TABLE I

Kinetic Data for Acylation of Amines in Benzene Solution, 30.0°C.

Acid Chloride	Conc'n $\times 10^3$, *M*	Amine	Conc'n $\times 10^3$, *M*	Benzene Solvent	$k_2 \times 10^2$ l. mole^{-1} sec.$^{-1}$
Dimethylcarbamyl chloride	5.67	Piperidine	18.3	Stock	4.95
Dimethylcarbamyl chloride	21.7	Piperidine	43.8	Stock	4.27
Ethyl chloroformate	11.15	*cis*-2,6-Dimethylpiperidine	21.8	Stock	2.18
Ethyl chloroformate	6.38	*cis*-2,6-Dimethylpiperidine	31.2	Stock	2.41
Ethyl chloroformate	5.87	*cis*-2,6-Dimethylpiperidine	22.3	Dry	2.70

cis-2,6-Dimethylpiperidine, b.p. 127.8–128.1°, n_D^{20} 1.4372, was obtained by the hydrogenation of 2,6-lutidine over ruthenium dioxide at 130° and 2000 lb. pressure. *Benzene* was Baker and Adamson Analytical Reagent. Its water content was checked by a Karl Fischer titration.

Acyl chlorides. These were purified as described previously.[2]

Kinetics procedure. Aliquots (5–50 ml.) of standard solutions of the reactants were pipetted into a series of small glass-stoppered separatory-funnels immersed in the bath. Zero time was taken as the moment delivery of the second reactant was begun. At intervals 25 ml. of 0.10 *N* nitric acid and 25 ml. of chloroform or carbon tetrachloride[3] were added together to a funnel. The mixture was shaken momentarily, the lower organic layer was discarded, and the aqueous layer run into a 125-ml. Erlenmeyer flask. The separatory-funnel was rinsed thoroughly with water, which was added to the aqueous layer. Titration of the aqueous layer for chloride ion was performed by the method of Cavanagh as modified by Dostrovsky and Halmann.[4] When contact was made to the titration solution from a *p*H 3.2 buffer across an unlubricated joint, the results appeared to depend on the acidity of the titration solution. Accordingly a salt bridge (6-mm. tubing, 3% Agar, 5% sodium perchlorate) was used to connect the titration solution to a quinhydrone electrode consisting of a 50-ml. Erlenmeyer flask containing a citrate buffer at *p*H 3.2, quinhydrone, and a platinum wire. The potential was measured with a Beckman model G *p*H meter.

Calculations. For the bimolecular reactions at differing initial concentrations, the following formula was used:

$$\log (a - 2x)/(b - x) = (a - 2b)k_2t/2.30 + \log a/b$$

where a is initial concentration of amine, b is that of acid chloride, and x is that of chloride ion. When the initial concentrations of amine and acid chloride were equivalent or nearly so, the following formula[5] was used:

$$1/(d - x) - 1/d = 2k_2t, \text{ where } \frac{a}{2} - s = d,\ b + s = d,$$

where s is the difference between a and b.

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(3) By using solvents denser than water, the hydrolyzable acid chloride is removed in the first separation.

(4) Dostrovsky and Halmann, *J. Chem. Soc.*, 506 (1953).

(5) See Frost and Pearson, *Kinetics and Mechanism*, John Wiley and Sons, Inc., New York, 1953, p. 19.

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Preparation of 2-Hydroxyethylammonium Acetate

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In the course of preparing N-acetylethanolamine (I) in this laboratory, the reaction between acetic anhydride and ethanolamine was investigated. According to Jones[1] the reaction of acetic anhydride and ethanolamine in methanol solution gave a 97% yield of I upon distillation of the product under reduced pressure. We have found, following his technique, that the product consists of an equimolecular mixture of I and the previously unreported 2-hydroxyethylammonium acetate (II).

$$(CH_3OO)_2O + 2\ NH_2CH_2CH_2OH \rightarrow CH_3CONHCH_2CH_2OH\ (I) + CH_3CO\bar{O}H_3\overset{+}{N}CH_2CH_2OH\ (II)$$

Upon distillation at reduced pressure the lower-boiling II is easily separated from I and crystallizes on standing to a hydroscopic, low-melting, solid. On further heating II is converted to I, but only under conditions such that II cannot distill. Vacuum distillation of an equimolecular mixture of acetic acid and ethanolamine, without prior heating, gives a quantitative yield of II.

The isolation of II in this way is surprising in view of a preparation of I by Wenker[2] which consists of merely heating glacial acetic acid and ethanolamine at atmospheric pressure until the stoichiometric amount of water is evolved and then distilling under a vacuum. (A duplication of Wenker's technique gave I in excellent yield). The amide-forming reaction begins at about 160° and is completed when the temperature of the mixture reaches 200–220°. Thus, if the crude product obtained by Jones[1] is distilled at the pressure he re-

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(1) Jones, *J. Org. Chem.*, **9**, 484 (1944).

(2) Wenker, *J. Am. Chem. Soc.*, **57**, 1079 (1935).

ports (2 mm.), II is not converted to I and can be recovered in essentially theoretical yield.

It is of interest to note that Frankel and Cornelius[3] isolated a hydroscopic solid, m.p. 63–65° from the reaction of acetyl chloride and ethanolamine which they erroneously identified as I. Their description indicates it may have been the hydroscopic salt (m.p. 65–66°) described in the present communication.

The identity of II was established by elementary analysis, by conversion to I on continued heating, and by preparation of derivatives of both ethanolamine and acetic acid. The previously unreported 3,5-dinitrobenzoate of N-acetylethanolamine was prepared to assist in the identification of I.

EXPERIMENTAL

To a mechanically stirred solution of 61 g. (1.0 mole) of ethanolamine in 150 ml. of absolute methanol was added 51 g. (0.5 mole) of acetic anhydride over a period of 45 min. The temp. was maintained at 15–25° by external cooling. The reaction mixture then was stirred and heated on the steam-bath for one hour or until it reached a temp. of 90–92°. The residue was distilled through an 8-inch Vigreaux column and two fractions collected. Fraction (1), boiling at 100–110° (2 mm.), solidified in the receiver, wt. 57.5 g. Fraction (2), boiling at 137–138° (0.5 mm.), remained a colorless, viscous oil, wt. 45.5 g. A small intermediate fraction and the pot residue weighed a total of 8 g.

Fraction (2) was identified as *N-acetylethanolamine* (I), n_D^{25} 1.4701 (lit. value, n_D^{25} 1.4710).[4]

Anal. Calc'd for $C_4H_9NO_2$: N, 13.59. Found: N, 13.38.

On warming at 140–150° with less than the calculated amount of 3,5-dinitrobenzoyl chloride, the *3,5-dinitrobenzoate*, m.p. 164–165°, was obtained. It showed no depression in a mixture m.p. determination with a sample prepared from authentic I.

Anal. Calc'd for $C_{11}H_{11}N_3O_7$: C, 44.45; H, 3.73; N, 14.14. Found: C, 44.98; H, 3.88; N, 13.92.

Fraction (1) crystallized with the generation of a large amount of heat. Due to extreme hygroscopicity the melting point was taken after drying under a vacuum on a microscope hot plate,[5] m.p. 65–66°. Redistillation gave b.p. 103–104° (0.7 mm.). Elementary analysis indicated it was *2-hydroxyethyl ammonium acetate* (II).

Anal. Calc'd for $C_4H_{11}NO_3$: C, 39.66; H, 9.15; N, 11.56. Found: C, 39.42; H, 8.88; N, 11.49.

II yielded a *picrate*,[6] m.p. 158–160°, and *dibenzoate*,[7] m.p. 88–89°, neither of which showed depression when mixed with the corresponding derivative of authentic ethanolamine. II also yielded a *p-bromophenacyl ester*,[8] m.p. 84.5–85.0°, which was not depressed on admixture with the *p*-bromophenacyl ester of authentic acetic acid.

II was heated on a hot plate until bubbling had largely ceased (maximum temperature reached was 210°). The oily product was identified as I.

Anal. Calc'd for $C_4H_9NO_2$: N, 13.59. Found: N, 13.65.

The liquid product yielded a 3,5-dinitrobenzoate, m.p. 164°, which was not depressed in a mixture melting point determination with the corresponding derivative of authentic I.

Acetic acid (0.5 mole) was added to ethanolamine (0.5 mole) in 100 ml. of methanol. The solvent was removed at the water pump and the residue was distilled, b.p. 103–104° (0.6 mm.), to give an essentially quantitative yield of II.

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[3] Frankel and Cornelius, *Ber.*, **51**, 1657 (1918).

[4] D'Alelio and Reid, *J. Am. Chem. Soc.*, **59**, 111 (1937).

[5] Kindly performed by Mr. D. G. Grabar.

[6] Klamerth, *Ber.*, **84**, 254 (1951).

[7] Goldberg and Kelly, *J. Chem. Soc.*, 1922 (1948).

[8] Judefind and Reid, *J. Am. Chem. Soc.*, **42**, 1048 (1920).

The Structure and Reactions of Gossypol. III. Aliphatic Anil Derivatives of Gossypol[2]

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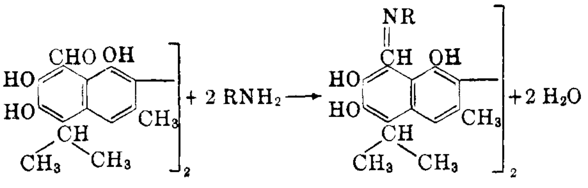
The formation of a derivative of gossypol (I) by its reaction with aniline is a long-known[3] and useful process. The resulting dianilinogossypol (II, R = phenyl) is a stable, crystalline product and its formation has provided the means of removal of gossypol from cottonseed products and detoxification of the gossypol in cottonseed meal. Miller and Adams,[4] prepared some additional aromatic anil derivatives and also isolated a rather unstable diaminogossypol (II, R = H) from the action of liquid ammonia on gossypol. These workers also reported that methylamine, dimethylamine, and piperidine did not form derivatives of gossypol which were sufficiently stable to permit purification.

We have been able to produce stable anils from gossypol and a variety of primary aliphatic amines by heating equivalent quantities of the reactants in isopropyl alcohol. For example, gossypol and dodecylamine produce didodecylaminogossypol (II, R = $C_{12}H_{25}$) in 95% yield. Crude gossypol acetic acid complex can also be used to produce these anils in good yields. The results of a series of experiments are summarized in Table I. Since gossypol and its derivatives are characterized by high melting points with decomposition, the lower melting points



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[1] Preceding paper, Shirley and Dean, *J. Am. Chem. Soc.*, **77**, 6077 (1955).

[2] A report of work conducted under contract with the U. S. Department of Agriculture and authorized by the Research and Marketing Act. The contract is being supervised by the Southern Regional Research Laboratory of the Agricultural Research Service.

[3] Carruth, *J. Am. Chem. Soc.*, **40**, 647 (1918).

[4] Miller and Adams, *J. Am. Chem. Soc.*, **59**, 1736 (1937).