Available online at www.sciencedirect.com

SCIENCE DIRECT®

Tetrahedron Letters 45 (2004) 2189–2192

Tetrahedron Letters

A nonconcerted cycloaddition of fused 2-vinylthiophenes with dimethyl acetylenedicarboxylate ☆

Aleš Machara,[a] Milan Kurfürst,[a] Václav Kozmík,[a] Hana Petříčková,[b] Hana Dvořáková[c] and Jiří Svoboda[a,*]

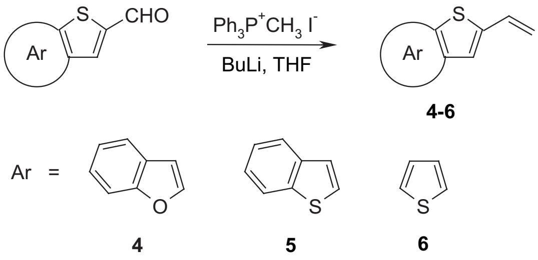
[a] *Department of Organic Chemistry, Institute of Chemical Technology, Technická 5, CZ-166 28 Prague 6, Czech Republic*
[b] *Department of Solid State Chemistry, Institute of Chemical Technology, Technická 5, CZ-166 28 Prague 6, Czech Republic*
[c] *Central Laboratories, Institute of Chemical Technology, Technická 5, CZ-166 28 Prague 6, Czech Republic*

Received 11 September 2003; revised 22 December 2003; accepted 9 January 2004

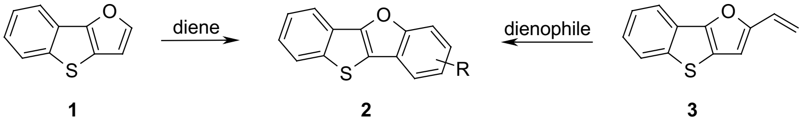
Abstract—Fused thiopyrans along with products of subsequent reactions of the primary adducts of the title compounds are obtained by nonconcerted [4π + 2π] processes. The course of the reactions and formation of all products discussed.

The Diels–Alder reaction[1] represents an essential instrument for the synthesis of various carbocycles and heterocycles. Recently[2] we showed that [1]benzothieno[3,2-*b*]furan (**1**), due to its low furan aromaticity, possesses dienophilic behaviour and reacts with electron-rich dienes with formation of a new heterocyclic [1]benzothieno[3,2-*b*][1]benzofuran system (**2**). Further we reported[3] that introduction of a vinyl moiety in the 2 position of **1** created a reactive diene (**3**), which reacted with various dienophiles. Thus, both cycloaddition reactions led to new derivatives of heterocycle **2** substituted in the 'benzofuran part' of the heterocyclic system (Scheme 1).

In order to utilize analogous cycloaddition reactions to obtain the heterocycle **2** substituted in the 'benzothiophene' part, we changed the topology of **3** to the isomeric 2-vinylthieno[3,2-*b*][1]benzofuran (**4**). A study of its reactivity was further extended to the new and structurally related [3,2-*b*]fused 2-vinylthiophene systems of 2-vinyl[1]thieno[3,2-*b*][1]benzothiophene (**5**) and 2-vinylthieno[3,2-*b*]thiophene (**6**) (Scheme 2), the reactivities of which have not been studied. In association with the known reactivity of 2-vinylthiophene[4] and



Scheme 2. Synthesis of 2-vinyl derivatives **4**–**6**.



Scheme 1. Formation of [1]benzothieno[3,2-*b*][1]benzofurans.

Keywords: Vinylthiophenes; Cycloaddition; Nonconcerted process.

☆ Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2004.01.030

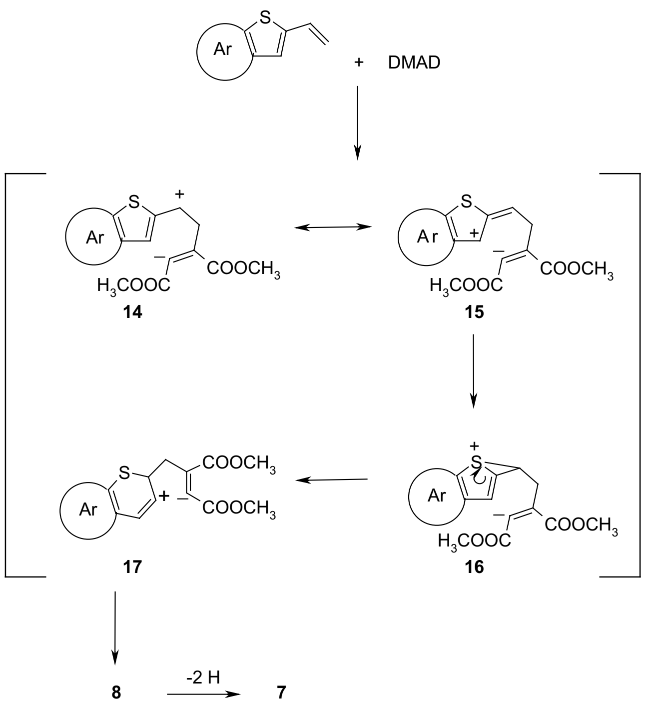
* Corresponding author. Tel.: +420-224-311-877; fax: +420-224-354-288; e-mail: jiri.svoboda@vscht.cz

0040-4039/$ - see front matter © 2004 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tetlet.2004.01.030

2-vinyl[1]benzothiophene,[5] analogous behaviour of **4–6** was anticipated. This paper summarizes the results of the different courses of their reactions with dimethyl acetylenedicarboxylate (DMAD).

The starting 2-vinyl derivatives **4–6** were obtained by standard Wittig methylenation of the corresponding aldehydes[6,7] (Scheme 2) with methylene(triphenyl)phosphorane in 54–76% yield after chromatographic purification. Cycloaddition reactions were performed by heating **4–6** (1.2 mmol) with DMAD (3.6 mmol) in toluene (10 mL) to reflux under a nitrogen atmosphere. When the starting compound had disappeared, the products formed were separated by careful column chromatography followed by multiple preparative TLC chromatographic purification. The yields of the isolated products are summarized in Table 1 and their structures[8] are shown in Scheme 3.

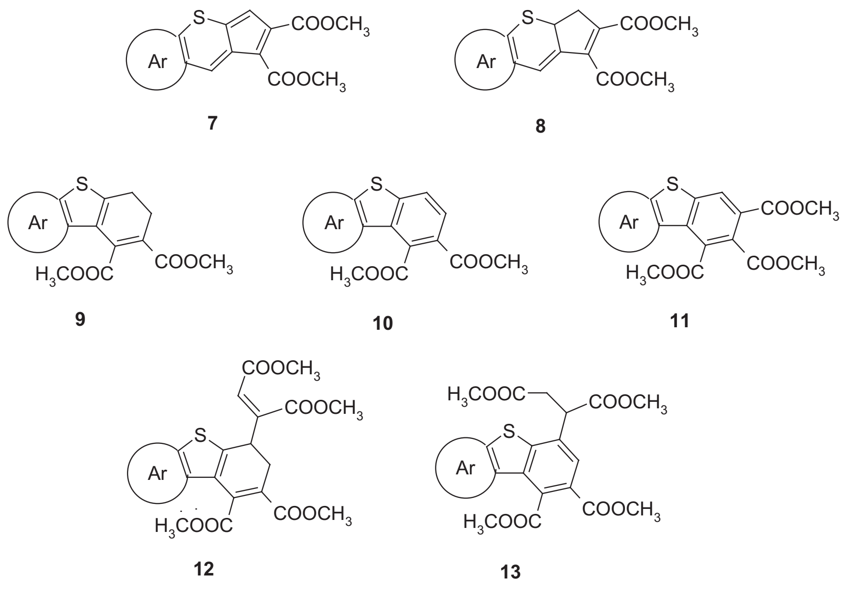
It is evident from the structures of the thiopyran **7** and the dihydro derivatives **8** that the reactions proceed by a nonconcerted process. Assuming that zwitterionic species are involved in $[4\pi + 2\pi]$-cycloadditions with strongly electro-deficient dienophiles,[9] the electron-rich vinyl double bond in **4–6** has added to the DMAD with formation of the zwitterionic intermediate **14** (Scheme 4). Furthermore, it rearranged with formation of other unstable species **15–17**, all of which may play key roles in the formation of products **7–13**. Formation of the fused system of **7** involves a thiophene–thiopyran ring enlargement. It can be explained by the creation of the thiiranium ion **16**, which rearranges to ion **17**. Analogous thiiranium species have been involved in fused thiopyran-fused thiophene ring contractions.[10–13]



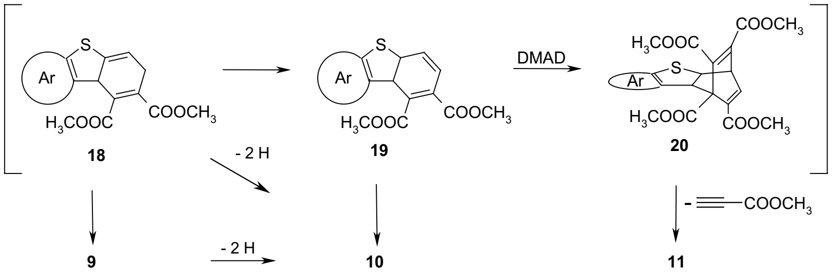
Scheme 4. Formation of products **7** and **8**.

Table 1. Product distribution and yields

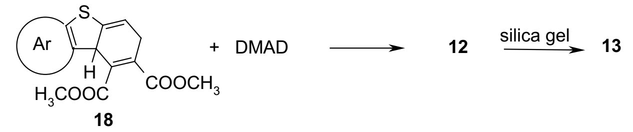
Comp.	Reaction time, h	Products and yields, %											
4	58	**7a**	19	**8a**	16	**9a**	20	**10a**	20	**11a**	17	**12a + 13a**	3
5	54	**7b**	10	**8b**	11	**9b**	25	**10b**	21	**11b**	23	**12b + 13b**	2
6	48	**7c**	10	**8c**	4	**9c**	9	**10c**	11	**11c**	9	**12c + 13c**	6



Scheme 3. Structures of the isolated products **7–13**.



Scheme 5. Transformation of **18** leading to esters **9**–**11**.



Scheme 6. Ene-reaction leading to tetraesters **12** and **13**.

Attachment of the diester residue leads to the dihydro derivatives **8**. Spontaneous aromatization of the unstable products **8** to the thiopyranes **7** completes the process. To our best knowledge, the formation of a thiopyran system by a thiophene ring enlargement is unique and has not been described in the literature. In addition, the dihydro derivatives **8** spontaneously aromatized during their storage even at −18 °C to thiopyrans **7**. Oxidation of **8b** with DDQ in dichloromethane at room temperature afforded **7b** as the sole product within 30 s. Thus, the reactivities of the fused 2-vinylthiophene systems **4**–**6** differ substantially from those of simple vinylthiophene derivatives.[4,5]

The closure of a six-membered ring in the zwitterion **15** leads to the important intermediate **18** (Scheme 5). Its structure also corresponds to that of the primary product of a concerted [4π + 2π] process. The adduct **18**, which could not be detected by any analytical method, stabilizes very rapidly by a double bond shift reforming the aromatic thiophene moiety in compound **9**. Dehydrogenation of **18** and/or **9** affords the fully aromatized diester **10**. A second double bond shift in **18** leads to formation of the nonisolable intermediate **19**, which undergoes a second cycloaddition with DMAD possibly creating the bridged structure **20**. Although such thermal 1,3-hydrogen shifts are expected to be high energy processes, the energy gain due to the rearomatization, to give **9**, favours this transformation. A *retro*-cycloaddition with elimination of methyl propiolate affords the final triester **11**. A similar cycloaddition with DMAD and **3** has been observed earlier.[3]

The tetraesters **12** are apparently formed by an ene-reaction of the intermediate **18** with another molecule of DMAD (Scheme 6). Formation of a structurally related tetraester was observed in the cycloaddition reaction of 2-vinylthiophene described earlier.[4] In addition, we found that the esters **12** partly rearrange during chromatographic separation of the reaction products to the more stable and fully aromatized tetraesters **13**.

In conclusion, reactions of fused 2-vinylthiophene heterocycles with DMAD leads to a broad range of products. The structures of thiopyrans **7** and dihydrothiopyrans **8** confirm that a nonconcerted mechanism is involved. These results are in contrast with the reactivity of simple 2-vinylthiophene derivatives. By this route, in addition to the 'expected' adducts, new interesting, electron-rich fused thiopyran derivatives were obtained. A more detailed study of fused vinylthiophene cycloaddition reactions and their mechanisms is in progress.

Acknowledgements

Financial support from the Grant Agency of the Czech Republic (project no. 202/02/0840) and the Ministry of Education, Youth and Sport (project no. MSM 223100001) is gratefully acknowledged.

References and notes

1. Carruthers, W. *Cycloaddition Reactions in Organic Synthesis*; Pergamon: New York, 1990.
2. Pihera, P.; Paleček, J.; Svoboda, J. *Collect. Czech. Chem. Commun.* **1998**, *63*, 681–697.
3. Pihera, P.; Dvořáková, H.; Svoboda, J. *Collect. Czech. Chem. Commun.* **1999**, *64*, 389–407.
4. Abarca, B.; Ballesteros, R.; Enriquez, E.; Jones, G. *Tetrahedron* **1985**, *41*, 2435–2440.
5. Ghosh, A.; Maiti, S. B.; Chatterjee, A.; Raychaudhuri, S. R. *Indian J. Chem.* **1989**, *28B*, 724–727.
6. Svoboda, J.; Pihera, P.; Sedmera, P.; Paleček, J. *Collect. Czech. Chem. Commun.* **1996**, *61*, 888–900.
7. Váchal, P.; Pihera, P.; Svoboda, J. *Collect. Czech. Chem. Commun.* **1997**, *62*, 1468–1480.
8. Structures of all products were assigned by the ^{1}H and ^{13}C NMR spectra and if necessary by ^{1}H–^{1}H COSY, HMBS, HMQC and NOE experiments. To establish the structure of thiopyran derivatives **7**, a single-crystal X-ray diffraction study of **7a** was accomplished, see the supplementary crystallographic data, CCDC registration number 205665. These data can be obtained free of charge via www.ccdc.cam.ac.uk/conts/retrieving.html (or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB2 1EZ, UK; fax: +44-1223-336033; or deposit@ccdc.cam.ac.uk).
9. Baldwin, J. E. In *Comprehensive Organic Synthesis*; Trost, B. M., Ed.; Pergamon: Oxford, 1991; Vol. 5, pp 70–77.

10. McKenzie, N. E.; Thomson, R. H. *J. Chem. Soc., Perkin. Trans. 1* **1982**, 395–402.
11. Smith, D. G. *J. Chem. Soc., Perkin. Trans. 1* **1990**, 3187–3191.
12. Rane, D. F.; Pike, R. E.; Puar, M. S.; Wright, J. J.; McPhail, A. T. *Tetrahedron* **1988**, *44*, 2397–2402.
13. Aso, Y.; Iyoda, M.; Nakagawa, M. *Tetrahedron Lett.* **1982**, *23*, 2473–2474.