was also obtained. *Anal.*[11] Calcd. for $C_5H_{11}OClHg$: Hg, 62.07. Found: Hg, 61.3.

This experiment suggests that many unusual hydroxyalkyl compounds might be synthesized with a trialkylsiloxyalkylmagnesium halide as a convenient reagent.

PITTSBURGH, PENNA. RECEIVED APRIL 25, 1951

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(11) Analysis was by the method of F. C. Whitmore and R. J. Sobatski, THIS JOURNAL, **55**, 1128 (1933).

[CONTRIBUTION FROM THE CHEMICAL FOUNDATION LABORATORY AND THE CHEMISTRY DEPARTMENT OF THE UNIVERSITY OF COLORADO]

Some Reactions of the Sodium Salts of Certain Amides[1]

BY JOSEPH D. PARK, ROBERT D. ENGLERT[1a] AND JOHN S. MEEK

The reactions of the sodium salts of some amides with certain halohydrocarbons were studied. The products formed when alkylene dihalides were used were explained on the basis of inductive effects of the halogen atoms and the relative nucleophilic power of the attacking ion toward hydrogen and carbon. The products were tested for their insecticidal action against the roach, *Periplaneta americana*, and the per cent. knockdown and per cent. kill observed.

In connection with the program in this Laboratory on insecticides, it was of interest to study the reactions of the sodium salts of amides with certain halogen-containing compounds.

Three main methods of synthesis were used: Hepp's[2] procedure using an amide and sodium in an inert solvent such as toluene followed by the addition of a halohydrocarbon; Pictet's[3] method using an amide, potassium hydroxide and a halohydrocarbon in ethyl alcohol; and a method utilizing sodium hydride in much the same manner as has recently been described by Fones.[4]

It was necessary in Hepp's method to use large volumes of solvent and vigorous stirring to complete the reaction of the sodium with the amide reactant. When using sodium hydride, the sodium salt of the amide would coat the granules of the hydride and hinder its complete reaction. It was found that the halohydrocarbon could be included with the initial reactants provided it had no active hydrogen, whereupon the halogen compound would continuously react with the sodium salt of the amide eliminating to a great extent any coating of the sodium hydride granules. By such a procedure the yield of product was considerably increased over that found when using Hepp's method. Both Hepp's procedure and the utilization of sodium hydride to form the sodium salt failed to produce an alkylated product when the amide reactant was a benzenesulfonamide derivative and the insolubility of the sodium salt of the amide in toluene is suggested as a reason for this result. The same benzenesulfonamide derivative was easily alkylated by the method of Pictet in which the sodium salts are soluble in the alcohol solvent.

Titherley[5] found that the reaction between sodamide derivatives of the type RCONHNa reacted normally with various halogen compounds such as alkyl halides, acid chlorides and halogen-substituted esters if R was an aryl group. However, if R was an alkyl group, only small quantities (if any) of product was formed owing to unexpected side reactions.

A much easier way of replacing the sodium atom in the sodium derivatives by alkyl groups, and thus synthesizing various alkyl-substituted amides, is by heating the sodamide with potassium alkyl sulfates (R and R′ = alkyl or aryl)

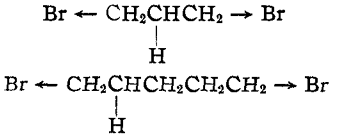
$$RCONHNa + KR'SO_4 \longrightarrow RCONHR' + KNaSO_4$$

This method, however, was not used in the synthesis of the products tested in this program.

Pictet's method has been described as producing good yields of alkylated products from such compounds as acetanilide; however, it was found to fail with a compound such as N-ethylacetamide. Acetanilide has a much greater resonance stabilization than N-ethylacetanilide which would favor the release of the proton.

Sodium N-ethylacetamide was allowed to react with pentamethylene chloride for a week, but only a poor yield of 1,5-bis-(N-ethylacetamide)-pentane was isolated. A good yield of the same product was obtained in 24 hours from pentamethylene bromide. Allylic compounds such as benzyl chloride reacted in a shorter time to produce good yields of alkylated products.

When sodium N-ethylacetamide was treated with pentamethylene bromide the bis-amide was produced; however, with trimethylene bromide N-allyl-N-ethylacetamide was formed. With trimethylene bromide an elimination reaction must have occurred first followed by the usual alkylation reaction. The elimination mechanism (E2) was favored by the inductive (−I) effects of both bromine atoms affecting the same or beta carbon atom favoring the release of a proton. In pentamethylene bromide the inductive effects must pass over a longer carbon chain and consequently a substitution mechanism (S_N2) is favored.



$$Br \leftarrow CH_2\underset{\displaystyle H}{\underset{|}{C}}HCH_2 \rightarrow Br$$

$$Br \leftarrow CH_2\underset{\displaystyle H}{\underset{|}{C}}HCH_2CH_2CH_2 \rightarrow Br$$

When sodium N-ethylbenzenesulfonamide was allowed to react with trimethylene bromide, 1,3-bis-(N-ethylbenzenesulfonamide)-propane was produced. Using the same alkylene dibromide, elimination or substitution can occur as determined by the

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(1) This paper represents part of a thesis submitted by Robert D. Englert to the Graduate School, University of Colorado, in partial fulfillment of the requirements for the degree Doctor of Philosophy, August, 1949.

(1a) Chemical Foundation Fellow in Chemistry.

(2) P. Hepp, *Ber.*, **10**, 327 (1877).

(3) A. Pictet, *ibid.*, **20**, 3422 (1887).

(4) W. W. Fones, Abstracts of Papers of the 115th Meeting of the A.C.S., San Francisco, Calif., March 27–April 1, 1949, p. 60L.

(5) A. W. Titherley, *J. Chem. Soc.*, **79**, 391 (1901).

relative nucleophilic power of the attacking ion toward carbon and hydrogen. A weak base such as the N-ethylbenzenesulfonamido ion produces a substitution reaction with trimethylene bromide, while a strong base such as the N-ethylacetamido ion goes by an elimination mechanism.

The products were tested for their insecticidal activity against the roach, *Periplaneta americana*, but none possessed a high activity. Of the compounds tested N-allyl-N-ethylacetamide and N-benzyl-N-ethylacetamide possessed the highest activities. These data are summarized in Table I.

TABLE I

SUMMARY OF INSECTICIDE TESTING

Compound	Knock-down in 15 min. at concn. 5%	Knock-down in 15 min. at concn. 10%	Kill in 24 hr. at concn. 5%	Kill in 24 hr. at concn. 10%
N-Amyl-N-ethylacetamide		50		20
N-Allyl-N-ethylacetamide	0	20	60	100
N-Ethyldiacetamide		0		60
N-Benzyl-N-ethylacetamide	0	30	40	100
1,5-Bis-(N-ethylacetamido)-pentane[a]	0	0	20	60
1,3-Bis-(N-ethylbenzenesulfonamido)-propane[b]				
Deobase	0	0	0	0

[a] Applied as a suspension since not very soluble in deobase. [b] Not applied since it was a solid insoluble in deobase.

Experimental Part

Melting points were taken on a Fisher–Johns melting point block. Nitrogen analyses were carried out by a modification of a semimicro borate method of Cole and Parks,[6] and bromine was analyzed by a semimicro Volhard method.

Acknowledgment is given to Sharples Chemicals, Inc., Philadelphia, Pennsylvania, for their generous supply of N-ethylacetamide.

N-*n*-Amyl-N-ethylacetamide. Method A.—Toluene (approximately 800 ml.) was distilled over sodium into a two-liter three-necked flask equipped with a mercury-sealed stirrer, a delivery tube and a Friedrich condenser which were protected by calcium chloride tubes. Five and three-quarter grams (0.25 mole) of sodium was added in small pieces to the toluene and the latter was brought to reflux. When the sodium melted, the stirrer was started. Twenty-three and nine-tenths grams (0.275 mole) of N-ethylacetamide was added, and the reaction was refluxed and stirred for about 24 hours. At the end of this reaction period, usually no traces of sodium could be seen, and the mixture would appear as a thin gruel. Thirty-seven and three-tenths grams (0.25 mole) of *n*-amyl bromide was added and the mass again refluxed for about 24 hours. The reaction mixture was cooled and filtered, and the residue washed with toluene. The combined filtrate and washings were stripped of toluene, and the liquid residue distilled. A 7.5-g. (34%) fraction distilling at 82–88° (3 mm.) was collected. On redistillation the compound gave satisfactory analyses; $n^{20}\text{D}$ 1.4458; d^{20}_{20} 0.8921; *MR* calcd. 47.58, found 46.91.

Anal. Calcd. for $C_9H_{19}NO$: N, 8.92. Found: N, 8.87.

Method B.—The same reaction was run using sodium hydride instead of sodium. The amyl bromide was added before all the sodium hydride had reacted. The reaction mixture was worked up as in method A. Fractions distilling at 200–214° and 214–218° (622 mm.) were collected (79.6%). Physical properties were taken on the latter fraction; $n^{20}\text{D}$ 1.4458; d^{20}_{20} 0.8850; *MR* calcd. 47.58, found 47.29.

Method C.—Using Pictet's method, equimolar amounts of potassium hydroxide, N-ethylacetamide and *n*-amyl bromide were allowed to react in ethyl alcohol. On distillation, no amylethylacetamide was isolated.

***n*-Amylethylamine Hydrobromide.**—The compound from method B of the preceding experiment was refluxed for one hour in 80% sulfuric acid. The mixture was neutralized and extracted with ether. The ether extracts were dried over anhydrous sodium sulfate and distilled. A fraction distilling at 126–132° (627 mm.) was collected ($n^{20}\text{D}$ 1.4162). The amine was treated with an excess of 48% hydrobromic acid and evaporated to dryness. The salt was decolorized in *n*-amyl alcohol with charcoal, filtered, and poured into petroleum ether. After filtration and washing with petroleum ether, the process was repeated and a white crystalline compound was obtained melting at 188–189°. The bromine analysis was checked by the Clark Microanalytical Laboratory, Urbana, Illinois.

Anal. Calcd. for $C_7H_{18}BrN$: Br, 40.82. Found: Br, 40.71. Found (Clark): Br, 40.47, 40.49.

N-Allyl-N-ethylacetamide. Method A.—Twenty-three grams (1.0 mole) of sodium in about one liter of technical xylene (distilled over sodium) was allowed to react for about 24 hours with 87 g. (1.0 mole) of N-ethylacetamide at the reflux temperature of the xylene and with vigorous stirring. One hundred and two grams (0.5 mole) of trimethylene bromide was added and the mixture heated and stirred overnight. The mixture was worked up as usual. Fractions distilling at 75–80° and 80–85° (5 mm.) were collected which amounted to a total of 37.9 g. (59.7%). These fractions were combined and distilled with about 25 ml. of acetic anhydride. On purification through further distillation, a water-white product was collected at 185–186° (633 mm.); $n^{20}\text{D}$ 1.4550; d^{20}_{20} 0.9303; *MR* calcd. 36.78, found 36.75. The nitrogen analysis was done by H. J. Gerjovich of this Laboratory.

Anal. Calcd. for $C_7H_{13}NO$: N, 11.02. Found: N, 11.02.

Method B.—The reaction was run as in method A except allyl bromide was used instead of trimethylene bromide and toluene was the solvent medium. On distillation fractions distilling at 75–87° (5 mm.) were collected (60.3%). The combined fractions were distilled with about 20 ml. of acetic anhydride. On purification through further distillation, a fraction was collected at 185–189° (629 mm.); $n^{20}\text{D}$ 1.4555; d^{20}_{20} 0.9413; *MR* calcd. 36.78, found 36.64.

Anal. Calcd. for $C_7H_{13}NO$: N, 11.02. Found: N, 11.09.

N-(2,3-Dibromo-*n*-propyl)-N-ethylacetamide Monohydrate.—N-Allyl-N-ethylacetamide from method A was treated with bromine and the solid that formed was decolorized in and recrystallized from ethyl alcohol. A second recrystallization gave a white crystalline solid melting at 169°. The nitrogen analyses were done by W. A. Harris of this Laboratory. The analyses for bromine, carbon and hydrogen were done by the Clark Microanalytical Laboratory, Urbana, Illinois.

Anal. Calcd. for $C_7H_{15}Br_2NO_2$: N, 4.59; Br, 52.45; C, 27.54; H, 4.92. Found: N, 4.59, 4.64; Br, 51.73, 52.07; C, 27.78; H, 4.79.

N-Allyl-N-ethylacetamide from method B was treated with bromine and the solid purified as before. This solid melted at 169°, and gave no depression of a melting point with the compound derived from the N-allyl-N-ethylacetamide of method A. The nitrogen analysis was done by W. A. Harris.

Anal. Calcd. for $C_7H_{15}Br_2NO_2$: N, 4.59. Found: N, 4.62.

N-Allyl-N-ethyl-3,4-dichlorobenzenesulfonamide.—Hydrolysis of N-allyl-N-ethylacetamide was effected in 15% aqueous sodium hydroxide solution. An 80% yield of N-allyl-N-ethylamine[7,8] distilling at 72–74° (625 mm.) was obtained. Reaction of this amine with 3,4-dichlorobenzenesulfonyl chloride in the presence of dilute sodium hydroxide gave a solid compound which was crystallized twice from alcohol, m.p. 22–23°. The nitrogen analysis was done by H. J. Gerjovich.

Anal. Calcd. for $C_{11}H_{13}Cl_2NO_2S$: N, 4.76. Found: N, 4.61.

N-Ethyldiacetamide.—The last fraction when distilling the reaction mixture from method A of the synthesis of N-allyl-N-ethylacetamide had a distilling range and refractive index near to those of N-ethylacetamide. As elimination occurred in this synthesis, 50% of the amide reactant should

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(6) J. O. Cole and C. R. Parks, *Ind. Eng. Chem., Anal. Ed.*, **18**, 61 (1946).

(7) A. Rinne, *Ann.*, **168**, 262 (1873).

(8) C. Liebermann and C. Paal, *Ber.*, **16**, 523 (1883).

be found in the distillate of the reaction mixture. About 30% was accounted for. The last fraction was distilled with some acetic anhydride, and on purification through further distillation, a product was collected at 183–185° (633 mm.); n^{20}D 1.4513; d^{20}_{20} 1.0166; *MR* calcd. 33.81, found 34.13. Only the density and boiling point are reported in the literature, and the compound had been prepared by a different procedure.[9] The nitrogen analysis was done by H. J. Gerjovich.

Anal. Calcd. for $C_6H_{11}NO_2$: N, 10.84. Found: N, 10.98.

N-Benzyl-N-ethylacetamide.—Exactly 5.75 g. (0.25 mole) of sodium reacted in about 700 ml. of toluene with 23.9 g. (0.275 mole) of N-ethylacetamide for about 48 hours. Thirty-one and six-tenths grams (0.25 mole) of benzyl chloride was added and allowed to react overnight. On distillation, 15 g. (33.9%) of a light yellow liquid was collected at 133–137° (3.5 mm.); n^{20}D 1.5289; d^{20}_{20} 1.0274; *MR* calcd. 52.72, found 53.12. The nitrogen analysis was done by H. J. Gerjovich.

Anal. Calcd. for $C_{11}H_{15}NO$: N, 7.91. Found: N, 7.95.

Gerjovich[10] had previously prepared this compound by alkylation and acetylation of benzylamine. He found that the light yellow liquid distilled at 133–136° (3 mm.), n^{20}D 1.5283.

1,5-Bis-(N-ethylacetamido)-pentane. Method A.—Exactly 11.5 g. (0.5 mole) of sodium reacted for about 24 hours with 47.8 g. (0.55 mole) of N-ethylacetamide. Thirty-five and three-tenths grams (0.25 mole) of pentamethylene chloride was added and reacted for a week. On working up and distilling, 3.5 g. (2.9%) of a viscous oil was collected at 170–202° (2.5 mm.).

Method B.—Exactly 7.67 g. (0.33 mole) of sodium was reacted overnight with 32 g. (0.368 mole) of N-ethylacetamide in about 800 ml. of toluene at its reflux temperature. Thirty-eight and three-tenths grams (0.35 mole) of pentamethylene bromide was then added and reacted overnight. On working up and distilling, 7.6 g. (18.9%) of a viscous oil was collected at 199–200° (3 mm.). On removing the stopcock grease by treatment with charcoal in water, the resulting light yellow oil gave a low nitrogen analysis, calcd. 11.57, found 10.93.

Method C.—Eight grams (0.333 mole) of sodium hydride was reacted overnight in about 800 ml. of toluene with 30 g. (0.345 mole) of N-ethylacetamide and 38.3 g. (0.167 mole) of pentamethylene bromide. After working up and distilling, 16.3 g. (40.4%) of a light yellow, viscous liquid was collected at 197–203° (2.5 mm.). The material was redistilled and filtered through a bed of cotton to remove stopcock grease; n^{20}D 1.4799; d^{20}_{20} 0.9911; *MR* calcd. 69.88, found 69.23.

Anal. Calcd. for $C_{13}H_{26}N_2O_2$: N, 11.57. Found: N, 11.52.

Method D.—Exactly 11.5 g. (0.5 mole) of sodium reacted in about one liter of absolute isopropyl alcohol. When all the sodium had reacted, 44.5 g. (0.511 mole) of N-ethylacetamide was added. The reaction mixture was warmed gently for 15 minutes, and then 57.5 g. (0.25 mole) of pentamethylene bromide was added. Gentle heat was applied for 15 hours, and then the reaction was refluxed vigorously for 24 hours. The reaction mixture was cooled and filtered. On distillation of the filtrate, only N-ethylacetamide was isolated, $n^{19.2}$D 1.4332. Forty-nine grams (95%) of sodium bromide was obtained.

1,5-Bis-(N-ethylbenzenesulfonamido)-propane. Method A.—Eighteen and one-half grams (0.1 mole) of N-ethylbenzenesulfonamide reacted with 2.3 g. (0.1 mole) of sodium in about one liter of toluene for 24 hours. Ten and two-tenths grams (0.05 mole) of trimethylene bromide was added and reacted for 24 hours. The mass was cooled and filtered, and the residue washed with petroleum ether. Distillation of the filtrate gave no isolable product.

Method B.—Thirty-seven grams (0.2 mole) of N-ethylbenzenesulfonamide reacted with 4.8 g. (0.2 mole) of sodium hydride and 20.2 g. of trimethylene bromide in about 800 ml. of toluene for 60 hours. The reaction mass was cooled and filtered and the residue was washed with toluene. Distillation of the filtrate gave no isolable amounts of product.

Method C.—The residue from method A was transferred to an erlenmeyer flask and 100 ml. of ethyl alcohol and 5.1 g. (0.025 mole) of trimethylene bromide was added. The reaction mass was then put on the steam-bath under a reflux condenser for 48 hours. The mixture was filtered and evaporated. An ether solution of the resulting mass was washed with sodium hydroxide solution followed by washing with water until washings were neutral to hydrion paper. The ether was evaporated and the crude product steam distilled to remove any traces of trimethylene bromide. The residue was extracted with ether and the ether extracts dried over magnesium sulfate. On filtration and evaporation of the solvent, a viscous, yellow oil was obtained. This, upon desiccation, amounted to 6.5 g. (63%). It would not crystallize when chilled in a Dry Ice–acetone-bath and was slowly brought to room temperature while scratching the container with a stirring rod. The material was unstable when distilled at atmospheric pressure, but a small portion was microdistilled without decomposition at 190° (11 mm.). The distillate crystallized in the ice-box. On seeding the residue from the microdistillation and the original oil followed by chilling, small crystals started forming. Addition of alcohol caused complete crystallization, and a white solid was isolated and melted at 63–63.5°. Recrystallization from ethyl alcohol gave a white crystalline solid melting at 66–66.5°. A mixed melting point with N-ethylbenzenesulfonamide was 36.5–41°. The nitrogen analyses were done by W. A. Harris.

Anal. Calcd. for $C_{19}H_{26}N_2O_4S_2$: N, 6.83. Found: N, 6.93, 6.79.

Method D.—Five grams (0.027 mole) of N-ethylbenzenesulfonamide was treated with 1.5 g. (0.027 mole) of potassium hydroxide and 2.75 g. (0.0135 mole) of potassium hydroxide and 2.75 g. (0.0135 mole) of trimethylene bromide in about 75 ml. of alcohol. After 24 hours reaction on the steam-bath, the reaction mass was treated as in method C. Four and one-half grams (80.9%) of a yellow oil was isolated which crystallized on seeding. Addition of alcohol completed crystallization and a white compound was isolated melting at 63.5–64.5°. There was no depression in melting point with the material from method C which melted at 63–63.5°.

Insecticide Investigation.—The fog method used was an easy and rapid way to determine relative insecticidal efficacy of organic compounds. The apparatus employed has been used extensively by the West Disinfectant Company, New York, with success. A Lucite cylindrical chamber of approximately one cubic foot volume, 18 inches in height and 12 inches in diameter, was used. It was equipped with a lid in the center of which an aspirator could be placed. One milliliter of 5 or 10% solution (weight:volume) of the candidate insecticide in deobase (deodorized kerosene) was aspirated by nitrogen gas into the chamber. Five to ten roaches, *Periplaneta americana*, were kept in contact with the fog for 15 minutes, after which time they were removed to clean petri dishes for observation. The per cent. knockdown (when a roach is on its back) in 15 minutes, and the per cent. kill (when a roach no longer responds to any stimuli) in 24 hours were noted.

BOULDER, COLORADO RECEIVED JULY 23, 1951

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[9] *Jahresber. Chem.*, **7**, 566 (1854).

[10] H. J. Gerjovich, private communication.