[CONTRIBUTION FROM THE KEDZIE CHEMICAL LABORATORY, MICHIGAN STATE COLLEGE]

The Effect of Strain in Cycloalkylcarbinols on their Reactivity with Benzene in the Presence of Aluminum Chloride

BY R. C. HUSTON AND K. GOODEMOOT[1]

It has been shown in previous papers[2] that those alcohols in which the *alpha* carbon atom is either a member of the benzene ring or is double bonded condense with benzene in the presence of aluminum chloride. It appears that the degree of reactivity of the alcoholic hydroxyl is dependent upon the degree of unsaturation or strain. Since allyl alcohol, which is the simplest member of the series of cycloalkyl carbinols, condenses with benzene, one expects that the next higher members of the series will condense less readily as the methylene groups are increased in number. The introduction of a methylene group into the ring at the beginning of the series should cause a relatively great reduction of strain. Since the strain becomes reduced to a minimum in the six-membered ring, one expects cyclohexylcarbinol to have the same order of activity as that of primary aliphatic alcohols which do not condense with benzene.

For this study, cyclohexyl, cyclopentyl and cyclobutyl carbinols were prepared. The results of an attempt to prepare cyclopropylcarbinol will be reported in a later publication.

Condensations.—All condensation reactions were carried out with one mole of alcohol and four to five moles of benzene in the presence of two-thirds of a mole of aluminum chloride. For all alcohols, condensation reactions were operated at low temperatures, 25–35°, and at high temperatures, 75–80°.

(1) Cyclohexylcarbinol

(a) **Low Temperatures.**—Thirty-eight grams of cyclohexylcarbinol[3] [b. p. 89–91° (18 mm.)] was mixed with 120 g. of benzene in a 500-cc. round-bottomed three-necked flask. The flask was provided with a condenser, a mercury sealed mechanical stirrer and a thermometer. While the mixture was stirred, 31 g. of aluminum chloride was added over a period of five hours, after which stirring was continued for eight hours. After standing for twelve hours, the contents of the flask were decomposed by ice and hydrochloric acid. The benzene layer was separated, the aqueous layer extracted several times with ether and the extract added to the benzene solution, after which the whole was dried over anhydrous potassium carbonate. Upon fractionation, practically all of the alcohol was recovered. One to two grams of residue remained from which we were unable to isolate cyclohexylphenylmethane.

(b) **High Temperatures.**—The high temperature condensation was carried out in exactly the same manner and with the same quantity of materials as that at low temperature, with the exception that the reaction flask was placed in a water-bath maintained at a temperature of 75–80°. Upon distillation of the reaction product, under 16 mm. pressure, the following fractions were obtained: 28 g. at 65–100°; 4.5 g. at 100–120°; 2–3 g. residue. The product boiling at 100–120° from five such condensation reactions when combined and fractionated under atmospheric pressure with a 25-cm. column was found to be cyclohexylphenylmethane,[4] b. p. 239.5–241.5° (736 mm.).

Anal. Calcd. for $C_{13}H_{13}$: C, 89.67; H, 10.43. Found: C, 89.34; H, 10.34.

(2) Cyclopentylcarbinol

(a) **Low Temperature.**—Fifteen grams of cyclopentylcarbinol[5] [b. p. 67–70° (15 mm.)] was mixed with 47 g. of benzene in the same apparatus as for the condensation of cyclohexylcarbinol. Ten grams of aluminum chloride was added over a period of half an hour. After the addition of all the aluminum chloride, the reaction mixture was stirred for six hours longer and then allowed to stand for twelve hours. The reaction product was treated in the usual manner and upon fractionation 11 g. of the alcohol was recovered. No product boiling above the alcohol was obtained.

(b) **High Temperature.**—Thirty-eight grams of alcohol with 125 g. of benzene was treated with 30 g. of aluminum chloride. The reaction was carried out in the same manner as that given for the high temperature condensation of cyclohexylcarbinol. The reaction products were isolated in the usual manner and upon distillation (16 mm.) gave the following fractions: 5 g. at 65°; 32 g. at 80–120°; and 8–10 g. of residue. The liquid boiling at 80–120° was fractionated under atmospheric pressure and finally yielded twenty-five grams of cyclopentylmethane,[6] b. p. 234.5–236° (736 mm.).

Anal. Calcd. for $C_{12}H_{16}$: C, 89.97; H, 10.07; mol. wt., 160. Found: C, 89.55; H, 10.15; mol. wt., 167, 166.

From the residue a substance crystallized out which was purified by recrystallizing from hot alcohol. This compound consisted of white plates, m. p. 101.5–102° (yield, 1.5 g.). Analysis and molecular weight determination indicated dicyclopentylmethylbenzene.

Anal. Calcd. for $C_{18}H_{26}$: C, 89.18; H, 10.82; mol. wt., 242. Found: C, 88.95; H, 10.72; mol. wt., 249.

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[1] From a dissertation presented by K. Goodemoot to the Faculty of Michigan State College in partial fulfilment for the requirements for the degree of Doctor of Philosophy.

[2] R. C. Huston and collaborators, THIS JOURNAL, **38**, 2527 (1916); **40**, 785 (1918); **48**, 1955 (1926).

[3] "Organic Syntheses," Vol. IV, p. 22.

[4] Klages, *Ber.*, **40**, 2366 (1907).

[5] This was prepared from chlorocyclopentane by the Zelinsky method, *ibid.*, **41**, 2629 (1908).

[6] Zelinsky and Titz, *ibid.*, **64**, 187 (1931).

Since the methyl group is ortho and para directing, one may assume that the second cyclopentylmethyl group takes either of these two positions. The symmetrical structure is the more probable because, under similar conditions, para dibenzylbenzene is found in addition to the main product, diphenylmethane, when benzyl alcohol is condensed with benzene.[7]

(3) Cyclobutylcarbinol

Diethyl cyclobutane-1,1-dicarboxylate[8] was converted into the acid ester by modification of Marguery's method.[9,10] When heated to 190° this was readily converted into the monocarboxylic ester,[11] b. p. 150.2–151.2°.[12] The carbinol which was formed by reduction[13] was purified by the addition of a solution of bromine in chloroform until a faint color of bromine remained and subsequent fractionation, b. p. 141–144° (745 mm.).

(a) **Low Temperature.**—Twenty-five grams of cyclobutylcarbinol mixed with 100 g. of benzene was treated with 24 g. of aluminum chloride. The aluminum chloride was added over a period of five hours and then the reaction mixture was stirred for eight hours. A noticeable amount of hydrogen chloride was liberated. After standing for twelve hours, the contents of the flask were treated in the usual manner. Upon distillation, the following fractions were obtained: 3 g. at 100–120° (740 mm.); 6 g. at 200–217.5°, 12 g. at 217.5–219.5° and 5 g. above 220°.

(b) **High Temperature.**—Except that the temperature was maintained between 75 and 80°, this condensation was carried out in the same manner as that for cyclobutylcarbinol at low temperatures. Upon distillation of the reaction products, the following fractions were obtained: 6 g. at 100–210° (740 mm.); 12 g. at 210–220°, 10–12 g. above 220°. The fraction boiling at 210–220° was constant at 217–220°. It was combined with the corresponding fraction obtained from the low temperature condensation and fractionated to a constant boiling point of 218–219° (736 mm.).

Anal. Calcd. for $C_{11}H_{14}$: C, 90.34; H, 9.65; mol. wt., 146. Found: C, 89.94; H, 9.71; mol. wt., 153, 152.

Discussion

The yield of cyclohexylphenylmethane was 7% at high temperatures. Cyclopentylphenylmethane was formed in yields of 45% at high temperatures but was not formed at low temperatures. On the other hand, cyclobutylphenylmethane was produced at low temperatures in 29% yields and at high temperatures in 21% yields. In these condensations of cyclobutylcarbinol at high and at low temperatures practically all of the alcohol reacted. These facts are in accord with the suggested theory: (a) that the lowest members of the cycloalkylcarbinol series react with benzene in the presence of aluminum chloride; (b) that the reactivity of the alcohols decreases as one ascends the series; and (c) that in cases where strain is minimum, as in the six-membered ring, the reactivity becomes of the same order as that of primary aliphatic alcohols.

Molecular Volumes, Parachors and Molecular Refractions.—Determination of density, surface tension[14] and index of refraction was made on each of the purified reaction products and upon allylbenzene. The results are summarized in the table.

TABLE I

Compound		Allyl-benzene	Cyclo-butyl-phenyl-methane	Cyclo-pentyl-phenyl-methane	Cyclo-hexyl-phenyl-methane
d_4^{20}		0.8930[15]	0.9556	0.9418	0.9281
V_m^{20}		132.23	152.92	170.05	187.65
Eff. of polymethylene ring		26.65	14.80	15.65	16.99
γ^{20}		36.33	35.17	34.76	33.81
Parachor	Calcd.	310.6	374.6	411.6	449.4
	Found	310:3	371.2	412.85	452.5
n_D^{20}		1.5126[16]	1.5265	1.5245	1.5132
M_D^{20}	Calcd.	36.69	47.2	51.81	56.43
	Found	39.72	46.99	52.06[15]	56.41

The effect of the polymethylene ring upon molecular volume was determined in each case by subtracting from the observed molecular volume the calculated value for the normal alkylbenzene containing the same number of carbons after deducting the value of two hydrogen atoms (32.05 cc.). It will be noted that the influence of the double bond is normal[17] and that of the four-membered ring does not differ greatly from the effect in cyclobutane (16.6 cc.). However, instead of a progressive decrease for the five- and six-membered rings, there is shown a slight progressive increase. In explanation, it is suggested that the increase in size of the polymethylene ring brings its members in closer contact with the phenyl group with an increase in eurogenic effect.

In calculating parachors, the atomic and structural constants of Mumford and Phillips[18] were used with the exception that a decrement of

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(7) Huston, THIS JOURNAL, **38**, 2527 (1916).

(8) Huston, *ibid.*, **43**, 680 (1921).

(9) Marguery, *Bull. soc. chim.*, [3] **33**, 542 (1905).

(10) The method of Cope and McElvain, THIS JOURNAL, **54**, 4319 (1932), which gives excellent yields of phenylpropionic ester, from benzylmalonic ester, did not give satisfactory results.

(11) This absorbed bromine, indicating the presence of allylacetic ester, b. p. 144–146°.

(12) Perkin, *J. Chem. Soc.*, **51**, 1 (1887), gives 151°. Freund and Gudeman, *Ber.*, **21**, 2692 (1888), report 159–160°.

(13) Demjanow, *ibid.*, **40**, 4959 (1907).

(14) Surface tension measurements were made by the drop weight method by Mr. Wallace Fox under the direction of Dr. D. T. Ewing.

(15) Agejewa, *Chem. Centr.*, **76**, II, 1017 (1905).

(16) Tiffeneau, *Compt. rend.*, **139**, 482 (1904).

(17) Kauffmann, "Beziehungen zwischen physikalischen Eigenschaften und chemischer Konstitution," Verlag F. Enke, Stuttgart, Germany, 1920, pp. 82–91.

(18) Mumford and Phillips, *J. Chem. Soc.*, **II**, 2112–2118 (1929).

-3 was used in the case of allylbenzene which contains one ring and a decrement of -6 in the three compounds containing both an aromatic and a polymethylene ring. The use of this decrement is, we believe, justified by the fact that a ring carbon atom attached to a side chain acts as a heaping center.[19] We have, therefore, in effect the equivalent of a —CHR_2 group.[18]

The greatest deviation (0.9%) of the observed parachor from the calculated is found in cyclobutylphenylmethane, where the unknown effect of the strain of a four-membered ring is a factor.

Summary

1. In condensation reactions with benzene in the presence of aluminum chloride the cycloalkylcarbinols show a progressive increase in activity as the number of carbon atoms of the ring is reduced from six to four.

2. Physical constants of allylbenzene, cyclobutylphenylmethane, cyclopentylphenylmethane are recorded and discussed.

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(19) Kaufmann, *loc. cit.*, pp. 93, 97.

[CONTRIBUTION FROM THE PATHOLOGICAL DIVISION, BUREAU OF ANIMAL INDUSTRY]

Lupine Studies. VIII. The Alkaloids of Lupinus Palmeri, S. Wats.

BY JAMES FITTON COUCH

Lupinus palmeri, S. Wats. is a perennial species of lupine found in certain parts of Utah and neighboring states. Its systematic position has been doubtful, some botanists referring it to the species caudatus, others naming some specimens of *L. caudatus*, *L. palmeri*. Chemical examination of authentic specimens of these two species demonstrates that their alkaloidal constituents are quite distinct and do not vary in different years.

The study of *L. palmeri* has resulted in the isolation of three lupine alkaloids, two of which are new, lupinine, tetralupine[1] and pentalupine. Sparteine, which has hitherto always accompanied lupinine in this genus, was found absent, which fact, coupled with the discovery of sparteine and absence of lupinine in *L. barbiger*,[2] demonstrates that there is no biochemical necessity for their occurring together. Tetralupine is of interest because it is isomeric with lupinine and isolupinine[3] and is found in nature while isolupinine is not naturally occurring. Whether it is the allolupinine postulated by Winterfeld and Holschneider[4] remains to be determined.

Experimental Part

Collection of Plant Material.—The plant used in this study was collected by my colleague, Mr. A. B. Clawson, on July 9, and on August 7 and 8, 1931, at a point 10 miles south of Cove Fort, Utah. Most of the plants were then in bloom, a few had developed pods and a few had not yet bloomed. The material was identified as *L. palmeri* by Mr. W. W. Eggleston of the Bureau of Plant Industry. The material was air dried, bagged and shipped to this Laboratory, where it was ground to a coarse powder.

Moisture.—The ground material contained 8.94% of matter volatile at 110°.

Extraction of the Alkaloids.—60.9 kg. of ground plant was extracted with alcohol. The solvent was distilled and the residual extract was boiled with successive portions of water until all soluble matter was removed.

The concentrated water solutions were treated with an excess of a mixture of neutral and basic lead acetates, filtered and freed from excess of lead with sulfuric acid. The filtrate was concentrated, made alkaline with sodium hydroxide, and shaken out with chloroform. The solvent was distilled from the separated solution and left the crude alkaloids in the form of a reddish sirup that weighed 2222 g. This sirup contained nearly 25% of its weight of chloroform that could not be distilled off at water-bath temperature and ordinary pressure. Much of it might be removed by heating under reduced pressure but some of the alkaloids were volatile under these conditions and would have been lost. The chloroform was expelled by adding enough methanol to the mixture to form the azeotropic mixture with the chloroform which boils at 53.6° and distilling the solution. The last traces of chloroform could be removed by repeating the process twice. By this means 1668 g. of crude alkaloid corresponding to 3.00% of the dry plant material was obtained. The mixture gave a very faint modified Grant test.[5]

Isolation of Lupinine

A portion of 310 g. of the crude alkaloid mixture was poured into a flask and warmed under 20 mm. pressure to remove volatile matter. When the residual solvent (traces only) had been removed, the pressure sank to 6 mm. and a crystalline sublimate formed on the walls of the flask.

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(1) Nomenclature, *cf.* THIS JOURNAL, **56**, 155 (1934).

(2) Couch, *ibid.*, **54**, 1691 (1932).

(3) Steinsiek, Dissertation, Marburg, 1928.

(4) Winterfeld and Holschneider, *Ber.*, **64**, 137–150 (1931).

(5) Couch, *Am. J. Pharm.*, **97**, 37 (1925).