tively. The shorter of these two bands approximates the type of change produced in the short wave band of 2-aminopyrimidine with variations in *p*H, although the effect is much more pronounced by reason of the introduction of the hydroxy group into the molecule. It will be noted from a comparison with Fig. 4 that the wave length separation of the peaks in acid and basic solution is approximately the same in guanine under the same experimental conditions. A further indication that the spectra of isocytosine are as reported in this communication, is seen in the data on isocytosine-4-acetic acid (1,2,4,6-tetrahydro-2-imino-6-ketopyrimidine-4-acetic acid), where, even not considering the influence of the acid, it will be noted (Fig. 5) that in aqueous solution the broad band can be resolved into two bands with centers at 2630 and 2820 Å., respectively, and that the shorter of the two shifts with *p*H as does that of isocytosine. Finally on the assumption that the absorption of these compounds is, to at least a certain extent, additive, the absorption curve of 2-aminopyrimidine and that of 2,4-dimethyl-6-hydroxypyrimidine[10] were combined and gave a curve similar to that of isocytosine. A like addition of 4,6-dimethyl-2-hydroxypyrimidine and 6-aminopyrimidine results in a curve indicative of cytosine in aqueous solution.

The discrepancy between these results and those of Heyroth and Loofbourow might be attributed to the possibility of contamination of products when the isomers are prepared simultaneously. Since the isocytosine is the less stable it could very easily be lost. Personal communication with Dr. Heyroth shed no light on this, and unfortunately there is none of the original samples from which comparison might be made under present conditions.

As was pointed out in the work on thymine desoxyriboside[11] the nucleoside does not show up as markedly as does the free base. However, guanosine does present under varying *p*H a much more characteristic picture (Fig. 6) than the former, and in biologic extracts may be differentiated from adenosine (Fig. 7)[12] as well. In conclusion it may be remarked that a general similarity can be traced through the various 2-aminopurines and pyrimidines, which is much more pronounced than a similar comparison involving the 6-amino compounds.

Summary

The ultraviolet absorption spectra of cytosine and isocytosine are not of similar type.

ADRIAN, MICHIGAN RECEIVED MAY 28, 1945

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[10] Williams, Buchman and Ruehle, THIS JOURNAL, **57**, 1093 (1935).

[11] Stimson and Reuter, *ibid.*, **67**, 847 (1945).

[12] Loofbourow, Cook and Stimson, *Nature*, **142**, 573 (1938); Cook, Loofbourow and Stimson, Xth Intern. Cong. Chem., Rome, May, 1938; Cook, Hart and Stimson, *Biochem. J.*, **34**, 1580 (1940).

[CONTRIBUTION FROM THE IPATIEFF HIGH PRESSURE AND CATALYTIC LABORATORY, DEPARTMENT OF CHEMISTRY, NORTHWESTERN UNIVERSITY AND THE UNIVERSAL OIL PRODUCTS COMPANY]

Isomerization Accompanying Alkylation. IV.[1] Reaction of Cycloheptanol and Cycloheptene with Benzene. Synthesis of Cycloheptylbenzene

BY HERMAN PINES, ALEXANDER EDELEANU[2] AND V. N. IPATIEFF

In the preceding paper of this series it was shown that a skeletal isomerization of the alkyl group during alkylation of aromatic hydrocarbons may take place; this work has now been extended to include cycloalkylation. The present paper deals with the reaction of cycloheptanol and cycloheptene with benzene using, respectively, aluminum chloride, hydrogen fluoride and sulfuric acid as catalysts.

Sidorova and Tsukervanik[3] reported that cycloheptanol on reaction with benzene in the presence of aluminum chloride yielded cycloheptylbenzene. These authors compared the monoacetamino and monobenzamino derivatives of the obtained hydrocarbon with that of synthetically prepared 1-methyl-2-phenylcyclohexane and phenylcyclohexylmethane. Since the melting point of these derivatives did not compare with each other they concluded that the hydrocarbon they obtained was cycloheptylbenzene. In view of the fact that cycloheptane undergoes isomerization to methylcyclohexane[4] in the presence of aluminum chloride and that the formation of cycloheptylbenzene was not proved conclusively by Sidorova and Tsukervanik it was decided to reinvestigate this reaction.

In order to determine whether cycloheptylbenzene was produced in the reaction studied, this hydrocarbon was prepared synthetically and its physical constants, infrared absorption spectra and solid derivatives compared with those obtained from cycloalkylation.

By repeating the experiment of Sidorova and Tsukervanik it was found that the cycloalkylation of benzene with cycloheptanol in the presence of aluminum chloride was accompanied by isomerization. Contrary to the statement made

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[1] For the preceding paper of this series see H. Pines, L. Schmerling and V. N. Ipatieff, THIS JOURNAL, **62**, 2901 (1940).

[2] At present with the United States Army.

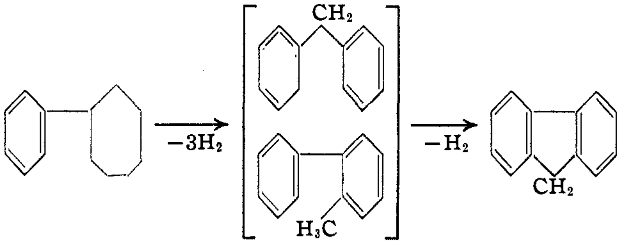
[3] N. G. Sidorova and I. P. Tsukervanik, *J. Gen. Chem.* (*U. S. S. R.*), **10**, 2073 (1940).

[4] M. B. Turova-Polak and F. P. Sidelkovskaya, *ibid.*, **11**, 817 (1941).

by the previous investigators, it was found by us that the monocycloalkylated benzene fraction contained only 10% of cycloheptylbenzene, the remainder being probably isomeric methylphenylcyclohexanes of which 1-methyl-4-phenylcyclohexane in the amount of 20% was identified by means of infrared absorption and by monoacetamino derivative. In order to determine whether during the reaction a methyl group migrated from the cyclohexyl ring to the phenyl group, a reaction probable when catalyzed with aluminum chloride, a sample of the cycloalkylated benzene was oxidized; the fact that benzoic acid was the only acid produced indicated that the cycloalkylation yielded only mono-substituted benzene.

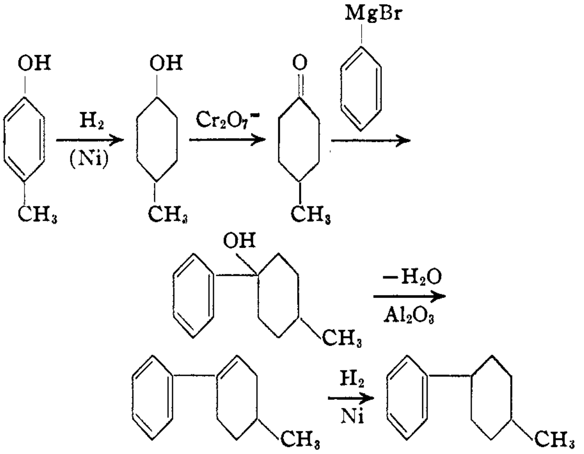
The reaction of cycloheptanol with benzene in the presence of 80% sulfuric acid at 80° was also accompanied by isomerization. The monocycloalkylated benzene fraction contained 40% of cycloheptylbenzene (8% of the theoretical) and about 10% of 1-methyl-4-phenylcyclohexane as determined by infra-red analysis. In view of the fact that the product obtained consisted of a mixture of hydrocarbons, the derivatives prepared did not melt sharply and it required several crystallizations to reach a constant melting point; even then it was not certain whether the derivatives prepared were not composed of a mixture of isomers. It was found that a good yield of cycloheptylbenzene could be obtained by treating benzene with cycloheptene in the presence of hydrogen fluoride or 96% sulfuric acid at 5–10°. This reaction was not accompanied by isomerization. The cycloheptylbenzene produced was about 95% pure when compared with the infrared absorption spectra of the synthetically produced hydrocarbon. The structure of the hydrocarbons produced was also determined by means of solid derivatives.

When, however, aluminum chloride–hydrogen chloride was used as a catalyst for the reaction of cycloheptene with benzene, isomerization accompanied the cycloalkylation. The monocycloalkylated benzene formed consisted probably of isomeric methylphenylcyclohexanes. The presence of cycloheptylbenzene could not be detected by either solid derivatives or infrared absorption analysis; migration of a methyl group from the cyclohexyl to the phenyl ring did not occur as might have been expected when aluminum chloride is used as a catalyst. It is probable that the product obtained was 1-methyl-3-phenylcyclohexane. This conclusion is based on the fact that the product formed did not correspond, according to its physical constants and its solid derivatives, to 1-methyl-2-phenylcyclohexane,[3] 1-methyl-4-phenyl cyclohexane or to phenylcyclohexylmethane[3]; its physical constants agreed, however, with those of 1-methyl-3-phenylcyclohexane.[5,6] It was thought that dehydrogenation of some of the products of reaction followed by a subsequent oxidation might facilitate the establishment of their structure. In order to determine the behavior of cycloheptylbenzene toward dehydrogenation, this hydrocarbon was passed over platinized alumina at 380° according to the procedure described previously.[7] A solid was obtained melting at 115°; it was identified as fluorene. This product was probably formed through the isomerization of the cycloheptyl ring to a methylcyclohexyl ring with subsequent cyclodehydrogenation.[8,9]



Cycloheptylbenzene was synthesized by dehydration of 1-phenylcycloheptanol by means of activated alumina. The 1-phenylcycloheptene produced was then hydrogenated under mild conditions to phenylcycloheptane.

1-Methyl-4-phenylcyclohexane was prepared according to the scheme



Experimental

Synthesis of Material Used

Cycloheptanol.—Four hundred and eight grams of cycloheptanone was dissolved in 200 cc. of ethanol and hydrogenated at 120° in a 3500-cc. capacity autoclave in the presence of 40 g. of nickel–kieselguhr catalyst and under 102 atmospheres of hydrogen measured at 25°. After the removal of ethanol, 92% of the product distilled at 186–187°, $n^{20}D$ 1.4760.

Cycloheptene.—Cycloheptanol was passed over 10–14 mesh activated alumina at 350° at an hourly liquid space velocity of one. The hydrocarbons obtained were separated from the water, dried and distilled over sodium.

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(5) N. Kursanov, *J. Russ.-Phys. Chem. Soc.*, **38**, 1304 (1906), *C. A.*, **1**, 2093 (1907).

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(7) H. Pines, A. V. Grosse and V. N. Ipatieff, THIS JOURNAL, **61**, 640 (1939).

(8) N. D. Zelinsky, I. N. Titz and M. V. Gaverdovskiĭ, *Ber.*, **59**, 2590 (1926).

(9) N. D. Zelinsky and I. N. Titz, *ibid.*, **62**, 2869 (1929).

TABLE I

		1	2	3	4	5	[e]	6	7		
Cycloalkylation agent....		Cycloheptanol		Cycloheptene			Cycloheptanol	Synthetic hydrocarbons			
Catalyst................		$AlCl_3$	H_2SO_4	H_2SO_4	HF	$AlCl_3$	$AlCl_3$	Cycloheptylbenzene	1-Methyl-4-phenylcyclohexane	1-Methyl-2-phenylcyclohexane	Phenylcyclohexylmethane
Monocycloalkylated benzene, b. p. (mm.)		94–95° (7)	75–78° (3.5)	108° (8)[f]	108° (7)	98° (7)	132–135° (28)	108° (7)	130° (21)[g]	91–92° (2)	
Monocycloalkylated benzene, n^{20}_D		1.5252	1.5238	1.5269	1.5280	1.5237	1.5217 (23°)	1.5309	1.5210	1.5360 (18.5°)	
Monocycloalkylated benzene, d^{20}_4		0.9433	0.9474	0.9460	0.9478	0.9427	0.9410 (23°)	0.9482	0.9442	0.9569 (18.5°)	
Monocycloalkylated benzene, M. R. at 20°		56.54	56.35	56.54	56.51	56.45		56.01[h]	56.11		
Derivatives	Monoacetamino[i]	137	131			157	137	173	142	liq.	170
	Diacetamino[i]	202	214–220	240	240	213–216		241			
	Monobenzamino[i]			172	170	170	173	173	197	169–174	162
	Sulfonamide[j]	105	97			109		131	164		
N Analyses, %[k]	Monoacetamino[a] N%		6.13			5.90		5.96	6.37		
	Diacetamino[b] N%		8.67	9.13		7.74					
	Monobenzamino[c] N%					4.35		4.84	4.78		
	Sulfonamide[d] N%					5.75		5.72	5.45		

[a] Calculated for $C_{15}H_{21}ON$: N, 5.96. [b] Calculated for $C_{17}H_{24}O_2N_2$: N, 8.45. [c] Calculated for $C_{20}H_{23}ON$: N, 5.05. [d] Calculated for $C_{13}H_{19}O_2NS$: N, 5.53. [e] Data reported by Sidorova and Tsukervanik (ref. 3). [f] Anal. calculated for $C_{13}H_{18}$: C, 89.59; H, 10.41. Found: C, 89.89; H, 10.18. [g] Anal. calculated for $C_{13}H_{18}$: C, 89.59; H, 10.41. Found: C, 90.04; H, 10.40. [h] Calculated $M^{20}D$: 55.20. [i] V. N. Ipatieff and L. Schmerling, THIS JOURNAL, **59**, 1056 (1937); **60**, 1476 (1938). [j] E. H. Huntress and J. S. Autenrieth, *ibid.*, **63**, 3446 (1941). [k] Analyses were made by Dr. T. S. Ma, University of Chicago.

Mixed melting points, approximately equal weights of derivatives were used:

Monoacetamino:	Expts. 1 and 2	M. p. at 127–129° (depression)
Diacetamino:	Expts. 2 and 6	M. p. 226–232°
	Expts. 2 and 5	M. p. 214–216°
	Expts. 1 and 5	M. p. 206–207°
Monobenzamino:	Expts. 5 and 6	M. p. 162–164° (depression)
Sulfonamide:	Expts. 1 and 5	M. p. 104–106°
	Expts. 1 and 2	M. p. 88–95° (depression)

Ninety and five-tenths per cent. of the product distilled at 115–116° at 756 mm., $n^{20}D$ 1.4576; 8% distilled at 110–114, n^{20}_4 1.4500 suggesting the presence of methylcyclohexene. A sample of the cycloheptene b. p. 115–116° obtained was hydrogenated at 29° to cycloheptane under 100 atmospheres of hydrogen pressure using nickel–kieselguhr catalyst. The product obtained distilled at 119°, $n^{20}D$ 1.4440, indicating that the main fraction of the cycloheptene was free of any methylcyclohexane.

Expt. 7: Synthesis of 1-Methyl-4-phenylcyclohexane. (a) **4-Methylcyclohexanol** was prepared by hydrogenation of *p*-cresol.

(b) **4-Methylcyclohexanone.**—To a solution consisting of 60 g. (0.2 *M*) of sodium dichromate 50 g. (0.48 *M*) of 96% sulfuric acid in 300 cc. of water and heated at 58° was added with stirring 33 g. (0.29 *M*) of 4-methylcyclohexanol. After all of the alcohol was added, the reaction mixture was maintained at 58° for an additional two hours. The ketone formed was extracted with ether, dried with sodium sulfate and distilled. The boiling point was 168°: yield 13.8 g., 47%.

(c) **4-Methyl-1-phenylcyclohexanol.**—To an ether solution of phenylmagnesium bromide prepared from 23.5 g. (0.15 *M*) of bromobenzene and 3.6 g. (0.15 atom) of magnesium was added 13 g. (0.13 *M*) of methylcyclohexanone. The product was poured into ice, neutralized with hydrochloric acid; the ether layer was separated, dried with potassium carbonate and distilled. The boiling point was 145° at 15 mm.; m. p. 64°; yield 11.1 g., 45%.

Phenylurethan, in the form of prisms melted at 135°.

(d) **4-Methyl-1-phenylcyclohexene.**—Ten grams of 4-methyl-1-phenylcyclohexanol was dehydrated by passing it over 30 cc. of activated alumina (10–14 mesh) at 330°. The hydrocarbon formed was separated, dried and distilled: b. p. 137° at 16 mm.; $n^{20}D$ 1.5558; yield 92%.

(e) **1-Methyl-4-phenylcyclohexane.**—Seven grams of 4-methyl-1-phenylcyclohexene dissolved in 10 cc. of *n*-pentane was hydrogenated in a 125-cc. autoclave at 36° in the presence of 2 g. of nickel–kieselguhr catalyst and 85 atmospheres of hydrogen. One mole of hydrogen was absorbed per mole of aromatic hydrocarbon charged. The material after hydrogenation was free of olefins, as determined by means of potassium permanganate test. The 4-methyl-1-phenylcyclohexene produced distilled at 120° at 21 mm.; yield 90%.

Physical constants and derivatives are given in Table I.

Preparation of Cycloheptylbenzene. (a) **1-Phenylcycloheptanol.**—This was prepared by treating phenylmagnesium bromide with cycloheptanone according to the procedure described by Kleene:[10] yield 71%; b. p. 136° (8 mm.); $n^{20}D$ 1.5493. The alcohol formed long white crystals melting at 23°.

(b) **Phenylcycloheptene.**—Twenty-two grams of 1-phenylcycloheptanol, dissolved in 20 cc. of ethanol, was passed over activated alumina catalyst at 334° with a rate of 0.5 cc. per minute. The ethanol, which at this temperature does not undergo dehydration, was added to prevent any isomerization of the seven-membered to a six-membered ring. The phenylcycloheptene formed was separated, dried over sodium sulfate and distilled under vacuum in the presence of sodium to remove any traces of unreacted phenylcycloheptanol. The phenylcycloheptene produced distilled at 113–115° at 8 mm.; yield 85%; $n^{20}D$ 1.5624; d^{20}_4 0.9859; $M^{20}D$ calculated 55.96; $M^{20}D$ found 55.02.

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(10) R. D. Kleene, THIS JOURNAL, **63**, 1482 (1941).

(c) **Cycloheptylbenzene.**—Nine and a half grams of phenylcycloheptene dissolved in 15 cc. of *n*-pentane was hydrogenated in a 125-cc. autoclave at 50° in the presence of nickel–kieselguhr catalyst and under 109 atmospheres of hydrogen measured at 29°. One mole of hydrogen was absorbed per mole of phenylcycloheptene charged. The product was filtered, pentane removed and the phenylcycloheptane distilled; yield 95%.

Cycloalkylation of Benzene

Expt. 1. Reaction of Benzene with Cycloheptanol in the Presence of Aluminum Chloride.—The procedure used was that of Sidorova and Tsukervanik.[3] The reaction was carried out in a three-necked flask provided with a mechanical stirrer, dropping funnel and a reflux condenser. Eighty-eight grams of benzene and 20 g. (0.15 *M*) of aluminum chloride were placed in the flask. To this mixture was added over a period of half an hour a solution of 17 g. (0.15 *M*) of cycloheptanol dissolved in 50 cc. of benzene. At first, no apparent reaction occurred; after fifteen minutes of stirring, however, a vigorous reaction took place. The product was refluxed for two hours; a homogeneous mixture was obtained which was allowed to stand at room temperature for sixteen hours. The content of the flask was poured into water, washed with sodium hydroxide solution, water, dried over calcium chloride and distilled. Eight grams (31% yield) of monocycloalkylated benzene was obtained.

Expt. 2. Reaction of Benzene with Cycloheptanol in the Presence of 80% Sulfuric Acid.—The apparatus consisted of a 3-necked 1000-cc. flask, provided with a mechanical stirrer; 400 cc. of 80% sulfuric acid and 29.5 g. of benzene were placed in the flask and heated to 70°. Thirty and nine-tenths grams (0.27 *M*) of cycloheptanol dissolved in 29 g. of benzene was added to the mixture over a period of half an hour; the contents of the flask were heated for an additional two hours. The resulting product was very dark and the hydrocarbon layer which was hardly visible was separated by adding water. It was washed with alkali, water, dried and distilled. Eleven grams (23% yield) of monocycloalkylated product was obtained.

Expt. 3. Reaction of Cycloheptene with Benzene in the Presence of Sulfuric Acid.—To a mixture consisting of 56 g. of 96% sulfuric acid and 15.6 g. of benzene and maintained at 5° was added with stirring over a period of half an hour, a solution of 19.2 g. (0.2 *M*) of cycloheptene in 15.6 g. of benzene. The stirring was continued for an additional fifty minutes. The mixture was allowed to stand for half an hour. An upper hydrocarbon layer separated which was washed, dried and distilled. The yield of cycloheptylbenzene produced amounted to 48%.

Expt. 4. Reaction of Cycloheptene with Benzene in the Presence of Hydrogen Fluoride.—In a copper flask provided with a copper stirrer was placed 30 g. of hydrogen fluoride and 15 g. of benzene. To these reagents maintained at 5°, was added slowly a solution composed of 19.2 g. (0.2 *M*) of cycloheptene and 16.2 g. of benzene. The content of the flask, after being stirred for forty-five minutes, was poured into ice precooled to −50°, neutralized with alkali. The hydrocarbon layer was separated, washed and dried. The yield of cycloheptylbenzene produced amounted to 71%.

Expt. 5. Reaction of Cycloheptene with Benzene in the Presence of Aluminum Chloride–Hydrogen Chloride.—Thirty grams of benzene and 5 g. of resublimed aluminum chloride were placed in a 250-cc. three-necked flask provided with a stirrer and maintained at 5–8°. About two bubbles of hydrogen chloride per second were passed into the reaction mixture. A solution composed of 15 g. (0.16 *M*) of cycloheptene dissolved in 15 g. of benzene was then added over a period of half an hour. The mixture was stirred for an additional hour; hydrogen chloride was bubbled during all that time. The contents of the flask which were dark consisted of two layers; the lower layer weighed 18 g. while the upper hydrocarbon layer, after being washed and dried, weighed 46 g. It contained 7.9 g. of monocycloalkylated hydrocarbons, representing a yield of 29%.

Acknowledgment.—The authors wish to thank Professor Herbert C. Brown of Wayne University, to whom they are indebted for the cycloheptanone, and Dr. W. S. Gallaway of the Universal Oil Products Company, for the infrared absorption analysis.

Summary

The cycloalkylation of benzene with cycloheptanol and with cycloheptene in the presence of aluminum chloride, hydrogen fluoride and sulfuric acid has been studied.

Contrary to the observation made by the previous investigators the reaction of cycloheptanol with benzene in the presence of aluminum chloride is accompanied by isomerization; the monocycloalkylated benzene formed contained only 10% of cycloheptylbenzene corresponding to a 3% yield.

When cycloheptene reacted with benzene in the presence of sulfuric acid or hydrogen fluoride, cycloheptylbenzene in respective yields of 48 and 71% was obtained; in the presence of aluminum chloride isomerization occurred, resulting in the formation of methylphenylcyclohexane.

Cycloheptanol on reaction with benzene in the presence of sulfuric acid yielded cycloheptylbenzene and methylphenylcyclohexanes.

Cycloheptylbenzene and 1-methyl-4-phenylcyclohexane have been synthesized.

Cycloheptylbenzene on dehydrogenation yielded fluorene.

RIVERSIDE, ILLINOIS
EVANSTON, ILLINOIS

RECEIVED JULY 23, 1945