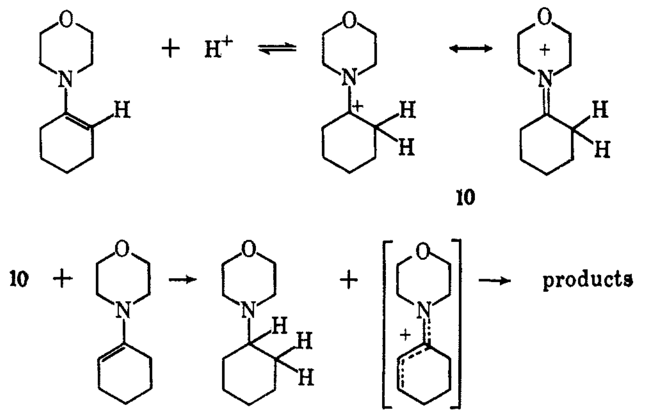

Enamines have been reduced previously to the corresponding saturated amines by heating with equimolar quantities of 98% formic acid.[3] The initial step was proved to be protonation followed by hydride transfer from the formate anion to form the saturated amine and carbon dioxide.

Experimental Section

Gas chromatographic analyses were performed on an Aerograph Model A-350-B chromatograph equipped with an Igepal Co-990 column (30 wt % on 60–80 mesh Chromosorb P packed in a 5 ft × 0.25 in. stainless steel column). Helium was used as the carrier gas (50 ml/min) and the column temperature was maintained at 204–205°. The relative areas of the enamine and saturated amine were measured by a Disc integrator and were converted to weight ratios by applying the appropriate weight relative response factors for the thermal conductivity detector. Infrared spectra were measured on a Perkin-Elmer Infracord Model 137B. The nmr spectra were measured in $CDCl_3$ solution using a Varian Associates V-4311 spectrometer operated at 60 Mcps. Tetramethylsilane was used as an internal reference standard. Mass spectra were measured on a Consolidated Electrodynamics Corp. Model 1030 spectrometer.

Materials.—1-Morpholino-1-cyclohexene, bp 109° (9 mm) [lit.[4] bp 104–106° (12 mm)] and 1-pyrrolidino-1-cyclohexene, bp 109–110° (16 mm) [lit.[4] bp 105–107° (13 mm)], were prepared by the method of Stork, Brizzolara, Landesmann, Szmuszkovicz, and Terrell[4] using catalytic quantities of p-toluenesulfonic acid. N-cyclohexylmorpholine (Abbott Laboratories) and p-toluenesulfonic acid monohydrate (Eastman Organic Chemicals) were used without further purification. Prepurified nitrogen (Air Reduction Co., Inc.) was used for the inert atmosphere.

Conversion of 1-Morpholino-1-cyclohexene to N-Cyclohexylmorpholine.—1-Morpholino-1-cyclohexene (33.4 g, 0.2 mole) and p-toluenesulfonic acid (1.0 g) were heated together at 175–180° for 24 hr in a nitrogen atmosphere. Gas chromatographic samples were obtained by hypodermic syringe inserted through a rubber septum and were taken at time 0 and hourly thereafter. The new product formed during the reaction was collected by preparative-scale gas chromatography and was identified as N-cyclohexylmorpholine by infrared, nmr, and mass spectra, and by gas chromatographic comparison of retention time and peak enhancement with an authentic sample. Distillation of the reaction mixture showed that 85.6% of the 1-morpholino-1-cyclohexene had been converted to products with a selectivity of 22.6% to N-cyclohexylmorpholine. Cyclohexanone (0.63 g), morpholine (1.47 g), higher boilers (0.4 g), and 12 g of residue were also obtained.

No N-cyclohexylmorpholine was formed when 1-morpholino-1-cyclohexene was heated in a nitrogen atmosphere at 175–180° for 23 hr. Excess morpholine was added to this mixture and it was heated for an additional 52 hr at reflux (143–145°). No N-cyclohexylmorpholine was formed.

Conversion of 1-Pyrrolidino-1-cyclohexene to N-Cyclohexylpyrrolidine.—1-Pyrrolidino-1-cyclohexene (30.2 g, 0.2 mole) and p-toluenesulfonic acid (1.0 g) were heated together at 178–180° for 22 hr in a nitrogen atmosphere. Gas chromatographic samples were obtained by a hypodermic syringe inserted through a rubber septum and were taken at time 0 and hourly periods thereafter.

Samples of the new product formed during this reaction were collected by preparative-scale gas chromatography and identified by infrared, nmr, and mass spectra. The infrared spectrum showed absorptions at λ_{max}^{neat} 3.64 (s), 3.72 (s), 6.94 (s), 7.3 (m), 7.45 (m), 8.4 (m), 8.88 (s), 9.3 (w), 9.66 (w), 9.82 (w), 9.92 (w), and 11.3 (s) μ. The nmr spectrum ($CDCl_3$) showed unresolved multiplets centered at 1.23 and 1.78 ppm (15 protons) for the cyclic protons and an unresolved multiplet centered at 2.60 ppm (four protons) for the protons α to the nitrogen in the pyrrolidine ring. Mass spectral analysis showed the molecular weight to be 153. Other major peaks were observed at m/e 110, 97, 96, 70, 69, 55, 42, 41, and 39 which are characteristic of pyrrolidine and cyclohexylamine type structures.

Registry No.—**9**, 670-80-4; **8**, 6425-41-8; 1-pyrrolidino-1-cyclohexene, 1125-99-1; N-cyclohexylpyrrolidine, 7731-02-4.

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[3] N. J. Leonard and R. R. Sauers, *J. Am. Chem. Soc.*, **79**, 6210 (1957).

[4] G. Stork, A. Brizzolara, H. Landesmann, J. Smuszkovicz, and R. Terrell, *ibid.*, **85**, 207 (1963).

Arylethanolamines from Diaroylfurazan Oxides

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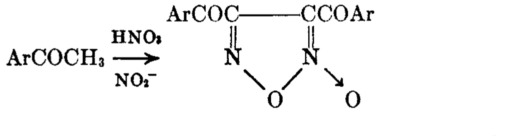
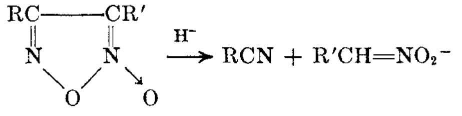
In a previous paper from this laboratory[1] the production of diaroylfurazan oxides from methyl aryl ketones was described. As a continuation of that work other furazans have been prepared by this method and these have been reduced by the use of lithium aluminum hydride to yield aryl-substituted ethanolamines.

Furazan oxides, containing two ArCO groups, are readily prepared by the action of nitric acid, containing a catalytic amount of nitrite ion, on aryl methyl ketones in acetic acid.



The reduction of furazan oxides (also commonly called furoxans) has been brought about with several different reducing agents including phosphorus pentachloride,[2] which removes the exocyclic oxygen atom to form a furazan, zinc and acetic acid,[3] which leads to dioximes, and sodium borohydride which also produces dioximes. In all these cases the 3,4 carbon–carbon bond in the 1,2,5-oxadiazole ring remains intact. Dornow, Fust, and Jordan[4] employed lithium aluminum hydride in the reduction of mixed furazan oxides to produce primary amines. They propose an initial cleavage of the furazan oxide to yield a nitrile and an anion of a nitro compound.



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[1] D. A. Shirley, B. H. Gross, and M. J. Danzig, *J. Org. Chem.*, **23**, 1024 (1958).

[2] H. Wieland and L. Semper, *Ann.*, **358**, 36 (1907).

[3] R. Scholl, *Ber.*, **21**, 506 (1888); **23**, 3490 (1890).

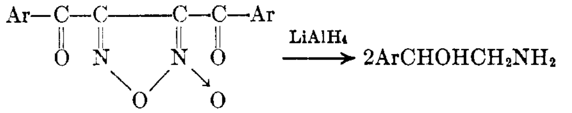
[4] A. Dornow, K. J. Fust, and H. O. Jordan, *ibid.*, **90**, 2124 (1957).

TABLE I

Ketone (ArCOCH$_3$)	Diaroylfurazan oxide Yield, %	 Mp, °C (found)	 Mp, °C (reptd)	N-Benzamide, derivative of redn prod, ArCHOHCH$_2$NHCOC$_6$H$_5$ Yield, %	 Mp, °C (found)	 Mp, °C (reptd)
Ar = phenyl	70	85.5–86.5	86–87[a]	43	148.5–150	149.5–150[c]
Ar = *p*-anisyl	73	140–140.5	139[b]	35	152.5–153	152.0[d]
Ar = 2-thienyl	72	114–115	New	58	122–123	121–122[e]
Ar = 1-naphthyl	48	151–152	New	56	145–146.5 (acetamide derivative)	145–146[f]

[a] A. F. Holleman, *Ber.*, **20**, 3360 (1887); **21**, 2838 (1888). [b] A. F. Holleman, *Rec. Trav. Chim*, **10**, 216 (1891) [c] S. M. Gordon, *J. Am. Pharm. Assoc.*, **17**, 1195 (1928). [d] V. Evdokimoff, *Gazz. Chim. Ital.*, **81**, 725 (1951). [e] C. F. Huebner, P. A. Diassi, and C. R. Scholz, *J. Org. Chem.*, **18**, 21 (1953). [f] A. Pictet and B. Manevitch, *Arch. Sci. Phys. Nat.*, **35**, 40 (1913).

We considered that the reduction of a molecule of diaroylfurazan oxide with lithium aluminum hydride might lead to two molecules of the corresponding β-aryl-β-hydroxyethylamine. Should the reaction produce the substituted ethanolamine in good yield, it would afford a simple, two-step procedure for obtaining these physiologically active types from methyl ketones. This has proved to be the case.



The amines appeared to be the only organic product. They were converted into benzamide or acetamide derivatives for identification.

Four typical aryl methyl ketones were converted to the diaroylfurazan oxides which were reduced to the amines. The results are summarized in Table I.

Experimental Section

Reaction of Methyl 2-Thienyl Ketone with Nitric Acid.—To a mixture of 50 ml of nitric acid (sp gr 1.42) and 100 ml of glacial acetic acid containing a small amount of sodium nitrite, was added, over a period of 10 min, 31.6 g (0.25 mole) of methyl 2-thienyl ketone dissolved in 50 ml of glacial acetic acid. The solution became pale yellow after addition but slowly darkened to a deep amber color after 2.5 hr. The temperature rose slowly from 30 to 50° over a 3-hr period. No external cooling was required. The mixture was then allowed to stand overnight. The resulting mass of needlelike crystals was filtered out, washed with cold ethanol, and air dried. A further yield of crystals could be obtained by pouring the filtrate over 200 g of ice; however, much by-product was mixed with the furazan oxide and purification was difficult. The furazan oxide was recrystallized from ethanol–ethyl acetate and the pale yellow product melted at 114–115°. The yield was 72%.

Anal. Calcd for $C_{12}H_6N_2O_4S_2$: C, 47.05; H, 1.97; N, 9.15. Found: C, 47.17; H, 1.99; N, 9.19.

Similar runs were carried out with acetophenone and *p*-methoxyacetophenone. Both furazans have been previously reported as indicated in Table I. In the case of the reaction of acetophenone, the temperature of the reaction mixture rose to 90° at which point the mixture was cooled to prevent further temperature rise.

1-Acetylnaphthalene was likewise converted into furazan oxide. In the first trial the temperature was raised to 86° and in the second to 51°. No furazan oxide could be isolated but a heavy, oily liquid, which set up as a glassy solid on cooling, was formed. In the third trial the temperature was held below 35°. After standing overnight a yellow, crystalline mass of furazan oxide had separated. No furazan oxide could be isolated from the filtrate.

Anal. Calcd for $C_{24}H_{14}N_2O_4$: N, 7.10. Found: N, 7.00, 7.22.

Preparation of 2,4-Dinitrophenylhydrazone of 3,4-Bis(2'-thienoyl)furazan Oxide.—Hayes and O'Keefe[5] had carried out the preparation of a 2,4-dinitrophenylhydrazone of 3,4-di(2-furoyl)furazan oxide in which they use iodine to catalyze the reaction. To 3.0 g of furazan in 100 ml of 95% EtOH was added several small crystals of iodine, 4.0 g of 2,4-dinitrophenylhydrazine, and 5 ml of concentrated HCl. The mixture was heated under reflux for 1 hr. The resulting, orange powder was filtered off and recrystallized from ethanol–ethyl acetate mixture. The product melted with decomposition at 180.5–182°. Although Hayes and O'Keefe obtained the bis-2,4-dinitrophenylhydrazone of the 2-furoyl compound, only one molecule of 2,4-dinitrophenylhydrazine was taken up by the 2-thienoyl compound.

Anal. Calcd for $C_{18}H_{10}N_6O_7S_2$: C, 44.44; H, 2.07; N, 17.27. Found: C, 44.70; H, 2.14; N, 17.60.

Reduction of Furazan Oxides with Lithium Aluminum Hydride.—A solution of the furazan oxide in 1,4-dioxane was prepared. In the typical case, 1.53 g (0.005 mole) of 3,4-bis-(2'-thienoyl)furazan oxide was dissolved in 25 ml of dioxane and mixed with 25 ml of anhydrous ether. The solution was added dropwise to a well-stirred mixture of 0.88 g of LiAlH$_4$ suspended in 100 ml of dry ether. A vigorous reaction resulted in a heavy, white precipitate. Excess LiAlH$_4$ was destroyed with moist ether and water. The ether layer was separated and the water layer was twice extracted with 50-ml portions of ether. The combined organic layers were dried over anhydrous MgSO$_4$, and the solvent was removed by distillation under reduced pressure. The oily ethanolamine was not crystallized but was converted into the benzamide.[6] Data from individual reactions are given in Table I.

Registry No.—$C_{12}H_6N_2O_4S_2$, 7733-96-2; $C_{24}H_{14}N_2O_4$, 7757-40-6.

Acknowledgment.—The authors wish to thank the National Science Foundation for a Research Participation grant for the summer of 1966 which made this study possible.

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(5) K. Hayes and C. O'Keefe, *J. Org. Chem.*, **19**, 1901 (1954).

(6) R. L. Shriner, R. C. Fuson, and D. Y. Curtin, "Identification of Organic Compounds," John Wiley and Sons, Inc., New York, N. Y., 1956, p 226.

Reduction of Silyl Esters of Amino Acids[1]

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A number of methods are available for the reduction of optically active amino acids to the corresponding optically active amino alcohols, but none is entirely satisfactory for use on a preparative scale. Direct reduction of the free amino acids with lithium aluminum

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(2) To whom inquiries should be directed.