

Anal. Calcd. for $C_{27}H_{45}NO_3$: C, 75.13; H, 10.51. Found: C, 74.88; H, 10.50.

The acetate **IIa**, prepared in the usual manner (acetic anhydride-pyridine, 1-hr. refluxing) and purified through chromatography (alumina), afforded white prisms: m.p. 197–199°; $[\alpha]^{20}_D -26.7 \pm 1.0^\circ$ (c 1.01, ethanol); $\lambda_{max}^{CS_2}$ 2.77 (OH), 5.75 and 8.07 (3-AcO), and 6.02 μ (N-Ac).

Anal. Calcd. for $C_{31}H_{49}NO_3$: C, 72.19; H, 9.58. Found: C, 72.36; H, 9.64.

The mother liquor, after removal of **II**, yielded 68 mg. of a substance whose R_f value (t.l.c.) was slightly lower than that of 9 α -hydroxydihydrosolasodine and which gave a green coloration on spraying with sulfuric acid (50%). **II** gave a violet coloration with sulfuric acid. The impure crystals of **III** were repeatedly crystallized from methanol-ether until homogeneity was achieved as shown by t.l.c. Needles, m.p. 216–219°, $[\alpha]^{20}_D -37.6 \pm 1^\circ$ (c 1.0, $CHCl_3$), were obtained. **III** analyzed for a monohydroxydihydrosolasodine and agreed in properties (melting point, mixture melting point, and infrared spectrum) with a sample of 7 β -hydroxydihydrosolasodine (**III**, solasodane-3 β ,7 β -diol) prepared by the reduction of 7 β -hydroxysolasodine.⁵ Molecular rotation difference ($\Delta M_D = M_D$ of **III** - M_D of **I**) of 102 also agrees well for a 7 β -hydroxy-5 α -steroid listed as +110.⁷

Anal. Calcd. for $C_{27}H_{45}NO_3$: C, 75.13; H, 10.51. Found: C, 75.26; H, 10.73.

The acetate **IIIa** failed to crystallize but t.l.c. and g.l.c. indicated it to be a homogenous product. It analyzed for a O,O,N-triacetyl derivative: $[\alpha]^{20}_D +7^\circ$ (c 0.578, $CHCl_3$); $\lambda_{max}^{CS_2}$ 5.76 and 8.05 (OAc), and 6.02 μ (N-Ac).

Anal. Calcd. for $C_{33}H_{51}NO_3$: C, 71.06; H, 9.22. Found: C, 70.84; H, 9.52.

Hydrogenation of 9 α -Hydroxysolasodine.—A solution of 43 mg. of 9 α -hydroxysolasodine⁵ in 5 ml. of glacial acetic acid was reduced over 40 mg. of palladium-charcoal (10%) catalyst until slightly more than 1 mmole of hydrogen was absorbed. The product, when chromatographed on alumina (Woelm, grade II) and eluted with 0.5 ~ 2.5% methanol in ether, afforded 5.2 mg. of crystalline substance of m.p. 220–223° from methanol-ether. The properties of this compound were in agreement (melting point mixture melting point, and infrared spectrum) with those obtained from the microbial hydroxylation of 5,6-dihydrosolasodine.

Hydrogenation of 7 β -Hydroxysolasodine.—To a solution of 30 mg. of 7 β -hydroxysolasodine⁵ in 6 ml. of ethyl acetate was added 50 mg. of 10% palladium-charcoal and the mixture was hydrogenated until 1 mole equiv. of hydrogen was absorbed. Thin layer chromatography and infrared spectrum indicated the product to be a mixture of the hydroxy- and ketodihydrosolasodine. The presence of the latter was suspected as due to impure starting material. The crystalline residue was therefore dissolved in 5 ml. of pyridine and reduced with 30 mg. of sodium borohydride. The residue was then submitted to alumina chromatography (Woelm, grade I). The fractions eluted with chloroform yielded needles of m.p. 216–218° from acetone and were identical (melting point and infrared spectrum) with the product from the microbiological hydroxylation.

(7) L. F. Fieser and M. Fieser, "Steroids," Reinhold Publishing Corp., New York, N. Y., 1959, p. 179.

The Reaction of Organic Azides with Benzyne

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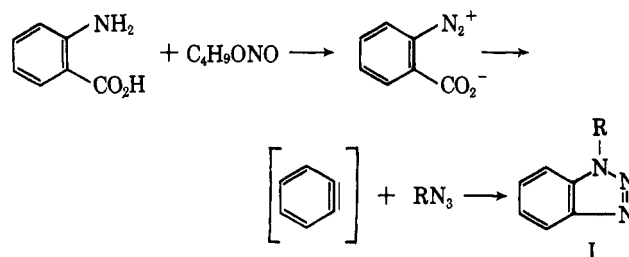
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Organic azides react rather sluggishly with olefins and acetylenes to yield triazolines and triazoles.¹ Since the incorporation of the double bond in strained cyclic compounds greatly accelerates the reaction rate, it was thought that benzyne, which contains a strained triple

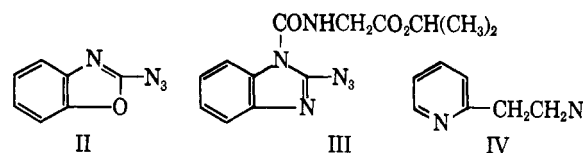
bond, should react readily with azides. This was confirmed several years ago when phenyl azide was treated with benzyne and 1-phenylbenzotriazole was obtained in small yield. The difficulty and danger involved in the preparation of benzyne² discouraged further investigation of this reaction.³ The recent publication of a convenient synthesis for benzyne⁴ led to a renewed interest in the problem.

Benzyne has been found to react readily with aromatic, aliphatic, and certain heterocyclic azides. The over-all reaction, including the preparation of the benzyne, is shown in the following reaction sequence. The

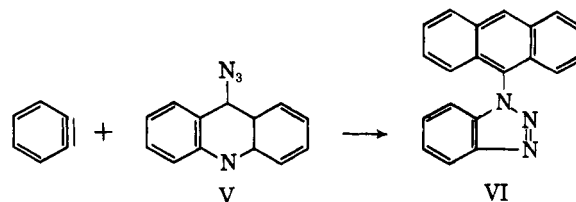


experimental procedure consisted in the slow addition of an acetone solution of anthranilic acid to a refluxing chloroform solution of butyl nitrite and the organic azide, thus eliminating the isolation of the explosive diazobenzoate. The substituted benzotriazoles that were prepared by the procedure are listed in Table I. It is evident that substituents and unsaturation on the aromatic azide do not affect the reaction adversely. It is thought that higher yields of product would be obtained if a metering pump had been used to obtain slower addition of the acetone solution of anthranilic acid. The higher yields of product that were obtained from the aliphatic azides are probably due to better recovery of the product from the reaction mixture.

The results obtained with heterocyclic azides were more complex. The azides **II**, **III**, and **IV** were treated with benzyne by the procedure just described, but the azides were recovered unchanged. It was thought that



these azides might not be typical because of interaction between the azide group and the heterocyclic nitrogen atom. The reaction was repeated with 9-azidoacridine (**V**) which should not be subject to this type of interaction, and 1-(9-acridyl)benzotriazole (**VI**) was obtained in 47% yield.




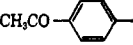
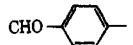
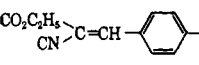
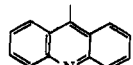
(2) M. Stiles and R. G. Miller, *J. Am. Chem. Soc.*, **82**, 3802 (1960).

(3) At about this time, Wittig reported that 1-phenylbenzotriazole was formed from phenyl azide and benzyne which was prepared by a different procedure: G. Wittig and R. W. Hoffman, *Angew. Chem.*, **73**, 435 (1961).

(4) L. Friedman and F. M. Logullo, *J. Am. Chem. Soc.*, **84**, 1549 (1963).

(1) J. H. Boyer and F. C. Canter, *Chem. Rev.*, **54**, 1 (1954).

TABLE I
 1-SUBSTITUTED BENZOTRIAZOLES

R	M.p. or b.p. (mm.), °C.	Yield, %	Calcd., %			Found, %		
			C	H	N	C	H	N
	89-90	52	73.8	4.6	21.6	74.0	4.5	21.5
	160-161	50	71.0	4.7	17.8	71.2	4.5	17.8
	156-157	50	70.0	4.0	18.8	69.7	4.0	18.6
	180-181	55	67.9	4.4	17.6	67.5	4.3	17.9
C_6H_{12}	135-136 (0.2)	70	71.0	8.4	20.7	71.0	8.6	21.0
C_6H_5	127-128 (0.2)	68	68.5	7.4	24.0	68.3	7.5	23.8
	250 dec.	47	77.0	4.1	18.9	76.6	4.2	18.8

Experimental

General Procedure.—A solution of 7 g. (0.051 mole) of anthranilic acid in 60 ml. of acetone was added over a 2-hr. period to a refluxing mixture of 0.05 mole of the azide and 6 g. (0.058 mole) of butyl nitrite in 200 ml. of dichloromethane. The volatile components were stripped from the reaction mixture with an aspirator to leave a brown gum. In the examples with aliphatic azides, the residues were distilled. The residue obtained from the reaction with phenyl azide and with V were dissolved in benzene, chromatographed through Florisil, and, after evaporation of the benzene, the residues were recrystallized from petroleum ether (b.p. 35-60°) and ethanol, respectively. The brown gums obtained in the other examples listed on Table I were all recrystallized from benzene. Azides II, III, and IV were treated in the same manner as phenyl azide, but evaporation of the solution which had been passed through the chromatography column yielded only the starting azide.

Phenylacetyl Derivatives of Methylhydrazine¹

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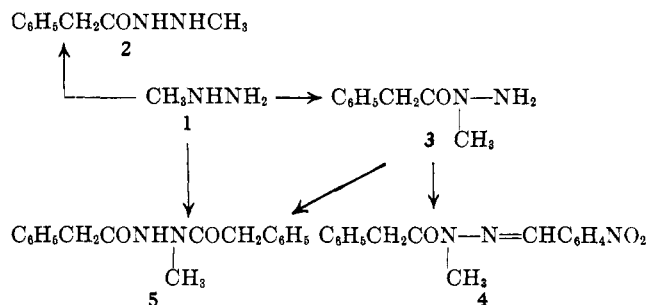
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The only systematic studies of the acylation of alkylhydrazines have been reported by Hinman and Fulton,² who found that their action of methylhydrazine with esters gave mainly 1-acyl-2-methylhydrazines and with anhydrides, 1-acyl-1-methylhydrazines. Most of the products were characterized by paper chromatography. In connection with a projected pyridazone synthesis, we had occasion to examine the reactions of methylhydrazine (1) with various derivatives of phenylacetic acid, and have confirmed the earlier conclusions on the course of these acylations.

On refluxing 1 with ethyl phenylacetate, crystalline 2-methyl-1-phenylacetylhydrazine (2) was obtained in 76% yield; the n.m.r. spectrum³ contained two one-

proton peaks at 260 c.p.s. (broad, -CONHNHCH₃) and 434 c.p.s. (-CONHNHCH₃) which were exchangeable with D₂O. The reaction of 1 with phenylacetic anhydride gave an oil which was characterized as 1-methyl-1-phenylacetylhydrazine (3) by conversion to the *p*-nitrobenzalhydrazone (4). In each of these reactions a minor amount of the other isomer, 3 from the ester and 2 from the anhydride, was detected in the product mixture by thin layer chromatography. The bis(phenylacetyl) derivative 5 was obtained from either 1 or 3 by treatment with phenylacetyl chloride; an intermediate monoacyl product could not be isolated.



Experimental⁴

1-Methyl-2-phenylacetylhydrazine (2).—A solution of 0.87 g. (18.8 mmoles) of methylhydrazine and 3.1 g. (18.8 mmoles) of ethyl phenylacetate in 1.6 ml. of ethanol was refluxed for 12 hr. On cooling, 1.59 g. (76%) of a fluffy crystalline precipitate, m.p. 113-116°, separated. Recrystallization from ethanol-ether gave white plates of 2: m.p. 126-127°; λ^{KBr} 3.02 and 6.13 μ ; n.m.r., 149 (singlet, 3), 208 (s, 2), 260 (broad, 1), and 434 c.p.s. (multiplet, 6).

Anal. Calcd. for C₉H₁₂N₂O: C, 65.83; H, 7.37. Found: C, 65.76; H, 7.42.

The ethanolic mother liquor from 2 showed three spots on a t.l.c. plate, corresponding, in order of decreasing *R_f* value, to ethyl phenylacetate, 3 and 2.

1-Methyl-1-phenylacetylhydrazine (3).—To a solution of 887 mg. (19.3 mmoles) of methylhydrazine in 1.0 ml. of benzene was

(3) N.m.r. spectra were obtained in CDCl₃ solutions (tetramethylsilane) with a Varian A-60 instrument.

(4) Melting points were observed on a Fisher-Johns block with a calibrated thermometer. Infrared spectra were obtained with a Perkin-Elmer Infracord. Thin layer chromatography was carried out on silica gel C in chloroform-methanol (25:2); the spots were visualized with iodine vapor.

(1) Supported by Grant DA-CmL-18-108-61-G-24 from the Army Chemical Corps.

(2) R. L. Hinman and D. Fulton, *J. Am. Chem. Soc.*, **80**, 1895 (1958).