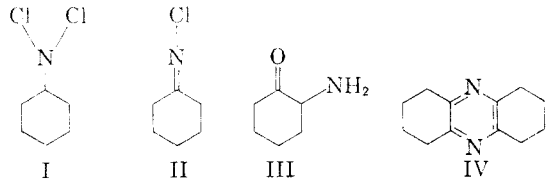
the *N*-chloroimine. The *N*-chloroimine being isoelectronic with the oxime tosylate can then undergo closure to an azirine intermediate, evidence for which has already been presented.[2] Positive evidence that the *N*-chloroimine is an intermediate is now submitted.



I II III IV

Treatment of *N,N*-dichlorocyclohexylamine, I, with potassium acetate in ethanol at the reflux temperature gave *N*-chlorocyclohexylimine, II,[5,6] as a colorless liquid. The compound was characterized by its infrared spectrum, elemental analysis and by its conversion to cyclohexanone on hydrolysis with aqueous acid. Treatment of II with one mole of sodium methoxide in absolute methanol gave an excellent yield of 2-aminocyclohexanone, III, isolated and characterized by its conversion to 1,2,3,4,6,7,8,9-octahydrophenazine, IV.[7]

The conversion of II to III with one mole of base proceeds at least as well as the conversion of I to III with two moles of base, so that the *N*-chloroimine II appears to be an intermediate in the *N,N*-dichloro-*sec*-alkylamine rearrangement.

EXPERIMENTAL

N-Chlorocyclohexylimine. To a solution of 25 g. (0.25 mole) of potassium acetate in 130 ml. of absolute ethanol at the reflux temperature was added dropwise over a period of 30 min. 16.8 g. (0.1 mole) of *N,N*-dichlorocyclohexylamine.[1] The reaction mixture was heated for a further 3 hr., cooled to room temperature and 200 ml. of ether and 100 ml. of benzene added. The ethereal solution was washed with 3 × 100 ml. of water, then with 3 × 50 ml. of 2*N* hydrochloric acid and again with water. The solvent layer was dried with calcium sulfate and the solvent removed at room temperature under vacuum. The residue consisted of 13 g. of an oil which was submitted to vacuum distillation through a column at 3 mm. of mercury. After a small forerun, the product distilled at 53–54°. The product was redistilled to give 7.5 g. (57%) of *N*-chlorocyclohexylimine, b.p. 36°/1.5 mm., n_D^{25} 1.5056. The infrared spectrum showed absorption due to C=N at 1612 cm.$^{-1}$, probably displaced from its normal position because of the chlorine.

Anal. Calcd. for $C_6H_{10}ClN$: C, 54.75; H, 7.66; Cl, 26.94; N, 10.65. Found: C, 54.92; H, 7.82; Cl, 26.68; N, 10.53.

Acid hydrolysis of N-chlorocyclohexylimine. A solution of 0.2 g. of *N*-chlorocyclohexylimine in aqueous ethanol was heated on the steam bath with 1 ml. of concd. hydrochloric acid for 30 min. The reaction mixture was treated with 2,4-dinitrophenylhydrazine reagent and on cooling cyclohexanone 2,4-dinitrophenylhydrazone, m.p. and mixture m.p. 160–162° crystallized.

Rearrangement of N-chlorocyclohexylimine. A solution of 1.0 g. (0.0075 mole) of *N*-chlorocyclohexylimine in 20 ml. of methanol was treated with 8 ml. of a 1.0*N* solution of sodium methoxide in methanol at the reflux for 1 hr. The solution was cooled and 30 ml. of dry ether added. The sodium chloride produced was filtered and amounted to 410 mg. (92%). The ethereal solution was extracted with 3 × 70 ml. of 10% hydrochloric acid and with water. The combined aqueous extracts were heated on the steam bath for 15 min., 30 ml. of 50% sodium hydroxide solution and 5 ml. of 30% hydrogen peroxide were then added, and the heating was continued for a further 15 min. The reaction mixture was cooled in ice and the precipitate filtered. The solid was recrystallized from acetone giving 530 mg. (74%) of 1,2,3,4,6,7,8,9-octahydrophenazine, m.p. 108–109°; mixture melting point with an authentic sample[7] was not depressed.

Acknowledgment. The authors are indebted to Dr. B. Katlafsky for the interpretation of the infrared spectra.

ORGANIC CHEMICALS DIVISION
ST. LOUIS RESEARCH DEPARTMENT
MONSANTO CHEMICAL CO.
ST. LOUIS, MO.

(5) S. Reid and D. Sharpe of Central Research Laboratories, Monsanto Chemical Company, Dayton, Ohio (private communication) have also prepared this compound by a different method.

(6) U. S. Patent 2,894,028 claims the preparation of this compound as a crystalline solid, m.p. 20°, by the action of chloramine on cyclohexanone; however, no analysis is given and in our hands the compound failed to crystallize.

(7) P. A. S. Smith, *J. Am. Chem. Soc.*, **70**, 323 (1948).

Three 2-Fluoroalkyl-5-nitrofurans

WILLIAM R. SHERMAN, MORRIS FREIFELDER, AND GEORGE R. STONE

Received May 5, 1960

In an excellent series of papers[1] sulfur tetrafluoride has recently been introduced as a unique fluorinating agent. By means of this reagent aldehydes and ketones are readily converted to *gem*-difluoro compounds and carboxylic acids to trifluoromethyl derivatives. Using sulfur tetrafluoride we have been able to obtain three 2-fluoroalkyl-5-nitrofurans. This type of nitrofuran has not previously been reported. Thus sulfur tetrafluoride reacted with 5-nitro-2-furaldehyde to form 2-difluoromethyl-5-nitrofuran, with 2-acetyl-5-nitrofuran to give 2-(α,α-difluoroethyl)-5-nitrofuran, and with 5-nitro-2-furoic acid to produce 2-trifluoromethyl-5-nitrofuran.

All of the fluoroalkylnitrofurans had antibacterial activity. The most active member of the group was 2-difluoromethyl-5-nitrofuran. In a two-fold agar dilution test[2] this compound completely inhibited the growth of *Escherichia coli* and *Salmonella typhimurium* at a concentration of 6 mcg. per ml., *Staphylococcus aureus* at 12 mcg. per ml. and *Proteus vulgaris* at 25 mcg. per ml.

(1) W. C. Smith, *et. al.*, *J. Am. Chem. Soc.* **81**, 3165 (1959); C. W. Tullock, *et. al.*, *J. Am. Chem. Soc.*, **82**, 539 (1960); W. R. Hasek, *et. al.*, *J. Am. Chem. Soc.*, **82**, 543 (1960); W. C. Smith, *et. al.*, *J. Am. Chem. Soc.*, **82**, 551 (1960).

(2) Carried out by R. J. Otto and staff of Abbott Laboratories.

EXPERIMENTAL[3]

2-Trifluoromethyl-5-nitrofuran. 5-Nitro-2-furoic acid (15.7 g., 0.1 mole) was placed in a 183 ml. stainless steel bomb, which was sealed and cooled in an acetone–Dry Ice bath. After evacuation to about 0.3 mm. pressure, the vessel was charged with sulfur tetrafluoride[4] (43 g., 0.4 mole). After allowing the mixture to warm to room temperature, the reactor was heated to 120° for 7 hr. under autogenous pressure. Following the reaction the cooled bomb was vented and the oily residue taken up in chloroform. The chloroform extract was washed with sodium carbonate solution followed by water, then dried and the solvent removed. The residual oil was fractionally distilled to give 5.47 g. of a light yellow liquid with a camphor-like odor, b.p. 108° (102 mm), n_D^{25} 1.4368. When the sodium carbonate extract was neutralized with acetic acid and cooled, 3.5 g. of the sodium salt of 5-nitro-2-furoic acid (explodes at 247°) was obtained. Based on recovered starting material the yield of pure trifluoromethyl compound was 37%.

Anal. Calcd. for $C_5H_2F_3NO_3$: C, 33.16; H, 1.11; N, 7.74. Found: C, 33.39; H, 1.39; N, 7.60.

2-Difluoromethyl-5-nitrofuran. Sulfur tetrafluoride (42 g., 0.39 mole) was added to 5-nitro-2-furaldehyde (26.4 g., 0.187 mole) in the manner described above. After heating for 8 hr. at 65°, the bomb was cooled and vented. The residue was worked up as before and distilled to provide 6.7 g. of the difluoromethyl compound, b.p. 96–98° (13 mm), $n_D^{21.3}$ 1.4910–1.4922 and 6.2 g. of starting nitrofuraldehyde. Based on recovered starting material the yield was 28%.

Anal. Calcd. for $C_5H_3F_2NO_3$: C, 36.82; H, 1.85; N, 8.59. Found: C, 36.88; H, 1.99; N, 8.56.

2-(α,α-Difluoroethyl)-5-nitrofuran. A mixture of 2-acetyl-5-nitrofuran (31 g., 0.2 mole) and water (1 ml.) was charged with sulfur tetrafluoride (63.0 g., 0.575 mole) as described above. The addition of water was necessary in order to generate hydrofluoric acid to catalyze the reaction. After heating at 75° for 10 hr., the reaction was worked up in the usual way to give 8.9 g. (25%) of the difluoroethyl derivative b.p. 58–60° (0.5 mm.), n_D^{25} 1.4717. When the reaction was carried out at 55–60° for 10 hr., the yield was increased to 34%.

Anal. Calcd. for $C_6H_5F_2NO_3$: C, 40.68; H, 2.84; N, 7.91. Found: C, 40.81; H, 3.09; N, 7.98.

In an attempt to prepare the difluoroethyl compound by carrying out the reaction with catalyst at 40° for 10 hr. only starting ketone was recovered, in 70% yield. When the reaction was run at 75° for 10 hr. in the absence of catalyst, starting material was again recovered, this time in 50% yield. At 110° only tars were formed.

ORGANIC CHEMISTRY DEPARTMENT
RESEARCH DIVISION, ABBOTT LABORATORIES
NORTH CHICAGO, ILL.

(3) Boiling and melting points are uncorrected. Analyses were carried out by E. F. Shelberg and staff of Abbott Laboratories.

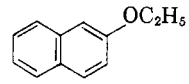
(4) Purchased from E. I. du Pont de Nemours and Company.

Novel Synthesis of Heterocyclic Ketones

WILLIAM C. ANTHONY

Received March 3, 1960

The introduction of an aldehyde function into aromatic (I)[1] and heterocyclic (II)[2] compounds

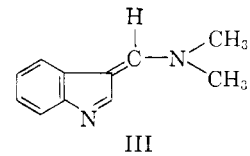


I

II

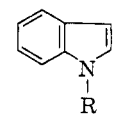
by use of phosphorus oxychloride and methyl formanilide or dimethylformamide has been described in the literature. In this paper we report the introduction of a ketone function into certain indoles and pyrroles by means of phosphorus oxychloride and the appropriate amide. The compounds which were prepared by this method are listed in Table I. All attempts to acylate β-ethoxynaphthalene, thiophene, dimethylaniline, and fluorene by this method failed.

It has been stated[1] that only *one* replaceable hydrogen on the aromatic system is necessary for the reaction with formamides to proceed. Smith[3] has applied this procedure to the preparation of indole-3-carboxaldehyde. He isolated and characterized the intermediate III and proposed a reaction mechanism which would require two replaceable hydrogens on the nucleophile.



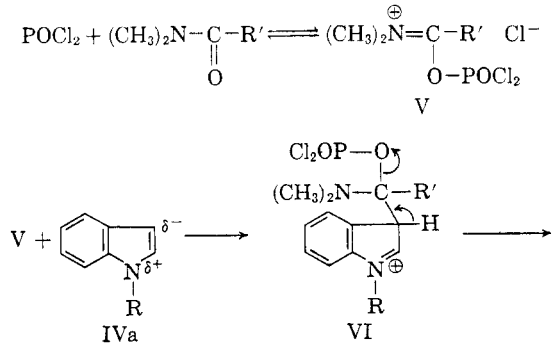
III

In the course of our investigation of indole and pyrrole ketone formations, we have found that an indole compound (IV) with only one replaceable hydrogen, is also convertible into a ketone. With such a starting material, an intermediate similar to III is not possible.



IV R = ethyl

The following reaction scheme may apply to acylations of indoles and pyrroles which contain either one or two replaceable hydrogens:



V

IVa VI

(1) *Org. Syntheses*, Coll. Vol. III, 98 (1955).

(2) E. Campaigne and W. L. Archer, *J. Am. Chem. Soc.*, **75**, 989 (1953).

(3) G. F. Smith, *J. Chem. Soc.*, 3842 (1954).