

desoxycodeine-C, is described, and its relationship to tetrahydrodesoxycodeine shown.

4. Dihydrodesoxycodeine-C, from electrolytic reduction of chlorodihydrocodide, is correctly described, and its relationship to tetrahydrodesoxycodeine shown.

5. The preparation of dihydrodesoxycodeine-D by catalytic reduction of β -chlorocodide is described, its relationship to the non-phenolic desoxycodeine-C pointed out, and its further reduction to tetrahydrodesoxycodeine accomplished.

6. The existence of dihydrodesoxycodeine-E is verified.

7. There is no evidence in the desoxycodeine series justifying the assumption of stereoisomerism due to spatial relationships on C-14. Until the existence of such an isomerism in the desoxycodeine or other series of morphine derivatives is demonstrated, it is improbable that more than six desoxycodeines can exist (three of which are known), and five dihydrodesoxycodeines, all of which have been described.

UNIVERSITY, VIRGINIA

[CONTRIBUTION FROM THE RESEARCH LABORATORY OF ORGANIC CHEMISTRY,
MASSACHUSETTS INSTITUTE OF TECHNOLOGY, No. 69]

CONDENSATIONS BY SODIUM INSTEAD OF BY THE GRIGNARD REACTION. I. TERTIARY CARBINOLS

BY AVERY A. MORTON AND JOSEPH R. STEVENS

RECEIVED FEBRUARY 25, 1931

PUBLISHED JUNE 8, 1931

Sodium and magnesium show many similar properties in organic reactions, for example, in the Wurtz-Fittig synthesis, in the formation of pinacones, and in the condensation of acetylene derivatives. Many investigators¹ have observed the behavior of metal alkyls and aryls which may be likened to that of the Grignard reagent. The literature² also indicates that sodium may be used in mixtures of the halide and carbonyl compounds³

¹ Among others see Frankland, *J. Chem. Soc.*, **13**, 191 (1830); Acree, *Am. Chem. J.*, **29**, 588 (1903); Schorigin, *Ber.*, **41**, 2711 (1908); *ibid.*, **43**, 1938 (1910); Schlenk and Ochs, *ibid.*, **49**, 608 (1916); Schlenk and Holtz, *ibid.*, **50**, 262 (1917); Schlubach, *ibid.*, **52**, 1910 (1919); Ziegler and Schnell, *Ann.*, **437**, 227 (1924); Ziegler and Colonius, *ibid.*, **479**, 135 (1930).

² For reactions run without isolation of an intermediate aryl and alkyl see (a) Kekulé, *Ann.*, **137**, 181 (1866); (b) Frey, *Ber.*, **28**, 2515 (1895); (c) Acree, *Am. Chem. J.*, **29**, 588 (1903); (d) Schorigin, *Ber.*, **40**, 3114 (1907); (e) Schorigin, *ibid.*, **41**, 2711 (1908); (f) Nagai, Ogata and Takata, *J. Pharm. Soc. Japan*, No. 407, 3; *Chem. Abstracts*, **10**, 1186 (1916); (g) Blicke, *THIS JOURNAL*, **46**, 2560 (1924); **47**, 229 (1925); (h) Rodd and Linch, *J. Chem. Soc.*, 2174 (1927).

³ Schorigin, *Ber.*, **40**, 3111 (1907), has definitely stated that the halogen alkyls react with esters or acid chlorides in the presence of sodium in a manner similar to the behavior of the Grignard compounds. His conclusion is based on a limited number of experiments which included bromides only, and the aromatic esters and acid chlorides.

to give the same product as if the condensation had been brought about through the intermediate formation of a metal alkyl or aryl. We have begun, therefore, a systematic study of the use of sodium in such condensations as are commonly brought about step-wise through the Grignard reagent. Our work brings out several points which deserve special consideration. Thus very good results are obtained with chlorobenzene.⁴ In fact, in the preparation of triphenylcarbinol from chlorobenzene and ethyl benzoate in the presence of sodium, nearly theoretical yields of crude material were obtained. This is in striking contrast to the great difficulty of causing any reaction between chlorobenzene and magnesium.⁵ Again we may use solvents other than anhydrous ether. This fact has been observed before^{2a,e,h} but has never been properly emphasized. We have obtained very good yields of triphenylcarbinol in benzene and in gasoline. One other very important point is the simplicity of carrying out the reaction. In contrast to the common practice with magnesium, which includes the initial preparation of the Grignard reagent followed by the addition of the carbonyl compound and the long period of refluxing and stirring necessary to complete the reaction, we obtain the carbinol by putting the organic halide, the carbonyl compound and sodium together in a bottle with ether, benzene, or other suitable solvent and setting aside for a day or such time as is necessary for the sodium to disappear completely.

In this paper we describe the preparation of triphenylcarbinol from phenyl halides with ethyl benzoate, diethyl carbonate, or diethyl oxalate and sodium. We also record a few experiments on the synthesis of some aliphatic and mixed tertiary carbinols, using reagents such as ethyl propionate and diethyl ketone, compounds which might be expected to enolize or polymerize in the presence of sodium. No attempt has been made to obtain maximum yields by this method. The work is intended to show the strength of sodium as a condensing agent, particularly in its action with chlorides. Without doubt a study of optimum conditions for some of these reactions would lead to good preparative methods.

We are continuing our studies in the use of sodium in condensations commonly carried out by the Grignard reaction, stressing those conditions in which its use appears to be of considerable advantage, *viz.*, the use of chlorides and of solvents other than ether. The more powerful action of

⁴ The observation that chlorides may be used with sodium in these condensations has been made only once before by Rodd and Linch,^{2h} who condensed chlorobenzene, chlorotoluene and similar compounds with Michler's ketone to form dyestuffs.

⁵ Gilman and St. John, *Rec. trav. chim.*, **49**, 717 (1930), and Gilman and Brown, *THIS JOURNAL*, **52**, 3330 (1930), have published methods for improved yields of phenylmagnesium chloride from magnesium and chlorobenzene but the processes involve either very long heating to initiate and complete the reaction or heating in the absence of a solvent to 150–160° for three hours.

the sodium enables one to synthesize tertiary carbinols such as triphenylcarbinol, which have hitherto been prepared by a very long procedure, and to obtain organic acids from the reaction of carbon dioxide with chlorides. We have also studied the reaction with nitriles. The details of these and other reactions will be published in succeeding papers.

Experiments

The results in the preparation of triphenylcarbinol are grouped in Table I. The procedure was somewhat similar in all of these cases. The halide, carbonyl compound and sodium were usually put into a bottle or flask with the solvent. The container was then stoppered tightly and the mixture set aside until the sodium had reacted or longer. At the beginning some heat was evolved. It was therefore desirable to set the container in cold water for a time, although this was omitted frequently. When the reaction was completed the contents were decomposed with water (usually a little alcohol was added first to decompose any unchanged sodium) and the mixture steam distilled. Crude triphenylcarbinol was obtained in the residue, which was spread out on paper and left to dry. This crude carbinol

TABLE I
REACTIONS

Halide	Mole	Carbonyl compound	Mole	Sodium, mole	Solvent	Cc.	Time	Crude triphenylcarbinol, %
Chlorobenzene	0.2	Ethyl benzoate	0.1	0.4 ^a	Ether	200	2 Days	73
Chlorobenzene	.2	Ethyl benzoate	.1	.4 ^b	Ether	200	2 Days	80
Chlorobenzene	.06	Methyl benzoate	.03	.12 ^a	Ether	25	2 Days	75
Chlorobenzene	.2	Ethyl benzoate	.1	.4 ^c	Ether	200	6 Days	98
Bromobenzene	.2	Ethyl benzoate	.1	.4 ^c	Ether	200	6 Days	98
Iodobenzene	.2	Ethyl benzoate	.1	.4 ^c	Ether	200	6 Days	85
Chlorobenzene	.2	Ethyl benzoate	.1	.43 ^c	Benzene	200	8 Days	84
Chlorobenzene	4.5	Ethyl benzoate	1.0	4 ^a	Gasoline	2000	3 ^d Week	67
Chlorobenzene	0.1	Diethyl carbonate	0.33	0.2 ^a	Ether	200	24 Hours	23
Chlorobenzene	.12	Diethyl oxalate	.02	.12 ^a	Ether	200	4 Days	19
Bromobenzene	.02	Benzyl ^e benzoate	.01	.022 ^a	Ether	20	2 Days	38

^a Sodium sand. ^b Single lump of sodium. ^c Sodium wire 1½ mm. O. D. ^d Because of the larger quantity and the heat evolved, the sodium wire was added in four portions at intervals of two days.

^e This experiment was suggested by the fact that Blicke, *THIS JOURNAL*, 46, 2560 (1924), obtained some triphenylcarbinol from bromobenzene, benzaldehyde and sodium. He also obtained benzyl benzoate from the reaction, which, as seen by our experiment, may have caused the formation of his triphenylcarbinol.

undoubtedly contained some solvent and diphenyl. That it was chiefly the carbinol, however, is shown by the fact that in every case except in the product obtained from the reaction in gasoline, a single digestion with a small quantity of alcohol gave a product melting at 160° or better.

In Table II we have grouped the results obtained in the preparation of a few other tertiary carbinols. These experiments were intended to show that sodium could be used with aliphatic compounds in spite of the great tendency of the latter to enolize and condense with themselves. The runs were made with the bromide since at this stage of the work we held to the prevailing prejudice that chlorides were rather unreactive. As in the case of the preparation of triphenylcarbinol, no attempt was made to obtain optimum conditions. The solvent was 200 cc. of anhydrous ether. The reaction flask was set in an ice-bath and the mixture stirred for seven hours, after which the mass was allowed to stand overnight; 0.2 mole of sodium was used in each experiment. The usual method of isolation was to decompose the product with water, dry the ether layer over potassium carbonate and distil the product.

TABLE II

RESULTS IN PREPARATION OF TERTIARY CARBINOLS			
Halide, 0.1 mole	Carbinol compound, 0.1 mole	Product	%
Bromobenzene	Diethyl ketone	Phenyldiethylcarbinol ^a	25
Ethyl bromide	Diethyl ketone	Triethyl carbinol ^b	17
Ethyl bromide	Ethyl propionate	Triethylcarbinol ^b	9
Ethyl bromide	Benzaldehyde	Phenylethylcarbinol ^c	14

^a Boiling point 221–229°. Klages, *Ber.*, 36, 3692 (1903), records 223–224°. Distillation with a trace of hydrochloric acid formed the unsaturated compound, 3-phenylpentene-2, b. p. 104–107°. Klages records 107–108°.

^b Boiling point 135–142°. Weigert, *Ber.*, 36, 1009 (1903), records 142°. When distilled with oxalic acid the unsaturated compound (b. p. 95–97°) was formed. Saytzeff, *J. prakt. Chem.*, [2] 57, 39 (1898), records 97–98° for 3-ethyl pentene-2.

^c Boiling point 208–214°. Phenylethylcarbinol boils at 212° as shown by Schorigin, *Ber.*, 41, 2721 (1908). When distilled from oxalic acid an unsaturated liquid (b. p. 175–177°) was obtained. *Sym.*-phenylmethylethylene is reported by Klages, *Ber.*, 36, 2574 (1903), as boiling at 177°.

Conclusions

A systematic study of the use of sodium as the condensing agent in reactions hitherto considered typical of magnesium through the Grignard reagent has been started.

Sodium has been found to be better than magnesium in the preparation of triphenylcarbinol in that chlorobenzene can be used, solvents other than ether are permissible and the reaction can be carried out in one step.

The preparation of some aliphatic and mixed tertiary carbinols by means of sodium is described.