two compounds are very similar it would seem that the *n*-butyl radical on oxygen is deficient in some way in its relation to the lipoids of the nervous system.

Summary

The preparation of various substituted urethans and of 1,3-diphenyl-2-iminobarbituric acid is described.

A preliminary study of the physiological action of acetylphenylurethan is reported.

SASKATOON, CANADA

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

THE CONDENSATION OF MESITYL OXIDE WITH ALIPHATIC KETONES

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Introduction

The simplest of the unsaturated cyclic ketones that can be prepared by the condensation of an aliphatic ketone is 1,3,3-trimethyl-cyclohexenone-5, or the well-known isophorone. Recently methylethyl ketone[2] and diethyl ketone[3] have been subjected to the action of condensing agents and the corresponding homologs of isophorone have been isolated. In the case of methylethyl ketone it was shown that four isomeric homologs of isophorone are theoretically possible, and two of them were isolated, 1,2,3,6-tetramethyl-3-ethyl-cyclohexenone-5 and 1,3-diethyl-3,4-dimethyl-cyclohexenone-5, which have been designated, respectively, as γ- and δ-homoisophorones, each with the empirical formula $C_{12}H_{20}O$. The structure of these compounds was proved by the same method originally used by Knoevenagel.[4] In the case of diethyl ketone the only homolog of isophorone theoretically possible, 1,3,3-triethyl-2,4,6-trimethyl-cyclohexenone-5, having the empirical formula $C_{15}H_{26}O$, was prepared.

Thus by condensing the saturated aliphatic ketones, unsaturated cyclic ketones are formed, bearing the type formula $C_nH_{2n-4}O$. As the homologous series is ascended, it is apparent that for a carbon increment of one in the initial ketone, the carbon increment in the final product is three; thus, acetone (C_3H_6O) $\longrightarrow$ $C_9H_{14}O$; methylethyl ketone (C_4H_8O) $\longrightarrow$ $C_{12}H_{20}O$; diethyl ketone ($C_5H_{10}O$) $\longrightarrow$ $C_{15}H_{26}O$.

Other members of this cyclic series should exist, containing an interme-

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[1] From a thesis submitted by M. Scott Carpenter to the Graduate Faculty of the University of Colorado in partial fulfilment of the requirements for the degree of Doctor of Philosophy.

[2] Ekeley and Howe, THIS JOURNAL, **45**, 1917 (1923).

[3] Ekeley and Carpenter, *ibid.*, **46**, 446 (1924).

[4] Knoevenagel, *Ann.*, **289**, 10 (1895); **299**, 160 (1897).

diate number of carbon atoms, C_{10}, C_{11}, C_{13}, C_{14}, etc. It seemed desirable that this series should be filled out, and the present investigation had for its purpose the preparation of some of these intermediate members.

We have condensed mesityl oxide with the following ketones: methylethyl, methylpropyl, diethyl, methylbutyl and methyl*iso*butyl. In all cases except that of diethylketone four isomers are theoretically possible. Diethyl ketone should yield but two. In no case was it possible by fractional distillation to isolate more than one product.

All of the compounds prepared have the general characteristics of isophorone and appear to belong to an homologous series. They immediately decolorize bromine water and dilute permanganate solution, give wine-red to violet colorations with ferric chloride and, very strangely, possess similar boiling points. The molecular refractions of these compounds are quite high, as compared to the values calculated for the keto form. They readily form semicarbazones that are insoluble in water and that crystallize in small, glistening plates from absolute alcohol. The semicarbazones are hydrolyzed almost instantly by dilute mineral acids, but are fairly stable in the presence of dil. acetic acid and alkalies. These derivatives possess melting points quite close to one another.

Experimental Part

Reagents.—Sodium ethylate was chosen for the condensing agent because it gives purer products than acid reagents. When concd. sulfuric acid is used the products are nearly always contaminated with sulfonic acids which sometimes are difficult to eliminate, while hydrogen chloride has a tendency to form hydrogen-chloride addition products which nearly always cause a darkening of the oils with time, regardless of the care which has been taken to free the products from these impurities. The sodium ethylate was prepared according to the method of Claisen, described by Lassar-Cohn.[5] The mesityl oxide used was prepared by the method of Locquin.[6] The methylethyl ketone used was purchased from the Eastman Kodak Company's Organic Laboratory and all the others were prepared by Kahlbaum. All the ketones were of a high degree of purity and were redistilled before use until they boiled constant to 0.5°.

Method.—A mixture of one molecular proportion of the ketone and one of mesityl oxide was cooled by immersing the flask in chipped ice. To this solution was added gradually while constantly shaking the flask 0.5 molecular proportion of powdered sodium ethylate. The solution, now of a pasty consistency, had assumed a deep reddish-brown color. The contents of the flask were protected from the atmosphere by means of a calcium chloride tube and set aside at a temperature of about 5°.

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[5] Lassar-Cohn, "Arbeitsmethoden für Organisch-Chemische Laboratorien," pp. 492, 729 (1923).

[6] Locquin, *Ann. chim.*, **19**, 32 (1923).

After about ten days an equal volume of water was added to the condensation mixture, whereupon a deep brown, oily layer floated on the surface of the aqueous alkaline layer. The oily layer was separated and washed repeatedly with water until the washings were clear and reacted neutral to litmus. The aqueous alkaline layer was neutralized with acetic acid, which caused the further separation of a small quantity of oil. This oil was extracted with ether, the ethereal solution washed with water and added to the main body of the oil. Anhydrous sodium sulfate was added to the ethereal solution which was then allowed to stand overnight.

The solution was filtered from sodium sulfate and the ether distilled on the water-bath. The residual oil was subjected to fractional distillation under diminished pressure until a product was obtained showing a constant refractive index. The yields were small on account of the many possibilities of condensation.

Many attempts were made to isolate more than one of the four expected isomers and to increase the yield of the condensation. The proportions of ketone, mesityl oxide and condensing agent were altered over wide ranges; the duration of the condensation was lengthened to a month and shortened to a day; the temperature was varied from that of ice to that of a boiling water-bath; the reaction was carried out in the presence of sunlight and in the dark; sodium methylate, sodamide, barium hydroxide, diethylamine and piperidine were used in place of sodium ethylate. Trials were also made, using sodium in methyl and ethyl alcohol, in which the mixtures were immediately heated over a water-bath without preliminary standing in the cold. Yields much poorer than that given by the original procedure were obtained in many cases, but none better, and in no case was more than one product isolated. A certain amount of ketone seems doomed to be transformed into a thick, tarry mass, and a corresponding quantity of the ketone is recovered as such and as a polymerized condensation product.

Preparation of the Semicarbazones.—Semicarbazide hydrochloride was dissolved in the minimum quantity of water and sufficient sodium acetate added to neutralize the hydrochloric acid. An equimolecular quantity of the unsaturated ketone was added, and enough alcohol to form a clear solution. This solution was allowed to stand overnight at a temperature of 5–8°, at the end of which time an abundant crop of white crystals had separated. These were filtered from the mother liquor and washed repeatedly on the suction filter with cold 50% alcohol. Several recrystallizations from absolute alcohol yielded small glistening plates, insoluble in water, fairly soluble in alcohol and melting from 170° to 176° with decomposition beginning just before melting. The crystals were found to be hydrolyzed almost instantly by warm, dilute mineral acids, but were fairly stable in the presence of acetic acid and alkalies, and not noticeably affected by long contact with boiling water, in which they are quite insoluble.

TABLE I

ANALYSES

A. Condensation Products from Various Ketones

From ketone	Formula	Calcd. C, %	Calcd. H, %	Found C, %		Found H, %	
Methylethyl	$C_{10}H_{16}O$	78.88	10.59	78.67		10.25	
Methylpropyl	$C_{11}H_{18}O$	79.45	10.92	79.70	79.51	10.74	10.61
Diethyl	$C_{11}H_{18}O$	79.45	10.92	79.62	79.36	10.43	10.46
Methylbutyl	$C_{12}H_{20}O$	79.93	11.19	79.86	80.01	10.65	10.61
Methyl*iso*butyl	$C_{12}H_{20}O$	79.93	11.19	79.83	79.70	10.50	10.51

B. Semicarbazones

From ketone product	Formula	M. p., °C.	N, % Calcd.	N, % Found	
Methylethyl	$C_{11}H_{19}ON_3$	176	20.10	20.30	20.00
Methylpropyl	$C_{12}H_{21}ON_3$	172	18.83	18.62	18.87
Diethyl	$C_{12}H_{21}ON_3$	170	18.83	18.82	18.92
Methylbutyl	$C_{13}H_{23}ON_3$	172	17.71	17.53	17.83
Methyl*iso*butyl	$C_{13}H_{23}ON_3$	170	17.71	17.55	17.75

For comparative purposes, the physical constants of the unsaturated ketones are listed in Table II.

TABLE II

PHYSICAL CONSTANTS

Compound from	$CH_3COC_2H_5$ $C_{10}H_{16}O$	$CH_3COC_3H_7$ $C_{11}H_{18}O$	$(C_2H_5)_2CO$ $C_{11}H_{18}O$	$CH_3COC_4H_9$ $C_{12}H_{20}O$	$CH_3COCHCH(CH_3)_2$ $C_{12}H_{20}O$
B. p., °C.	99.5–100	122–126	102–105	119–121	101–104
Pressure, mm.	4.5	13	4	11	3
d_4^{20}	0.92811	0.92372	0.93062	0.92004	0.92616
n_D^{20}	1.5048	1.5112	1.5218	1.5130	1.5222
M_D	48.640	53.917	54.451	58.878	59.341
Exaltation from keto form	2.916	3.575	4.109	3.918	4.381

It will be noticed that the refractive indices and exaltations of all the compounds prepared from methyl ketones progress regularly as the series is ascended, while the diethyl compound presents an irregularity. The authors have no explanation to offer for the unusually high exaltations of the molecular refraction that have been observed. An exaltation is to be expected, since the first member of the series, isophorone, exhibits an exaltation of one unit, but an exaltation of more than four units as the series is ascended was entirely unlooked for.

Summary

1. Mesityl oxide has been condensed with the following ketones: methylethyl, methylpropyl, diethyl, methylbutyl and methyl*iso*butyl. In each case only one condensation product was isolated.

2. The semicarbazones of the unsaturated ketones have been prepared.

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