transformed to pseudodiosgenin diacetate.

5. Pseudokryptogenin and its diacetate have been reduced catalytically to pseudodiosgenin and its diacetate, respectively.

6. Three practical methods for the transformation of kryptogenin into steroidal hormone intermediates have been described.

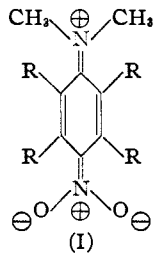
MEXICO, D. F. RECEIVED APRIL 15, 1948

[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY OF THE UNIVERSITY OF MINNESOTA]

Steric Effect of Methylene Groups. IV

BY RICHARD T. ARNOLD AND JOHN RICHTER[1]

By making use of a large variety of physical and chemical methods,[2] it has been clearly demonstrated that resonance in aromatic nitro compounds is hindered by ortho substituents R which inhibit coplanarity of the benzenoid ring and the electron-donor (*i. e.*, $(CH_3)_2N$–) or electron-acceptor (*i. e.*, $-NO_2$) groups.

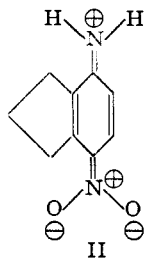


(I)

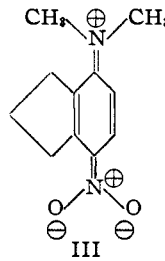
p-Nitro-N,N-dimethylaniline (I, R = H) is essentially a flat molecule due to the contribution of the quinoidal structure to the resonance. As the group R increases in size, there is an increasing repulsion between R and the amino[3] and nitro[4] groups. Remington[3] has shown that the marked ultraviolet absorption (near 380 mμ) of certain nitrobenzene derivatives is associated with the quinoidal limiting structure (I). The intensity of this band is steadily reduced as the group R increases in volume.

We have made use of this fact in a determination of the relative steric influence of methylene groups in five- and six-membered rings.

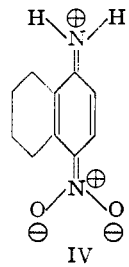
Compounds II–V (represented above in their quinoidal limiting structures) have been prepared



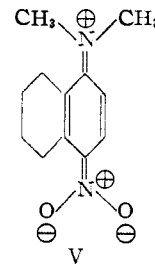
II



III



IV



V

and examined in the ultraviolet region. Table I includes a summary of the pertinent absorption maxima and intensities.

TABLE I[a]

	Compound	Max. (in mμ)	(Molar)
II	4-Amino-7-nitrohydrindene	376	13,900
	(*p*-Nitroaniline)	(374)	(15,700)
III	4-N,N-Dimethylamino-7-nitrohydrindene	387	12,600
	(N,N-Dimethyl-*p*-nitroaniline)	(386)	(18,290)[3]
IV	5-Amino-8-nitro-1,2,3,4-tetrahydronaphthalene	383	11,400
V	5-N,N-Dimethylamino-8-nitro-1,2,3,4-tetrahydronaphthalene	364	5,900

[a] Measurements were made in 95 per cent. ethanol using a Beckman spectrophotometer.

The free amino groups in II and IV are not appreciably affected by the ortho substituents.[3] Presumably the difference between II and IV can be attributed largely to a steric repulsion between the nitro and methylene groups.

When *p*-nitroaniline is converted into *p*-nitro-N,N-dimethylaniline a considerable increase is observed in the absorption band near 380 mμ. This is, perhaps, largely due to the electron repelling effects of the methyl groups which increase the basicity and facilitate electron release toward the nitro group as indicated in I. This effect is more than counterbalanced, however, when ortho substituents are present, and increases with the size of the substituent due to steric inhibition of the resonance.

Differences in the extinction coefficients of II and IV and the changes brought about when these two compounds are methylated to give III and V strongly support, we believe, the view that methylene groups in hydrindene provide a smaller steric

(1) This manuscript was written from the Ph.D. thesis of John Richter. Present address: Merck & Company, Rahway, New Jersey.

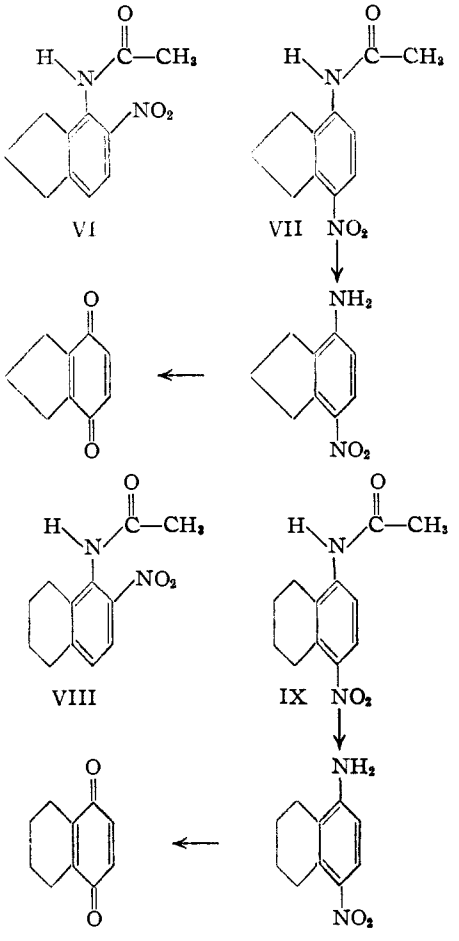
(2) G. W. Wheland, "The Theory of Resonance," John Wiley and Sons, Inc., New York, N. Y., 1944, p. 136.

(3) Remington, THIS JOURNAL, **67**, 1838 (1945).

(4) Brown and Reagan, *ibid.*, **69**, 1032 (1947).

influence than those in the corresponding six-membered ring of tetralin.

The nitroamines examined above were prepared by nitration of the appropriate acetanilide followed by hydrolysis and methylation. Structure proof consisted of converting the para derivatives to the known para-quinones.



Acetamido groups when *o*-disubstituted resist hydrolysis,[5] and thus IX was readily separated from VIII by partial hydrolysis. As suspected from the above stereo considerations, compound VI is cleaved rapidly enough in acid media so that its separation from VII proved quite difficult.

The authors are grateful to Dr. Donald Wheeler and Mr. David Terry of the General Mills Research Laboratory for the separation of 4- and 5-nitrohydrindenes by means of a Podbielniak column.

Experimental

4-Nitrohydrindene.—A mixture of 4- and 5-nitrohydrindene (399 g.) was separated by distillation through a Podbielniak column. About one-third of the material (129 g.) distilled at 105–107° (6 mm.) and crystallized in the receiver. Recrystallization from alcohol gave 117 g. (17% based on hydrindene used); m. p. 44–45°. Reduction with hydrogen and Raney nickel followed by acetylation gave 4-acetamidohydrindene in a yield of 82%.

Nitration of 4-Acetamidohydrindene.—To a well-stirred solution of 4-acetamidohydrindene (23 g.) in sulfuric acid (100 ml. cooled to −5°), a cold mixture of nitric acid (8.5 ml.) and sulfuric acid (10 ml.) was added slowly enough so that the solution temperature did not exceed 0°. After pouring onto ice (450 g.) the solution was boiled for two hours to hydrolyze the acetylamines. After cooling to 0°, concentrated sulfuric acid (100 ml.) was added cautiously and the whole was left at 0° overnight. The precipitated sulfate (Fraction 1) was collected on a filter. To the filtrate was added water (900 ml.) and orange needles (4.8 g.) separated at 0°. This was designated Fraction 2. Neutralization of the filtrate with ammonium hydroxide gave a brown precipitate. This on sublimation at 0.01 mm. and recrystallization from benzene gave 4-amino-7-nitrohydrindene; wt. 6.8 g.; m. p. 140–141°.

Anal. Calcd. for $C_9H_{10}N_2O_2$: C, 60.65; H, 5.65. Found: C, 60.40; H, 5.76.

Fraction 1 was triturated with hot benzene (250 ml.) and filtered. Treatment of the residue with ammonium hydroxide gave a mixture of amines. Trituration with hot cyclohexane gave a residue consisting of 4-amino-7-nitrohydrindene (1.4 g.). From the solution 4-amino-6-nitrohydrindene (1.9 g.) crystallized; m. p. 109–110°.

Anal. Calcd. for $C_9H_{10}N_2O_2$: C, 60.65; H, 5.65. Found: C, 60.88; H, 5.78.

Fraction 2 was recrystallized from cyclohexane and then from alcohol to give 4-amino-5-nitrohydrindene; m. p. 106–107°; wt. 3.8 g.

Anal. Calcd. for $C_9H_{10}N_2O_2$: C, 60.65; H, 5.65. Found: C, 60.90; H, 5.79.

4-Acetamido-5-nitrohydrindene.—A mixture of 4-amino-5-nitrohydrindene (0.5 g.) and acetic anhydride (6 ml.) was refluxed for ninety minutes and poured into ice water. After neutralizing with ammonium hydroxide, the product was recrystallized from alcohol; m. p. 146–147°.

Anal. Calcd. for $C_{11}H_{12}N_2O_3$: C, 59.98; H, 5.46. Found: C, 59.88; H, 5.60.

4-Acetamido-6-nitrohydrindene.—The *m*-nitroamine was acetylated as above; m. p. 189–190°.

Anal. Calcd. for $C_{11}H_{12}N_2O_3$: C, 59.98; H, 5.46. Found: C, 59.79; H, 5.54.

4-Acetamido-7-nitrohydrindene.—Prepared as in the case of the other isomers, this compound melted at 172–173°.

Anal. Calcd. for $C_{11}H_{12}N_2O_3$: C, 59.98; H, 5.46. Found: C, 60.25; H, 5.74.

Structure Proof.—(a) 4-Amino-7-nitrohydrindene (0.5 g.) was reduced with hydrogen using platinum in acetic acid (30 ml.). After removing the catalyst a solution containing concentrated sulfuric acid (4 ml.), potassium dichromate (4.0 g.) and water (50 ml.) was added quickly to the filtrate. From the steam distillate there was obtained 4,7-hydrindenequinone; m. p. 39–40°.[6]

(b) From 5-amino-8-nitro-1,2,3,4-tetrahydronaphthalene there was formed (using the above procedure) 1,2,3,4-tetrahydro-5,8-naphthoquinone; m. p. 55–56°.[6]

(c) A solution of 4-amino-5-nitrohydrindene (0.5 g.) in absolute ethanol (30 ml.) was reduced with hydrogen (at 10 pounds pressure) in the presence of platinum. The catalyst was removed by filtration and concentrated hydrochloric acid (10 ml.) was added to precipitate the diamine hydrochloride. A mixture of the diamine hydrochloride (0.57 g.), 9,10-phenanthraquinone (0.55 g.) and acetic acid (30 ml.) was heated under reflux for two hours. The precipitated phenazine melted at 245–246°.

Anal. Calcd. for $C_{28}H_{16}N_2$: C, 86.26; H, 5.04. Found: C, 86.18; H, 5.36.

This isolation of dibenza[a,c]cyclopenta[j]phenazine proves the relative position of nitro and amino groups as that of ortho.

(5) Verkade and Witjens, *Rec. trav. chim.*, **62**, 202 (1943).

(6) Arnold and Zaugg, THIS JOURNAL, **63**, 1317 (1941).

4-N,N-Dimethylamino-7-nitrohydrindene.—A mixture containing 4-amino-7-nitrohydrindene (4 g.), sodium hydroxide (4 g.), methyl iodide (17 g.) and methanol (20 ml.) was heated at 140–150° for six hours. The solution was extracted with benzene after having been made alkaline and the benzene was removed by steam distillation. The residue was refluxed with acetic anhydride (30 ml.) for three hours and decomposed with water. Extraction with benzene followed by extraction of the benzene layer with hydrochloric acid (6 *N*) and then neutralization gave 4-N,N-dimethylamino-7-nitrohydrindene. Recrystallization from alcohol gave 2.9 g. of pure product; m. p. 81–82°.

Anal. Calcd. for $C_{11}H_{14}N_2O_2$: C, 64.06; H, 6.85. Found: C, 64.01; H, 7.00.

5-Amino-8-nitro-1,2,3,4-tetrahydronaphthalene.—5-Acetamido-1,2,3,4-tetrahydronaphthalene (18 g.) dissolved in sulfuric acid (100 ml.) and nitrated at 0° with nitric acid (6.3 ml.) dissolved in sulfuric acid (30 ml.). The residue obtained after decomposition with ice (800 g.) was taken up in hot alcohol (200 ml.). To this was added hydrochloric acid (80 ml., 6 *N*) and the whole was heated under reflux for thirty minutes. One-half of the alcohol was removed by distillation, water (300 ml.) was added and the solution was neutralized with ammonium hydroxide. The solid which formed was dried, dissolved in nitrobenzene (250 ml.) and treated with dry hydrogen chloride for fifteen minutes at 0°. A solid (hydrochloride) weighing 14.1 g. was formed. Neutralization by alkali followed by recrystallization from alcohol gave 5-amino-8-nitro-1,2,3,4-tetrahydronaphthalene; wt. 10.2 g.; m. p. 114.5–116°.[7]

5-N,N-Dimethylamino-8-nitro-1,2,3,4-tetrahydronaphthalene.—Following the procedure for methylation as described above for the corresponding hydrindene derivative, there was obtained from the amino compound (4 g.) a 45% yield of the anticipated methylated product; m. p. 61–62°.

Anal. Calcd. for $C_{12}H_{16}N_2O_2$: C, 65.45; H, 7.32; N, 12.7. Found: C, 65.76; H, 7.35; N, 12.7.

Summary

1. A number of nitroamines in the hydrindene and tetralin series have been prepared.

2. The ultraviolet spectra of these compounds have been used to support the view that methylene groups in five-membered rings offer less steric hindrance than those in six-membered rings.

(7) Schroeter, *Ann.*, **426**, 60 (1922).

MINNEAPOLIS, MINNESOTA RECEIVED APRIL 30, 1948

NOTES

The Homogeneity of the Phenylosazone Prepared from D-Fructose

BY W. W. BINKLEY[1] AND M. L. WOLFROM

Wolfrom, Thompson and Evans[2] have reported an instance of phenylosazone formation, in 1-desoxy-D-psicose, in which the carbonyl carbon and the secondary hydroxyl of carbon three were concerned. It was considered of interest to investigate the phenylosazone formation from the ketose D-fructose to determine if the phenylosazone produced might be a mixture of the 1,2 and 2,3 derivatives.[3] To this end the phenylosazone produced from D-fructose was converted to the phenylosotriazole. The phenylosotriazole obtained was found to be identical with that obtained from D-glucose and which Hann and Hudson[4] had found to be homogeneous and to produce on periodate oxidation 2-phenyl-4-formyl-osotriazole with the concomitant formation of 1 mole of formaldehyde and 2 moles of formic acid. These oxidation results were confirmed by us on our product and we report further that the oxidation with lead tetraacetate, a homogeneous reaction (the periodate oxidations are heterogeneous), yielded the same over-all result. Any 2,3-osazone present would have yielded a phenylosotriazole that would have consumed 2 moles of oxidant with the concomitant formation of 1 mole of formaldehyde, 1 mole of formic acid and 2-phenyl-4-formyl-5-hydroxymethyl-osotriazole.

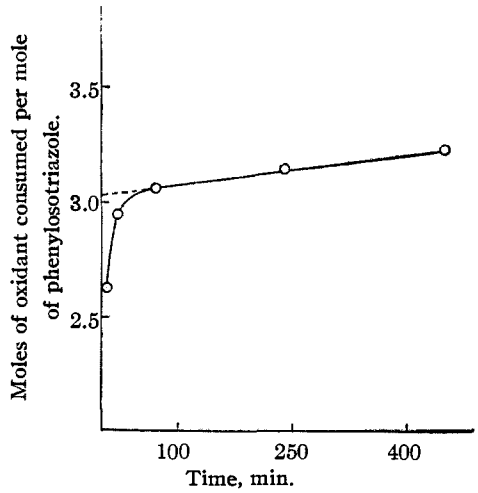


Fig. 1.—Lead tetraacetate oxidation of phenylosotriazole from D-fructose in 97.5% acetic acid at 25°. Points shown corrected for reagent blanks.

Thus it has been determined that in the normal procedures for preparing phenylosazones and

(1) Sugar Research Foundation Associate of The Ohio State University Research Foundation (Project 190).

(2) M. L. Wolfrom, A. Thompson and E. F. Evans, THIS JOURNAL, **67**, 1793 (1945).

(3) See E. G. V. Percival, *Advances in Carbohydrate Chem.*, **3**, 44 (1948).

(4) R. M. Hann and C. S. Hudson, THIS JOURNAL, **66**, 735 (1944).