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On the ring-contraction of 1,4-dithiins to 1,3-dithiole derivatives

Raquel Andreu, Javier Garín,* Jesús Orduna and José M. Royo

Departamento de Química Orgánica, ICMA, Universidad de Zaragoza-CSIC, E-50009 Zaragoza, Spain

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Abstract—The effect of different factors (pK_a of the base, nature of the counterion and dissociation of the ion pairs) on the course of the base-induced rearrangement of 1,4-dithiins to 1,3-dithiole derivatives is discussed. Ab initio calculations account for the driving force of these isomerisations. © 2001 Elsevier Science Ltd. All rights reserved.

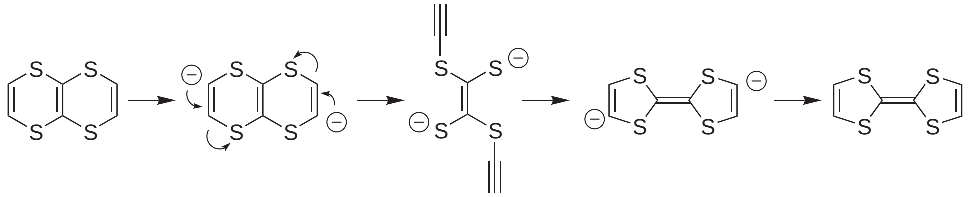
1. Introduction

1,4-Dithiins have attracted much attention because of their structural and electronic properties, their ability to act as electron donors and the wide variety of synthetic transformations they undergo.[1] On the other hand, there are only scant reports in the literature concerning the metallation of these heterocycles and they show widely different results. Thus, while some 1,4-dithiin derivatives can be metallated with LDA,[2] BuLi[3] or even weaker bases, such as KO*t*-Bu,[4] NaOMe[5] or tetrabutylammonium hydroxide,[6] others can be recovered unchanged after treatment with BuLi.[3c,7] Moreover, the metallated species, when generated, can react in several ways, giving rise to substitution,[2,3a,b] ring-opening[3a,c] or ring-contraction (isomerisation)[2,4–6] products.

1,4,5,8-Tetrathianaphthalene (TTN, **1**)[2c,4,8] is a most interesting 1,4-dithiin derivative since its base-induced isomerisation affords tetrathiafulvalene (TTF, **2**) in very good yield (Scheme 1). To that end, both LDA[2] and KO*t*-Bu[4] have been successfully used, whereas NaOEt is unable to carry out the isomerisation.[4] In this paper we report the effect of different factors on the course of this rearrangement and the results obtained with other monocyclic and benzo-fused 1,4-dithiin derivatives. An explanation for the driving force of these rearrangements is also proposed.

2. The ring-contraction of TTN and 1,4-dithiins to TTF and 1,4-dithiafulvenes

The fact that KO*t*-Bu, unlike NaOEt, is able to isomerise **1** to **2** has been ascribed[4] to the higher pK_a of *t*-BuOH compared to EtOH (*ca.* 19 and 16, respectively). This reasonable guess is, nevertheless, an oversimplification as demonstrated by the following experiments (refluxing THF was used in every case): (a) **1** was recovered unchanged after treatment with NaH; (b) treatment of **1** with KOEt led to complete destruction of TTN and afforded a complex mixture from which TTF was isolated in 16% yield; and (c) reaction of **1** with KOH (28 h) led to an 87:13 mixture of **1**/**2** (as determined by ^{1}H NMR) in 64% yield, whereas the use of NaOH led to recovery of the starting material. It is



Scheme 1.

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* Corresponding author. Fax: +34-976-761194; e-mail: jgarin@posta.unizar.es

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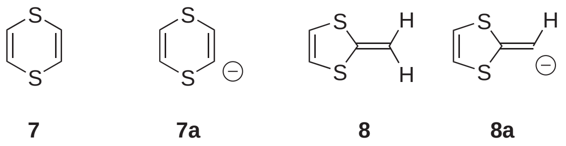
Table 1. Effect of cations and added crowns on the **1** to **2** isomerisation[a]

Base	Crown	Time (h)	Temp (°C)	**1**/**2**[b]
KO*t*-Bu	–	0.5	Reflux	0:100[c]
NaO*t*-Bu	–	1	Reflux	100:0
LiO*t*-Bu	–	7	Reflux	100:0
NaO*t*-Bu	18-c-6	2	25	77:23
NaO*t*-Bu	15-c-5	2	25	80:20
NaO*t*-Bu	15-c-5	14	50	70:30
LiO*t*-Bu	15-c-5	6	Reflux	90:10

[a] Experimental conditions: **1** (1 mmol) and base (5 mmol) in THF (7 ml).
[b] Molar ratio determined by ^{1}H NMR.
[c] 99% yield (lit.[4]).

also noteworthy that **1** did not rearrange to **2** when TBA OH in refluxing MeCN was used, a system which is reported to isomerise some 1,4-dithiin derivatives to 1,4-dithiafulvenes, even at room temperature.[6] Thus, the extent of the isomerisation seems to be not only dependent on the pK_a of the base, but also on the counterion. This factor was ascertained by the lack of reaction of **1** with either NaO*t*-Bu or LiO*t*-Bu in refluxing THF (for 1 and 7 h, respectively). These bases with smaller cations form larger aggregates than those with larger cations (such as K^+) and the enhanced dissociation of the ion pairs in the latter case leads to an increase of the reactivity of the base.[9] This point was further confirmed by addition of crown ethers to the reaction medium; some representative results are collected in Table 1 and show that complexation of Na^+ or Li^+ ions by the crowns leads to partial conversion of **1** to **2**.

These results are in line with the different course of the lithiation reactions of **1** with LDA in THF or Et_2O (70 and 0% yield of **2**, respectively), formation of contact ion pairs in the latter solvent being considered to inhibit the rearrangement.[2a,b] A similar conclusion can be drawn from our experiments: for the rearrangement to be synthetically useful, an alkoxide with p$K_a \geq 19$ is needed, provided the ion pairs are dissociated enough in the reaction medium. These conditions are fulfilled by KO*t*-Bu in THF, so we decided to use this combination in the attempted isomerisation of other 1,4-dithiins. To that end, compounds **3a**–**c**[10] and **4**[11] were prepared and their reactions with KO*t*-Bu (5 equiv.) in refluxing THF afforded the corresponding 1,4-dithiafulvenes **5a**–**c**[12] and **6**,[11,13] respectively, in medium to good yields (Scheme 2). On the other hand, very low conversions (for **3b** and **3c**) or no isomerisation at all (for **3a** and **4**) were observed when excess NaO*t*-Bu and longer reaction times (11–24 h) were used, thus confirming the importance of the cation in these rearrangements.

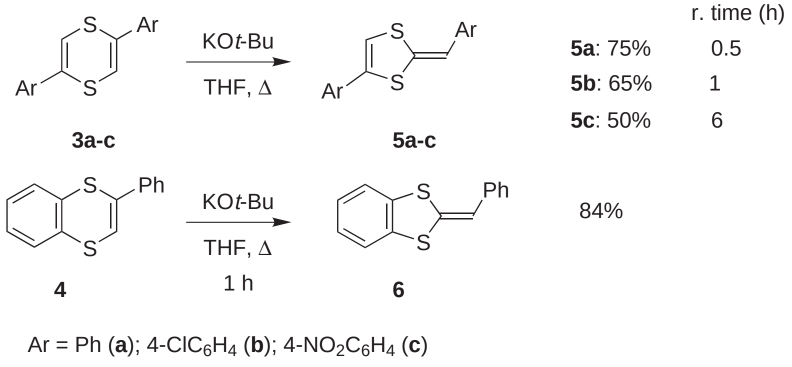


Scheme 3.

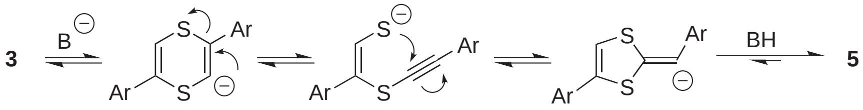
3. The driving force of the rearrangement

The fact that **1** rearranges to **2** has been accounted for by the greater thermodynamic stability of the latter;[4,14] nevertheless, no clear conclusion has been presented for the analogous isomerisation of compounds **4** to **6**, since semi-empirical calculations show that both isomers are close in energy.[6] Here we suggest an alternative explanation which accounts for all experimental facts.

These rearrangements are supposed to proceed by an E1cB mechanism, since trapping of the metallated species with electrophilic reagents is sometimes possible.[2,3a,b] Thus, we have carried out ab initio calculations[15] at the HF/6-311+G**//HF/6-311+G** level[16] on compounds **1**, **1a**, **2**, **2a** and model compounds **7**, **7a**, **8** and **8a** (Scheme 3). Concerning the isomerisation of **1** to **2**, not only **2** is more stable than **1**, but ΔG (**1a**→**2a**)$=-13.55$ kcal mol^{-1}. For the isomerisation of **7** to **8**, $\Delta G=-3.26$ kcal mol^{-1} but, more important, the protonation of **8a** is more exergonic than that of **7a** by 12.5 kcal mol^{-1}, which implies that **7** is a stronger acid by ca. 9 pK_a units. Therefore, in the case of compounds **3** it can be assumed that the equilibrium established between the corresponding anions is driven to the right by the protonation of the anion of **5**, which is a strongly favoured step (Scheme 4). Moreover, this explanation accounts for the fact that all of these rearrangements take place in the presence of the conjugated acid of the base.[2,4–6]



Scheme 2.



Scheme 4.

To sum up, the pK_a of the base and the dissociation of the ion pairs play a key role on the ring-contraction of 1,4-dithiin derivatives. It is the combination of these two factors that makes KO*t*-Bu the reagent of choice for carrying out these rearrangements. Moreover, the greater thermodynamic stability of 1,3-dithiole derivatives, together with the weaker acidity of dithiafulvenes, account for the course of these rearrangements.

Acknowledgements

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