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 $C_4H_6Br_2N_2O_3$: 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 tetrahydrofuran[2] (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.

Acknowledgment.—Support of this work by the Office of Naval Research is gratefully acknowledged.

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

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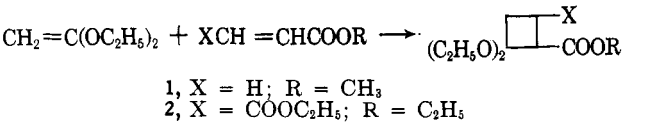
In an earlier paper of this series,[1] some cycloaddition reactions of enamines with electrophilic olefins were described. In this Note, a limited investigation of similar reactions of ketene acetals, O,N-acetals, and N,N-acetals is described.

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

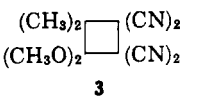


1, X = H; R = CH_3
2, X = $COOC_2H_5$; R = C_2H_5

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.

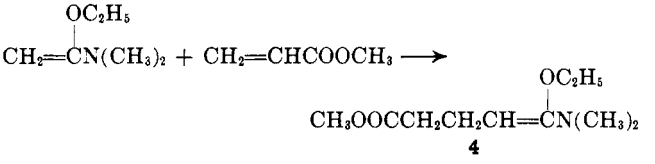
Ketene diethyl acetal reacted more slowly with diethyl fumarate in refluxing acetonitrile to give a poor yield of adduct 2.

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 ethenetetracarbonitrile[2] to give adduct 3.



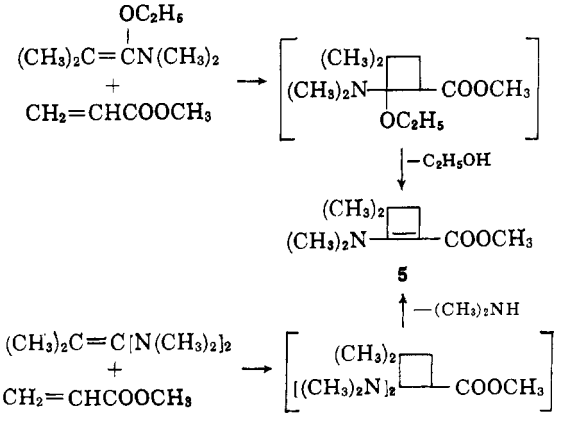
3

No cycloaddition products were obtained from the reactions of 1-ethoxy-N,N-dimethylvinylamine with electrophilic olefins. Instead, as shown for methyl acrylate, the Stork[3] adduct 4 was obtained.



4

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.



5

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

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

(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).

ethoxide. Yields of 73 and 70% of 1-ethoxy-N,N-dimethylvinylamine, b.p. 124–125°, were obtained in runs of 1 and 3 moles, respectively.

1-Ethoxy-N,N,2-trimethylpropenylamine.—The procedure of Meerwein,[4] modified as described above, was applied to the preparation of this compound from N,N-dimethylisobutyramide. The product, b.p. 148–150° (63–65° at 40 mm.), $n^{20}D$ 1.4367, was obtained in 49% yield. Satisfactory elemental analyses were not obtained, possibily because the product reacted with atmospheric moisture. However, its physical properties, including infrared and n.m.r. spectra, were in agreement with the proposed structure. The infrared spectrum contained a strong absorption for >N—C=C< at 5.98 μ. The n.m.r.[5] spectrum consisted of the following absorptions (chemical shift, multiplicity, and assignment are shown): 3.63, quartet, O–CH_2–; 2.64, singlet, N–CH_3; 1.58, singlet, C=C–CH_3; 1.18 p.p.m., triplet, C–CH_3.

N,N,N′,N′,2-Pentamethyl-1-propene-1,1-diamine.—To a solution of N,N-dimethylisobutyramide (57.5 g., 0.5 mole) in tetrahydrofuran (250 ml.) was added phosgene (60 g., 0.6 mole). The resulting mixture was heated at 50–65° with stirring under a Dry Ice-cooled condenser for 1.5 hr., while carbon dioxide was evolved and the mixture separated into two liquid phases. The entire mixture was transferred to a heated dropping funnel and added rapidly to a mixture of dimethylamine (70 g., 1.55 moles), dioxane (150 ml.), and 48 g. of a 50% dispersion of sodium hydride in mineral oil, while the temperature was maintained at 0–10°. The resulting viscous slurry was allowed to stand for 18 days at room temperature, while protected from atmospheric moisture by drying tubes. The mixture was filtered, and the filtrate was distilled *in vacuo* to yield 22.5 g. (32%) of product, b.p. 60–62° (35 mm.), and 15 g. (26%) of recovered amide. Again, satisfactory elemental analyses could not be obtained. However, the infrared spectrum showed a strong absorption at 6.02 μ and the n.m.r. spectrum consisted of singlet absorptions at 2.6 and 1.5 p.p.m. assigned to N–CH_3 and C=C–CH_3 protons, respectively.

Methyl 2,2-Diethoxycyclobutanecarboxylate.—Ketene diethyl acetal (20 g., 0.172 mole), methyl acrylate (15 g., 0.174 mole), and acetonitrile (50 ml.) were combined and refluxed for 190 hr. Distillation of the mixture through a 6-in. Vigreux column gave 22 g. (63%) of methyl 2,2-diethoxycyclobutanecarboxylate, b.p. 52–55° (0.9 mm.), $n^{20}D$ 1.4324. The infrared spectrum showed no absorption between 5.9 and 6.7 μ, and the n.m.r. spectrum showed no olefinic proton absorption.

Anal. Calcd. for $C_{10}H_{18}O_4$: C, 59.4; H, 9.0. Found: C, 59.4; H, 9.2.

The 2,4-dinitrophenylhydrazone (prepared in methanol) melted at 143–145°.

Anal. Calcd. for $C_{12}H_{12}N_4O_6$: C, 46.7; H, 3.9. Found: C, 46.6; H, 4.2.

Hydrolysis of Methyl 2,2-Diethoxycyclobutanecarboxylate.—A mixture of methyl 2,2-diethoxycyclobutanecarboxylate (10 g., 0.049 mole), water (15 ml.), concentrated hydrochloric acid (5 drops), and enough methanol to produce a homogeneous solution was heated on the steam bath for 3.5 hr. in an open beaker. The mixture was cooled and filtered. The solid was recrystallized from benzene to give 4.8 g. (72%) of glutaric acid, which was identical with an authentic sample.

Diethyl 3,3-Diethoxy-1,2-cyclobutanedicarboxylate.—A mixture of ketene diethyl acetal (30 g., 0.259 mole), diethyl fumarate (41 g., 0.24 mole), and acetonitrile (75 ml.) was refluxed for 190 hr. Distillation of the mixture through a 3-in. Vigreux column gave 12 g. (17%) of diethyl 3,3-diethoxy-1,2-cyclobutanedicarboxylate, b.p. 103–109° (0.2 mm.), $n^{20}D$ 1.4421.

Anal. Calcd. for $C_{14}H_{24}O_6$: C, 58.3; H, 8.4. Found: C, 58.5; H, 8.3.

3,3-Diethoxy-4,4-dimethyl-1,1,2,2-cyclobutanetetracarbonitrile.—Dimethylketene dimethyl acetal (4.4 g., 0.038 mole) was added over a 5-min. period to ethenetetracarbonitrile (3.2 g., 0.025 mole) in acetonitrile (25 ml.). The temperature rose to 38° and then dropped to room temperature. The solvent was removed *in vacuo*, and the residue was recrystallized from acetone–hexane to give 5.2 g. (85%) of 3,3-dimethoxy-4,4-dimethyl-1,1,2,2-cyclobutanetetracarbonitrile, m.p. 136–137°.

Anal. Calcd. for $C_{12}H_{12}N_4O_2$: C, 58.9; H, 5.0. Found: C, 59.0; H, 5.3.

Methyl 5-Dimethylamino-5-ethoxy-4-pentenoate.—Methyl acrylate (25.8 g., 0.3 mole) was combined with N,N-dimethyl-1-ethoxyvinylamine (34.5 g., 0.3 mole). The temperature of the mixture rose to 60° over a 0.5-hr. period and then dropped slowly to room temperature. Distillation gave 38 g (61%) of methyl 5-dimethylamino-5-ethoxy-4-pentenoate, b.p. 63–67° (1 mm.), $n^{20}D$ 1.4574. The infrared spectrum showed, besides the ester band, a strong absorption at 6.04 μ, and the n.m.r. spectrum contained an olefinic proton triplet at 3.2 p.p.m.

Anal. Calcd. for $C_{10}H_{19}NO_3$: C, 59.7; H, 9.5; N, 7.0. Found: C, 60.0; H, 9.5; N, 6.9.

The same product was formed when the reaction was carried out at 10° and, on the basis of infrared spectral data, was present prior to distillation. When the analogous compound from ethyl acrylate, b.p. 67–70° (0.5 mm.), $n^{20}D$ 1.4536, was dissolved in ethanol and the resulting solution was added to dilute hydrochloric acid, there was obtained on distillation a 58% yield of diethyl glutarate, identical with an authentic sample.

Methyl 2-Dimethylamino-3,3-dimethyl-1-cyclobutene-1-carboxylate.—A mixture of 1-ethoxy-N,N,2-trimethylpropenylamine (24.8 g., 0.17 mole), methyl acrylate (15 g., 0.17 mole), and acetonitrile (75 ml.) was refluxed for 16 hr. Distillation of the reaction mixture gave 10 g. (40% recovery) of the ethoxyamine starting material and 8.5 g. (44% based on unrecovered starting material) of the product, b.p. 65–68° (0.8 mm.), $n^{20}D$ 1.5121.

Anal. Calcd. for $C_{10}H_{17}NO_2$: C, 65.5; H, 9.3; N, 7.6. Found: C, 65.7; H, 9.3; N, 7.4.

The infrared spectrum showed strong bands at 6.0 and 6.2 μ, and the n.m.r. spectrum was compatible with the proposed structure.

The compound gave the 2,4-dinitrophenylhydrazone of methyl 3,3-dimethyl-2-oxocyclobutanecarboxylate, m.p. 128.5–130°.

Anal. Calcd. for $C_{14}H_{16}N_4O_6$: C, 50.0; H, 4.8; N, 16.6. Found: C, 50.3; H, 5.1; N, 16.3.

Methyl 2-dimethylamino-3,3-dimethyl-1-cyclobutene-1-carboxylate also was obtained in 23% yield from methyl acrylate and N,N,N′,N′,2-pentamethyl-1-propene-1,1-diamine. Some of the diamine was recovered, apparently admixed with methyl 3-dimethylaminopropionate, which was formed by addition of dimethylamine to methyl acrylate.

(5) N.m.r. absorptions are reported in parts per million (p.p.m.) relative to tetramethylsilane.

Evidence Supporting the Occurrence of a 4,5-Dehydropyrimidine in Aminations of Halopyrimidines[1]

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The elimination–addition (benzyne) mechanism for nucleophilic aromatic substitution has been invoked in many heterocyclic systems; included among these are pyridines,[2] quinolines,[3] and pyridazines.[4] This mode of substitution apparently has not been postulated yet for such transformations in pyrimidines.

Because reactions involving a benzyne-type intermediate generally occur in cases of nonactivated aryl halides, 2-methyl-5-chloropyrimidine (I) was selected as a precursor for the 4,5-dehydropyrimidine. The C-5 of the pyrimidine ring is relatively electron-rich

(1) This investigation was supported by Grant CA-02857 from the National Cancer Institute, National Institutes of Health, U. S. Public Health Service.

(2) For pertinent references, see (a) T. Kauffmann and F.-P. Boettcher, *Chem. Ber.*, **95**, 1528 (1962); (b) R. J. Martens and H. J. den Hertog, *Tetrahedron Letters*, **No. 15**, 643 (1962).

(3) T. Kauffmann, F.-P. Boettcher, and J. Hansen, *Ann.*, **659**, 102 (1962).

(4) T. Kauffmann and A. Risberg, *Tetrahedron Letters*, **No. 22**, 1459 (1963).