TABLE II

DERIVATIVES OF ALIPHATIC THIOETHERS AND MERCAPTANS

Compound	M. p., °C.	Form[a]	Solvent	Formula	Analyses, % Calcd. Hg	Calcd. Pd	Found Hg	Found Pd
$(i\text{-}C_5H_{11}S)_2Hg$	59–60	Silky needles	Dil. alc.	$C_{10}H_{22}HgS_2$	49.2		49.36	
$(i\text{-}C_4H_9SC_2H_4)\cdot 2HgCl_2$	107–108	Prisms	Bz	$C_6H_{14}SHg_2Cl_4$	60.84		61.40	
$(i\text{-}C_5H_{11}SC_2H_4)\cdot 2HgCl_2$	86–87	Glistening flakes	Dil. acetone	$C_7H_{16}SHg_2Cl_4$	59.40		60.03	
$(s\text{-}i\text{-}C_5H_{11}SC_2H_4)_2\cdot PdCl_2$	92.5–94	Yel. rect. prisms	Dil. acetone	$C_{14}H_{32}S_2PdCl_2$		24.14		23.94
$(n\text{-}C_4H_9SC_4H_9\text{-}i)_2\cdot PdCl_2$	73.5	Yellow-orange flakes	Dil. alc.	$C_{16}H_{36}S_2PdCl_2$		22.71		22.85

[a] All mercury derivatives were colorless.

Acetic acid was added until the solution was slightly acid to phenolphthalein, then 10 cc. of aqueous solution of mercuric cyanide was added (hood!). The mercaptide was separated by filtration and recrystallized from dilute ethanol.

The ester prepared by the addition of thioacetic acid to trimethylethylethylene yielded on saponification a mercaptan whose mercury salt was an oil. The mercaptan was converted to a sulfide by the following procedure. Nine grams (0.06 mole) of the ester was saponified by refluxing fifteen minutes with a solution of 6.72 g. (0.12 mole) of potassium hydroxide in 50 cc. absolute alcohol. To the warm solution was added 20 g. of ethyl iodide and the reaction completed by boiling the mixture fifteen minutes. The product was isolated by dilution of the reaction mixture with water, extraction with ether, and distillation under reduced pressure. The palladous chloride complex of the sulfide melted at 92.5–94°, mixed melting point with the complex of the sulfide formed by the addition of ethyl mercaptan to trimethylethylene was 93–94°.

Summary

Aliphatic mercaptans, thioacetic acid and hydrogen sulfide add to aliphatic olefins to give good yields of thioethers, thioesters and mercaptans, respectively. The aliphatic mercaptans and thioacetic acid resemble thiophenol and differ from hydrogen sulfide in that they add to the olefins more readily and in better yields, and in that they add practically completely in accordance with Markownikoff's rule.

In all cases the yield of addition product increases with increasing branching of the olefins.

RIVERSIDE, ILLINOIS RECEIVED OCTOBER 14, 1938

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, YALE UNIVERSITY]

Researches on Pyrimidines. CLX. The Catalytic Hydrogenation of 5-Benzyl- and 6-Benzyluracils[1]

BY JOSEPH C. AMBELANG[2] AND TREAT B. JOHNSON

The structural relationship of hydrouracils to β-amino acids, paralleling that of hydantoins to α-amino acids, has been pointed out in a previous paper[3] from this Laboratory. In that paper was discussed the possible synthesis of difficultly accessible β-amino acids from the corresponding hydrouracils. Brown and Johnson prepared their hydrouracil by hydrogenation of uracil at 75° over the Adams catalyst. Although the same catalyst was effective for the hydrogenation of ethyl uracil-6-acetate[4] and of 1-methyluracil,[4] it failed in the case of N-1-methyl-6-phenyluracil-N-3-acetic acid[5] and its methyl ester.[5]

In the present study hydrogenation of 5-benzyl- and 6-benzyluracils was attempted at elevated temperatures and pressures over Raney nickel and copper–chromium oxide catalysts, which in the desoxouracils[6] investigated by Folkers and Johnson made possible selective hydrogenation of the benzene and pyrimidine nuclei, respectively.

Over Raney nickel at 175° 6-benzyluracil (I) was hydrogenated with moderate ease to 6-benzylhydrouracil (III); at 225° over the same catalyst 2-keto-6-benzylhexahydropyrimidine (IV) resulted. No products of further reduction, other than a gum, were in evidence. Oxidation of 2-keto-6-benzylhexahydropyrimidine (IV) with the formation of benzoic acid demonstrated the failure of the benzene ring to undergo hydrogenation. Hydrolysis with barium hydroxide in aqueous methanol yielded 4-phenyl-1,3-butanediamine

(1) Constructed from a dissertation presented by Joseph C. Ambelang in June, 1938, to the Graduate Faculty of Yale University in partial fulfilment of the requirements for the degree of Doctor of Philosophy.

(2) Sterling Professorship of Chemistry Research Assistant 1938–1939.

(3) Brown and Johnson, THIS JOURNAL, **45**, 2702 (1923).

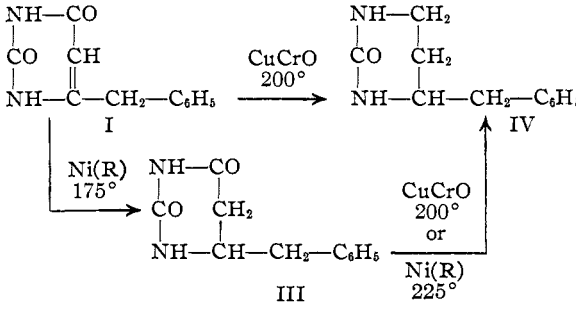
(4) Hilbert, *ibid.*, **54**, 2078 (1932).

(5) Evans and Johnson, *ibid.*, **52**, 500 (1930).

(6) Folkers and Johnson, *ibid.*, **56**, 1180 (1934).

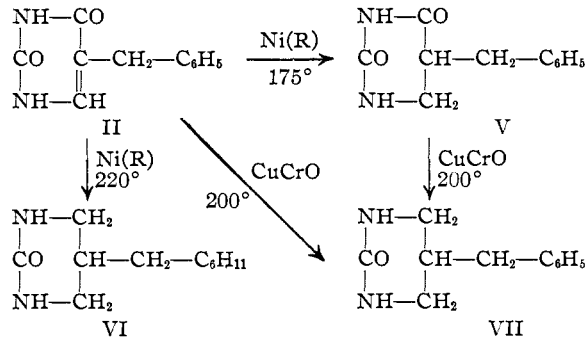
from 2-keto-6-benzylhexahydropyrimidine (IV) and 4-phenyl-3-butenoic acid from 6-benzylhydrouracil (III).

Reduction of 6-benzyluracil (I) over copper–chromium oxide at 200° could be effected only in small portions, the single product isolated being 2-keto-6-benzylhexahydropyrimidine (IV). This compound could not be hydrogenated further over Raney nickel at 225°. The same product resulted from the reduction of 6-benzylhydrouracil (III) under similar conditions over copper–chromium oxide. Of attempts at reduction of samples of 6-benzyluracil (I) larger than three grams in 100 cc. of ethanol no solid save unaltered 6-benzyluracil could be isolated from the reaction mixture, and the red color of the catalyst indicated deactivation.



The isomeric 5-benzyluracil (II) was hydrogenated over Raney nickel at 175° to 5-benzylhydrouracil (V) either in dioxane or ethanol solutions, but more rapidly in the latter solvent. All the samples of 5-benzylhydrouracil appeared on the basis of analysis to contain more highly reduced material for whose removal further recrystallization seemed ineffective. Since the 2-ketohexahydropyrimidines because of their high solubility should not persist, the impurity was believed to be 5-hexahydrobenzylhydrouracil, whose solubility would probably be very similar to that of 5-benzylhydrouracil.

Prolonged reduction treatment of II over Raney nickel at 200–220° in ethanol yielded 2-keto-5-hexahydrobenzylhexahydropyrimidine (VI). Over copper–chromium oxide at 200° 5-benzyluracil (II) in dioxane solution absorbed hydrogen very slowly. In ethanol at the same temperature 2-keto-5-benzylhexahydropyrimidine (VII) was formed. A mixture of 5-benzyluracil (II) and 5-benzylhydrouracil (V), obtained by partial hydrogenation of the former in dioxane solution over Raney nickel, when subjected to further reduction in ethanol, gave rise to the same 2-ketohexahydropyrimidines obtained when 5-benzyluracil was the starting material.



The higher rate of reaction in the case of 6-benzyluracil may be explained by the greater solubility of this isomer, or perhaps by the protective action of the benzyl group substituted on a carbon adjacent to one of the nitrogen atoms. Adkins and co-workers[7] observed the greater ease of hydrogenation of pyridinoid rings when certain substituents, notably benzyl- and carbethoxyl-occupied the 2- or the 2,6-positions of the pyridine cycle. Lessening the tendency of the nitrogen to combine with the catalyst was the mechanism they proposed to explain the effect of the substituents in these positions.

Hydrogenolysis of the carbon to oxygen bond (carbonyl) in the 4-position of both pyrimidines, even in the presence of Raney nickel suggests greater lability of this unsaturated bond in the compounds studied than in the open chain amides reduced by Adkins and Wojcik.[8] Nickel is ordinarily regarded as nearly inactive toward amide linkages.[9]

Failure of the benzenoid ring in 6-benzyluracil (I) to undergo hydrogenation over Raney nickel is unexpected in view not only of the behavior of the isomeric 5-benzyluracil (II) but also of the hydrogenation of the aryl substituted desoxouracils investigated by Folkers and Johnson.[6] The desoxouracil, 2-keto-6-benzylhexahydropyrimidine would be expected to yield the corresponding cyclohexanoid compound, *viz.*, 2-keto-6-hexahydrobenzylhexahydropyrimidine. No evidence of the latter was uncovered. Purification of the 6-benzyluracil (I) by refluxing in alcoholic solution with Raney nickel appeared to have no effect on either the course or the rate of reduction.

(7) Adkins, Kuick, Farlow and Wojcik, THIS JOURNAL, **56**, 2425 (1934).

(8) Adkins and Wojcik, *ibid.*, **56**, 2419 (1934).

(9) Adkins, "Reactions of Hydrogen," University of Wisconsin Press, Madison, Wis., 1937, p. 11.

TABLE I

HYDROGENATION AND HYDROGENOLYSIS OF 5-BENZYL- AND 6-BENZYLURACILS

Starting material	G.	Catalyst	G.	Abs. EtOH, cc.	Temp., °C.	H_2, atm.	Time, hours	Yield, %	Reduction product
5-Benzyluracil	1.3	Ni(R)[11]	1	45	175	165	6.5	53	5-Benzylhydrouracil
5-Benzyluracil	1.2	CuCrO[12]	1.5	100	200	195	4.0	27	2-Keto-5-benzylhexahydropyrimidine
5-Benzylhydrouracil[a]	1.0	CuCrO	1.5	100	200	210	6.0	32	2-Keto-5-benzylhexahydropyrimidine
5-Benzylhydrouracil[a]	1.0	Ni(R)	1	100	200	200	6.5	..	.....
					220	200	3.5	26	2-Keto-5-hexahydrobenzylhexahydropyrimidine
6-Benzyluracil	5.7	Ni(R)	1	50	175	165	3.5	59	6-Benzylhydrouracil
6-Benzyluracil	6.7	Ni(R)	1	44	220	175	6.0	..	.....
					225	165	3.0	42	2-Keto-6-benzylhexahydropyrimidine
6-Benzyluracil	2.0	CuCrO	2.0	100	200	210	3.0	64	2-Keto-6-benzylhexahydropyrimidine
6-Benzylhydrouracil	1.8	CuCrO	1.5	100	200	195	4.0	60	2-Keto-6-benzylhexahydropyrimidine

[a] A mixture containing 5-benzyluracil in addition to 5-benzylhydrouracil and obtained by hydrogenation of the former in dioxane solution.

TABLE II

MELTING POINTS AND ANALYSES OF THE REDUCTION PRODUCTS

Reduction product	M. p., °C.	Carbon, % Calcd.	Carbon, % Found		Hydrogen, % Calcd.	Hydrogen, % Found		Nitrogen, % Calcd.	Nitrogen, % Found	
5-Benzylhydrouracil	232	64.69	64.71	64.63	5.92	6.41	6.28	13.72	13.92	13.98
2-Keto-5-benzylhexahydropyrimidine	214–215	69.44	69.40	69.64	7.42	7.63	7.44	14.73	14.51	14.61
2-Keto-5-hexahydrobenzylhexahydropyrimidine	221–223	67.30	67.18	67.42	10.27	10.03	9.90	14.27	14.35	14.21
6-Benzylhydrouracil	223–224	64.69	64.58	64.75	5.92	6.14	5.88	13.72	13.78	13.62
2-Keto-6-benzylhexahydropyrimidine	184–185	69.44	69.18	69.53	7.42	7.33	7.20	14.73	14.68	14.81

Experimental Part

5-Benzyl- and 6-Benzyluracil.—These two uracil derivatives were prepared by the methods described in a previous paper of this series.[10] For hydrogenation experiments 5-benzyluracil was recrystallized once from glacial acetic acid and once from dioxane; 6-benzyluracil was recrystallized once from glacial acetic acid and twice from 95% ethanol. The data applying to the catalytic reduction experiments are recorded in Table I.

The apparatus used was essentially that described by Adkins.[13]

Reaction mixtures containing the hydrouracils were filtered while hot through fluted paper. The reduction product separated after cooling, and concentration of the mother liquor yielded an additional amount. The resulting pyrimidine was purified by recrystallization from 95% ethanol. Reaction mixtures containing the 2-ketohexahydropyrimidines were filtered while hot through sintered glass and concentrated to 15 cc. volume. The crystals which separated after cooling were purified by recrystallization from 95% or more dilute ethanol.

The hydrouracils are soluble in 5% sodium hydroxide solution but insoluble in concentrated aqueous ammonia, which dissolves the unreduced benzyluracils.

The 2-ketohexahydropyrimidines are soluble in concentrated hydrochloric acid but insoluble in 5% sodium hydroxide solution.

Oxidation of 2-Keto-6-benzylhexahydropyrimidine.—This pyrimidine was oxidized in the manner described for the oxidation of 5-bromo-6-benzyluracil.[10] The resulting product melted at 122–123° and when mixed with benzoic acid showed no depression in melting point.

Hydrolysis of 6-Benzylhydrouracil.—No crystalline entity was isolated from the reaction mixture when hydrolysis was effected with concentrated hydrochloric acid at 150°.

After digestion under atmospheric pressure with barium hydroxide in aqueous methanol for twenty-four hours, distillation of the hydrolysate into standard acid and titration revealed that virtually no ammonia had been evolved.

One and three-tenths grams of 6-benzylhydrouracil was suspended in 70 cc. of methanol and 50 cc. of water together with 10 g. of barium hydroxide and heated in a bomb at 145–155° for eight hours. A strong odor of ammonia was observed when the bomb was opened. The barium carbonate was filtered off and the rest of the barium removed by neutralization with dilute sulfuric acid. The solution was made faintly alkaline with barium hydroxide, evaporated to dryness and the gummy residue extracted with hot absolute ethanol. The remaining solid was dissolved in water and the solution acidified with dilute hydrochloric acid. The solid, 0.1 g., separating as the solution cooled, decolorized bromine water. It melted at 88–89°. The reported melting point for β-benzalpropionic acid is 88°.[14] Neutralization equivalent. Calcd. for $C_{10}H_{10}O_2$: 162. Found: 162.

4-Phenyl-1,3-butanediamine Sulfate.—One and seven-tenths grams of 2-keto-6-benzylhexahydropyrimidine was hydrolyzed in the manner described above. After removal of the barium sulfate the solution was concentrated to 5 cc. volume and 5 cc. of ethanol was stirred in. Cooling in an ice-bath and stirring resulted in crystallization of 1.1 g. of the hygroscopic diamine sulfate.

4-Phenyl-1,3-butanediamine Hydrochloride.—Three-tenths gram of the diamine sulfate was added to 6 cc. of 15% sodium hydroxide solution and the free diamine extracted with two 8-cc. portions of ether. After drying the extract with anhydrous sodium sulfate and finally with drierite, the extract was treated with an ethereal solution of hydrogen chloride. The hydrochloride separated as an oil which crystallized after standing overnight. It

(10) Johnson and Ambelang, THIS JOURNAL, **60**, 2941 (1938).
(11) Covert and Adkins, *ibid.*, **54**, 4116 (1932).
(12) Connor, Folkers and Adkins, *ibid.*, **54**, 1138 (1932).
(13) Adkins, *Ind. Eng. Chem., Anal. Ed.*, **4**, 342 (1932).
(14) Buchner and Dessauer, *Ber.*, **25**, 1155 (1892).

was dissolved in absolute ethanol and reprecipitated with dry ether; m. p. 145–146°.

Anal. Calcd. for $C_{10}H_{18}N_2Cl_2$: N, 11.81. Found: N, 11.68, 11.63.

N,N'-Dibenzoyl-4-phenyl-1,3-butanediamine.—When 0.8 g. of the above diamine sulfate was mixed with 12 cc. of 15% sodium hydroxide solution, an oil appeared on the surface of the alkali. Addition of 1.35 g. of benzoyl chloride and shaking precipitated 1.1 g. of the colorless benzoyl derivative which was recrystallized from ethanol; m. p. 174–175°.

Anal. Calcd. for $C_{24}H_{24}O_2N_2$: N, 7.52. Found: N, 7.58, 7.62.

Summary

1. 5-Benzyl- and 6-benzyluracil have been reduced catalytically to the corresponding hydrouracils, and to the corresponding 2-ketohexahydropyrimidines.

2. The benzene ring in the benzyl group occupying the 5-position was attacked, one of the products of reduction of 5-benzyluracil being 2-keto-5-hexahydrobenzylhexahydropyrimidine. No hydrogenation was observed of the benzene ring in the isomeric 6-benzyluracil.

3. The structures of the reduction products of 6-benzyluracil were established by hydrolysis of 6-benzylhydrouracil to β-benzalpropionic acid, and of 2-keto-6-benzylhexahydropyrimidine to 4-phenyl-1,3-butanediamine.

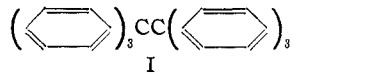
NEW HAVEN, CONN. RECEIVED OCTOBER 28, 1938

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE UNIVERSITY OF ILLINOIS]

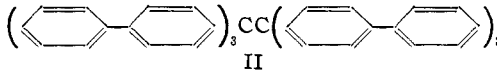
Effect of Substitution on the Dissociation of Hexaarylethanes. VI. Hexa-*m*-biphenylethane[1]

BY C. S. MARVEL, EMANUEL GINSBERG AND MAX B. MUELLER

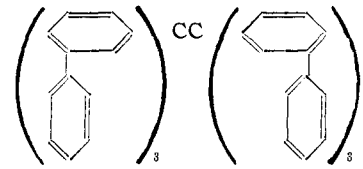
The effect of substituting phenyl groups for the para-hydrogen atoms in hexaphenylethane (I) has been studied by Schlenk and his students.[2] Whereas hexaphenylethane is dissociated to the extent of only 2.5%, tetraphenyldibiphenylethane exists to the extent of 15% as a free radical, the corresponding tetrabiphenyl derivative is 80% free radical and the hexa-*p*-biphenyl derivative (II) is completely dissociated. The increased possibility for resonance in the *p*-biphenyl derivative has been cited as one reason for this marked increase in dissociation.[3] On this basis the *m*-biphenyl group would not be expected to have a much greater effect than an unsubstituted phenyl group. Hence it seemed of interest to prepare hexa-*m*-biphenylethane (III) and to determine the degree of dissociation by the magnetic susceptibility method.[4]



I



II



III

m-Bromobiphenyl was prepared from *m*-bromoaniline and benzene according to the general method devised by Gomberg and Bachmann[5] for the preparation of substituted biphenyls. Conversion of the *m*-bromobiphenyl to the Grignard reagent and addition of this to ethyl carbonate gave tri-*m*-biphenylcarbinol. The chloride and ethane (III) were obtained by the usual procedures.[6] The ethane was not isolated but the solution was exposed to the air and the peroxide thus produced was characterized.

A light red, 0.025 molar solution of hexa-*m*-biphenylethane in benzene was prepared by shaking the chloromethane in benzene with silver for ten hours and then filtering the solution. Experiments showed that a 0.1 molar solution such as was used in the earlier work[6] could not be prepared because of low solubility of the ethane. Also it was found in these preliminary experiments that shaking the solutions used in the preparation of the ethane for more than ten hours caused a

(1) For the fifth communication in this series see THIS JOURNAL, **59**, 2622 (1937).

(2) Schlenk, Weikel and Herzenstein, *Ann.*, **372**, 1 (1910); *Ber.*, **43**, 1753 (1910).

(3) Pauling and Wheland, *J. Chem. Phys.*, 1, 362 (1933).

(4) Müller, *et al.*, *Ann.*, **520**, 235 (1935); **521**, 89 (1935); see also ref. 1.

(5) Gomberg and Bachmann, THIS JOURNAL, **46**, 2339 (1924).

(6) Copenhaver, Roy and Marvel, *ibid.*, **57**, 1311 (1935).