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Hetero Diels–Alder reactions (HDAR) of α,α′-dioxothiones on solid support

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Abstract—Solid-supported α,α′-dioxothiones are easily obtained starting from β-ketoester modified Wang and hydroxymethylated polystyrene resins. The hetero Diels–Alder reactions (HDAR) of these species, used either as electron-poor dienes or dienophiles, followed by a simple cleavage of the products from the resin by trans-esterification with sodium methoxide, allowed the isolation of the desired cycloadducts in overall yields up to 90%.
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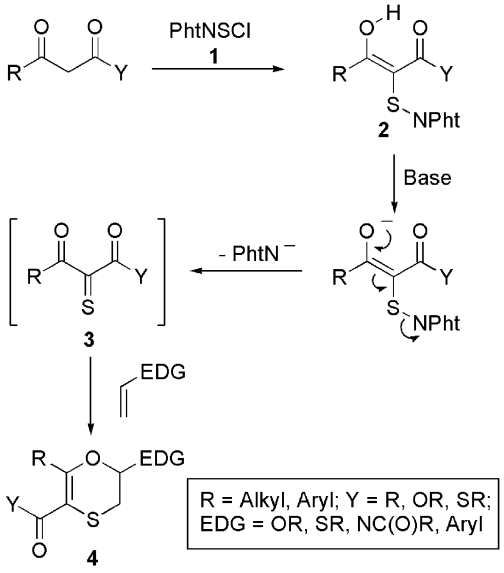
1. Introduction

Hetero Diels–Alder reactions represent one of the more efficient and valuable tool for the construction of six-membered heterocycles which, in turn, probably are the most common cyclic moiety encountered in bio-organic and medicinal chemistry.[1] The development of [4+2] cycloadditions on solid-phase represents an appreciated target either for a possible simplification of the synthetic procedure or for their potential application in combinatorial chemistry.

We have developed a practical procedure for the formation of α,α′-dioxothiones and studied their behaviour as electron-poor heterodienes in inverse electron demand hetero Diels–Alder reactions with a plethora of electron-rich alkenes (Scheme 1). The reaction of β-dicarbonyls with the phthalimidesulfenyl chloride **1** (PhtNSCl, Pht= Phthaloyl) affords the corresponding α,α′-dioxothiophthalimides **2** which, in the presence of weak bases like Pyridine or Et_3N, undergo a 1,4-elimination at sulfur of the phthalimide anion causing the formation of the transient thiones **3** (Scheme 1). These species react smoothly with vinyl ethers, vinyl sulfides, vinyl amides, and styrenes to give 1,4-oxathiin heterocyclic systems **4** with a total control of chemo- and regiochemistry.[2–4]

Due to the simplicity, mildness, generality and usefulness of this approach,[5] we decided to study the possibility of its extension to solid support. In this paper, we report the results, scope and limitations of this methodology when applied to solid-supported α,α′-dioxothiones.[6]



Scheme 1. General procedure for the generation and trapping of α,α′-dioxothiones in solution-phase.

2. Results and discussion

Following the general protocol optimized for this chemistry

Keywords: Phthalimidesulfenyl chloride; Dioxothiones; Hetero Diels–Alder reactions; Solid-phase synthesis; Sulfur heterocycles.
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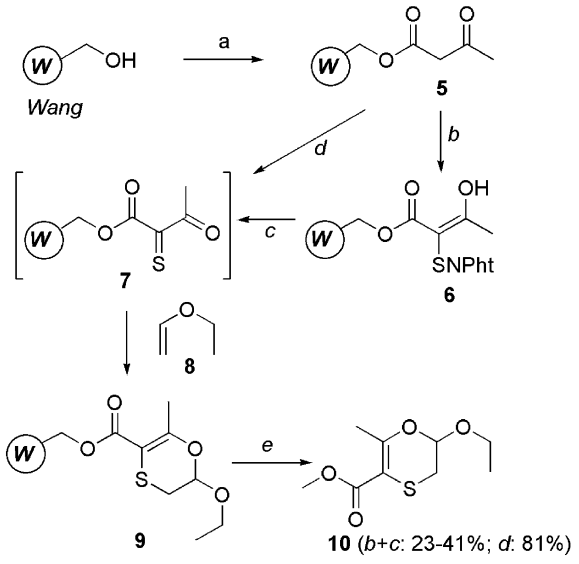
in solution-phase, we tried to transform a resin-linked β-ketoester into the corresponding acylthione. Using the Wang resin as solid support, the β-ketoester function was attached after considering several possible methods,[7] by direct trans-esterification with *tert*-butylacetoacetate[8] in toluene at 110 °C, to obtain immobilised ketoester **5** (Scheme 2). The reaction of a DCM pre-swelled suspension of resin **5** with 1.4 equiv of phthalimidesulfenyl chloride (**1**) at room temperature, allowed the transformation into the α,α′-dioxothiophthalimide modified resin **6** (Scheme 2). Eventually, the reaction of **6** with 1 equiv of Pyridine in $CHCl_3$ at room temperature afforded the solid-supported α,α′-dioxothione **7** that, in the presence of 5 equiv of ethyl vinyl ether (**8**), underwent an inverse electron demand HDAR to give the resin-linked oxathiin **9** as reported in Scheme 2.



Scheme 2. General procedure for the generation and trapping of an α,α′-dioxothione on solid-phase. Reagents: (a) *tert*-butylacetoacetate, toluene, 110 °C, 24 h; (b) **1**, DCM, rt, 5 h; (c) Py or Et_3N, ethyl vinyl ether (**8**), $CHCl_3$, rt −60 °C, 18–22 h; (d) **1**, Et_3N, **8**, DCM, 60 °C, 19 h; (e) MeONa/MeOH, THF, rt, 5 h.

After each step, the resin was repeatedly washed with DCM, MeOH, Et_2O, DCM and dried under vacuum over KOH. The progress of the reactions and the formation of intermediates **5**, **6** and **9** was monitored by FTIR and ^1H NMR.[9]

The use of Wang resin would have allowed the cleavage of the cycloadduct from the solid-phase by reaction with TFA in DCM, however, we found that oxathiin cycloadducts of type **4** (or **9**) are unstable under these conditions. Alternatively, a clean cleavage was achieved by trans-esterification with a freshly prepared methanolic sodium methoxide solution in dry THF; the isolation of cycloadduct **10** was thus possible in 23% yield (Scheme 2). Despite the low yield, these preliminary results were quite encouraging due to the simplicity of the entire procedure and since **10** was obtained as a pure compound (purity >95% by ^1H NMR) directly after evaporation of the solvents used to wash the resin (see Section 4). Identification of **10** was easily obtained by comparison with an authentic sample obtained in solution-phase reactions from methylacetoacetate[3] (R=Me, Y=OMe, EDG=OEt) as described in Scheme 1.

Several examples of Diels–Alder reactions on solid phase have been reported[10] but, at the best of our knowledge, this is the first example of hetero cycloaddition employing a solid-supported acylthione. We studied how to improve the yield of sequence reported in Scheme 2. A first advance was easily obtained using a stronger base to generate the thione **7** and performing the cycloaddition at higher temperature. As a matter of fact repeating the procedure as depicted in Scheme 2 but using 2 equiv of Et_3N on step c and carrying on the cycloaddition of **7** with **8** at 60 °C for 18 h, after cleavage with MeONa, derivative **10** was isolated in a 41% yield. Other simple modifications to the procedure, among those often suggested to optimize a reaction on solid-phase, such as duplication of trans-esterification and/or sulfenylation steps (a and/or b steps in Scheme 2) did not allow, in our case, any satisfactory improvement.

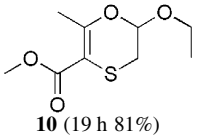
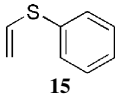
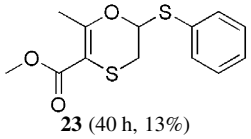
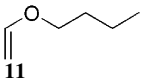
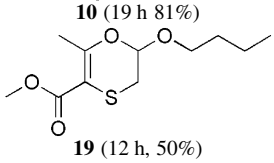
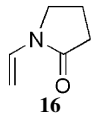
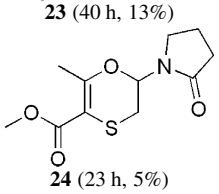
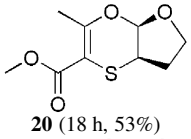
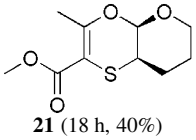
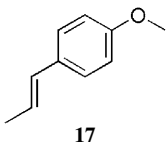
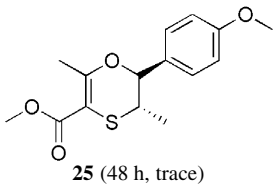
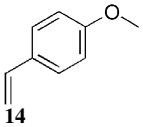
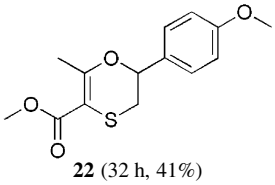
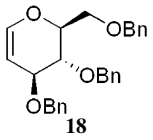
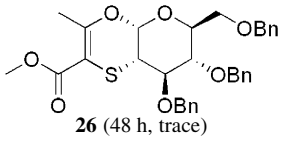
A crucial enhance was eventually obtained using a simplified procedure that allowed to run the cycloaddition without the isolation of the intermediate dioxothiophthalimide derivative, and we recently verified to be valuable for the cycloaddition of thiones obtained from acid sensitive sugar-containing β-ketoesters.[11] In particular 2 equiv of **1** and 2.5 equiv of Et_3N were added in sequence to resin **5** at room temperature in DCM, followed, after 20 min, by the addition of vinyl ether **8** (Scheme 2, step d). The reaction mixture was heated to 60 °C for 19 h; the obtained resin-linked oxathiin **9** was then reacted with MeONa to give **10** in a 81% yield. This satisfactory result indicated that each of the five steps carried out on solid-phase to isolate **10** (i.e., introduction of the β-ketoester, sulfenylation, formation of the thione, cycloaddition and cleavage) must occur with almost quantitative yield. The nearly simultaneous addition of **1** and Et_3N to **5**, which avoids the formation of a high concentration of HCl, the obvious by-product of the sulfenylation step, and consequently the acid decomposition of the Wang resin, can likely explain this successful result. However, it must be mentioned that the analysis of the solvents used to wash the resin **6** after sulfenylation (i.e., step b in Scheme 2) did not show any compound deriving from a possible deterioration of the resin **5**.

We decided to verify the generality of this solid-supported HDAR repeating the cycloaddition with the electron-rich alkenes **11–18** as dienophiles as reported in Table 1.

In any case, the supported thione **7** was generated following the simplified procedure without isolation of the sulfenylated resin **6** and the final yields refer to the cycloadducts **19–26** isolated as pure compounds (>95% by ^1H NMR) after cleavage with MeONa (see Section 4). Apart from the reaction with enol ether **8**, all the other results are for oxathiin cycloadducts obtained in a single run without optimization. Identification of compounds **19–26** was achieved by comparison with authentic samples previously prepared in solution-phase.[3]

Data reported in Table 1 are in good agreement with the informations, we have accumulated during the last years for these cycloaddition reactions. In fact when the dienophile

Table 1. Oxathiins **10**, **19–26** obtained by cycloaddition of solid-supported thione **7**

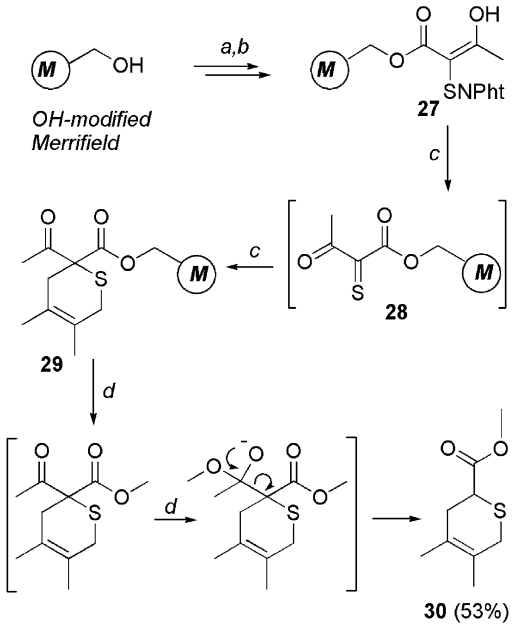
Dienophil	Cycloadduct (reac. time, yield)	Dienophile	Cycloadduct (reac. time, yield)
 **8**	 **10** (19 h 81%)	 **15**	 **23** (40 h, 13%)
 **11**	 **19** (12 h, 50%)	 **16**	 **24** (23 h, 5%)
 **12**	 **20** (18 h, 53%)		
 **13**	 **21** (18 h, 40%)	 **17**	 **25** (48 h, trace)
 **14**	 **22** (32 h, 41%)	 **18**	 **26** (48 h, trace)

chosen presents either a poor reactive HOMO orbital, that is an high gap between the LUMO of the thione and the HOMO of the alkene,[4] or a remarkable steric demand[2–4,12] the reaction time becomes very long and the yields decrease. In such circumstances the cycloaddition on solid-phase, which requires, as expected, harsher reaction conditions, becomes poorly efficient for dienophiles like vinyl pyrrolidone **16**, anethole **17** or tri-*O*-benzylglucal **18** that allowed the isolation of only trace amounts of the corresponding oxathiins **24**, **25** or **26**.

On the other hand, the methodology depicted in Scheme 2 (path d) is valuable and more convenient, in terms of simplicity and overall yields, than the procedure in solution-phase for reactive steric undemanding dienophiles.

A further development of this methodology we studied was, the possibility of using different solid-supporting resins for the generation of α,α'-dioxothiones. Thus, a β-ketoester group was inserted on a hydroxymethyl polystyrene (OH-modified Merrifield) resin following the same procedure reported in Scheme 2. In this case, due to the insensitivity of this resin to acid hydrolysis, the sulfenylation reaction was carried out using an excess of **1** and repeated twice since to have an exhaustive transformation to the resin-linked dioxothiophathalimide **27** (Scheme 3). Indeed, we verified that generating the supported thione **28** from **27** and Et_3N, in the presence of ethyl vinyl ether (**8**), after 18 h at 60 °C and cleavage with MeONa, the oxathiin **10** was isolated in 77% yield.

With completely sulfenylated resin **27** in hand we could also carry out cycloaddition reactions in solvents like DMF, that are not suitable for the one-pot [(i) sulfenylation (ii) thione generation] procedure. With minute amounts[13] of DMF as



Scheme 3. Formation of the modified Merrifield supported-thione **28**, and its trapping as electron-poor dienophile. Reagents: (a) *tert*-butylacetoacetate, toluene, 110 °C, 24 h; (b) **1**, DCM, rt, 5 h; (c) Et_3N, 2,3-dimethyl-1,3-butadiene, $CHCl_3$, 60 °C, 20 h; (d) MeONa/MeOH, THF, rt, 5 h.

solvent and prolonging the reaction times we observed a little, but promisingly, further improvement on the total yield of some cycloadditions, including those that had given poor results with resin **5**. Thus, under these conditions derivatives **10**, **23**, **24** and **25** were isolated in 92, 28, 12 and 13% yield, respectively.

Another noticeable reaction of α,α′-dioxothiones[14] is their participation as electron-poor dienophiles in direct electron demand Diels–Alder reactions with 1,3-dienes.[2] We tried to trap solid-supported α,α′-dioxothione **28** as dienophile using 2,3-dimethyl-1,3-butadiene. In this case, cycloaddition afforded the dihydrothiopyran OH-modified Merrifield resin **29**, that, when reacted with MeONa in dry THF, allowed the isolation of derivative **30** in 53% yield (Scheme 3).

The modification of the heterocyclic ring structure with loss of the acetyl group was expected since we have already observed[15] that basic hydrolysis, or trans-esterification with alkoxides, in α-keto-α′-carboxythiopyrans is associated with a very easy and unavoidable retro-Claisen rearrangement that causes the formation of a 2-carboxythiopyran of type **30** (Scheme 3). However, the isolation of derivative **30**, proving the formation of thiopyran **29**, indicates that α,α′-dioxothiones retain their double nature of efficient electron-poor dienes and dienophiles in HDAR on solid-support as well.

As already mentioned, α,α′-dioxothiones **3** are transient species that cannot be isolated or detected. When α-keto-α′-carboxy-*N*-thiophthalimides of type **2** (R = Me, Y = OMe, OEt) are reacted with a base in the absence of a suitable trapping agent, the produced thiones **3** undergo a base catalysed reversible self-condensation process with formation of a dimeric species which, in turn, can be isolated and identified.[2] It has been recently reported[16] that the formation of a quinone methide on a solid support allowed its spectroscopic characterization since the resin acts as an appropriate 'isolator' for such highly reactive species.

We speculated whether this possibility exists also for α,α′-dioxothione **28**. Operatively, resin **27** was reacted with Et_3N in dry DCM for 2 h at room temperature in the dark. After being thoroughly washed and dried, the resin **28** formally containing the free thione moiety was reacted with **8** in dry DCM at 60 °C for 18 h. Satisfactorily, after the usual cleavage, oxathiin **10** was isolated in 16% yield indicating that, under this condition, a monomeric α,α′-dioxothione moiety is, at least in part, stable on the resin **28**.[17]

3. Conclusion

In this paper, we reported the successful extension on solid-phase of the *N*-thiophthalimide mediated generation of α,α′-dioxothiones. Using the easily available Wang or OH-modified Merrifield resins as solid-supports and avoiding the introduction of any linker, dioxothiones were obtained under very mild reaction conditions and reacted in HDAR either as electron-poor dienes or dienophiles. Using highly reactive small dienophiles the isolation from the solid phase of the oxathiin cycloadducts was more simple and convenient than the parallel solution-phase procedure. Further developments and applications of this new aspect of dioxothiones chemistry are under study.

4. Experimental

4.1. General

DCM, DMF, $CHCl_3$, THF, CH_3OH, toluene, Pyridine and Et_3N were dried using standard procedures. All commercial reagents were used without further purification. Solution phase ^1H NMR spectra were recorded in $CDCl_3$ at 200 or 400 MHz, using residual $CHCl_3$ at δ_H 7.26 as reference. Phthalimidesulfenyl chloride **3** was prepared as published elsewhere.[18] Oxathiins **19–26** were identified by comparison of the ^1H NMR spectra with authentic samples previously prepared in solution.[3]

4.2. Solid-phase synthesis

Wang and hydroxymethylated Merrifield resins were purchased from Novabiochem. They are all based on 1% cross-linked divinylbenzene-styrene copolymer and are 100–200 mesh with a loading of 1.2 and 0.98 mmol/g. Solid-phase reactions were carried in sure sealed vials and the resin suspensions transferred by plastic-pipettes. Solid-phase work-up was carried out by means of the plastic-siring technique. Flat-bottom PE syringes were equipped with sintered Teflon filters, teflon tubing and valves which allow suction to be applied to the syringe from below. Functionalized resins were analysed with FTIR and/or MAS solid-phase NMR. MAS solid-phase NMR were acquired on a 400 MHz Varian MercuryPlus spectrometer using a PFG-ID-Varian Nanoprobe (Pulsed Field Gradient, Indirect Detection), at 25 °C using $CDCl_3$ as solvent with a CPMG modified sequence to minimise the resin signals. In the following ^1H NMR spectra of the intermediated resins **5**, **6**, **9** the signals due to the resin's protons are omitted apart from the terminal benzilic CH_2. Unless otherwise stated reactions were worked-up as it follows: the resin was transferred from the vial to the syringe, filtered and washed with DCM (four times), MeOH (four times), Et_2O (four times) and DCM (four times), and dried under vacuum over KOH for 2–24 h before to run the following step.

4.2.1. Immobilised β-ketoester 5.[8] Wang resin (1 g, 1.2 mmol/g) was swelled at room temperature in dry toluene (5 mL) for 2 h. *tert*-Butylacectoacetate (1.9 g, 12 mmol) was added and the mixture heated at 110 °C for 24 h. The general work-up afforded 1.064 g of resin **5**.

IR (KBr) 1742 (s, C=O ester), 1717 (s, C=O ketone) cm^{-1}.[7,8] ^1H NMR (400 MHz, $CDCl_3$) δ: 2.32 (s, C=$COCH_3$, 3H), 3.55 (s, $OCOCH_2CO$, 2H), 5.23 (s, resin-$ArCH_2OCO$, 2H).

4.2.2. Sulfenylated resin 6. β-Ketoester functionalised resin **5** (1.070 g, 1.2 mmol) was swelled at room temperature in dry DCM (6.5 mL) for 1 h. Sulfenyl chloride **1** (0.356 g, 1.7 mmol) was added and the mixture kept at room temperature for 5 h. The general work-up afforded 1.081 g of resin **6**.

IR (KBr) 1785+1740+1718 (N–C=O Pth+C=O ester) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ: 2.73 (s, C=$COCH_3$, 3H), 5.25 (s, resin-$ArCH_2OCO$, 2H); 7.70–7.90 (m, Phthaloyl, 4H), 13.93 (s, C=COH, 1H).

4.2.3. Immobilised oxathiin 9 from sulfenylated resin 6. Sulfenylated resin **6** (180 mg, 0.15 mmol) was swelled in dry $CHCl_3$ (4 mL) at room temperature for 2 h, then ethyl vinyl ether (**8**) (56 mg, 0.78 mmol) and Et_3N (33 mg, 0.32 mmol) were added in sequence and the mixture heated to 60 °C for 18 h. The general work-up afforded 164 mg of resin **9**.

IR (KBr) 1702 (s, C=O ester conjugated), 1600 (s, C=C conjugated) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ: 1.30 (bs, OCH_2CH_3, 3H), 2.40 (s, C=$COCH_3$, 3H), 2.95–3.05 (m, SCH_2, 2H), 3.87–3.92 (m, OCH_2CH_3, 1H), 4.01–4.06 (m, OCH_2CH_3, 1H), 5.25 (bs, OCHO, 1H), 5.40 (s, resin-$ArCH_2OCO$, 2H).

4.2.4. Immobilised oxathiin 9 from resin 5: simplified procedure. To a pre-swelled suspension of resin **5** (153 mg, 0.17 mmol) in dry DCM (2.5 mL) at room temperature for 1 h, PhtNSCl **1** (75 mg, 0.35 mmol) in dry DCM (1.5 mL) and dry Et_3N (44 mg, 0.43 mmol) were added in succession. After 20 min at room temperature vinyl ether **8** (62 mg, 0.86 mol) was introduced and the mixture heated to 60 °C for 19 h. The general work-up afforded 170 mg of resin **9**.

4.2.5. Resin 9 cleavage with MeONa: oxathiin 10. The resin **9** (170 mg, 0.16 mmol) was swelled in dry THF (6 mL) at room temperature for 1 h; a solution of freshly prepared MeONa 1.6 M in MeOH (0.5 mL, 0.8 mmol) was added by syringe and the mixture kept at room temperature for 5 h. The resin was washed with Et_2O (four times) and DCM (four times), the organic solvents recollected, washed with saturated aqueous NH_4Cl and brine and dried over anhydrous Na_2SO_4. Evaporation of the solvent afforded cycloadduct **10** (28 mg, 81%) as a pale yellow oil identical to an authentic sample.[3]

^1H NMR (200 MHz, $CDCl_3$) δ: 1.25 (t, J=7.5 Hz, 3H), 2.32 (s, 3H), 2.76–2.94 (AB part of an ABX system, J_{AB}= 13.5 Hz, 2H), 3.64–3.76 (m, 1H), 3.73 (s, 3H), 3.84–3.96 (m, 1H); 5.24 (X part of an ABX system, J=4.0, 2.0 Hz, 1H).

All the above reported procedures can be considered as representative also for the functionalization of the hydroxymethyl polystyrene (OH-modified Merrifield) resin, and for all the cycloadditions described in Table 1.

4.2.6. Cycloadduct 23 from resin 27 in DMF. To a pre-swelled sulfenylated resin **27** (260 mg, 0.20 mmol) in dry DMF (1 mL) at room temperature for 2 h, phenyl vinyl sulfide (**15**) (136 mg, 1.00 mmol) and Et_3N (21 mg, 0.21 mmol) were added in sequence and the mixture heated to 60 °C for 52 h. The general work-up afforded 239 mg an oxathiin-immobilised resin, which was dried and reacted with MeONa in dry THF as described above. Evaporation of the solvent gave cycloadduct **23** (16 mg, 28%) as a pale yellow oil with spectroscopic data identical of those reported in the literature.[3]

^1H NMR (200 MHz, $CDCl_3$) δ: 2.37 (s, 3H), 3.01 (AB part of an ABX system, J_{AB}=13.2 Hz, 2H), 3.77 (s, 3H), 5.68 (X part of an ABX system, J=5.4, 2.7 Hz, 1H), 7.30–7.60 (m, 5H).

4.2.7. Thiopyran 30. To a pre-swelled sulfenylated resin **27** (160 mg, 0.12 mmol) in dry $CHCl_3$ (4 mL) at room temperature for 2 h, 2,3-dimethyl-1,3-butadiene (54 mg, 0.66 mmol) and Et_3N (14 mg, 0.14 mmol) were added in sequence and the mixture heated to 60 °C for 20 h. The general work-up afforded 154 mg of immobilised thiopyran resin **29** which was dried and reacted with MeONa in dry THF as described above. Evaporation of the solvent gave thiopyran **30** (13 mg, 53%) as a colourless oil with spectroscopic data identical of those reported in the literature.[19]

^1H NMR:[17] (200 MHz, $CDCl_3$) δ: 1.69 (bs, 3H), 1.71 (bs, 3H), 2.45 (AB system, 2H, J=6.2 Hz), 3.08 (AB system, 2H, J=16.2 Hz), 3.6 (t, 1H, J=6.2 Hz), 3.73 (s, 3H).

4.2.8. Immobilised monomeric thione 28. In a flat-bottom PE syringe equipped with two sintered Teflon filters, resin **27** (212 mg, 0.16 mmol) was swelled in dry DCM (2 mL) at room temperature for 1 h, then the syringe was covered with aluminium foil and Et_3N (49 mg, 0.50 mmol) was added in the dark. After 2 h at room temperature the deep pink resin obtained was washed with dry DCM, until no trace of Et_3N was detected in the washing, transferred into a vials with dry DCM (2 mL) and vinyl ether **8** (36 mg, 0.50 mmol) and heated to 60 °C for 18 h. The usual work-up and cleavage with MeONa gave cycloadduct **10** in 16% isolated yield.

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References and notes

1. Nicolaou, K. C.; Snyder, S. A.; Montagnon, T.; Vassilikogiannakis, G. *Angew. Chem., Int. Ed.* **2002**, *41*, 1668–1698 and reference cited therein.
2. Capozzi, G.; Nativi, C.; Menichetti, S.; Rosi, A.; Valle, G. *Tetrahedron* **1992**, *48*, 9023–9032.
3. Capozzi, G.; Franck, R. W.; Mattioli, M.; Menichetti, S.; Nativi, C.; Valle, G. *J. Org. Chem.* **1995**, *60*, 6416–6426.
4. Capozzi, G.; Dios, A.; Franck, R. W.; Geer, A.; Marzabadi, C.; Menichetti, S.; Nativi, C.; Tamarez, M. *Angew. Chem., Int. Ed.* **1996**, *35*, 777–779.
5. Menichetti, S.; Nativi, C. Hetero Diels–Alder approach to oxathiins. In *Targets in Heterocyclic Systems—Chemistry and Properties*, 2003; Vol. 7, pp 108–139.
6. A preliminary report of this work has been presented at 21st

International Symposium on the Organic Chemistry of Sulfur, ISOCS-XXI, Madrid, Spain, July 4–9, 2004.

7. (a) Tietze, L. F.; Hippe, T.; Stainmetz, A. *Synlett* **1996**, 1043–1044. (b) Witzeman, J. S. *Tetrahedron Lett.* **1990**, *31*, 1401–1404. (c) Tietze, L. F.; Evers, H.; Hippe, T.; Steinmetz, A.; Töpken, E. *Eur. J. Org. Chem.* **2001**, 1631–1634.
8. Strohmeier, G. A.; Kappe, O. C. *J. Comb. Chem.* **2002**, *4*, 154–161.
9. FTIR and ^{1}H NMR spectra registered on the resin immobilised compounds **5**, **6**, **9** were compared with those of the corresponding *O*-benzylester derivatives previously prepared in solution-phase (i.e. in Scheme 1: R=Me, Y=OBn, EDG=OEt).
10. (a) Lorsbach, B. A.; Kurth, M. J. *Chem. Rev.* **1999**, *99*, 1549–1581. (b) Yli-Kauhaluoma, J. *Tetrahedron* **2001**, *57*, 7053–7071 and reference cited therein.
11. Bartolozzi, A.; Pacciani, S.; Benvenuti, C.; Cacciarini, M.; Liguori, F.; Menichetti, S.; Nativi, C. *J. Org. Chem.* **2003**, *68*, 8529–8533.
12. Leconte, S.; Dujardin, G.; Brown, E. *Eur. J. Org. Chem.* **2000**, 639–643.
13. Alexandros Kiriazis, A.; Leikoski, T.; Mutikainen, I.; Yli-Kauhaluoma, J. *J. Comb. Chem.* **2004**, *6*, 283–285.
14. We demonstrated that α,α'-dioxothiones are also involved in ene-reactions: Capozzi, G.; Fragai, M.; Menichetti, S.; Nativi, C. *Eur. J. Org. Chem.* **2000**, 3653–3657.
15. A similar Retro-Claisen rearrangement was observed on α-keto-α'-carboxythiopyrans obtained by cycloaddition of thiones **3** (R=Me, Y=OMe, OEt) with anthracene: (a) Capozzi, G.; Menichetti, S.; Nativi, C.; Vergamini, C. *Synthesis* **1998**, 915–918. (b) Capozzi, G.; Giacomelli, S.; Menichetti, S.; Nativi, C. *Synthesis* **2001**, 409–412.
16. Zanaletti, R.; Freccero, M. *Chem. Commun.* **2002**, 1908–1909.
17. Preliminary attempts to identify the dioxothione moiety on resin **28** either by FTIR or ^{13}C NMR were unsatisfactory.
18. Boccardo, G.; Capozzi, G.; Giuntini, M.; Menichetti, S.; Nativi, C. *Tetrahedron* **1997**, *53*, 17383–17394.
19. Shimizu, H.; Kudo, N.; Kataoka, T.; Hori, M. *J. Chem. Soc., Perkin Trans 1* **2001**, 2269–2276.