A Ketenimine from the Addition of a Carbene to an Isocyanide

ENGELBERT CIGANEK

Contribution No. 1599 from the Central Research Department, Experimental Station, E. I. du Pont de Nemours and Company, Wilmington, Delaware 19898

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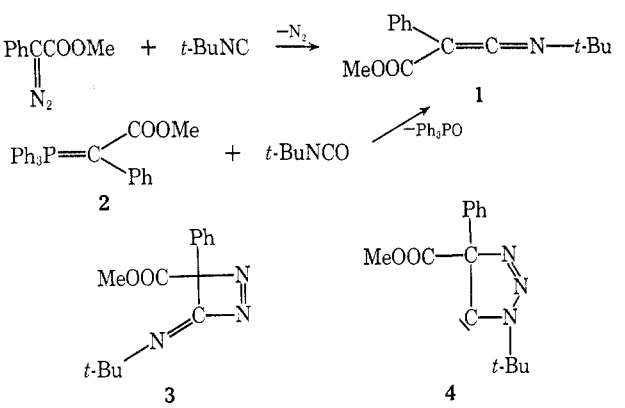
Although carbenes and isocyanides, two formally divalent species, might be expected to react with each other to give ketenimines, only one attempt to demonstrate such an addition appears to have been recorded. Dichlorocarbene, generated from potassium trichloroacetate in alcohols, reacts with cyclohexyl isocyanide to give N-cyclohexyldichloroacetimidates, the adducts of alcohols to dichloroketene-N-cyclohexylimine.[1] We find that the ketenimine **1** is obtained in 51% yield on thermolysis of methyl phenyldiazoacetate in *t*-butyl isocyanide (Scheme I). An authentic sample of **1** was prepared by a Wittig reaction between *t*-butyl isocyanate and the phosphorane **2**. On the basis of the available evidence, it cannot be ruled out completely that the diazo ester initially adds to *t*-butyl isocyanide to form intermediates such as **3** or **4**, which then lose nitrogen to give **1**. However, the most likely reaction path involves initial nitrogen loss from methyl phenyldiazoacetate followed by α addition of phenylmethoxycarbonylcarbene to *t*-butyl isocyanide, especially since the reaction requires heating to a temperature at which methyl phenyldiazoacetate is known[2] to decompose with loss of nitrogen.

SCHEME I



Experimental Section

Thermolysis of Methyl Phenyldiazoacetate in *t*-Butyl Isocyanide.—A mixture of 3.10 g of methyl phenyldiazoacetate[3] and 8.87 g of *t*-butyl isocyanide was placed in a Carius tube. The tube was sealed under vacuum and heated to 140° for 6 hr. Removal of the excess isocyanide and short-path distillation of the residue at 120–140° bath temperature (2 μ) gave 2.07 g (51%) of phenylmethoxycarbonylketene-N-*t*-butylimine, identified by comparison of its infrared and nmr spectra with those of an authentic sample (see below).

Phenylmethoxycarbonylketene-N-*t*-butylimine.—A mixture of 6.55 g of methyl triphenylphosphoranylidenephenylacetate[4] and 20 ml of *t*-butyl isocyanate, contained in a sealed Carius tube, was stirred at 103° for 24 hr. The excess *t*-butyl isocyanate was removed under vacuum; ethyl acetate (15 ml) was added to the residue; the mixture was heated to the boiling point, cooled, and filtered. The solids were washed with ethyl acetate and dried to give 3.38 g of triphenylphosphine oxide, identified by its infrared spectrum. The combined filtrates were concentrated to dryness, and the residue was short-path distilled at a bath temperature of 100–130° (0.2 μ) to give 3.39 g (92% yield) of phenylmethoxycarbonylketene-N-*t*-butylimine as a very pale yellow oil: uv max (cyclohexane) 300 mμ (sh, ϵ 5500), 268 (10,000), and 243 (9300); ir (CCl_4) 2040 and 1710 cm^{-1}, among others; nmr ($CDCl_3$) τ 2.0–2.7 (m, 5, phenyl), 6.0 (s, 3, COOMe), and 8.2 (s, 9, CMe_3).

Anal. Calcd for $C_{14}H_{17}NO_2$: C, 72.70; H, 7.41; N, 6.06. Found: C, 72.41; H, 7.66; N, 5.83.

Registry No.—**1**, 22979-24-4.

(1) A. Halleux, *Angew. Chem.*, **76**, 889 (1964).
(2) E. Ciganek, unpublished observation.
(3) E. Ciganek, *J. Org. Chem.*, **35**, 862 (1970).
(4) H. J. Bestmann and H. Schulz, *Ann.*, **674**, 11 (1964).

α-Aryl- and α-Cyanodiazoacetic Esters

ENGELBERT CIGANEK

Contribution No. 1600 from the Central Research Department, Experimental Station, E. I. du Pont de Nemours and Company, Wilmington, Delaware 19898

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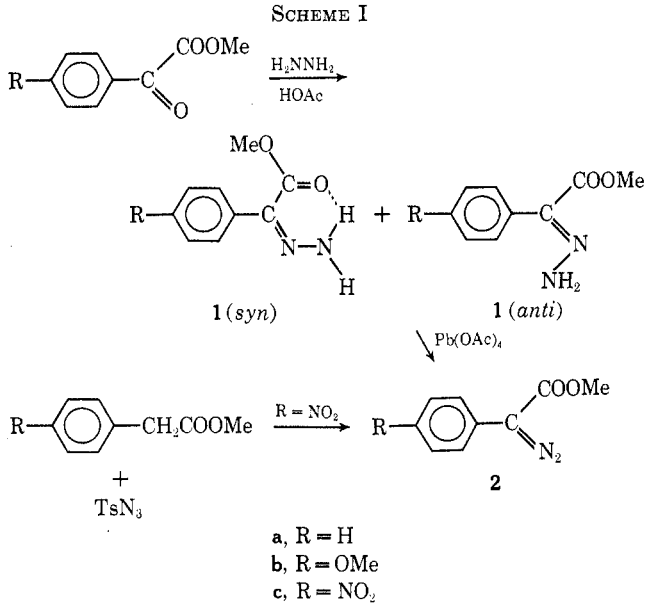
For a study of the effect of substituents on the norcaradiene–cycloheptatriene equilibrium,[1] we required, among others, methyl phenyldiazoacetate (**2a**) and its *p*-methoxy (**2b**) and *p*-nitro derivatives (**2c**), as well as methyl cyanodiazoacetate (**5**). Impure ethyl phenyldiazoacetate has been prepared in poor yield by diazotization of ethyl phenylglycinate.[2] The Bamford–Stevens reaction of methyl phenylglyoxylate *p*-toluenesulfonylhydrazone has been reported[3] to give methyl phenyldiazoacetate (**2a**), also of only 63% purity. Ethyl *p*-nitrophenyldiazoacetate has been prepared by reaction of *p*-toluenesulfonyl azide with ethyl *p*-nitrophenylacetate.[4] We find that pure methyl phenyldiazoacetate (**2a**) can be obtained in 89% overall yield from commercially available methyl phenylglyoxylate *via* lead tetraacetate oxidation[5] of the hydrazones **1a** (Scheme I). Reaction of methyl phenylglyoxylate with hydrazine in glacial acetic acid gave a mixture of two isomeric hydrazones **1a** in a ratio of 60:40.[6] The two isomers could be separated; the major isomer was assigned the intramolecularly hydrogen-bonded *syn*[7] structure on the basis of its lower boiling point, the lower field chemical shift of the amino protons (τ 1.5 *vs.* 3.8 in the *anti* isomer), and the insensitivity of the N–H

(1) The synthesis and structure determination of the benzene adducts of the carbenes derived from the diazo compounds described in this note will be the subject of a forthcoming publication.
(2) T. Curtius and E. Müller, *Ber.*, **37**, 1261 (1904); *cf.* A. Kossel, *ibid.*, **24**, 4145 (1891).
(3) I. Moritani, T. Hosokawa, and N. Obata, *J. Org. Chem.*, **34**, 670 (1969).
(4) (a) W. Pelz, U. S. Patent 2,950,273 (1960); *Chem. Abstr.*, **55**, 2116 (1961); (b) M. Regitz, *Chem. Ber.*, **98**, 1210 (1965).
(5) E. Ciganek, *J. Org. Chem.*, **30**, 4198 (1965).
(6) One of the two isomers of **1a** has recently been prepared by a more circuitous route: H. Neunhoeffer, *Ann. Chem.*, **722**, 38 (1969); no stereochemistry was assigned but on the basis of the reported melting point it appears to be the *anti* isomer.
(7) The terms *syn* and *anti* refer to the relationship of the amino to the methoxycarbonyl group in **1**.

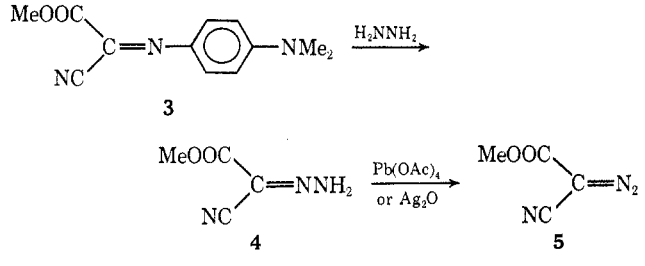
SCHEME I



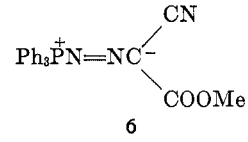
stretching absorptions in the infrared spectrum to changes in concentration (see Experimental Section). The two isomers do not interconvert in solution at room temperature. It has not been established whether the isomer composition reflects the thermodynamic equilibrium or whether it is a consequence of kinetic control.

A 20:80 mixture of the *ortho* and *para* isomers of methyl methoxyphenylglyoxylate was obtained on Friedel–Crafts addition of methyl chloroglyoxylate to anisole. Treatment of this mixture with hydrazine in glacial acetic acid gave two hydrazones in a ratio of 87:17. Since the minor isomer was most likely the hydrazone of methyl *o*-methoxyphenylglyoxylate,[8] only one of two possible isomers of **1b** appeared to have been formed. Infrared data indicate that it is the *syn* isomer. Pure **1b** (43% yield based on methyl *p*-methoxyphenylglyoxylate) was obtained by crystallization of the isomer mixture. Oxidation with lead tetraacetate gave the diazo ester **2b** in 84% yield. Methyl *p*-nitrophenyldiazoacetate (**2c**) was prepared by the method of Regitz.[4b]

Hydrazinolysis[9] of methyl (*p*-dimethylaminophenylimino)cyanoacetate (**3**)[10] gave methyl cyanoglyoxylate hydrazone (**4**) in low yield. Judging from the chemical



shift of the amino protons and the absence of concentration dependence of the N–H stretching bands, only the isomer having the amino and methoxycarbonyl groups in *syn* relationship was isolated. Oxidation of **4** with silver oxide or lead tetraacetate gave methyl cyanodiazoacetate as a yellow oil. In view of the potential hazards,[5] purification by distillation was not attempted. The diazo ester was characterized by its infrared and nmr spectra, and by conversion, in 93% yield, to the triphenylphosphazine **6**.



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Experimental Section

Methyl Phenylglyoxylate Hydrazone (*syn* **and** *anti* **Isomers**).—Hydrazine hydrate (110 ml) was added to a stirred and cooled mixture of 180 ml of water and 180 ml of acetic acid, keeping the temperature below 25°. Methyl phenylglyoxylate (177.4 g; material obtained from Columbia Organic Chemicals Co. was redistilled) was added followed by sufficient methanol to produce a homogeneous solution (*ca.* 550 ml). The mixture stood at room temperature for 65 hr and was then concentrated at room temperature under vacuum, using a rotary evaporator. Water and methylene chloride were added to the residue, the layers were separated, and the aqueous phase was extracted several times with methylene chloride. The combined extracts were washed with 5% hydrochloric acid, 5% sodium bicarbonate solution, water, and concentrated sodium chloride solution, and dried ($MgSO_4$). Removal of the solvent and rapid short-path distillation of the residue gave 176.7 g (92%) of a mixture of the *syn* and *anti* isomers of methyl phenylglyoxylate hydrazone, boiling at a bath tempeature of 70–130° (0.1 μ). The ratio of the *syn* and *anti* isomers in the crude product before distillation was 60:40 as determined by integration of the nmr spectrum. Slow molecular distillation at 0.1 μ resulted in almost complete separation of the isomers, the *syn* isomer boiling at a bath temperature of 70°, the *anti* isomer at 110–130°. Both solidified on standing. An analytical sample of the *syn* isomer was prepared by two crystallizations from hexane–benzene (5:3) at −20°: mp 40–41°; uv max (cyclohexane) 298 mμ (ϵ 7700) and 232 (10,800); ir (KBr) 3450, 3280, 1695, and 1575 cm^{-1}, among others; (CCl_4) 3470, 3280, 1700, 1570, and 1530 cm^{-1}, among others (there is no change on dilution); nmr (in $CDCl_3$) τ 1.5 (broadened singlet, 2, NH_2), 2.5–3.1 (m, 5, phenyl), and 6.5 (s, 3, COOMe).

Anal. Calcd for $C_9H_{10}N_2O_2$: C, 60.66; H, 5.65; N, 15.72. Found: C, 60.48; H, 5.79; N, 15.70.

An analytical sample of the *anti* isomer, mp 70–71° (lit.[6] mp 70–71°), was prepared by crystallization from benzene–cyclohexane. To remove all solvent the sample had to be ground and heated to 56° (0.1 mm) for 2 hr: uv max (cyclohexane) 258 mμ (ϵ 7100) and 218 (sh, 9400) (Beer's law was not followed; the extinction coefficients are for a 6×10^{-5} *M* solution); ir (KBr) 3400, 3280, 3180, 1725, 1620, and 1550 cm^{-1}, among others, and (CCl_4) 3500, 3400, 3280, 3200, 1725, 1610, and 1575 cm^{-1}, among others (the band at 3500 is very weak at high concentration but becomes the strongest of the N–H bands at low concentration; conversely the band at 3200 becomes weaker on dilution; the intensities of the other N–H and the COOMe bands do not appear to change); nmr ($CDCl_3$) 2.5–3.1 (m, 5, phenyl), 3.7 (broad singlet, 2, NH_2), and 6.5 (s, 3, COOMe).

Anal. Calcd for $C_9H_{10}N_2O_2$: C, 60.66; H, 5.65; N, 15.72. Found: C, 60.99; H, 5.68; N, 16.00.

Methyl Phenyldiazoacetate.—The acetic acid was removed from a commercial sample of lead tetraacetate (22.46 g) by heating to 40° (0.1 mm) for 30 min. Nitrogen was admitted and 100 ml of methylene chloride was added. The mixture was cooled with ice, and a solution of 5.74 g of methyl phenylglyoxylate hydrazone (mixture of *syn* and *anti* isomers) in 20 ml of methylene chloride was added, with mechanical stirring, over 5 min. Stirring was continued for 5 min, Celite and water (50 ml) were added, and the mixture was filtered after another 5 min. The solids were washed twice with methylene chloride. The layers of the filtrate were separated; the organic phase was washed with

(8) The aromatic region in the nmr spectrum of the crude mixture appeared to be too complex for a mixture of two *para*-disubstituted phenyl derivatives.

(9) The procedure is an adaptation of the method of Shechter and Bernard, to whom we are grateful for the experimental details prior to publication.

(10) F. Bell, *J. Chem. Soc.*, 516 (1957).

water and concentrated sodium chloride solution, and dried ($MgSO_4$). Removal of the solvent and short-path distillation gave 5.50 g (97%) of methyl phenyldiazoacetate, boiling at a bath temperature of 62–64° (0.3 μ): $n^{25}D$ 1.5779; uv max (cyclohexane) 440 mμ (ε 65) 298 (sh, 5700), 280 (9300), 275 (sh, 9100), 253 (sh, 14,000), and 246 (15,000); ir (CCl_4) 2090 and 1715 cm^{-1}, among others; nmr ($CDCl_3$) τ 2.6–3.2 (m, 5, phenyl) and 6.3 (s, 3, COOMe).

Anal. Calcd for $C_9H_8N_2O_2$: C, 61.35; H, 4.58; N, 15.90. Found: C, 61.73; H, 4.94; N, 16.31.

Methyl *p*-Methoxyphenylglyoxylate Hydrazone.—Friedel–Crafts addition[11] of methyl chloroglyoxylate[12] to anisole gave, in 77% yield, a mixture of methyl *o*- and *p*-methoxyphenylglyoxylate (ratio *ca.* 20:80): bp 94–102° (1 μ), $n^{25}D$ 1.5486–1.5519, as a pale yellow oil which solidified on standing. Hydrazine hydrate (42 ml) was added slowly to a cooled mixture of 70 ml of glacial acetic acid and 70 ml of water, followed by 58.27 g of the above mixture of isomers and 200 ml of methanol. After the mixture had been stirred at room temperature for 64 hr, most of the methanol was removed under reduced pressure. Water and methylene chloride were added to the residue, the layers were separated, and the aqueous phase was extracted several times with methylene chloride. The combined extracts were washed with water, 5% hydrochloric acid, 5% sodium bicarbonate solution, and concentrated sodium chloride solution, and dried. Removal of the solvent gave 64.4 g of a semisolid, the nmr spectrum of which indicated that it was a mixture of methyl *o*- and *p*-methoxyphenylglyoxylate hydrazone (ratio 17:83). Crystallization from benzene (100 ml) gave 21.5 g (43%) of methyl *p*-methoxyphenylglyoxylate hydrazone, mp 140–142°. An analytical sample (ethyl acetate) had mp 142–143°; nmr ($CDCl_3$) 2.7–3.1 (m, 4, phenyl), 3.6 (broad singlet, 2, NH_2), and 6.2 (two singlets, separation 1.5 cps, three each, OMe and COOMe); uv max (dioxane) 270 mμ (ε 10,000) and 228 (13,100); ir (KBr) 3400, 3290, 3230, and 1715 cm^{-1}, among others; the N–H stretching region is insensitive to concentration changes (in CH_2Cl_2).

Anal. Calcd for $C_{10}H_{12}N_2O_3$: C, 57.68; H, 5.81; N, 13.46. Found: C, 57.69; H, 5.85; N, 13.54.

Methyl *p*-Methoxyphenyldiazoacetate.—To a solution of 61.1 g (weight after removal of the acetic acid) of lead tetraacetate in 400 ml of methylene chloride was added, with external cooling (ice bath), 19.17 g of methyl *p*-methoxyphenylglyoxylate hydrazone. The mixture was stirred at room temperature for 5 min, Celite and water (100 ml) were added, and the mixture was filtered after being stirred for 1 min. The layers of the filtrate were separated; the organic layer was washed with concentrated sodium chloride solution and dried. Removal of the solvent and crystallization of the residue from 30 ml of cyclohexane gave 15.06 g of methyl *p*-methoxyphenyldiazoacetate, mp 50.5–51.5°, in the form of orange crystals. An additional 0.82 g of this product was obtained by removal of the solvent from the mother liquor and crystallization of the residue from 6 ml of cyclohexane: combined yield 15.88 g (84%); nmr ($CDCl_3$) τ 2.6–3.1 (AB quartet, split further, 4, phenyl) and 6.2 (two singlets, three each, OMe and COOMe); uv max (cyclohexane) 450 mμ (ε 103), 283 (11,000), and 250 (18,000); ir (CCl_4) 2100, 1720 cm^{-1}; (KBr) 2095, 1705 cm^{-1}.

Anal. Calcd for $C_{10}H_{10}N_2O_3$: C, 58.24; H, 4.89; N, 13.59. Found: C, 58.01; H, 4.94; N, 13.25.

Methyl *p*-nitrophenyldiazoacetate was prepared in 60% yield from methyl *p*-nitrophenylacetate by the method of Regitz.[4b] The product had mp 149–150° dec (crystallization from ethyl acetate); nmr ($CDCl_3$) 1.8–2.5 (AB quartet, split further, 4, phenyl) and 6.1 (s, 3, COOMe); uv max (cyclohexane) 440 (sh, ε 120), 330 (17,000), and 272 (11,000); ir (CCl_4) 2110, 1735 cm^{-1}; (KBr) 2100, 1715 cm^{-1}.

Anal. Calcd for $C_9H_7N_3O_4$: C, 48.87; H, 3.19; N, 19.00. Found: C, 48.66; H, 3.17; N, 18.74.

Methyl Cyanoglyoxylate Hydrazone.—To a stirred mixture of 11.0 g of methyl (*p*-dimethylaminophenylimino)cyanoacetate[10] and 250 ml of glacial acetic acid was added, dropwise, 12 g of anhydrous hydrazine. After the mixture had been stirred at 80° for 1 hr, most of the acetic acid was removed under vacuum. Methylene chloride and concentrated sodium chloride were added to the residue, the mixture was filtered, and the insoluble crystalline solid was washed with water and methylene chloride and dried, to give 0.51 g of methyl cyanoglyoxylate hydrazone. The layers of the filtrate were separated, and the aqueous phase was extracted repeatedly with methylene chloride (a total of 400 ml). The combined extracts were washed with concentrated sodium chloride solution and dried. Removal of the solvent gave another 1.05 g of methyl cyanoglyoxylate hydrazone, yield of crude product 1.56 g (25%). This material was used directly for the preparation of methyl cyanodiazoacetate. An analytical sample, mp 171–171.5°, was obtained by sublimation (1 μ; 100–110° bath temperature) followed by chromatography on Florisil (elution with tetrahydrofuran–methylene chloride 5:95) and crystallization from acetonitrile: nmr ($(CD_3)_2CO$) τ 0.7–1.8 (broad band, 2, NH_2) and 6.1 (s, 3, COOMe); uv max (MeCN) 280 mμ (14,100); ir (KBr) 3330, 3180, 2970, 2220, 1715, 1650, 1550 cm^{-1}, among others.

Anal. Calcd for $C_4H_5N_3O_2$: C, 37.80; H, 3.97; N, 33.06. Found: C, 37.53; H, 3.82; N, 33.06.

Methyl Cyanodiazoacetate.—A mixture of 244 mg of methyl cyanoglyoxylate hydrazone, 1.4 g of silver oxide, 2.4 g of magnesium sulfate, and 20 ml of methylene chloride was stirred at room temperature for 2 hr. Removal of the solvent from the filtered solution gave 241 mg of methyl cyanodiazoacetate as a yellow oil: ir (neat) 2225, 2140, and 1720 cm^{-1}, among others; nmr ($CDCl_3$) τ 6.1 (s, COOMe). To a solution of 230 mg of this material in 5 ml of ether was added 502 mg of triphenylphosphine. Methyl cyanodiazoacetate triphenylphosphazine (660 mg, 93% yield based on methyl cyanoglyoxylate hydrazone), mp 189–190° dec, precipitated immediately (the melting point remained unchanged on crystallization from benzene): nmr ($CDCl_3$) τ 2.1–2.7 (m, 15, phenyl) and 6.2 (s, 3, COOMe); uv max (MeCN) 325 mμ (ε 27,000), 275 (6500), 268 (6500) 262 (sh, 5600), and 225 (sh, 28,000); ir (KBr) 2200, 1735 cm^{-1}, among others.

Anal. Calcd for $C_{22}H_{18}N_3O_2P$: C, 68.21; H, 4.69; N, 10.85; P, 7.99. Found: C, 68.26; H, 4.61; N, 10.85; P, 7.90.

Registry No.—**1a** (*syn*), 22979-32-4; **1a** (*anti*), 22979-33-5; **1b** (*syn*), 22979-34-6; **2a**, 22979-35-7; **2b**, 22979-36-8; **2c**, 22812-58-4; **4** (*syn*), 22979-25-5; **5**, 22979-38-0; **6**, 23031-07-4.

(11) K. Kindler, W. Metzendorf, and D. Y. Kwok, *Ber.*, **76**, 308 (1943).
(12) S. J. Rhoads and R. E. Michel, *J. Amer. Chem. Soc.*, **85**, 585 (1963).

Sodium Borohydride Reduction of Aza Lactones[1]

PRICE TRUITT AND J. CHAKRAVARTY

Department of Chemistry, North Texas State University, Denton, Texas 76203

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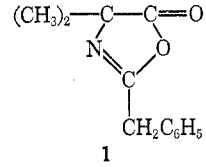
The recent report of Meyers and coworkers[2] concerning the sodium borohydride reduction of dihydrooxazines for the production of aldehydes prompted us to investigate the reduction of some 2-oxazoline-5-ones (aza lactones) with the view of producing aldehydes from these easily formed compounds.

2-Benzyl-4,4-dimethyl-2-oxazoline-5-one (**1**) and 2-phenyl-2-oxazoline-5-one (**2**) were selected as representative aza lactones for this study.



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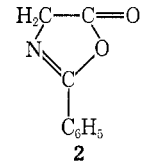

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(1) This investigation was supported by Research Grant No. CA-10530 from the National Cancer Institute.
(2) A. I. Meyers, A. Nabeya, H. W. Adickes, and I. R. Politzer, *J. Amer. Chem. Soc.*, **91**, 763 (1969).