TABLE I

Compound	Color	M.p., °C.	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found	Methoxyl, % Calcd.	Methoxyl, % Found	2,4-Dinitrophenylhydrazone M.p., °C.	2,4-Dinitrophenylhydrazone Empirical formula	2,4-Dinitrophenylhydrazone Nitrogen, % Calcd.	2,4-Dinitrophenylhydrazone Nitrogen, % Found
2′,4-Dihydroxy-3,3′-dimethoxychalcone ($C_{17}H_{16}O_5$)	Orange	128–129	67.89	67.8	5.37	5.36	20.7	20.7	241–242	$C_{23}H_{20}O_8N_4$	11.7	12.3
2′-Hydroxy-3,3′,4-trimethoxychalcone[a,b] ($C_{18}H_{18}O_5$)	Red	128–129.5	68.77	68.9	5.77	5.79	29.6	29.8	190–191 d	$C_{24}H_{22}O_8N_4$	11.33	11.44
3′4′8-Trimethoxyflavanone ($C_{18}H_{18}O_5$)	Colorless	142–143	68.77	68.7	5.77	5.7	29.6	29.7	.....	.....	...	...
2,2′3,3′-Tetramethoxychalcone[c] ($C_{19}H_{20}O_5$)	Yellow	71–74	69.5	69.6	6.14	6.12	37.8	37.8	177–179	$C_{25}H_{24}O_8N_4$	11.9	10.4

[a] Acetyl derivative described in Experimental. [b] Yield 26.7%. [c] Yield 21.8%.

occurred to a limited extent under the reaction conditions.

Attempts to prepare 4-hydroxy-2′,3,3′-trimethoxy- and 4-acetoxy-2′,3,3′-trimethoxychalcones by both acid- and alkali-catalyzed condensation of 2,3-dimethoxyacetophenone with vanillin and vanillinmonoacetate, respectively, were unsuccessful.

Experimental[4]

General Procedure.—To a stirred solution of equimolar quantities of the aldehyde and ketone in the minimum amount of absolute alcohol was added portionwise an aqueous alkali hydroxide solution. The flask was stoppered and allowed to stand for 24 hours. The mixture was diluted with ice-water, and acidified with hydrochloric acid to congo red. If the resulting precipitate was crystalline or a semi-solid, it was dried and crystallized repeatedly from alcohol or an alcohol–water mixture with the aid of decolorizing charcoal.

Isolation of 3′,4′,8-Trimethoxyflavanone.—The mother liquor from the crystallization of 2′-hydroxy-3,3′,4-trimethoxychalcone (0.3-mole run) was concentrated to about 126 ml., and cooled overnight. The pale orange crystals were recrystallized from alcohol with the aid of decolorizing charcoal to yield a colorless crystalline product. Qualitative tests for unsaturation and the hydroxyl group were negative. This material gave the characteristic yellow color reaction for flavanones with an aqueous solution of sodium hydroxide, and with hot aqueous solution of sodium bicarbonate or sodium carbonate. The colorless crystalline product was identified by analysis as 3′,4′,8-trimethoxyflavanone; yield 0.9 g.

2′-Acetoxy-3,3′,4-trimethoxychalcone.—Direct acetylation of an anhydrous pyridine solution of 2′-hydroxy-3,3′,4-trimethoxychalcone (0.0016 mole) with freshly distilled acetyl chloride (1.5 ml.) yielded the acetoxy derivative of this chalcone. The reaction mixture was worked up in the usual manner, and the crude product was twice recrystallized from an ethanol–water mixture (50%) with the aid of decolorizing charcoal, yielding a yellow crystalline product, m.p. 107–109°, yield 0.15 g. (26.7%).

Anal. Calcd. for $C_{20}H_{20}O_6$: acetyl, 12.0. Found: acetyl, 11.7.

Preparation of 2′,4-Dihydroxy-3,3′-dimethoxychalcone.[5]—The general procedure failed to give the desired chalcone, and the following technique was used: Alcoholic solutions containing equimolar quantities (0.066 mole) of vanillin and 2-hydroxy-3-methoxyacetophenone, respectively, were combined, stirred and cooled to −5°. With continued stirring, 152 ml. of potassium hydroxide solution (60%) was added portionwise, and the salts that formed were redissolved by adding an alcohol–water mixture, and heating on the steam-bath for 3 hours. After standing at room temperature for 15 days (with occasional shaking) excluded from air, the reaction product was diluted with ice-water, and acidified with hydrochloric acid to congo red. The acid solution was decanted, and the gummy mass was washed three times with water. An ether solution of the gummy material was extracted with water until neutral, then dried, and the solvent was removed by distillation and evaporation. The ether-free, dried, semi-crystalline material was steam distilled, and the product was twice recrystallized from an alcohol–water mixture with the aid of decolorizing charcoal; yield 2.0 g. (10.2%).

(4) Melting points are uncorrected.

(5) Modification of the cold condensation technique described by T. A. Geissman and R. O. Clinton, THIS JOURNAL, **68**, 697 (1946).

DEPARTMENT OF CHEMISTRY
BRADLEY UNIVERSITY
PEORIA, ILLINOIS

The Isomerization of D-Glucose by a Strong Base Resin

BY JOHN C. SOWDEN

RECEIVED APRIL 14, 1954

In a recent communication,[1] Rebenfeld and Pacsu described the isomerization of D-glucose by the strongly basic anion-exchange resin Amberlite IRA-400.[2] They analyzed the isomerized mixture by a combination of the alkaline hypoiodite and Somogyi methods, neither of which are specific for individual sugars, and recorded the results as "% glucose" and "% fructose." Finally, they concluded that "—it appears that the presently accepted ene–diol mechanism for the Lobry du Bruyn transformation does not hold in this case, as evidenced by the absence of mannose in the glucose–fructose interconversion."

It is apparent that the above data alone cannot validly be used to conclude that D-mannose is not formed in the isomerization reaction. Moreover, since D-mannose is a very minor constituent[3,4] of the alkaline isomerization products from D-glucose, failure to detect it on a paper chromatogram of the reaction mixture would constitute at best a tenuous basis for assuming its absence.

Since the conclusion reached by Rebenfeld and Pacsu concerning the reaction mechanism would be, if correct, of considerable importance, it was desirable to repeat their isomerization experiment in order to determine the presence or absence of D-mannose in the products. In the present work it was observed that D-mannose *is* formed from D-glucose in the presence of Amberlite IRA-400-(OH) to approximately the same extent as from D-glucose in the presence of dilute aqueous sodium hydroxide. The interpretation placed on their work by Rebenfeld and Pacsu therefore must be considered invalid.

Experimental

Ten grams (dry weight, chloride form) of Amberlite IRA-400 was cycled several times through the chloride and hydroxide forms. To the conditioned, moist resin in the hydroxide form was added a solution of 2.0 g. of D-glucose

(1) L. Rebenfeld and E. Pacsu, THIS JOURNAL, **75**, 4370 (1953).

(2) A product of Rohm and Haas Co., Philadelphia, Pa.

(3) M. L. Wolfrom and W. L. Lewis, THIS JOURNAL, **50**, 837 (1928); R. D. Greene and W. L. Lewis, *ibid.*, **50**, 2813 (1928).

(4) J. C. Sowden and R. Schaffer, *ibid.*, **74**, 499 (1952).

in 90 ml. of carbon dioxide-free water and the mixture was allowed to stand at room temperature under nitrogen. A control solution of 2.0 g. of D-glucose in 100 ml. of water, but containing no resin, also was prepared. After 188 hours, the isomerization mixture was filtered from the resin, with washing, and was concentrated at reduced pressure to a volume of 20 ml. The control solution was similarly concentrated. Both solutions then were treated at 0° with solutions containing 1 ml. of phenylhydrazine, 4 ml. of water and 5 drops of acetic acid. After 18 hours at 0°, filtration, washing and drying were performed as described previously.[4] The control solution yielded no product, whereas the isomerization solution yielded 60.5 mg. of D-mannose phenylhydrazone, m.p. 190–191°. When this yield is corrected for destruction of sugar to acidic products[1] and for the solubility of the phenylhydrazone,[4] the calculated production of D-mannose is 3.8% of the total remaining sugar. This value is in reasonable agreement with that observed[3,4] from D-glucose in dilute aqueous alkali.

The identity of the D-mannose phenylhydrazone was confirmed by converting it to the known anhydro-*O*-tetraacetate,[5] m.p. and m.m.p. 123–124°; $[\alpha]^{25}D$ 12° in pyridine (*c* 4).

(5) M. L. Wolfrom and Mary Grace Blair, THIS JOURNAL, **68**, 2110 (1946). The author is indebted to Dr. Blair for an authentic sample of this compound.

DEPARTMENT OF CHEMISTRY
WASHINGTON UNIVERSITY
SAINT LOUIS, MISSOURI

Some Amines Derived from 3-Phenyl-1-indanone

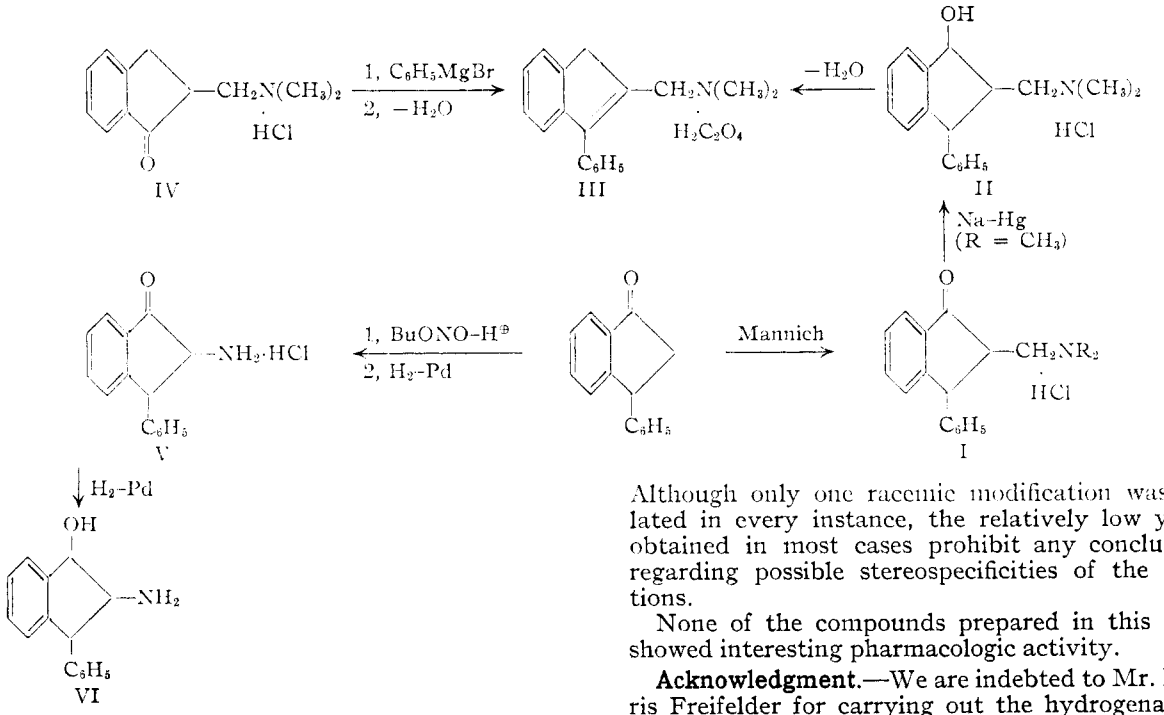
BY HAROLD E. ZAUGG AND BRUCE W. HORROM

RECEIVED MAY 13, 1954

Amines derived from the Mannich reaction of 1-indanone show definite pharmacologic activity.[1,2] For this reason similar products derived from 3-phenyl-1-indanone were prepared in the present work which is summarized in the accompanying flow sheet. The Mannich products I obtained from the four amines, dimethylamine, diethylamine, piperidine and morpholine, were all formed in poor yield and seemed to be even less stable than the simpler Mannich products from 1-indanone (type IV). Like the latter,[2] the hydrochlorides of type I also split off the starting amine hydrochlorides at or near their melting points. Reduction with sodium amalgam of the Mannich product from dimethylamine (I, R = CH_3) led to the carbinol II which on dehydration gave the same indene derivative III (isolated as the bioxalate) obtained by dehydration of the phenyl Grignard adduct of IV. Rearrangement of the double bond, formed initially on dehydration of II, to the position shown in III must occur as a result of stabilization gained from conjugation with both aromatic rings.[3]

Stepwise catalytic hydrogenation of 2-isonitroso-3-phenyl-1-indanone led first to the aminoindanone V isolated as the hydrochloride, and finally to the aminoalcohol VI isolated in the form of the solid free base. All attempts to prepare N-disubstituted amines of type V by reaction of 2-bromo-3-phenyl-1-indanone with secondary amines failed. Likewise, reduction of this bromoketone with aluminum isopropoxide to 2-bromo-3-phenyl-1-indanol followed by reaction with secondary amines failed to produce N-disubstituted analogs of VI.

Most of the compounds prepared in this work contain either two or three asymmetric carbon atoms. The authors feel that all of the products isolated were relatively pure diastereoisomers.



Although only one racemic modification was isolated in every instance, the relatively low yields obtained in most cases prohibit any conclusions regarding possible stereospecificities of the reactions.

None of the compounds prepared in this work showed interesting pharmacologic activity.

Acknowledgment.—We are indebted to Mr. Morris Freifelder for carrying out the hydrogenations and to Mr. E. F. Shelberg for the microanalyses.

Experimental

2-Dimethylaminomethyl-3-phenyl-1-indanone Hydrochloride (I, R = CH_3).—To a stirred refluxing solution of 31.2 g.

(1) K. Hoffmann and H. Schellenberg, *Helv. Chim. Acta*, **27**, 1782 (1944); U. S. Patent 2,441,069 (1948), 2,479,744 (1949).

(2) J. O. Jilek, M. Borovička and M. Protiva, *Coll. Czech. Chem. Comm.*, **18**, 257 (1953).

(3) Compare C. F. Koelsch and R. A. Scheiderbauer, THIS JOURNAL, **65**, 2311 (1943).