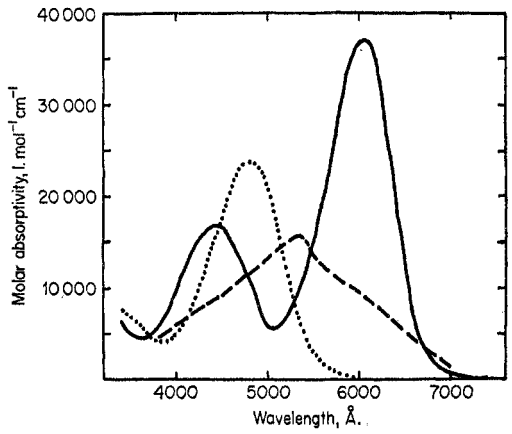
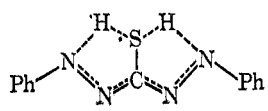


Figure 1.—Electronic spectra of three forms of diphenylthiocarbazone: ———, methylene chloride at room temperature; ·····, alkaline methylene chloride–methanol at room temperature (~0.005 *N* NaOH in 95% (vol) methylene chloride–5% methanol); – – – –, hexane at ~1°, while irradiated with the full intensity of the near-infrared tungsten lamp in the Cary 14.

(or at least broadening) of the τ −2.03 peak at low temperature instead of the slight narrowing which was observed.

We propose structure **1** to represent the green form existing in neutral solutions of dithizone.



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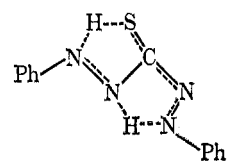

2

Structure **2**, which can be obtained by isomerization about a carbon–nitrogen double bond, may be responsible for the red, metastable form. The nmr spectrum of this form cannot be studied, since the incident light beam is completely absorbed at the surface of the concentrated solutions required for nmr. Consequently only a small fraction of the molecules is converted to the metastable form.

The exact explanation for the intensity of the long-wavelength peak in the spectrum of the green form is still lacking, but it appears unlikely that a simple thiol–thione tautomeric system can account for the spectrum.

Registry No.—Dithizone, 60-10-6.

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Reaction of Diazomethane with Some α,β-Unsaturated Acetals and Aldehydes

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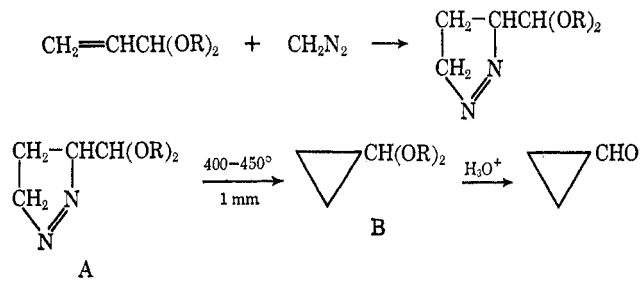
A fairly recent report[1] has described an improved method of synthesis of cyclopropanecarboxaldehyde by ceric nitrate oxidation of cyclopropylcarbinol. We wish to report a new synthesis of this aldehyde which represents at least a more economical method, since cyclopropylcarbinol is a relatively expensive starting material. This procedure involves a three-step sequence with various acrolein acetals as starting materials—each step being accomplished in good to excellent yields. Acrolein acetals, including the cyclic 2-vinyl-1,3-dioxolanes and 2-vinyl-1,3-dioxanes, can be obtained commerically or may be conveniently prepared from acrolein.[2] Reaction of diazomethane with the unsaturated acetal forms a 1-pyrazoline. This can be readily pyrolyzed to the corresponding acetal of cyclopropane carboxaldehyde, which is then hydrolyzed to the aldehyde. Overall yields for the three steps ranged as high as 50%. Table I lists yields, physical



constants, and elementary analytical data for compounds of types A and B as prepared from different acrolein acetals.

The pyrazolines obtained from all of the acrolein acetals used were of the indicated Δ^1 structure, as evidenced by the lack of an NH absorption band near 3400 cm^{-1} and the presence of an N=N absorption at 1540 cm^{-1} in the infrared spectra. The direction of addition of diazomethane to the double bond is assumed to be that demonstrated for alkene linkages having other adjacent electron-withdrawing groups.[3]

Vapor phase pyrolysis of the pyrazolines, following the method used by McGreer,[4] gave yields of 73–96%. These pyrazolines proved to be relatively more heat stable, and higher temperatures (400–450°) and lower pressure (1 mm) were necessary than for the conjugated pyrazolines pyrolyzed in McGreer's work. A number of unsuccessful attempts were made to photolyze these pyrazolines, using a 450-W Hanovia lamp.

The most difficult step for which to develop good yields proved to be the final hydrolysis. Use of inorganic acid solutions resulted in very poor yields. The best method developed during our study involved the use of a minimum amount of trichloroacetic acid to effect the water solution. With the cyclic acetals, yields of cyclopropanecarboxaldehyde were much better than with the diethyl acetal, owing to the difficulty of complete separation of ethanol from the aldehyde in the latter case.

An investigation was also made of the reaction of diazomethane with acrolein itself, in the hope of realizing a two-step synthesis of cyclopropanecarboxaldehyde. Although a rapid reaction occurred, it proved to be impossible to isolate the simple addition

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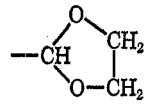
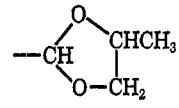
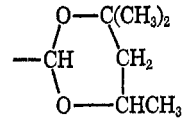
(4) D. E. McGreer, W. Wai, and G. Carmichael, *Can. J. Chem.*, **38**, 2410 (1960).

TABLE I

Compd	Acetal group	Compd type[a]	Yield, %	Bp, °C (mm)	$n^{25}D$	Molecular formula	Calcd, % C	Calcd, % H	Found, % C	Found, % H
1		a	80	76–77 (1)	1.4774	$C_6H_{10}N_2O_2$	50.69	7.09	50.47	6.91
2		a	68–75	85–86 (1)	1.4677	$C_7H_{12}N_2O_2$	53.83	7.74	54.00	7.90
		b	73–79	78–79 (60)	1.4326	$C_7H_{12}O_2$	65.58	9.45	65.39	9.59
3		a	77	79–81 (0.3)	1.4632	$C_{10}H_{18}N_2O_2$	60.58	9.15	60.59	9.24
		b	82–96	85–86 (10)	1.4436	$C_{10}H_{18}O_2$	70.56	10.66	70.69	10.52
4	$-CH(OC_2H_5)_2$	a	58	68–69 (1)	1.4435	$C_8H_{16}N_2O_2$	55.80	9.36	55.64	9.46
		b	82	47–48 (18)	1.4090	$C_8H_{16}O_2$	66.63	11.18	66.41	10.98

[a] a, 1-Pyrazolinecarboxaldehyde acetals; b, cyclopropanecarboxaldehyde acetals.

product, pyrazoline-3-carboxaldehyde, in even a fair yield. A competing reaction of diazomethane with the aldehyde group resulted in a second product, 3-acetyl-2-pyrazoline. Thus mixtures of the desired aldehyde and the ketone were formed when a 1:1 ratio of diazomethane and acrolein was used. With a 2:1 ratio of diazomethane to acrolein, good yields of 3-acetylpyrazoline were obtained. This compound was identical with that formed by addition of diazomethane to methyl vinyl ketone and is apparently a mixture of the tautomeric Δ^1- and Δ^2-pyrazolines. An infrared absorption band at 1550 cm^{-1}, ascribed to N=N stretching, indicated that some Δ^1-pyrazoline structure was present, although only conjugated carbonyl was indicated by absorption at 1670 cm^{-1}. No previous report of this reaction of acrolein was found, but the corresponding reaction of cinnamaldehyde has been reported[5] to give 4-phenyl-2-pyrazoline-3-carboxaldehyde. When we repeated this reaction with a 1:1 ratio of reactants, an unstable mixture was obtained. Using an excess of diazomethane, 3-acetyl-4-phenylpyrazoline could be isolated in fairly good yield. Again as with the acrolein product, the infrared spectrum indicated that both 1-pyrazoline and 2-pyrazoline structures were present. Methacrolein and diazomethane reacted in the same manner and, with an excess of diazomethane, 3-acetyl-3-methyl-1-pyrazoline was obtained.

Experimental Section

Elemental analyses were performed by Galbraith Laboratories, Knoxville, Tenn. Infrared spectra were obtained with a Beckman Model IR-5.

Acrolein Acetals.—Acrolein diethyl acetal was prepared according to the method of VanAllan.[6] Various 2-vinyl-1,3-dioxolanes or 2-vinyl-1,3-dioxanes were prepared from acrolein and the appropriate glycol in the presence of a catalytic amount of *p*-toluenesulfonic acid as described by Fischer and Smith:[2] **2-vinyl-1,3-dioxolane**, bp 109–113° (690 mm), $n^{25}D$ 1.4281; **2-vinyl-4-methyl-1,3-dioxolane**, bp 50–51° (50 mm), $n^{25}D$ 1.4218; **2-vinyl-4,4,6-trimethyl-1,3-dioxane**, bp 88–90° (53 mm), $n^{25}D$ 1.4359.

Reaction of Diazomethane with Acrolein Acetals.—An ether solution of diazomethane, prepared by potassium hydroxide hydrolysis of *p*-tolylsulfonylmethylnitrosoamide ("Diazald," Aldrich Chemical Co.)[7] was distilled directly into a stirred and externally cooled solution of the acrolein acetal in ether. After addition was complete, stirring was continued for 1 hr and the solution was then poured into precooled pressure bottles which were sealed and kept at room temperature for 1–3 days. Removal of ether and vacuum distillation gave the product pyrazolines (see Table I, compound type a). Prepared were 2-(3-pyrazolinyl)-1,3-dioxolane (**1a**); 2-(3-pyrazolinyl)-4-methyl-1,3-dioxolane (**2a**); 2-(3-pyrazolinyl)-4,4,6-trimethyl-1,3-dioxane (**3a**); and pyrazoline-3-carboxaldehyde diethyl acetal (**4a**).

Pyrolysis of the Pyrazoline-3-carboxaldehyde Acetals (a).—A preheated sample of the pyrazolinyl acetal was placed in a dropping funnel equipped with a pressure-equalizing tube and attached to the top of a glass column packed to a distance of 20 cm with pieces of broken Pyrex glass tubing. A filter flask chilled externally with ice was attached to the bottom of the column and a tube from the side arm led to another filter flask chilled with Dry Ice. The column was heated to a temperature of 400–450° by a furnace, and the system was maintained at a pressure of 1 mm during dropwise addition of the pyrazoline. Products were directly distilled under reduced pressure. (See Table I, compound type **b**.)

Hydrolysis of the Cyclopropanecarboxaldehyde Acetals.—To 0.02 mol of the acetal was added 2–5 ml of 1 *N* trichloroacetic acid, sufficient to form a homogeneous solution upon stirring. Some warming helped with the higher molecular weight acetals. The mixture was usually stirred for 3–5 hr. It was then dried ($MgSO_4$) and distilled, or directly distilled to give a two-phase mixture of cyclopropanecarboxaldehyde and water, dried ($MgSO_4$), and redistilled. Yields ranged from 60 (for **4b**) to 96% (for **2b**), bp 92–95° (690 mm), $n^{25}D$ 1.4280 [lit.[8] bp 97–100° (740 mm), $n^{20}D$ 1.4302].

Reaction of Excess Diazomethane with α,β-Unsaturated Aldehydes. A. With Acrolein.—An ether–diazomethane mixture, prepared as previously described from 0.3 mol of Diazald, was distilled into an ice-cooled, stirred, 10% solution of 0.1 mol of acrolein in ether. Some amorphous orange solid, which was apparently polymeric, precipitated during the addition. The mixture was sealed in a pressure bottle and kept in a refrigerator overnight. The solution was decanted from the gummy solid and distillation gave a yellow liquid, bp 60° (0.5 mm), which quickly crystallized to an orange solid. Three recrystallizations from 10:1 ether–petroleum ether (bp 30–60°) resulted in light yellow crystals of 3-acetyl-2-pyrazoline: mp 60–62°; ir (CCl_4), 3400 (NH), 1670 (conjugated C=O), 1550 (N=N), and 1410 cm^{-1}. This compound was identical in melting point and ir spectrum with the product of addition of diazomethane to methyl vinyl ketone, and a mixture melting point determination showed no depression.

B. With Methacrolein.—A procedure similar to that above yielded 67% of colorless, liquid 3-acetyl-3-methyl-1-pyrazoline: bp 44–45° (0.2 mm); $n^{25}D$ 1.4625; ir (neat) 1720 (C=O), 1545 (N=N), and 1447 cm^{-1}.

(5) K. Kratzl and E. Wittman, *Monatsh. Chem.*, **85**, 7 (1954).

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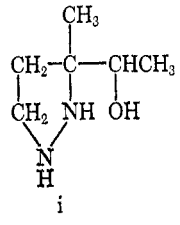
Anal. Calcd for $C_6H_{10}N_2O$: C, 57.12; H, 7.99. Found: C, 56.92; H, 8.22.

The phenylhydrazone melted at 119–120°. The semicarbazone did not have a sharp melting point, deforming and carmellizing at 230–240°.

Anal. Calcd for $C_6H_{11}N_5O$: C, 42.60; H, 6.54. Found: C, 42.49; H, 6.49.

A sample of the ketone in ethanol was hydrogenated with Raney nickel catalyst at 1000 psi and room temperature. Distillation gave a very viscous, colorless liquid assumed to be i, bp 89° (0.5 mm), $n^{29}D$ 1.4891.



i

Anal. Calcd for $C_6H_{14}N_2O$: C, 55.35; H, 10.84; N, 21.52. Found: C, 55.31; H, 10.27; N, 21.62.

C. With Cinnamaldehyde.—An ether–diazomethane solution, prepared as described before, was distilled into a solution of cinnamaldehyde in ether. The product solution was sealed in a precooled pressure bottle and let stand for 2 days. Removal of the ether gave a high yield of crude product, but an attempt to distil this material resulted in decomposition of a considerable amount of the desired product. The distillate crystallized to light yellow crystals. Three recrystallizations from ether–petroleum ether gave colorless crystals, mp 100–101° [lit.[9] light yellow crystals, mp 101° (with some indication of lower melting Δ^1 isomer), prepared from benzalacetone and diazomethane]. The infrared spectrum in CCl_4 showed bands at 3400 (NH), 1720 (C=O), 1670 (conjugated C=O), 1545 (N=N), and 1410 cm^{-1}, indicating a mixture of the 1-pyrazoline and 2-pyrazoline isomers.

Registry No.—**1a**, 23936-71-2; **2a**, 23936-72-3; **2b**, 23936-73-4; **3a**, 23936-74-5; **3b**, 23936-75-6; **4a**, 23936-76-7; **4b**, 23936-77-8; 3-acetyl-3-methyl-1-pyrazoline, 1567-95-9; 3-acetyl-3-methyl-1-pyrazoline phenylhydrazone, 23936-79-0; diazomethane, 334-88-3; semicarbazone of 3-acetyl-3-methyl-1-pyrazoline, 23936-81-4; i, 23936-80-3.

Acknowledgment.—This research was supported in part by a grant from the Petroleum Research Fund of the American Chemical Society. Grateful acknowledgment is made to the donors of this fund.

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N Acylation of D-Glucosamine by a New Method

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N-Acyl derivatives of D-glucosamine are of great interest in biochemical studies. Several methods for the preparation of N-acyl derivatives of D-glucosamine have been reported in the literature.[2-7] The latest method reported by Inouye, *et al.*,[8] for preparing N-acyl derivatives of D-glucosamine required the treatment of a supersaturated solution of D-glucosamine hydrochloride in methanol with sodium methoxide solution followed by removal of precipitated sodium chloride before any acid chloride or anhydride was added for the reaction.

We wish to report here a new method for N acylation of D-glucosamine, in which *p*-nitrophenyl esters were used as acylating agents.

Bodanszky[9] first reported that amino groups of tyrosine and serine with unprotected hydroxyl groups could be selectively acylated by *p*-nitrophenyl esters. We found this reagent to be very effective for the N acylation of amino sugars. This method was found to be simple, direct, and more convenient than all previously reported methods.

Three typical N-acyl derivatives of D-glucosamine were prepared by using *p*-nitrophenyl esters of acetic, benzoic, and stearic acids.

Analytical data and physical constants for the three N-acyl-D-glucosamines prepared are given in Table I. All the three compounds show absorption maxima at 510, 545, and 585 nm when submitted to the Morgan Elson color reaction as reported previously.[10]

Experimental Section

Melting points were taken in open capillaries and are uncorrected. Infrared spectra were determined with a Perkin-Elmer Model 521 infrared spectrophotometer, and absorption spectra in the visible range were obtained in Hilger Uvispeck spectrophotometer, Model H700. Optical rotations were measured with Hilger-Watts Model M-511 microptic photoelectric polarimeter.

Preparation of N-Acyl Derivatives of D-Glucosamine.—A representative experimental procedure is as follows. To a solution of *p*-nitrophenyl acetate (181 mg, 1 mmol) in 1.4 ml of freshly distilled dimethyl sulfoxide (DMSO) were added D-glucosamine hydrochloride (107 mg, 0.5 mmol) and triethylamine (0.07 ml, approx 0.5 mmol). Higher proportions of DMSO were required to dissolve *p*-nitrophenyl benzoate and *p*-nitrophenyl stearate. The mixture was stirred for 1 hr at room temperature, and, after standing for 4 days at 20°, the yellow mixture was diluted with 15 vol of dry methylene chloride (*ca.* ten times the volume of DMSO used). Excess of *p*-nitrophenyl acetate and triethylamine hydrochloride remained in solution and N-acetyl-D-glucosamine gradually separated out. The mixture was centrifuged after being allowed to stand for 2 hr, and the residue was washed twice with methylene chloride and three times with dry ether and finally dried over concentrated sulfuric acid. The yield was almsost quantitative. The crude material was crystallized from methanol by addition of ether to incipient turbidity.

Preparation of *p*-Nitrophenyl Stearate.—Stearic acid (2.3 g, 0.008 mol) was refluxed with thionyl chloride (3 ml, 0.04 mol) on water bath for 4 hr and kept overnight at 20°. Excess thionyl chloride was removed *in vacuo* at 100°. To the reaction product in the flask, dry pyridine (5 ml) was added while the flask was cooled in ice, and then, to this mixture, *p*-nitrophenol (2 g, 0.015 mol) in dry pyridine (10 ml) was added. Some solid appeared in the flask which was dissolved by heating to 50°. The reaction mixture was kept at 20° for 40 hr and then poured in crushed ice. The mixture was acidified to congo red with H_2SO_4, cooled in ice

(1) To whom correspondence should be addressed.

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