

**B. 1-Hydroxy-2-methoxymethyl-4,4-dimethyl-3-pentanone (methoxy alcohol 7)**, bp 97–98° (2.0 mm),  $n_D^{20}$  1.4403, was isolated in 12% conversion. The sample showed infrared absorption bands at 2.87 (medium), 5.92 (strong), and 9.04  $\mu$  (strong).

Gas-liquid partition chromatographic analysis showed the presence of 10–20% of dimethyl ether 6 which could not be separated by fractional distillation. 7 was therefore characterized by conversion to 1-acetoxy-2-methoxymethyl-4,4-dimethyl-3-pentanone(methoxyacetate 8) employing the procedure described above for diacetate 4. Compound 8 was obtained in 86% yield, bp 80° (0.4 mm),  $n_D^{20}$  1.4327. This sample showed strong infrared absorption bands at 5.73, 5.85, and 9.02  $\mu$ .

*Anal.* Calcd for  $C_{12}H_{20}O_5$ : C, 61.11; H, 9.26. Found: C, 61.08; H, 9.38.

**4-Hydroxy-3,3-dimethylbutanone (9)**.—This compound was prepared by the reaction of methyl isopropyl ketone with formaldehyde described by Decombes.<sup>11</sup> 9 boiled 94–96° (24 mm) and had infrared absorption bands at 2.85 (medium) and 5.91  $\mu$  (strong).

The alcohol was acetylated following the procedure described above for diacetate 4 to produce 4-acetoxy-3,3-dimethylbutanone 10, bp 108–111° (32 mm). The infrared absorption band for the ketone carbonyl was found to be 5.85  $\mu$ .

**2-Benzoyl-3-methoxy-1-propene (13)**.—This compound was prepared by the method of Beets and Heeringa,<sup>15</sup> and boiled at 88–89° (0.1 mm),  $n_D^{20}$  1.5312.

**2-Methoxymethyl-4,4-dimethyl-1-penten-3-one (14)**.—Dichloride 5 (40.6 g, 0.205 mole) was dissolved in 200 ml of methanol and the solution chilled to –50° with an acetone–Dry Ice bath. A solution of sodium methoxide (freshly prepared from sodium (8.74 g, 0.38 mole) and 100 ml of anhydrous methanol) was added slowly over 1 hr while maintaining the reaction mixture at –50°. The mixture was stirred 2 hr at –50°, then permitted to warm to room temperature, and stand overnight.

Precipitated sodium chloride (21.9 g, 0.374 mole) was removed by filtration, and the filtrate was distilled to give a fraction, bp 86–89° (30 mm, 23.0 g). Gas-liquid partition chromatography (2% diethylene glycol succinate on Gas Chrom P) showed this fraction to be principally the desired 14. Purification was effected by redistillation and collection from the gas chromatograph. Pure material showed  $n_D^{20}$  1.4360 and infrared absorption bands at 5.96 (strong) and 6.02  $\mu$  (strong, shoulder).

*Anal.* Calcd for  $C_9H_{16}O_2$ : C, 69.19; H, 10.32. Found: C, 69.07; H, 10.22.

**Vinyl Analyses.**<sup>12</sup> **A. Activated Vinyl Compounds.**—The analytical method used is that described by American Cyanamid Co. for acrylonitrile using *n*-dodecyl mercaptan,<sup>16</sup> with the exception that reaction times in the alkaline mercaptan medium were extended to 0.5 hr. Under these conditions, mercaptan consumptions were measured: 13, 2.0 moles; and 14, 1.3 moles.

**B. "Latent" Vinyl Compounds.**—The elimination reaction in the presence of mercaptan is conducted similarly, except that more base (0.5 *N* potassium hydroxide in ethanol) is added to compensate for that consumed by the acid formed on elimination, and to maintain alkaline conditions during the analysis. In this analysis, mercaptan consumptions were measured: 4, none; 8, none; 10, none; and 11, 0.9 moles. Under similar conditions, base consumptions were measured: 4, 2.04; 8, 1.1; 10, 1.1; and 11, 1.05 moles.

**Acknowledgments.**—We wish to thank Dr. G. C. Tesoro for helpful discussion and advice during this work, Mr. Frank Draugelis for assistance with the experiments, and Mr. Chester Becker for running the infrared spectra and gas chromatograms.

(16) *The Chemistry of Acrylonitrile*, 2nd ed, American Cyanamid Co., New York, N. Y., 1959, pp. 61–63.

## The Reaction of Formates and Formamides with Base<sup>1</sup>

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*Received March 1, 1966*

Formates react with strong bases such as sodium hydride, potassium *t*-butoxide, and triphenylmethylsodium to produce alkoxides and carbon monoxide. Formamides undergo a similar transformation with sodium hydride. The usefulness of these reactions in synthesis and attempts to trap possible intermediate carbanions is discussed.

The reaction of alkoxides with carbon monoxide under pressure to yield formates is a well-documented process.<sup>4</sup> This reaction is reversible and formates can be decomposed into alcohols and carbon monoxide by alkali alkoxides.<sup>5,6</sup> The exact course of formate, decompositions has been clouded by several unexplainable observations. Adkins, for example, found that sodium reacted with formates with evolution of only 66% of the theoretical amount of carbon monoxide.<sup>7</sup> Scheibler in a series of papers describes the

isolation of "carbonite ions" from the reaction of formates with bases.<sup>8</sup> Adickes later showed that these so called "carbonite ions" were in fact either alkoxides or products from the addition of alkoxides to formates.<sup>9</sup>

**Formates.**—Ethyl formate reacts rapidly with sodium hydride at room temperature with the evolution of carbon monoxide and hydrogen. We first noticed this reaction while performing some condensation reactions using sodium hydride as a base and ethyl formate as the solvent. Since this reaction seemed quite interesting and potentially useful if carbanionic intermediated could be trapped, we decided to investigate this process further. In order to simplify isolation and purification of products, most of our subsequent work was carried out with *n*-butyl formate.

Butyl formate reacted rapidly with sodium hydride in diethyl ether with the evolution of gas. Upon work-up of the reaction mixture, a 68% yield of 1-butanol was obtained. When the reaction was car-

(1) A preliminary account of some of the investigations reported in this paper has appeared: J. C. Powers, R. Seidner, and T. G. Parsons, *Tetrahedron Letters*, 1713 (1965).

(2) National Science Foundation summer undergraduate research participant, 1964.

(3) National Science Foundation summer undergraduate research participant, 1965.

(4) B. S. Lacy, R. G. Dunning, and H. H. Storch, *J. Am. Chem. Soc.*, **52**, 926 (1930); A. Staher, *Ber.*, **47**, 580 (1914); J. C. Gjaldback, *Acta Chem. Scand.*, **2**, 683 (1948).

(5) (a) J. Hine, "Physical Organic Chemistry," McGraw-Hill Book Co., Inc., New York, N. Y., 1962, p 311; (b) J. Hine, "Divalent Carbon," Ronald Press Co., New York, N. Y., 1964, p 79.

(6) H. J. Ringold [*J. Am. Chem. Soc.*, **78**, 816 (1956)] reports that a steroidal formate is decomposed by aluminium isopropoxide under conditions of the Oppenauer oxidation.

(7) (a) H. E. Carswell and H. Adkins, *ibid.*, **50**, 235 (1928); (b) G. J. Pfeiffer and H. Adkins, *ibid.*, **53**, 1043 (1931).

(8) H. Scheibler, *Ber.*, **59B**, 1022 (1926); **60B**, 554 (1927); **67B**, 312, 314 (1934).

(9) F. Adickes, *ibid.*, **60B**, 272 (1927); **63**, 3016, 3022 (1930); F. Adickes and P. P. Peckelhoff, *ibid.*, **68B**, 1138 (1935).

ried out in refluxing dimethoxyethane, 1.85 equiv of gas were evolved/equiv of formate. Mass spectral analysis of the gas mixture demonstrated the presence of carbon monoxide.

Bases other than sodium hydride also catalyzed the decarbonylation of formates (see Table I). The rates

TABLE I

Formate (mole)	Base (mole)	Solvent, temp (°C)	Products
Ethyl	NaH	C <sub>2</sub> H <sub>5</sub> , 25	C <sub>2</sub> H <sub>5</sub> OH
Ethyl	Na	Dimethoxyethane, 84	C <sub>2</sub> H <sub>5</sub> OH, gas (64) <sup>a</sup>
Ethyl	NaOCH <sub>3</sub>	None, 25	C <sub>2</sub> H <sub>5</sub> OH, gas (70)
Ethyl	NaOCH <sub>3</sub>	Methanol	No reaction
<i>n</i> -Butyl	NaH	Ether	C <sub>4</sub> H <sub>9</sub> OH (68)
<i>n</i> -Butyl	NaH	Dimethoxyethane, 84	C <sub>4</sub> H <sub>9</sub> OH, gas (92)
<i>n</i> -Butyl	Na	Dimethoxyethane, 84	Gas (84)
<i>n</i> -Butyl (0.1)	NaOCH <sub>3</sub> (0.5) CH <sub>3</sub> OH (0.5)	DMSO, 25	No reaction
<i>n</i> -Butyl	(C <sub>6</sub> H <sub>5</sub> ) <sub>3</sub> CNa	DMSO, 25	Gas (33%)
<i>n</i> -Butyl	KOC(CH <sub>3</sub> ) <sub>3</sub>	Dimethoxyethane, 84	C <sub>4</sub> H <sub>9</sub> OH, gas (50)
<i>n</i> -Butyl	KOC(CH <sub>3</sub> ) <sub>3</sub>	DMSO, 25	C <sub>4</sub> H <sub>9</sub> OH
<i>n</i> -Butyl	NaH	Dimethoxyethane, 84	C <sub>4</sub> H <sub>9</sub> OCH <sub>2</sub> C <sub>6</sub> H <sub>5</sub> (43)

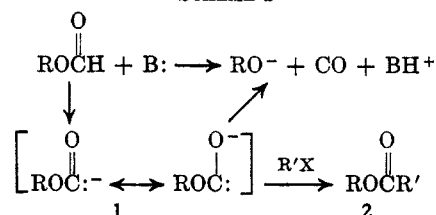
<sup>a</sup> The gas evolved was measured by collecting it over water. The values in parentheses are the percentages of calculated theoretical gas evolution that were observed during the reaction.

of the reactions with sodium hydride, triphenylmethylsodium, or potassium *t*-butoxide were qualitatively similar. Decarbonylation using an alkoxide as the base, on the other hand, was much slower. When a formate and alkoxide reacted without solvent, gas evolution was rapid at first. The reaction, however, became progressively slower as the concentration of alcohol was built up. More complete reaction could be effected by the addition of sodium to consume the alcohol as formed. No reaction took place at room temperature between formates and sodium methoxide in the presence of methanol. Evidently, sodium methoxide is not a strong enough base to carry out the decarbonylation reaction in alcoholic solution. Formation of small amounts of methanol during the reaction of formates with alcohol-free methoxide decreases the basicity of the alkoxide immensely, and decarbonylation no longer occurs.<sup>10</sup> Adkins has utilized the evolution of carbon monoxide from formates in the presence of alkoxides and sodium to perfect an analytical method for formates.<sup>7</sup> Contrary to his results, we were unable to detect any methanol when *n*-butyl formate was decomposed with sodium.

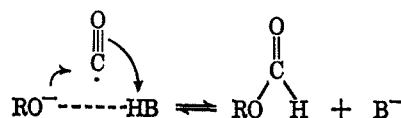
Two mechanisms can be visualized for these decarbonylation reactions. The first would involve abstraction of a proton by the base to give a carbanion 1 which would probably fall apart quite readily to an alkoxide and carbon monoxide. The second would involve a simple concerted decomposition. Intermediate carbanions, "carbonite ions," have been reported.<sup>8</sup> However, this work was later discredited by Adickes.<sup>9</sup> In order to explore the possibility of trapping any intermediates (1), we carried out some formate decompositions in the presence of alkylating agents. Thus, we hoped that the decomposition of

ethyl formate or *n*-butyl formate with sodium hydride in the presence of benzyl bromide would yield some of the ethyl or butyl ester of phenylacetic acid (1 → 2). Neither of these products could be isolated. Instead from the reaction of *n*-butyl formate with sodium hydride there was obtained a 43% yield of benzyl *n*-butyl ether, a product formed by alkylation of the alkoxide ion produced from the decomposition of the formate (see Scheme I).

SCHEME I



Several attempts were made to trap the carbanions 1 under high pressures of carbon monoxide, but all of these were unsuccessful. For example, decomposition of formates with sodium hydride in the presence of benzyl bromide with an atmosphere of 1500 psi of carbon monoxide yielded only ethers; no phenylacetic acid esters were formed. Similarly, decomposition of formates with base or the carbonylation of alkoxides in aprotic solvents in the presence of benzaldehyde and 4000 psi of carbon monoxide gave no mandelic acid or esters of mandelic acid. These consistently negative results would seem to demand that a concerted mechanism is involved in these carbonylation and decarbonylation reactions. One likely possibility is direct reaction of carbon monoxide with an alkoxide ion hydrogen bonded to the conjugate acid of a base as shown below. There seems to be no valid



reason to postulate a carbanionic mechanism<sup>5</sup> for either of these reactions.

While attempting to obtain evidence for a carbanion (1) intermediate, we carried out a partial decomposition of *n*-butyl formate with potassium *t*-butoxide in deuterated dimethyl sulfoxide. Potassium *t*-butoxide has been shown to possess several molecules of *t*-butyl alcohol of solvation and this rapidly exchanges with DMSO-*d*<sub>6</sub>. Thus the active protonating agent should be (CH<sub>3</sub>)<sub>3</sub>COD. When the reaction of potassium *t*-butoxide with *n*-butyl formate in DMSO-*d*<sub>6</sub> was carried to 70–80% completion, the recovered ester contained (ca.) 1–1.5% deuterium. Analysis of the mass spectrum<sup>11</sup> of the deuterated *n*-butyl formate showed that most if not all of the deuterium was attached to the carbonyl group. One explanation for this incorporation of deuterium would be a discrete carbanion intermediate 1 which could pick up deuterium from the solvent and give the deuterated product. This seems highly unlikely since loss of carbon monoxide from 1 would lead to increased stability of the system

(10) Addition of 5 mole % of methanol to a mixture of sodium methoxide in DMSO decreases the basicity of the medium by a factor of 10<sup>4</sup>. See, for example, R. Stewart, J. O'Donnell, D. J. Cram, and B. Rickborn, *Tetrahedron*, **18**, 917 (1962); E. C. Steiner and J. M. Gilbert, *J. Am. Chem. Soc.*, **85**, 3054 (1963).

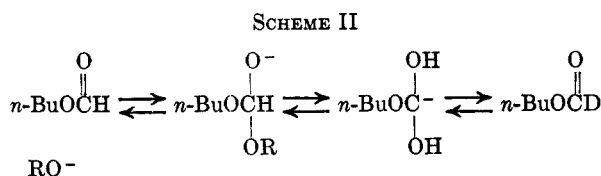
(11) See the Experimental Section for an analysis of the mass spectral results.

TABLE II

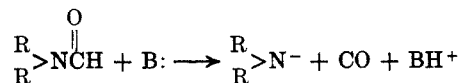
Formamide	Base	Solvent	Products (%)
N-Methylformanilide	NaH		C <sub>6</sub> H <sub>5</sub> NHCH <sub>3</sub> (70) Gas (86)
N-Methylformanilide C <sub>6</sub> H <sub>5</sub> CH <sub>2</sub> Br	NaH		C <sub>6</sub> H <sub>5</sub> NHCH <sub>3</sub> (11) C <sub>6</sub> H <sub>5</sub> N—CH <sub>2</sub> C <sub>6</sub> H <sub>5</sub> (6)
N-Methylformanilide	(C <sub>6</sub> H <sub>5</sub> ) <sub>3</sub> C <sup>-</sup> Na <sup>+</sup>	DMSO	No reaction
N-Methylformanilide	Potassium <i>t</i> -butoxide	DMSO	No reaction
N,N-Diethylformamide	NaH	Dimethoxyethane (reflux)	Gas (50) Et <sub>2</sub> NH (20) <sup>a</sup>
C <sub>6</sub> H <sub>5</sub> NCH <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub> NC <sub>6</sub> H <sub>5</sub>	NaH	Dimethoxyethane (reflux)	C <sub>6</sub> H <sub>5</sub> NHCH <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub> NHC <sub>6</sub> H <sub>5</sub> (79)

<sup>a</sup> The low yield of diethylamine is probably due to difficulty in the isolation procedure. No formamide was left in the reaction mixture and no other organic compounds could be detected.

and all of our previous attempts to trap the carbanion 1 were unsuccessful. A more likely explanation for the deuteration results is that a slower base-catalyzed exchange reaction is competing with the decarbonylation. The mechanism presented in Scheme II below has some merit.<sup>12,13</sup>



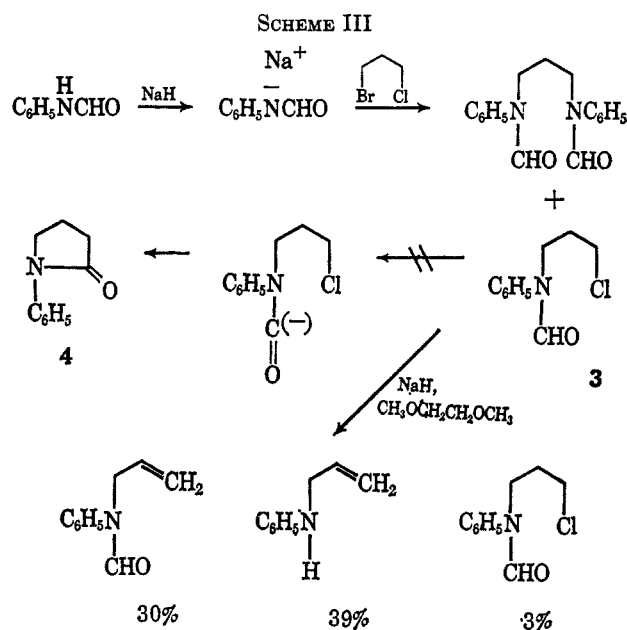
**Formamides.**—Formamides were also decomposed by sodium hydride (see results in Table II).<sup>14</sup> Carbon monoxide was detected in the gaseous product from the sodium hydride decomposition of N-methylformanilide. These decompositions took considerably longer than the formates. The approximate half-



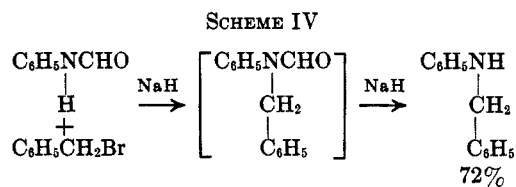
lives of the reactions with sodium hydride in refluxing dimethoxyethane were: *n*-butylformate, 20 min; N-methylformanilide, 45 min; N,N-diethylformamide, 50 hr. This order is in agreement with decreasing stability of the carbanionic product (*e.g.*, alkoxide or amide ion) produced in the decarbonylations.

In order to again explore the possibility of a carbanionic intermediate, the decomposition of N-(3-chloropropyl)formanilide (3) was investigated. (Scheme III). None of the lactam 4 could be detected in the reaction mixture. Instead 70% of the products could be accounted for by simple elimination or decarbonylation reactions.

The decarbonylation of formamides can be utilized in a one-pot synthesis of secondary amines. This involves reaction of a primary formamide with NaH in the presence of an alkylating agent to give a secondary



formamide which is then decarbonylated with excess sodium hydride. An example of this procedure is given in Scheme IV.



**Aldehydes and Imino Esters.**—The possibility that aldehydes might be decarbonylated was investigated but no success was achieved. Gas evolution in the sodium hydride reactions was minimal and no decarbonylation products could be detected. The reaction of substituted benzaldehydes (5) with sodium hydride led simply to reduction products (6) or to the various products from Cannizzaro-type reactions (Scheme V).<sup>15</sup>

The reaction of the imino ester 7<sup>16</sup> with sodium hydride in dimethoxyethane produced the amidine 9

(15) F. W. Swamer and G. R. Hauser [*J. Am. Chem. Soc.*, **68**, 2647 (1946)] report the formation of benzyl benzoate from the reaction of benzaldehyde with sodium hydride. G. E. Lewis [*J. Org. Chem.*, **30**, 2433 (1965)] report the formation of *p*-nitrobenzyl alcohol and *p*-nitrobenzoic acid from the reaction of *p*-nitrobenzaldehyde with sodium hydride in THF. The reaction of *p*-nitrophenyl-CDO with NaH followed by injection of the reaction mixture into water led to no loss of D.

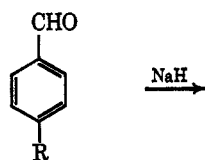
(16) R. M. Roberts, *J. Am. Chem. Soc.*, **77**, 3801 (1955).

(12) This mechanism was suggested by Professor D. J. Cram.

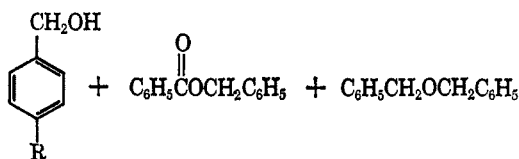
(13) A similar process must be involved in the exchange of sodium formate in 0.1 N NaOH in D<sub>2</sub>O at 1000: F. Münzberg and W. Oberst, *Z. Physik. Chem.* (Leipzig), **B51**, 18 (1935).

(14) Dimethylformamide reacts with sodium to give a mixture of products, including dimethylamine, formaldehyde, N,N-dimethylglyoxylic amide, and glycollic aldehyde. Most of the products can be rationalized by assuming that acyloin-like reactions are occurring: "DMF," Du Pont Product Information Bulletin, 1958. See also Leo L. Contois, Jr., U. S. Patent 2,961,465 (1960); *Chem. Abstr.*, **55**, 8295<sup>d</sup> (1961); **52**, 8420<sup>e</sup> (1958).

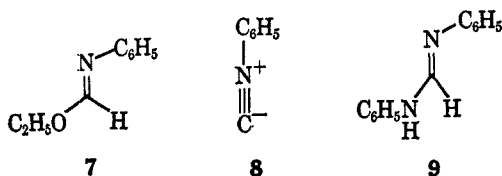
SCHEME V



5, R = H, NO<sub>2</sub>, OCH<sub>3</sub>



as the only isolable product. Phenylisocyanide (8), the product formed if a process similar to decarbonylation occurred, could be detected by its characteristic odor, but was not isolated.



### Experimental Section

Microanalyses were performed by Miss Heather King, University of California at Los Angeles. Melting points were determined with a Büchi melting point apparatus and are uncorrected. Infrared spectra were measured on a Perkin-Elmer Model 127 infracord. A Varian Associates A-60 instrument was used for recording nmr spectra. Peak positions are given in  $\tau$  values. The gas-liquid partition chromatograms were obtained with 3-ft columns packed with 20% by weight suspension of SE-30 silicone oil on firebrick. The fractions, eluted with helium, were detected with a thermal conductivity cell.

***n*-Butyl Formate and Sodium Hydride.**—A mixture of 10.2 g (0.1 mole) of *n*-butyl formate and 2.4 g of sodium hydride in 200 ml of ether was stirred at room temperature for 3 hr. The reaction mixture was poured into water and the aqueous layer was extracted with ether. The combined ether extracts were dried over magnesium sulfate and the ether was removed by distillation. Distillation of the residue through a 40-cm spinning-band column gave 5.0 g (67.5%) of 1-butanol which was identified by infrared and gas chromatographic comparison with an authentic sample. No *n*-butyl formate or other organic products could be detected.

In another experiment, 3 ml (0.025 mole) of *n*-butyl formate was allowed to react with 0.6 g (0.025 mole) of sodium hydride in dimethoxyethane. There was evolved 1180 ml (1.85 equiv) of gas. The gas was collected and was shown to contain carbon monoxide by mass spectrometric analysis.

A plot of gas evolution vs. time gave a half-life of 20 min for the reaction of sodium hydride with *n*-butyl formate in refluxing 1,2-dimethoxyethane.

No reaction occurred between *n*-butyl formate and sodium hydride at  $-20^\circ$ .

**Formates and Alkoxides.**—A mixture of 1.5 g (0.02 mole) of ethyl formate and 1.1 g (0.02 mole) of sodium methoxide reacted with evolution of 344 ml (0.70 equiv) of gas. The reaction proceeded very rapidly at first, but later slowed down.

No reaction was observed between *n*-butyl formate (0.1 mole), sodium methoxide (0.1 mole), and 0.2 mole of methanol in dimethyl sulfoxide.

A white solid was obtained when ethyl formate was allowed to react with sodium methoxide in ether followed by removal of the volatile components by distillation under reduced pressure. No gas evolution was obtained when water was added to this salt.

***n*-Butyl Formate and Sodium.**—A mixture of 2.04 g (0.02 moles) of *n*-butyl formate and sodium (excess) was heated at reflux in 1,2-dimethoxyethane for 6 hr while 410 ml (0.84 equivalents) of gas was evolved. Work-up of the reaction mixture yielded 1-butanol (40%). No methanol or starting material

could be detected in the reaction mixture. Ethyl formate reacted likewise with the evolution of 0.64 equiv of gas.

***n*-Butyl Formate and Triphenylmethylsodium.**—A solution of triphenylmethylsodium (0.05 mole) in dimethyl sulfoxide was prepared by Corey's procedure. Addition of 5.1 g (0.05 mole) of *n*-butyl formate led to a vigorous reaction with the discharge of the red color and the evolution of 0.95 equiv of gas. The only detectable product was 1-butanol.

No reaction was observed between *n*-butyl formate and triphenylmethyl sodium at  $-20^\circ$ .

***n*-Butyl Formate, Benzyl Bromide and Sodium Hydride.**—A mixture of 11 ml (0.1 mole) of *n*-butyl formate, 12 ml (0.1 mole) of benzyl bromide, and 2.3 g (0.1 mole) of sodium hydride was heated at reflux in 100 ml of benzene for 18 hr. The reaction mixture was poured into water and extracted with benzene. The benzene extract was dried over magnesium sulfate and the solvents were then removed by distillation. Distillation of the residue through a 40-cm spinning-band column yielded 7 g (43%) of *n*-butyl benzyl ether. This was identified by infrared and gas chromatographic comparison with an authentic sample synthesized by the reaction of sodium *n*-butoxide with benzyl bromide. Careful search failed to reveal the presence of any *n*-butyl phenylacetate.

**Decomposition of *n*-Butyl Formate in DMSO-*d*<sub>6</sub>.**—Butyl formate (0.102 g, 0.001 mole), 0.5 ml of DMSO-*d*<sub>6</sub>, and 100 mg of potassium *t*-butoxide ( $\sim 0.001$  mole) were allowed to react for 4 min. The reaction mixture was poured into water and extracted with ether. Vapor phase chromatographic analysis of the reaction mixture showed the reaction to be ca. 80% complete (ratio of alcohol/ester was 4/1). The *n*-butyl formate was collected from the vpc and analyzed by mass spectroscopy (see below). Results obtained in two different experiments were 1.49 and 1.34% deuteration.

**Analysis of the Mass Spectrum of Deuterated *n*-Butyl Formate.**—The molecular ion of *n*-butyl formate was too weak to obtain an accurate isotope ratio on our instrument (Consolidated Electrodynamics Corp. Model 21-620). Therefore we obtained an isotope ratio using a peak at  $m/e$  73 and  $m/e$  29 in the mass spectrum. The 73 peak arises by loss of ethyl to give  $(\text{CH}_2\text{CH}_2\text{O}_2\text{CH})^+$  and the peak at 29 is due to  $\text{H}^+\text{C}=\text{O}$  and  $\text{C}_2\text{H}_5^+$ .<sup>17</sup> We obtained the isotope ratios for the 73/74 peaks and 29/30 peaks from a pure sample of *n*-butyl formate and from the deuterated samples. The per cent deuteration was calculated from these measured ratios using the following relationships:  $x/y$  = ratio of the two peaks in the undeuterated sample,  $z$  = per cent deuteration, and  $(x + zy)/[(1 - z)y]$  = ratio of two peaks in the deuterated sample. The results obtained are as follows for the first and second peaks, respectively: 73 peak, 1.49 and 1.34%; 29 peak, 0.35 and 0.40%.

**N-Methylformanilide and Sodium Hydride.**—N-Methylformanilide (6.15 ml, 0.05 mole) and 1.2 g (0.05 mole) of sodium hydride were refluxed in 200 ml of dimethoxyethane, evolving 2150 cc of gas (86% of 1 equiv). Half-life for the reaction was 45 min. The gas was shown to contain carbon monoxide by mass spectroscopy. Extraction of the reaction mixture with dilute hydrochloric acid solution yielded 3.7 g of N-methylaniline (70%). The N-methylaniline was identified by comparison of its infrared spectrum and vpc retention time with those of an authentic sample.

**N-Methylformanilide, Benzyl Bromide, and Sodium Hydride.**—N-methylformanilide (24 ml, 0.2 mole), 48 ml (0.4 mole) of benzyl bromide, and 0.2 mole of sodium hydride were refluxed for 48 hr in 200 ml of dimethoxyethane. The reaction mixture was extracted with dilute hydrochloric acid solution giving a 10% yield of N-methyl-N-benzylaniline, an 11% yield of N-methylaniline, and a 6% yield of the original N-methylformanilide. The products were identified by comparison of infrared spectra and vpc retention times with those of authentic samples.

**N,N-Diethylformamide and Sodium Hydride.**—Diethylformamide (10 g, 0.1 mole) and 2.5 g of sodium hydride were refluxed for 18 hr in 200 ml of dimethoxyethane. The reaction mixture was extracted into ether, and the ether was extracted with dilute hydrochloric acid solution which was washed with more ether, basified, and extracted with ether. The extract was dried over magnesium sulfate and distilled through a 40-cm spinning-band column. A 20% yield of diethylamine was isolated and identified by comparison of its infrared spectrum and vpc retention times

(17) J. H. Benyon, *Anal. Chem.*, **33**, 221 (1961); A. G. Sharkey, *ibid.*, **31**, 87 (1959).

with those of an authentic sample. No other organic compounds were detectable by vpc.

**Synthesis of N-(3-Chloropropyl)formanilide.**—Sodium hydride (2.4 g, 0.1 mole) was added to 12.1 g (0.1 mole) of formanilide dissolved in dimethoxyethane. The salt which formed was added to 31.4 g (0.2 mole) of 1-bromo-3-chloropropane dissolved in 100 ml of dimethoxyethane, and the resulting mixture stirred for 18 hr at room temperature. The reaction mixture was poured into water, extracted with chloroform, and fractionated through a 40-cm spinning-band column. The product had bp 135° (10 mm). The nmr spectrum consisted of two triplets (two protons) at  $\tau$  6.09 and 6.53, a multiplet (two protons) at 8.02, a five-proton multiplet at 2.74, and a one-proton singlet at 1.67.

**Synthesis of N,N'-Diformyl-N,N'-diphenyltrimethylenediamine.**—Formanilide (100 g, 0.83 mole) was added dropwise to a suspension of 20 g of sodium hydride in dimethoxyethane over a period of 1 hr. To this was added 167 g (0.83 mole) of 1,3-dibromopropane, and the resulting mixture was stirred for 3 hr, poured into water, and extracted with ether. The ether extract was washed with water, dried over magnesium sulfate, and evaporated. The product crystallized on cooling and was recrystallized from benzene-hexane giving crystals, mp 105–109°.

*Anal.* Calcd for  $C_{17}H_{18}N_2O_2$ : C, 72.32; H, 6.43; N, 9.92. Found: C, 72.47; H, 6.54; N, 10.13.

**Preparation of N,N'-diphenyltrimethylenediamine from N,N'-Diformyl-N,N'-diphenyltrimethylenediamine.**—A mixture of 2.4 g (0.0085 mole) of N,N'-diformyl-N,N'-diphenyltrimethylenediamine and 0.0085 mole of sodium hydride was refluxed for 2 hr in dimethoxyethane until gas evolution had stopped. The reaction mixture was poured into water and extracted with chloroform, the chloroform was washed with dilute hydrochloric acid, and the aqueous solution was basified and extracted with chloroform. The yield after distillation of the diamine was 1.5 g (79%).

The product had an identical infrared spectrum and tlc  $R_f$  value as an authentic sample.<sup>18</sup>

**Reaction of N-(3-Chloropropyl)formanilide with Sodium Hydride.**—To 28 g (~0.1 mole) of N-(3-chloropropyl)formanilide dissolved in 200 ml of dimethoxyethane was added 2.4 g (0.1 mole) of sodium hydride. Gas was evolved. The reaction mixture was refluxed for 18 hr, poured into water, and extracted with chloroform. The chloroform was extracted with dilute hydrochloric acid, which was basified and extracted with chloroform. Vapor phase chromatography showed the presence of N-allylformanilide and N-(3-chloropropyl)formanilide in the neutral fraction. No other peaks were observed. In the basic fraction, only N-allyl aniline was identified. The original mixture was shown by vpc analysis to consist of 39% N-allylaniline, 30% N-allylformanilide, and 3% N-(3-chloropropyl)formanilide. No 1-phenyl-2-pyrrolidinone<sup>19</sup> was detected.

**Synthesis of N-Benzylaniline.**—To a solution of 6 g (0.05 mole) of formanilide in 100 ml of dimethoxyethane at 25° was added 1.2 g (0.05 mole) of sodium hydride, and the mixture was refluxed for 1 hr. Benzyl bromide (5.9 ml, 0.05 mole) was then added and the mixture refluxed for 18 hr. The reaction was poured into water and extracted with ether, which was dried over magnesium sulfate. The solution was concentrated with a rotary evaporator and the product was chromatographed on a column of activated alumina and recrystallized from methanol-water, giving white needles, mp 36–37°.

**Acknowledgment.**—The authors wish to thank the University of California at Los Angeles Research Committee for financial support.

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## Chloroindoles<sup>1</sup>

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Contribution No. 1966 from the Department of Chemistry, University of California at Los Angeles, Los Angeles, California 90024

Received December 29, 1965

A systematic investigation of the reaction of simple indoles with chlorinating agents is described. Oxindoles react with phosphorus oxychloride to yield 2-chloroindoles, the first examples of unsubstituted 2-haloindoles. Both 2- and 3-chloroindoles are hydrolyzed to oxindoles, thus demonstrating that acidic hydrolysis is unsuitable for differentiating 2-halo- from 3-haloindoles. N-Chlorosuccinimide reacted with 2-methylindole to yield 3-chloro-2-methylindole, and phosphorus pentachloride reacted to yield 3-dichlorophosphoryl-2-methylindole. Skatole reacted with chlorinating agents to give oxindolic products.

The bromination and iodination of simple indoles has been extensively studied.<sup>2,3</sup> These electrophilic substitution reactions preferentially occur at the  $\beta$  position of the indole ring. Blockage of this position allows reaction to take place either  $\alpha$  or in the benzenoid system.<sup>3</sup> Because of this selectivity in the reactions of indole, it is not surprising that there are no authentic syntheses of unsubstituted 2-haloindoles.<sup>4</sup> In this paper, we wish to describe the first preparation of 2-chloroindoles, a systematic investigation of the reactions of simple indoles with chlorinating agents

and solution of the old problem of hydrolysis of 2- and 3-haloindoles yielding the same product.

**Indole.**—Chlorination of indole with sulfuryl chloride produces a mixture of 2,3-dichloroindole and 3-chloroindole (mp 91.5).<sup>5</sup> A cleaner synthetic method for securing the monochloride involves the action of chlorine on 1-benzoylindole followed by alkaline hydrolysis.<sup>6,7</sup> Mazzara and Borgo<sup>5</sup> incorrectly assumed that the monochloride produced in the sulfuryl chloride reaction was substituted at the 2 position since oxindole was obtained from its acidic hydrolysis. This behavior is not unique and several other workers have observed that supposed 3-haloindoles yielded oxindole upon hydrolysis. In order to bury the problem of the structure and hydrolysis of haloindoles, we have prepared authentic 2- and 3-chloroindole and have compared their behavior upon hydrolysis.

The syntheses of 2-chloroindole utilized the Vils-

(1) Presented in part at the Western Regional Meeting of the American Chemical Society, Los Angeles, Calif., Nov 1965.

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(3) K. Piers, C. Meimaroglou, R. V. Jardine, and R. K. Brown, *Can. J. Chem.*, **41**, 2399 (1963); R. M. Acheson and R. W. Snaith, *Proc. Chem. Soc.*, 344 (1963); V. Franzen, *Chem. Ber.*, **87**, 1148 (1954); L. A. Yanovskaya, *Dokl. Akad. Nauk SSSR*, **71**, 693 (1950); *Chem. Abstr.*, **44**, 8354h (1950); A. P. Terent'ev, L. I. Belen'kii, L. A. Yanovskaya, *Zh. Obshch. Khim.*, **24**, 1265 (1954); *Chem. Abstr.*, **49**, 1232f (1955); R. D. Arnold, W. M. Nutter, and W. L. Stepp, *J. Org. Chem.*, **24**, 117 (1959); J. Szmuszkovicz, *ibid.*, **29**, 178 (1964).

(4) Halogenation of 3-substituted indoles occasionally yields substituted 2-haloindoles; see, for example, Q. Mingola, *Gazz. Chim. Ital.*, **60**, 509 (1930).

(5) G. Mazzara and A. Borgo, *ibid.*, **35**, 320, 563 (1905).

(6) R. Weissgerber, *Chem. Ber.*, **46**, 651 (1913).

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