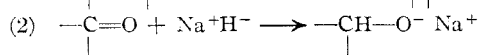
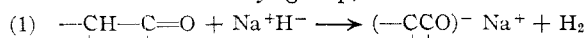


[CONTRIBUTION FROM THE CHEMISTRY DEPARTMENT OF DUKE UNIVERSITY]

The Action of Sodium Hydride on Certain Carbonyl Compounds. Condensations¹ and Reductions

BY FREDERIC W. SWAMER AND CHARLES R. HAUSER

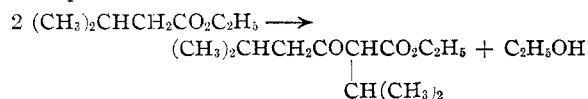
Like other strongly basic anions, the hydride ion of sodium hydride might be expected to react with a carbonyl compound either at an α -hydrogen or at the carbonyl group; the first type of reaction would result in the removal of the α -hydrogen as a proton to form the anion of the carbonyl compound, whereas the second would involve the reduction of the carbonyl group, thus



Actually both types of reaction have been realized, although the reduction of the carbonyl group has been observed only with aldehydes or ketones having no α -hydrogen.

The conversion of esters and ketones having α -hydrogen to their anions by means of sodium hydride has previously been realized by Hansley and Carlisle² in connection with various Claisen condensations in which the ester or ketone anion is the reactive intermediate. However, it was not clear from their results whether the formation of the ester or ketone anion and the condensation were effected by the hydride ion or by alkoxide ion formed from sodium hydride and a trace of alcohol.

We have found that ethyl *i*-valerate is self-condensed in good yield in the presence of sodium hydride at 90–100° and that the temperature at which reaction occurs is not lowered by the presence of small amounts of sodium ethoxide (formed by the addition of ethanol). Since Roberts and McElvain³ have shown that this ester fails to self-condense in the presence of sodium ethoxide even under forced conditions (in which alcohol formed in the condensation is removed by distillation), it appears that the hydride ion actually converts the ester to its anion and effects the condensation. Sodium hydride is a convenient reagent for effecting this condensation,⁴ which may be represented as



Ethyl *i*-butyrate, however, has failed to self-

(1) Paper XXXVI on "Condensations"; paper XXXV, *THIS JOURNAL*, **68**, 2742 (1946).

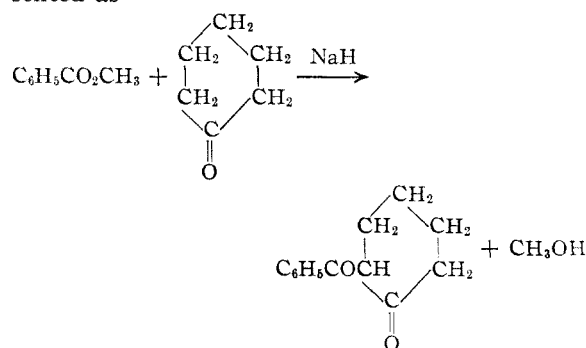
(2) Hansley and Carlisle, *Chem. Eng. News*, **23**, 1332 (1945); Hansley, V. L., U. S. Patent 2,158,071 (May 16, 1939); Hansley, U. S. Patent 2,218,026 (October 15, 1940).

(3) Roberts and McElvain, *THIS JOURNAL*, **59**, 2007 (1937).

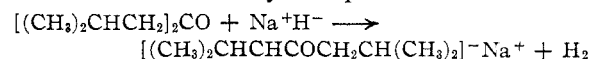
(4) See Hauser and Hudson, "Organic Reactions," Roger Adams, Editor-in-Chief, John Wiley and Sons, Inc., New York, N. Y., 1942, Vol. I, pp. 276–277; also Levine, Baumgarten and Hauser, *THIS JOURNAL*, **66**, 1230 (1944).

condense in the presence of sodium hydride at temperatures up to 120°. It is possible that this condensation might be effected with sodium hydride by the use of more drastic conditions.

Since satisfactory yields for the benzylation of cyclohexanone have not previously been reported⁵ we have studied the use of sodium hydride for this purpose. It has been found that with methyl benzoate and this reagent a 40% yield of the β -diketone is obtained. The reaction may be represented as

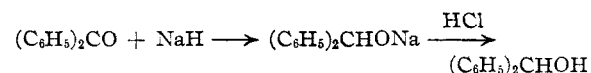


Attempts to prepare ketone anions independently of the Claisen condensation have not been entirely satisfactory, since the conditions required for hydrogen evolution are also generally favorable for the self-condensation of the ketone. Thus with acetone or methyl *i*-butyl ketone high boiling products were obtained. However, with di-*i*-butyl or di-*i*-propyl ketone, which self-condenses very slowly or not at all, the ketone was largely recovered. The conversion of di-*i*-butyl ketone to its anion may be represented as



Judging from these results it appears that the procedure of first preparing the ketone anion and then adding the ester, found particularly satisfactory with sodium amide,⁶ is probably not generally suitable with sodium hydride.

Reduction of the carbonyl group has been realized with benzophenone, which has no α -hydrogen. With sodium hydride in boiling xylene, this ketone is reduced, in good yield, to benzhydrol.

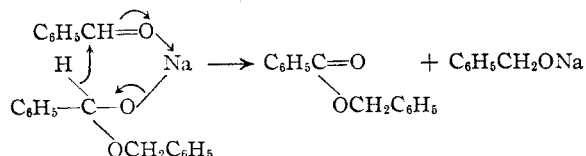
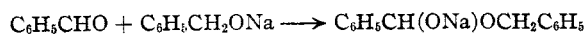


With benzaldehyde only a small amount of so-

(5) Bauer (*Ann. chim. phys.*, [9] **1**, 393 (1914)) reported a very poor yield with ethyl benzoate using sodium amide. However, in this laboratory, good yields have been obtained with methyl or phenyl benzoate using this reagent; the results will be published shortly.

(6) Adams and Hauser, *THIS JOURNAL*, **66**, 1220 (1944).

dium hydride reacts, but an excellent yield (92%) of product, benzyl benzoate, is produced. Evidently a small amount of benzaldehyde is first reduced by the hydride ion of sodium hydride to form sodium benzyloxide, which then catalyzes the reduction of the benzaldehyde to the ester. As indicated by Hammett,⁷ the latter well known reaction⁸ also probably involves a hydride ion reduction. The mechanism may be represented thus



Methyl benzoate fails to reduce in the presence of sodium hydride, even in boiling xylene. The greater stability of the ester group, compared to the aldehyde or ketone group, toward sodium hydride may be ascribed to its considerably larger resonance.⁹

A further study of the action of sodium hydride on various functional groups is in progress.

Experimental¹⁰

The apparatus used in this work consisted of a 500 ml., three-necked flask equipped with a mercury-sealed stirrer, thermometer, dropping funnel and a reflux condenser to which was attached a tube leading through a Dry Ice-ether trap to a wet test meter. The solvent¹¹ was placed in the flask and the sodium hydride was weighed out and added under an atmosphere of nitrogen in a dry box. The system was then assembled and purged with nitrogen.

Self Condensation of Ethyl Isovalerate.—The suspension of sodium hydride (7.2 g., 0.3 mole) in ethyl isovalerate (157 g., 1.2 mole) was stirred for one hour at room temperature. No reaction was apparent. The temperature was then gradually raised, by means of an oil-bath, to 60° during three hours, 1 ml. of absolute ethanol being added at the end of each hour. Upon each addition of ethanol a small amount of gas was evolved, but reaction did not continue. The temperature was then raised to 100°. At this temperature the reaction proceeded smoothly (indicated by the evolution of hydrogen), being complete in two hours. The mixture was cooled to room temperature and a small amount of ethanol was added to destroy any excess sodium hydride. The mixture was poured onto 200 g. of ice and 20 g. of glacial acetic acid. Ether (100 ml.) was added and the mixture was stirred thoroughly. The ether layer was washed with water, dried over drierite, and the ether distilled. Excess ethyl isovalerate (120 g., b. p. 131–134°) was recovered at atmospheric pressure, through a 25-cm. Vigreux column. The residue was distilled *in vacuo*, yielding 15.8 g. (60% based on the sodium hydride; 52% based on the ester) of ethyl α -isovaleryl

isovalerate boiling at 117–119° (14 mm.).⁴ The experiment was repeated without adding the ethanol; the reaction occurred at 90–100°.

Acylation of Cyclohexanone with Methyl Benzoate.—To the stirred suspension of sodium hydride (9.6 g., 0.4 mole) in 100 ml. of dry ether at 35° was added a solution of 55.0 g. (0.4 mole) of methyl benzoate in 50 ml. of ether. Cyclohexanone (19.5 g., 0.2 mole) in 50 ml. of dry ether was then added dropwise during thirty minutes. The mixture was stirred at 35–40° for five hours and then allowed to stand overnight at room temperature. The product was cooled below 10° in an ice-bath and the excess sodium hydride destroyed with ethanol (15 ml.). Water (100 ml.) was added slowly, keeping the temperature below 10°. The mixture was then poured onto 100 g. of ice in a separatory funnel and shaken thoroughly. The aqueous phase was acidified with 10% hydrochloric acid and the liberated β -diketone extracted with ether. The ether extract was washed with 50 ml. of saturated sodium bicarbonate solution, then with water, and dried over drierite. The solvent was distilled and the residue, which solidified in an ice-bath, was recrystallized from dilute ethanol. The yield of α -benzoylcyclohexanone, m. p. 87–88°,¹² was 16.5 g., 41% based on the ketone.

Preparation of Ketone Anions.—The ketone in a suitable solvent was allowed to react with a 5% molecular excess of sodium hydride until 80–100% of the hydrogen had been evolved; the mixture was then worked up as described for benzophenone.

With acetone in ether at 30–45° (actually some hydrogen was evolved at 10°) the calculated amount of hydrogen was evolved; only high boiling products were obtained. With methyl isobutyl ketone in xylene at 80°, 80% of the hydrogen was evolved in five hours; there was obtained 17% of the original ketone, 41% of a product, b. p. 76–78° (3 mm.), and 41% of material, b. p. 145–152° (3 mm.). With di-*i*-propyl ketone in toluene at 120°, 80% of the hydrogen was evolved in five hours and the ketone was largely recovered; there was no high boiling material. With di-*i*-butyl ketone in xylene at 140°, the calculated amount of hydrogen was evolved in five hours, after which the ketone was largely recovered along with 5% of material boiling at 67–155° (18 mm.).

Reduction of Benzophenone.—Benzophenone (45.5 g., 0.25 mole) was added to the stirred suspension of sodium hydride (7.3 g., 0.3 mole) in 75 ml. of xylene and the temperature was raised slowly to 145°. The color of the mixture became deep blue. During six hours at 145° the blue color gradually disappeared with the formation of a white precipitate. (After three hours 50 ml. of xylene was added to keep the mixture fluid.) The product was cooled in an ice-bath and 100 ml. of ether added. Neutralization was effected and excess sodium hydride destroyed by dropwise addition of 19 g. of glacial acetic acid in 80 ml. of water, keeping the temperature below 20°; then the mixture was stirred at room temperature for about twenty minutes to assure complete decomposition of any remaining sodium hydride. The evolved hydrogen during neutralization amounted to only 0.011 mole. The organic phase was washed with water, dried over drierite, and the solvent distilled (using an aspirator at 100 mm. pressure). The residue was distilled in a von Braun flask yielding 38 g. (83%) of benzhydrol (b. p. 178–182° (20 mm.)) and 4.5 g. of high boiling material which decomposed on attempted distillation. The benzhydrol, after recrystallization from ligroin, melted at 66–67° (mixed m. p. 66–67°).

Reduction of Benzaldehyde.—To the stirred suspension of sodium hydride (12.6 g., 0.525 mole) in 75 ml. benzene was added 53 g. (0.5 mole) of freshly distilled benzaldehyde. The temperature was then raised gradually, during forty-five minutes, to 80° and held there for five hours. The reaction mixture was worked up as described above for benzhydrol, except that the organic phase was extracted

(12) This melting point agrees with that observed for a sample prepared by means of sodium amide, which gave the correct analysis. Bauer⁴ reported 92°.

(7) Hammett, "Physical Organic Chemistry," McGraw-Hill Book Co., New York, N. Y., 1940, p. 352.

(8) "Organic Syntheses," Coll. Vol. I, 104 (1941).

(9) The relatively large amount of resonance energy that becomes tied up in formation of the ester group in the catalytic reduction of benzaldehyde by sodium benzyloxide (represented above) appears to furnish the main free energy decrease of the reaction.

(10) We are indebted to the Electrochemicals Department, E. I. du Pont de Nemours and Co., Niagara Falls, New York, for the sample of sodium hydride used in this investigation.

(11) In the condensation of ethyl isovalerate, excess ester was used as solvent.

with sodium bicarbonate solution. The hydrogen evolved during neutralization amounted to 0.5 mole. Distillation of the product *in vacuo* yielded 1.0 g. (1.9%) of benzyl alcohol (b. p. 91–93° (10 mm.)) and 45.6 g. (86.5%) of benzyl benzoate (b. p. 172–173° (10 mm.)). The ester was identified by hydrolysis to benzoic acid (m. p. 121°; m. p. of amide 128–129°) and benzyl alcohol (b. p. 91–93° (10 mm.); m. p. of 3,5-dinitrobenzoate 111.5°).

The reaction was also carried out using only 1.2 g. (0.05 mole) of sodium hydride to 106 g. (1.0 mole) of benzaldehyde. The yield of benzyl benzoate (b. p. 172–173° (10 mm.)) was 97.6 g. (92%).

Action on Methyl Benzoate.—A mixture of 12.0 g. (0.5 mole) of sodium hydride, 34.0 g. (0.25 mole) of methyl benzoate, and 75 ml. of xylene was stirred at 140° for three hours and then worked up as described for benzophenone. The evolved hydrogen on neutralization amounted to 0.49 mole and 29.4 g. (87%) of essentially pure methyl benzoate was recovered. No other product was found.

Summary

1. Certain carbonyl compounds having α -hydrogen are converted by sodium hydride to their anions, which may enter into Claisen condensations, whereas certain of those having no α -hydrogen are reduced.

2. Ethylisovalerate has been self-condensed and cyclohexanone has been benzoylated with methyl benzoate. Di-*i*-propyl and di-*i*-butyl ketones have been converted to their anions and recovered.

3. Benzophenone has been reduced to benzhydrol and benzaldehyde to benzyl benzoate. The mechanism for the latter reaction and the failure of methyl benzoate to reduce is discussed.

DURHAM, NORTH CAROLINA RECEIVED AUGUST 24, 1946

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, DUKE UNIVERSITY]

The Vapor Pressures of Some Organic Fluorides^{1,2}

BY FRANK H. FIELD AND JOHN H. SAYLOR

The measurements reported in this paper were made in connection with a general program of research in this Laboratory concerning the physical properties of fluorine compounds.

Experimental

The method used was a modification of that devised by Ramsay and Young³ and has been previously described.⁴

Two different manometers were used as before; a mercury U-gage⁵ for pressures above 15 mm. of mercury and an oil manometer⁶ for all pressures below 15 mm. of mercury.

All of the compounds used except the benzotrifluoride were prepared by workers in this Laboratory under the direction of Dr. C. K. Bradsher. The benzotrifluoride was procured from the Hooker Electrochemical Company. The materials were refluxed with sulfuric acid until the acid gave no test for chloride ion, were washed twice with sodium bicarbonate solution, three times with water and dried over Drierite. The dried material was distilled at a

high reflux ratio through a two-and-one-half foot glass column packed with glass helices using calibrated thermometers.

The extent of the purification was somewhat limited by the quantities of materials available. The 4-chloro-*m*-xylene hexafluoride boils within one degree of 2-chloro-*p*-xylene hexafluoride and was likely contaminated with a small amount of the latter compound. All boiling points were corrected to 760 mm. by means of Craft's rule.

Results

Approximately ten individual measurements were made on each compound at temperatures ranging from about 2 to 80°. The data were fitted by the method of least squares to the following equation.^{4,7}

$$\log p = -\frac{A}{T-C} + B$$

In the calculations, 0° = 273.16° K.

The mean deviation between the observed pressures and those calculated from the equation varied from 2 parts per 1000 for 5-chloro-*m*-xylene hexafluoride to 9 parts per 1000 for 4-chloro-*m*-xylene hexafluoride.

Heats of vaporization were calculated from the Clapeyron equation approximation obtained by differentiating the vapor pressure equation and multiplying the result by RT^2 . These values together with the constants for the vapor pressure equation are given in Table I.

Booth, Elsey and Burchfield⁸ have measured the vapor pressures of benzotrifluoride which are the only values reported for any of the four compounds measured here. The agreement with the present data is good.

Summary

The vapor pressures of benzotrifluoride, *m*-xylene hexafluoride, 5-chloro-*m*-xylene hexafluo-

(7) Thomson, *Chem. Rev.*, **38**, 1 (1946).

(8) Booth, Elsey and Burchfield, *THIS JOURNAL*, **57**, 2066 (1935).

TABLE I

BOILING POINTS, CONSTANTS OF THE VAPOR PRESSURE EQUATION AND HEATS OF VAPORIZATION

Substance	B. p. range, °C.	Constants of the equation			ΔH_{25° kcal./mole
		$\log p = \frac{A}{T-C} + B$	A	B	
Benzotrifluoride	102.30 ± 0.05	1148.7	6.642	70.90	9.0
<i>m</i> -Xylene hexafluoride	116.0–116.1	1488.8	7.315	52.16	10.0
5-Chloro- <i>m</i> -xylene hexafluoride	138.20–138.25	1992.7	8.119	26.54	11.0
4-Chloro- <i>m</i> -xylene hexafluoride	149.1–149.2	1959.4	7.981	33.61	11.4

(1) This research program was sponsored by the Naval Research Laboratory.

(2) This paper was taken in part from the thesis submitted by Frank H. Field to the Graduate School of Duke University in partial fulfillment of the requirements for the degree of Master of Arts, June, 1944.

(3) Ramsay and Young, *J. Chem. Soc.*, **47**, 42 (1885).

(4) Stuckey and Saylor, *THIS JOURNAL*, **62**, 2922 (1940).

(5) Zimmerli, *Ind. Eng. Chem., Anal. Ed.*, **10**, 283 (1938).

(6) Hickman, *Rev. Sci. Instruments*, **5**, 161 (1934).