tion was identified as cyclohexylidene cyclohexanone by an analysis and a comparison of its semicarbazone (m. p. 177°) with that of an authentic sample. The yields were 34 g. or 68% of cyclohexanol and 11.6 g. or 26% of cyclohexylidene cyclohexanone from 49 g. of the ketone.

From the foregoing account it is evident that under the conditions favored by Grignard and Blanchon, at least 94% of the product of the reaction between cyclohexanone and isopropylmagnesium bromide is composed of substances which are not due to enolization but to reduction and to condensation. Lower temperatures, which according tot he French authors are less favorable to enolization, are in reality less favorable to reduction, the reduction product being in part replaced by the normal addition product. Thus at −5° the yield of cyclohexanol was only 28%.

In view of these results we are compelled to conclude that Grignard and Blanchon were misled by the method of Job and Reich, and that they mistook cyclohexyl acetate for cyclohexenyl acetate, cyclohexanol for cyclohexenol. Grignard reagents containing secondary and tertiary hydrocarbon residues frequently act as condensing and reducing agents, but we can find no evidence that they are more effective than others in inducing enolization, and we also fail to find any evidence that any Grignard reagents can convert mono ketones into enolates unless the hindrance to addition is prohibitive.

Summary

An examination of the reaction between isopropyl magnesium bromide and cyclohexanone showed that Grignard and Blanchon must have mistaken reduction for enolization.

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Some New Local Anesthetics Containing the Piperazine Ring

BY JOHN H. GARDNER AND JOHN H. SCHNEIDER

As piperazine can be regarded as a double secondary amine, it seemed of interest to prepare and study a series of esters of piperazine-dialkanols, which could be regarded as compounds of the procaine type and therefore would be expected to possess local anesthetic activity. The only compound of this type noted in the literature was β-1,4-piperazine-diethyl benzoate which was described by Pyman. He stated that this substance shows[1] marked local anesthetic activity but is quite toxic.

In the present investigation, β-1,4-piperazine-diethanol and γ-1,4-piperazine-dipropanol were prepared by the condensation of piperazine

(1) Pyman, *J. Chem. Soc.*, **93**, 1802 (1908).

with ethylene chlorohydrin or with trimethylene chlorohydrin. γ-1,4-Piperazine-dipropyl benzoate was prepared by the action of benzoyl chloride on the corresponding alcohol in pyridine solution. The phenyl urethans were formed by the action of phenyl isocyanate on the alcohols in anhydrous acetone, and the cinnamates were prepared with cinnamoyl chloride in acetone. The hydrochlorides were prepared by treating alcoholic solutions of the esters with hydrogen chloride in alcohol.

No quantitative pharmacological data have as yet been obtained on these compounds, but all show decided local anesthetic activity on the tongue. All of the compounds give rather acid solutions and are precipitated from solution at rather low P_H values.

Experimental

β-1,4-Piperazine-diethanol.—This was prepared by the method of Pyman.[1]

γ-1,4-Piperazine-dipropanol.—This was prepared in a similar manner, using trimethylene chlorohydrin in place of ethylene chlorohydrin; yield, 48%, m. p. 142–143°.

Anal. Calcd. for $C_{10}H_{22}O_2N_2$: N, 13.88. Found: N, 13.87.

Ester Hydrochlorides.—The yields, properties and composition of the new hydrochlorides are shown in Table I.

TABLE I

-1,4-Piperazine hydrochloride	Yield, %	M. p., °C. corr.	Analyses, % Calcd. Cl	Calcd. N	Found Cl	Found N
β-Diethyl phenylurethan	86	260–261	14.62	11.55	14.50	11.64
β-Diethyl cinnamate	66	261–262	13.98	5.48	13.78	5.60
γ-Dipropyl benzoate	45	251–252	14.69	5.80	14.64	5.74
γ-Dipropyl phenylurethan	52	250–251	13.82	10.91	13.60	10.73
γ-Dipropyl cinnamate	47	254–255	13.16	5.20	13.06	5.24

Summary

Five new esters of piperazine-dialkanols have been prepared. These compounds have been found to be local anesthetics, but to give highly acid solutions.

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