[Contribution from the Department of Chemistry of the Illinois Institute of Technology]

# ALKYLIDENE AND ARYLIDENE DERIVATIVES OF DIAMINOGUANIDINE[1]

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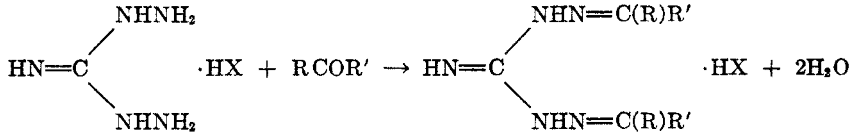
The objectives of this investigation were to study the reactions of diaminoguanidine, in the form of its nitrate salt, with mono-functional aldehydes and ketones in order to provide a background for the study of its reactions with polyfunctional aldehydes and ketones and to extend the number of alkylidene and arylidene derivatives beyond that reported in the literature.

The first reaction of an aromatic aldehyde with diaminoguanidine was reported by Sgolle and Hofmann (1) in 1904. They prepared dibenzylidenediaminoguanidine hydrochloride and the corresponding free base. The same compounds were also reported by Pellizzari and Cantoni (2) and Phillips and Williams (3). Pellizzari and Cantoni (2) also prepared the hydrobromide salt of dibenzylidenediaminoguanidine and Pellizzari and Gaiter (4) prepared the corresponding nitrate salt. Gaiter (5) prepared the *m*-nitrobenzylidene and salicylidene derivatives of diaminoguanidine hydrobromide and the corresponding free bases. Gaiter (5) also reacted glyoxal with a diaminoguanidine salt and conjectured that a heptagonal ring was probably formed. The only ketone derivative reported is that of *p*-acetophenonearsonic acid prepared by Albert (6).

The reaction of monofunctional aldehydes and ketones with salts of diaminoguanidine may be represented as follows:



$$\mathrm{HN{=}C}\begin{matrix}\diagup\ \mathrm{NHNH_2}\\ \diagdown\ \mathrm{NHNH_2}\end{matrix}\cdot\mathrm{HX} + \mathrm{RCOR'} \rightarrow \mathrm{HN{=}C}\begin{matrix}\diagup\ \mathrm{NHN{=}C(R)R'}\\ \diagdown\ \mathrm{NHN{=}C(R)R'}\end{matrix}\cdot\mathrm{HX} + 2\mathrm{H_2O}$$

where R′ is hydrogen in the case of aldehydes. The reaction is acid-catalyzed and proceeds rapidly with aromatic carbonyl compounds in good yield. The salt can be converted to the free base by treating the compound with sodium carbonate solution or dilute ammonium hydroxide. The alkylidene derivatives of diamoguanidine nitrate could not be obtained in the form of crystals. Attempts to obtain crystals resulted in semi-solid gums and oils; however, the picrate salt precipitates readily on addition of a saturated aqueous solution of picric acid. The compounds prepared are summarized in Table I and a few representative preparations are presented in detail in the experimental section.

A number of the arylidene derivatives of diaminoguanidine nitrate were observed to turn light red when exposed to light. These are the diaminoguanidine

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[1] Abstracted from the Senior Research Thesis of Edwin J. Strojny, Illinois Institute of Technology, June 1951.

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TABLE I

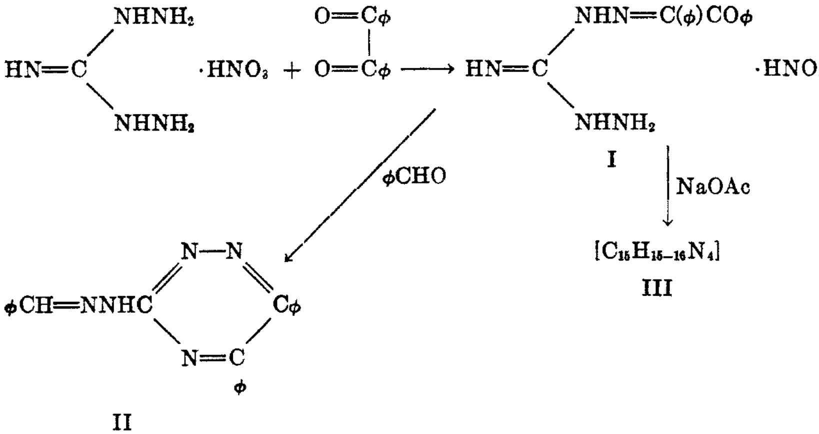
ALKYLIDENE AND ARYLIDENE DERIVATIVES OF DIAMINOGUANIDINE

| REACTION OF DIAMINOGUANIDINE NITRATE WITH | FORM ISOLATED | YIELD, % | CRYSTAL FORM | M.P., °C. | FORMULA | ANALYSIS N |  |
|---|---|---|---|---|---|---|---|
|  |  |  |  |  |  | Calc'd | Found |
| Acetaldehyde | Picrate | 38[a] | Yellow needles | 167–168 | $C_{11}H_{14}N_8O_7$ | 30.26 | 30.21 |
| Cinnamaldehyde | Free base | 91[a] | Yellow powder | 234–236d. | $C_{19}H_{19}N_5$ | 22.07 | 21.62 |
| Cinnamaldehyde | Nitrate | 92[a] | Yellow needles | 207–209d. | $C_{19}H_{20}N_6O_3$[b] | 22.09 | 21.87 |
| *o*-Chlorobenzaldehyde | Free base | 82[c] | Yellow plates | 198–201 | $C_{15}H_{13}Cl_2N_5$ | 20.96 | 21.14 |
| *o*-Chlorobenzaldehyde | Nitrate | 93[a] | White needles | 246.5d. | $C_{15}H_{14}Cl_2N_6O_3$ | 21.16 | 21.02 |
| *p*-Hydroxybenzaldehyde | Nitrate | 95[d] | Straw-colored powder | 240–246d. | $C_{15}H_{16}N_6O_5$ | 23.33 | 23.02 |
| *m*-Nitrobenzaldehyde | Free base | 92[c] | Orange powder | 250–251d.[e] | $C_{15}H_{13}N_7O_4$ | 27.60 | 27.36 |
| *m*-Nitrobenzaldehyde | Hydrobromide | 69 | Orange powder | 292–293d.[f] |  |  |  |
| Piperonal | Nitrate | 82[a] | Cream powder | 206–210d. | $C_{17}H_6N_6O_7$ | 20.19 | 20.10 |
| Propionaldehyde | Picrate | 90[a] | Yellow needles | 168–170d. | $C_{13}H_{18}N_8O_7$ | 28.13 | 28.04 |
| Salicylaldehyde | Free base | 37[a] | Yellow plates | 210–211d.[g] |  |  |  |
| Salicylaldehyde | Nitrate | 65[a] | White powder | 232–234d. | $C_{15}H_{16}N_6O_5$ | 23.33 | 23.56 |
| Acetone | Nitrate | 25[c] | White crystals | 177–179 | $C_7H_{16}N_6O_3$ | 36.19 | 36.55 |
| Acetophenone | Nitrate | 91[h] | White needles | 174d. | $C_{17}H_{20}N_6O_3$ | 23.58 | 23.36 |
| Benzil[i] | Nitrate | 83[c] | White needles | 166–168d. | $C_{15}H_{16}N_6O_4$ | 24.41 | 24.35 |
| Benzophenone | Nitrate | 70[a] | Yellow powder | 188–189d. | $C_{27}H_{24}N_6O_3$ | 17.49 | 17.30 |
| *p*-Bromoacetophenone | Nitrate | 93[a] | White powder | 261–263d. | $C_{17}H_{18}Br_2N_6O_3$ | 16.35 | 16.34 |

[a] Recrystallized from abs. ethyl alcohol. [b] Calc'd: C, 59.99; H, 5.30; Found: C, 60.36; H, 5.68. [c] Recrystallized from methanol. [d] Recrystallized from a 1:1 water-ethyl alcohol mixture. [e] Gaiter (5) reported m.p. 240–242°d. [f] Gaiter (5) reported m.p. 290°d. [g] Gaiter (5) reported m.p. 201–203°d. which corresponds to our uncorrected m.p. of 205°. [h] Recrystallized from a mixture of 40% water in ethyl alcohol. [i] The mono-(aminoguanyl)hydrazone.

derivatives of salicylaldehyde, *o*-chlorobenzaldehyde, *p*-hydroxybenzaldehyde, and piperonal. The initially light yellow color of dicinnamylidenediaminoguanidine nitrate became a deeper yellow when exposed to light, the change taking place only on the surface of the crystals. The time of exposure necessary to bring about a color change varies with the individual compound. The cause of the color change is at present being investigated and will subsequently be reported upon.

From the bifunctional nature of benzil and diaminoguanidine a large number of alicyclic and heterocyclic condensation products could be predicted. However, the reaction of benzil and diaminoguanidine nitrate in a 1:1 and 1:2 molar ratio always resulted in the formation of benzil mono(aminoguanyl)hydrazone (I) in yields as high as 85 percent. The presence of the free hydrazine group in (I) can readily be demonstrated with ammoniacal silver nitrate; however, attempts to react this group with benzaldehyde result in ring closure with the formation of the benzylidene derivative of 3-hydrazino-5,6-diphenyl-1,2,4-triazine (II). Evidence for this structure is based upon the elementary analysis and the data reported by Thiele and Bihan (8) for the reaction of aminoguanidine with aromatic α-diketones. A number of attempts to isolate the free base of I or its cyclized derivative 3-hydrazino-5, 6-diphenyl-1, 2, 4-triazine resulted in the formation of a yellow crystalline compound (III), decomposing at 173–175°. This was quite reproducible and mixture melting points of independent preparations showed no depression. We have as yet been unable to account for the loss of an atom of nitrogen or for the high hydrogen content and attempts to fit the empirical formula into the various possible heterocylic structures have failed. We are continuing our investigation of this substance.



## EXPERIMENTAL[3]

*Aldehydes and ketones.* The various aldehydes and ketones used in this study were purified to accord with the physical properties as reported in the literature.

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[3] All melting points were obtained with a Fisher-John's block and are corrected. Microanalyses are by Micro-Tech Laboratories, Skokie, Illinois.

*Diaminoguanidine nitrate.* This compound was prepared from thiosemicarbazide according to the procedure of Keim, Henry, and Smith (7).[4]

Diethylidene derivative of diaminoguanidine picrate. Diaminoguanidine nitrate (2.00 g., 0.013 mole) was dissolved in about 5 ml. of water. Then 1.20 g. (0.027 mole) of acetaldehyde was added. The reaction mixture was shaken vigorously and allowed to stand at room temperature for about one hour. A saturated water solution of picric acid was added until no further precipitation could be observed upon further addition. The product was washed with water and dried. The crystals were obtained as yellow needles when recrystallized slowly from ethanol. They were found to be insoluble in water, slightly soluble in ether, and soluble in ethyl and methyl alcohols.

*Derivative of acetophenone and diaminoguanidine nitrate.* Diaminoguanidine nitrate (1.00 g., 0.0066 mole) was dissolved in ethanol and acidified with 6 drops of nitric acid. Then 1.56 g. (0.013 mole) of acetophenone was dissolved in 15 ml. of ethanol and the two solutions were mixed and allowed to stand at room temperature for 2 days. The product was collected and dried. A yield of 2.1 g. (91%) was obtained. The compound was found to be slightly soluble in hot water, insoluble in benzene and ether, and soluble in methyl and ethyl alcohols. The derivative was recrystallized first from 40% ethanol, then from 60% ethanol, and a third time from 10% ethanol. In each case the solvent was acidified with 1-2 drops of nitric acid. White cotton-like needles were obtained which decomposed at 174°.

*Dicinnamylidene diaminoguanidine.* (a) *Nitrate salt.* Diaminoguanidine nitrate (1.0 g., 0.0066 mole) was dissolved in 75 ml. of water and 25 ml. of ethanol and acidified with 6 drops of nitric acid. Then 1.72 g. (0.013 mole) of cinnamaldehyde was added and the mixture was agitated. After the product had formed it was collected and dried. A yield of 2.30 g. (92%) was obtained. The derivative was found to be insoluble in hot water, ether, and benzene and soluble in hot ethyl and methyl alcohols. The compound was recrystallized 3 times from ethyl alcohol acidified with 1-2 drops of nitric acid. Light yellow, cotton-like crystals were obtained. A decomposition point of 207–209° was observed. The compound gave a positive $HNO_3$ test with diphenylamine in $H_2SO_4$.

(b) *Free base.* Dicinnamylidenediaminoguanidine nitrate (0.46 g.) was heated in a dilute solution of $NH_4OH$ for about half an hour. The crystals were collected and washed with water. A yield of 0.31 g. (91%) was obtained. The crystals were insoluble in water and only slightly soluble in hot ethanol and methanol. Recrystallization was made from ethyl alcohol. The yellow powder obtained decomposed at 234–236°.

*Benzil mono(aminoguanyl)hydrazone nitrate.* (I). Diaminoguanidine nitrate (3.00 g., 0.020 mole) was dissolved in 20 ml. of water and diluted with 75 ml. of ethyl alcohol. The solution was acidified with 1 ml. of nitric acid. Then 4.17 g. (0.020 mole) of benzil was dissolved in 75 ml. of ethyl alcohol and the two solutions were mixed and heated to about 75° for about 20 minutes. The solution was then concentrated to about half-volume by evaporation of the solvent with the aid of an air jet. The solution was then cooled to 5° and the precipitate collected and washed with ether. A yield of 5.40 g. (83%) was obtained. The compound was found to be slightly soluble in water, insoluble in ether and benzene, and soluble in ethanol and methanol. The compound was recrystallized twice from methyl alcohol. After each recrystallization the crystals were washed with ether. White needles were obtained which decomposed at 166–168°. The test for $HNO_3$ and the free hydrazino-group were positive.

*Benzylidene-3-hydrazino-5,6-diphenyl-1,2,4-triazine.* (II). Benzil mono(aminoguanyl)-hydrazone nitrate (I) (0.50 g., 0.00145 mole) was dissolved in ethyl alcohol and 0.2 ml. (0.002 mole) of benzaldehyde was added. The solution was then evaporated down to near dryness at room temperature with the aid of an air jet. The compound obtained was recrys-

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[4] The conversion of S-methylthiosemicarbazide hydriodide to a diaminoguanidine salt by hydrazinolysis was first carried out by A. H. Greer, Ph.D. Thesis, Polytechnic Institute of Brooklyn, 1949.

tallized twice from methyl alcohol. Yellow crystals, 0.10 g. (19%), were obtained which decomposed at 253°. Tests for $HNO_3$ and hydrazino-groups were negative.

*Anal.* Calc'd for $C_{22}H_{17}N_5$: C, 75.19; H, 4.88; N, 19.93.
Found: C, 75.23; H, 5.11; N, 20.01.

*Reaction of benzil mono(aminoguanyl)hydrazone nitrate* (I) *with sodium acetate. Preparation A.* Compound I (0.50 g.) was dissolved in methanol; then 0.12 g. of sodium acetate was dissolved in methanol and the two solutions were mixed. The solution turned yellow immediately and after a short while precipitation occurred. The product was recrystallized twice from a methanol-water mixture and a yellow compound was obtained which decomposed at 173–175°. Tests for $HNO_3$ and hydrazino-groups were negative.

*Preparation B.* Compound I (0.50 g.) was dissolved in 5 ml. of methyl alcohol and 0.12 g. of sodium acetate was dissolved in 5 ml. of methyl alcohol and combined with the first solution. This was then diluted to 20 ml. with methanol and heated on the steam-bath for 15 minutes. Hot water was then added to the cloud point and the solution was heated 20 minutes longer. The solution was cooled and the precipitate collected. The product was recrystallized twice from a methyl alcohol-water mixture and finally from methyl alcohol. A yellow powder was obtained which gave m.p. 172–175°. A mixture m.p. with *Preparation A* showed no depression.

*Anal.* Found (*Preparation A*): C, 71.53; H, 6.06; N, 22.10.
(*Preparation B*): C, 71.38; H, 6.09; N, 22.01.

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## SUMMARY

Monofunctional aliphatic and aromatic aldehydes and ketones react with diaminoguanidine nitrate to form the corresponding dialkylidene and diarylidene derivatives. The aliphatic aldehyde derivatives of diaminoguanidine can be obtained in the form of picrate salts. Benzil reacts with diaminoguanidine nitrate to form benzil mono(aminoguanyl)hydrazone nitrate (I). This product is obtained exclusively when benzil and diaminoguanidine nitrate are reacted in a 1:1 or 1:2 ratio. Reaction of I with benzaldehyde yields benzylidene-3-hydrazino-5,6-diphenyl-1,2,4-triazine. A total of 14 new aldehyde and ketone derivatives of diaminoguanidine have been prepared and characterized.

CHICAGO, ILLINOIS

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