Preparation of 1,3-Dithiolan-2-ylium Tetrafluoroborate and Its Reaction with Enol Trimethylsilyl Ethers

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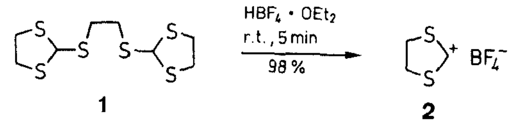
Received 8 July 1991; revised 2 August 1991

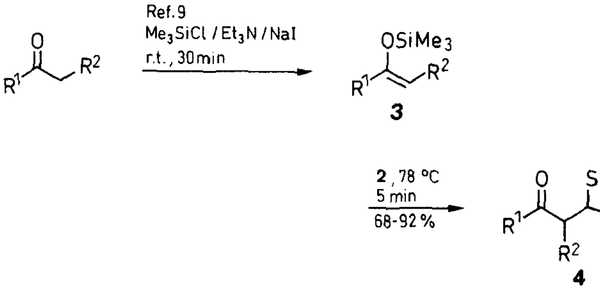
1,3-Dithiolan-2-ylium tetrafluoroborate (**2**) has been prepared and is found to be a good C-alkylating agent for the β-1,3-dithiolaniation of carbonyl compounds through their enol trimethylsilyl ethers.

2-Chloro-1,3-dithiane,[1] and 2-ethoxy-1,3-dithiolane[2] have been successfully employed as formyl cation equivalents. Thus, morpholino enamines react with 2-chloro-1,3-dithiane directly at ambient temperature to provide the selectively protected β-dicarbonyl compounds in moderate yields.[1] Similarly, 2-ethoxy-1,3-dithiolane readily alkylates the enol silyl ethers in good yields in the presence of Lewis acids such as zinc chloride, boron trifluoride - diethyl ether complex and titanium tetrachloride.[2] The electrophile responsible for these reactions is not well defined, but may involve the partially dissociated Lewis acid complex with the reagent, the extent of dissociation being determined by the substrate reactivity. Paterson and Price[3] alkylated regioselectively several enol silyl ethers using the preformed six-membered ring 1,3-dithienium tetrafluoroborate.[4] Such alkylations involving the lower homolog, 1,3-dithiolan-2-ylium cation salt **2** is not known. The only isolated cation of this system is the 1,3-dithiolan-2-ylium perchlorate.[5] Presumably because of the potentially explosive nature of perchlorates,[6] synthetic applications of this cation were not explored.[7] Now we have synthesized stable five-membered ring 1,3-dithiolan-2-ylium tetrafluoroborate (**2**) and explored the synthetic potential of this reactive reagent with enol silyl ethers.



Reaction of the bis-1,3-dithiolane **1** which is readily prepared from 1,2-ethanedithiol and triethylorthoformate[8] with tetrafluoroboric acid - diethyl ether complex in anhydrous chloroform solution resulted in instantaneous precipitation of 1,3-dithiolan-2-ylium tetrafluoroborate (**2**) (isolated in 98 % yield). Although the salt **2** proved to be hygroscopic, it could be handled conveniently under an inert atmosphere, and is stable for several days at room temperature under nitrogen atmosphere. The solubility of this salt is rather limited, being practically insoluble in the usual solvents like diethyl ether, dichloromethane, and chloroform. However, it is soluble in nitromethane, and the solutions can be kept at 0 °C for several days without any appreciable loss of activity.

Next, we explored the reactivity of salt **2** with enol silyl ethers. A heterogeneous reaction involving **2** and cyclohexanone enol trimethylsilyl ether in dichloromethane, although exothermic initally, did not proceed to any significant completion. However, a nitromethane solution of this salt reacted with several enol trimethylsilyl ethers, including cyclohexanone enol trimethylsilyl ether even at − 78 °C, very rapidly and provided the β-carbonyl 1,3-dithiolanes in good to excellent yields (Table 1).



Thus, virtually any enolizable carbonyl compound can be converted to the corresponding β-dithiolanylium derivative through this procedure. The required enol silyl ethers were conveniently prepared using Duboudin's procedure.[9]

Our results are comparable to Hatanaka's procedure,[2] wherein he used 2-ethoxy-1,3-dithiolane to alkylate enol silyl ethers. However, the preparation[10] of 2-ethoxy-1,3-dithiolane from 1,2-ethanedithiol is not as efficient (30 % isolated yield). In conclusion the easy, high yield isolation of 1,3-dithiolan-2-ylium tetrafluoroborate, a formyl cation equivalent, should provide impetus for further studies with other nucleophiles such as phenols, amines and indoles.

Starting carbonyl compounds were purchased from Aldrich and used as received. Silyl enol ethers were prepared following the literature method.[9] 2,2′-[1,2-Ethanediylbis(thio)]bis-1,3-dithiolane (**1**) was synthesized following Houghton and Dunlop's procedure.[8] All solvents used in this study were dried and distilled prior to use. NMR spectra were obtained on a Varian Associates Model VXR-200 spectrometer equipped with a broad-band switchable probe. GC-Mass spectrometric studies were carried out on a Finnigan-Mat Incos-50 spectrometer.

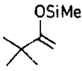
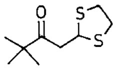
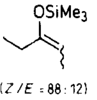
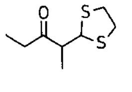
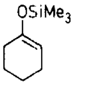
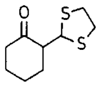
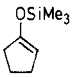
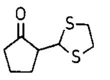
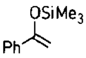
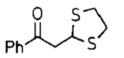
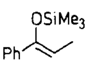
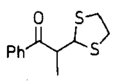
Dithiolanium Tetrafluoroborate (2):

The bis-1,3-dithiolane **1**[8] (15 g, 0.049 mol) dissolved in anhydrous $CHCl_3$ (100 mL) was placed in a 250-mL round-bottom flask equipped with a magnetic stirrer, a N_2 inlet and serum cap. $HBF_4 \cdot OEt_2$ (24.1 g, 0.15 mol) was added to the contents through a hypodermic syringe. The reaction was instantaneous, and the 1,3-dithiolan-2-ylium tetrafluoroborate (**2**) appeared as a white precipitate. The precipitate was filtered under N_2 atmosphere, washed with copious amounts of $CHCl_3$, Et_2O, and dried under N_2. The salt (14.9 g, 98 %) was stored in a flask under N_2 atmosphere. The salt was very hygroscopic, but is stable under N_2 atmosphere for several days.

^1H NMR (CD_3NO_2/TMS): δ = 4.46 (s, 4 H, CH_2), 11.3 (s, 1 H, CH).

^{13}C NMR (CD_3NO_2/TMS): δ = 45.9 (t, J = 151 Hz, CH_2), 221.1 (d, J = 194 Hz, CH).

Table. 1,3-Dithiolaniation of Enol Trimethylsilyl Ethers

Reactant	Product[a]	Yield[b] (%)	^1H NMR ($CDCl_3$/TMS) δ, J (Hz)	^{13}C NMR ($CDCl_3$/TMS) δ	MS m/z (%)
 **3a**	 **4a**	81	1.03 (s, 9H, t-C_4H_9), 3.0 (d, $J = 7$, 2H, CH_2), 3.14 (s, 4H, SCH_2CH_2S), 4.75 (t, $J = 7$, 1H, SCHS)	26.1 (CH_3), 34.0 ($\underline{C}CH_3$), 38.3 (SCH_2CH_2S), 46.96 (CH_2), 47.2 (SCHS), 213.1 (C=O)	204 (M^+, 12.6), 147 (50.0), 119 (7.4), 105 (66.6), 91 (10.0), 57 (100)
 (Z/E = 88:12) **3b**	 **4b**	73	0.96 (t, $J = 7.2$, 3H, CH_3CH_2), 1.13 (d, $J = 7$, 3H, CH_3CH), 2.31–2.49 (m, 2H, CH_2), 2.66– 2.75 (m, 1H, CH), 3.09 (s, 4H, SCH_2CH_2S), 4.56 (d, $J = 9.5$, 1H, SCHS)	7.53 (CH_3), 16.8 (CH_3), 35.7 (CH_2), 38.3, 38.5 (SCH_2CH_2S), 54.7 (SCHS), 54.9 ($\underline{C}HCO$), 213.2 (C=O)	190 (M^+, 8.9), 175 (1.7), 161 (16.4), 133 (4.3), 105 (100), 85 (4.3)
 **3c**	 **4c**	86	1.5–2.1 (m, 6H, CH_2), 2.2–2.4 (m, 2H, CH_2CO), 2.55–2.7 (m, 1H, CH), 3.07 (s, 4H, SCH_2CH_2S), 4.66 (d, $J = 7.9$, 1H, SCHS)	25.1 (CH_2), 28.2 (CH_2), 32.3 (CH_2), 38.4, 38.7 (SCH_2CH_2S), 42.3 ($\underline{C}H_2CO$), 52.1 (SCHS), 59.0 (CH), 211.3 (C=O)	202 (M^+, 32.9), 141 (5.7), 105 (100), 103 (6.7), 85 (10.0)
 **3d**	 **4d**	69	1.8–2.4 (m, 6H, CH_2), 2.5–2.7 (m, 1H, CH), 3.16 (s, 4H, SCH_2CH_2S), 4.90 (d, $J = 4.9$, 1H, SCHS)	20.2 (CH_2), 23.2 (CH_2), 26.3 ($\underline{C}H_2CO$), 38.9, 39.3 (SCH_2CH_2S), 52.0 (SCHS), 55.7 (CH), 217.4 (C=O)	188 (M^+, 19.7), 171 (1.1), 154 (2.6), 127 (4.4), 105 (100)
 **3e**	 **4e**	92	3.27 (s, 4H, SCH_2CH_2S), 3.59 (d, $J = 7$, 2H, CH_2), 5.03 (t, $J = 6.9$, 1H, SCHS), 7.44–7.59 (m, 3H_{arom}, H-3′,4′,5′), 7.96 (d, $J = 7$, 2H_{arom}, H-2′,6′)	38.6 (SCH_2CH_2S), 47.3 (SCHS), 48.97 (CH_2), 128.1 (C_{arom}, C-3′,5′), 128.7 (C_{arom}, C-2′,6′), 133.4 (C_{arom}, C-4′), 136.3 (C_{arom}, C-1′), 197.4 (C=O)	224 (M^+, 26.9), 196 (3.8), 163 (12.9), 120 (20.7), 105 (100)
 **3f**	 **4f**	68	1.36 (d, $J = 7.1$, 3H, CH_3), 3.19–3.23 (m, 4H, SCH_2CH_2S), 3.66– 3.76 (m, 1H, CH), 4.88 (d, $J = 9.5$, 1H, SCHS), 7.47–7.58 (3H_{arom}, H-3′,4′,5′), 7.96 (d, $J = 9.5$, 2H_{arom}, H-2′,6′)	18.3 (CH_3), 38.4, 38.6 (SCH_2CH_2S), 50.3 (SCHS), 55.5 (CH), 128.5 (C_{arom}, C-3′,5′), 128.7 (C_{arom}, C-2′,6′), 133.3 (C_{arom}, C-4′), 136.0 (C_{arom}, C-1′), 202.6 (C=O)	238 (M^+, 38.8), 223 (9.6), 177 (7.1), 133 (12.8), 105 (100)

[a] All products are known in the literature and were obtained as oils.

[b] Yield of isolated pure product.

1-(1,3-Dithiolan-2-yl)-3,3-dimethyl-2-butanone (4a); Typical Procedure):

2-Trimethylsiloxy-3,3-dimethyl-1-butene (**3a**; 1 g, 5.8 mmol) dissolved in anhydrous dichloromethane (10 mL) was placed in a 50 mL 3-necked round-bottom flask, equipped with a magnetic stirrer, N_2 inlet, and serum cap, and was cooled at – 78 °C in a dry ice–acetone bath. 1,3-Dithiolan-2-ylium tetrafluoroborate (**2**; 6.94 mL of a 1 M solution in $MeNO_2$) was then added to the contents through a syringe in 3 min at – 78 °C, stirred for 5 min, and was warmed to r.t. The contents were then poured into water (100 mL), and were extracted with CH_2Cl_2 (2 × 20 mL). The combined organic layers were washed with 10% $NaHCO_3$, dried ($MgSO_4$), and the solvents were removed on a rotary evaporator under vacuum. The product was purified by flash chromatography on a silica gel column eluting with 50% pentane in CH_2Cl_2. Compound **4a** was obtained as a colorless liquid; yield: 0.95 g (81 %) (Table).

Support of our work by Loker Hydrocarbon Research Institute is gratefully acknowledged. Prof. G.A. Olah is thanked for his kind support and encouragement.

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The corresponding methoxy analog has been prepared in 37 and 46% isolated yields starting from **1** following two different procedures (see Ref. 8).