No evidence for the acetylation of VI was obtainable, using acetic anhydride in pyridine or in glacial acetic acid. Also V was unacetylated by treatment with acetic anhydride and sodium acetate at 100°.

Summary

Ethylacetonylbarbituric acid may be made in good yields from sodium ethylbarbiturate and chloroacetone in the presence of a little sodium iodide. Several cyclic acetals were prepared by reaction of ethylacetonylbarbituric acid with glycols, including a nitro glycol. The nitro acetal was hydrogenated to an amino acetal, and the latter was acetylated with ketene to an acetamido acetal. Pharmacological toxicity data and anticonvulsant tests are included.

EVANSTON, ILLINOIS RECEIVED DECEMBER 8, 1947

NOTES

Amide Vinylogs

BY ROBERT H. BAKER AND ARTHUR H. SCHLESINGER[1]

In a survey of the behavior of ethoxymethylenediketones and esters as alkylating agents toward amines, amides, the Grignard reagent and in Friedel–Crafts and other type reactions some new compounds have been encountered and are described below.[2]

Ethoxymethyleneacetoacetic ester reacts readily with aminoacetic ester and with progressive difficulty with *p*-aminobenzoic ester and urethan to produce open chain amide vinylogs which are cleaved by hydrogen (PtO_2, 2 atm., 25°) as are derivatives of typical amines.[3] Thiourea reacts to form the mercaptopyrimidine similar to the cyclization product of the urea derivatives.[3]

Experimental[4]

Ethyl α-(N-Carbethoxyaminomethylene)-acetoacetate.—Equimolar quantities of ethyl ethoxymethyleneacetoacetate and ethyl carbamate were heated at 143–165° for 1.7 hours and then cooled at 0° for three hours to induce crystallization. Three crystallizations from cyclohexane, employing activated alumina as decolorizing agent, produced yellow needles, m. p. 40.5–41.0°; 13% yield.

Anal. Calcd. for $C_{10}H_{15}NO_5$: C, 52.3; H, 6.55; N, 6.11. Found: C, 52.4; H, 6.90; N, 6.10.

Ethyl α-(*p*-Carbethoxyanilinomethylene)-acetoacetate.—This was produced similar to the above from ethyl *p*-aminobenzoate at 110–135° for one hour. It was decolorized in hot ethanol solution by alumina. Five crystallizations from ethanol, then from cyclohexane and finally ethanol gave colorless crystals, m. p. 105°, 70% yield.

Anal. Calcd. for $C_{16}H_{19}NO_5$: C, 63.0; H, 6.26; N, 4.60. Found: C, 63.2; H, 6.50; N, 4.50.

Ethyl α-(N-Carbethoxymethylaminomethylene)-acetoacetate.—Slow addition of freshly distilled glycine ethyl ester to an equivalent of the ethoxymethylene compound at 0° produced a vigorous reaction, and the contents of the reaction flask were solid within thirty minutes. Two crystallizations from 70% ethanol gave matted colorless needles, m. p. 71.0–71.5°; 66% yield.

Anal. Calcd. for $C_{11}H_{17}NO_5$: C, 54.4; H, 7.00; N, 5.76. Found: C, 55.2; H, 7.15; N, 5.58.

Ethyl 2-Mercapto-4-methylpyrimidine-5-carboxylate.—Thiourea and an equivalent of the ester vinylog were heated at 150° for thirty minutes. The mixture frothed vigorously and a hard, red solid was obtained which was purified by digestion on the steam-bath with ethanol. The liquors upon chilling gave a red powder which was treated three more times in a similar manner. The red product, 52% yield, failed to melt but sintered at 160° and decomposed. Sublimation *in vacuo* failed to improve its appearance. It is soluble in 10% sodium hydroxide solution and decolorizes iodine.

Anal. Calcd. for $C_6H_{10}N_2O_2S$: N, 14.10. Found: N, 13.94.

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(1) Allied Chemical and Dye Corporation Fellow, 1946–1947.

(2) Except toward amines the results were largely of a negative nature and cannot be published here, *cf.* A. H. S., Ph.D. Thesis, 1947.

(3) Baker and Schlesinger, THIS JOURNAL, **68**, 2009 (1946).

(4) Microanalyses by Patricia Craig and Nelda Mold.

Some Quaternary Ammonium Salts of Substituted Thiazoles

BY CARL T. BAHNER, DONALD PICKENS[1] AND DOROTHY BETTIS BALES[2]

The biological results obtained by Shear and associates[3] at the National Cancer Institute using quaternary salts derived from pyridine and its homologs and benzologs have led us to prepare similar quaternary salts containing the thiazole ring. Particular interest attaches to this series in view of the fact that thiamin chloride is a quaternary salt containing this ring. The substituted thiazoles which we have used are 4-methyl-2-β-hydroxyethylthiazole, 2,4-dimethylthiazole, 2-ethyl-4-methylthiazole, 4-methylthiazole, benzothiazole, and 2-methylbenzothiazole. These have been caused to react with phenacyl and substituted phenacyl bromides and with phenylethyl and cyclohexylethyl halides. Most of these bases reacted with the phenacyl bromides readily upon

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(3) Shear, *et al.*, in "Approaches to Cancer Chemotherapy," American Association for the Advancement of Science, F. R. Moulton, Editor, Washington, D. C., 1947, p. 236 ff.; Hartwell and Kornberg, THIS JOURNAL, **68**, 1131 (1946).

TABLE I

Salt from benzothiazole and	Empirical formula	M. p.,[a] °C.	Yield, %	Ionic halogen, % Calcd.	Found
β-Cyclohexylethyl bromide	$C_{15}H_{20}NSBr$	181	40	26.80	26.75
p-Iodophenacyl bromide	$C_{15}H_{11}NSOBrI$	249–254 dec.	60	17.34	17.26
Phenacyl bromide	$C_{15}H_{12}NSOBr$	244 dec.	65	23.93	24.07[b]
Phenacyl bromide oxime[c]	$C_{15}H_{13}N_2SOBr$	197	30		
β-Phenylethyl iodide	$C_{15}H_{14}NSI$	176	45	34.56	34.39
p-Phenylphenacyl bromide	$C_{21}H_{16}NSOBr$	248	50	19.49	19.57
2,4-Dimethylthiazole and					
β-Cyclohexylethyl bromide	$C_{13}H_{22}NSBr$	193	35	26.25	26.09
p-Iodophenacyl bromide	$C_{13}H_{13}NSOBrI$	227 dec.	55	18.25	18.25
Phenacyl bromide	$C_{13}H_{14}NSOBr$	235[d]	60	25.60	25.57
β-Phenylethyl iodide	$C_{13}H_{18}NSI$	233	45	36.70	36.66
2-Ethyl-4-methylthiazole and					
p-Bromophenacyl bromide oxime	$C_{14}H_{16}N_2SOBr_2$	215–222 dec.	50	19.02	18.80
p-Iodophenacyl bromide oxime	$C_{14}H_{16}N_2SOBrI$	206–212 dec.	50	17.11	16.98
p-Methylphenacyl bromide	$C_{15}H_{18}NSOBr$	142	45	23.49	23.20
m-Nitrophenacyl bromide	$C_{14}H_{15}N_2SO_3Br$	200–215 dec.	70	21.53	21.31
2-Methylbenzothiazole and					
β-Phenylethyl iodide	$C_{16}H_{16}NSI$	195	60	33.29	33.24
4-Methyl-5-β-hydroxyethylthiazole and					
p-Iodophenacyl bromide	$C_{14}H_{15}NSO_2BrI$	242 dec.	45	17.07	17.18
Phenacyl bromide	$C_{14}H_{16}NSO_2Br$	172–173	55	23.35	23.34
β-Phenylethyl iodide	$C_{14}H_{18}NSOI$	160	30	33.83	33.73
4-Methylthiazole and					
β-Cyclohexylethyl bromide	$C_{12}H_{20}NSBr$	155	70	27.54	27.48
p-Iodophenacyl bromide	$C_{12}H_{11}NSOBrI$	228–235 dec.	70	18.85	18.85
p-Iodophenacyl bromide oxime	$C_{12}H_{12}N_2SOBrI$	202 dec.	40	18.20	18.20
m-Nitrophenacyl bromide	$C_{12}H_{11}N_2SO_3Br$	231–232 dec.	60	23.29	23.25
Phenacyl bromide	$C_{12}H_{12}NSOBr$	211	90	26.80	26.75

[a] Melting points below 200° are corrected. Others are uncorrected. [b] Also analyzed for C and H by Dr. Carl Tiedcke. Calcd.: C, 53.89; H, 3.59. Found: C, 53.78; H, 3.72. [c] Made by treating phenacylbenzothiazolium bromide with hydroxylamine hydrochloride, a method which gave a very small yield, and also in better yield by mixing benzothiazole with phenacyl bromide oxime prepared by the method given by Korten and Seboll for obtaining the *syn*-form; *Ber.*, **34**, 1907 (1901). On account of difficulty in carrying out a Volhard analysis on this particular compound a Kjeldahl nitrogen analysis was made by Marvel Fielden. Calcd.: N, 8.02. Found: N, 7.91. [d] A melting point of 216° was reported for this compound, crystallized from a different solvent by Kondo and Nagasawa, *J. Pharm. Soc. Japan*, **57**, Abstracts, 308–310 (1937).

heating to 100° for about five minutes, using a small amount of chloroform or ethanol as solvent in those cases where the starting materials alone did not form a homogeneous liquid at 100°, but the benzothiazole and 4-methyl-2-β-hydroxyethylthiazole reacted somewhat more slowly. The phenylethyl and cyclohexylethyl halides were much less reactive and were usually heated with the base three or four days at 100° in a sealed tube. Some substituted benzothiazoles, such as 2-chlorobenzothiazole, 2-methylmercaptobenzothiazole, and 2-phenylbenzothiazole gave little or no crystalline quaternary salt on heating with phenacyl bromide.

The quaternary salts obtained were purified by recrystallization from ethanol and the ionic halogen content determined by Volhard analysis. (Hartwell and Kornberg[4] had found that some compounds which gave satisfactory combustion analyses held the halogen in non-ionic form and appeared not to be the expected quaternary salts.)

(4) Hartwell and Kornberg, THIS JOURNAL, **68**, 868 (1946).

Samples of the salts listed in Table I have been submitted to the National Cancer Institute for testing. Results of the screening tests will be taken into account in planning further syntheses in this series.

Intermediates.—Phenacyl bromide, *p*-bromophenacyl bromide, *p*-phenylphenacyl bromide, β-cyclohexylethyl bromide, benzothiazole, 2-methylmercaptobenzothiazole, 2-phenylbenzothiazole, 2-chlorobenzothiazole, and 2-methylbenzothiazole were purchased from Eastman Kodak Company and phenylethyl iodide from Edcan Laboratories. The 4-methyl-2-β-hydroxyethylthiazole was furnished by Merck and Company. The other halides used were prepared in the usual way by halogenation of the corresponding methylaryl ketones or by the Friedel–Crafts reaction of bromoacetyl bromide with the proper substituted aromatic hydrocarbon. The other substituted thiazoles were made by the method of Schwarz.[5]

(5) W. E. Bachmann, "Organic Syntheses," Vol. XXV, John Wiley and Sons, New York, N. Y., 1945, p. 35.

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CONTRIBUTION FROM THE
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Density Data for Two Methylchlorosilanes

BY E. W. BALIS, W. F. GILLIAM, E. M. HADSELL, H. A. LIEBHAFSKY AND E. H. WINSLOW

Density data for dimethyldichlorosilane (DDS) and for methyltrichlorosilane (MTS), which were used several years ago to lay the foundation for a successful routine method to aid in controlling chlorosilane distillation, are given below. There appear to be no comparable earlier published data.

Pure Compounds.—As a by-product of painstaking distillation work done in 1943, the details of which are to be published later, the following densities (g./ml. at 25°) were obtained on chlorosilanes among the purest ever prepared here: for DDS, 1.0663; for MTS, 1.2691. The corresponding weight percentages of chlorine by hydrolysis were: DDS, 54.93 *vs.* 54.95 (theor.); MTS, 71.19 *vs.* 71.17 (theor.), the deviations from the theoretical being comparable with the possible uncertainty in the atomic weight of silicon.[1]

Temperature Coefficients.—For the interval 25–30°, dilatometric measurements on the best materials available from the pilot plant in 1944[2] yielded the following values for the change in density with temperature (g./ml./°C.): DDS, 0.00145; MTS, 0.00173. These precise results are in good agreement with older data (0.0015 and 0.0018, respectively) obtained on a Westphal balance.

The 50-ml. dilatometer was designed and manipulated to give a precision better than 0.005% in a density determination. Special techniques were required to mitigate the difficulty of handling the methylchlorosilanes, and the dilatometer itself did not change weight by more than a few tenths milligram—if at all—during the measurements.

Volume Additivity.—In order to establish whether any volume change on mixing DDS and MTS is negligible for purposes of routine control, the routine density-balance (to be described elsewhere) was used on DDS[2] and MTS[2], and on six solutions carefully prepared by weight therefrom. The measured densities are given in Table I alongside densities calculated for the solutions on the assumption of volume additivity.

TABLE I

VOLUME ADDITIVITY OF DDS AND MTS AT 27°

Weight fraction DDS	Measured densities, g./ml.	Calculated densities, g./ml.
MTS	1.2593	....
DDS	1.0618	....
0.81450	1.0939	1.0936
.66014	1.1217	1.1216
.42930	1.1665	1.1662
.42930	1.1659	1.1662
.29397	1.1940	1.1940
.14036	1.2275	1.2273

The measured densities tend to exceed those calculated by an amount comparable with the experimental error; consequently, volume additivity could permissibly be assumed in the control work. The data in Table I indicate that this pair of methylchlorosilanes belongs among those for which volume additivity comes closest to being realized, which suggests that a thorough investigation of these and other chlorosilanes along lines laid down by Young[3] would be welcome.

(1) Baxter, Guichard and Whytlaw-Gray, THIS JOURNAL, **69**, 731 (1947). The chlorine titrations were not of atomic weight precision. Correction of the final average chlorine contents for all conceivable sources of error would lower the percentages by 0.02; taking 28.10 as the atomic weight of silicon would produce the same change in the theoretical values. The density data have been corrected for all conceivable sources of error.

(2) The methylchlorosilanes used in the work on temperature coefficients and volume additivity were sufficiently pure for these purposes as the following data show. DDS, density at 25°, 1.065 g./ml.; wt. % Cl by hydrolysis, 54.72, 54.64. MTS, density at 25°, 1.263 g./ml.; wt. % Cl by hydrolysis, 70.64, 70.69.

(3) Young, "Distillation Principles and Processes," Macmillan and Co., Limited, London, England, 1922, pp. 31 *et seq.*

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SCHENECTADY, NEW YORK RECEIVED DECEMBER 17, 1947

p-Bromobenzyl Bromide in the Identification of Some Aromatic Carboxylic Acids

BY B. A. FIEKERS AND E. M. DI GERONIMO

As part of a study of suitable derivatives for the identification of organic acids, *p*-bromobenzyl esters of benzoic acid, some of its derivatives and similar acids have been prepared and characterized in this Laboratory. The general preparation of these esters is given by the equation.

$$p\text{-BrC}_6\text{H}_4\text{CH}_2\text{Br} + \text{NaOCOR} \longrightarrow \text{NaBr} + p\text{-BrC}_6\text{H}_4\text{CH}_2\text{OCOR}$$

Experimental

***p*-Bromobenzyl Bromide.**—This was prepared from *p*-bromotoluene by bromination of the side-chain, using ultraviolet light, quartzware and heat.[1] The solid product was purified by recrystallization from alcohol until a constant melting point (61.5°) was obtained.

Preparation of the Esters.—The sodium salt of the acid was formed by dissolving a slight excess of the acid in 5 ml. of 0.5 *M* sodium carbonate solution. The mixture was refluxed on a steam-bath and water was added sparingly, when necessary, until solution was complete. 1.25 g.

(1) Weizmann and Patai, THIS JOURNAL, **68**, 150 (1946).