with 400 cc. of ethanol and 500 cc. of acetone. On long standing in the cold, the product crystallized as stout, colorless needles, wt. 0.90 g. (63%), m.p. greater than 300°. A 0.60-g. sample of this product was further purified by dissolving it in 10 cc. of water and diluting the solution with 150 cc. of ethanol and 250 cc. of acetone. On cooling, the product separated slowly as colorless, crystalline needles, wt. 0.45 g., m.p. greater than 300°.

Anal. Calcd. for $C_{10}H_{11}N_3O_2 \cdot HCl$: C, 49.7; H, 5.01; N, 17.4. Found: C, 49.6; H, 5.17; N, 17.6.

1-(3,4-Ureidophenyl)-2-N-methylaminoethanol Hydrochloride (VI).—A 1.32-g. (0.004 mole) sample of V and 0.3 g. of 10% palladium-on-charcoal catalyst[5] was placed in 30 cc. of water and shaken at room temperature under 50 lb./in.^{2} of hydrogen pressure for 18 hours. The theoretical hydrogen absorption was observed. The solution was filtered and concentrated to dryness to give 0.85 g. (89%) of product as a colorless solid. This was redissolved in 3 cc. of hot water, filtered and diluted with 75 cc. of hot alcohol. On cooling, the product separated slowly as colorless, crystalline plates, wt. 0.55 g. (58%). The material decomposes above 261°. Recrystallization of this material in the same manner gave 0.25 g. of crystalline product decomposing above 256°.

Anal. Calcd. for $C_{10}H_{13}N_3O_2 \cdot HCl$: C, 49.3; H, 5.79; N, 17.2. Found: C, 49.3; H, 5.91; N, 17.1.

5-Butyrylbenzimidazolone-2 (VIII).—A 67-g. (0.5 mole) sample of anhydrous powdered aluminum chloride was added with good stirring over a 10-minute period to a mixture of 13 g. (0.1 mole) of benzimidazolone-2 and 23 g. (0.2 mole) of butyryl chloride in 76 g. (1 mole) of carbon disulfide and the reaction mixture was then heated for 2 hours on the steam-bath. The dark brown oily reaction mixture was poured onto 250 g. of cracked ice and hydrolyzed by addition of 10–15 drops of concentrated hydrochloric acid. The resulting brown solid was filtered off, washed with water and recrystallized (Darco) from 400 cc. of 50% ethanol to

(3) All melting points were taken on a Fisher–Johns block and are corrected. We are indebted to Dr. J. A. Kuck and his staff, of these laboratories, for the microanalyses.

(4) A. Kaufmann and H. Muller, *Ber.*, **51**, 123 (1918).

(5) Obtained from Baker & Co., Inc., Newark, N. J.

(6) W. Borsche and J. Barthenheier, *Ann.*, **553**, 250 (1942).

(7) N. H. Cromwell, R. D. Babson and C. E. Harris, THIS JOURNAL, **65**, 312 (1943).

(8) A satisfactory value for carbon was not obtained on this compound.

give 20 g. of crude, yellow product. This was purified by two crystallizations (Darco) from 50% ethanol followed by three crystallizations from 95% ethanol to give 5.2 g. (25%) of product as colorless crystals, m.p. 261–263°.

Anal. Calcd. for $C_{11}H_{12}N_2O_2$: C, 64.7; H, 5.93; N, 13.7. Found: C, 64.9; H, 5.95; N, 13.5.

5-(α-Bromobutyryl)-benzimidazolone-2.—A 22.5-g. (0.11 mole) sample of VIII was dissolved with warming in 300 cc. of glacial acetic acid and a solution of 17.6 g. (0.11 mole) of bromine in 50 cc. of glacial acetic acid was added dropwise at 50–60° over a 20-minute period. The reaction mixture was then concentrated by vacuum distillation to leave the product as a light tan, crystalline residue. This was recrystallized from a mixture of 350 cc. of ethyl acetate and 150 cc. of ethanol to give 20.1 g. (65%) of product as colorless crystals, m.p. 233–234° dec. Concentration of the filtrate until crystallization began and recooling yielded an additional 8.7 g. (28%) of product also melting at 233–234° dec. These crops were combined and recrystallized as above to give 22.7 g. (73%) of product melting at 235–236° dec.

Anal. Calcd. for $C_{11}H_{11}BrN_2O_2$: C, 46.7; N, 9.9. Found: C, 46.5; N, 10.2.

5-[α-(N-Benzohydrylamino)-butyryl]-benzimidazolone-2 Hydrochloride (IX).—A 2.8-g. (0.01 mole) sample of 5-(α-bromobutyryl)-benzimidazolone-2 and 3.6 g. (0.02 mole) of benzohydrylamine[9] were dissolved in 25 cc. of absolute ethanol and the solution heated under reflux for 3 hours. The ethanol was then removed by distillation and the light yellow residue was triturated with ether to dissolve the product and leave benzohydrylamine hydrobromide as a colorless residue. The ether solution was shaken with 75 cc. of 10% hydrochloric acid to precipitate an oil phase which slowly crystallized on standing for several hours; wt. 3.9 g. (93%), m.p. 180–200°. Two recrystallizations from ethanol–isopropyl alcohol (1:1) gave 2.9 g. (69%) of product as colorless needles, m.p. 182–184°.

Anal.[10] Calcd. for $C_{24}H_{23}N_3O_2 \cdot HCl$: C, 68.3; H, 5.73. Found: C, 68.2; H, 5.99.

1-(3,4-Ureidophenyl)-2-aminobutanol Hydrochloride (X).—A 2.8-g. (0.007 mole) sample of IX and 0.3 g. of 10% palladium-on-carbon catalyst[5] were placed in 30 cc. of absolute alcohol and shaken at room temperature under 50 lb./in.^{2} of hydrogen pressure for 7 hours. The theoretical amount of hydrogen was absorbed. The hydrogenation mixture was diluted with 50 cc. of alcohol, heated to boiling, and filtered to remove the catalyst. Dilution of the filtrate with 1 liter of acetone caused the product to precipitate as a colorless, crystalline powder, wt. 1.1 g. (65%). Concentration of the filtrate gave an additional 0.35 g. (21%) of crystalline solid. Both solids darkened above 200° and charred without melting between 215–250°. The first crop was recrystallized by dissolving it in 75 cc. of absolute ethanol and diluting the solution with 500 cc. of acetone and 250 cc. of ether. The product separated as a colorless crystalline powder, wt. 0.90 g. (82% recovery), having the same decomposition characteristics as described above.

Anal. Calcd. for $C_{11}H_{15}N_3O_2 \cdot HCl$: C, 51.3; H, 6.26; N, 16.3. Found: C, 51.7; H, 6.20; N, 16.2.

This product was further characterized by acetylation using acetic anhydride in the presence of sodium acetate to give **1-(3,4-ureidophenyl)-2-acetylaminobutyl acetate (XI).** This derivative was obtained as colorless needles by crystallization from 50% ethanol; m.p. 183–184°.

Anal.[10] Calcd. for $C_{15}H_{19}N_3O_4$: C, 59.0; H, 6.27. Found: C, 59.0; H, 5.90.

2-Methyl-5-(ω-bromoacetyl)-benzimidazole (XII).—A solution of 11.5 g. (0.066 mole) of 2-methyl-5-acetylbenzimidazole[6] in 100 cc. of glacial acetic acid at 70° was irradiated with an 100-watt light bulb and treated dropwise with a solution of 10.6 g. (0.066 mole) of bromine in 25 cc. of glacial acetic acid. The reaction required 4 hours. The excess acetic acid was removed by distillation and the tarry residue was converted to a white solid by stirring for several hours with two 300-cc. portions of 30–70° petroleum ether. Crystallization of the material from 100 cc. of 1:1 ethanol–isopropyl alcohol gave 6.1 g. (36.5%) of product as colorless granules. On rapid heating the material melts with decomposition at approximately 180°, but on slow heating it darkens above 250° but does not melt below 300°. This material was used in the next step without further purification.

2-Methyl-5-(N-benzyl-N-methylaminoacetyl)-benzimidazole (XIII).—A 3.8-g. (0.015 mole) sample of crude XII and 3.6 g. (0.03 mole) of benzylmethylamine were placed together in 25 cc. of ethanol. An exothermic reaction occurred and rapidly subsided. The mixture was refluxed for 1 hour and then concentrated to a red oil. This was triturated with ether to cause solidification and the solid was taken up in alcoholic hydrogen chloride and precipitated with ether. This process was repeated from isopropyl alcohol–ether to give a solid which, after crystallization from ethanol–ether, melted at 238–240° dec., yield 1.0 g. (25%). The material was not purified further.

2-Methyl-5-methylaminoacetylbenzimidazole Dihydrochloride (XIV) and 1-(2-Methyl-5-benzimidazolyl)-2-methylaminoethanol Dihydrochloride (XV).—A 1.0-g. (0.0033 mole) sample of crude XIII was placed in 30 cc. of water with 0.2 g. of 10% palladium-on-charcoal[5] and the mixture shaken at room temperature under a hydrogen pressure of 40 lb./in.^{2}. Two equivalents of hydrogen were absorbed in 2 hours. The solution was filtered, treated with Darco and concentrated to yield 0.50 g. (63%) of a crystalline solid. This was recrystallized from 40 cc. of 85% ethanol (Darco) to give 0.11 g. of colorless crystalline needles which darken above 240° and decompose above 275°. Recrystallization of this from 30 cc. of 95% alcohol gave 0.08 g. of colorless needles melting in the same fashion. Analysis of this material indicates that it is XIV.

Anal. Calcd. for $C_{11}H_{13}N_3O \cdot 2HCl$: C, 47.8; H, 5.48; N, 15.2; Cl^-, 25.7. Found: C, 47.6; H, 5.31; N, 15.2; Cl^-, 25.4.

On dilution of the original alcoholic mother liquor (40 cc. of 85% alcohol) with 5–6 cc. of ether, 0.2 g. of a colorless, crystalline product separated. This was recrystallized from 50 cc. of 95% alcohol as colorless needles which decompose above 275°.

Anal. Calcd. for XV, $C_{11}H_{15}N_3O \cdot 2HCl$: C, 47.5; H, 6.16; N, 15.1. Found: C, 47.1; H, 5.78; N, 15.1.

MEDICINAL CHEMICAL SECTION
RESEARCH DIVISION
AMERICAN CYANAMID COMPANY
STAMFORD, CONNECTICUT

(9) C. F. Winans and H. Adkins, THIS JOURNAL, **55**, 2051 (1933).

(10) A satisfactory nitrogen value was not obtained on this compound.

Formation of Neopentyl Alcohol from Isobutylene in the Hydroformylation Reaction

BY IRVING WENDER, JULIAN FELDMAN, SOL METLIN, BERNARD H. GWYNN AND MILTON ORCHIN

RECEIVED MAY 11, 1955

Considerations of the mechanism of the hydroformylation reaction have been influenced by the rule formulated by Keulemans, Kwantes and van Bavel which states that "addition of the formyl group to a tertiary carbon atom does not occur, so that no quaternary carbon atoms are formed."[1] During an investigation of the cobalt carbonyl catalyzed reaction of *t*-butyl alcohol with carbon monoxide and hydrogen in a continuous unit, a large amount of product was obtained. A distillation of this material after hydrogenation resulted in the isolation of a solid product which was shown to be neopentyl alcohol. Previous work has shown that *t*-butyl alcohol reacts rapidly at 150° to give isoamyl alcohol in good yield[2]; presumably the alcohol is dehydrated[2–4] to isobutylene which then undergoes the hydroformylation reaction.

(1) A. I. M. Keulemans, A. Kwantes and Th. van Bavel, *Rec. trav. chim.*, **67**, 298 (1948).

(2) I. Wender, R. Levine and M. Orchin, THIS JOURNAL, **71**, 4160 (1949).

(3) K.-H. Ziesecke, *Brennstoff-Chem.*, **33**, 385 (1952).

(4) R. C. Anderson, Abstracts of the 123rd Meeting of the American Chemical Society, Chicago, Ill., Sept., 1953.