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Papers

Synthesis of 4-methylene-2-(1-nitromethylidene)-1,3-dithiolane and 4-methyl-2-(1-nitromethylidene)-1,3-dithiole from dipotassium 2-nitro-1,1-ethylenedithiolate*

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The reaction of dipotassium 2-nitro-1,1-ethylenedithiolate **1** with propargyl bromide has provided isomeric 4-methylene-2-(1-nitromethylidene)-1,3-dithiolane **4** and 4-methyl-2-(1-nitromethylidene)-1,3-dithiole **6** *via* novel mono-alkylation-cyclization.

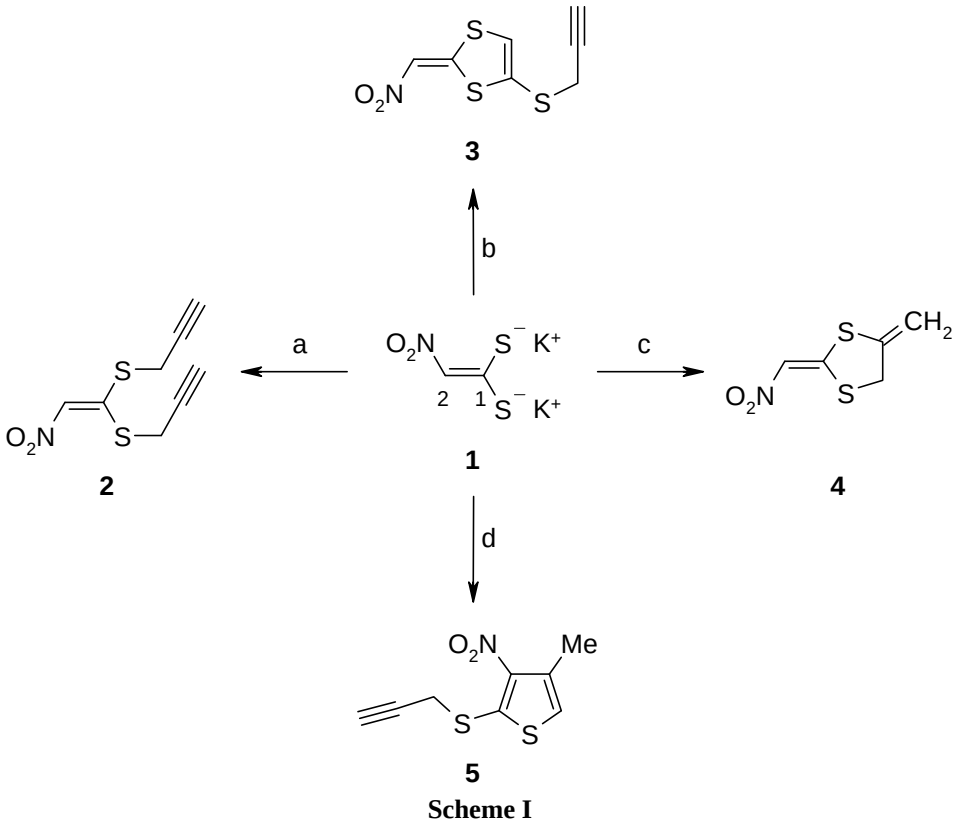
Keywords: Ketene acetal, dithiolane, dithiole

The salt, dipotassium 2-nitro-1,1-ethylenedithiolate **1** is a well known intermediate in the synthesis of nitroketene dithioacetals and their further transformation to heterocyclic compounds[1]. It is also an intermediate in the synthesis of anti-ulcer drugs ranitidine® and nizatidine®. It can be prepared in bulk scale from carbon disulfide, nitromethane and potassium hydroxide. The alkylation of **1** with different alkyl halides in methanol / water mixture provides a wide variety of the bis-alkylated products, i.e., 1,1-di(alkylsulfanyl)-2-nitroethylenes of the type **2** (ref. 2). Nevertheless, when the alkylation of **1** is carried out with sterically hindered alkyl halides the reaction takes a different course to provide 4-(alkylsulfanyl)-2-[(*Z*)-1-nitromethylidene]-1,3-dithioles of the type **3** (ref. 3). The 1,3-dithiols, in general, have found good application as materials exhibiting non-linear optical properties and as organic conductors[4]. In this context, it would be interesting to study alkylation of salt **1** with allyl bromide, because, the bis-allylated product of the type **2** could undergo symmetry allowed 3,3-sigmatorpic rearrangement to provide C-2 allylated products. Unfortunately, the alkylation of **1** with allyl bromide under a variety of conditions led to extensive decomposition of the reaction-mixture and it was not possible isolate any characterizable products. In continuation of this study, the reaction of the salt **1** with propargyl bromide is conducted.

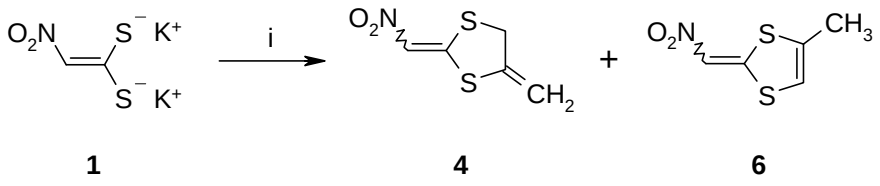
The reaction of salt **1** with propargyl bromide could provide the bis-alkylated product 1,1-di(2-propynylsulfanyl)-2-nitroethylene **2** (route a, **Scheme I**) or 4-(2-propynylsulfanyl)-2-[(*Z*)-1-nitromethylidene]-1,3-dithiole **3** (route b) in line with the previous findings[2]. On the other hand, the reaction could provide 4-methylene-2-[(*E*)-1 - nitromethylidene]-1,3-dithiolane **4** resulting from monoalkylation followed by cyclization (route c). Alternatively, the bis-alkylated product or its precursors could undergo cyclization followed by aromatization to provide 4-methyl-3-nitro-2-(2-propynylsulfanyl)thiophene **5** (route d). It was found that the reaction of salt **1** and propargyl bromide takes route c (**Scheme I**) to furnish dithiolane **4** and its isomer **6** (**Scheme II**).

The salt **1** was treated with propargyl bromide in MeOH, H_2O (2:1) at 0°C and then left at rt for 8 hr to furnish a mixture of isomeric products, 4-methylene-2-(1-nitromethylidene)-1,3-dithiolane **4** and 4-methyl-2-(1-nitromethylidene)-1,3-dithiole **6** in 47% yield. The ^{1}H NMR spectrum of **4** revealed that it was a mixture of *E* and *Z* isomers. The spectrum exhibited two triplets at δ 4.12 and 4.14 ppm (J = 1.8 Hz) for methylene, two sets of quartets at 5.14 and 5.43 and a multiplet at 5.54 for olefinic CH_2 and two singlets at 7.48 and 7.49 ppm for nitromethylidene hydrogens. The ^{13}C NMR spectrum of **4** revealed two sets of five signals confirming the presence of *E* and *Z* isomers in the ratio of 55:45. The predominance of *E* isomer was indicated on the basis of comparison of the spectral data with data on similar compounds[5]. However, since

* Part 6 in the series on ketene acetal chemistry



Scheme I



Reagents and conditions: HC≡CCH$_2$Br, MeOH, H$_2$O (2:1), 0°C to rt, 8hr, 47%.

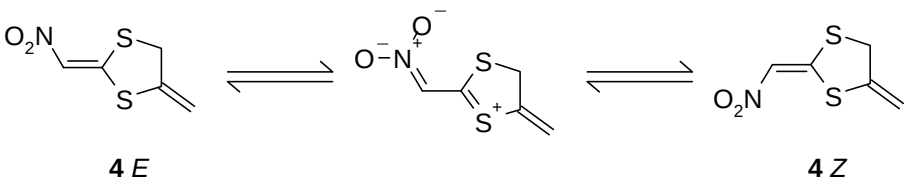
Scheme II

4 is a polarized ketene acetal the *E* and *Z* isomers could inter-convert as shown in **Figure 1**.

The ^{1}H NMR spectrum of the dithiole **6** showed that it was also a mixture of *E* and *Z* isomers. The spectrum displayed two sets of doublets at δ 2.36 and 2.38 ppm (J = 1.2 Hz) for methyl, a multiplet at 6.66 for olefinic hydrogen and a broad singlet and a doublet at 7.70 and 7.72 (J = 1.2 Hz) ppm for nitromethylidene hydrogens, to account for its structure. The ^{13}C NMR spectrum of **6** exhibited two sets of five signals confirming the presence of *E* and *Z* isomers. Similar to **4** (**Figure 1**), the *E* and *Z* isomers of **6** also can inter-convert.

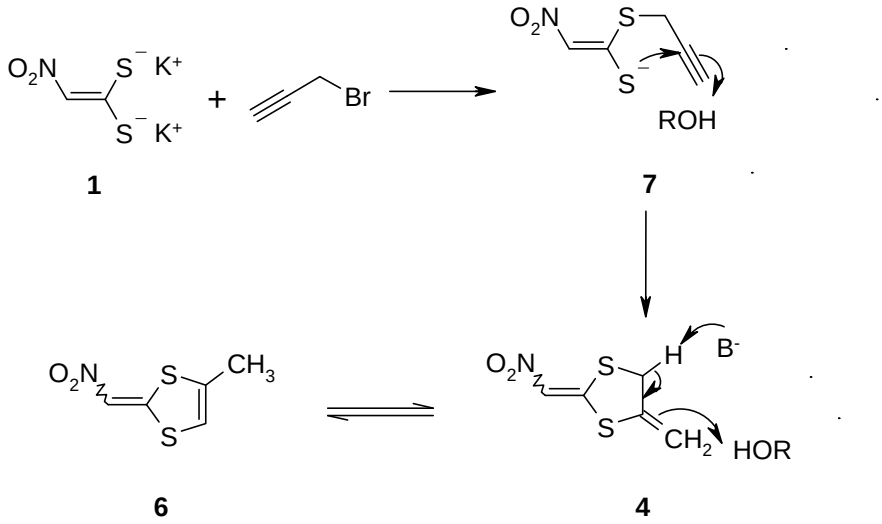
Possible mechanism for the formation of dithiolane **4** and the dithiole **6** is given **Scheme III**. The mono-alkylation of the salt **1** with propargyl bromide gives intermediate **7**. Next, the cyclization in exo-trig manner provides dithiolane **4**. Under the reaction conditions **4** could rearrange *via* tautomeric shift of hydrogen to generate **6**. To evaluate if the isomerization of **4** to equilibrium-mixture of **4** and **6** also takes place under acidic conditions, the $CDCl_3$ solution of pure **4** was treated with catalytic quantity of CF_3COOH and the isomerization was monitored by ^{1}H NMR spectroscopy. Indeed, the equilibration of **4** to **6** took place at 55°C in 24 hr to provide a mixture of **4** and **6** in the ratio of 55:45. At room temperature the equilibration was slow.

In conclusion, it is shown that the reaction of salt **1** with propargyl bromide provides dithiolane **4** and the dithiole **6**. Both **4** and **6** were obtained as *E* and *Z* isomeric mixtures. The dithiolane **4** and the dithiole **6** were found to equilibrate in the presence of strong acid at 55°C.



4 *E* **4** *Z*

Figure 1



1 **7** **6** **4**

Scheme III

Experimental Section

The TLC (Acme Chemicals or Silica gel GF E Merck) technique was used to monitor the progress of the reactions. Iodine vapors were used to visualize of the spots in the developed TLC plates. Column purifications of the crude products were performed on silica gel 100-200 mesh using hexane : ethyl acetate solvent mixtures ranging from 95:5 to 70:30. Melting points were noted using a Gallenkemp melting point apparatus. The IR spectra were recorded as KBr solutions using ABB Bomem MB104 FT IR spectrometer. ^{1}H and ^{13}C NMR spectra were recorded as solutions in $CDCl_3$ solvent using Bruker 300 MHz NMR spectrometer. Dipotassium 2-nitro-1,1-ethylenedithiolate **1** was prepared according to the literature procedure[2d].

4-Methyl-3-nitro-2-(2-propynylsulfanyl)thiophene 5 and 4-methyl-2-[(*E*)-1-nitromethylidene]-1,3-dithiole 6

To a well-stirred and cooled (0°C) solution of dipotassium salt of 2-nitro-1,1-ethylenedithiolate **1** (1 g, 4.7 mmole) in 20 mL of 66% aqueous methanol, propargyl bromide (600 mg, 5 mmole) was added drop-wise during 10 min. The stirring was continued at room temperature for 8 hr for completion of the reaction (TLC). The reaction-mixture was diluted with of ice-cold water (50 mL) and the product was extracted by dichloromethane (25 mL × 2). The organic layer was washed with water (25 mL × 2) brine (25 mL) then dried over anhydrous Na_2SO_4. Evaporation of solvent under reduced pressure resulted in the crude product having pungent smell. The crude product was purified by column chromatography using silica gel (100 – 200 mesh) and eluting with hexane:ethyl acetate (95:5 to 70:30) solvent mixtures. The fractions with the desired products were pooled and the solvent removed to furnish dithiolane **4** and dithiole **6**. The solid products were recrystallized with dichloromethane and hexanes solvent mixtures.

4-Methylene-2-[(*E, Z*)-1-nitromethylidene]-1,3-dithiolane 4

Obtained as a unseparable mixture of *E* and *Z* isomers present in the ratio of 55:45. The NMR spectra displayed separate set of signals for each isomer as given below. MF = $C_5H_5O_2NS_2$, R_f = 0.62 (90:10 hexane:ethyl acetate), Yield = 25%. IR (KBr): 3051, 2866, 1526, 1312, 926 cm^{-1}. *E*-isomer: ^{1}H NMR

(300 MHz, $CDCl_3$): δ 4.12 (t, *J* = 1.8 Hz, 2H, CH_2), 5.14 (q, *J* = 1.8 Hz, 1H, =CH), 5.53 (q, *J* = 1.8 Hz, 1H, =CH), 7.49 (s, 1H, =CH); ^{13}C NMR (75 MHz, $CDCl_3$): δ 40.2 (CH_2), 112.95 (CH_2), 123.9 (CH), 143.4 (C), 165.3 (C); *Z*-isomer: ^{1}H NMR (300 MHz, $CDCl_3$): δ 4.14 (t, *J* = 1.8 Hz, 2H, CH_2), 5.38 (q, *J* = 1.8 Hz, 1H, =CH), 5.53 (q, *J* = 1.8 Hz, 1H, =CH), 7.48 (s, 1H, =CH); ^{13}C NMR (75 MHz, $CDCl_3$): δ 42.8 (CH_2), 112.9 (CH_2), 123.9 (CH), 139.6 (C), 166.01 (C); EIMS: M^+ 175 (100), 104 (35), 89 (45), 71 (32), 45 (40); HRMS Calcd for $C_5H_5O_2NS_2$: 174.9262. Found: 174.9267.

4-Methyl-2-[(*E*)-1-nitromethylidene]-1,3-dithiole 6

Obtained as a unseparable mixture of *E* and *Z* isomers in the ratio of 55:45. The NMR spectra displayed separate set of signals for each isomer as given below. MF = $C_5H_5O_2NS_2$, R_f = 0.37 (90:10 hexane:ethyl acetate), Yield = 22%. IR (KBr): 3067, 2866, 1546, 1332, 921 cm^{-1}; *E*-isomer: ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.36 (d, *J* = 1.2 Hz, 3H, CH_3), 6.60 (m, 1H, =CH), 7.70 (s, 1H, =CH); ^{13}C NMR (75 MHz, $CDCl_3$): δ 15.5 (CH_3), 114.8 (CH), 119.8 (CH), 134.8 (C), 167.5 (C); *Z*-isomer: ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.38 (d, *J* = 1.2 Hz, 3H, CH_3), 6.60 (m, 1H, =CH), 7.72 (d, *J* = 1.2 Hz, 1H, =CH); ^{13}C NMR (75 MHz, $CDCl_3$): δ 15.5 (CH_3), 119.2 (CH), 119.8 (CH), 137.1 (C), 167.6 (C); EIMS: M^+ 175 (100), 145 (35%), 89 (42), 71 (21), 45 (40). HRMS Calcd for $C_5H_5O_2NS_2$: 174.9262. Found: 174.9265.

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