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Reaction of Dihydropyran with Substituted Benzenesulfonyl Azides

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REACTION OF DIHYDROPYRAN WITH SUBSTITUTED BENZENESULFONYL AZIDES

by

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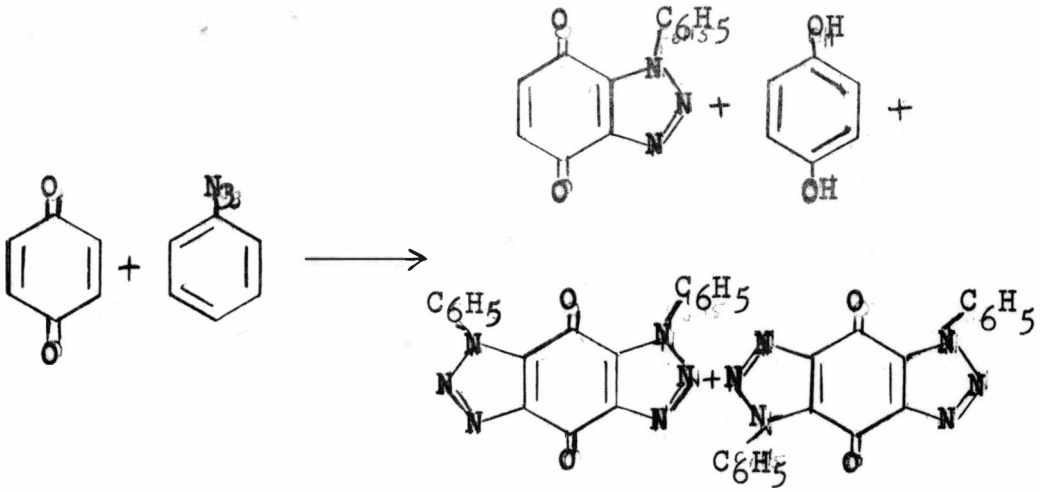
INTRODUCTION

The intent of this investigation was to study the addition of arylsulfonyl azides to vinyl ethers, specifically 2,3-dihydro-4H-pyran, and to establish by chemical and physical methods the structure of the adduct.

HISTORICAL

Addition of Azido Compounds to Carbon-Carbon Double Bonds

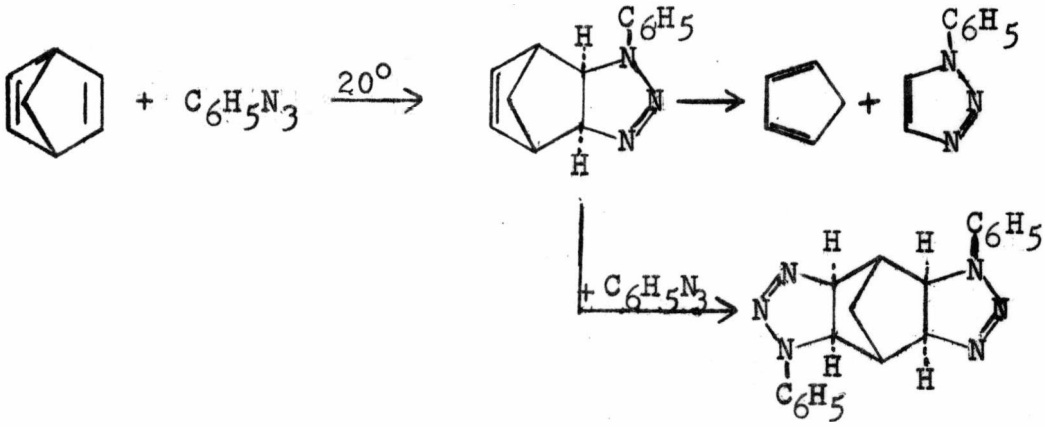
The addition of an azide group to an olefinic linkage was first reported by Wolff[1] who obtained the mono- and two bis-adducts with phenyl azide and p-benzoquinone.



The introduction of a p-nitro group on the N-phenyl substituent renders the triazole so unstable that it decomposes at once to the aziridine.[2]

A variety of olefins have undergone this addition reaction with azides.[3-14] Generally, addition to a double bond in conjugation with an aromatic system occurs sluggishly, if at all, whereas addition to a double bond in a cyclic system in which there is considerable ring strain occurs readily.

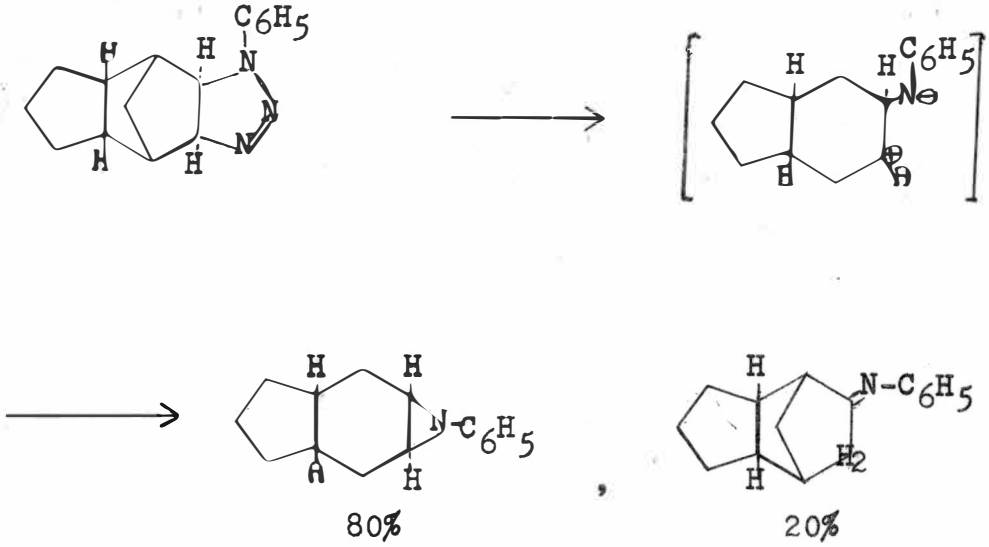
The most thoroughly studied azide addition reactions are those taking place at the angle-strained double bonds of bicyclo(2.2.1)heptene derivatives. Alder and Stein[15] using phenyl azide developed a diagnostic tool for the bicyclo(2.2.1)heptene double bond. For example norbornene and dicyclopentadiene react exothermically and quantitatively with phenyl azide.[16c] Norbornadiene is able to add two moles of phenyl or p-nitrophenyl azide. The monoadduct, obtained when an excess of norbornadiene is used, easily decomposes in a retro-Diels-Alder reaction giving cyclopentadiene and 1-aryltriazole.[16b]



Aliphatic azides also combine with norbornadiene and dicyclopentadiene but with lower yields.[17]

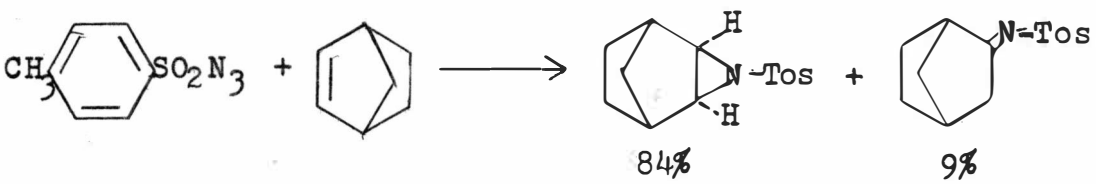
The adducts formed by organic azides and bicycloheptene derivatives are relatively stable to heat. Elimination of nitrogen takes place only at 150° with formation

of a mixture of an aziridine and a Schiff base, as illustrated below for dihydrodicyclopentadiene.[3]



The presumed zwitterion intermediate[16a] shown above could either stabilize itself through ring closure or by a hydride shift. This intermediate has not been detected experimentally.

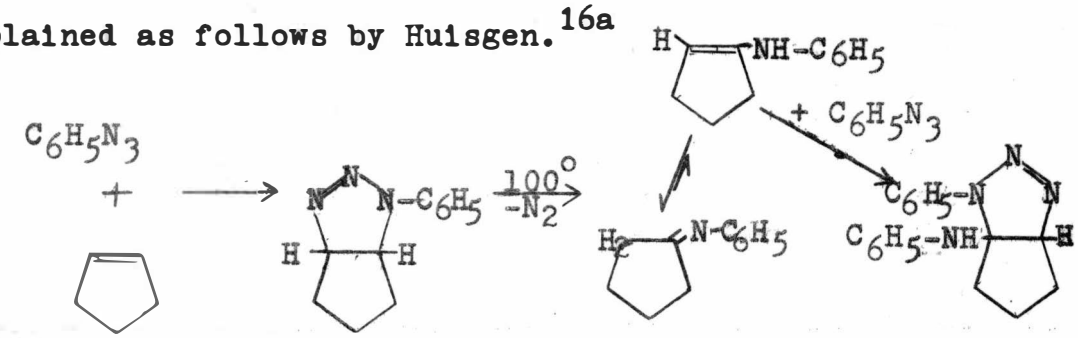
The benzoyl substituted triazoline derivative formed from the reaction of benzoyl azide and norbornene cannot be isolated and decomposes to give a 65% yield of a N-benzoyl aziridine derivative and a 25% yield of a substituted oxazoline. A comparable situation exists in the addition of p-toluenesulfonyl azide to bicyclo(2.2.1)heptene.[16f]



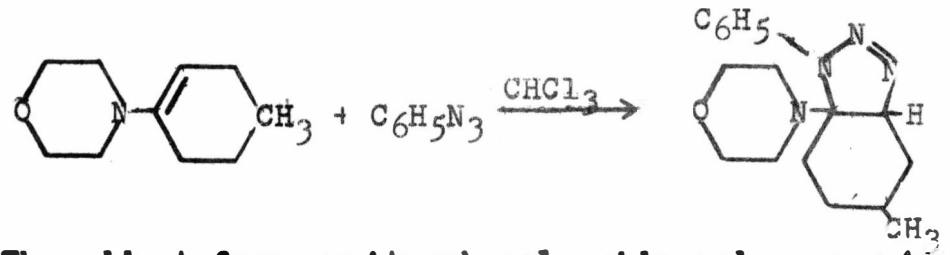
The only evidence for stereoselectivity in the cycloaddition of azides comes from Zalkow's and Ohlschlager's[11] work on addition to trans-cyclooctene. They found that phenyl azide adds exothermically to the trans while the diastereoisomeric triazoline from the cis isomer requires several months to form.[3] The enhanced reactivity of the trans configuration is also apparent in higher cyclic olefins.[18] Cyclopentene and other relatively unstrained cycloalkenes, like cis-cyclooctene, require more vigorous conditions.[3,16d] The triazoline from cyclopentene and phenyl azide loses nitrogen below 100° with quantitative formation of cyclopentanone anil[3] and it is claimed that in the analogous reaction with tosyl azide nitrogen is evolved even at 40°.[16b]

Addition of Azides to Enamines and the Related Enol Ethers

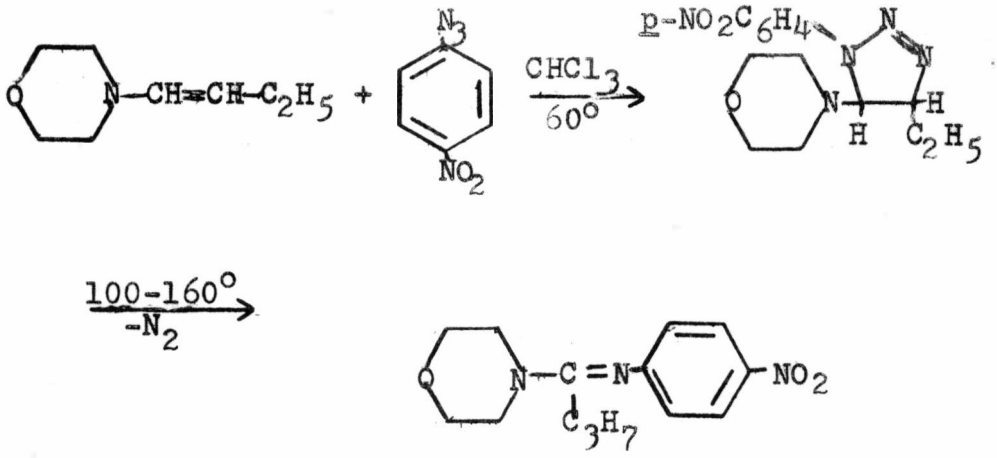
Particularly susceptible to attack by organic azides are the electron-rich double bonds of enamines. Alder and Stein[3] noted that heating cyclopentene with excess phenyl azide leads to a product with four nitrogen atoms, explained as follows by Huisgen.[16a]



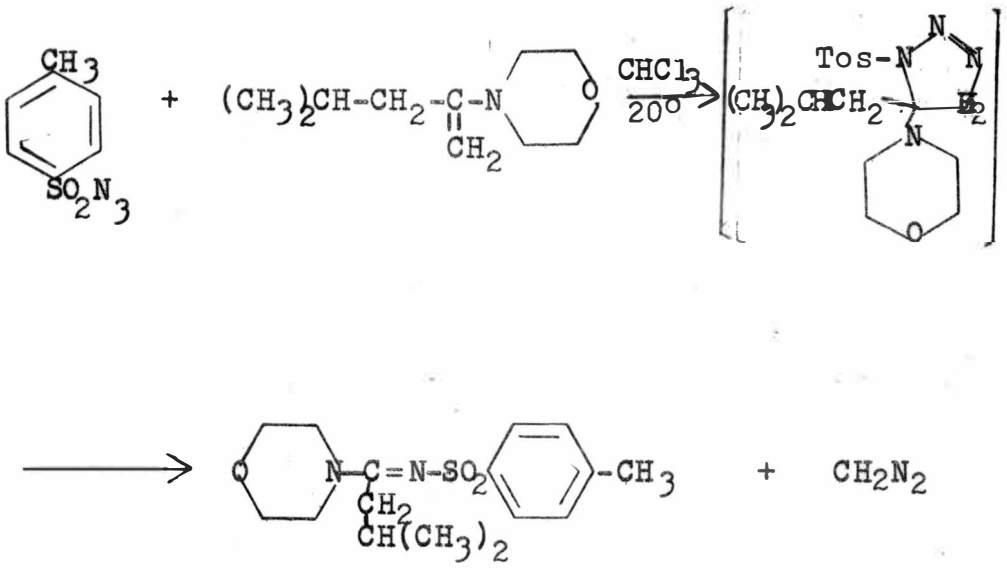
Fusco and others[19] have studied the addition of aromatic azides to enamines.



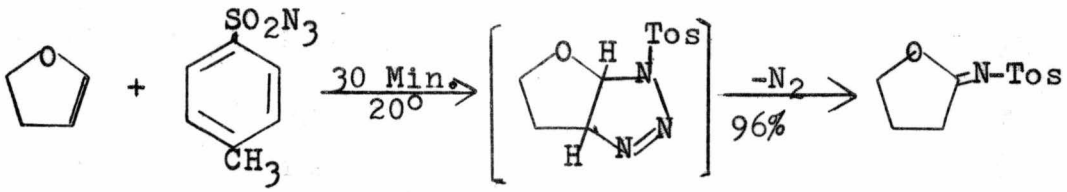
The adduct from p-nitrophanyl azide and an enamine rearranges on pyrolysis with elimination of nitrogen and formation of an amidine.[19]



Fusco and associates[19] have shown that adducts from tosyl azide and enamines undergo an interesting 1,3-dipolar elimination. The tosyl azide adduct from 2-morpholino-4-methylpent-1-ene at room temperature decomposes to diazomethane and an amidine having one less carbon atom.



In unpublished results Huisgen and co-workers[16a] claimed to have prepared the adducts from enol ethers, 2,3-dihydropyran and 2,3-dihydrofuran, and aromatic[16d] and tosyl[16b] azides.



Franz and Osuch[6] reacted p-toluenesulfonyl azide with 2,3-dihydropyran and n-butyl vinyl ether but failed to characterize or isolate the adduct although comparison of the infrared spectra of the reaction mixture and an enamine adduct had a similarity.

EXPERIMENTAL

General

All melting points, expressed in degrees centigrade, are corrected. Galbraith Microanalytical Laboratories performed the analyses. The analytical samples were dried *in vacuo* over phosphorous pentoxide for four days before analysis. Infrared spectra were measured with a Beckman I.R.-8 spectrophotometer and only bands of moderate to strong intensity are cited. Nuclear magnetic resonance spectra of samples at a concentration of 0.2 M were determined with a Varian A-60 spectrometer using deuterated chloroform or dimethylsulfoxide as solvent and tetramethylsilane as an internal reference. The assignment of splitting pattern and coupling constants are only tentative. Xylene and benzene were dried over sodium metal. Tetrahydrofuran and p-dioxane were dried over sodium hydroxide pellets and calcium hydride respectively.

Preparation of Substituted Benzenesulfonyl Azides

o-NITROBENZENESULFONYL AZIDE (I). — A solution of 30.00 g. (0.135 mole) of o-nitrobenzenesulfonyl chloride in 50 ml. of acetone was added dropwise with stirring to 10.00 g. (0.154 mole) of sodium azide in 75 ml. of water and 35 ml. of acetone at 0° over a 20 min. period. The

reaction mixture was stirred for 1 hr. at 0°, allowed to come to room temperature, and then poured over 500 ml. of crushed ice with vigorous stirring. The solid was collected by suction filtration, washed with cold water and recrystallized from hot absolute ethanol, to yield 23.95 g. (78%) of yellow needles, m.p. 71-72.5° (lit.[20] m.p. 71-73°); $\nu_{max.}$(Nujol) 2170, 1585, 1548, 1530, 1310, 1192, 1170, 1140, 1117, 1050, 963, 886, 849, 780, 753, 735, 728, 693, and 648 cm.$^{-1}$.

p-NITROBENZENESULFONYL AZIDE (II). — To 75 ml. of a 50% aqueous acetone solution containing 5.00 g. (0.077 mole) of sodium azide was added dropwise at -10°, 15.00 g. (0.068 mole) of p-nitrobenzenesulfonyl chloride dissolved in 75 ml. of acetone. Stirring was continued at -10° for 1 hr. and at room temperature for an additional hour. The mixture was then diluted with 500 ml. of ice water and a yellow solid precipitated which was collected on a filter, washed with cold water and dried. The product was dissolved in 150 ml. of warm absolute ethanol and the resulting solution was filtered. Cooling caused separation of slender light yellow needles which were collected by vacuum filtration, washed with cold ethanol and dried to give 13.60 g. (88%), m.p. 101-102°, of product; $\nu_{max.}$(Nujol) 2130, 1600, 1535, 1400, 1340, 1300, 1170, 1150, 1100, 1078, 1010, 982, 971, 960, 865, 850, 765, 758, 740, 727, and 677 cm.$^{-1}$.

Anal. Calcd. for $C_6H_4N_4O_4S$: C, 32.02; H, 1.75; N, 24.56. Found: C, 31.73; H, 1.90; N, 24.84.

In another experiment 30.00 g. (0.135 mole) of p-nitrobenzenesulfonyl chloride was dissolved in 50 ml. of acetone and added over a 20 min. period with stirring to 10.00 g. (0.154 mole) of sodium azide dissolved in 75 ml. water-20 ml. acetone at 0°. The reaction mixture was stirred for 1 hr. at 0°, brought to room temperature, and processed as before to yield 26.13 g. (85%) of product, m.p. 101-102°.

m-NITROBENZENESULFONYL AZIDE (III). — A solution of 10.00 g. (0.154 mole) of sodium azide in 75 ml. of 50% aqueous acetone was cooled to 0°. To this was added dropwise over a 20 min. interval 30.00 g. (0.135 mole) of m-nitrobenzenesulfonyl chloride in 50 ml. of acetone. The solution was stirred an additional hour at 0°, brought to room temperature and stirred for 30 min. The reaction mixture was poured with stirring into 500 ml. of crushed ice. The crude material, 30.59 g., was collected by vacuum filtration and washed. Recrystallization from hot ethanol gave 27.23 g. (88%) of white needles, m.p. 78-81°. An analytical sample, prepared by recrystallizing from absolute ethanol four times, melted at 79-81°; $\nu_{max.}$(Nujol) 2130, 1595, 1525, 1345, 1300, 1270, 1170, 1115, 1095, 1073, 1063, 993, 944, 908, 876, 816, 765, 742, 730, 664, and 656 $cm.^{-1}$.

Anal. Calcd. for $C_6H_4N_4O_4S$: C, 32.02; H, 1.75; N, 24.56. Found: C, 31.74; H, 1.87; N, 24.72.

In a second experiment the sodium azide was dissolved in 70% instead of 50% aqueous acetone and the stirring was continued for 2 hr. instead of 1 hr. after the m-nitrobenzenesulfonyl chloride addition. The yield was 30.55 g. (99%), m.p. 78-80°.

p-BROMOBENZENESULFONYL AZIDE (IV). — To 75 ml. of 50% aqueous acetone containing 5.00 g. (0.077 mole) of sodium azide, cooled to 0°, was added dropwise with stirring 17.25 g. (0.067 mole) of p-bromobenzenesulfonyl chloride in 75 ml. of acetone. After stirring 1 hr. at 0° the solution was allowed to come to room temperature. The reaction mixture was poured with stirring into 300 ml. of crushed ice. A white solid separated which was collected by vacuum filtration, washed with cold water, and recrystallized from ethanol to yield 17.71 g. (86%) of short white needles, m.p. 51-53°. Four recrystallizations from absolute ethanol provided an analytical sample, m.p. 53-53.5°; $\nu_{max.}$(Nujol) 2127, 1565, 1530, 1300, 1275, 1260, 1172, 1080, 1060, 1005, 968, 890, 832, 819, 770, 755, 730, and 687 $cm.^{-1}$.

Anal. Calcd. for $C_6H_4N_3BrO_2$: C, 27.48; H, 1.53; N, 16.03. Found: C, 27.70; H, 1.52; N, 16.22.

In a second experiment 34.55 g. (0.135 mole) of p-bromobenzenesulfonyl chloride in 100 ml. of acetone was

added dropwise to 10.00 g. (0.154 mole) of sodium azide in 100 ml. water. The reaction mixture was stirred 2 hr. at 0° and 2 hr. at room temperature and gave 34.18 g. (97%) of product when processed as before.

3,4-DICHLOROBENZENESULFONYL AZIDE (V). — Ten grams (0.154 mole) of sodium azide was dissolved in 100 ml. of water. To this solution, chilled to 0°, was added dropwise with stirring 33.15 g. (0.135 mole) of 3,4-dichlorobenzenesulfonyl chloride in 100 ml. acetone. After stirring at 0° for 2 hr. the mixture was brought to room temperature and was worked up as usual. The product was obtained as fine white needles, 30.24 g. (89%), m.p. 59-61°. Recrystallization four times from absolute ethanol afforded an analytical sample which melted at 60-61°; $\nu_{max.}$(Nujol) 2135, 1305, 1273, 1253, 1178, 1136, 1092, 1030, 890, 825, 742, 718, 696, 676, and 665 cm.$^{-1}$.

Anal. Calcd. for $C_6H_3N_3Cl_2O_2S$: C, 28.57; H, 1.19; N, 16.67. Found: C, 28.81; H, 1.23; N, 16.90.

In another experiment 10.00 g. (0.154 mole) of sodium azide dissolved in 75 ml. of water and 35 ml. of acetone was cooled to 0°. To this was added dropwise 33.15 g. (0.135 mole) of 3,4-dichlorobenzenesulfonyl chloride in 50 ml. of acetone. After stirring 1 hr. at 0° and 30 min. at room temperature the product was isolated in the usual manner. The product, 32.89 g. (97%), showed the characteristic azide band at 2135 cm.$^{-1}$, with a m.p. 59-61°.

2,5-DICHLOROBENZENESULFONYL AZIDE (VI). — To 10.00 g. (0.154 mole) of sodium azide dissolved in 100 ml. of water was added dropwise 100 ml. of an acetone solution containing 33.15 g. (0.135 mole) of 2,5-dichlorobenzenesulfonyl chloride at 0°. After stirring 2 hr. at 0° the solution was brought to room temperature then processed in the manner previously described. The product was obtained as white needles, 31.13 g. (92%), m.p. 50-53°. A sample, submitted for analysis after three recrystallizations from absolute ethanol, melted at 51-53°; $\nu_{max.}$ (Nujol) 2140, 1300, 1265, 1225, 1190, 1178, 1140, 1113, 1102, 1028, 976, 893, 834, 822, 740, 720, and 681 cm.$^{-1}$.

Anal. Calcd. for $C_6H_3N_3Cl_2O_2S$: C, 28.57; H, 1.19; N, 16.67. Found: C, 28.64; H, 1.30; N, 16.82.

In a second experiment 10.00 g. (0.154 mole) of sodium azide was dissolved in 75 ml. of 50% aqueous acetone. This solution, cooled to 0°, was combined with 28.57 g. (0.112 mole) of 2,5-dichlorobenzenesulfonyl chloride over a 20 min. period. The mixture was stirred 1 hr. at 0° and 10 hr. at room temperature and the product was isolated as before. The product, 27.35 g. (97%), m.p. 50-52.5°, had an infrared spectra identical to that of the compound prepared by the above procedure.

2,5-DIBROMOBENZENESULFONYL CHLORIDE (VII). — A mixture of 107.8 g. (0.46 mole) of p-dibromobenzene and

213.2 g. (1.83 mole) of chlorosulfonic acid was warmed at 63-67° for 2 hr., allowed to stand 12 hr. at room temperature and heated on a steam bath 2 hr. After pouring the solution into 500 ml. of crushed ice a grayish solid was collected by suction filtration and was washed with cold water. Recrystallization from 60% ethanol gave 97.6 g. (59%) of white platelets, m.p. 70-71.5° (lit[21] m.p. 71°).

2,5-DIBROMOBENZENESULFONYL AZIDE (VIII). — A solution of 26.62 g. (0.080 mole) of VII in 70 ml. of acetone was added dropwise to 75 ml. of water containing 6.50 g. (0.100 mole) of sodium azide at 0°. After stirring at 0° for 2 hr. and at room temperature for 1 hr. the product was isolated in the usual manner. The product was obtained as large white platelets, 20.36 g. (76%), m.p. 65-66°. Three recrystallizations from absolute ethanol afforded an analytical sample which melted at 65-67.5°; $\nu_{max.}$(Nujol) 2140, 1548, 1265, 1255, 1195, 1170, 1144, 1110, 1098, 1078, 1070, 1020, 964, 888, 831, 790, 730, 683, and 665 cm.$^{-1}$.

Anal. Calcd. for $C_6H_3N_3Br_2O_2S$: C, 21.11; H, 0.88; N, 12.32. Found: C, 21.32; H, 1.10; N, 12.58.

In a second preparation 10.00 g. (0.154 mole) of sodium azide was dissolved in 75 ml. of 50% aqueous acetone. To this solution at 0°, 43.89 g. (0.131 mole) of VII in 50 ml. of acetone was added dropwise over a 20 min. period.

After stirring at 0° for 2 hr. and at room temperature for 30 min. the product was isolated as usual to give 41.30 g. (92%), m.p. 65-67°.

p-TOLUENESULFONYL AZIDE (IX). — The method of Leffler and Tsuno[20] was used in two experiments in which 19.00 g. (0.100 mole) of p-toluenesulfonyl chloride and 13.00 g. (0.200 mole) of sodium azide afforded 16.16 g. (82%) and 16.95 g. (86%) of product melting at 18-20° (lit[20] m.p. 19-20°); $\nu_{max.}$ (liquid film) 2340, 2130, 1920, 1800, 1750, 1650, 1585, 1490, 1440, 1395, 1360, 1310, 1290, 1180, 1119, 1081, 1038, 1016, 970, 950, 810, 797, 742, 700, 662, and 631 $cm.^{-1}$.

In an additional preparation 19.00 g. (0.100 mole) of p-toluenesulfonyl chloride dissolved in 50 ml. of acetone was added to 75 ml. of ice-cold 50% acetone containing 13.00 g. (0.200 mole) of sodium azide during a 30 min. interval. After stirring at 0° for 2 hr. the reaction mixture was allowed to come to room temperature and subsequently was diluted with an equal volume of water. The solution was extracted thrice with 100 ml. portions of diethyl ether. The combined ether extracts were washed twice with 50 ml. of ice water and dried over anhydrous calcium chloride. Upon concentration in vacuo the etheral solution yielded 16.04 g. (82%) of product, m.p. 18.5-20.5°.

p-METHOXYBENZENESULFONYL AZIDE (X). — A 75 ml. portion of a 50% water-acetone solution containing 10.00 g.

(0.154 mole) of sodium azide was cooled to 0°. To this well-stirred solution was added 27.90 g. (0.135 mole) of p-methoxybenzenesulfonyl chloride in 50 ml. of acetone over a 60 min. period. After 1 hr. of stirring at 0° the reaction mixture was allowed to come to room temperature and was then diluted with 400 ml. of crushed ice. White platelets separated which were collected by suction filtration and washed with cold water. Recrystallization from ethanol afforded 26.85 g. (93%) of product, which melted at 51-52.5° and decomposed at 135° (lit.[22] decomposed 135°); $\nu_{max.}$ (Nujol) 2230, 1590, 1570, 1490, 1440, 1414, 1345, 1315, 1295, 1265, 1184, 1162, 1108, 1080, 1018, 830, 815, 803, 742, 712, and 664 $cm.^{-1}$.

Preparation of N-(Arylsulfonyl)-δ-Pentanimidolactones

PREPARATION OF N-(m-NITROBENZENESULFONYL)-δ-PENTANIMIDOLACTONE (XI). — To 2.28 g. (0.01 mole) of III was added 10.1 g. (0.12 mole) of dihydropyran at room temperature and within 1 min. gas evolution was noted. After standing at room temperature for 30 hr. no further nitrogen evolution occurred. Dilution with xylene to a total volume of 40 ml. followed by cooling and scratching the sides of the flask resulted in the separation of a white solid. The product was collected by suction filtration, washed with cold xylene and recrystallized from hot xylene to yield 2.12 g. (75%) of fine colorless

needles, m.p. 100-102°. Eight recrystallizations from benzene-petroleum ether gave an analytical sample which melted at 100-101°; $V_{max.}$(Nujol) 1580, 1525, 1350, 1320, 1310, 1275, 1169, 1155, 1119, 1080, 1069, 1056, 997, 975, 937, 892, 877, 827, 812, 760, 733, 720, 680, 669, and 655 cm.$^{-1}$; n.m.r. ($CDCl_3$) 117 (quintet, J=3), 164 (triplet, J=6), 271 (triplet, J=6), 465 (triplet, J=8), 510 (triplet, J=7), and 532 c.p.s. (triplet, J=2 c.p.s.).

Anal. Calcd. for $C_{11}H_{12}N_2O_5S$: C, 46.48; H, 4.23; N, 9.86; mol. wt., 284. Found: C, 46.66; H, 4.23; N, 9.73; mol. wt. (Rast), 250.

In a second experiment 5.0 g. (0.06 mole) of dihydropyran was added to 2.28 g. (0.01 mole) of III dissolved in 20 ml. of tetrahydrofuran at room temperature. The solution was stirred for 30 hr. after which time no further nitrogen evolution occurred. The total volume was brought to 40 ml. with xylene. On cooling and scratching the sides of the flask a white solid, collected by vacuum filtration and washed with cold xylene, separated. The 2.38 g. (84% yield) of product melted at 99.5-101°. The infrared spectra was identical to that of the above product.

In a third experiment 5.0 g. (0.06 mole) of dihydropyran was added to 2.28 g. (0.01 mole) of III in 20 ml. of benzene. After 30 hr. of standing at room temperature the product was isolated as before. It melted at 100-101°; yield, 2.32 g. (82%).

In a fourth experiment 5.0 g. (0.06 mole) of dihydropyran and 2.28 g. (0.01 mole) of III in 15 ml. of p-dioxane were stirred for 36 hr. at room temperature. The product, worked up as in the previous experiments, melted at 100-102°; yield 2.33 g. (82%).

In a fifth experiment 5.0 g. (0.06 mole) of dihydropyran was added to 2.28 g. (0.01 mole) of III in 20 ml. of xylene at room temperature. A white solid began to separate 30 hr. later. After cooling in an ice bath the small needles were collected by suction filtration and washed with cold xylene to give 2.34 g. (82%) of product, m.p. 100-101°.

All products isolated using the various reaction solvents had identical infrared spectra.

PREPARATION OF N-(o-NITROBENZENESULFONYL)-δ-PENTANIMIDOLACTONE (XII). — To 2.28 g. (0.01 mole) of I dissolved in 20 ml. of tetrahydrofuran was added 5.0 g. (0.06 mole) of dihydropyran. After warming at 50° for 20 hr. the reaction mixture was cooled to 25° and made to a total volume of 40 ml. with xylene. On cooling and scratching the sides of the flask, 2.43 g. (86%) of fine white needles separated, m.p. 75-77°. Recrystallizing four times from xylene afforded an analytical sample of constant melting range, 75-76°; $\nu_{max.}$ (Nujol) 1580, 1525, 1400, 1360, 1345, 1310, 1295, 1285, 1173, 1152, 1121, 1080, 1070, 1051, 980, 954, 917, 892, 872, 852, 829, 808, 773, 740, 723,

700, and 659 cm.$^{-1}$; n.m.r. ($CDCl_3$) 113 (quintet, J=3), 163 (triplet, J=6), 263 (triplet, J=6), 468 (doublet, J=1), and complex multiplet centered at 493 c.p.s. (J=2-3 c.p.s.), with a peak area ratio of 4:2:2:4:1.

Anal. Calcd. for $C_{11}H_{12}N_2O_5S$: C, 46.48; H, 4.23; N, 9.86. Found: C, 46.53; H, 4.38; N, 10.03.

In a second experiment 5.0 g. (0.06 mole) of dihydropyran was added to 2.28 g. (0.01 mole) of I in 20 ml. of xylene at room temperature. Within 2 min. nitrogen evolution began. Fourteen hours later there was no perceptible gas evolution. Stirring an additional hour and then cooling caused separation of a white solid which was collected and washed to yield 2.23 g. (79%) of product.

In a third experiment 2.28 g. (0.01 mole) of I was shaken with 10.0 g. (0.12 mole) of dihydropyran. The solution was warmed at 55-60° for 10 min. and then allowed to stand for 10 hr. at room temperature. After dilution with three volumes of xylene and cooling, the product separated and was collected and washed. The 2.40 g. obtained represents a yield of 85%.

The product, XII, isolated in all experiments gave identical infrared spectra and melting ranges ± 1°.

PREPARATION OF N-(p-NITROBENZENESULFONYL)-δ-PENTANIMIDOLACTONE (XIII). — A mixture of 10.1 g. (0.12 mole) of dihydropyran and 2.28 g. (0.01 mole) of II was warmed at 55° for 10 min. then allowed to stand at room temperature

for 10 hr. Dilution with an equal volume of xylene and cooling resulted in separation of 2.70 g. (95%) of a colorless solid which was collected by vacuum filtration and washed with cold xylene, m.p. 127-130°. An analytical sample of fine white needles melting at 130-132° was prepared by recrystallizing the crude product four times from hot xylene; $\nu_{max.}$(Nujol) 1600, 1520, 1340, 1295, 1270, 1192, 1170, 1141, 1090, 1083, 1048, 1006, 969, 956, 950, 930, 890, 850, 827, 820, 775, 742, 733, 720, 698, 677, 666, and 632 cm.$^{-1}$; n.m.r. (CD_6SO) 112 (quintet, J=3), 165 (triplet, J=6), 269 (triplet, J=6), and a complex multiplet at 487-513 c.p.s.

Anal. Calcd. for $C_{11}H_{12}N_2O_5S$: C, 46.48; H, 4.23; N, 9.86. Found: C, 46.69; H, 4.45; N, 10.05.

In a second experiment a solution of 5.0 g. (0.06 mole) of dihydropyran and 2.28 g. (0.01 mole) of II in 20 ml. of p-dioxane was kept at 50° for 20 hr. and subsequently cooled to room temperature and made to a total volume of 40 ml. with xylene. With cooling fine colorless needles formed which were collected by suction filtration and washed with cold xylene to yield 2.27 g. (80%) of the product.

In a third experiment the same quantities of reactants used in the preceding preparation were dissolved in 20 ml. of tetrahydrofuran (instead of p-dioxane) and allowed to stand at 55° for 20 hr. Cooling resulted in

separation of a pale yellow solid which was worked up as usual to give 2.65 g. (90% yield) of product.

In a fourth experiment again the same quantities of reactants were dissolved in 20 ml. of xylene. After standing at room temperature for 36 hr. and cooling the product was collected and washed with cold xylene; yield 1.94 g. (68%).

In a fifth experiment 4.56 g. (0.02 mole) of II dissolved in 15 ml. of benzene was mixed with 10.1 g. (0.12 mole) of dihydropyran at room temperature. The solution was warmed at 53° for 1 hr. and at room temperature for 14 hr. during which time a light yellow solid deposited. The 4.32 g. (76%) of product was collected by vacuum filtration and washed with cold benzene.

In each preparation the products obtained gave identical infrared spectra and melting ranges ± 1.5°.

PREPARATION OF N-(p-BROMOBENZENESULFONYL)-δ-PENTANIMIDOLACTONE (XIV). — To a 20 ml. benzene solution containing 5.24 g. (0.02 mole) of IV was added 3.4 g. (0.04 mole) of dihydropyran. After warming at 40° for 20 hr. and making the total volume 40 ml. with xylene, cooling with scratching of the flask's sides resulted in the separation of a white solid. The product was collected by vacuum filtration and washed with cold xylene to give 3.36 g. (53%) of colorless blunt needles. Five recrystallizations from hot xylene afforded an analytical sample

which melted at 108-111°; $\nu_{max.}$(Nujol) 1575, 1345, 1312, 1265, 1167, 1141, 1088, 1051, 1008, 970, 940, 917, 897, 842, 810, 770, 740, 720, and 680 cm.$^{-1}$; n.m.r. ($CDCl_3$) 112 (quintet, J=4), 160 (triplet, J=6), 264 (triplet, J=6), and a complex multiplet 452-486 c.p.s., with a peak area ratio of 2:1:1:2.

Anal. Calcd. for $C_{11}H_{12}NBrO_3S$: C, 41.51; H, 3.77; N, 4.40. Found: C, 41.49; H, 3.73; N, 4.39.

In a second experiment 5.24 g. (0.02 mole) of IV dissolved in 20 ml. of xylene was shaken with 3.4 g. (0.04 mole) of dihydropyran. The mixture discolored after heating at 75° for 4 hr. With cooling and scratching the flask's sides a white solid deposited which was worked up as before to give 1.12 g. (18%) of product.

In a third experiment a mixture of 2.62 g. (0.01 mole) of IV and 10.1 g. (0.12 mole) of dihydropyran was warmed at 60° for 15 min. then allowed to stand at room temperature 60 hr. After dilution to 30 ml. with xylene the product was isolated in the usual manner to give 1.00 g. (31%) of product.

In a fourth experiment a solution of 2.62 g. (0.01 mole) of IV dissolved in 20 ml. of tetrahydrofuran and 5.0 g. (0.06 mole) of dihydropyran stood at 55° for 48 hr. then was diluted to 40 ml. with xylene. Cooling and scratching the sides of the flask caused separation of a white solid which was filtered and washed. The 1.23 g. of product obtained represents a 39% yield.

All products isolated in these experiments gave identical infrared spectra and had melting ranges within ± 1°.

PREPARATION OF N-(2,5-DIBROMOBENZENESULFONYL)-δ-PENTANIMIDO LACTONE (XV). — To a 20 ml. tetrahydrofuran solution containing 3.41 g. (0.01 mole) of VIII was added 5.0 g. (0.06 mole) of dihydropyran. After stirring 26.5 hr. at 25° the mixture was diluted to a total volume of 40 ml. with xylene. With cooling and scratching of the flask's sides a white powder separated which was collected then washed and recrystallized from xylene to give 2.61 g. (66%) of product, m.p. 125-127.5°. A sample for analysis was prepared by recrystallizing three times from xylene; $\nu_{max.}$ (Nujol) 1600, 1435, 1383, 1360, 1348, 1338, 1311, 1270, 1245, 1190, 1170, 1153, 1132, 1110, 1096, 1083, 1055, 1021, 972, 943, 933, 888, 827, 806, 788, 768, 762, 743, 705, 683, and 664 cm.$^{-1}$; n.m.r. ($CDCl_3$) 113 (quintet, J=3), 164 (triplet, J=6), 265 (triplet, J=6), and 456 c.p.s. (doublet, J=1 c.p.s.), with a peak area ratio of 4:2:2:2:1.

Anal. Calcd. for $C_{11}H_{11}NBr_2O_3S$: C, 33.25; H, 2.75; N, 3.53. Found: C, 33.30; H, 2.75; N, 3.38.

In another experiment 3.41 g. (0.01 mole) of VIII was shaken with 10.1 g. (0.12 mole) of dihydropyran at room temperature. After 26.5 hr. at 25° nitrogen evolution had ceased and a white solid had deposited. Upon

making the total volume 40 ml. with xylene, the product, 3.28 g. (82%), was isolated in the usual manner.

In a third reaction a mixture of 3.41 g. (0.01 mole) of VIII dissolved in 10 ml. of p-dioxane and 5.0 g. (0.06 mole) of dihydropyran was stirred at room temperature for 26.5 hr. then diluted with three volumes of xylene. A fine white powder separated after cooling. It was filtered, washed and recrystallized to give 2.00 g. (50%) of product.

In a fourth experiment 3.41 g. (0.01 mole) of VIII dissolved in 15 ml. of xylene was shaken with 5.0 g. (0.06 mole) of dihydropyran. After standing at 25° for 29 hr. the product was obtained as before, 3.44 g. (87%).

All products isolated using the various reaction solvents had identical infrared spectra and melting ranges within ± 1°.

PREPARATION OF N-(3,4-DICHLOROBENZENESULFONYL)-δ-PENTANIMIDOLACTONE (XVI). — To a 20 ml. xylene solution containing 2.52 g. (0.01 mole) of V was added 5.0 g. (0.06 mole) of dihydropyran. After stirring at 25° for 30 hr. the mixture was diluted to a total volume of 40 ml. with xylene. Cooling and scratching the sides of the flask caused separation of small colorless needles which were collected by suction filtration, washed with cold xylene and recrystallized from hot xylene to give 2.89 g. (94%) of product. An analytical sample was prepared by

four recrystallizations from xylene, m.p. 104-105°; $\nu_{max.}$ (Nujol) 1565, 1410, 1365, 1342, 1320, 1310, 1270, 1160, 1152, 1091, 1068, 1050, 1028, 977, 936, 892, 826, 802, 728, 697, 684, 671, and 627 cm.$^{-1}$; n.m.r. ($CDCl_3$) 115 (quintet, J=3), 162 (triplet, J=6), 268 (triplet, J=6), a complex multiplet 452-476, and 485 c.p.s. (doublet, J=1 c.p.s.), with a peak area ratio of 4:2:2:1:1:1.

Anal. Calcd. for $C_{11}H_{11}NCl_2O_3S$: C 42.86; H, 3.57; N, 4.55. Found: C, 43.02; H, 3.76; N, 4.53.

In another experiment a solution of 2.52 g. (0.01 mole) of V and 10.1 g. (0.12 mole) of dihydropyran was warmed at 55° for 15 min. then allowed to stand at 25° for 60 hr. During the last 48 hr. a white solid separated. After dilution with two volumes of xylene (20 ml.) and cooling, the product deposited and 1.70 g. (55%) was isolated in the usual manner.

In a third experiment 5.04 g. (0.02 mole) of V in 25 ml. of benzene was shaken with 10.1 g. (0.24 mole) of dihydropyran. After warming at 53° for 4 hr. and standing at 25° for 4 hr. the solution was triturated with petroleum ether and cooled. Scratching of the flask's sides resulted in the separation of a white powder which was collected by suction filtration and recrystallized from xylene to give 5.30 g. (86%) of product.

All products obtained using the various solvents had identical infrared spectra and melting ranges within ± 2.0°.

PREPARATION OF N-(2,5-DICHLOROBENZENESULFONYL)-δ-PENTANIMIDOLACTONE (XVII). — A mixture of 2.52 g. (0.01 mole) of VI and 10.1 g. (0.12 mole) of dihydropyran was stirred 35 hr. at room temperature. The volume was adjusted to 40 ml. with xylene. After cooling and scratching the sides of the flask a fine white powder separated which was vacuum filtered and washed with cold xylene to yield 1.48 g. (48%) of product. Three recrystallizations from xylene afforded an analytical sample melting at 96.5-97.5°; $\nu_{max.}$ (Nujol) 1600, 1350, 1338, 1320, 1275, 1241, 1170, 1155, 1125, 1112, 1097, 1058, 1037, 973, 940, 890, 833, 812, 770, 746, 708, 689, and 677 cm.$^{-1}$.

Anal. Calcd. for $C_{11}H_{11}NCl_2O_3S$: C, 42.86; H, 3.57; N, 4.55. Found: C, 42.96; H, 3.66; N, 4.51.

In another experiment 2.52 g. (0.01 mole) of VI in 11 ml. of benzene was stirred with 5.0 g. (0.06 mole) of dihydropyran for 35 hr. at 25°. After dilution to 30 ml. with xylene 1.51 g. (49%) of product was isolated in the usual manner.

In a third experiment 2.52 g. (0.01 mole) of VI in 20 ml. of xylene was stirred with 5.0 g. (0.06 mole) of dihydropyran for 30 hr. at room temperature. After dilution to 40 ml. with xylene, cooling, and scratching the sides of the flask, a white solid separated. It was collected and washed to give 1.09 g. (36%) of product.

All products obtained had identical infrared spectra and melting ranges within ± 1.5°.

PREPARATION OF N-(p-TOLUENESULFONYL)-δ-PENTANIMIDOLACTONE (XVIII). — To a 20 ml. benzene solution containing 1.97 g. (0.01 mole) of IX was added 5.0 g. (0.06 mole) of dihydropyran. After 11 days of standing at 25° only a light yellow oil remained. Upon stirring with 10 ml. of diethyl ether a white solid formed which was collected by vacuum filtration and washed with a small amount of ether to yield 2.17 g. (86%) of product. Three recrystallizations from warm xylene afforded an analytical sample of small colorless needles, m.p. 74-75°; $\nu_{max.}$(Nujol) 1570, 1405, 1345, 1305, 1298, 1292, 1281, 1175, 1150, 1085, 1067, 1053, 1014, 980, 934, 894, 822, 805, 793, 727, 704, 687, 664, and 652 cm.$^{-1}$.

Anal. Calcd. for $C_{12}H_{15}NO_2S$: C, 56.92; H, 5.93; N, 5.53. Found: C, 57.12; H, 6.09; N, 5.39.

PREPARATION OF N-(p-METHOXYBENZENESULFONYL)-δ-PENTANIMIDOLACTONE (XIX). — A mixture of 2.13 g. (0.01 mole) of X and 10.1 g. (0.12 mole) of dihydropyran was warmed at 47° for 96 hr. The resulting yellow oil was dissolved in 10 ml. of benzene and triturated with ether. The short colorless needles which separated after three days in the refrigerator were collected by suction filtration and washed with cold xylene. Recrystallization from xylene gave 1.27 g. (47%) of product, m.p. 93-95°. An additional xylene recrystallization provided an analytical sample, m.p. 93-94.5°; $\nu_{max.}$(Nujol) 1580, 1400,

1345, 1310, 1290, 1265, 1176, 1147, 1108, 1083, 1050, 1020, 970, 890, 833, 818, 800, 770, 720, 683, and 660 cm.$^{-1}$.

Anal. Calcd. for $C_{12}H_{15}NO_4S$: C, 53.53; H, 5.58; N, 5.20. Found: C, 53.30; H, 5.58; N, 5.33.

Reactions Related to Structure Assignment and Mechanism

p-NITROBENZENESULFONAMIDE (XX). — To 50 ml. of concentrated ammonium hydroxide was added 4.43 g. (0.02 mole) of p-nitrobenzenesulfonyl chloride. After 20 min. of gentle boiling the solution was cooled and diluted with 100 ml. of water. Colorless needles separated which were collected by suction filtration and washed with ice water. Recrystallization from 60% ethanol yielded 3.66 g. (91%) of material, m.p. 178-180° (lit.[23] m.p. 179-180°); $\nu_{max.}$(Nujol) 3340, 3250, 1610, 1565, 1520, 1400, 1345, 1310, 1285, 1177, 1161, 1110, 1091, 1009, 899, 852, 822, 775, 745, 740, 720, and 682 cm.$^{-1}$.

m-NITROBENZENESULFONAMIDE (XXI). — By the same procedure used to prepare XX, 4.43 g. (0.02 mole) of m-nitrobenzenesulfonyl chloride and 50 ml. of concentrated ammonium hydroxide afforded 3.00 g. (74%) of white needles, m.p. 166.5-167.5° (lit.[23] m.p. 167-168°); $\nu_{max.}$(Nujol) 3360, 3270, 1605, 1530, 1350, 1333, 1305, 1185, 1160, 1120, 1083, 1070, 995, 905, 873, 817, 757, 737, 720, 670, and 659 cm.$^{-1}$.

o-NITROBENZENESULFONAMIDE (XXII). — By the procedure used to prepare XX, 2.50 g. (0.01 mole) of o-nitrobenzenesulfonyl chloride and 30 ml. of concentrated ammonium hydroxide gave 1.70 g. (75%) of white needles, m.p. 190-192° (lit.[23] m.p. 193°); $\nu_{max.}$(Nujol) 3385, 3270, 1590, 1530, 1350, 1335, 1300, 1159, 1123, 1060, 965, 920, 852, 782, 737, 725, 700, and 655 $cm.^{-1}$.

N-(2-TETRAHYDROPYRANYL)-4-METHYLBENZENESULFONAMIDE (XXIII). — A mixture of 17.4 g. (0.21 mole) of dihydropyran, 34.20 g. (0.20 mole) of p-toluenesulfonamide, and 0.20 g. of p-toluenesulfonic acid in 50 ml. of benzene reacted exothermically. After the initial reaction had subsided the mixture was refluxed for 1 hr. then cooled to room temperature. To neutralize the catalyst 1.00 g. of anhydrous potassium carbonate was added which caused the reaction mixture to solidify. The product and excess potassium carbonate were collected by vacuum filtration and washed with cold ether until the washings were colorless. The crude material was dissolved in hot benzene then filtered and cooled to give 23.5 g. (45%) of a fine white powder, m.p. 105-106.5° (lit.[24] m.p. 106-107.5°); $\nu_{max.}$(Nujol) 3230, 1335, 1325, 1300, 1200, 1165, 1144, 1118, 1089, 1070, 1047, 1017, 940, 910, 879, 852, 848, 837, 807, and 664 $cm.^{-1}$.

HYDROLYSIS OF XII. — A solution of 2.00 g. (0.007 mole) of XII in 20 ml. of 95% ethanol was refluxed for 5 hr.

Cooling to room temperature caused white needles to separate from the yellow solution. The product was collected by suction filtration, washed with a small amount of cold 95% ethanol and recrystallized from 60% ethanol. Concentration of the filtrate gave another small crop for a total yield of 1.34 g. (95%) of o-nitrobenzenesulfonamide, m.p. 191-192° (lit.[23] m.p. 193°). The product gave an identical infrared spectrum with XXII and the melting point failed to be depressed when mixed with XXII.

The filtrate was diluted to a total volume of 20 ml. with absolute ethanol. After addition of 0.60 ml. (0.007 mole) of 95% hydrazine the solution was refluxed for 7½ hr. Reducing the volume in vacuo resulted in the separation of white platelets which were collected by suction filtration and washed with cold ethanol, m.p. 105-105.5°. Recrystallization from absolute ethanol afforded 0.37 g. (47%) of 5-hydroxypentanoyl hydrazide, m.p. 104-106° (lit. m.p. 105° [25] and 107° [26]); $\nu_{max.}$ (Nujol) 3325, 3160, 3140, 3050, 1640, 1530, 1335, 1295, 1275, 1245, 1220, 1178, 1150, 1063, 1045, 1025, 988, 957, 740, 731, 720, and 680 cm.$^{-1}$.

HYDROLYSIS OF XI. — A solution of 3.17 g. (0.011 mole) of XI in 20 ml. of 95% ethanol was refluxed for 5 hr. The product was isolated as it was in the preceding hydrolysis reaction to give 2.12 g. (94%) of m-nitrobenzenesulfonamide, m.p. 166-168° (lit.[23] m.p. 167-168°).

The product gave an identical infrared spectrum with and failed to depress the melting point of XXI.

The filtrate was evaporated to dryness and the resulting oil taken up in 10 ml. of absolute ethanol. After addition of 1.00 ml. (0.012 mole) of 95% hydrazine the solution was heated at reflux for 7 hr. White platelets separated upon reducing the volume of the solution in vacuo. The product was collected by vacuum filtration and washed with cold ethanol. Recrystallization from absolute ethanol gave 0.78 g. (53%) of the 5-hydroxypentanoyl hydrazide, m.p. 104-106°, lit. m.p. 105° [25] and 107° [26]. The product gave an identical infrared spectrum with that of the hydrazide formed in the hydrolysis of XII.

HYDROLYSIS OF XIII. — In a procedure similar to that used in hydrolyzing XI and XII the hydrolysis of 4.22 g. (0.015 mole) of XIII gave 2.60 g. (87%) of XX, m.p. 177-179° and 1.11 g. (56%) of the hydrazide, m.p. 105.5-107°.

ATTEMPTED REDUCTIONS OF XVIII TO XXIII. — To 0.42 g. (0.002 mole) of XVIII suspended in 5 ml. of absolute ethanol was added with swirling 0.07 g. (0.002 mole) of sodium borohydride at an average rate of 0.01 g./min. Gas evolution was observed immediately. The reaction flask was jacketed with a water bath at room temperature and after standing 16 hr. a solid separated. Forty-three hr. later the reaction mixture was diluted with 10 ml. of ice water and extracted three times with 10 ml. portions of

diethyl ether. After drying over sodium sulfate the ether layer was triturated with petroleum ether and allowed to cool. The colorless solid which separated was collected by vacuum filtration, washed with petroleum ether and dried to yield 0.30 g. of product of an uncertain identity which melted at 58-59.5°; $\nu_{max.}$(Nujol) 3470, 3110, 1310, 1305, 1285, 1180, 1150, 1119, 1090, 1059, 1025, 947, 938, 806, 755, 720, 706, and 662 cm.$^{-1}$.

In an attempted catalytic reduction 3.80 g. (0.015 mole) of XVIII was dissolved in 250 ml. of p-dioxane which contained 0.19 g. of 85.66% platinum oxide. After shaking under a hydrogen atmosphere at low pressure for 30 min. at 25° approximately 0.015 mole of hydrogen had been consumed. After standing at room temperature over night the hydrogenation mixture was flushed with nitrogen and filtered. The green filtrate was reduced to a dark oil which was dissolved in 100 ml. of benzene and decolorized with charcoal. The resulting yellow filtrate was again reduced *in vacuo* to a yellow oil which failed to crystallize.

REACTION OF ARYLSULFONYL AZIDES WITH BENZENE. — Separate 20 ml. benzene solutions containing 2.62 g. (0.01 mole) of IV, 2.52 g. (0.01 mole) of V, 2.28 g. (0.01 mole) of I, and 2.28 g. (0.01 mole) of II were warmed at 45-50° for 22 hr. The reaction mixtures were then evaporated to dryness *in vacuo*. In each case 99%

of the starting material was recovered unchanged, verified by melting points and infrared spectra. Notably no (-N-H) stretching absorptions were found in the spectra of the recovered materials. This suggests that no sulfonamides or anilides were formed.

DISCUSSION

Evaluation of Preparative Procedures

Six new substituted benzenesulfonyl azides have been prepared from the reaction of sodium azide and various arylsulfonyl chlorides in aqueous acetone.

Leffler and Tsuno[20] were first to employ aqueous acetone as a reaction medium for the preparation of arylsulfonyl azides from sodium azide and arylsulfonyl chloride. The small number of previously synthesized arylsulfonyl azides had been run in aqueous ethanol[22, 27] or in aqueous ether.[28]

In this investigation little variation in the yields was noted when the reaction medium was changed from 50% to 75% acetone. In the preparation of IX, previously reported by Leffler and Tsuno[20] who used aqueous ethanol, changing the solvent to aqueous acetone had no significant effect on the yield.

All of the new substituted benzenesulfonyl azides had the characteristic azide band from 2230-2127 cm.$^{-1}$

in Nujol mulls. Other notable infrared absorption bands include those for: $-SO_2-$, 1184-1169 cm.$^{-1}$; $-NO_2-$, 1535-1525 cm.$^{-1}$; and appropriate aromatic substitution bands for C-H out-of-plane bending.

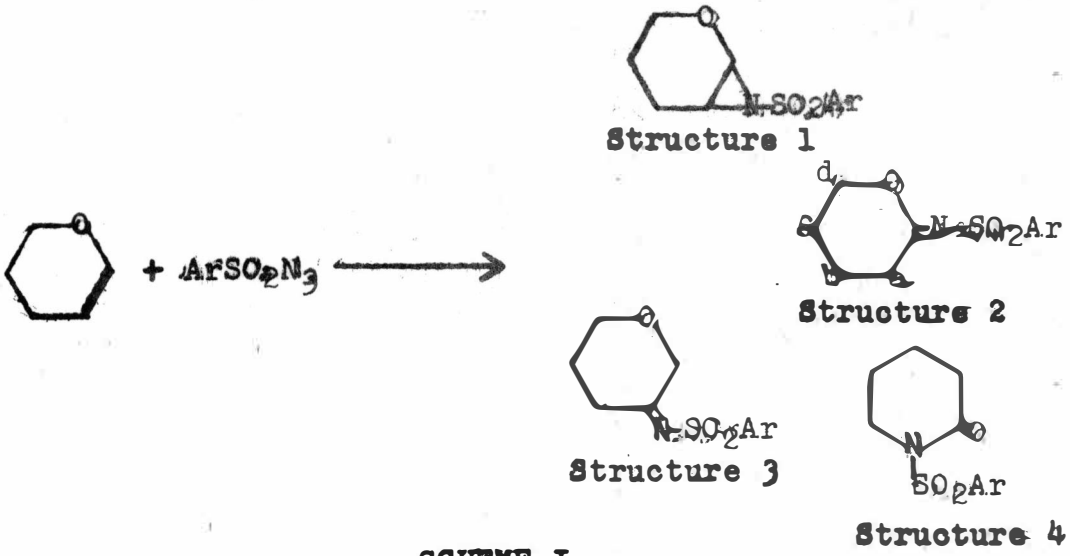
The addition of arylsulfonyl azides to dihydropyran resulted in nitrogen evolution within 3-20 min. after mixing, depending on the type of benzenesulfonyl azide. The reaction conditions employed are summarized in Table I. For a given substituent it can be seen that the nature of the reaction medium has little influence on the yield of product. In the only experiment attempted at an elevated temperature of any time duration the yield of XIV was decreased one half to one third.

After attempting to utilize a wide spectrum of aprotic solvents and solvent systems, xylene was the best solvent found for recrystallization of the adducts.

Evaluation of Chemical and Physical Evidence for a Structural Assignment

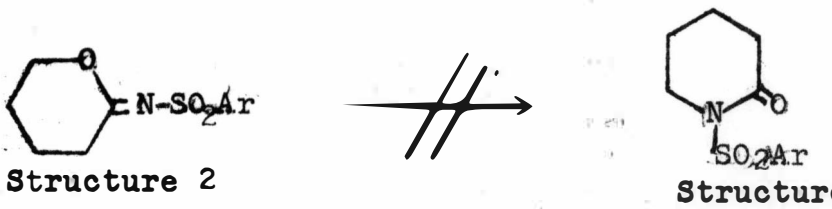
The structural assignment to the adduct of substituted benzenesulfonyl azides and dihydropyran was made on the basis of elemental analysis, a molecular weight determination, n.m.r. and infrared spectra, and the hydrolysis products of XI, XII, and XIII. Elemental analysis, a molecular weight determination and the observation of nitrogen evolution during the course of the reaction indicate the product has one of the four possible

structures shown below (Scheme I).



SCHEME I

The N-(arylsulfonyl)-2-pyridone (Structure 4) could be formed by a Chapman Rearrangement of the N-(arylsulfonyl)-δ-pentanimidolactone (Structure 2).

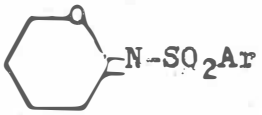


However, such reactions usually occur only on pyrolysis of the imidic acid.

The infrared spectra of the adducts obtained, summarized in Table II, showed a very strong absorption in the range of 1565-1600 cm.$^{-1}$. This indication of a $-C=N-SO_2-$ function[30] eliminates possible adduct structures 1 and 4. The presence of a -C-O-C- band also rules out the Chapman Rearranged product (Structure 4). The other absorption bands are consistent with adduct structures 1, 2 and 3.

TABLE I.

YIELDS AND SUMMARY OF REACTION CONDITIONS FOR THE PREPARATION OF



Compound Number	Aryl Substituent	Solvent	Temp. °C	Time hr.	Yield %
XI	m-Nitro-	Dihydropyran	25[a]	30	75
		Tetrahydrofuran	25[a]	30	84
		Benzene	25[a]	30	82
		p-Dioxane	25[a]	36	82
		Xylene	25[a]	30	82
XII	o-Nitro-	Tetrahydrofuran	50	20	86
		Xylene	25[a]	15	79
		Dihydropyran	55-25[a]	10	85
XIII	p-Nitro-	Dihydropyran	55-25[a]	10	95
		p-Dioxane	50	20	80
		Tetrahydrofuran	55	20	90
		Xylene	25[a]	36	68
		Benzene	53-25[a]	15	76
XIV	p-Bromo-	Benzene	40	20	53
		Xylene	75	4	18
		Dihydropyran	60-25[a]	60	31
		Tetrahydrofuran	55	48	39

(a) At 25° or ambient temperature.

TABLE I.
continued

Compound Number	Aryl Substituent	Solvent	Temp. °C	Time hr.	Yield %
XV	2,5-Dibromo-	Tetrahydrofuran	25[a]	26.5	66
		Dihydropyran	25[a]	26.5	83
		p-Dioxane	25[a]	26.5	50
		Xylene	25[a]	29	87
XVI	3,4-Dichloro-	Xylene	25[a]	30	94
		Dihydropyran	55-25[a]	60	55
		Benzene	53-25[a]	8	86
XVII	2,5-Dichloro-	Dihydropyran	25[a]	35	48
		Benzene	25[a]	35	49
		Xylene	25[a]	30	36
XVIII	p-Methyl-	Benzene	25[a]	264	86
XIX	p-Methoxy	Dihydropyran	47	96	47

(a) At 25° or ambient temperature.

TABLE II.

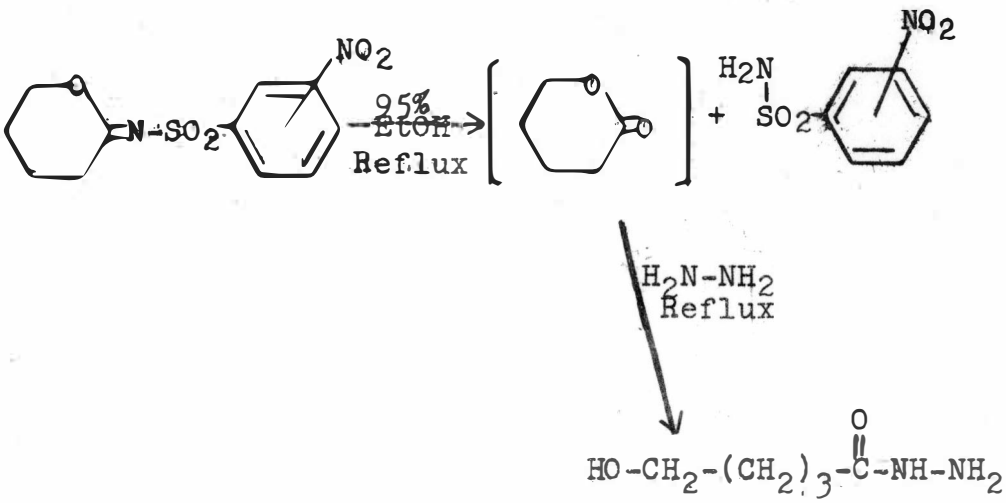
SUMMARY OF INFRARED SPECTRA[a] AND THE STRUCTURAL INTERPRETATION[29] FOR ADDUCTS OF DIHYDROPYRAN AND ARYLSULFONYL AZIDES

Compound Number	SO_2-N=C[b]	C-O-C[c]	Ar-SO_2-N[d]	-NO_2[e] (if any)	C-H[f] Out-Of-Plane Bending
XI	1580	1056	1350 1169 1155	1525	812
XII	1580	1051	1345 1173 1152	1525	740
XIII	1600	1048	1340 1170 1141	1520	827
XIV	1575	1051	1345 1167 1141	—	810
XV	1600	1055	1348 1170 1153	—	806
XVI	1565	1050	1342 1160 1152	—	802
XVII	1600	1058	1350 1170 1155	—	812
XVIII	1570	1053	1345 1175 1150	—	822
XIX	1580	1050	1345 1176 1147	—	818

(a) Absorption maxima are expressed in cm.$^{-1}$.
(b) Very strong; (c) Moderate; (d) Strong; (e) Strong;
(f) Moderate to strong.

Nuclear magnetic resonance spectra of six of the different adducts synthesized showed quintets from 112-117 c.p.s., triplets from 160-165 c.p.s., and triplets from 263-271 c.p.s. with peak area ratios of 4:2:2 respectively. These multiplets support Structure 2 with the quintets from 112-117 c.p.s. assigned to the two equivalent methylene groups, b and c; triplets from 160-165 c.p.s. to a methylene function, a; and the triplets from 263-271 c.p.s. to the methylene attached to the oxygen in the lactone ring, d. The lines in the 452-519 c.p.s. region can be attributed to the type of arylsulfonyl group substituted on the nitrogen of the imidate lactone.

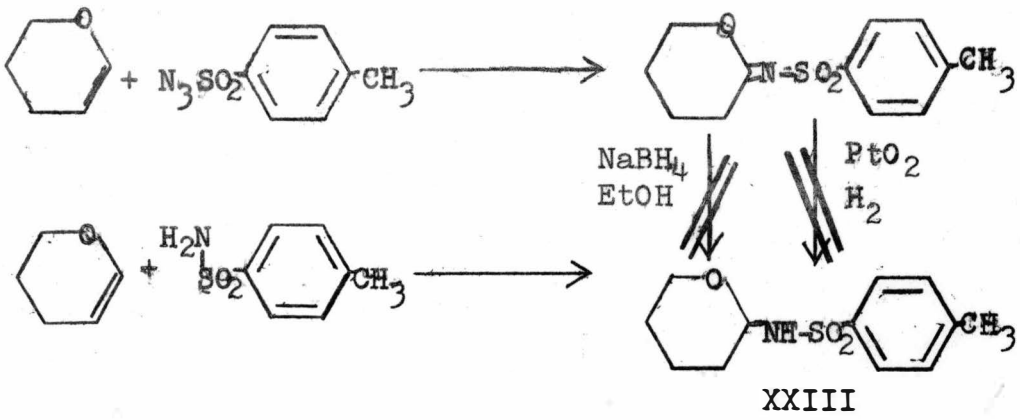
Chemical evidence for the assignment of Structure 2 comes from the hydrolysis of the adducts in 95% ethanol. The adducts, XI, XII, and XIII, gave the corresponding sulfonamide and δ-valerolactone which was isolated as its hydrazide.



SCHEME II

The suspected sulfonamides from the hydrolysis were isolated and compared with authentic sulfonamides and proved to be identical. The 5-hydroxypentanoyl hydrazide's melting point agreed with that which has been previously reported[25, 26] and gave an infrared spectra consistent with such a compound.

Attempts to reduce XVIII to XXIII by chemical and catalytic methods were unsuccessful (Scheme III).



SCHEME III

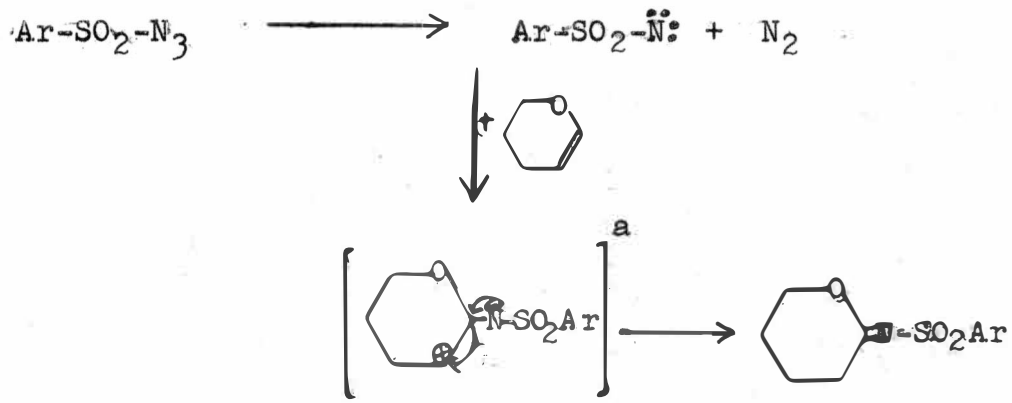
The reduced product, XXIII, has previously been reported[24] and was synthesized from dihydropyran and p-toluenesulfonamide using hydrogen chloride in ether as a catalyst. In this investigation employment of p-toluenesulfonic acid as catalyst increased the yield from 22 to 46%.

Supporting evidence for the structural assignments can be found in a recent review article[16a] authored by Huisgen and others describing some of their unpublished work.[16b] These investigators reacted p-toluenesulfonyl

azide with 2,3-dihydrofuran and 2,3-dihydropyran to obtain compounds proposed to be substituted imidic acid lactones. However, no experimental evidence was reported to substantiate their structural assignments. Franz and Osuch[6] have reported that they obtained adducts by reacting vinyl ethers with various sulfonyl azides. The adducts had infrared spectra similar to that of an eniminesulfonyl azide reaction product; but definite structural assignments were not made to the compounds derived from the vinyl ethers.

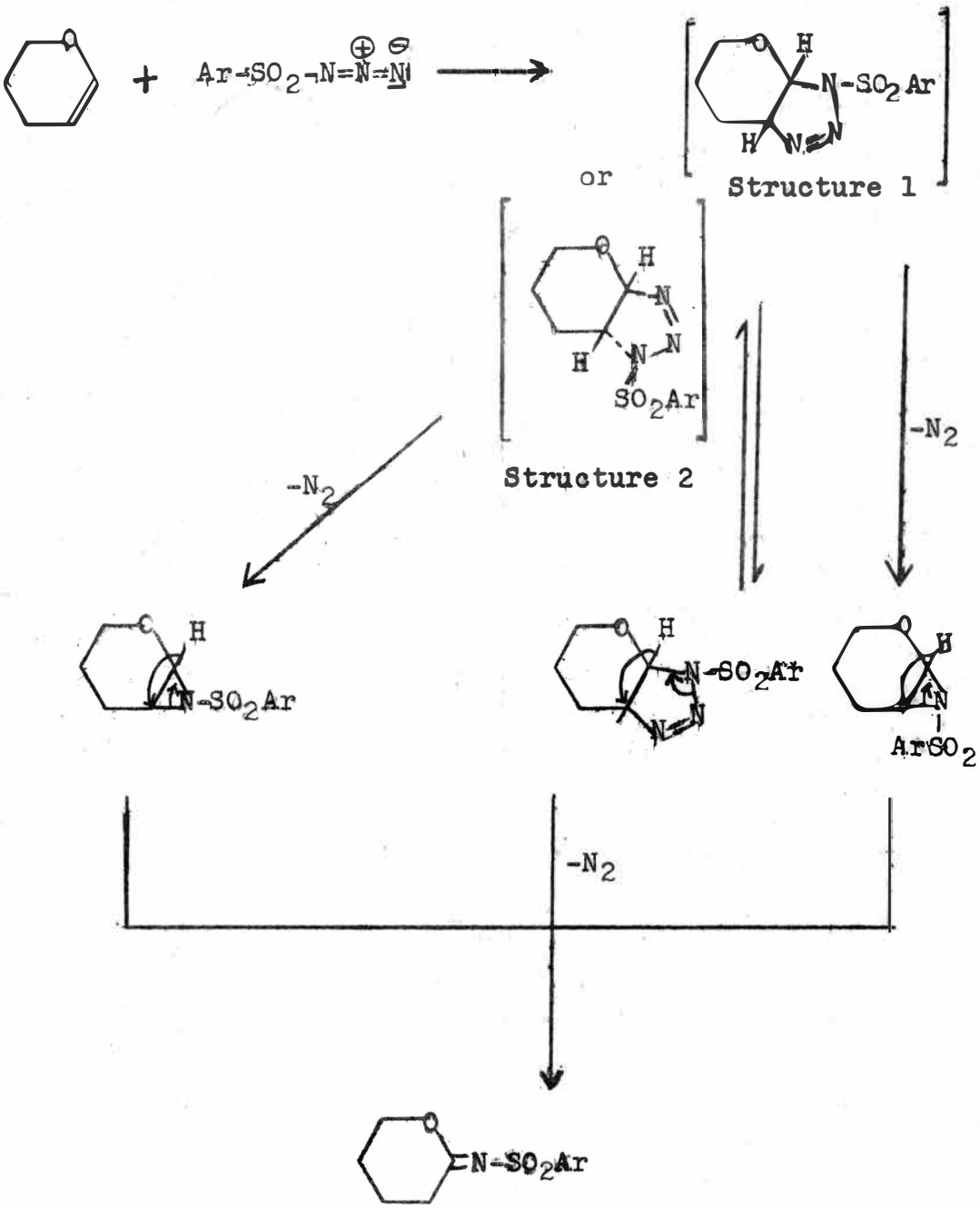
Possible Mechanisms for Adduct Formation

Speculation concerning the mechanism of addition of arylsulfonyl azides to 2,3-dihydro-4H-pyran suggests two general types of intermediates; a "nitrene" intermediate shown in Scheme IV, or one of two or both triazoline type intermediates described in Scheme V.



SCHEME IV

(a) Other intermediates involving addition of the nitrene to dihydropyran are possible.



SCHEME V

Heacock and Edmison[31] have decomposed benzenesulfonyl azide in various aromatic solvents to obtain sulfonamides and substituted anilides. They suggest that a "nitrene"

intermediate forms initially then proceeds to give the isolated products by a radical substitution mechanism:

$C_6H_5SO_2N_3 \longrightarrow C_6H_5SO_2N: + N_2$

$C_6H_5SO_2N: + ArH \longrightarrow C_6H_5SO_2NH\cdot + Ar\cdot$

$Ar\cdot + C_6H_5SO_2N_3 \longrightarrow C_6H_5SO_2\dot{N}Ar + N_2$

$C_6H_5SO_2\dot{N}Ar + ArH \longrightarrow C_6H_5SO_2NHAr + Ar\cdot$

$C_6H_5SO_2NH\cdot + ArH \longrightarrow C_6H_5SO_2NH_2 + Ar\cdot$

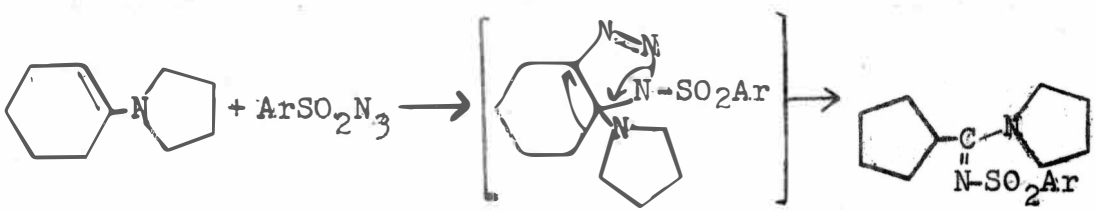
The "nitrene" intermediate has also been proposed by other workers[20] in the decomposition of various arylsulfonyl azides.

Infrared spectra of the dihydropyran-arylsulfonyl azide adduct crude products showed no absorption in the N-H stretching frequency region. Several of the arylsulfonyl azides prepared were stirred at conditions used to form the adducts except the dihydropyran was deleted. Evaporation of the solvent gave quantitative recovery of the starting materials with infrared spectra unchanged. That is, no sulfonamides or substituted anilides were formed. Consequently the possibility of a "nitrene" intermediate being generated under conditions used in forming the adducts is remote.

The triazoline intermediate (Scheme V) is consistent with the previously reported reactions involving additions of azides to olefins.[3, 6, 16a, 19] Such an intermediate would require bond bending in the azide function.

In the azide group sp hybridization of the bonds of the central nitrogen atom leads to a linear chain of three nitrogen atoms in the ground state. So the first and third nitrogen atoms may make contact with the π bond of an olefinic dipolarophile in the course of a cycloaddition, bending of the linear azide system is required. An LCAO calculation by Roberts[32] has shown that such bending is possible without too great an expenditure of energy. Huisgen and co-workers[16a] suggest that the energy lost in breaking one bond is partially compensated for by a gain in energy through rehybridization.

The next consideration in the triazoline intermediate structure is the orientation of the arylsulfonyl moiety. Two possible orientations are possible as depicted in Scheme V. On the hypothesis that the dominate orientation factor, stabilization of a positive charge by the neighboring oxygen atom, is equivalent to that in the enamine case, Huisgen and others[16a] propose Structure 1 in Scheme V. The mechanism put forth by Franz and Osuch[6] for the addition of arylsulfonyl azides to enamines in described in Scheme VI.

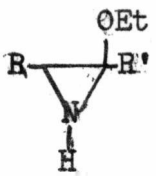


SCHEME VI

An identical mechanism has been postulated by Fusco and associates[19] in the reaction of tosyl azide with 2-morpholino-4-methylpent-1-ene. Further strong support of Structure 1 in Scheme V comes from the product of the addition of tosyl azide to ethinyl ethers.[33]

$$HC{\equiv}C\text{-}OC_2H_5 + ArSO_2\text{-}\underline{N}{=}\overset{\oplus}{\underline{N}}{=}\overset{\ominus}{\underline{N}} \longrightarrow N_2CH\text{-}\overset{NSO_2Ar}{\overset{|}{C}}\text{-}OCH_2CH_3$$

If one accepts the intermediate of Structure 1 in Scheme V the next step in the mechanism cannot be easily discerned. The product may be formed by first eliminating nitrogen to form an aziridine which with a 1,2-hydride shift forms the product or by a concerted process to eliminate nitrogen and form the product with the hydride shift in one step. It is worthy to note that aziridines of this type have been reported by House and Berkowitz[34] and Hatch and Cram[35].



SUMMARY

The adducts from 2,3-dihydro-4H-pyran and various arylsulfonyl azides have been prepared in a variety of reaction mediums. By a combination of chemical and physical methods the structure of the adducts was found to be N-(arylsulfonyl)-δ-pentanimidolactones.

A possible "nitrene" intermediate in the mechanism of the reaction has been discounted. The absence of a "nitrene" is suggested by the failure to detect sulfonamides and substituted anilides in the crude products. "Nitrenes" do exist in reactions at temperatures near the arylsulfonyl azide's decomposition point. Such vigorous conditions were not used in this investigation. The mechanism proposed involves a triazoline which eliminates nitrogen by one and/or two possible modes to give the isolated products. A triazoline intermediate is supported by previously proposed mechanisms for addition of organic azides to olefinic and acetylenic functions.

The arylsulfonyl azides and their adducts have been submitted to the Cancer Chemotherapy National Service Center for evaluation against cancer. A few of these have shown activity in the Walker 256 Carcinoma.

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VITA

Douglas Lou Rector was born January 30, 1942 in Grand Rapids, Michigan. After completing his secondary education in the Vicksburg Community School System, Vicksburg, Michigan he enrolled at Western Michigan University in September 1959. He received a B. S. degree with a major in chemistry in July 1963.

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The author and his wife, the former Judith Frye, have a daughter and a son.

The author is a member of The American Chemical Society.