

TABLE I  
 PROPOXYMETHYL ALKYL (OR PHENYL) KETONES, C<sub>3</sub>H<sub>7</sub>OCH<sub>2</sub>COR      2,4-DINITROPHENYLHYDRAZONES

C <sub>3</sub> H <sub>7</sub>	R	Yield, %	B. p., (cor.), mm.	n <sub>D</sub> <sup>20</sup>	d <sub>4</sub> <sup>20</sup>	Molec. refract.		Carbon, %		Hydrogen, %		M. p., °C. (cor.)	Nitrogen, %		
						Calcd.	Found	Calcd.	Found	Calcd.	Found		Calcd.	Found	
<i>n</i> -	-CH <sub>3</sub>	52	49 <sup>a</sup>	6	1.4052	0.9020	31.56	31.55	62.04	61.88	10.41	10.36			
<i>i</i> -	-CH <sub>3</sub>	48	35	10	1.4004	.8918	31.56	31.59	62.04	62.11	10.41	10.40	144	18.92	19.03
<i>n</i> -	-C <sub>2</sub> H <sub>5</sub>	46	56	4	1.4122	.8940	36.18	36.17	64.57	64.26	10.84	10.68			
<i>i</i> -	-C <sub>2</sub> H <sub>5</sub>	41	47	11	1.4082	.8875	36.18	36.18	64.57	64.24	10.84	10.98	103	18.06	18.16
<i>n</i> -	<i>n</i> -C <sub>3</sub> H <sub>7</sub>	64	64	4	1.4155	.8858	40.80	40.80	66.62	66.42	11.18	11.02			
<i>i</i> -	<i>n</i> -C <sub>3</sub> H <sub>7</sub>	42	56	8	1.4120	.8786	40.80	40.82	66.62	66.72	11.18	11.20	98	17.28	17.39
<i>i</i> -	<i>i</i> -C <sub>3</sub> H <sub>7</sub>	35	79	60	1.4147	.8847	40.80	40.80	66.62	66.49	11.18	11.19			
<i>i</i> -	<i>i</i> -C <sub>3</sub> H <sub>7</sub>	8	42	6	1.4095	.8790	40.80	40.56	66.62	65.86	11.18	11.02	89	17.28	17.43
<i>n</i> -	<i>n</i> -C <sub>4</sub> H <sub>9</sub>	51	81	12	1.4210	.8815	45.42	45.44	68.31	68.02	11.47	11.36			
<i>i</i> -	<i>n</i> -C <sub>4</sub> H <sub>9</sub>	37	63	7	1.4196	.8761	45.42	45.38	68.31	68.03	11.47	11.51	78	16.57	16.66
<i>i</i> -	<i>i</i> -C <sub>4</sub> H <sub>9</sub>	25	56	5	1.4138	.8674	45.42	45.54	68.31	68.01	11.47	11.57	95	16.57	16.65
<i>i</i> -	<i>s</i> -C <sub>4</sub> H <sub>9</sub>	11	50	5	1.4165	.8763	45.42	45.33	68.31	67.70	11.47	11.17	61	16.57	16.72
<i>n</i> -	<i>n</i> -C <sub>5</sub> H <sub>11</sub>	48	120	45	1.4240	.8783	50.03	50.04	69.72	69.47	11.70	11.49	73	15.91	16.08
<i>i</i> -	<i>n</i> -C <sub>5</sub> H <sub>11</sub>	45	83	8	1.4209	.8709	50.03	50.12	69.72	69.83	11.70	11.89	77	15.91	16.07
<i>n</i> -	<i>i</i> -C <sub>5</sub> H <sub>11</sub>	46	111	26	1.4230	.8726	50.03	50.02	69.72	69.43	11.70	11.56	79	15.91	16.36
<i>i</i> -	<i>i</i> -C <sub>5</sub> H <sub>11</sub>	30	83	9	1.4189	.8691	50.03	50.02	69.72	69.36	11.70	11.78	82	15.91	16.03
<i>n</i> -	-C <sub>6</sub> H <sub>5</sub>	37	118	6	1.5150	1.0333	51.71 <sup>b</sup>	51.94	74.13	73.87	7.92	7.87			
<i>i</i> -	-C <sub>6</sub> H <sub>5</sub>	40	112	6	1.5129	1.0290	51.71 <sup>b</sup>	51.97	74.13	74.01	7.92	7.77			

<sup>a</sup> Gauthier [*Ann. chim. phys.*, [8] 16, 289 (1909)] reported b. p. 145° (732 mm.); we record b. p. 150° (763 mm.).

<sup>b</sup> Includes 0.65 for exaltation due to C<sub>6</sub>H<sub>5</sub>CO grouping [*J. prakt. Chem.*, [2] 84, 35 (1911)].

viscous reaction mixture to continue. Hydrolysis of the adduct was accomplished with cold hydrochloric acid, usually yielding a deeply red-colored solution. After repeated fractionation, the ketones are stable, colorless liquids with characteristic odor. They decompose slightly when heated to their respective boiling points at atmospheric pressure.

### Summary

The synthesis is reported of sixteen new keto ethers containing either the normal or isopropoxy grouping.

AUSTIN, TEXAS

RECEIVED JANUARY 29, 1942

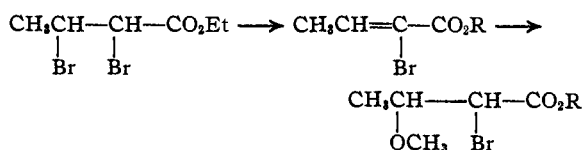
## NOTES

### Synthesis of $\alpha$ -Bromo- $\beta$ -methoxy-*n*-butyric Acid

BY HERBERT E. CARTER AND LUMAN F. NEV

As an intermediate in the synthesis of threonine West and Carter<sup>1</sup> used the mixture of  $\alpha$ -bromo- $\beta$ -methoxy-*n*-butyric acids obtained by brominating a mercuration product of crotonic acid. This mixture of bromomethoxybutyric acids contains approximately 50% of the threonine<sup>2</sup> precursor. Recently Wood and du Vigneaud<sup>3</sup> reported the conversion of ethyl  $\alpha,\beta$ -dibromopropionate to ethyl  $\alpha$ -bromo- $\beta$ -ethoxypropionate by the action of sodium ethylate. It seemed probable that ethyl  $\alpha$ -bromo- $\beta$ -methoxy-

*n*-butyrate might be prepared from ethyl  $\alpha,\beta$ -dibromo-*n*-butyrate in a similar manner. Therefore we have made a study of the reactions



The reaction of ethyl  $\alpha,\beta$ -dibromo-*n*-butyrate with one mole of sodium methylate gives ethyl  $\alpha$ -bromocrotonate together with a small amount of ethyl  $\alpha$ -bromo- $\beta$ -methoxy-*n*-butyrate. However, in the presence of slightly larger quantities of sodium methylate the dibromo ester is converted into the bromomethoxy ester in yields of 80–90%. Ethyl  $\alpha$ -bromocrotonate also gives an excellent yield of bromomethoxy ester when treated with sodium methylate and hence may be considered an intermediate in the above reaction.

(1) West and Carter, *J. Biol. Chem.*, 119, 109 (1937).

(2)  $\alpha$ -Amino- $\beta$ -hydroxy-*n*-butyric acids exist in two racemic forms, *dl*-threonine and *dl*-allo-threonine. Threonine has the same spatial configuration as does threonine, hence the name [Meyer and Rose, *J. Biol. Chem.*, 115, 721 (1936)]. The second form was designated as allthreonine by West and Carter<sup>1</sup> to express its relation to threonine.

(3) Wood and du Vigneaud, *ibid.*, 134, 413 (1940).

The approximate composition of the product was determined by hydrolyzing the ester, aminating the bromo acid, and separating the mixture of aminomethoxybutyric acids thus obtained through the benzoyl derivatives. The yield of benzoylamino-methoxybutyric acid was 50-55% calculated on the ethyl crotonate originally used. Approximately 85% of the product consisted of benzoyl-*dl*-O-methylallothreonine. This series of reactions therefore provides an excellent method for the preparation of allothreonine, while the mercuration procedure remains the preferable method for the synthesis of threonine. It is interesting to note that the addition of sodium methylate to ethyl  $\alpha$ -benzoylamino-crotonate gives mainly the threonine isomer in marked contrast to the behavior of ethyl  $\alpha$ -bromocrotonate.

### Experimental

Each of the reactions was repeated a number of times. Typical results are described below.

**Ethyl  $\alpha,\beta$ -dibromo-*n*-butyrate.**<sup>4</sup>—Ethyl crotonate (570 g. or 5 moles) was placed in a 5-liter three-necked flask fitted with a mechanical stirrer and a dropping funnel. The flask was cooled in an ice-bath and 800 g. (5 moles) of bromine was added slowly with vigorous stirring over a period of seventy-five minutes. The reaction mixture was stirred for fifteen minutes after the bromine addition was completed. The product was distilled under reduced pressure giving 1300 g. (95% yield) of ethyl  $\alpha,\beta$ -dibromo-*n*-butyrate; b. p. 103-104° (17 mm.).

**Ethyl  $\alpha$ -Bromo- $\beta$ -methoxy-*n*-butyrate.**—The reaction of ethyl  $\alpha,\beta$ -dibromobutyrate with sodium methylate was carried out at temperatures ranging from -5 to 25°. No significant difference in the composition of the product was observed over this range.

**Ethyl  $\alpha,\beta$ -dibromo-*n*-butyrate** (1096 g. or 4 moles) was placed in a 5-liter three-necked flask fitted with a stirrer, dropping funnel and calcium chloride tube. The flask was cooled in an ice-bath and a solution of 115 g. (5 moles) of sodium in 2000 cc. of absolute methyl alcohol was added over a period of seventy-five minutes. The stirring was continued for one hour (with cooling). The reaction mixture was then poured into 5 liters of cold water containing 200 cc. of concentrated hydrochloric acid. The ester layer was separated. The aqueous layer was extracted with three 1-liter portions of ether and the ether extracts were combined with the ester layer. This solution was washed with a saturated solution of calcium chloride, then with water and was dried over sodium sulfate. The ether was removed and the residue was distilled under reduced pressure. The yield of ethyl  $\alpha$ -bromo- $\beta$ -methoxy-*n*-butyrate was 720-810 g., 80-90%; b. p. 90-100° (18 mm.).

**$\alpha$ -Bromo- $\beta$ -methoxy-*n*-butyric Acid.**—The bromomethoxy ester (1125 g.) and 1 liter of 0.5 *N* sodium hydroxide were placed in a 5-liter three-necked flask fitted with a

stirrer, dropping funnel and thermometer. The flask was cooled in an ice-bath and vigorously stirred while 1 liter of 5 *N* sodium hydroxide was added at such a rate that the temperature of the reaction mixture was maintained at 15-20°; the addition required about one hour. The ice-bath was then removed and the stirring was continued for thirty minutes. The flask was again cooled while 500 cc. of concentrated hydrochloric acid was added slowly. The bromo acid layer was separated. The aqueous layer was extracted three times with 1-liter portions of ether. The combined ether extracts and bromo acid were washed once with cold water and dried over sodium sulfate. The ether was distilled and water was removed under reduced pressure giving a nearly quantitative yield of crude  $\alpha$ -bromo- $\beta$ -methoxy-*n*-butyric acid. The benzoylamino-methoxybutyric acids were prepared from this material as previously described.<sup>1</sup>

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RECEIVED JANUARY 19, 1942

### The Heat Capacity of Organic Vapors. III. Nitromethane<sup>1</sup>

BY THOS. DE VRIES AND BEN. T. COLLINS<sup>2</sup>

Recently Pitzer and Gwinn<sup>3</sup> published values for the heat capacity of nitromethane and from their data calculated the potential of the barrier to rotation about the C-N bond. At that time similar measurements for nitromethane were completed in this Laboratory and since our data are in excellent agreement with those of Pitzer and Gwinn they are published here in confirmation of their results.

**Experimental.**—A good grade of nitromethane, produced by Commercial Solvents Corporation, was dried over calcium chloride and rectified. Only the middle fraction, approximately 60%, having a boiling range of less than 0.1° was collected for use.

The apparatus and experimental technique described in a previous article<sup>4</sup> was used. Since the values obtained at atmospheric pressure were so much higher than expected,<sup>5</sup> it was decided to make measurements at reduced pressures which were held constant to  $\approx 2$  mm. of mercury pressure. The calibration of the ten-junction thermel at the completion of the research was found to be unchanged.

(1) Abstracted from a thesis to be submitted by B. T. Collins in partial fulfillment of the requirements for the degree of Doctor of Philosophy.

(2) Present address: Stanolind Gas and Oil Co., Tulsa, Okla.

(3) Pitzer and Gwinn. *THIS JOURNAL*, **63**, 3313 (1941).

(4) De Vries and Collins. *ibid.*, **63**, 1343 (1941).

(5) E. B. Wilson, Jr., private communication, 1941.

(4) Goss, Ingold and Thorpe, *J. Chem. Soc.*, **123**, 3342 (1923).