leave a residue. The dichloromethane solution (200 mL) of the residue was washed with water (50 mL), 0.1 N NaOH solution (50 mL), and water (50 mL), dried over sodium sulfate, and filtered. After removal of the dichloromethane, the residue (3.0 g) was distilled at 86 °C (0.3 mm) by a Kugelrohr apparatus to give 2.9 g (90%) of **5a** as a colorless oil which solidified on cooling, mp 26–27 °C.

3-Methyl-5-phenyl-1,2,4-thiadiazole (5b). Process A. To a solution of 4.12 g (0.020 mol) of **2b** in 50 mL of anhydrous dichloromethane at 0 °C was added dropwise a solution of 4.30 g (0.020 mol) of MSH in 25 mL of anhydrous dichloromethane over a period of 1–2 min. The reaction mixture was stirred at room temperature for 2 h and then diluted with 80 mL of dichloromethane. The dichloromethane solution was washed with saturated sodium bicarbonate solution, decolorized with activated carbon (Darco), and filtered through a Celite pad. After removal of the dichloromethane, the residue was recrystallized from 5 mL of hexane to give 2.9 g (82%) of **5b**: mp 54–56 °C (lit. 50 °C,[10] 54–55.5 °C[11]); NMR ($CDCl_3$) δ 2.76 (s, 3 H), 7.2–7.6 (m, 3 H), 7.7–8.1 (m, 2 H); mass spectrum, *m/e* 176 (M^+) (calcd for $C_9H_8N_2S$ 176.24); IR (KBr) 1515, 1493, 1460, 1370, 1324, 1307, 1235, 1020, 934.6, 826.4, 775.2, 694.2, 673.4 cm^{-1}.

Process B. To a suspension of 4.12 g (0.020 mol) of **2b** in a mixture of 3.2 mL (0.040 mol) of pyridine and 50 mL of absolute ethanol at room temperature was added rapidly a solution of 2.48 g (0.022 mol) of HSA in 30 mL of absolute methanol. The reaction mixture was stirred at room temperature for 1 h. The solvents were removed under reduced pressure at room temperature to leave a residue. The dichloromethane solution (200 mL) of the residue was washed successively with water (50 mL), 0.1 N NaOH solution (50 mL), and water (50 mL), dried over Na_2SO_4, and filtered. After removal of the dichloromethane, the residue was recrystallized from 4 mL of hexane to give 3.21 g (91%) of **5b** as colorless crystals, mp 54–56 °C.

Acknowledgment. We thank Dr. W. Gore and Mr. G. Morton and staff for the measurement and interpretation of spectral data and Mr. L. Brancone and staff for microanalyses.

Registry No. 2a, 52421-65-5; **2b**, 67229-59-8; **2c**, 74466-79-8; **2d**, 74466-80-1; **2e**, 74466-81-2; **2f**, 74466-82-3; **2g**, 74466-83-4; **2h**, 74466-84-5; **2i**, 74466-85-6; **2j**, 59819-37-3; **2k**, 74466-86-7; **2l**, 74466-87-8; **2m**, 74466-88-9; **5a**, 74466-89-0; **5b**, 50483-77-7; **5c**, 74466-90-3; **5d**, 74466-91-4; **5e**, 74466-92-5; **5f**, 74466-93-6; **5g**, 74466-94-7; **5h**, 74466-95-8; **5i**, 74466-96-9; **5j**, 74466-97-0; **5k**, 74466-98-1; **5l**, 74466-99-2; **5m**, 17467-18-4; thiobenzamide, 2227-79-4; *N,N*-dimethylformamide dimethyl acetal, 4637-24-5; *N,N*-dimethylacetamide dimethyl acetal, 18871-66-4; phenylthiourea, 103-85-5; *p*-fluorophenylthiourea, 459-05-2; *m*-(trifluoromethyl)phenylthiourea, 1736-70-5; MSH, 36016-40-7; HSA, 2950-43-8.

Some 1,3-Dipolar Cycloaddition Reactions of Nitrile *N*-Sulfides with Acetylenes and Olefins

Michael J. Sanders and John R. Grunwell*

Department of Chemistry, Miami University, Oxford, Ohio 45056

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The generation of nitrile *N*-sulfides from iminosulfur difluorides is general. Trifluoroacetonitrile *N*-sulfide was allowed to react with some acetylenes and olefins. For example, *N*-phenylmaleimide gave *N*-phenyl-3-trifluoromethyl-1,2-thiazoline-4,5-carboximide in 74% yield.

The reaction between benzonitrile *N*-sulfide and monosubstituted electron-deficient acetylenes produced a mixture of 4- and 5-substituted isothiazoles.[1,2,7] The purpose of this research was to investigate the generality of the formation of nitrile *N*-sulfides from iminosulfur difluorides and the influence of substituents on the regiospecificity of the 1,3-dipolar cycloaddition reactions between methyl propiolate and some nitrile *N*-sulfides as well as the reactions between trifluoroacetonitrile *N*-sulfide and electron-deficient olefins.

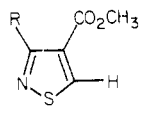
Results and Discussion

The iminosulfur difluorides were synthesized by reacting sulfur tetrafluoride with the appropriate primary amine.[3] In the case of (benzylimino)sulfur difluoride, trimethylamine was employed as a solvent and base to react with the hydrogen fluoride produced with the formation of the iminosulfur difluoride.[4] The use of trimethylamine in the preparation of ((2,2,2-trifluoroethyl)imino)sulfur difluoride was complicated by the similarity of the boiling points of the amine and the difluoride. Since 2,2,2-trifluoroethylamine is expensive, the nonvolatile base *N,N,N',N'*-tetramethyl-1,8-diaminonaphthalene was employed. An inert solvent, having a low freezing point, because the highly exothermic reaction between amine and sulfur tetrafluoride is best conducted at −45 °C, and having a fairly high boiling point, in order to allow its convenient separation from the iminosulfur difluoride, was desirable. Toluene (fp −95 °C, bp 110 °C) was found to satisfy those requirements although it was never possible to completely remove all traces of toluene from any sample of the iminosulfur difluoride. Solutions of the iminosulfur difluoride dissolved in toluene were satisfactory for conducting the 1,3-dipolar cycloaddition reactions and therefore the need to completely remove all toluene from the iminosulfur difluoride was eliminated. (Ethylimino)sulfur difluoride was obtained by reaction of ethylamine with sulfur tetrafluoride in the absence of any solvent or other base.[5] The major disadvantage of this procedure was the formation of diethylsulfur diimide which could be easily separated from the iminosulfur difluoride by high-vacuum distillation.

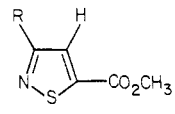
(1) M. J. Sanders, S. L. Dye, A. G. Miller, and J. R Grunwell, *J. Org. Chem.*, **44**, 510 (1979).
(2) R. K. Howe, J. A. Gruner, L. D. Carter, L. L. Black, and J. E. Franz, *J. Org. Chem.*, **43**, 3736 (1978).
(3) R. Cramer, *J. Org. Chem.*, **26**, 3476 (1961).
(4) J. R. Grunwell and S. L. Dye, *Tetrahedron Lett.*, 1739 (1975).
(5) B. Cohen and A. G. MacDiarmid, *J. Chem. Soc.*, 1780 (1966).

0022-3263/80/1945-3753$01.00/0

Table I. Isothiazole Isomer Ratios



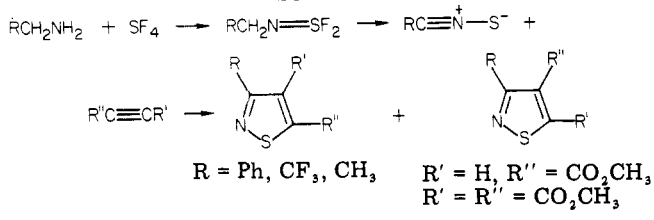
I



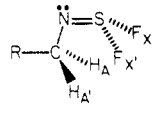
II

R	I/II
Ph	2:1
CH_3	1:1
CF_3	1:5

Scheme I



On the basis of the expected structure for iminosulfur difluorides, the methylene protons and the sulfur fluorines should comprise an AA'XX' spin system. However, be-



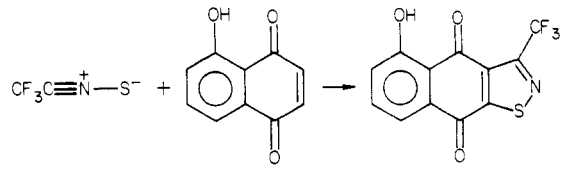
cause the $J_{AA'}$ and $J_{XX'}$ are large compared to the J_{AX} and J_{XX} is much greater than J_{AA}, the proton spectrum of the methylenes display a deceptively simple triplet with an apparent coupling constant of J_{AX} = 9.0–10.0 Hz. The spectrum of ((trifluoroethyl)imino)sulfur difluoride is further simplified to a sextet because the methyl and sulfur fluorines have the same coupling constant with the protons. The generation of acetonitrile *N*-sulfide and trifluoroacetonitrile *N*-sulfide from the corresponding iminosulfur difluoride was accomplished in sealed tubes because of the volatility of the iminosulfur difluorides. When the iminosulfur difluorides reacted with dimethyl acetylenedicarboxylate, modest yields of the corresponding isothiazoles were obtained.

The regiospecificity of the reaction between iminosulfur difluorides and methyl propiolate was significantly affected by the nitrile *N*-sulfide substituent, as shown in Table I. Thus, while benzonitrile *N*-sulfide (R = Ph) gave a 2:1 mixture of 4- and 5-(carbomethoxy)-3-phenyl-1,2-thiazole, trifluoroacetonitrile *N*-sulfide (R = CF_3) formed a 5:1 isomer ratio in favor of 5-(carbomethoxy)-3-(trifluoromethyl)-1,2-thiazole. Acetonitrile *N*-sulfide and methyl propiolate produced a 1:1 mixture of the 4- and 5-substituted isothiazole (Scheme I).

The identity of the (trifluoromethyl)(carbomethoxy)-isothiazoles was established by proton NMR spectroscopy and mass spectrometry. The major isomer had a resonance at δ 8.0 and is similar to other 5-isomers in the benzonitrile *N*-sulfide series. The resonance was assigned to the proton in the four position. The minor isomer showed a loss of hydrogen fluoride (M – 20) while the major isomer did not in the mass spectrum. The proximity of the trifluoromethyl and the carbomethoxy group in the 4-isomer allows for the synchronous loss of hydrogen fluoride, while the groups are not close enough for this process to occur in the 5-isomer.

It was not possible to separate the methyl(carbomethoxy)isothiazole isomers by gas or column chromatography. The NMR spectrum of the mixture showed two peaks of equal intensity at δ 9.2 and 7.5 for the isothiazole ring

Scheme II



protons, corresponding to the 4- and 5-substituted carbomethoxy isomers, respectively. The mass spectrum of 3-methyl-4,5-bis(carbomethoxy)-1,2-thiazole showed a significant (99% relative intensity) peak corresponding to the loss of methanol (M – 32) from the molecular ion and is analogous to the loss of methanol from *o*-methyl toluate. The mass spectrum of the mixture of 4- and 5-(carbomethoxy)isothiazoles also had a peak at M – 32, probably arising from the 4-isomer which has the methyl group and carbomethoxy group substituted on adjacent carbons.

The application of MO theory toward understanding the experimental results is complicated by at least two factors. First, the method of generation of the *N*-sulfide produces hydrogen fluoride which we have shown increases the amount of MO dipole control by protonating the ester carbonyl. The same amount of hydrogen fluoride generated at approximately the same rate from each *N*-sulfide cannot be assumed. Second, although the products are stable to the reaction conditions, the low yields of the adducts make mechanistic conclusions risky.

The reaction between *p*-chlorobenzonitrile *N*-sulfide and N-substituted maleimides gave adducts in good yield.[6] We found trifluoroacetonitrile *N*-sulfide and *N*-phenylmaleimide gave the corresponding isothiazoline in 74% yield, while acetonitrile *N*-sulfide and the imide produced only polymer and sulfur. In contrast to benzonitrile *N*-sulfide,[7] trifluoroacetonitrile *N*-sulfide reacted with 1,4-naphthoquinone and juglone to form adducts in 11% and 14% yield, respectively.

The exact structure for the adduct produced from juglone was not established. The structure shown in Scheme II was deduced from consideration of the mass spectrum. The adducts are isothiazoles because the initially formed isothiazolines were oxidized by unreacted naphthoquinone.

The mass spectrum of the juglone adduct had a small but significant M – 20 peak corresponding to the loss of hydrogen fluoride. This peak is absent in the spectrum of the naphthoquinone adduct. Thus, the hydroxyl hydrogen was responsible for the loss of hydrogen fluoride. Of the two possible regioisomers, the one with the hydroxyl and trifluoromethyl groups on the same side of the ring system could lose hydrogen fluoride by the mechanism shown in Scheme III.

Experimental Section

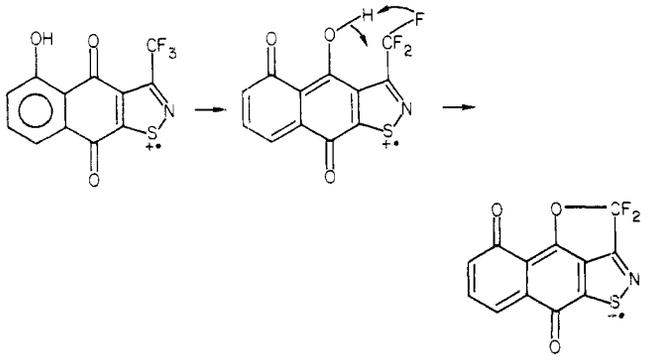
All melting and boiling points are uncorrected. Infrared spectra were recorded with a Perkin-Elmer IR-237, mass spectra were taken on a single-focusing Hitachi RMU-6 spectrometer, and proton NMR spectra were run with a JEOL-C-60H with Me_4Si as an internal standard.

Microanalysis were performed by Galbraith Laboratories, Inc. Methyl propiolate was obtained from Farchan Chemical Co. Naphthoquinone, dimethyl acetylenedicarboxylate and 2,2,2-trifluoroethylamine hydrochloride were purchased from Aldrich Chemical Co., Inc.

((2,2,2-Trifluoroethyl)imino)sulfur Difluoride. In a dried flask fitted with a condenser maintained at –78 °C (dry ice–acetone) were placed 25 g of 2,2,2-trifluoroethylamine, 50 g of Proton Sponge (Aldrich), and 25 mL of toluene. The flask was

(6) R. K. Howe and J. E. Franz, *J. Org. Chem.*, **43**, 3472 (1978).
(7) J. E. Franz and L. L. Black, *Tetrahedron Lett.*, 1381 (1970).

Scheme III



cooled to −45 °C (chlorobenzene slush) and 25 mL of sulfur tetrafluoride was added slowly. After completion (about 2 h) of the reaction, the flask was connected to a high-vacuum line (10^{-4} mm) and the contents were distilled into a trap cooled with liquid nitrogen. The material in the liquid nitrogen trap was allowed to warm to room temperature and was fractionated through four traps cooled to −30 °C (bromobenzene slush), −45 °C (chlorobenzene slush), −78 °C (dry ice–acetone), and −189 °C (liquid nitrogen). The material in the −78 °C trap contained a toluene solution (usually 50% iminosulfur difluoride) of the desired iminosulfur difluoride which was separated from toluene by distillation (atmospheric pressure) as needed for other experiments. The −45 °C trap also contained a toluene solution of the difluoride; ^{1}H NMR ($CH_3C_6H_5$) δ 3.8 (sexet, J = 9.0 Hz).

4,5-Bis(carbomethoxy)-3-(trifluoromethyl)-1,2-thiazole. Freshly distilled ((2,2,2-trifluoroethyl)imino)sulfur difluoride (2.0 g, 0.01 mol), 3.4 g (0.01 mol) of dimethyl acetylenedicarboxylate, 1.9 g of NaF, and 0.31 g of 18-crown-6 polyether were placed in a tube sealed under vacuum. The tube was heated at 130 °C for 18 h in an oil bath. The contents of the tube were dissolved in hot benzene. The benzene was evaporated at the aspirator and the remaining residue was chromatographed over silica gel and eluted with petroleum ether (bp 30–60 °C) followed by benzene. Evaporation of the first fractions gave white crystals which were recrystallized from heptane to give 0.9 g (30%) of the isothiazole: mp 54.5–55.5 °C; mass spectrum, m/e (relative intensity) 269 (6), 250 (4), 238 (100), 110 (11), 82 (10), 69 (12), 59 (28); ^{1}H NMR ($CDCl_3$) δ 3.94 (s); IR (KBr) 1733 cm^{-1}. Anal. Calcd for $C_8H_6F_3NO_4S$: C, 35.69; H, 2.25; F, 21.17; N, 5.20; S, 11.91. Found: C, 35.81; H, 2.20; F, 21.14; N, 5.19; S, 12.40.

4- and 5-(Carbomethoxy)-3-(trifluoromethyl)-1,2-thiazoles. Methyl propiolate (4.7 g, 0.056 mol), 2.3 g of NaF, and 0.36 g of 15-crown-5 polyether were placed in a tube which was evacuated and into which was added 5 g of a toluene solution containing 2.5 g (0.03 mol) of ((2,2,2-trifluoroethyl)imino)sulfur difluoride. The tube was sealed under vacuum and heated in an oil bath for 24 h at 120 °C. The tube contents were dissolved in acetone. The acetone was evaporated and the residue subjected to gas chromatography using a 6 ft × 0.25 in. stainless-steel column packed with 10% SE-30 on Chromosorb Q. Two peaks in a 1:5 ratio were collected and found to be 4- and 5-substituted isothiazoles by mass spectrometry. The residue was chromatographed over silica gel with petroleum ether (bp 30–60 °C). The 5-isomer was isolated as an impure oil in 15% yield: ^{1}H NMR ($CDCl_3$) δ 8.0 (s, 1 H), 3.97 (s, 3 H); mass spectrum, m/e (relative intensity) 211 (29), 180 (100), 146 (47), 95 (32), 69 (64). Anal. Calcd for $C_6H_4F_3NO_2S$: C, 34.13; H, 1.91; N, 6.62. Found: C, 34.39; H, 2.16; N, 6.40.

The 4-isomer collected by gas chromatography gave the following mass spectrum: m/e (relative intensity) 211 (13), 191 (13), 180 (100), 152 (10), 83 (12), 69 (11).

***N*-Phenyl-3-(trifluoromethyl)-2-isothiazoline-4,5-dicarboximide.** In a tube were placed 2.0 g (0.01 mol) of *N*-phenylmaleimide, 2 g of NaF, and 1.5 g (0.01 mol) of ((2,2,2-trifluoroethyl)imino)sulfur difluoride. The tube was sealed under vacuum, allowed to warm to room temperature, and heated in an oil bath at 100 °C for 20 h. The contents of the tube were dissolved in benzene and filtered. The benzene was evaporated and the residue was chromatographed over silica gel, eluted with benzene, and recrystallized from cyclohexane/benzene to give 2.0 g (74%) of white needles: mp 138–139 °C; IR (KBr) 1770, 1710 cm^{-1}; ^{1}H NMR (acetone-d_6) δ 7.4 (br s, 5 H), 5.4 (AB q, 2 H, J = 11 Hz); mass spectrum, m/e (relative intensity) 300 (17), 173 (35), 153 (18), 129 (13), 119 (100), 91 (42), 78 (40), 69 (13). Anal. Calcd for $C_{12}H_7F_3N_2O_2S$: C, 48.00; H, 2.35; N, 9.33; S, 10.68; F, 18.98. Found: C, 48.22; H, 2.54; N, 9.28; S, 10.90; F, 18.78.

3-(Trifluoromethyl)-1,2-thiazolo[5,4-*b*][1,4]naphthoquinone. In a tube were placed 3 g (0.02 mol) of naphthoquinone and 3 g of NaF. While the tube was cooled in liquid N_2, 3 g (0.02 mol) of ((2,2,2-trifluoroethyl)imino)sulfur difluoride was added and the tube was sealed under vacuum. The tube was heated to 130 °C for 17 h in an oil bath. The contents of the tube were dissolved in benzene and chromatographed over silica gel, eluting with benzene. The yellow crystalline adduct was obtained in high purity, 0.55 g (11.4%): mp 194–196 °C; mass spectrum, m/e (relative intensity) 283 (10), 214 (10), 158 (100), 130 (54), 104 (85), 102 (76), 76 (96). Anal. Calcd for $C_{12}H_4F_3NO_2S$: C, 50.89; H, 1.42; N, 4.95; S, 11.32; F, 20.12. Found: C, 50.97; H, 1.46; N, 4.95; S, 11.24; F, 20.29.

5-Hydroxy-3-(trifluoromethyl)-1,2-thiazolo[5,4-*b*][1,4]naphthoquinone. In a tube were placed 5 g (0.03 mol) of juglone and 4 g of NaF, and after the solution cooled, 3.5 g (0.25 mol) of ((2,2,2-trifluoroethyl)imino)sulfur difluoride dissolved in 3.5 mL of toluene was added. The tube was sealed under vacuum and heated at 100 °C for 24 h in an oil bath. The contents of tube were dissolved in benzene and chromatographed over silica gel, eluting with benzene. The desired isothiazole obtained in this way was recrystallized from benzene to give 0.9 g (14%) of red-orange crystals: mp 150–151 °C; IR (KBr) 3200, 1680, 1670, 1640 cm^{-1}; mass spectrum, m/e (relative intensity) 299 (100), 279 (14), 251 (15), 230 (23), 204 (9), 202 (15), 120 (23). Anal. Calcd for $C_{12}H_4F_3NO_3S$: C, 48.17; H, 1.35; N, 4.68; S, 10.72; F, 19.04. Found: C, 48.05; H, 1.52; N, 4.43; S, 10.49; F, 18.90.

(Ethylimino)sulfur Difluoride.[5] Sulfur tetrafluoride (10.0 g, 0.09 mol) was condensed into a trap held at −189 °C under high vacuum. Dry ethylamine, 14.0 g (0.31 mol), was transferred to the trap by distillation. The trap was maintained at −130 °C (pentane slush) for 1 h. The trap was warmed to −78 °C and maintained at that temperature for 2 h. The contents of the trap were distilled through a −125 °C trap. The contents of the −125 °C trap were distilled from a −45 °C trap to a −78 °C trap which contained 5.0 g (48%) of (ethylimino)sulfur difluoride which was too heat sensitive to allow satisfactory elemental analysis. The residue remaining in the −45 °C trap was identified as sulfur bis(ethylimide). The spectral data for the difluoride are the following: ^{1}H NMR (neat) δ 2.2 (3 H, t, J = 7.5 Hz), 3.5 (2 H, t of q, J = 7.5, J = 9.0 Hz); mass spectrum, m/e (relative intensity) 113 (10), 112 (5), 98 (100), 76 (3), 43 (38), 42 (51), 29 (20).

4,5-Bis(carbomethoxy)-3-methyl-1,2-thiazole.[2] In a tube were placed 5.0 g (0.04 mol) of dimethyl acetylenedicarboxylate, 3.0 g of NaF, 0.4 g of 18-crown-6 polyether, and 5 mL of chlorobenzene. The tube was cooled to −189 °C and 2.0 g (0.02 mol) of (ethylimino)sulfur difluoride was added. The tube was sealed under vacuum and heated at 130 °C for 24 h. The contents of the tube were dissolved in benzene and the solution heated under high vaccum to remove benzene and dimethyl acetylenedicarboxylate. The residue remaining was chromatographed over silica gel and eluted with benzene to give 0.2 g (5%) of the isothiazole as a yellow oil previously reported:[2] ^{1}H NMR ($CDCl_3$) δ 2.60 (3 H, s), 3.95 (6 H, s); mass spectrum, m/e (relative intensity) 215 (17), 184 (100), 183 (99), 155 (17), 154 (13), 84 (55), 59 (55).

4- and 5-(Carbomethoxy)-3-methyl-1,2-thiazoles. In a tube were placed 14.0 g (0.167 mol) of methyl propiolate 1.0 g of 18-crown-6 polyether, and 7.0 g of NaF. To the cooled tube was added 4.5 g (0.04 mol) of (ethylimino)sulfur difluoride. The tube was sealed under vacuum and heated at 130 °C for 17 h in an oil bath. The contents were dissolved in acetone which was evaporated to give a residue that was chromatographed over silica gel to give 0.5 g (8%) of an oil. Data for 4-isomer: ^{1}H NMR ($CDCl_3$) δ 2.7 (3 H, s), 3.8 (3 H, s), 9.2 (1 H, s). For 5-isomer: ^{1}H NMR ($CDCl_3$) δ 2.5 (3 H, s), 3.85 (3 H, s), 7.5 (1 H, s). Analysis was obtained on the mixture of isomers which we were unable to separate. Anal. Calcd for $C_6H_7NO_2S$: C, 45.84; H, 4.49; N, 8.91. Found: C, 46.10; H, 4.69; N, 8.78.

Registry No. ((2,2,2-Trifluoroethyl)imino)sulfur difluoride,

74410-90-5; 2,2,2-trifluoroethylamine, 753-90-2; sulfur tetrafluoride, 7783-60-0; 4,5-bis(carbomethoxy)-3-(trifluoromethyl)-1,2-thiazole, 74410-91-6; dimethyl acetylenedicarboxylate, 762-42-5; methyl propiolate, 922-67-8; 4-(carbomethoxy)-3-(trifluoromethyl)-1,2-thiazole, 74410-92-7; 5-(carbomethoxy)-3-(trifluoromethyl)-1,2-thiazole, 74410-93-8; *N*-phenyl-3-(trifluoromethyl)-2-isothiazoline-4,5-carboximide, 74410-94-9; *N*-phenylmaleimide, 941-69-5; 3-(trifluoromethyl)-1,2-thiazolo[5,4-*b*][1,4]naphthoquinone, 74410-95-0; naphthoquinone, 130-15-4; 5-hydroxy-3-(trifluoromethyl)-1,2-thiazolo-[5,4-*b*][1,4]naphthoquinone, 74410-96-1; juglone, 481-39-0; (ethylimino)sulfur difluoride, 3880-02-2; 4,5-bis(carbomethoxy)-3-methyl-1,2-thiazole, 49570-33-4; 4-(carbomethoxy)-3-methyl-1,2-thiazole, 74410-97-2; 5-(carbomethoxy)-3-methyl-1,2-thiazole, 15901-54-9; ((phenylmethyl)imino)sulfur difluoride, 56973-71-8; 4-(carbomethoxy)-3-phenyl-1,2-thiazole, 21905-48-6; 5-(carbomethoxy)-3-phenyl-1,2-thiazole, 68438-26-6.

Intramolecular Cycloaddition Reactions of Olefinic Tosylhydrazones

Albert Padwa* and Hao Ku

Department of Chemistry, Emory University, Atlanta, Georgia 30322

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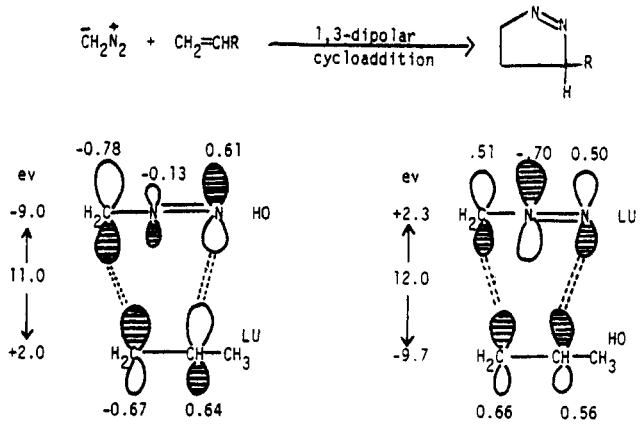
A series of olefinic tosylhydrazones were prepared, and their base- and acid-induced behavior was investigated. Thermolysis of the sodium salt of the tosylhydrazones generates diazoalkenes which undergo intramolecular 1,3-dipolar cycloaddition reactions. The exclusive formation of the tetrahydroindeno[1,2-*c*]pyrazole ring from thermolysis of *o*-allylbenzaldehyde tosylhydrazones is unusual and cannot be easily accounted for on the basis of frontier molecular orbital theory. Our results indicate that geometrical factors can force the reaction to occur in a manner opposite to that normally encountered. Further heating of several methyl-substituted indeno-[1,2-*c*]pyrazolines indicates that benzobicyclo[3.1.0]hexene formation proceeds with predominant inversion of configuration. The results are consistent with a mechanism involving C–N bond cleavage followed by rotation about the σ bond and back-side displacement of nitrogen. Treatment of the olefinic tosylhydrazones with boron trifluoride etherate resulted in a novel cyclization reaction. The regioselectivity associated with the acid-induced cyclization is the consequence of a carbocation pathway.

Although 1,3-dipolar cycloadditions have been successfully employed by chemists for decades,[1-3] it is only within the last few years that a fundamental understanding of the reactivity, stereoselectivity, and regioselectivity phenomena of the reaction has begun to emerge.[4-6] The additions of diazoalkanes to olefins are among the most thoroughly studied 1,3-dipolar cycloadditions.[1,7] Tosylhydrazones are commonly used as precursors to generate diazoalkanes. The cycloadditions of simple diazoalkanes are HO (1,3-dipole)–LU (dipolarophile) controlled.[5,6] Both conjugating and electron-attracting groups accelerate reactions of dipolarophiles with diazoalkanes as compared to ethylene. With these dipolarophiles, 3-substituted Δ^1-pyrazolines are favored, a result of the union of the larger diazoalkane HO coefficient on carbon with that of the larger dipolarophile LU coefficient on the unsubstituted carbon.[5] Huisgen has recently shown that introduction of a carbomethoxy group into diazomethane shifts the 1,3-dipole to a type II (Sustmann's classification)[8] in methyl diazoacetate and further toward a type III for dimethyl diazomalonate and methyl diazo(phenylsulfonyl)acetate.[9] Electron-releasing substituents in the diazoalkane, on the other hand, raise the HO energy and enhance the cycloaddition rate[10] (see Scheme I).

Simple diazoalkanes and alkylethylenes are rather unreactive as a result of the large energy gap between the frontier molecular orbitals. Surprisingly, the literature

Scheme I



contained very few examples of the regiochemistry of cycloaddition of diazoalkanes with simple monoalkylethylenes when we initiated our studies.[11-15] Very recently, it has been shown that 3-substituted pyrazolines are formed as the major products in the 1,3-dipolar cycloaddition of diazomethane with 1-alkenes.[16,17] With these systems, the difference between the two frontier orbital interactions is quite small, but the nearly equal magnitude of the terminal coefficients in the diazomethane LU suggests that the diazomethane HO determines product regiochemistry.

In spite of the copious literature dealing with bimolecular cycloaddition reactions of diazoalkanes, intramo-

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