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Regiospecific iodocyclization of *S*-allyl dithiocarbamates: synthesis of 2-imino-1,3-dithiolane and 2-iminium-1,3-dithiolane derivatives

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ABSTRACT

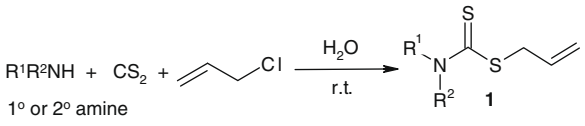
4-Alkyl-2-imino-1,3-dithiolanes and 4-alkyl-2-iminium-1,3-dithiolanes were prepared in excellent yields with complete regiospecificity under mild conditions by the iodocyclization of *S*-allyl dithiocarbamates. Dehydrohalogenation of the 4-alkyl-2-imino-1,3-dithiolanes gave 4-alkylidene-2-imino-1,3-dithiolanes in excellent yields.

The synthesis of compounds that protect crop plants from the action of herbicides without reducing the herbicidal effectiveness against weeds would be beneficial. It is well documented that 2-imino-1,3-dithiolane and 2-iminium-1,3-dithiolane derivatives are safe agents.[1] A variety of methods are available in the literature for the preparation of these biologically active compounds. Imino dithiolanes can be prepared from the reaction of *vic*-dithiocyanates in refluxing hydrochloric acid,[2] by the reaction of *vic*-dithiols and cyanogen chloride,[3] acid-catalyzed cyclization of propargyl, allylic, or β-hydroxy alkyl esters of dithiocarbamic acids,[4] and by photolysis of chlorinated *S*-allyl dithiocarbamate compounds.[1a,b] Unfortunately, difficulties are encountered due to the physical nature of the starting materials. The drawbacks of using *vic*-dithiols, the toxicity of cyanogen chloride, the corrosive character of mineral acids, and low yield of products are some limitations of these processes.

Iodocyclization of an unsaturated C–C bond with a wide variety of nucleophiles, including N, O, Se, and S, has been studied[5] extensively and it has become a powerful tool for the construction of various heterocycles.

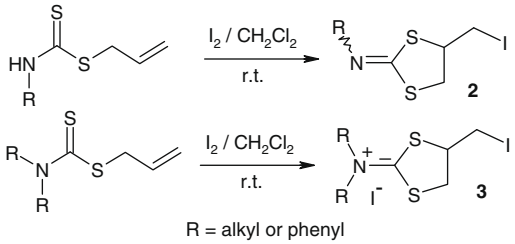
In previous work, we reported a simple, one-pot, and green method for the synthesis of dithiocarbamates from amines, CS_2, and different nucleophile acceptors, such as alkyl halides, activated olefins, and epoxides under solvent-free and aqueous conditions.[6] The starting *S*-allyl dithiocarbamate can be prepared from the reaction of an amine, carbon disulfide, and allyl chloride in water as outlined in Scheme 1.

In continuation of our interest in finding new and efficient methods for the synthesis of novel dithiocarbamate derivatives and the use of these intermediates in organic transformations, we report the iodocyclization of *S*-allyl dithiocarbamates using I_2 or NIS as the electrophile to give the corresponding 4-alkyl-2-imino-1,3-dithiolanes and 4-alkyl-2-iminium-1,3-dithiolanes in excellent yields (Scheme 2).



Scheme 1. One-pot synthesis of allyl dithiocarbamates in water.

After synthesizing the starting dithiocarbamates, we optimized the reaction conditions for the key iodocyclization by changing the number of equivalents of I_2, the solvent, and the temperature for the reaction of dithiocarbamate **1** with I_2. Next, the reactions of different *S*-allyl dithiocarbamates with iodine were investigated under our optimized conditions. The results are summarized in Tables 1 and 2.[7,8] The reaction of *S*-allyl dithiocarbamates based on primary amines was strongly influenced by the substituent present on the allyl group. *S*-Allyl dithiocarbamates gave excellent yields of 2-imino-1,3 dithiolanes (Table 1, entries 1–6). The reaction of (*Z*)- or (*E*)-*S*-(2-butenyl)dithiocarbamate with iodine gave



Scheme 2. Synthesis of 2-imino and 2-iminium-1,3-dithiolanes from dithiocarbamates.

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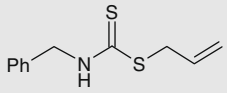
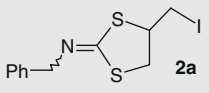
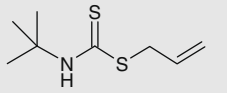
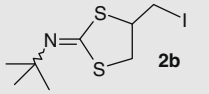
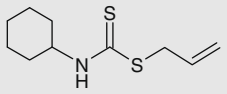
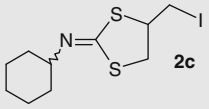
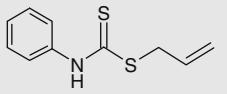
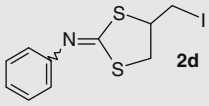
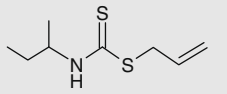
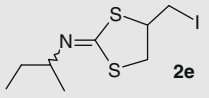
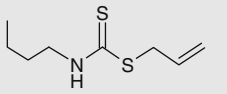
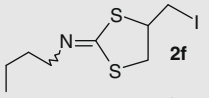
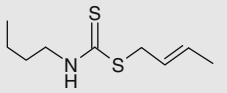
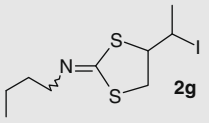
Table 1
Synthesis of 2-imino-1,3-dithiolanes from dithiocarbamates

Entry	Dithiocarbamate	Product	Yield[a,b] (%)
1		 **2a**	95
2		 **2b**	100
3		 **2c**	100
4		 **2d**	90
5		 **2e**	95
6		 **2f**	90
7		 **2g**	<10[c]

[a] Reaction conditions: dithiocarbamate (1 mmol), I_2 (1.5 mmol), rt, and CH_2Cl_2 (5 mL).
[b] Isolated yield.
[c] NIS as the electrophile.

a very low yield of product (entry 7). Even the use of NIS failed to deliver the desired product **2g** in an acceptable yield. The reaction shows complete regiospecificity for the five-membered ring. The ^1H and ^{13}C NMR spectra show 1:1 mixtures of *E/Z* stereoisomers of 2-imino-1,3 dithiolanes, **2**.

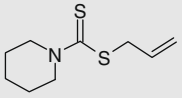
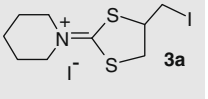
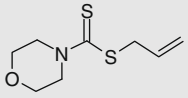
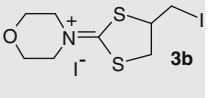
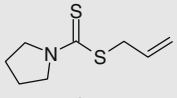
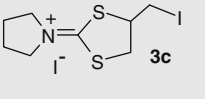
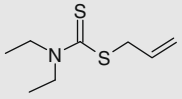
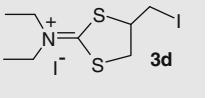
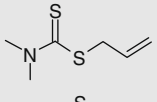
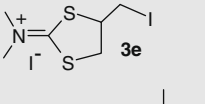
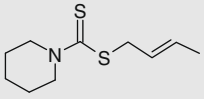
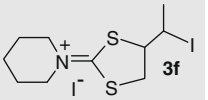
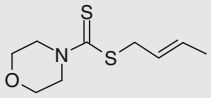
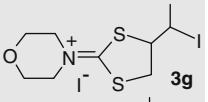
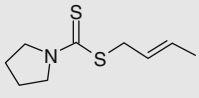
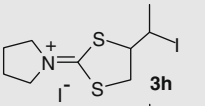
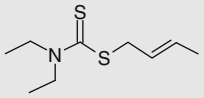
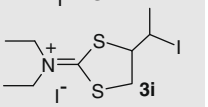
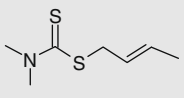
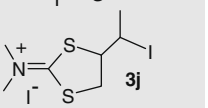
The reaction of *S*-allyldithiocarbamate prepared from secondary amines with I_2 was not influenced by the substitution on the γ-carbon and gave excellent yields of the five-membered 2-iminium-1,3-dithiolanes **3** with complete regiospecificity, (Scheme 2 and Table 2). The structures of the products were elucidated from their IR, ^1H, and ^{13}C NMR spectra, and by elemental analysis.

The presence of iodine in the products allowed further structural elaboration via dehydrohalogenation using DBU.[9] For example, when compound **2a** was treated with DBU, the corresponding 4-methylidene-2-imino-1,3-dithiolane, **4**, was obtained in excellent yield (Scheme 3).[10]

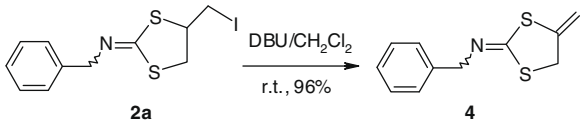
According to the literature,[5b,11] the CH_2I group in five-membered compounds is observed at 4–8 ppm in ^{13}C NMR, while the –CHI group in six-membered compounds appears above 14 ppm. The ^{13}C NMR spectra of the products given in Tables 1 and 2 are completely in agreement with the formation of five-membered rings. Also, ^1H NMR spectra indicated that dehydrohalogenation resulted in the formation of an exocyclic double bond and no endocyclic double bond. The DEPT spectrum showed three peaks for the CH_2 groups in compound **4**, which is in agreement with the five-membered ring. The NMR spectra (at 298 K) showed the presence of an *E/Z* (1:1) mixture of compound **4** due to the C=N double bond. Only one isomer was observed at temperatures above 320 K because of the rapid interconversion of *E* and *Z* isomers.

In conclusion, we have reported a new route for the iodocyclization reaction of *S*-allyl dithiocarbamates to give five-membered

Table 2
Synthesis of 2-iminium-1,3-dithiolanes from dithiocarbamates

Entry	Dithiocarbamate	Product[a,a,b]
1		 **3a**
2		 **3b**
3		 **3c**
4		 **3d**
5		 **3e**
6		 **3f**
7		 **3g**
8		 **3h**
9		 **3i**
10		 **3j**

[a] Reaction conditions: dithiocarbamate (1 mmol), I_2 (1.5 mmol), rt, and CH_2Cl_2 (5 mL).
[b] Isolated yield was quantitative in each case.



Scheme 3. Synthesis of 2-imino-4-methylidene-1,3-dithiolane by dehydrohalogenation.

2-imino- and 2-iminium-1,3-dithiolane derivatives with complete regiospecificity. Treatment of 2-imino-1,3-dithiolane **2a** with DBU led to the formation of a 2-imino-4-methylidene-1,3-dithiolane. The procedure is simple and gives excellent yields of potentially biologically significant products.

Acknowledgments

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7. *General procedure for the synthesis of 2-imino-1,3-dithiolanes:* In a round-bottomed flask equipped with a magnetic stirrer, *S*-allyl dithiocarbamate (1 mmol), I_2 (1.5 mmol), and CH_2Cl_2 (5 mL) were added. The mixture was stirred at room temperature until conversion of the starting material was complete (TLC). The reaction mixture was diluted with CH_2Cl_2 and was washed with aqueous $Na_2S_2O_3$ solution. (10 mL, 1 M). The organic phase was washed with brine, dried over Na_2SO_4, filtered, and evaporated in vacuo. In most cases, pure products were obtained. If needed, further purification was carried out by column chromatography on silica gel, using a 2:8 ratio of ethyl acetate and petroleum ether as eluent. Selected spectroscopic data: *E/Z* (1:1) mixture of **2c**: ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 1.25–1.35 (m, 10H), 1.48 (m, 2H), 1.78 (m, 8H), 3.15 (m, 2H), 3.45–3.69 (m, 6H), 3.78 (m, 2H), 4.08 (m, 1H) and 4.29 (m, 1H). ^{13}C NMR (125.7 MHz, $CDCl_3$): δ (ppm) 6.5 and 7.0, 25.0 and 25.1, 25.9 and 26.0, 33.2 and 33.3, 39.0 and 41.8, 50.3 and 53.7, 69.1 and 69.2, 164.5 and 164.6; *E/Z* (1:1) mixture of **2d:** ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 3.44–3.59 (m, 2H), 3.60–3.81 (m, 6H), 4.15 (m, 1H), 4.21 (m, 1H), 6.92–6.97 (m, 4H), 7.14 (m, 2H), 7.33–7.37 (m, 4H). ^{13}C NMR (125.7 MHz, $CDCl_3$): δ (ppm) 6.1 and 6.5, 39.5 and 42.1, 50.8 and 54.0, 120.5 and 120.6, 125.2 and 125.3, 129.4 and 129.5, 152.0 and 152.1, 167.2 and 167.8.
8. *General procedure for the synthesis of 2-iminium-1,3-dithiolanes:* In a round-bottomed flask equipped with a magnetic stirrer, were added *S*-allyldithiocarbamate (1 mmol), I_2 (1.5 mmol), and CH_2Cl_2 (10 mL). The mixture was stirred for 4 h at room temperature. After completion of the reaction, the solvent was evaporated in vacuo and the residue was triturated with diethyl ether to afford the products as yellow-brown precipitates. Filtration and washing of the precipitate with diethyl ether (three times) gave the pure products. Selected spectroscopic data: **3b**: IR (KBr) 1632 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 3.85–3.91 (m, 2H), 4.03 (m, 4H), 4.18 (m, 4H), 4.39 (m, 2H), 5.10 (m, 1H). ^{13}C NMR (125.7 MHz, $CDCl_3$): δ (ppm) 3.9, 44.5, 56.9, 57.2, 58.3, 65.4, 65.4, 196.2; Anal. Calcd for $C_8H_{13}I_2NOS_2$: C, 21.00; H, 2.84; N, 3.06. Found: C, 20.7; H, 2.49; N, 3.10. **3e:** IR (KBr) 1626 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 3.79 (s, 6H), 3.84–3.93 (m, 2H), 4.34 (dd, 1H, *J*= 12.78, 4.28 Hz), 4.41 (dd, 1H, *J*= 12.78, 5.17 Hz), 5.09 (m, 1H); ^{13}C NMR (125.7 MHz, $CDCl_3$): δ (ppm) 4.7, 45.5, 48.8, 49.1, 59.4, 194.2; Anal. Calcd for $C_6H_{11}I_2NS_2$: C, 17.35; H, 2.65; N, 3.37. Found: C, 17.16; H, 2.42; N, 3.41. **3f:** IR (KBr) 1630 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 1.88 (m, 2H), 2.02 (m, 4H), 2.09 (d, 3H, *J*= 6.76 Hz), 3.89–3.95 (m, 2H), 4.15–4.18 (m, 4H), 4.37 (dd, 1H, *J*= 12.75, 4.36 Hz), 4.42 (dd, 1H, *J*=12.75, 5.27 Hz). ^{13}C NMR (125.7 MHz, $CDCl_3$): δ (ppm) 14.5, 22.4, 25.9, 26.0, 26.1, 48.8, 58.3, 59.4, 68.3, 190.6. Anal. Calcd for $C_{10}H_{17}I_2NS_2$: C, 25.60; H, 3.62; N, 2.98. Found: C, 25.87; H, 3.52; N, 3.09.
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10. *Synthesis of compound 4 by dehydrohalogenation of* **2a**: DBU (1.5 mmol) was added to a solution of **2a** (1 mmol) in CH_2Cl_2 (5 mL), and the resulting mixture was stirred for 1 h at rt. The product was extracted with CH_2Cl_2 (2 $\times$ 10 mL). The combined organic layers were washed with water and brine and were dried over sodium sulfate, filtered, and evaporated in vacuo. The residue was pure enough to give satisfactory spectroscopic data. *E/Z* (1:1) mixture of **4**: IR (KBr) 1654 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 4.03 (s, 2H) and 4.20 (s, 2H), 4.50 (s, 2H) and 4.53 (s, 2H), 5.25 (s, 2H) and 5.39 (s, 1H) and 5.41 (s, 1H), 7.15–7.32 (m, 10H).^{13}C NMR (125.7 MHz, $CDCl_3$): δ (ppm) 39.8 and 43.0, 61.7 and 62.8, 110.2 and 111.1, 127.4 and 127.5, 128.1 and 128.2, 128.8 and 128.9, 138.8 and 139.0, 141.7 and 143.5, 164.3 and 165.3.
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