TABLE I

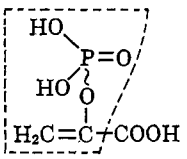
THE APPARENT MOLECULAR WEIGHT OF DICHLOROACETYL CHLORIDE AND BENZOYL CHLORIDE IN ETHYL ACETATE DETERMINED BY BOILING POINT ELEVATION

Acid chloride	Molality[a]	B.p. elevation, °C.[b] Calcd.	B.p. elevation, °C.[b] Obsd.	Mol. wt. Obsd.	Mol. wt. Actual	Mol. wt. ratio, obsd./actual
Dichloroacetyl chloride	0.436	0.59	1.02	89.4	147.4	0.59
Benzoyl chloride	0.617	0.85	1.64	72.4	140.5	0.52

[a] Solvent, ethyl acetate containing 0.005% water. For molecular weight of dichloroacetyl chloride: weight of ethyl acetate was 67.759 g.; weight of dichloroacetyl chloride was 4.360 g. For molecular weight of benzoyl chloride: weight of ethyl acetate was 71.134 g.; weight of benzoyl chloride was 6.170 g. [b] Cottrell boiling point apparatus employing a Beckman thermometer. All boiling points were determined in a nitrogen atmosphere.

form which retains acylating activity and which is not the free acid. These considerations lead to the suggestion that the hydrogen chloride is generated in the preceding manner which also gives rise to a reasonable structure that can be expected to be actively acylating and, additionally, accounts for the molecular weight observations.

The intermediate in brackets would essentially be a "high energy" anhydride type. Although there is no scientific reason why a precedent for the above compound type is necessary in order to validate the suggestion, some degree of precedence is found in the consideration of the structure of phosphoenol pyruvate,



wherein the difference with the proposed intermediate shown above is simply that one-half of the "anhydride" is phosphate in phosphoenol pyruvate and carboxylate in the proposed intermediate.

Upon reaction with amino acid (or amino acid hydrochloride), the intermediate would yield the acylated amino acid and free the hydrogen chloride as well as a molecule of solvent.

Other Experiments.—It was observed that the acylation of L-leucine by dichloroacetyl chloride did not proceed in the following solvents: triethyl orthoformate, methyl formate, N,N-dimethylformamide. The reaction does proceed in *n*-butyl acetate, *n*-propyl acetate, and methyl acetate. In each case, the product (dichloroacetyl-L-leucine) was identified by its m.p. 119–122°.[4] These results tend to support the acylating intermediate structure proposed above. It is of interest that the product from the methyl acetate reaction is difficult to crystallize, though success is eventually achieved; whereas, the product from the other acetates crystallizes fairly readily.

Although a quantitative study has yet to be undertaken, definite evidence was obtained that both particle size and form (flake or powder) of the amino acid affect the rate of reaction. This led to the use of a uniformly purified and treated batch of L-leucine throughout this study.

Acknowledgment.—The authors are indebted to Dr. Kenneth F. O'Driscoll of this department for his development of the rate equation and for his helpful discussions throughout this study.

The Preparation and Some Reactions of N′-Fluorodiimide N-Oxides,[1] R—N(O)=NF

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A variety of N-substituted N′-fluorodiimide N-oxides, R–N(O)=NF, have been prepared by the reaction of nitroso compounds with either tetrafluorohydrazine or pyridine–difluoramine mixtures. Some reactions of those novel azoxy compounds with nucleophilic reagents were investigated and a new synthesis of unsymmetrical azoxy compounds was discovered. Reduction yielded anilines or hydrazines.

The preparation and thorough characterization of N-trifluoromethyl-N′-fluorodiimide N-oxide (I, R = CF_3) was reported recently.[2] This N-fluoroazoxy compound was obtained from the ultraviolet or thermally activated reaction of trifluoronitrosomethane and tetrafluorohydrazine. Two convenient methods for the preparation of alkyl- and aryl-N′-fluorodiimide N-oxides from nitroso compounds in solution are reported here.

(1) This research was supported by the Advanced Research Projects Agency under Army Ordnance Contract No. DA-01-021 ORD-11909.

(2) J. W. Frazer, B. E. Holder, and E. F. Worden, *J. Inorg. Nucl. Chem.*, **24**, 45 (1962).

In inert solvents such as chlorobenzene, carbon tetrachloride, or methylene chloride, C-nitroso monomers absorb tetrafluorohydrazine (N_2F_4) at subatmospheric pressure and are converted to the corresponding N′-fluorodiimide N-oxide (Table I). The reaction proceeded readily at 0–20° if the blue-green color of the nitroso monomer were visible in the solution. Only with the last three nitroso dimers listed in Table I was heating necessary; at 60–80° in chlorobenzene solution sufficient monomer was present to cause these reactions to proceed at a reasonable rate. N′-Fluorodiimide N-oxides also were produced when di-

TABLE I

N-SUBSTITUTED N′-FLUORODIIMIDE N-OXIDES, R—N(→O)=NF

R	B.p. (mm.) and m.p., °C.	Yield, %	Calcd., % C	Calcd., % H	Calcd., % N	Found, % C	Found, % H	Found, % N	F^{19} n.m.r.,[a] c.p.s.
Phenyl[b]	78 (4)	53[c]	51.43	3.60	20.00	51.36	3.69	20.57	−4742
o-Tolyl	84 (2)	27[d]	54.54	4.58	18.18	54.74	4.68	18.39	−5167
m-Tolyl	54 (0.1)	49[d]	54.54	4.58	18.18	54.27	4.73	17.40	−4695
p-Tolyl	60 (0.2)	43[c]	54.54	4.58	18.18	54.57	4.72	17.74	−4642
o-Chlorophenyl	*e*	23[d]			16.05			16.22	−5264
p-Chlorophenyl	54	50[d]	41.28	2.31	16.05	41.56	2.37	15.70	−4807
p-Bromophenyl	83	60[c]	32.90	1.84	12.79	33.19	2.04	12.35	−4871
p-Nitrophenyl	108	*f*	38.93	2.18	22.70	39.20	2.27	21.67	−4951
t-Butyl	56 (64)	33[d]	39.99	7.55	23.32	41.02[i]	7.61	23.79	−4759
2-Nitro-2-propyl	62 (4.5)	38[d]	23.86	4.00	27.81	24.94[i]	3.70	27.95	−5063
2-Chloro-2-propyl	68 (59)	41[d]	25.63	4.30	19.93	27.17[i]	4.51	20.09	−4943
Trifluoromethyl	*g*	29[d]							−4748
Benzyl	70 (0.1)	60[c]	54.54	4.58	18.18	55.16	4.74	17.71	−5020
β-Phenylethyl[h]	80 (0.1)	85[c]	57.13	5.39	16.66	57.04	5.58	17.83	−5036
Cyclohexyl	70 (0.1)	90[c]	49.30	7.59	19.17	49.43	7.22	18.98	−4830

[a] At 40 Mc., relative to external trifluoroacetic acid. [b] Calcd. for F: 13.56. Found: 13.16. [c] Yield from tetrafluorohydrazine. [d] Yield from difluoramine method. [e] Sample chromatographed, not distilled. [f] Yield not determined. [g] Infrared and mass spectra of the product were identical with those published.[2] Sample isolated by fractionation *in vacuo*. [h] Calcd. for F: 11.3. Found: 11.4. [i] Efforts to effect purification and repeated combustion analyses failed to yield satisfactory C and H data.

$$R{-}NO \xrightarrow[HNF_2\text{–pyridine}]{N_2F_4\text{ or}} R{-}\underset{\displaystyle O}{\overset{\displaystyle \uparrow}{N}}{=}NF \quad (I)$$

fluoramine,[3] diluted with nitrogen as a carrier gas, was swept into a pyridine–methylene chloride solution of the nitroso compound. Table I summarizes these preparations.

The radical mechanism suggested to account for the formation[2] of I, R = CF_3, affords a logical explanation for these tetrafluorohydrazine reactions. Apparently the glass surface, the solvent, and the nitroso compound act as the fluorine acceptors in this reaction, since silicon tetrafluoride and fluorosilicates are by-products, and the F^{19} n.m.r. spectra of chlorobenzene solutions from the reactions show C–F absorption. Highly colored organic products also are formed.

$$R{-}NO + NF_2\cdot \longrightarrow \left[R\underset{\displaystyle \cdot +}{\overset{\displaystyle O^-}{N}}{-}NF_2 \right] \longrightarrow R{-}\underset{\displaystyle O}{\overset{\displaystyle \uparrow}{N}}{=}NF + [F\cdot]$$

Since tetrafluorohydrazine conceivably could arise from an oxidation–reduction reaction of difluoramine, pyridine, and a nitroso compound, the radical pathway may account for N′-fluorodiimide N-oxide formation in the difluoramine reactions. However, ionic (NF_2^-) and nitrene (:NF) mechanisms cannot be ruled out at this time.[4]

The infrared spectra of N′-fluorodiimide N-oxides (see Table II) are characterized by strong bands at 10.7–11.2 μ, which are probably due to the N–F stretching vibrations,[5] and at 6.7–6.8 μ which are characteristic of azoxy compounds.

Conclusive evidence for the structure assigned to these fluoroazoxy compounds was obtained from their reaction with Grignard reagents. In the aromatic series displacement of fluoride ion by the organometallic reagent gave azoxy compounds in respectable yields[6] (Table III[7]).

$$Ar{-}N(\nearrow O){=}NF + RMgX \longrightarrow Ar{-}\underset{\displaystyle O}{\overset{\displaystyle \uparrow}{N}}{=}N{-}R$$

Because unsymmetrical azoxy compounds may be obtained by a similar and simpler route,[7] no efforts were made to optimize the yield data of Table III. The experimental method of choice appeared to be the addition of a slight excess of the Grignard reagent to a solution of the N-fluoroazoxy compound at 0°. Aliphatic N′-fluorodiimide N-oxides could not be used successfully in this azoxy synthesis, probably because

TABLE II

SPECTRAL CHARACTERISTICS OF Ar—N(→O)=NF

Aryl group	Infrared absorption λN–F, μ	Ultraviolet spectra (cyclohexane) λmax, mμ	εmax
Phenyl	11.15	243	8,400
p-Tolyl	11.15	216	7,100
		253	7,400
o-Tolyl	11.2	No maximum	
m-Tolyl	10.7	247	8,600
p-Bromophenyl	11.15	258	12,100
o-Chlorophenyl	11.15	267	1,490
		273	1,480
p-Chlorophenyl	11.15	252	11,000

(3) J. P. Freeman, A. Kennedy, and C. B. Colburn, *J. Am. Chem. Soc.*, **82**, 5304 (1960).

(4) These species have been proposed as intermediates in the reactions of difluoramine with amines [C. L. Bumgardner, K. J. Martin, and J. P. Freeman, *ibid.*, **85**, 97 (1963)].

(5) The N–F stretching vibrations of difluorodiazine occur at 10–11 μ [R. H. Sanborn, *J. Chem. Phys.*, **33**, 1855 (1960)].

(6) A small amount of displacement on fluorine with the formation of fluorocarbon and N_2O apparently took place also. Methyl fluoride (*ca.* 11%) and N_2O (10%) were trapped from the nitrogen sweep of the reaction of the methyl Grignard reagent and N-*p*-chlorophenyl-N′-fluorodiimide N-oxide, and were identified by their mass spectra. Signals due to aromatic C–F groups could also be observed in the n.m.r. spectra of residues from reactions with aryl Grignard reagents.

(7) Characterization of the azoxy compounds reported in Table III was carried out in conjunction with the study of the reaction of Grignard reagents and organonitrosohydroxylamine tosylates, R—N(→O)=N—OTs, and was reported there [T. E. Stevens, *J. Org. Chem.*, **24**, 311 (1964)].

TABLE III

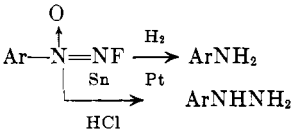
AZOXY COMPOUNDS FROM N′-FLUORODIIMIDE N-OXIDES

Diimide, Ar—N(O)=NF, Ar	Grignard reagent R	Azoxy compounds,[a] Ar—N(O)=N—R % yield
Phenyl	Phenyl	44
Phenyl	*p*-Chlorophenyl	74
p-Chlorophenyl	Phenyl	57
p-Bromophenyl	Phenyl	51
p-Chlorophenyl	*p*-Tolyl	62
Phenyl	*n*-Butyl	34
p-Bromophenyl	Ethyl	79[b]
p-Chlorophenyl	Methyl	46[c]
Phenyl	Ethyl	25

[a] See ref. 7. [b] Based on recovered starting material. [c] See ref. 6.

of the active hydrogen available to the organometallic reagent.

Reduction of the aromatic N′-fluorodiimide N-oxides was studied briefly. Catalytic hydrogenation with Adams catalyst in ethanol solution of the phenyl, *m*-tolyl, and *p*-tolyl isomers gave the corresponding aniline. Reduction with tin and hydrochloric acid converted I (R = phenyl), *p*-chlorophenyl, or *p*-bromophenyl, to the aromatic hydrazine.



Qualitatively, the aromatic diimides were much more stable than the aliphatic compounds. For example, the 2-chloro-2-propyl compound in refluxing chlorobenzene was converted to nitrous oxide and 2-chloropropene, but the aromatic diimides were not affected by similar treatment.[8] This thermal elimination reaction will be studied with other aliphatic azoxy compounds.

Experimental[9]

Reaction of Nitrosobenzene and Difluoramine.—A solution of 3.1 g. (29 mmoles) of nitrosobenzene in pyridine–methylene chloride (15:75 ml.) was stirred at about 20° while 30 mmoles of difluoroamine, generated by heating an acidified aqueous solution of difluorourea, was carried into the solution by a slow stream of nitrogen. When the difluoramine addition was complete, the methylene chloride–pyridine solution was poured into ice–water. The organic layer was separated and washed with water and dilute aqueous hydrochloric acid. The residue remaining after the methylene chloride had been removed at reduced pressure was combined with the residue from another nitrosobenzene–HNF_2 run of the same size. Distillation of the combined residues gave, after the removal of a small amount of nitrosobenzene that had sublimed into the condenser, N-phenyl-N′-fluorodiimide N-oxide, 3.4 g. (42%), b.p. 78° (4 mm.), $n^{20}D$ 1.5334.

Reaction of 2-Nitro-2-nitrosopropane and Difluoroamine.—A solution of 3.54 g. (30 mmoles) of 2-nitro-2-nitrosopropane in 30 ml. of pyridine and 90 ml. of methylene chloride was stirred at 20° while 40 mmoles of difluoramine was passed into the solution as described above. When the difluoramine addition was completed, the reaction mixture was poured into water and processed as described above. Distillation of the residue obtained on evaporation of the methylene chloride solvent gave N-(2-nitro-2-propyl)-N′-fluorodiimide N-oxide, 1.72 g. (38%), b.p. 62° (4.5 mm.), $n^{20}D$ 1.4349.

Reaction of Nitrosobenzene and Tetrafluorohydrazine.—A solution of 5.0 g. (46.6 mmoles) of nitrosobenzene in 50 ml. of chlorobenzene was stirred at 6° under 235-mm. pressure of tetrafluorohydrazine; the total volume of the system was about 2 l. The pressure began to drop immediately, and the solution was allowed to warm to 30° over 2 hr. No additional tetrafluorohydrazine was consumed (total pressure then was 128 mm.). A total of 23 mmoles of tetrafluorohydrazine was consumed and 0.73 mmole of silicon tetrafluoride and 1.9 mmoles of nitrous oxide were produced. The chlorobenzene solution was passed through a silica gel column packed in pentane. The material eluted by pentane–methylene chloride (2:1 and 1:1) was distilled to give N-phenyl-N′-fluorodiimide N-oxide, 3.45 g. (53%), b.p. 78° (4 mm.).

Reaction of Tetrafluorohydrazine and *p*-Bromonitrosobenzene.—A suspension of 1.0 g. of *p*-bromonitrosobenzene in 7 ml. of chlorobenzene was degassed on a vacuum line. The mixture was cooled to −196°, and tetrafluorohydrazine, 126 ml. (STP), was condensed into the U-tube. The cooling bath was removed and the reaction mixture was allowed to warm to room temperature. As the chlorobenzene melted, the solution darkened rapidly. After stirring at ambient temperature for 2 hr., the reaction mixture was chilled in ice while the gases were distilled through −80 and −196° traps. The −196° trap contained 94 ml. (STP); the mass spectrum of this fraction indicated a composition of 90% N_2F_4, 3% N_2O, 6% NO, and 1% of C–F material (the last product is a contaminant in the N_2F_4 used). A total of 1.85 mmoles (73%) of tetrafluorohydrazine was consumed. The chlorobenzene solution was removed from the U-tube and chromatographed on a pentane-packed silica gel column. Elution of the column with pentane–methylene chloride gave a solid fraction weighing 1.03 g. One recrystallization from hexane gave N-*p*-bromophenyl-N′-fluorodiimide N-oxide, 0.70 g. (60%), m.p. 82–84°.

Reaction of β-Phenylnitrosoethane Dimer and Tetrafluorohydrazine.—A solution of 3.55 g. (13.1 mmoles) of β-phenylnitrosoethane dimer[10] in 55 ml. of chlorobenzene was stirred at 55–70° under an atmosphere of tetrafluorohydrazine (a 3.85-g. sample of N_2F_4 gave a pressure of 347 mm. in volume of about 2 l.). After 3 hr. the pressure had decreased to 175 mm., and the gases were removed *in vacuo*. A total of 0.93 g. of tetrafluorohydrazine, 1.0 mmole of silicon tetrafluoride, 1.7 mmoles of nitric oxide, and 0.2 mmole of nitrous oxide were recovered (by mass spectrum). The chlorobenzene solution was chromatographed on a silica gel column. Elution of the column with pentane–methylene chloride gave N-β-phenylethyl-N′-fluorodiimide N-oxide, 3.76 g. (85%), as a pale yellow oil. A sample prepared earlier was isolated by distillation, b.p. 80° (0.1 mm.).

Reduction of N-*p*-Bromophenyl-N′-fluorodiimide N-Oxide.—To a mixture of 0.500 g. of the N-oxide and 2.1 g. of tin was added 3.7 ml. of concentrated aqueous hydrochloric acid over a 5-min. period. The mixture was warmed on the steam bath for 30 min., then allowed to stand overnight at room temperature. Water and enough 40% sodium hydroxide solution to make the solution basic were added, and the organic product was extracted with methylene chloride. Evaporation of the methylene chloride and recrystallization of the residue from hexane gave *p*-bromophenylhydrazine, 0.303 g. (71%), m.p. 104–106°, lit.[11] m.p. 105°.

Catalytic Hydrogenation of N-*p*-Tolyl-N′-fluorodiimide N-Oxide.—A 233-mg. sample of the N-oxide in 11 ml. of ethanol containing 25 mg. of platinum oxide was hydrogenated at atmospheric pressure and 26°. Hydrogen uptake began immediately; a total of 134 ml. (STP) of hydrogen was taken up in 70 min. (theory for 4 equiv. of hydrogen is 135.2 ml.). The catalyst was removed from the solution by filtration; the filtrate was stripped to dryness at reduced pressure. The solid residue was extracted with hot hexane. Evaporation of the hexane left 72 mg. (44%) of white crystals, the infrared spectrum of which was identical with that of *p*-toluidine. A 67-mg. portion of this solid was benzoylated in the Schotten–Baumann manner. The benzoyl derivative, after one recrystallization from hexane–methylene

(8) Aromatic N′-fluorodiimide N-oxides were recovered unchanged after being heated to reflux in acetic acid, diethylamine, concentrated aqueous hydrochloric acid, or methanolic sodium methoxide. They also were recovered after solution in concentrated sulfuric acid or boron trifluoride–ether at 25°. In concentrated sulfuric acid at 70° N_2, N_2O, NO, and SiF_4 were formed, but no organic product could be characterized.

(9) Melting points and boiling points are uncorrected.

(10) W. D. Emmons, *J. Am. Chem. Soc.*, **79**, 6522 (1959).

(11) J. E. Humphries, E. Bloom, and R. Evans, *J. Chem. Soc.*, **123**, 1766 (1923).

chloride, weighed 108 mg. (81%) and melted at 156–157°. A mixture melting point determination with the benzoyl derivative of *p*-toluidine (m.p. 157–158°) was 157–158°. The infrared spectra of the samples were identical.

Pyrolysis of N-(2-Chloro-2-propyl)-N′-fluorodiimide N-Oxide in Chlorobenzene.—A solution of 0.55 g. (3.9 mmoles) of the N′-fluorodiimide in 15 ml. of chlorobenzene was refluxed for 2 hr. while a nitrogen stream swept the off-gases through a −20° condenser and through traps cooled to −78 and −196°. The chlorobenzene solution was cooled while the nitrogen sweep was maintained. The −196° trap collected only N_2O (by mass spectrum), 85.5 ml. (STP), 3.8 mmoles. No SiF_4 was detected. The −78° trap collected 64.3 ml. (STP), 2.9 mmoles, of 2-chloropropene. The infrared and mass spectra were identical with those of an authentic specimen.

Reaction of N-Phenyl-N′-fluorodiimide N-Oxide and the *n*-Butyl Grignard Reagent.—A solution of 0.71 g. of the above diimide in 25 ml. of tetrahydrofuran was stirred at ice-bath temperature while 9.5 ml. of 0.8 *M* *n*-butyl Grignard reagent in tetrahydrofuran was added over 10 min. The reaction mixture was allowed to warm to 25° (90 min.), and then was poured over an ice–dilute hydrochloric acid mixture. The organic product was isolated by extraction with methylene chloride and was chromatographed on silica gel. Elution of the column with pentane–methylene chloride (1:1) gave N-phenyl-N′-*n*-butyldiimide N-oxide, 0.306 g. (34%), as a yellow oil; ultraviolet (cyclohexane), λ_{max} 246 mμ (ϵ_{max} 10,300).

Anal. Calcd. for $C_{10}H_{14}N_2O$: C, 67.39; H, 7.92; N, 15.72. Found: C, 67.46; H, 7.97; N, 16.08.

Reaction of the Phenyl Grignard Reagent and N-*p*-Chlorophenyl-N′-fluorodiimide N-Oxide.—A solution of 0.350 g. of the above diimide in 20 ml. of ether was stirred at ice-bath temperature while about 3 mmoles of the phenyl Grignard reagent in 2 ml. of ether was added dropwise. The reaction temperature was allowed to increase to 22° over 1 hr., then the mixture was quenched in ice–water and hydrochloric acid. The organic product was isolated by ether extraction. Chromatography of the organic residue over silica gel gave N-*p*-chlorophenyl-N′-phenyldiimide N-oxide, 0.264 g. (57%), m.p. 81–82°.[7]

Anal. Calcd. for $C_{12}H_9ClN_2O$: N, 12.04. Found: N, 12.23.

Reaction of the *p*-Chlorophenyl Grignard Reagent and N-Phenyl-N′-fluorodiimide N-Oxide.—A solution of 1.02 g. (7.3 mmoles) of the above diimide in 25 ml. of tetrahydrofuran was stirred at ice-bath temperature under an atmosphere of nitrogen while 7.7 ml. of 1.1 *M* *p*-chlorophenylmagnesium bromide in tetrahydrofuran was added dropwise. The mixture was allowed to warm to 20° over 1 hr., and then quenched in iced aqueous hydrochloric acid. The organic product was isolated by extraction with methylene chloride. The methylene chloride was removed at reduced pressure. The last traces of solvent were removed by pumping *in vacuo* through a −80° trap. An F^{19} n.m.r. scan of the material trapped at −80° showed peaks at −4800 c.p.s. (40 Mc., CF_3COOH standard), due to the starting N′-fluorodiimide, and at +1531 c.p.s., due to 4-chlorofluorobenzene. Chromatography of the residue over silica gel as usual gave an azoxybenzene fraction of 1.27 g. (74.6%). One recrystallization of this material from hexane gave N-phenyl-N′-*p*-chlorophenyldiimide N-oxide, 1.07 g., m.p. 68–69°, lit.[7] m.p. 68°.

Structure and Configuration of Isojervine[1]

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Isojervine, an isomer obtained on acid treatment of jervine, is shown to possess structure II from chemical and physical evidence.

The elucidated structure[2] of jervine (I) has been shown to explain all but one of the diverse reactions[3] of the alkaloid. Isojervine,[4] an unexpected product obtained on acid treatment of pseudojervine has received no generally accepted structural assignment.[5] In a preliminary communication[6] we reported that structure II was consonant with all chemical and spectral data obtained from isojervine[7] and the present paper describes the full details.

Isojervine (II), $C_{27}H_{39}O_3N$, m.p. 116–118°, was obtained in crystalline form by treatment of jervine according to Jacobs' procedure,[4] together with a new isomer, m.p. 262–263°. Isojervine is moderately stable toward acid and very sensitive to alkali, in contrast to jervine. It possesses a characteristic ultraviolet absorption spectrum[8] (Fig. 1), showing strong end absorption (ϵ 9200 at 220 mμ) with inflection at 252 mμ (ϵ 2900) and a maximum at 330 mμ, the intensity (ϵ 250) of which is considerably higher than that of usual ketones. The infrared spectrum[9] exhibits an α,β-unsaturated carbonyl peak at 1684 and 1630 $cm.^{-1}$ and the chemical data[4,8] show the presence of two hydroxyl groups and a secondary amino group; that is, the ether linkage of jervine is cleaved in isojervine. Isolation of 2-ethyl-3-hydroxy-5-methylpyridine on selenium dehydrogenation[10] proves that isojervine contains the same nitrogen ring skeleton as that of jervine.

Reduction of II with lithium in liquid ammonia at −70° in presence of methanol has now afforded "α-dihydrojervinol"[8] (III), showing that the carbocyclic ring system of jervine is still retained, and three double bonds are, therefore, present in isojervine. The result also established that not only the ketonic function of isojervine exists at C-11, but also that two hydroxyl groups are located at C-3 and C-23 in "α-dihydrojervinol" and isojervine.

The abnormal ultraviolet absorption spectrum of II and the higher pK_a value (7.12 in 50% ethanol) of N-methylisojervine (IV) than that (6.08) of N-methyljervine[11] (V) led us to assume, at first, that one of the three double bonds might be conjugated with nitrogen.

(1) Part I of "C-Nor-D-homosteroids and Related Alkaloids."

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(7) After we had completed this work, Dr. O. Wintersteiner of the Squibb Institute and Professor W. G. Dauben of California University informed us that they also have arrived at the same structure as ours. Their results have now been published in (a) *Tetrahedron Letters*, 795 (1962), and (b) *J. Org. Chem.*, **28**, 293 (1963), respectively.

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