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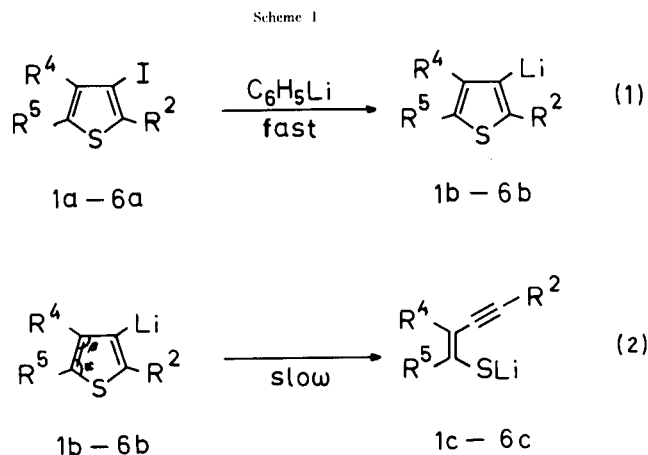
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The ring-opening rates of some substituted 3-thienyllithium derivatives have been measured and the activation parameters calculated for the ring-opening of 2,5-dimethyl-3-thienyllithium. Steric and electronic effects are discussed.

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It was previously shown that 2,5-dimethyl-3-selenienyllithium ring-opened much faster than the corresponding 3-thienyllithium derivative (1). Whereas the selenienyllithium derivative ring-opened to give lithium 2-hexen-4-yn-2-selenolate completely in less than 10 minutes at -70° (in ether), the 3-thienyllithium derivative did not ring-open at all even after 6 hours under the same conditions. The latter substance had to be heated to about -30° in order to give the ring-opening product, lithium 2-hexen-4-yn-2-thiolate (1c), at a convenient rate. It was also shown that 3-thienyllithium ring-opened much slower than 2,5-dimethyl-3-thienyllithium (2). This made it of interest to examine the substituent effects on the reaction (RO-I reaction (6)). For this reason kinetic measurements were performed with 2,5-dimethyl-3-thienyllithium (1b), 2-*t*-butyl-5-methyl-3-thienyllithium (2b), 5-methyl-2-phenyl-3-thienyllithium (3b), 2-methyl-5-phenyl-3-thienyllithium (4b) and 5-*t*-butyl-2-methyl-3-thienyllithium (5b) (Scheme 1). The results are shown in Table I and it is seen that the difference in the rates of formation of the enynethiolates 1c-5c spans over a relative range of approximately 1-100. With the assumption that the rate of formation of 1c-5c parallels the rate of ring-opening of the corresponding thienyllithium derivatives 1b-5b (7) the following order of reactivity is obtained: $1b > 2b > 3b > 4b > 5b$.

It is then somewhat surprising to find that the formation of lithium 6,6-dimethyl-2-hepten-4-yn-2-thiolate (2c) is slower than that of 1c. One would expect 2b to give 2c faster than 1b gives 1c if the inductive effect of the substituents were of any importance, since compound 1b ring-opens much faster than 3-thienyllithium and the corresponding 3-selenienyllithium derivatives behave similarly (1,2). Moreover, 3-thienyllithium and 3-selenienyllithium derivatives with strong -I substituents, such as 2,5-dichloro-3-thienyllithium and 2,5-dichloro-3-selenienyllithium, are more stable than those with +I substituents, such as the 2,5-dimethyl-3-lithio derivatives (8). In the selenophene series, however, the situation is complicated by the RO-II type reaction (6) of 3-selenienyllithium derivatives with -I substituents (9). The actual result indicates that the bulky *t*-butyl group exerts some steric hindrance for a lithium ion (or atom) to reach the sulfur atom. A similar reasoning can be applied on the conversion 3b \rightarrow 3c, but



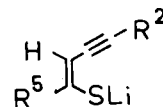
- 1 $R^2, R^5 = \text{CH}_3, R^4 = \text{H}$
- 2 $R^2 = \text{C}(\text{CH}_3)_3, R^5 = \text{CH}_3, R^4 = \text{H}$
- 3 $R^2 = \text{C}_6\text{H}_5, R^5 = \text{CH}_3, R^4 = \text{H}$
- 4 $R^2 = \text{CH}_3, R^5 = \text{C}_6\text{H}_5, R^4 = \text{H}$
- 5 $R^2 = \text{CH}_3, R^5 = \text{C}(\text{CH}_3)_3, R^4 = \text{H}$
- 6 $R^2, R^5 = \text{CH}_3, R^4 = \text{C}_6\text{H}_5$

here the -I effect of the phenyl group may also be involved, slowing down the reaction.

It is easier to explain why lithium 1-phenyl-1-penten-3-yn-1-thiolate (4c) and lithium 2,2-dimethyl-3-hepten-5-yn-3-thiolate (5c) are formed more slowly than 1b. In these cases, a bulky substituent is placed at the "reverse side" of the double bond to be formed. As the ring-opening proceeds the close approach of the 4-proton, the 5-substituent

Table I

Pseudo First Order Rate Constants for the Formation of 1c-5c from 1b-5b at -0.5°C in Ether



Pseudo first order rate constants $k \cdot 10^3 (\text{min}^{-1})$ (5)

1c	$R^2 = R^5 = \text{CH}_3$	104 \pm 1
2c	$R^2 = \text{C}(\text{CH}_3)_3, R^5 = \text{CH}_3$	36.9 \pm 0.6
3c	$R^2 = \text{C}_6\text{H}_5, R^5 = \text{CH}_3$	13.7 \pm 0.2
4c	$R^2 = \text{CH}_3, R^5 = \text{C}_6\text{H}_5$	3.22 \pm 0.07
5c	$R^2 = \text{CH}_3, R^5 = \text{C}(\text{CH}_3)_3$	1.24 \pm 0.03

Table II

Pseudo First Order Rate Constants and Activation Parameters for the Formation of **1c**

Temp K (°C)	$k \cdot 10^3$ (min ⁻¹) (5)	ΔH^* (kJ/mole)	ΔS^* (J/mole, deg)	ΔG^* (kJ/mole)
272.7 (-0.5)	104 ± 1	66.0 ± 3.7	-54 ± 14	80.6 ± 7.5
264.7 (-8.5)	57.3 ± 0.8			
256.2 (-17.0)	16.5 ± 0.2			
255.2 (-18.0)	13.6 ± 0.3			
244.2 (-29.0)	3.5 ± 0.1			

and the sulfur atom (due to the increase of the inner α -angle from 111° to 120° and the inner β -angle from 114° to 120°, *cf.* Scheme 1) will result in sterical crowding. This becomes more pronounced the bigger the 4- and 5-substituents are. It has *e.g.* been shown that atropisomerism arises in crowded styrenes (10). It was also noticed that the ethyl thioether related to lithium 3-phenyl-2-hexen-4-yn-2-thiolate (**6c**) was formed relatively slowly from 2,5-dimethyl-4-phenyl-3-thienyllithium (**6b**) in preparative work (12d). This could partly be due to slow ring-opening reaction but also to a slow alkylation at sulfur of **6c** by ethyl bromide, since if approaching planarity, **6c** should be less reactive due to some delocalisation of the negative charge.

The activation parameters of the ring-opening of 2,5-dimethyl-3-thienyllithium are shown in Table II and it is obvious that the enthalpy of activation is the main factor determining the free energy of activation. However, the entropy of activation is clearly negative and relatively large, which is hardly compatible with the opening of a ring. One would expect a positive entropy of activation since more degrees of freedom are gained in going from a cyclic to a non-cyclic structure. However, since the product (enynethiolate **1c**) probably has a more ionic character than the 3-thienyllithium derivative **1b**, it is quite possible that the negative entropy of activation is due to reorganisation of the solvent shell.

EXPERIMENTAL

Samples of 2,5-dimethyl-3-iodothiophene (**1a**), 2-*t*-butyl-3-iodo-5-methylthiophene (**2a**), 3-iodo-5-methyl-2-phenylthiophene (**3a**), 3-iodo-2-methyl-5-phenylthiophene (**4a**) and 5-*t*-butyl-3-iodo-2-methylthiophene (**5a**) (12) (0.4 mmole) were placed in nmr tubes, which were sealed with plastic caps and cooled to -70° in ethanol/dry ice. An excess of 1.0 *M* ethereal phenyllithium (0.50 ml.) was then injected with a syringe. The tubes were sealed off with a glass blower's torch and stored at -70° until just before the measurements. At this point the actual tube was heated to -30° (in the cases of **1a** and **2a**) (3) or to +20° (in the cases of **3a-5a**) (3) and turned upside down a couple of times in order to mix the reagents. The tube was placed in the probe of the nmr spectrometer (11) at a preset temperature (-0.5°). The increasing absorptions of the vinyl protons of the enyne thiolates **1c-5c** were then integrated at different times to give the integral values

I_g . The final integral values (complete reactions) were obtained by heating the tubes to +35° for 30 minutes after the measurements (the reactions were followed to 65% conversion except for **5d**, 35%) and then integrated again to give the integral values $I_{g\text{tot}}$ (4). Least squares treatment of the data to the expression $-\ln(I_{g\text{tot}} - I_g) = k \cdot t + 1$ (first order rate expression with respect to enyne thiolates) gave the rate constants presented in Table I. The activation parameters for the formation of **1c** in ether were obtained by measuring the pseudo first order rate constants at five different temperatures and then applying the Eyring equation ($\ln \frac{k}{T}$ was plotted against $\frac{1}{T}$).

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- (2) S. Gronowitz and T. Frejd, *Int. J. Sulfur Chem.*, **A2**, 165 (1972).
- (3) It was checked by GC that the halogen-metal exchange was complete under these conditions. Thus, there is no interference between reactions 1 and 2 in Scheme 1.
- (4) It is assumed that these conditions are sufficient for completion of the reactions since prolonged heating at +35° (1.5 hour) did not result in any significant increase of the vinyl proton integrals.
- (5) Correlation coefficients are better than 0.99 in all cases. Methodological errors are not accounted for and therefore the presented values should be regarded as preliminary ones.
- (6) The RO-I type reaction (RO for Ring-Opening) is defined as shown in eq. 2 Scheme 1, *i.e.* the ring-opening takes place by introducing an anionic centre in the β -position to the bond to be broken. On the other hand the RO-II type reaction is defined as a direct attack on the hetero atom of the ring by a nucleophile, followed by ring-opening with expulsion of a leaving group in the β -position to the bond in the ring that is cleaved. More examples of different base induced ring-openings of heterocyclic compounds will be given in a forthcoming review article (13).
- (7) As a first approximation it is assumed that possible dimer (oligomer) monomer equilibria of the 3-thienyllithium derivative do not significantly affect the ring-opening reactions.
- (8) S. Gronowitz and T. Frejd, *Acta Chem. Scand.*, **B30**, 439

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(9) T. Frejd, *Chem. Scr.*, **10**, 133 (1976).

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(11) The measurements were performed with a Jeol MH-100 NMR spectrometer equipped with a thermostate unit.

(12) Preparation of **1a**: S. Gronowitz and R. Beselin, *Ark. Kemi*, **21**, 349 (1963); **2a**, **5a**: R. Lantz and A.-B. Hörnfeldt, *Chem. Scr.*, **2**, 9 (1972); and S. Gronowitz and T. Frejd, *Acta Chem. Scand.*, **B30**, 287 (1976); **3a**, **4a**, and **6a**: S. Gronowitz and T. Frejd, *Acta Chem. Scand.*, **B30**, 485 (1976).

(13) S. Gronowitz and T. Frejd, manuscript in preparation.