

of the nitroindole in acetic acid solution with stannous chloride in hydrochloric acid. However, when the crude amine was acylated by the method devised by Lumière and Barbier⁹ 6-acetamino-2,3-dimethylindole was obtained in 78% yield. Attempts to prepare the free amine in higher yield by alkaline hydrolysis of the acylated amine gave only an uncrystallizable tarry material.

Experimental¹⁰

6-Amino-2,3-dimethylindole.—2,3-Dimethylindole⁸ was nitrated according to the directions of Plant and Tomlinson.¹ A solution of the 6-nitro-2,3-dimethylindole (10 g.) in 100 ml. of glacial acetic acid was cooled to 30° and 20 g. of stannous chloride dihydrate in 100 ml. of concentrated hydrochloric acid was slowly added, with stirring, so that a sharp rise in temperature of the reaction mixture was avoided. The mixture was then allowed to stand until the reaction temperature began to fall whereupon the clear, reddish solution was heated for one hour on a steam-bath. When cooled in ice, the solution deposited a brown tin double salt which was removed, washed with cold acetic acid and then dispersed in ice-water. Enough 40% sodium hydroxide was added to make the solution basic and remove the tin as the soluble sodium salts. The liberated amine remained in this alkaline solution for 12 hours to permit complete penetration of the solid particles. The greyish amine, which had suffered no apparent change in color during this period, was removed, washed thoroughly with water and dried as rapidly as possible between filter paper. The dried amine was dissolved in benzene and decolorized twice with norite. The clear solution when cooled deposited 1.1 g. (13%) of tan crystals, melting sharply at 119–120°. Since the amine discolors markedly on exposure to air, the filtrations and crystallizations of the benzene solutions were carried out under an atmosphere of nitrogen. However, even after one week's exposure, accompanied by extensive discoloration, the solid amine showed practically no change in its melting point from that of the freshly prepared material.

Anal. Calcd. for C₁₀H₁₂N₂: C, 75.0; H, 7.6. Found: C, 74.9; H, 7.6.

6-Acetamino-2,3-dimethylindole. (a) From 6-Amino-2,3-dimethylindole.—To 6-amino-2,3-dimethylindole (0.35 g.), dissolved in 20 ml. of dry benzene, was added 0.5 ml. of acetic anhydride. A slight rise in temperature occurred while the pale yellow solution first turned reddish, then deposited a colorless precipitate. Ten minutes later the mixture was cooled and the solid separated, washed with benzene and air-dried. The crude material (0.4 g., m.p. 210–212°) when recrystallized from diluted alcohol gave 0.32 g. (72%) of colorless needles melting at 211–212°.

Anal. Calcd. for C₁₂H₁₄N₂O: C, 71.3; H, 7.0. Found: C, 71.0, 71.1; H, 7.0, 6.9.

(b) From 6-Nitro-2,3-dimethylindole.—The crude amine, obtained from the reduction of 44 g. of 6-nitro-2,3-dimethylindole as described above, was dissolved in a slight excess of dilute hydrochloric acid. The clear solution heated to 60° was treated with norite and filtered. To the colorless filtrate was added in succession a slight excess of acetic anhydride, then excess sodium acetate dissolved in water, to liberate the amine from its hydrochloric acid salt.⁹ The crude acylated amine was removed from the cooled solution and air dried (37 g., m.p. 197–200°). Crystallization from diluted alcohol gave 29 g. (62%) of pure, colorless 6-acetamino-2,3-dimethylindole melting at 211–212°. A mixed melting point with the product obtained by method (a) showed no depression.

Two grams of the 6-acetamino-2,3-dimethylindole was refluxed for 2 hours with 100 ml. of 2.5 N aqueous alcohol (2:1). From the cooled solution was obtained 50 mg. of a brown amorphous powder which did not melt under 330°. Evaporation of the liquor to one-third its volume gave a dark precipitate which yielded only a small amount of the original 6-acetamino-2,3-dimethylindole and a tarry material from which no amine could be isolated.

(9) A. Lumière, L. Lumière and H. Barbier, *Bull. soc. chim.*, [3] **33**, 783 (1905); L. F. Fieser, "Experiments in Organic Chemistry," 2nd Ed., D. C. Heath and Co., New York, N. Y., 1941, p. 165.

(10) Melting points are corrected.

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DEPARTMENT OF CHEMISTRY
UNIVERSITY OF ALBERTA
EDMONTON, ALBERTA, CANADA

Preparation of a Series of Carbethoxymethyl Alkanoates¹

BY THEODORE M. BURTON AND WYNN B. FIFE

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Heintz² was able to prepare carbethoxymethyl acetate by the interaction of sodium acetate and ethyl monochloroacetate in a sealed tube. The same compound was obtained by Gal³ using the monobromo instead of the monochloro derivative, and he also prepared carbethoxymethyl butyrate from ethyl monobromoacetate and sodium butyrate. This reaction was further studied by Senff⁴ who prepared the corresponding derivatives from the sodium salts of propionic, butyric, isobutyric, benzoic, phthalic and salicylic acids, but did not purify the diester derivatives of the last three acids cited. Though he reported a reaction with sodium stearate, he was not able to isolate the ester.

When sodium iodide was used as a catalyst, it was found that the reaction of ethyl monochloroacetate with sodium acetate and sodium propionate showed an apparent increase in reaction rate over the uncatalyzed reaction as shown in Table I. However, it was found difficult to separate the diesters from the ethyl iodoacetate (b.p. 178–180°) formed in the course of the reaction. Since the reaction was found to take place at atmospheric pressure on continued refluxing, the carbethoxymethyl alkanoates were obtained in higher purity by the latter method without using a catalyst.

During the course of this investigation it was noted that the rate of reaction increased with increasing length of the carbon chain of the fatty acid. Branching of the carbon chain resulted in a large increase in the speed of the reaction.

Experimental

Ethyl Monochloroacetate.—This compound was prepared in an 85.5% yield, b.p. 136–136.6° (646 mm.), from the esterification of monochloroacetic acid using a modification of the procedure of Vanino.⁵

Sodium Salts of Fatty Acids.—Commercial sodium acetate was fused, cooled, ground in a mortar and used as such. The other salts of fatty acids used in this investigation were prepared from commercially available acids which were purified by careful rectification in a packed column. The slightly acid salts were pulverized in a mortar and dried in a vacuum drying oven for 12 hours at 95° (4 mm.) to remove excess water and acid before being used.

Carbethoxymethyl Alkanoates.—A 500-ml., 3-necked, round-bottomed flask with ground glass joints was equipped with a reflux condenser, a motor-driven Monel metal

(1) This paper contains material abstracted from the thesis of Wynn B. Fife submitted to the faculty of the Utah State Agricultural College in partial fulfillment of the requirements for the degree of Master of Science, June, 1951.

(2) K. Heintz, *Ann.*, **123**, 338 (1862).

(3) H. Gal, *ibid.*, **142**, 371 (1867).

(4) M. Senff, *ibid.*, **208**, 270 (1881).

(5) L. Vanino, "Präparativen Chemie," II Band, Organischen Teil, Verlag von Ferdinand Enke, Stuttgart, Germany, 1937, p. 107.

TABLE I
 CARBETHOXYMETHYL ALKANOATES

The effect of reaction time on yield is illustrated in the case of carbethoxymethyl acetate: 8 hours, 3% yield; 26 hours (with NaI cat.), 69% yield; 48 hours, 44% yield; and for carbethoxymethyl valerate: 1 hour, 14% yield; 24 hours, 82% yield; 48 hours, 55% yield. In this latter 48 hour run, 36.4 g. of a fraction boiling from 114–167° (2 mm.) was obtained. The nature of this higher-boiling fraction was not investigated further as no similar product was observed in any of the other experiments.

R value of acid	Time, hr.	Yield, %	B. p., °C. (60 mm.)	n_D^{20}	d_{20}^{20}	Carbon, %		Hydrogen, %		Saponif. equivalent		Molecular refract.	
						Calcd.	Found	Calcd.	Found	Calcd.	Found	Calcd.	Found
Methyl	48	44	108	1.40999	1.0893	49.31	49.05	6.90	6.81	73.1	71.5	33.22	33.24
Ethyl ^a	24	53	119	1.41296	1.0550	52.49	52.74	7.55	7.57	80.1	80.4	37.83	37.85
<i>n</i> -Propyl	49	61	131	1.41677	1.0314	55.16	54.99	8.10	8.08	87.1	86.9	42.40	42.45
Isopropyl	1 1/4	54	123	1.41354	1.0215	55.16	54.99	8.10	8.13	87.1	88.1	42.40	42.57
<i>n</i> -Butyl	24	77	144	1.42049	1.0159	57.43	57.48	8.57	8.58	94.1	94.8	47.07	46.96
Isobutyl	1	60	137	1.41880	1.0093	57.43	57.18	8.57	8.44	94.1	95.2	47.07	47.07
<i>s</i> -Butyl	1	81	136	1.41926	1.0109	57.43	57.28	8.57	8.54	94.1	93.9	47.07	47.05
<i>t</i> -Butyl	6	75	124	1.41507	1.0012	57.43	57.37	8.57	8.53	94.1	94.6	47.07	47.09
<i>n</i> -Amyl	36	70	155	1.42521	1.0011	59.38	59.30	8.97	8.89	101.1	100.3	51.69	51.68
<i>n</i> -Heptyl	2	91	179	1.42911	0.9723	62.58	62.45	9.63	9.67	115.6	113.4	60.92	61.08

^a In this run 4.0 g. of sodium iodide was used as a catalyst.

stirrer and a thermometer dipping into the reaction mixture. The flask was heated externally with a Glascol heating mantle controlled by a Variac variable transformer. In a typical run, a mixture of from 0.5 to 1.0 mole of the anhydrous sodium salt with a 50–100% excess of ethyl monochloroacetate was added to the reaction flask. The excess ethyl monochloroacetate was used as a solvent to give the mixture sufficient fluidity so that it could be stirred. The mixture was then stirred and heated and began to reflux gently when the temperature of the reaction mixture reached approximately 140°, but it was observed that the mixture became pasty during the heating process and stirring became difficult. Over a period of time the temperature gradually rose to a maximum and then began to drop slowly. At the maximum temperature the gel broke down and stirring became easier. The attainment of the maximum temperature was taken as the end of the reaction. The mixture was cooled, filtered with suction, the salt washed twice with anhydrous ether and the washings added to the filtrate. The ether and excess ethyl monochloroacetate were removed by distillation at atmospheric pressure. The pressure was then lowered and the residue rectified in a 9 mm., 16-inch column packed with 3/32-inch stainless steel helices to produce the yields given in Table I.

The individual esters were further purified by rerectification at 60 mm. pressure using a Unitized Cartesian type manostat⁶ to maintain constant pressure. A 9-mm., 16-inch column packed with 1/8-inch Pyrex glass helices was used to produce the pure esters whose physical constants are summarized in the table. The analytical values for carbon and hydrogen given in the table are the averages of two determinations, none of which varied more than ±0.15 unit from the average. The saponification equivalents cited in the table are also averages of two determinations.

Acknowledgment.—The authors are indebted to the Hooker Electrochemical Company, Niagara Falls, N. Y., and to the Applied Research Laboratories of Armour and Company, Chicago, Ill., for generous samples of their chemical products which were used in this investigation.

(6) R. Gilmont, *Anal. Chem.*, **23**, 157 (1951).

DEPARTMENT OF CHEMISTRY
 UTAH STATE AGRICULTURAL COLLEGE
 LOGAN, UTAH

Desulfuration of Thioamides

BY M. W. CRONYN AND JUDSON E. GOODRICH

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Since nitriles are readily converted into thioamides¹ under mild conditions, the reduction of a

(1) A. Cahours, *Compt. rend.*, **27**, 239 (1848); S. Gabriel and P. Heymann, *Ber.*, **23**, 158 (1890); K. Kindler, *Ann.*, **431**, 187 (1923).

nitrile to an aldehyde *via* Raney nickel desulfuration of the thioamide would be an attractive process if the yields obtainable in the desulfuration step were satisfactory.

At the time this desulfuration was studied there had been no examples of the reduction of a thioamide to an aldehyde reported in the literature^{2,3}; although two *N*-substituted thiobenzamides had been reduced to benzaldehyde. Ciusa,⁴ using zinc and potassium hydroxide, obtained a 42% yield of benzaldehyde from thiobenzanilide and Kindler¹ was able to convert *N,N*-dimethylthiobenzamide into benzaldehyde in 40% yield by electrolytic reduction.

With thiobenzamide as a model the desulfuration was studied under a variety of conditions. Several types of Raney nickel catalysts were used, W-2, the commercial catalyst,⁵ nickel deactivated by acetone at 25°, or at the refluxing temperature for an hour, or by acetone and ammonium hydroxide at 25°. The best results, 32% of benzaldehyde isolated as the 2,4-dinitrophenylhydrazone, were obtained with the last named catalyst in a ratio of 41:1 in ethanol at 25°. Usually, the reaction was complete in 15 minutes or less with yields ranging from 15 to 30%.

No better results were obtained in acetone or *t*-butyl alcohol and higher temperatures and longer reaction times gave less recovered starting thioamide and more reduction of the aldimine to the amine or condensation to hydrobenzamide.

Several thioanilides were treated with Raney nickel since it was expected that the resulting anils would be more stable than the corresponding aldimines. This was found to be the case and a

(2) After this work had been completed D. Brovet (*Arkiv Kemi*, **20**, 70 (1948); *C. A.*, **44**, 6830 (1950)) reported a 77% yield of benzaldehyde, isolated as the dinitrophenylhydrazone, by the desulfuration of thiobenzamide. There is a possibility that a suitably deactivated nickel might give such a yield, but this is not stated in Brovet's report.

(3) E. C. Kornfeld (*J. Org. Chem.*, **16**, 131 (1951)) has recently described the conversion of thioamides to amines by means of Raney nickel. C. D. Hurd and B. Rudner (*THIS JOURNAL*, **73**, 5157 (1951)) have also studied the desulfuration of several substituted thioamides.

(4) R. Ciusa, *Atti R. Accad. dei Lincei Roma*, [5] **15**, II, 381 (1906); *Chem. Zentr.*, **76**, I, 28 (1907).

(5) Obtained from the Gilman Paint and Varnish Co., Chattanooga, Tenn.