

The Alkyl Nitrate Nitration of Active Methylene Compounds. III. The Nitration of Aliphatic Amides^{1,2}

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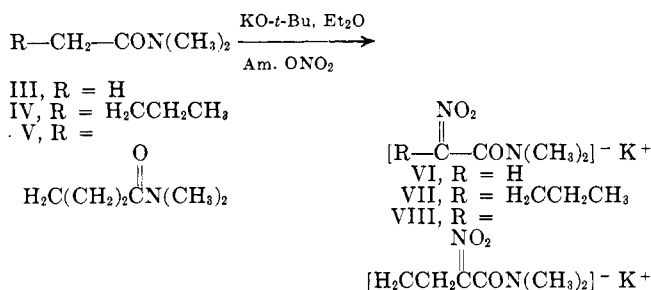
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In continuation of our studies² of the alkyl nitrate nitration of active methylene compounds, we are now reporting our results with aliphatic amides.

When butyramide (I) and N-methylbutyramide (II) were subjected to the alkyl nitrate nitration with potassium *t*-butoxide and amyl nitrate, the desired salts of the α -nitro amides were not obtained; instead only the potassium salts of I and II were formed.³ This was established by the fact that acidification of the salt of I gave essentially a quantitative recovery of I, and treatment of the salt of II with methyl iodide afforded N,N-dimethylbutyramide in a 98% yield.

Since these results indicated that the amido hydrogens interfered with the anion formation at the α -carbon atom which is essential for successful nitration to occur,² it was anticipated that the alkaline nitration would proceed readily with N,N-dialkyl-substituted amides.

When N,N-dimethylacetamide (III), N,N-dimethylbutyramide (IV), and N,N,N',N'-tetramethyladipamide (V) were subjected to the usual nitration conditions,² the expected salts of α -nitro-N,N-dimethylacetamide (VI), α -nitro-N,N-dimethylbutyramide (VII), and α,α' -dinitro-N,N,N',N'-tetramethyladipamide (VIII) were obtained in good yield. The best solvent for these nitration reactions was found to be

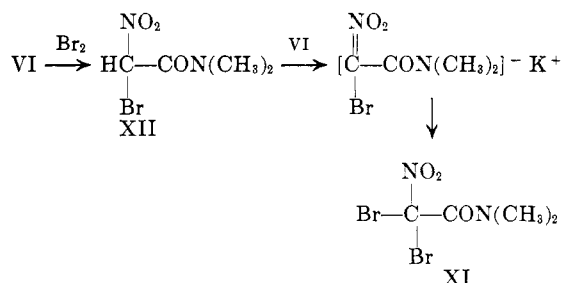


diethyl ether because salts VI, VII, and VIII precipitated during the reaction and could be removed from the reaction mixture by simple filtration. When tetrahydrofuran was employed as the solvent, the isolation

of the nitro salts was difficult because of their high solubility in this solvent.

The salts of these α -nitro amides were found to be highly hygroscopic and upon exposure to the atmosphere tended to decompose with charring because of their high heat of hydration. Attempts to convert these salts to the free α -nitro amides by acidification with hydrogen chloride in dry ether or with glacial acetic acid gave unstable products which evolved oxides of nitrogen.

The identity of these salts was established by conversion to their bromo derivatives² with correct analysis. Anhydrous bromination of salts VII and VIII proceeded normally to afford α -bromo- α -nitro-N,N-dimethylbutyramide (IX) and α,α' -dibromo- α,α' -dinitro-N,N,N',N'-tetramethyladipamide (X). However, bromination of VI gave α,α' -dibromo- α -nitro-N,N-dimethylacetamide (XI) instead of the expected monobromo compound (XII). Formation of XI can be explained by the interaction of unbrominated salt VI with XII to give the salt of XI which subsequently underwent reaction with bromine to give the final product (XI).



Experimental

α -Bromo- α -nitro-N,N-dimethylbutyramide (IX).—N,N'-Dimethylbutyramide⁴ (11.5 g., 0.1 mole), dissolved in 60 ml. of dry ether, was added in 30 min. with stirring to a mixture of 18.5 g. (0.165 mole) of sublimed potassium *t*-butoxide and 70 ml. of dry ether at -70° . This was followed by the dropwise addition (20 min.) of 14.6 g. (0.11 mole) of amyl nitrate dissolved in 30 ml. of dry ether. The Dry Ice bath was removed, and the stirred reaction mixture was allowed to reach room temperature. Collecting the solid through a pressure filtration apparatus under nitrogen, washing with three 50-ml. portions of ether, and drying for 2 days *in vacuo* (1 μ) gave 16.0 g. (81%) of crude potassium α -nitro-N,N-dimethylbutyramide (VII).⁵

A stirred suspension of 1.98 g. (0.01 mole) of VII in 30 ml. of dry ether was cooled to 3° and a solution of 0.8 g. (0.01 mole) of bromine in 30 ml. of dry carbon tetrachloride was added dropwise while maintaining the temperature at $3-5^\circ$. After the reaction mixture was allowed to attain room temperature, potassium bromide was filtered off, and the solvent was removed *in vacuo*. Distilling the remaining oil at 35° (2 μ) in a sublimator and repeating the operation twice gave 1.91 g. (80%) of α -bromo- α -nitro-N,N-dimethylbutyramide (IX), m.p. $73.5-74^\circ$ (overall yield based on N,N-dimethylbutyramide, 64.8%).

(1) From the Ph.D. thesis of B. F. Vincent, Jr., Purdue University, August, 1962.

(2) For previous publications, see H. Feuer, J. W. Shepherd, and C. Savides, *J. Am. Chem. Soc.*, **78**, 4364 (1956); H. Feuer and C. Savides, *ibid.*, **81**, 5826 (1959).

(3) J. N. Rakshit, *J. Chem. Soc.*, **103**, 1557 (1913).

(4) H. C. Brown and W. H. Bonner, *J. Am. Chem. Soc.*, **75**, 14 (1953).

(5) Care should be taken in handling the nitro amide salts because of their tendency to char on exposure to the atmosphere.

Anal. Calcd. for $C_6H_{11}BrN_2O_3$: C, 30.12; H, 4.60; Br, 33.47; N, 11.71. Found: C, 30.05; H, 4.55; Br, 33.39; N, 11.73.

α,α -Dibromo- α -nitro-*N,N*-dimethylacetamide (XI).—Potassium α -nitro-*N,N*-dimethylacetamide (VI, 13.5 g., 79% yield) was prepared from *N,N*-dimethylacetamide by the same procedure as described for VII.

Bromination of VI, as described for VII, gave 9.19 g. (41%) of α,α -dibromo- α -nitro-*N,N*-dimethylacetamide (XI), m.p. 78–79° (over-all yield based on *N,N*-dimethylacetamide, 32.3%).

Anal. Calcd. for $C_4H_8Br_2N_2O_3$: C, 16.55; H, 2.06; Br, 55.17; N, 9.65. Found: C, 16.62; H, 2.04; Br, 55.01; N, 9.62.

N,N,N',N'-Tetramethyladipamide (V).—Into a 1-l. three-necked flask, equipped with a stirrer, thermometer, and Dry Ice-cooled addition funnel topped by a drying tube, were placed 100 g. (0.546 mole) of adipyl chloride and 454 g. of dry ether. The flask was cooled to 3° and 100 g. (2.22 moles) of dimethylamine was added at such a rate that the reaction temperature did not exceed 10°. The reaction mixture then was stirred overnight at 3°, 500 ml. of water was added, and the solution was extracted continuously with ether for 4 days. Evaporating the solvent in a stream of air, recrystallizing the residue from hexane, and then subliming at 50° and 1 μ gave 30.3 g. (28%) of *N,N,N',N'*-tetramethyladipamide (V), m.p. 84–85°.

α,α' -Dibromo- α,α' -dinitro-*N,N,N',N'*-tetramethyladipamide (X).—Into a dried flask were placed 18.5 g. (0.165 mole) of potassium *t*-butoxide and 90 ml. of purified tetrahydrofuran² (THF). The temperature of the reaction mixture was lowered to –20° and 10.2 g. (0.05 mole) of V was added in about 15 min. by means of a solid addition device. Then, an additional 60 ml. of THF was added, the temperature was lowered to –70°, and a solution of 14.6 g. (0.11 mole) of amyl nitrate in 30 ml. of THF was added dropwise in 20 min. Working up the reaction mixture, as described in the preparation of VII, gave 16.2 g. (89%) of crude dipotassium α,α' -dinitro-*N,N,N',N'*-tetramethyladipamide (VIII).

Compound VIII (4.6 g.) was brominated as described in the preparation of IX. Sublimation (110° and 5 μ) of the solid which remained after evaporation of the solvent gave 2.7 g. (48%) of α,α' -dibromo- α,α' -dinitro-*N,N,N',N'*-tetramethyladipamide (X), m.p. 172–173° dec. (over-all yield based on V, 42.7%).

Anal. Calcd. for $C_{10}H_{16}Br_2N_4O_6$: C, 26.78; H, 3.57; Br, 35.71; N, 12.50. Found: C, 27.06; H, 3.89; Br, 35.90; N, 12.31.

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Enamine Chemistry. VII. Cycloaddition Reactions of Ketene Acetals, O,N-Acetals, and N,N-Acetals

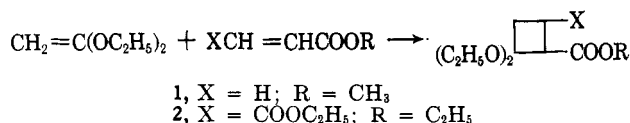
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In an earlier paper of this series,¹ some cycloaddition reactions of enamines with electrophilic olefins were described. In this Note, a limited investigation of similar reactions of ketene acetals, O,N-acetals, and N,N-acetals is described.

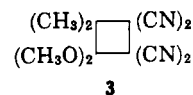
Ketene diethyl acetal was found to react slowly with methyl acrylate in refluxing acetonitrile to give the cycloaddition product 1 in good yield. Although 1



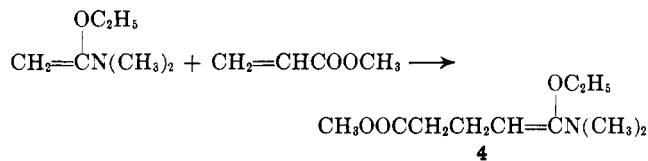
gave the 2,4-dinitrophenylhydrazone of the corresponding β -keto ester, we were not able to obtain the free β -keto ester itself. Moderately vigorous, acid-catalyzed hydrolysis of 1 gave glutaric acid.

Ketene diethyl acetal reacted more slowly with diethyl fumarate in refluxing acetonitrile to give a poor yield of adduct 2.

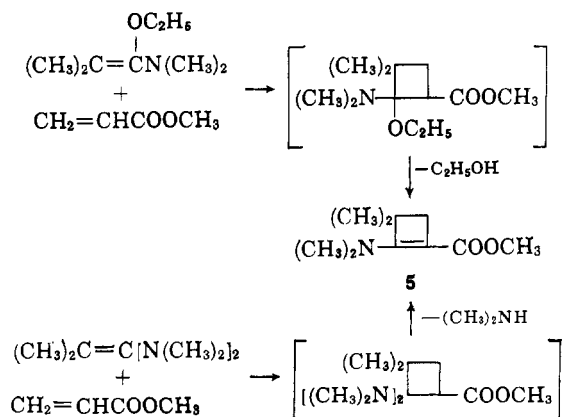
Under conditions comparable to those used with ketene diethyl acetal, no cycloaddition products were obtained from dimethylketene dimethyl acetal and either methyl acrylate or diethyl fumarate. Dimethylketene dimethyl acetal reacted readily with ethene-tetracarbonitrile² to give adduct 3.



No cycloaddition products were obtained from the reactions of 1-ethoxy-*N,N*-dimethylvinylamine with electrophilic olefins. Instead, as shown for methyl acrylate, the Stork³ adduct 4 was obtained.



Both 1-ethoxy-*N,N*,2-trimethylpropenylamine and *N,N,N',N'*,2-pentamethyl-1-propene-1,1-diamine reacted with methyl acrylate to give the cyclobutene derivative 5 in poor yield, presumably by loss of alcohol and dimethylamine, respectively, from the initially formed cyclobutanes.



Experimental

1-Ethoxy-*N,N*-dimethylvinylamine.—This compound was prepared from *N,N*-dimethylacetamide by the method of Meerwein,⁴ except that 1 mole of alcohol-free sodium ethoxide suspended in ether was used in place of excess ethanolic sodium

(2) J. K. Williams, D. W. Wiley, and B. C. McKusick, *J. Am. Chem. Soc.*, **84**, 2210 (1962).

(3) G. Stork, A. Brizzolara, H. Landesman, J. Szmuszkovicz, and R. Terrell, *ibid.*, **85**, 207 (1963).

(4) H. Meerwein, W. Florian, N. Schön, and G. Stopp, *Ann.*, **641**, 1 (1961).

(1) Part IV of this series: K. C. Brannock, A. Bell, R. D. Burpitt, and C. A. Kelly, *J. Org. Chem.*, **29**, 801 (1964).