Ring Cleavage and Ring Contraction of Nitro-Substituted 1-Methyl-2,5-diphenyl-1,4-dithiinium Tetrafluoroborates

Thomas E. Young* and Alan R. Oyler[1]

Department of Chemistry, Lehigh University, Bethlehem, Pennsylvania 18015

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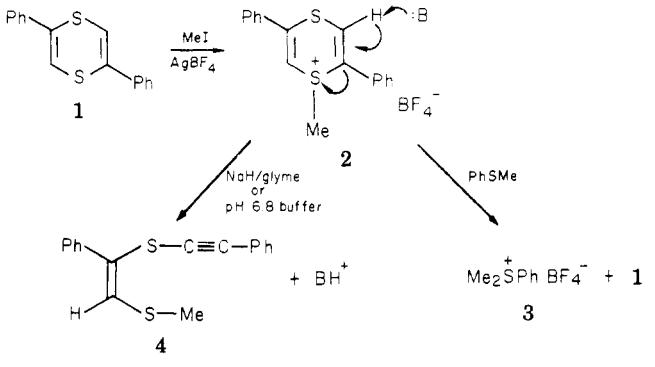
1-Methyl-2,5-diphenyl-1,4-dithiinium tetrafluoroborate (2) underwent selective abstraction of H-3 in aqueous phosphate buffer at pH 6.8 to yield the ring cleavage product (*Z*)-1-(phenylethynylthio)-2-(methylthio)-1-phenylethylene (4). Methylation of 3-nitro-2,5-diphenyl-1,4-dithiin (5) with MeI–$AgBF_4$ yielded as the major product 1-methyl-6-nitro-2,5-diphenyl-1,4-dithiinium tetrafluoroborate (8), which also underwent ring cleavage in acetonitrile on an alumina column, in pH 6.8 phosphate buffer or with triethylamine, to form (*Z*)-1-(phenylethynylthio)-2-(methylthio)-2-nitro-1-phenylethylene (14). The methylation of 5 also yielded a minor product, 3-(dimethylsulfonio)-5-nitro-2,4-diphenylthiophene tetrafluoroborate (13), apparently resulting from ring contraction of 1-methyl-3-nitro-2,5-diphenyl-1,4-dithiinium tetrafluoroborate (9), which appeared to be unstable. Demethylation of 13 with triethylamine yielded 3-(methylthio)-5-nitro-2,4-diphenylthiophene (12). More fully substituted dithiins, including 3,6-dinitro- and 3-bromo-6-nitro-2,5-diphenyl-1,4-dithiins, could not be methylated, whereas the 3,6-dibromo analogue (16) afforded only a 3% yield of 1-methyl-3,6-dibromo-2,5-diphenyl-1,4-dithiinium tetrafluoroborate (17).

In an earlier article[2] we reported that alkylation of 2,5-diphenyl-1,4-dithiin (1) with methyl iodide and silver tetrafluoroborate gave a high yield of 1-methyl-2,5-diphenyl-1,4-dithiinium tetrafluoroborate (2), which exhibited ambident behavior toward various bases (cf. Scheme I). For example, a variety of common nucleophiles, including triethylamine, anilines, and thioanisoles, effected S_N2 attack on the methyl group of 2, resulting in displacement of 1 and formation of the methylated nucleophiles (e.g., 3 from thioanisole); a detailed kinetic study of the aniline and thioanisole methylations by 2 in acetonitrile has been reported.[3] In contrast, an essentially nonnucleophilic base (B: in Scheme I) such as hydride ion (from NaH) abstracted the β-proton (H-3) of 2, resulting in ring cleavage to (*Z*)-1-(phenylethynylthio)-2-(methylthio)-1-phenylethylene (4).[2]

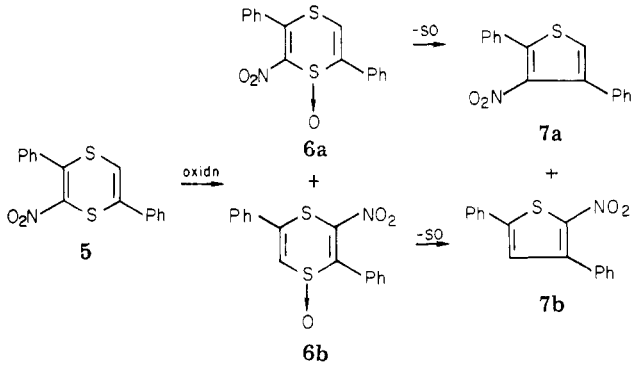
We have subsequently found that the ring cleavage (2 → 4) does not require such drastic treatment but occurs even in aqueous phosphate buffer at pH 6.8 and 37 °C (cf. Experimental Section). Ring scission under such mild conditions, presumably involving abstraction of the β-proton by hydrogen phosphate ion, was surprising and prompted us to explore the influence of nitro and bromo substituents on the dithiinium system (2). The results of these experiments, reported here, include a particularly interesting ring contraction of a nitro-substituted 1,4-dithiinium salt to a thiophene derivative.

Several nitro- and bromo-substituted derivatives of 1 were easily available by electrophilic substitution of 1, as described by Parham and co-workers,[4-6] and the mononitro derivative (5) was selected for first attention. Parham[4,6] found that oxidation of 3-nitro-2,5-diphenyl-1,4-dithiin (5) gave a mixture of two isomeric thiophenes (7a and 7b), which were formed by loss of sulfur monoxide from the two unstable intermediates (6a and 6b; Scheme II). It was not surprising, therefore, to find that methylation of 5 with

Scheme I



Scheme II



methyl iodide and silver tetrafluoroborate also yielded two products in a ratio of 3:1 (cf. Experimental Section). The major product, isolated in pure form by direct recrystallization of the crude product, was clearly 1-methyl-6-nitro-2,5-diphenyl-1,4-dithiinium tetrafluoroborate (8; Scheme III), which exhibited an NMR spectrum with a methyl singlet at δ 3.33, an aromatic multiplet for the two phenyl rings at δ 7.77, and a singlet at δ 8.05, corresponding to H-3 of the dithiinium ring, in the ratio of 3:10:1. Since the single vinyl proton of 8 appears in the strongly deshielded position comparable with that of the β-proton (H-3 at δ 8.15) of the parent 1-methyl-2,5-diphenyl-1,4-dithiinium salt (2),[2] the nitro group must be assigned to the 6-position as shown.

Chromatography of the crude 3:1 mixture from the methylation of 5 on an alumina column gave two products:

(1) Based in part on Alan R. Oyler, Ph.D. Dissertation, Lehigh University.
(2) T. E. Young and R. A. Lazarus, *J. Org. Chem.*, **33**, 3770 (1968).
(3) T. E. Young and A. R. Oyler, *J. Org. Chem.*, **41**, 2753 (1976).
(4) W. E. Parham and V. J. Traynelis, *J. Am. Chem. Soc.*, **77**, 68 (1955).
(5) W. E. Parham, I. Nicholson, and V. J. Traynelis, *J. Am. Chem. Soc.*, **78**, 850 (1956).
(6) W. E. Parham, E. T. Harper, and R. S. Berger, *J. Am. Chem. Soc.*, **82**, 4932 (1960).

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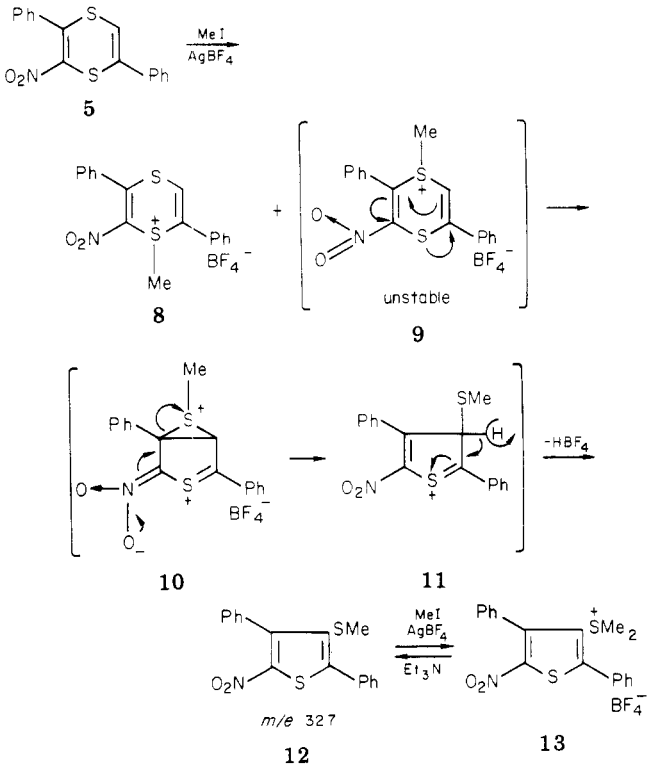
Scheme III



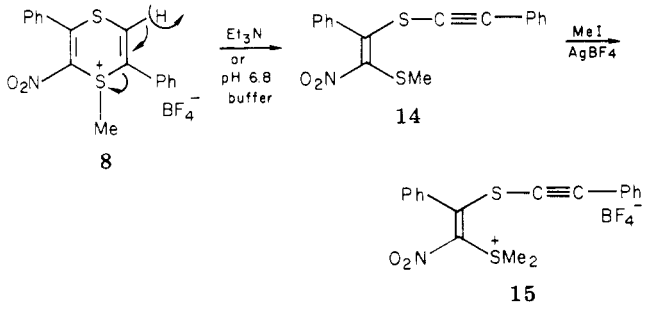
(a) the thiophene derivative (13) whose NMR spectrum was identical with that of the minor component in the original methylation mixture, and (b) compound 14, which resulted from ring cleavage of 8 during chromatography. Compound 8 itself was not eluted.

Assignment of the thiophene structure (13) to the minor methylation product from 5 was based on the following information. This secondary product (13) showed an NMR spectrum lacking the vinyl proton signals characteristic of the dithiinium cations but having an aromatic resonance band (essentially a singlet with only fine splitting) at δ 7.65 and a methyl singlet at δ 3.02 in the ratio of 10:6. Demethylation of this product (13) with triethylamine afforded a new compound (assigned structure 12), which showed a parent peak at m/e 327 in the mass spectrum, and an NMR spectrum which displayed an aromatic multiplet (sharp) centered at δ 7.45 and a methyl singlet at δ 1.78, which integrated in the ratio of 10:3. The structure 3-(dimethylsulfonio)-2,4-diphenyl-5-nitrothiophene tetrafluoroborate (13) is consistent with the data for the minor methylation product of 5, and 2,4-diphenyl-3-(methylthio)-5-nitrothiophene (12) is consistent with the data for the demethylation product of 13.

The probable mode of formation of the thienyldimethylsulfonium salt (13) is shown in Scheme III. Presumably, the initially formed 1-methyl-3-nitro-2,5-diphenyl-1,4-dithiinium tetrafluoroborate (9) is unstable and rearranges via transient cations 10 and 11, the latter of which then loses a proton to form 2,4-diphenyl-3-(methylthio)-5-nitrothiophene (12). This process is analogous with the known ring contractions of other 2,5-diphenyl-1,4-dithiin derivatives to the more stable thiophenes by extrusion of sulfur, sulfur dioxide, or sulfur monoxide (e.g., Scheme II).[4,6-8] The methylthio compound 12 is finally methylated in the reaction medium to form 13, which is ultimately isolated.

(7) W. E. Parham and V. J. Traynelis, *J. Am. Chem. Soc.*, 76, 4960 (1954).
(8) H. Szmant and L. M. Alfonso, *J. Am. Chem. Soc.*, 79, 205 (1957).

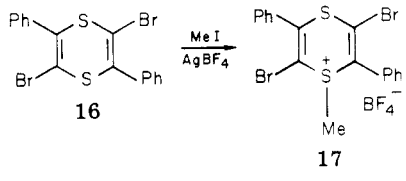
Scheme IV



As mentioned above, the 6-nitro-1,4-dithiinium salt (8) was not eluted from the alumina column during the chromatographic isolation of 13. Instead, 1-(phenylethynylthio)-2-methylthio-2-nitro-1-phenylethylene (14), resulting from ring cleavage of 8, was eluted (cf. Scheme IV). Compound 14 was also obtained as the sole product from the reaction of 8 with triethylamine and from the decomposition of 8 in aqueous phosphate buffer of pH 6.8. This reaction is entirely analogous with the transformation of 2 to 4 as shown in Scheme I. The structure of 14 was assigned on the basis of a triple bond stretch in the infrared spectrum and its NMR spectrum which exhibited a methyl singlet and a phenyl multiplet that integrated in the ratio 3:10. The mode of formation of 14 strongly suggests that it has the Z configuration, as illustrated.

Reaction of 14 with methyl iodide–silver tetrafluoroborate gave the dimethylsulfonium salt (15), which showed a triple bond stretch at 2160 cm^{-1} in the infrared and gave an NMR spectrum having only a methyl singlet at δ 3.38 and an aromatic multiplet at 6.8–7.8 ppm, integrating in the ratio of 6:10. Compound 15 was of interest since it had the same molecular composition as the minor product (13) obtained from the methylation of 5 and was originally considered as a possible structure for that minor methylation product. Compound 15 and the minor product, though isomeric, proved to be distinctly different, hence giving further support to the structural assignment (13) to the minor methylation product from 5.

Attempts to methylate 3,6-dinitro-2,5-diphenyl-1,4-dithiin and 3-bromo-6-nitro-2,5-diphenyl-1,4-dithiin with MeI–$AgBF_4$ were not successful. Only starting materials or thermal decomposition products of the dithiins could be isolated. 3,6-Dibromo-2,5-diphenyl-1,4-dithiin (16) gave only a 3% yield of the 1-methyldithiinium derivative (17); hence, these latter systems were not further investigated.



Experimental Section

Melting points were determined in capillary tubes using a calibrated Mel-Temp apparatus. Ultraviolet spectra were recorded on a Perkin-Elmer 402 spectrophotometer, and infrared spectra were taken on a Perkin-Elmer 257 instrument. NMR spectra were determined on a Hitachi Perkin-Elmer R20A high-resolution spectrometer using tetramethylsilane as internal standard. Data are reported in the order: δ (multiplicity, number of protons, assignment). Mass spectra were run at 70 eV by Dr. James E. Sturm using a Hitachi RMU-6E high-resolution instrument equipped with double-focusing sector. Microanalyses were performed by Robertson Laboratories, Florham Park, NJ. The silver tetrafluoroborate used was $AgBF_4 \cdot 4CH_3CN$, prepared as we described earlier.[2]

Decomposition of 1-Methyl-2,5-diphenyl-1,4-dithiinium Tetrafluoroborate (2) in Phosphate Buffer. 1-Methyl-2,5-diphenyl-1,4-dithiinium tetrafluoroborate (**2**)[2] (0.2 g, 0.00054 mol) was stirred in 160 mL of pH 6.8 phosphate buffer (0.025 M in both KH_2PO_4 and Na_2HPO_4) at 37 °C for 12 h. The solid material that separated was removed by ether extraction to give 0.08 g (53% yield) of white crystals with mp 71–72 °C (lit. mp 72–74 °C) and IR and NMR spectra identical with those reported earlier[2] for 1-(phenylethynylthio)-2-(methylthio)-1-phenylethylene (**4**).

Methylation of 3-Nitro-2,5-diphenyl-1,4-dithiin (5). To a stirred solution of 4.57 g (0.0146 mol) of 3-nitro-2,5-diphenyl-1,4-dithiin (**5**)[4] and 21 g (0.15 mol) of methyl iodide in 50 mL of methylene chloride was added 5.38 g (0.015 mol) of $AgBF_4 \cdot 4MeCN$ in 75 mL of nitromethane. The reaction flask was covered with aluminum foil to exclude light, and the mixture was stirred overnight. The yellow precipitate that formed was removed by filtration and washed with nitromethane and ether to give 3.35 g (95%) of silver iodide. The combined washings and filtrate were concentrated on a rotary evaporator to the point at which a red precipitate appeared. The least amount of methylene chloride necessary to redissolve this precipitate was then added. Slow addition of ether with constant stirring precipitated 3.02 g of an olive drab powder, which was recrystallized once from acetonitrile–ether to yield 2.34 g of a yellow solid. This solid was roughly a 3:1 mixture of 1-methyl-6-nitro-2,5-diphenyl-1,4-dithiinium tetrafluoroborate (**8**) and 3-(dimethylsulfonio)-2,4-diphenyl-5-nitrothiophene tetrafluoroborate (**13**) as determined by the ratio of the area of the NMR methyl peak of **8** to one-half the area of the NMR methyl peak of **13**. The ethereal filtrate was evaporated to yield a red solid which was recrystallized from ethyl acetate to give 0.92 g (20%) of unreacted **5**.

A. Isolation of 3-(Dimethylsulfonio)-2,4-diphenyl-5-nitrothiophene Tetrafluoroborate (13). The 2.34 g of the 3:1 mixture obtained above was stirred into 100 mL of pH 6.8 phosphate buffer (0.025 M in both Na_2HPO_4 and KH_2PO_4) and then kept at 25 °C for 2 h and then at 50 °C for another 2 h. The insoluble solid was removed and washed with benzene and ether to give 0.54 g of a white salt which showed only one of the two methyl groups originally present in the NMR spectrum of the mixture. An additional 0.05 g of product was obtained by evaporating the aqueous filtrate and recrystallizing the residual material from acetonitrile–ether. The total yield of 0.59 g (9.4% yield based on **5**) was recrystallized from absolute ethanol to yield material of mp 192 °C, having both NMR and IR spectra identical with those of the salt (**13**) isolated in the chromatographic separation described below.

In another experiment the 3:1 mixture prepared by a methylation reaction analogous to that described above was chromatographed on a column of alumina using acetonitrile as eluent. Evaporation of the initial fractions yielded a yellow oil which crystallized. Recrystallization from absolute ethanol gave yellow needles, mp 60–61.5 °C. This material was identical with 1-(phenylethynylthio)-2-(methylthio)-2-nitro-1-phenylethylene (**14**) described in a later experiment (vide infra).

After isolation of the yellow fraction, elution with acetonitrile was continued. Addition of ether to these later fractions precipitated a white salt, which was recrystallized from absolute ethanol to yield pure 3-(dimethylsulfonio)-2,4-diphenyl-5-nitrothiophene tetrafluoroborate (**13**): mp 194.5–195.5 °C; NMR (CD_3NO_2) δ 7.65 (m, 10, Ar H), 3.02 (s, 6, CH_3's); UV λ_{max} (MeCN) 320 nm (log ϵ 3.97); IR (KBr) 3030 (Ar H), 2930 (CH_3), 1535, 1505, 1445, 1425, 1320 (C–NO_2), 1380, 1220, 1350–950 (B–F), 860, 795, 755, 700 cm^{-1}.

Anal. Calcd for $C_{18}H_{16}NS_2O_2BF_4$: C, 50.36; H, 3.76; N, 3.26; S, 14.94; F, 17.70. Found: C, 50.05; H, 3.84; N, 3.23; S, 15.42; F, 16.95.

B. Isolation of 1-Methyl-6-nitro-2,5-diphenyl-1,4-dithiinium Tetrafluoroborate (8). A 3:1 mixture of **8** and **13** was again prepared in a similar fashion using 11.7 g (0.0374 mol) of **5**, 53 g (0.374 mol) of methyl iodide, and 26.8 g (0.0748 mol) of $AgBF_4 \cdot 4MeCN$. Recrystallization of the mixture from acetonitrile–ether (Norite A) gave 3.87 g (25% based on **5**) of a yellow solid with mp 151–152 °C and an NMR spectrum containing only one of the two methyl peaks present in the spectrum of the mixture. Further recrystallization gave analytically pure 1-methyl-6-nitro-2,5-diphenyl-1,4-dithiinium tetrafluoroborate (**8**): mp 150 °C dec; NMR (CD_3NO_2) δ 8.28 (s, 1, H-3), 7.9–7.5 (m, 10, Ar H), 3.38 (s, 3, CH_3); (CF_3COOD) δ 8.05 (s, 1, H-3), 7.9–7.5 (m, 10, Ar H), 3.33 (s, 3, CH_3); (CD_3CN) δ 8.20 (s, 1, H-3), 7.9–7.5 (m, 10, Ar H), 3.2 (s, 3, CH_3); UV λ_{max} 230 nm (log ϵ 4.22), 288 (4.14).

Anal. Calcd for $C_{17}H_{14}NS_2O_2BF_4$: C, 49.17; H, 3.40; N, 3.37; S, 15.44; F, 18.30. Found: C, 49.26; H, 3.49; N, 3.11; S, 15.20; F, 18.24.

2,4-Diphenyl-3-(methylthio)-5-nitrothiophene (12). Excess triethylamine was added to an NMR tube containing a concentrated solution of 3-(dimethylsulfonio)-2,4-diphenyl-5-nitrothiophene tetrafluoroborate (**13**) in CD_3CN. The spectrum, taken after 3 min, showed only peaks corresponding to 2,4-diphenyl-3-(methylthio)-5-nitrothiophene (**12**), triethylamine, and Et_3NMeBF_4. Addition of ether to the solution precipitated a white, hygroscopic solid with an NMR spectrum identical with that of Et_3NMeI, prepared by reacting triethylamine and methyl iodide. Evaporation of the filtrate gave a yellow solid, mp 88–91 °C. Recrystallization of this product from absolute ethanol gave yellow crystals of pure 2,4-diphenyl-3-(methylthio)-5-nitrothiophene (**12**): mp 90.5–91.0 °C; NMR ($CDCl_3$) δ 7.9–7.2 (m, 10, Ar H), 1.78 (s, 3, CH_3); IR (KBr) 3030 (Ar H), 2920 (CH_3), and strong bands at 1500 and 1310 (aromatic C–NO_2), 755, 690 cm^{-1}; UV λ_{max} (CH_3CN) 248 (log ϵ 4.05), 338 (3.90) nm; mass spectrum, *m/e* (rel intensity) 327 (100, M^+), 266 (9), 234 (24), 221 (14), 218 (10), 202 (15), 189 (17), 155 (8), 133 (12), 121 (34), 105 (13), 89 (15), 81 (35), and 77 (10).

Anal. Calcd for $C_{17}H_{13}NO_2S_2$: C, 62.36; H, 4.00; N, 4.28; S, 19.59. Found: C, 62.17; H, 4.23; N, 4.08; S, 19.50.

1-(Phenylethynylthio)-2-(methylthio)-2-nitro-1-phenylethylene (14). 1-Methyl-6-nitro-2,5-diphenyl-1,4-dithiinium tetrafluoroborate (**8**) (0.5 g, 0.0012 mol) was vigorously stirred in 100 mL of pH 7 buffer at 50 °C for 1.5 h. Filtration yielded 0.34 g (87%) of a gold solid, mp 58–60 °C. Recrystallization from absolute ethanol gave yellow needles of pure **14**: mp 64–65 °C; NMR (CCl_4) δ 7.5–6.7 (m, 10, Ar H), 2.45 (s, 3, CH_3); IR (KBr) 2170 (C≡C) cm^{-1}.

Anal. Calcd for $C_{17}H_{13}NO_2S_2$: C, 62.36; H, 4.00; N, 4.28; S, 19.59. Found: C, 62.13; H, 4.14; N, 4.10; S, 19.44.

Reaction of 1-Methyl-6-nitro-2,5-diphenyl-1,4-dithiinium Tetrafluoroborate (8) with Triethylamine. **8** (0.5 g, 0.0012 mol) and 0.122 g (0.0012 mol) of triethylamine were stirred in 25 mL of acetonitrile at 25 °C for 1 h. Ether (450 mL) was then added, and the mixture was stirred at 0 °C for 0.5 h to precipitate a hygroscopic white solid (Et_3NHBF_4) which was removed by filtration. Evaporation of the ethereal filtrate yielded 0.34 g (87%) of a golden yellow solid, mp 59–63 °C. One recrystallization from absolute ethanol gave yellow needles with mp 64–65 °C and NMR and IR spectra identical with those of 1-(phenylethynylthio)-2-(methylthio)-2-nitro-1-phenylethylene (**14**) described in the previous experiment.

1-(Phenylethynylthio)-2-(dimethylsulfonio)-2-nitro-1-phenylethylene Tetrafluoroborate (15) via Methylation of 14. To a stirred solution of 1-(phenylethynylthio)-2-(methylthio)-2-nitro-1-phenylethylene (**14**; 0.50 g, 0.00153 mol) and 2.2 g (0.015 mol) of methyl iodide in 10 mL of methylene chloride was added 0.55 g (0.00153 mol) of $AgBF_4 \cdot 4CH_3CN$ in 15 mL of nitromethane. The flask was covered with aluminum foil, and the mixture was stirred for 24 h. The silver iodide, removed by filtration and washed with nitromethane, weighed 0.34 g (94%). Ether was added to the combined filtrate and washings to precipitate 0.49 g (75% yield) of 1-(phenylethynylthio)-2-(dimethylsulfonio)-2-nitro-1-phenylethylene tetrafluoroborate (**15**), mp 178 °C dec. Recrystallization from acetonitrile–ether gave yellow crystals: mp 180–182 °C dec; NMR (CD_3NO_2) δ 7.9–7.0 (m, 10, Ar H), 3.39 (s, 6, 2 CH_3); IR (KBr) 2160 cm^{-1} (C≡C).

Anal. Calcd for $C_{18}H_{16}NS_2O_2BF_4$: C, 50.36; H, 3.76; N, 3.26; S, 14.94; F, 17.70. Found: C, 50.25; H, 3.88; N, 3.39; S, 15.03; F, 17.68.

1-Methyl-3,6-dibromo-2,5-diphenyl-1,4-dithiinium Tetrafluoroborate (17). To a stirred solution of 4.50 g (0.0105 mol) of 3,6-dibromo-2,5-diphenyl-1,4-dithiin (**16**)[5] and 14 g (0.10 mol) of methyl iodide in 310 mL of methylene chloride and 345 mL of nitromethane was added 3.78 g (0.0105 mol) of $AgBF_4 \cdot 4CH_3CN$ in 100 mL of nitromethane. The flask was covered with aluminum foil, and the mixture was stirred overnight. The silver iodide which had separated was collected by filtration and then washed with

methylene chloride, with nitromethane, and finally with ether. Concentration of the combined filtrate and washings to 100 mL on a rotary evaporator led to precipitation of 3.28 g (73% recovery) of unreacted starting material (**16**). About 800 mL of ether was then added to the filtrate to precipitate a brown solid, which was washed with benzene and ether. One recrystallization of this material from acetonitrile–ether gave 0.17 g (3% yield) of crude product, mp 156–157 °C. Further recrystallization gave pure 1-methyl-3,6-dibromo-2,5-diphenyl-1,4-dithiinium tetrafluoroborate (**17**): mp 161–163 °C; NMR (CD_3CN) δ 7.62 (m, 10, Ar H), 3.30 (s, 3, CH_3); UV λ_{max} 282 nm (log ϵ 4.11).

Anal. Calcd for $C_{17}H_{13}S_2Br_2BF_4$: C, 38.67; H, 2.48; S, 12.14. Found: C, 38.47; H, 2.61; S, 12.40.

Registry No. **2**, 17250-79-2; **4**, 17278-23-8; **5**, 6317-72-2; **8**, 72525-34-9; **12**, 72525-35-0; **13**, 72525-37-2; **14**, 72525-38-3; **15**, 72525-40-7; **16**, 6317-71-1; **17**, 72525-42-9; silver tetrafluoroborate, 14104-20-2; methyl iodide, 74-88-4.

Acid-Catalyzed Rearrangement of α-Aminoalkylidene-β-alkoxy β-Lactams

Yoshiro Hirai, Shun-ichi Hirokami, and Masanori Nagata

Laboratory of Chemistry, Toyama Medical and Pharmaceutical University, Sugitani, Toyama 930-01, Japan

Masayuki Morita and Takao Yamazaki*

Faculty of Pharmaceutical Sciences, Toyama Medical and Pharmaceutical University, Sugitani, Toyama 930-01, Japan

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Hydrolysis of six nonfused 4-methoxy β-lactams (**1–6**) on alumina gave the corresponding enamino ketone derivatives (**11–16**), whereas the fused β-alkoxy β-lactams (**7** and **8**) afforded the alkyl 2-piperidylideneacetoacetates **17** and **18**, respectively. The structures of the products (**11**, **17**, and **18**) were confirmed by synthesis. Treatment of the fused β-methoxy β-lactam **7** in ethanol solution containing water (11%) and a catalytic amount of acetic acid (1%) leads to a mixture of two products, **17** and enamino ketone derivative **21**. Similarly, treatment of the fused β-ethoxy β-lactam **8** in an acidic methanol solution containing water (11%) afforded **18** and **21**. Under similar conditions the fused β-alkoxy β-lactams **9** and **10** also gave the corresponding alkyl 2-(2-hexahydroazepinylidene)acetoacetate (**19** and **20**), enamino ketone derivative **22**, and 3-acetyl-β-alkoxy β-lactams (**23** and **24**), respectively. Furthermore, hydrolysis of **24** in a similar acidic solution gave the enol-type product **25**. Hydrolysis of fused CD_3O β-lactam **7a** and fused $CH_3{}^{18}O$ β-lactam **7b** on alumina gave methyl-d_3 2-piperidylideneacetoacetate (**17a**) and methyl 2-piperidylideneacetoacetate-*carboxy*-^{18}O (**17b**), respectively. These observations suggest that an intramolecular migration of the alkoxy group to the amide carbonyl carbon is responsible for the formation of the products (**17–20**).

Irradiation of 2,3,6-trialkyl-4-pyrimidinone derivatives in alcoholic solution gives α-aminoalkylidene-β-alkoxy β-lactams (**1–10**).[1b] The structure of the fused β-lactam **7** was unambiguously established by the X-ray analysis. The structures and properties of these β-lactams in solution were also studied in detail.

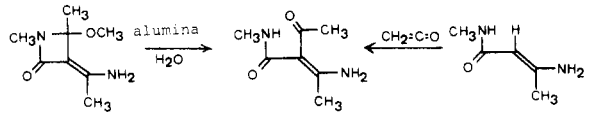
During the course of the investigation, we found that when the fused β-lactam **7** or **8** was eluted from a column of alumina with benzene, products **17** and **18** (about 90% yield), respectively,[1a] were obtained. The structures of these products were assigned by spectral data and confirmed by synthesis. However, the structure was inconsistent with those of compounds expected from the hydrolysis of the corresponding acyclic β-lactams.[2]

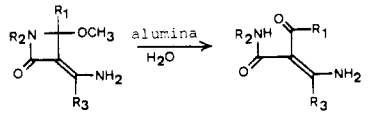
These β-lactams are of interest since these are model compounds related to the penicillin and cephalosporin antibiotics, and the hydrolysis of these β-lactams may provide important information about the stability of the β-lactams.

With this prospect in mind, we have now undertaken the hydrolysis of the β-alkoxy β-lactam under various experimental conditions.

Hydrolysis of α-Aminoalkylidene-β-alkoxy β-Lactams 1–6 on Alumina. The nonfused β-lactam **1** was not stable to alumina chromatography. The only product isolated from **1** on alumina was **11**, obtained in 34% yield.

Scheme I





compd	R_1	R_2	R_3
2, 12	CH_3	CH_2CH_3	CH_3
3, 13	CH_3	$CH_2CH_2CH_3$	CH_3
4, 14	CH_3	$CH_2C_6H_5$	CH_3
5, 15	CH_2CH_3	CH_3	CH_3
6, 16	CH_3	CH_3	CH_2CH_3

The ^1H NMR spectrum showed a doublet at δ 2.72 (J = 4.5 Hz, 3 H) and a quartet at 7.82 (J = 4.5 Hz, 1 H) which could be assigned to the secondary *N*-methyl group. The ^1H NMR spectrum also exhibited signals at δ 7.60 (br s, 1 H) and 10.14 (br s, 1 H) which, when considered in terms of the stretching bands at 3330, 3200, and 3100 cm^{-1}, indicated a primary amino group. The ^1H NMR spectrum (δ 10.14) showed that one of the hydrogen atoms in the primary amino group is bonded by an intramolecular hydrogen bond. The IR bands at 1640 and 1610 cm^{-1} sug-

(1) (a) T. Yamazaki, M. Nagata, S. Hirokami, Y. Hirai, and T. Date, *Heterocycles*, **9**, 505 (1978); (b) S. Hirokami, Y. Hirai, M. Nagata, T. Yamazaki, and T. Date, *J. Org. Chem.*, **44**, 2083 (1979).

(2) R. J. Stoodley, *Tetrahedron*, **31**, 2321 (1975).

0022-3263/80/1945-0936$01.00/0