

Unsaturated Heterocyclic Systems. XXXIX. Transannular Cyclizations in Medium-Sized Unsaturated Azalactams¹

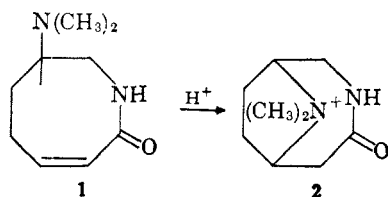
LEO A. PAQUETTE AND MALCOLM K. SCOTT

Department of Chemistry, The Ohio State University, Columbus, Ohio 43210

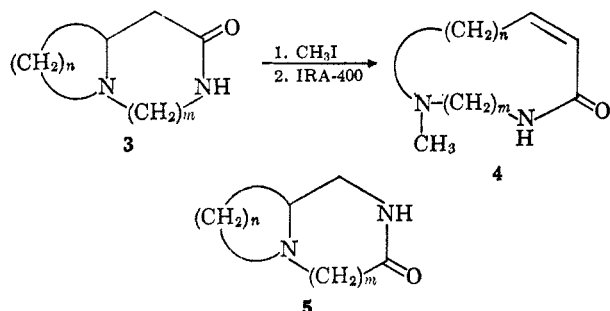
Received January 19, 1968

Two medium-sized α,β -unsaturated azalactams in which the tertiary nitrogen center forms a segment of the ring system have been prepared and their transannular cyclization in the presence of hydriodic acid was investigated. The synthetic route to these heteroatomic mesocycles consisted at its early stages in the Schmidt ring expansion of appropriate azabicyclic ketones in which the basic nitrogen atom occupies a bridgehead position. The consistent reactivity pattern manifested by these amino ketones toward hydrazoic acid is discussed.

In a recent paper, Paquette and Wise described a unique type of transannular reaction which involved the cyclization of an α,β -unsaturated lactam such as **1** in the presence of acid.² The transannular bonding process was found to be strongly dependent upon the preferred conformational orientations of the medium-sized heterocyclic rings. For example, the N-methyl lactam derived from **1** merely underwent protonation at the basic nitrogen center when exposed to acid, presumably because introduction of the methyl substituent effectively prevented the dimethylamino group from attaining a favorable bonding position with respect to the β -olefinic carbon atom.

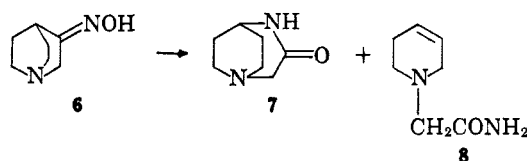


To examine the generality of such cyclizations, we were led to investigate possible transannular interactions in unsaturated lactams such as **4**. Since it had been established earlier that unsaturated lactam **1** and its congeners could be readily obtained by Hofmann degradation of the related quaternary ammonium salts, *e.g.*, **2**,^{2,3} it followed that **3** should likewise be convertible into **4**. From the synthetic viewpoint, therefore, it was desirable that a method be found which would lead to an amide such as **3** in preference to the isomeric amide **5**.

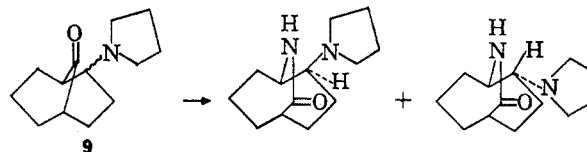


To this end, the possibility was considered that the requisite amides might be available by Schmidt ring expansion of the corresponding amino ketones or by Beckmann rearrangement of their ketoximes. A Russian group had reported that Beckmann rearrangement

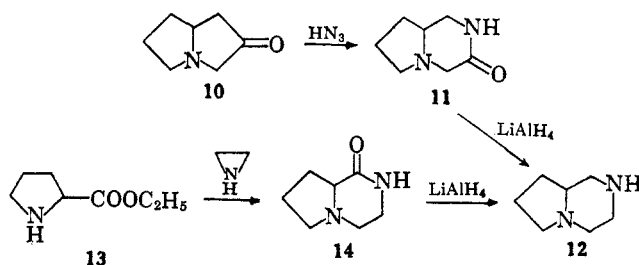
of 3-quinuclidone oxime (**6**) yielded 1,4-diazabicyclo[3.2.2]nonan-3-one (**7**, 28.3%) and Δ^3 -dehydropiperidinyl-1-acetamide (**8**, 56.6%).⁴ These same workers also



found that Schmidt ring expansion of 3-quinuclidone afforded a 50:50 mixture of **7** and **8** in a total yield of 54%.⁴ Plostniecks observed that exposure of amino ketone **9** to hydrazoic acid produced two isomeric amides, both resulting from migration of the bond closer to the nitrogen substituent.⁵ On the basis of Plostnieck's report and because conditions for Schmidt reactions on symmetrical amino ketones have been thoroughly investigated by earlier workers,^{2,3,6} this procedure was selected for further study.



When 1-azabicyclo[3.3.0]octan-3-one (**10**) was treated with hydrazoic acid, a single azalactam was obtained in good yield. This product was shown to be **11** on the basis of its lithium aluminum hydride reduction to diamine **12**, an authentic sample of which was synthesized in an unequivocal manner from 1,4-diazabicyclo[4.3.0]nonan-5-one (**14**) prepared in turn by the condensation of ethyl prolinatate (**13**) and ethylenimine.⁷



1-Azabicyclo[4.3.0]nonan-4-one (**15**) was similarly found to afford a single lactam (**16**) which again resulted

(1) For paper XXXVIII of this series, see L. A. Paquette and M. Rosen, *J. Org. Chem.*, **33**, 2130 (1968).

(2) L. A. Paquette and L. D. Wise, *J. Amer. Chem. Soc.*, **87**, 1561 (1965).

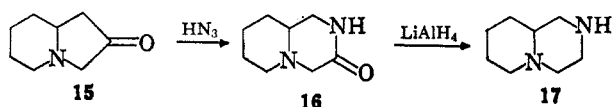
(3) L. A. Paquette and L. D. Wise, *J. Org. Chem.*, **30**, 228 (1965).

(4) E. E. Mikhлина and M. V. Rubtsov, *Zh. Obshch. Khim.*, **33**, 2167 (1963); M. V. Rubtsov, E. E. Mikhлина, V. Ya. Vorob'eva, and A. D. Yanina, *ibid.*, **34**, 2222 (1964); E. E. Mikhлина, V. Ya. Vorob'eva, V. I. Shedchenko, and M. V. Rubtsov, *Zh. Org. Khim.*, **1**, 1336 (1965).

(5) J. Plostniecks, *J. Org. Chem.*, **31**, 634 (1966).

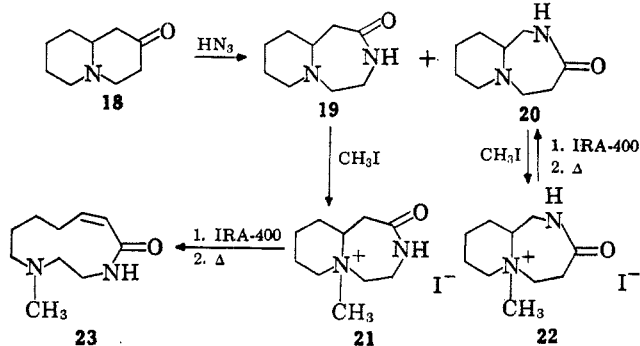
(6) R. J. Michaels and H. E. Zaugg, *ibid.*, **25**, 637 (1960).

(7) M. E. Freed and A. R. Day, *ibid.*, **25**, 2108 (1960).



exclusively from migration of the carbon-carbon bond most distant from the nitrogen atom. The structural assignment was confirmed by reduction to **17** which proved to be identical with an authentic sample prepared in a prescribed manner.⁷

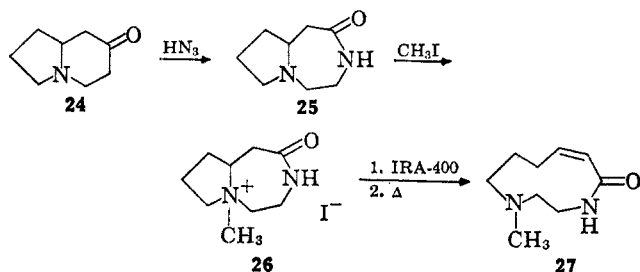
By contrast, in the Schmidt reaction of 1-azabicyclo[4.4.0]decan-4-one (**18**), **19** was found to predominate



over **20**. Assignment of structure was achieved indirectly by conversion of each azalactam (**19** and **20**) into its methiodide (**21** and **22**, respectively) and subjecting the individual quaternary ammonium salts to Hofmann elimination. Whereas **21** (as its methohydroxide) gave evidence of smooth loss of water to provide α,β -unsaturated lactam **23**, the methohydroxide of **22** proved to be quite resistant to degradation; instead, reconversion of **20** *via* demethylation was observed. This behavior was anticipated from our earlier observation that pyrolysis of the methohydroxide of **16** yielded the original lactam (**16**) as the only identifiable product.

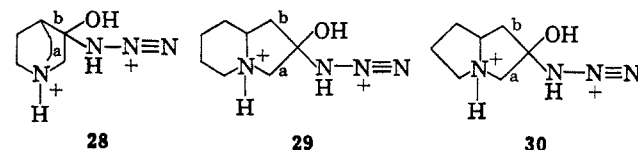
α,β -Unsaturated amide **23** exhibited principal infrared peaks in carbon tetrachloride solution at 3300 (N-H) and 1665 cm^{-1} (amide carbonyl group). The ultraviolet spectrum displayed only end absorption. In its nmr spectrum (CDCl_3), the chemical shifts of the two vinyl protons are close and the over-all pattern looks like a broad doublet centered at approximately δ 5.90 with two main peaks separated by 7 Hz; the N-methyl group is seen as a singlet at δ 2.30.

In the case of the last amino ketone to be examined, exposure of **24** to hydrazoic acid led to the formation of **25**. Although **25** was the only amide isolated (22% yield), the highly hygroscopic nature of the crude reaction mixture served to preclude isolation of the expected minor isomer. The structure of **25** follows from its facile conversion *via* methiodide **26** into the medium-sized unsaturated azalactam **27**. Although **27** could not be obtained as crystals, its spectra were totally consistent with the structural formulation. In this instance, the vinyl proton α to the carbonyl group was



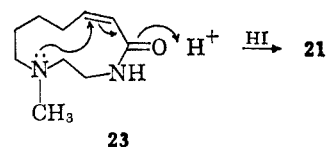
clearly seen as a doublet at δ 6.21 ($J = 7$ Hz). The small vinyl coupling constant would seem to indicate the presence of a *cis* olefinic bond in **27**,⁸ and its geometry has been assigned accordingly.

At this point, it was evident that a consistent reactivity pattern was being manifested by the amino ketones under Schmidt conditions. Thus, in intermediates such as **28-30** the strong electron-attracting characteristics of the protonated ring-nitrogen atom are seen to reduce the migratory aptitude of the neighboring carbon-carbon σ bond (labeled a) to electron-deficient azide nitrogen. The operation of this inductive effect permits the



alternative carbon-carbon σ bond (labeled b) to rearrange preferentially. The exclusive formation of **7**, **11**, and **16** gives evidence of this fact. Introduction of an additional methylene group between the ring nitrogen and the carbonyl group can be expected to diminish substantially this inductive effect and in such examples the migratory aptitudes of the two bonds would be expected to be comparable and to exhibit less directional specificity. This conclusion is supported by the behavior of **9**, **18**, and **24**.

In view of these developments, therefore, our study was restricted to a consideration of the behavior of α,β -unsaturated azalactams **23** and **27** in acid. Addition of ethanolic hydriodic acid to an ethereal solution of **23** afforded initially a gummy material which, after heating for a few minutes in methanol to complete the reaction, gave rise to a crystalline methiodide. Evidence that the reaction product was indeed the bicyclic methiodide **21** resulting from transannular ring closure was found in the superimposability of its infrared and nmr spectra upon those of **21**. A similar reaction readily transformed **27** into **26**. Therefore, we conclude that the introduction of a tertiary nitrogen atom into the



ring of a medium-sized α,β -unsaturated lactam does not adversely effect the propensity of such systems (*e.g.*, **1**) for protium-induced transannular cyclization. Also, the results described herein suggest that such transannular interactions may be of a general nature.

Experimental Section⁹

General Procedure for the Schmidt Reaction. 1,4-Diazabicyclo[4.3.0]nonan-3-one (11).—To a solution of 2.0 g (0.014

(8) O. L. Chapman, *J. Amer. Chem. Soc.*, **85**, 2014 (1963); G. V. Smith and H. Kriloff, *ibid.*, **85**, 2016 (1963).

(9) Melting points were determined with a Thomas-Hoover melting point apparatus and are corrected. Infrared spectra were recorded with a Perkin-Elmer Infracord Model 137 spectrometer fitted with sodium chloride prisms. Ultraviolet spectra were determined with a Cary 14 recording spectrometer. Nuclear magnetic resonance spectra were obtained with a Varian A-60 spectrometer purchased with funds made available through the National Science Foundation. The mass spectrum was measured with an AEI MS-9 mass spectrometer at an ionizing energy of 70 eV. The microanalyses were performed by the Scandinavian Microanalytical Laboratory, Herlev, Denmark.

mol) of 10^{10} in 40 ml of chloroform was added dropwise 9 ml of sulfuric acid while maintaining the temperature at 0° . Sodium azide (2.2 g, 0.033 mol) was added portionwise with vigorous stirring during 1 hr, the temperature being kept below 30° . The mixture was subsequently heated to 50° for 0.5 hr, cooled, and poured onto 20 g of crushed ice. Solid potassium carbonate was added until the evolution of gas had ceased. Aqueous 50% potassium hydroxide solution (20 ml) was added and the mixture was filtered to remove the inorganic salts. The chloroform layer in the filtrate was separated and the aqueous layer was extracted twice with 10-ml portions of chloroform. The combined organic layers were dried ($MgSO_4$), filtered, and evaporated to give 1.0 g (44%) of **11**: mp 120 – 121.5° , after recrystallization from ethyl acetate and sublimation; $\nu_{max}^{CCl_4}$ 3300, 3100 (N–H), and 1670 cm^{-1} (amide carbonyl).

For the purpose of characterization, **11** was converted into its methiodide by refluxing in ethanol with excess methyl iodide, mp 280 – 281.5° dec (methanol).

Anal. Calcd for $C_8H_{15}IN_2O$: C, 34.04; H, 5.36; N, 9.93. Found: C, 34.25; H, 5.42; N, 9.95.

1,4-Diazabicyclo[4.3.0]nonan-5-one (14).—A solution of 5.0 g (0.035 mol) of ethyl prolinatate (**13**) and 1.0 g of ethyl prolinatate hydrochloride in 45 ml of ethanol was heated to reflux and 1.55 g (0.036 mol) of ethylenimine in 15 ml of ethanol was added during 0.5 hr. The solution was refluxed for 24 hr, cooled, and evaporated, whereupon a crude liquid was obtained. Distillation of this material gave 1.2 g (25%) of **14**: bp 110 – 120° (0.4 mm); ν_{max}^{neat} 3250 cm^{-1} (NH) and 1670 cm^{-1} (amide carbonyl).

The methiodide of **14** melted at 250 – 252° dec (ethanol-methanol).

Anal. Calcd for $C_8H_{15}IN_2O$: C, 34.04; H, 5.36; N, 9.93. Found: C, 34.09; H, 5.37; N, 9.85.

1,4-Diazabicyclo[4.3.0]nonane (12). **A. Reduction of 12**.—A solution of 1.0 g (7.1 mmol) of **11** in 20 ml of dry tetrahydrofuran was added with stirring to a slurry of 600 mg of lithium aluminum hydride in 20 ml of the same solvent. The mixture was heated at reflux for 10 hr, cooled, and decomposed by the addition of water. The residue was filtered and extracted with dichloromethane. The combined filtrates were dried, filtered, and evaporated to give upon distillation 0.4 g (45%) of **12**: bp 69 – 70° (10 mm); ν_{max}^{neat} 3350 cm^{-1} (N–H).

The phenylthiourea of **12** melted at 122.5 – 124° (cyclohexane) [lit.⁷ mp 122 – 123°].

Anal. Calcd for $C_{14}H_{19}N_2S$: C, 64.33; H, 7.33; N, 16.08. Found: C, 64.33; H, 7.27; N, 16.08.

B. Reduction of 14.—From 1.0 g (0.007 mol) of **14** and 1.0 g of lithium aluminum hydride, there was obtained in like fashion 0.4 g (45%) of **12** which was converted directly into its crystalline phenylthiourea derivative, mp 123 – 125° (cyclohexane).

The infrared and nmr spectra of the phenylthioureas were superimposable and a mixture melting point of the two compounds was undepressed.

1,4-Diazabicyclo[4.4.0]decan-3-one (16).—Following the procedure outlined for the preparation of **11**, 4.7 g (0.054 mol) of **15**¹¹ and 4.1 g (0.055 mol) of sodium azide yielded 3.4 g (65%) of **16**: mp 111 – 113° , after recrystallization from ethyl acetate and sublimation; ν_{max}^{Nujol} 3360 (N–H) and 1670 cm^{-1} (amide carbonyl).

A sample of **16** was converted into its methiodide in the aforementioned manner, mp 273 – 275° (aqueous ethanol).

Anal. Calcd for $C_9H_{17}IN_2O$: C, 36.24; H, 5.73; N, 9.27. Found: C, 36.50; H, 5.78; N, 9.46.

Attempted Hofmann Elimination of 16.—An aqueous solution of 2.0 g of the above methiodide was passed through a column of Amberlite IRA-400 resin (hydroxide form) and the resulting aqueous solution of the methoxyhydroxide was evaporated to a syrupy residue. Pyrolysis of this residue gave a solid brown mass which was taken up in ethyl acetate. Addition of ether to this solution caused brown crystals to deposit; these were collected and recrystallized from benzene (charcoal decolorization) to give a white solid which was identified as **16** by infrared comparison and by mass spectral analysis (parent peak, m/e 154).

1,4-Diazabicyclo[4.4.0]decane (17).—A 500-mg (0.003 mol) sample of **16** was treated with 300 mg (0.005 mol) of lithium aluminum hydride in the manner described above. The resulting light yellow liquid (300 mg) was converted directly into its phenylthiourea derivative, mp 115 – 115.5° (cyclohexane) [lit.⁷

mp 118 – 119° (ethanol)]. An authentic sample of this derivative was prepared;⁷ the infrared and nmr spectra of the two samples were superimposable and a mixture melting point showed no depression.¹²

1,4-Diazabicyclo[5.4.0]undecan-5-one (19) and 1,5-Diazabicyclo[5.4.0]undecan-4-one (20).—Following the procedure outlined for the preparation of **11**, 10.5 g (0.067 mol) of **18**¹³ and 9.0 g (0.16 mol) of sodium azide yielded 10.5 g of a brown semisolid which was recrystallized twice from ethyl acetate to give 1.9 g (20%) of pure **19** as white needles: mp 135 – 136° ; $\nu_{max}^{CCl_4}$ 3200 , 3050 (N–H) and 1690 cm^{-1} (amide carbonyl).

Anal. Calcd for $C_9H_{16}N_2O$: C, 64.25; H, 9.59; N, 16.65. Found: C, 64.23; H, 9.67; N, 16.48.

The combined mother liquors were cooled and white rhomboid crystals, mp 95 – 105° , were deposited. Repeated fractional recrystallization of this solid from hexane–ethyl acetate failed to sharpen or alter its melting point. This purified material (0.8 g) was, therefore, treated directly with ethanolic methyl iodide. From this reaction, there could be isolated 0.2 g of a highly crystalline white solid, mp 234 – 236° dec (methanol), which proved to be the methiodide of **20**: ν_{max}^{KBr} 3500 , 3300 (N–H), and 1650 cm^{-1} (amide carbonyl).

Anal. Calcd for $C_{10}H_{19}IN_2O$: C, 38.70; H, 6.17; N, 9.03. Found: C, 38.73; H, 6.31; N, 9.07.

Attempted Hofmann degradation of this last methiodide by the procedure outlined above was found to produce **20**. The quantity isolated was too small for elemental analysis; however, the material displayed a mass spectral parent peak at m/e 168.

Preparation and Hofmann Elimination of Methiodide 21.—A solution of 2.3 g (0.0137 mol) of **19**, 3.5 g of methyl iodide, and 40 ml of ethanol was refluxed for 1.5 hr and cooled. The resulting crystalline solid was separated by filtration and recrystallized from methanol to give 3.1 g (73%) of **21**, mp 263 – 264° .

Anal. Calcd for $C_{10}H_{19}IN_2O$: C, 38.70; H, 6.17; N, 9.03. Found: C, 38.73; H, 6.31; N, 9.07.

An aqueous solution of 3.8 g (0.012 mol) of **21** was passed through a column of 70 g of Amberlite IRA-400 ion exchange resin (hydroxide form) and the solution of the methoxyhydroxide that was collected was evaporated to a syrupy residue which slowly solidified. Pyrolysis of this solid at 107 – 111° (0.22 mm) gave a white crystalline distillate, recrystallization of which from hexane afforded 0.7 g (30%) of **23**: mp 67 – 69° ; $\nu_{max}^{CCl_4}$ 3300 (NH) and 1670 cm^{-1} (amide carbonyl).

The methiodide of **23**, prepared in the customary manner, was found to melt at 229 – 231° (ethanol).

Anal. Calcd for $C_{11}H_{21}IN_2O$: C, 40.75; H, 6.53; N, 8.64. Found: C, 40.54; H, 6.60; N, 8.86.

1,4-Diazabicyclo[5.3.0]decan-5-one (25).—When a 4.0-g (0.029 mol) sample of **24**¹⁴ and 3.4 g (0.052 mol) of sodium azide were allowed to react in the manner described above a highly hygroscopic white solid was obtained. This material was recrystallized from hexane to give 1.0 g (22%) of **25**, mp 65 – 70° . Due to the hygroscopic nature of this solid, its methiodide (**26**) was formed directly, mp 234.5 – 236° (ethanol–methanol).

Anal. Calcd for $C_9H_{17}IN_2O$: C, 36.50; H, 5.79; N, 9.46. Found: C, 36.57; H, 5.67; N, 9.31.

Hofmann Elimination of 26.—An aqueous solution of 1.5 g (0.5 mmol) of **26** was passed through a column of Amberlite IRA-400 ion exchange resin (hydroxide form) and the aqueous eluate of the methoxyhydroxide was evaporated to leave a syrupy residue. Pyrolysis of the residue at a pot temperature of 100 – 150° (0.1 mm) gave 0.4 g (20%) of **27** as a liquid: ν_{max}^{neat} 3350 , 3100 (NH) and 1640 (amide carbonyl) and 1620 cm^{-1} (C=C); λ_{max}^{EtOH} end absorption; $\delta_{TMS}^{CDCl_3}$ 6.21 (doublet, $J = 7\text{ Hz}$, 1 H, vinyl proton adjacent to carbonyl), 5.54 (overlapping doublets, $J = 7$ and 7 Hz , 1 H, vinyl proton β to carbonyl), 2.33 (singlet, 3 H, N-methyl group).

Because of the limited quantity, this material was not purified further.

Transannular Cyclization of 23.—A solution of 0.10 g (0.6 mmol) of **23** in 5 ml of ether was treated with a 1:1 solution of 50% hydriodic acid in ethanol until no cloudiness persisted. The ether was decanted and the residue was taken up in several millimeters of boiling methanol. After the solution was allowed

(12) Subsequent to the completion of this work, we became aware of yet another synthesis of **17**: T. Yamazaki, M. Nagata, K. Ogawa, and F. Nohara, *Yakugaku Zasshi*, **87**, 668 (1967); *Chem. Abstr.*, **67**, 90770 (1967).

(13) G. R. Clemo, T. P. Metcalfe, and R. Raper, *J. Chem. Soc.*, 1429 (1936).

(14) R. T. Holden and R. Raper, *ibid.*, 2545 (1963).

(10) G. R. Clemo and T. A. Melrose, *J. Chem. Soc.*, 424 (1942).

(11) M. J. Martell, Jr., and T. O. Soine, *J. Pharm. Sci.*, **52**, 331 (1963).

to cool, the crystalline solid which formed was collected by filtration to give 0.049 g (29%) of 21, mp 264.5–265.5°. The infrared and nmr spectra of this material were identical with those of authentic 21.

Transannular Cyclization of 27.—A solution of 0.4 g of 27 and 5 ml of ether was treated with 0.2 ml of a 1:1 solution of 50% hydriodic acid in ethanol. The ether was decanted and the residue was taken up in methanol. Because a crystalline solid was not deposited from the methanolic solution, the solvent was evaporated to leave a thick residue which was dried at 50° (1.0 mm) over phosphorous pentoxide for 2 days. The infrared and nmr spectra of the dried residue (0.45 g) proved to be superimposable on those of 26.

The Preparation of 2-Hydroxyamino- α,α,α -trifluoro-*p*-toluenesulfonamide by Catalytic Hydrogenation and Its Use in the Synthesis of 2,3-Dihydro-4H-1,2,4-benzothiadiazin-4-ol 1,1-Dioxides. Studies in Infrared and Proton Magnetic Resonance Spectra

HARRY L. YALE

The Squibb Institute for Medical Research, New Brunswick, New Jersey 08903

Received December 5, 1967

The hydrogenation of 2-nitro- α,α,α -trifluoro-*p*-toluenesulfonamide (1) over a palladium catalyst in ethanol proceeded rapidly (0.5 hr) at room temperature; hydrogen uptake ceased with the absorption of 2 molar equiv to give a 90% yield of pure 2-hydroxyamino- α,α,α -trifluoro-*p*-toluenesulfonamide (2). Reduction of 2 to the amine (3) required a temperature of 50–60° and about 3 hr. The acid-catalyzed cyclization of 2 with formaldehyde and acetaldehyde led to the novel 2,3-dihydro-4H-1,2,4-benzothiadiazin-4-ol 1,1-dioxides (4a, b). The ir and pmr spectra of these and related reference compounds have made possible precise spectral assignments to the several different types of NH protons in these compounds.

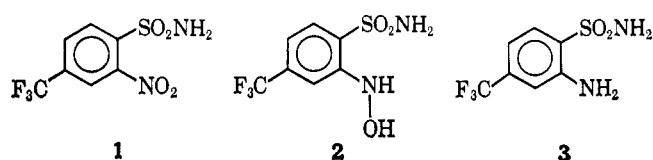
A recent paper¹ has described the intramolecular trapping of the intermediate hydroxyamino derivatives formed during the platinum-catalyzed reductions in ethanol of 2-nitro-2'-carboxy-, 2-nitro-2'-carbalkoxy-, and 2-nitro-2'-cyanobiphenyl; in addition, these hydrogenations formed appreciable amounts of the cyclization products arising *via* the intramolecular cyclization of the corresponding amine derivatives. The one exception was found in the reduction of 2,2'-dinitro-6,6'-dicyanobiphenyl; here, the 2,2'-dihydroxyamino-6,6'-dicyanobiphenyl which formed neither underwent intramolecular cyclization nor conversion to the diamino derivative during hydrogenation, but did cyclize during subsequent recrystallization. This report was noteworthy, since the literature contains but one earlier reference² to the isolation of any product other than amines (or their derivatives) from the catalytic hydrogenation of nitro compounds and that reference also involved the intramolecular trapping of the hydroxyamino and amino derivatives formed during the reduction of ethyl 2-nitrophenylacetate.

We have studied the palladium-catalyzed hydrogenation of a suspension of 2-nitro- α,α,α -trifluoro-*p*-toluenesulfonamide (1) in ethanol. At *ca.* 20–25°, hydrogen uptake is rapid (\sim 0.5 hr) and ceases after the absorption of 2 molar equiv of hydrogen. Filtration of the suspended catalyst, concentration of the filtrate, and recrystallization of the residual solid gave a 90% yield of pure hydroxyamino derivative (2). If, however, following the absorption of the 2 molar equiv of hydrogen, the temperature was raised to 50–60° a slow uptake of hydrogen was initiated and *ca.* 3.5 hr

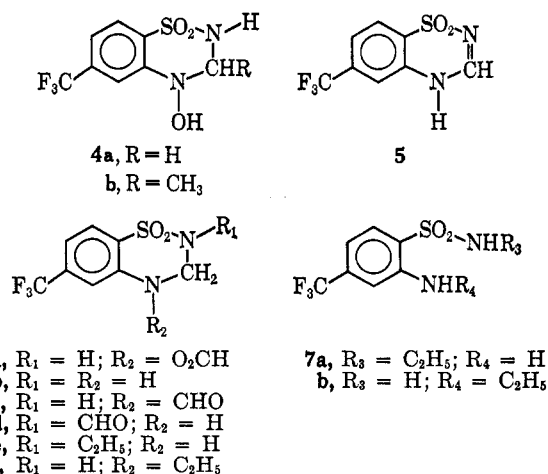
Registry No.—11, 16620-83-0; methiodide of 11, 16620-59-0; 12, 5654-83-1; 14, 16620-61-4; methiodide of 14, 16620-62-5; 16, 15932-74-8; methiodide of 16, 16620-64-7; 19, 16620-84-1; methiodide of 20, 16620-85-2; 21, 16620-86-3; 23, 16620-88-5; methiodide of 23, 16620-87-4; 25, 16620-89-6; 26, 16620-90-9; 27, 16620-91-0.

Acknowledgment.—The authors are grateful to Dr. Rodger Foltz for the mass spectral determinations.

were required to complete the reduction to the amine (3) even though 2 was completely in solution. Finally, when the isolated 2 was subjected to hydrogenation with fresh solvent and catalyst at 50–60° a similar slow reduction to 3 was observed.



The acid-catalyzed cyclization reactions³ of 2 with formaldehyde and acetaldehyde gave the novel 2,3-dihydro-4H-1,2,4-benzothiadiazin-4-ol 1,1-dioxides (4a and b). The reaction of 4a with formic acid for 1 hr at 90° gave two compounds, 5, the expected dehydration product, and 6a, the 4-formyl ester.



(1) C. W. Muth, J. R. Elkins, M. L. DeMatte, and S. T. Chiang, *J. Org. Chem.*, **32**, 1106 (1967).

(2) F. J. DiCarlo, *J. Amer. Chem. Soc.*, **68**, 1420 (1944).

(3) H. L. Yale and J. T. Sheehan, *J. Org. Chem.*, **26**, 4315 (1961).