Electrophilic Cyclisation of Bis(4-methoxybenzylthio)acetylene − Competition Between Ar_2-6 and Ar_1-5 Routes, Yielding 1*H*-2-Benzothiopyrans or Spiro Derivatives of Cyclohexadienone

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Treatment of bis(4-methoxybenzylthio)acetylene (**1**) with iodine monochloride yields different products in the presence or absence of nucleophiles such as water or alcohols. Normally, the electrophilic cyclisation of bis(benzylthio)acetylenes produces 1*H*-2-benzothiopyrans **2** by intramolecular *ortho* attack on the aromatic ring by a vinyl cation formed in situ (Ar_2-6 cyclisation). In the case of **1**, however, the high electron density in the *ipso* position of the aromatic ring favours *ipso* attack (Ar_1-5 route). The fate of the *ipso* σ complex is determined by the presence or absence of nucleophiles in the reaction medium. When nucleophiles are excluded, the σ complex is stabilised by 1,2-migration and formation of 1*H*-2-benzothiopyran **2a**. In the presence of water, the σ complex yields spirocyclohexadienone dihydrothiophenes **3a** and **3d**. In the presence of 3-methylbenzyl alcohol, the methoxy substituent of the 2-benzothiopyran ring is exchanged by the 3-methylbenzyloxy group in product **2d**. These findings are consistent with the formation of **2a**, **2c**, **2d** and **2f** by *ipso* – and not *ortho* – attack on the 4-methoxyphenyl ring. Similar results were obtained both with ICl and from a proton-induced cyclisation. In one-pot syntheses, **3a** and **3d** were transformed into 2-benzothiopyrylium salts **4a** and **4b** by tritylium tetrafluoroborate, and **3a** and **3b** were rearranged into the 6-hydroxy-substituted 2-benzothiopyrans **2b** and **2g** by proton catalysis.

Introduction

We recently described an efficient synthesis of 1*H*-2-benzo- and 1*H*-2-naphthothiopyrans involving a ring-closure of symmetrical bis(arylmethylthio)acetylenes in the presence of iodine monochloride or bromine, with methanol/chloroform as reaction medium.[1] In a related cyclisation of dialkynyl sulfides, 2*H*-benzothiopyran derivatives were obtained.[2] These Ar_2-6 cyclisations were regarded as intramolecular electrophilic substitutions of the aromatic ring by a vinyl cation formed in situ from the acetylenes and halonium ions. In agreement with this, when bis(4-methoxybenzylthio)acetylene (**1**) was treated with iodine monochloride, 3-iodo-6-methoxy-4-(4-methoxybenzylthio)-1*H*-benzothiopyran (**2a**) was produced in good yield.[1] In view of the known Ar_2-6/Ar_1-5 (*ortho*/*ipso*) competition in electrophilic cyclisation and substitution reactions of electron-rich aromatic ring systems,[3−5] we studied the cyclisation of **1** in the presence either of iodine monochloride or of protons in more detail. It was found that − as well as the 1*H*-2-benzothiopyran pathway − there is indeed also an intramolecular *ipso* attack on the 4-methoxyphenyl ring in **1** by the intermediate vinyl cation (Ar_1-5 pathway), which yields spiro derivatives **3**. For this *ipso* pathway, the presence of nucleophiles such as water in the reaction medium is necessary. In order to obtain an insight into the mechanism of the cyclisation in the presence of iodine monochloride, methanol from the reaction medium was replaced by 3-methylbenzyl alcohol. In this case the nucleophilic alcohol was introduced into the 1*H*-2-benzothiopyran **2d** as a benzyloxy substituent, identified by a NOESY experiment. Conclusions regarding the mechanism have been drawn. The spiro derivatives **3** are valuable synthons. Their rearrangement into 1*H*-2-benzothiopyran derivatives with new substitution patterns is described.

Results

Bis(4-methoxybenzylthio)acetylene (**1**) was subjected to conditions that had resulted in electrophilic Ar_2-6 cyclisation of other symmetrically substituted bis(arylmethylthio)acetylenes.[1] However, depending on the conditions, different products or mixtures were observed (Scheme 1). Only with strict exclusion of water (i) was the expected benzothiopyran **2a** obtained in high yield (84%). As a by-product, traces of 1*H*-2-benzothiopyran **2a′** were formed by

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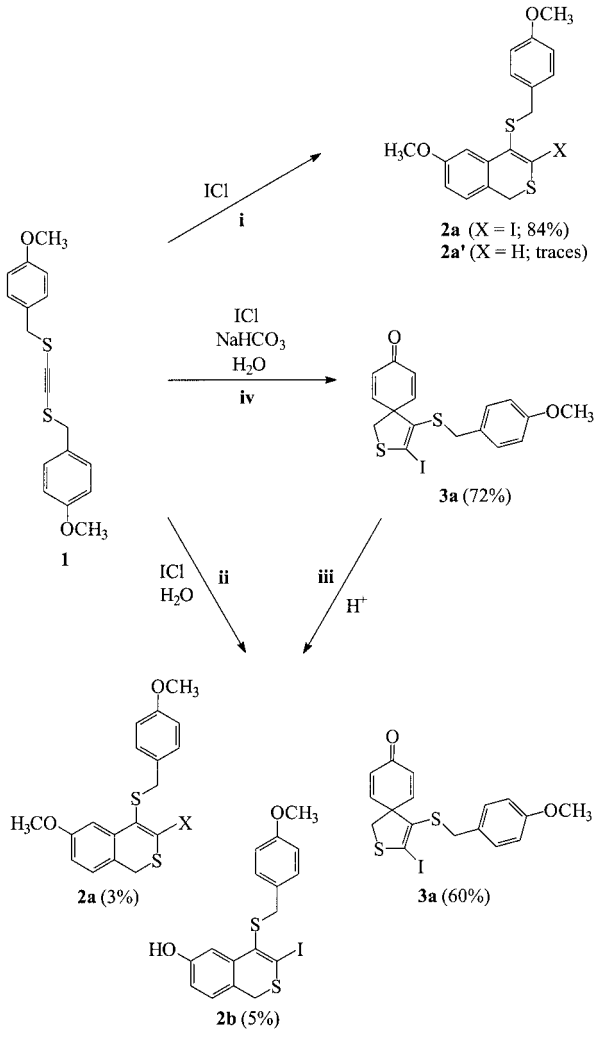
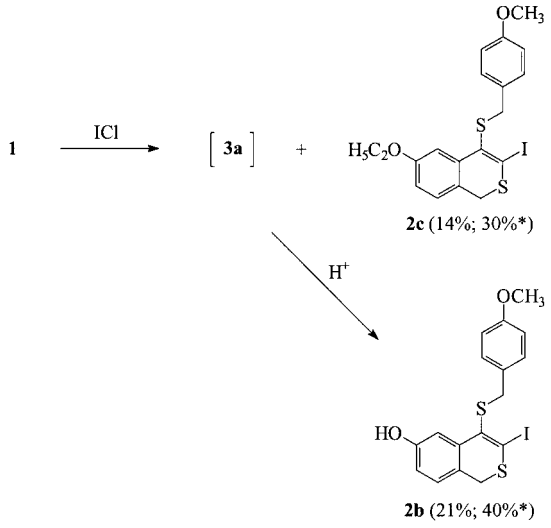
proton-induced cyclisation of **1**. Compound **2a′** was identified by ^{1}H NMR spectroscopy by comparison of its spectrum with that of an authentic specimen. In the presence of small amounts of water (ii), the spiro compound **3a** became the main product. By-products were **2a** and the 6-hydroxy-3-iodo-substituted 1*H*-2-benzothiopyran **2b**. The 1*H*-2-benzothiopyran **2b** was formed (iii) from **3a** by a proton-catalysed rearrangement (see cyclohexadienone/phenol rearrangement),[4,6,7] as verified by an independent experiment (treatment of **3a** with trifluoroacetic acid in acetonitrile). Use of sodium bicarbonate together with water (iv) shifted the product relation in favour of **3a**.



Scheme 1. Electrophilic cyclisation of bis(4-methoxybenzylthio)acetylene (**1**) in the presence of ICl in CH_3OH/CH_2Cl_2 with or without water in the reaction medium

In dry ethanol/dichloromethane, the spirocyclic ketone **3a** was formed as intermediate and rearranged into the isolated product **2b** (Scheme 2). In addition, the 6-ethoxy-substituted 1*H*-2-benzothiopyran **2c** was obtained and its structure was elucidated by NOESY experiments. An NOE was found between 5-H and the methylene protons of the 6-ethoxy group.



Scheme 2. Electrophilic cyclisation of **1** in the presence of ICl in C_2H_5OH/CH_2Cl_2; * yields according to ^{1}H NMR analysis

The structure of **3a** was deduced from its ^{1}H and ^{13}C NMR spectroscopic data and the precise molecular structure was established by an X-ray analysis (Figure 1). The bond angles around the spiro atom are weakly distorted tetrahedral [range 105.3(3)−112.1(3)°]. Within the crystal, the molecules are connected by I1···O1 contacts of 2.949(4) Å, considerably shorter than the sum of the corresponding van der Waals radii (3.50 Å)[8] and arranged in chains running parallel to the crystallographic *y* axis (Figure 2). The chains are stacked in the *x* direction and neighbouring stacks of chains are interlocked by the methoxybenzyl fragments of the molecules.

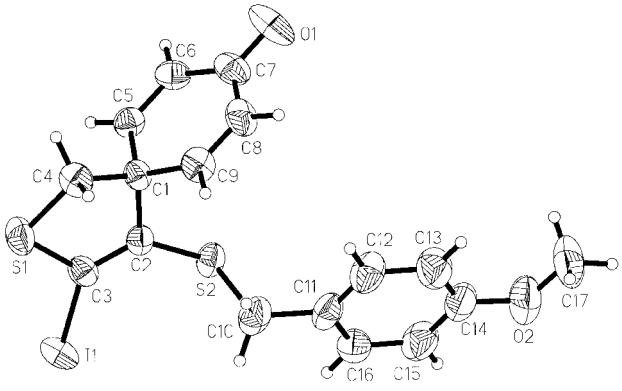


Figure 3. Molecular structure of **3a** (displacement ellipsoids at the 50% probability level, H atoms as small circles of arbitrary size); selected bond lengths [Å]: C1−C2 1.536(5), C1−C4 1.550(5), C1−C5 1.491 (5), C1−C9 1.510 (5), C3−I1 2.074(4), C7−O1 1.216(5)

To elucidate the mechanism of the cyclisation reaction of **1** in the presence of ICl, the methanol of the reaction medium was replaced by 3-methylbenzyl alcohol (Scheme 3).

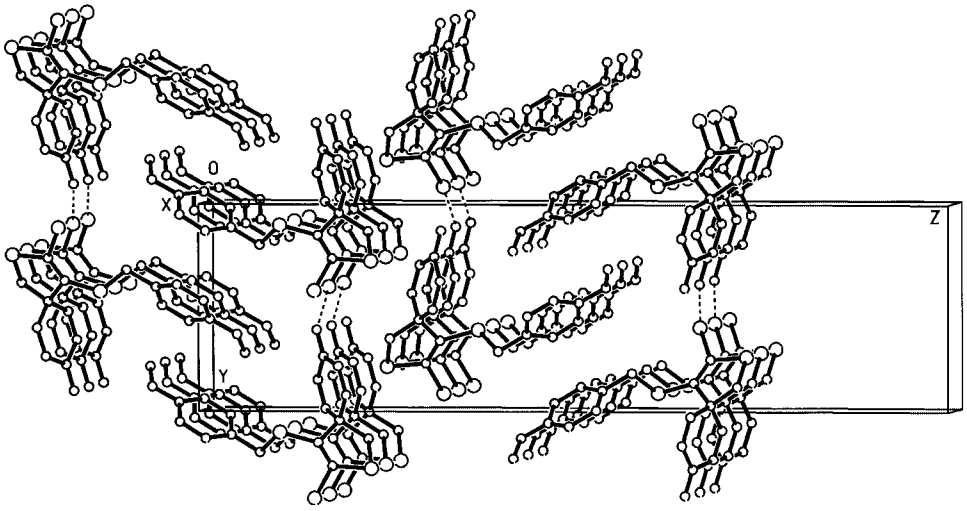
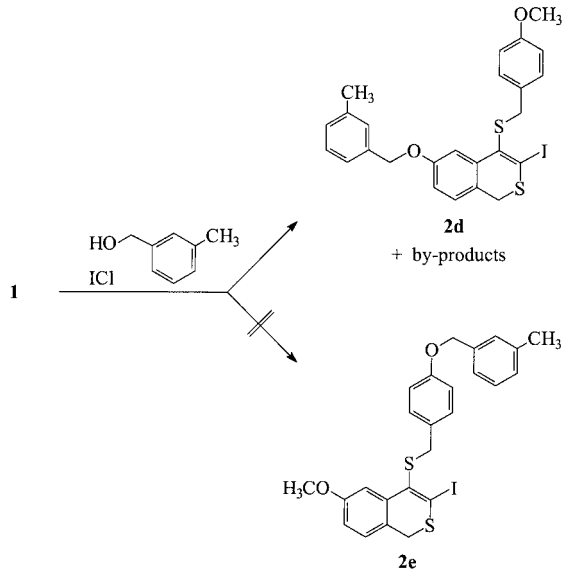


Figure 2. Molecular packing in the crystals of **3a**; I···O interactions are denoted by broken lines

This alcohol was chosen in order to avoid β-elimination from an expected *ipso* σ complex and to use the methyl and/or methylene group as indicators in the NMR spectroscopic product analysis. Under the standard conditions for the formation of 1*H*-2-benzothiopyrans a mixture of products was obtained. Separation of the individual compounds by column chromatography on silica gel was only partially successful. By comparison of the ^{1}H NMR spectra of separated fractions containing enriched components with the spectra of **2a** and **3a**, it was possible to rule out that the latter compounds had been formed in this experiment. From some fractions the 6-(3-methylbenzyloxy)-1*H*-2-benzothiopyran **2d** was separated and identified by NOESY experiments. An NOE was found between the proton in the 5-position of the 1*H*-2-benzothiopyran ring and the methylene protons of the 3-methylbenzyloxy substituent, as well as between the protons of the methoxy group and the adjacent aromatic protons of the 4-(4-methoxybenzylthio) side chain of **2d**. No indication of the formation of **2e** as an isomer of **2d** was found. A prepurified sample of the reaction mixture (the 3-methylbenzyl alcohol was separated by distillation and chromatography) was treated with tritylium tetrafluoroborate (solvent: MeCN) in order to convert 1*H*-2-benzothiopyrans and products of type **3** into the corresponding thiopyrylium salts. The products were analysed by ESI mass spectrometry. Besides the molecular ion peak of the pyrylium cation derived from **2d** (m/z = 545), other peaks were also observed. These corresponded to the pyrylium cations of **2a** (traces), a derivative of **2a** in which both methoxy groups are displaced by 3-methylbenzyloxy groups (m/z = 635) and further derivatives of **2a**, **2d**, and the compound with m/z = 635, in which one hydrogen atom is substituted by the C_8H_9O (3-methylbenzyloxy) group. These side-products are not considered in further discussions.[9]

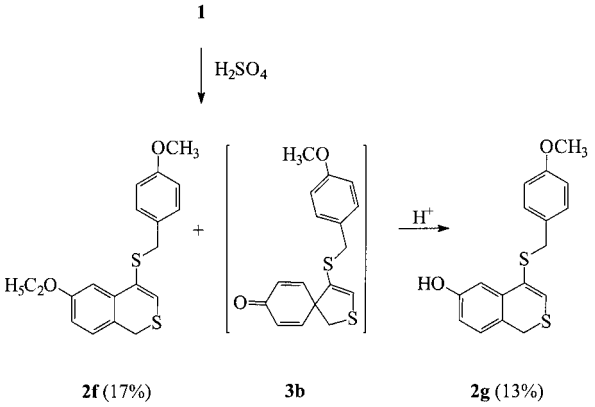
The electrophilic cyclisation of **1** could also be achieved in ethanol by high proton concentrations (Scheme 4). Here, no spiro derivative **3b** was isolated, but **2g** was formed from



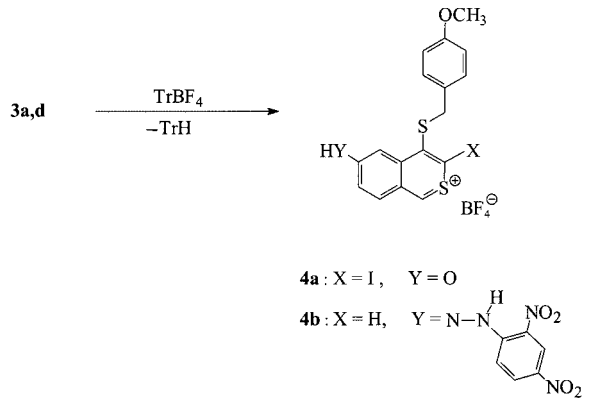
Scheme 3. Electrophilic cyclisation of **1** in the presence of ICl in 3-methylbenzyl alcohol

the intermediate **3b** by the proton-catalysed rearrangement described above. As a second reaction product, the 6-ethoxy-1*H*-2-benzothiopyran **2f** was chromatographically separated and identified by ^{1}H NMR spectroscopy. NOEs were again found by NOESY experiments, between 5-H of the 2-benzothiopyran ring and the methylene protons of the ethoxy group, as well as between the methoxy substituent of the side chain and the neighbouring aromatic protons.

To trap the spirocyclic intermediate **3b** formed from **1**, the cyclisation was performed in a solution of 2,4-dinitrophenylhydrazine in ethanol/sulfuric acid (Scheme 5). The low solubility of the hydrazone of **3b** in the reaction medium and the high water concentration influence the com-

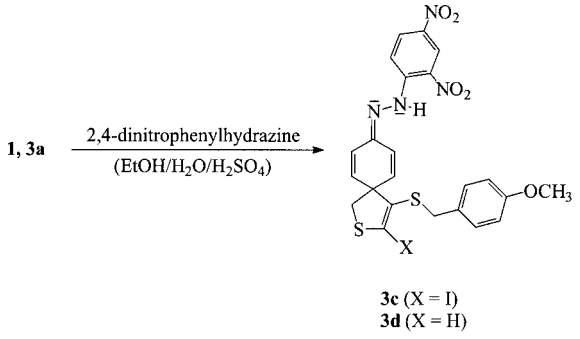


Scheme 4. Electrophilic cyclisation of **1** in the presence of H_2SO_4 in C_2H_5OH/H_2O



Scheme 6. 2-Benzothiopyrylium salts through rearrangement and hydride abstraction

petition between Ar_1-5 and Ar_2-6 cyclisation in favour of the former. The hydrazone **3d** was obtained in high yield (90%). From **3a** and 2,4-dinitrophenylhydrazine, the hydrazone **3c** was synthesised (Scheme 3).



3c (X = I)
3d (X = H)

Scheme 5. 2,4-Dinitrophenylhydrazones of 2-thiaspiro[4.5]deca-3,6,9-trien-8-ones from different starting materials

The 2-benzothiopyrylium salts **4a** and **4b** were obtained from the spiro derivatives **3a** or 3**d** and tritylium tetrafluoroborate in one-pot reactions by Lewis acid induced rearrangement[3] and hydride abstraction (Scheme 6).

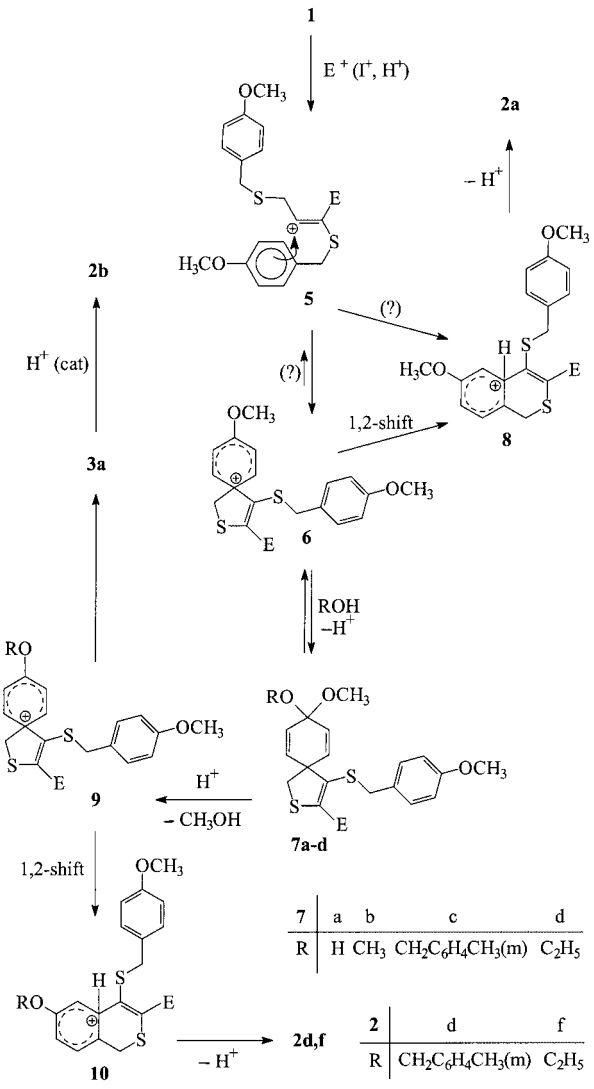
Discussion

Spiro derivatives **3** were formed in good yields by electrophilic cyclisation of **1** in the presence of ICl or protons and of nucleophiles in the reaction medium. Ar_1-5 cyclisation competes successfully with the Ar_2-6 cyclisation under these reaction conditions. The formation of 3-methylbenzyloxy-substituted 1*H*-2-benzothiopyran **2d** by replacement of the methanol used for the Ar_2-6 pathway by 3-methylbenzyl alcohol, or the formation of the ethoxy-substituted products **2c** and **2g** in ethanol, are clear indications of a σ complex formed by *ipso* substitution (Ar_1-5 pathway). This σ complex is also the first intermediate in the formation of 1*H*-2-benzothiopyrans **2** from **1** in the absence of nucleophiles in the reaction medium.

Reaction Mechanism of the Formation of 2 or 3 from 1

Aromatic *ipso* substitution is normally observed for rings containing strongly electron-withdrawing groups *para* to another substituent.[5,10,11] Our results are analogous, but in the special context of an intramolecular reaction proceeding through a stabilised electrophilic intermediate (vinyl cation). Products of intramolecular *ipso* substitution have been described in the literature,[12] but the mechanism giving rise to their formation was not provided. Scheme 7 therefore presents mechanistic details. Compound **3** is formed from **1** through the vinyl cation **5** and the σ complex **6**. By addition of water or alcohols the σ complex **6** is transformed into the hemiketal **7a**, which upon acid-induced elimination of methanol yields the spirocyclic ketone **3a** via **9**. This mechanism agrees with literature results.[3,7,13] A radical pathway (see refs.[14,15]) is less probable under the reaction conditions employed here.

From the σ complex **6**, the thermodynamically favoured 1*H*-2-benzothiopyran **2a** is formed either by a 1,2-migration or, less probably, by an equilibrium reaction through the stabilised vinyl cation **5**. In methanol it is not possible to distinguish between these two pathways. On the creation of competition between the methoxy-substituted σ complex **6** and a high concentration of 3-methylbenzyl alcohol, the methoxy substituent would be expected to be exchanged by this alcohol if the exchange reaction is fast in comparison to the product-forming steps. Since **2a** was formed only in traces (determined by ESI mass spectrometry) from **1** in the presence of 3-methylbenzyl alcohol, and the benzyloxy-substituted 1*H*-2-benzothiopyran **2d** was the main product, a fast exchange reaction can be assumed. Furthermore, the exclusive formation of **2d** rather than a mixture of **2d** and **2e** strongly argues for the 1,2-migration in the σ complexes **6** and **9** − and not an equilibrium with a vinyl cation of type **5** followed by an *ortho* attack − as the product-determining step.



Scheme 7. Proposed mechanism for product formation

Further experiments support the decisive role of the *ipso* σ complexes for product formation. An exchange of the methoxy group by an ethoxy group in the 1*H*-2-benzothiopyran ring when using **1** and ICl in dry ethanol/dichloromethane or protons in ethanol/water is a clear argument for an *ipso* complex as the product-determining intermediate in electrophilic cyclisation reactions of **1**. This mechanism is further substantiated by the formation of **3a** through an assumed β-elimination from **9**.

Conclusion

The mechanism of the electrophilic cyclisation of bis(arylmethylthio)acetylenes is described in a special case. Normally, 1*H*-2-benzothiopyrans are formed from these acetylenes, through intramolecular *ortho* attack of vinyl cations on the aromatic ring (Ar_2-6 ring closure). However, the regioselectivity of this reaction depends on the substituents on the aromatic ring and therefore on the free activation enthalpy of the transition states of the intermediates. In the case of bis(4-methoxybenzylthio)acetylene (**1**), *ipso* attack of the vinyl cation **5** on the 4-methoxyphenyl ring is kinetically favoured. The isolated and/or identified 1*H*-2-benzothiopyrans **2a**−**2d**, **2f** and **2g** (some with exchanged alkoxy substituents), as well as the spirocyclic ketones **3a** and **3c**, substantiate this mechanistic proposal. As far as we know, no other reaction in which the spiro derivatives **3** are obtained in good yields has been described. The synthetic potential of **3** is high, due to their conversion into 1*H*-2-benzothiopyrans **2** or the corresponding thiopyrylium salts **4**.

Experimental Section

General Remarks: Melting points were determined with a micro melting point apparatus and are corrected. ^1H and ^{13}C NMR spectra were recorded with Varian spectrometers (Gemini 300, Unity 500). Chemical shifts are reported as values in ppm from internal TMS. Standard Varian software was employed for all NMR experiments. The NOEs were measured by 2D NOESY; the mixing time was 200−800 ms. The samples were degassed by at least two freeze-thaw cycles. The ESI mass spectra were performed with a Finnigan MAT LCQ spectrometer (solvent: MeCN; flow: 8 L/min; ESI spray voltage 4.6 kV; cap. temp. 200 °C; cap. voltage 34 V). UV/Vis absorptions are given as λ in nm (ε in L/mol·cm). All reported elemental analyses were averaged from two independent determinations. Prefabricated silica gel sheets (Sigma-Aldrich) were used for TLC. Reagents were obtained from commercial sources. The synthesis of bis(4-methoxybenzylthio)acetylene (**1**) and 3-iodo-6-methoxy-4-(4-methoxybenzylthio)-1*H*-2-benzothiopyran (**2a**) has already been described.[1]

3-Iodo-4-(4-methoxybenzylthio)-1*H*-2-benzothiopyran-6-ol (2b): Compound **3a** (90 mg, 0.2 mmol) was dissolved in dry CH_3CN (3 mL), and CF_3COOH (0.3 mL) was added. The mixture was stirred at room temperature for 10 h and then concentrated in vacuo to 1 mL. After neutralization with saturated $NaHCO_3$ solution (5 mL), diethyl ether (10 mL) was added. The organic phase was separated and the water phase was extracted five times with diethyl ether (3 mL each). The combined organic phases were washed twice with water and dried with $MgSO_4$. The solvent was evaporated in vacuo and the residue was dissolved in CH_2Cl_2. Compound **2b** (53 mg, 59%) precipitated upon addition of a fivefold volume of *n*-hexane. TLC (cyclohexane/ethyl acetate, 4:1): R_f(**3a**) = 0.25, R_f(**2b**) = 0.40; slightly yellow crystals, m.p. 118−120 °C. ^1H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 3.47 (s, 2 H, CH_2), 3.75 (s, 3 H, OCH_3), 3.79 (s, 2 H, CH_2), 6.72−6.77 (m, 3 H), 6.92 (d, J = 8.1 Hz, 1 H), 6.98 (d, J = 8.5 Hz, 2 H), 7.40 (d, J = 2.4 Hz, 1 H) ppm. ^{13}C NMR (300 MHz, $CDCl_3$, 25 °C): δ = 35.35 (CH_2), 39.22 (CH_2), 55.29 (OCH_3), 98.39, 113.59, 114.40, 115.17, 122.79, 127.76, 128.91, 130.24, 133.67, 134.70, 155.34, 158.62 ppm. UV/Vis (CH_3CN): λ_{max} = 227 (26900), 250 (sh, 14300), 319 (5660), 339 (sh, 5180) nm. IR (KBr): $\tilde{\nu}$ = 3355 cm^{-1} (broad). $C_{17}H_{15}IO_2S_2$ (442.34): calcd. C 46.16, H 3.42, S 14.50; found C 46.53, H 3.59, S 14.36.

6-Ethoxy-3-iodo-4-(4-methoxybenzylthio)-1*H*-2-benzothiopyran (2c) and 2b: Compound **1** (100 mg, 0.3 mmol) was dissolved in dry CH_2Cl_2 (1.5 mL), and absolute ethanol (4 mL) was added. The solution was cooled to −70 °C with stirring and under exclusion of water. ICl (54 mg, 0.34 mmol) in CH_2Cl_2 (1.5 mL) was added drop-

wise to the suspension formed. The mixture was stirred for 30 min at −70 °C and the solution was then allowed to warm to room temperature for 10 min. The solvent was evaporated in vacuo (temperature of the bath 25 °C, p = 150−20 mbar) and the obtained residue was separated chromatographically on silica gel with cyclohexane/ethyl acetate, 4:1. **Compound 2c (1st Fraction):** 19 mg (14%), R_f = 0.64. ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 1.41 (t, J = 7 Hz, 3 H, CH_3-ethoxy), 3.48 (s, 2 H, CH_2-benzyl), 3.77 (s, 3 H, OCH_3), 3.80 (s, 2 H, CH_2-thiopyran), 4.04 (q, J = 7 Hz, 2 H, CH_2-ethoxy), 6.73 (d, J = 8.7 Hz, 2 H), 6.80 (m, 2 H), 6.95 (dd, J = 8.3, 3.1 Hz, 2 H), 7.48 (d, J = 2.4 Hz, 1 H) ppm. **2b (2nd Fraction):** 28 mg (21%), R_f = 0.40.

3-Iodo-4-(4-methoxybenzylthio)-6-(3-methylbenzyloxy)-1*H*-2-benzothiopyran (2d): Compound **1** (100 mg, 0.3 mmol) was dissolved in CH_2Cl_2 (1.5 mL), and 3-methylbenzyl alcohol (4 mL) was added. The solution was stirred under argon and cooled to −10 °C. A solution of ICl (54 mg, 0.3 mmol) in CH_2Cl_2 (1.5 mL) was added dropwise to the suspension formed. After 1 h of stirring at −5 °C and 30 min at room temperature, the solvent was removed in vacuo (bath temperature 85 °C, p = 0.1 mbar) and the residue was separated chromatographically on silica gel with cyclohexane/ethyl acetate, 9:1. Fractions of eluate (10 mL) were analysed by TCL. The fractions containing pure **2d** (R_f = 0.63) were collected and the solvent was evaporated in vacuo. The oily residue of **2d** crystallised after some hours. **Compound 2d:** 30 mg (18%), m.p. 123−124 °C. ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 2.35 (s, 3 H, CH_3-tolyl), 3.45 (s, 2 H, CH_2-thiopyran), 3.65 (s, 2 H, CH_2-benzyl), 3.74 (s, 3 H, OCH_3), 5.05 (s, 2 H, CH_2-tolyl), 6.71 (d, J = 8.6 Hz, 2 H), 6.86−6.91 (m, 2 H), 6.96 (d, J = 8.3 Hz, 1 H), 7.11−7.27 (m, 4 H), 7.52 (d, J = 2.3 Hz, 1 H) ppm. ^{13}C NMR (300 MHz, $CDCl_3$, 25 °C): δ = 22.32 (CH_3-tolyl), 36.28 (CH_2-thiopyran), 39.99 (CH_2-benzyl), 56.22 (CH_3O), 71.25 (CH_2O), 98.74 (C−I), 114.65, 114.89, 115.10, 116.30, 124.11, 125.65, 128.60, 129.30, 129.67, 129.89, 130.08, 130.50, 131.32, 134.54, 136.28, 137.96, 139.48, 159.68, 159.81 ppm. MS ESI (**2d** + Ph_3CBF_4): m/z (%) = 545 (100) $[M]^+$, 418 (15) $[M^+ - I]$.

6-Ethoxy-4-(4-methoxybenzylthio)-1*H*-2-benzothiopyran (2f) and 4-(4-Methoxybenzylthio)-1*H*-2-benzothiopyran-6-ol (2g): Compound **1** (198 mg, 0.6 mmol) was dissolved in ethanol (10 mL), and a mixture of ethanol (5 mL), H_2O (1.5 mL) and concd. H_2SO_4 (1.5 mL) was added. After the mixture had been kept for 19 h at room temperature, H_2O (5 mL) was added to the dark solution, and the mixture was extracted six times with CH_2Cl_2 (5 mL each). The organic phases were pooled and washed twice with $NaHCO_3$ solution and H_2O, and then dried with $MgSO_4$. After evaporation of the solvent, the residue obtained was separated on silica gel with cyclohexane/ethyl acetate, 4:1. **Compound 2f (1st Fraction):** 36 mg (17%); R_f = 0.82, colourless oil. ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 1.41 (t, J = 7 Hz, 3 H, CH_3-ethoxy), 3.63 (s, 2 H, CH_2-benzyl), 3.76 (s, 3 H, OCH_3), 3.79 (s, 2 H, CH_2-thiopyran), 4.04 (q, J = 7 Hz. 2 H, CH_2-ethoxy), 6.63 (s, 1 H), 6.76−6.82 (m, 3 H), 7.02 (t, J = 8.0 Hz, 1 H), 7.04 (d, J = 8.2 Hz, 2 H), 7.44 (d, J = 2.4 Hz, 1 H) ppm. ^{13}C NMR (300 MHz, $CDCl_3$, 25 °C): δ = 14.82 (CH_2-ethoxy), 30.31 (CH_2-benzyl), 38.37 (CH_2-thiopyran), 55.21 (OCH_3), 63.59 (CH_2-ethoxy), 111.74, 113.70, 114.51, 121.77, 127.67, 128.92, 129.51, 130.06, 130.46, 133.87, 158.57, 158.73 ppm. **Compound 2g (2nd Fraction):** 8 mg (13%), R_f = 0.61, colourless crystals, m.p. 93−95 °C. ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 3.62 (s, 2 H, CH_2), 3.76 (s, 3 H, OCH_3), 3.77 (s, 2 H, CH_2), 6.63 (s, 1 H), 6.73 (m, 1 H), 6.75 (d, J = 8.2 Hz, 2 H), 6.98 (d, J = 8.1 Hz, 1 H), 7.04 (d, J = 8.4 Hz, 2 H), 7.36 (d, J = 2.4 Hz, 1 H) ppm. ^{13}C NMR (300 MHz, $CDCl_3$, 25 °C): δ = 30.29 (CH_2), 38.43 (CH_2), 55.27 (CH_3O), 112.60, 113.76, 115.22, 121.79, 127.97, 128.40, 129.38, 129.54, 130.11, 134.20, 155.53, 158.61 ppm. UV/Vis (CH_3CN): λ_{max} = 226 (10353), 280 (3817), 426 (959) nm. IR (KBr): $\tilde{\nu}$ = 3436 cm^{-1} (broad).

3-Iodo-4-(4-methoxybenzylthio)-2-thiaspiro[4.5]-deca-3,6,9-trien-8-one (3a): Compound **1** (248 mg, 0.75 mmol) was dissolved in CH_2Cl_2 (4 mL), methanol (6 mL) and H_2O (1 mL). $NaHCO_3$ (630 mg, 7.5 mmol) was added to the solution in order to neutralise HCl formed by the reaction in situ. The mixture was cooled to −78 °C with solid CO_2/acetone. ICl (134 mg, 0.84 mmol) in CH_2Cl_2 (2 mL) was added dropwise over 10 min. The reaction was complete after a further 10 min at −78 °C [monitoring by TLC with cyclohexane/ethyl acetate, 4:1; R_f(**1**) = 0.55, R_f(**3a**) = 0.22−0.25. The solvent was removed in vacuo (bath temperature 25 °C, p = 150−50 mbar). The remaining solid was extracted with CH_2Cl_2 (3 mL), the solution was filtered, and **3a** was precipitated with cyclohexane (10 mL). Light, voluminous crystals were formed after some minutes. Yield 240 mg (72%); m.p. 111−112 °C. ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 3.35 (s, 2 H, CH_2), 3.78 (s, 3 H, OCH_3), 3.80 (s, 2 H, CH_2), 6.19 (d, J = 10 Hz, 2 H), 6.55 (d, J = 10 Hz, 2 H), 6.81 (d, J = 8.5 Hz, 2 H), 7.10 (d, J = 8.5 Hz, 2 H) ppm. ^{13}C NMR (300 MHz, $CDCl_3$, 25 °C): δ = 39.75 (CH_2), 43.86 (CH_2), 55.32 (OCH_3), 57.52, 102.58, 113.61, 128.74, 129.95, 130.57, 131.00, 147.20, 159.12, 185.25 (C=O) ppm. UV/Vis (CH_3CN): λ_{max} = 280 (8100), 301 (sh) nm. IR (KBr): $\tilde{\nu}$ = 1660 cm^{-1}. MS EI: m/z (%) = 442 (14) $[M^+]$, 316 (3) $[C_{17}H_{15}S_2O_2^+]$, 253 (6) $[C_5H_2IS_2^+]$, 227 (6) $[C_{15}H_{15}S_2^+]$, 215 (3) $[C_2IS_2^+]$, 149 (4) $[C_8H_5SO^+]$, 135 (3) $[C_7H_3SO^+]$, 127 (5) $[I^+]$, 121 (100) $[C_8H_9O^+]$, 58 (15) $[C_2H_2S^+]$, 43 (33) $[C_3H_7^+]$. $C_{17}H_{15}IO_2S_2$ (442.34): calcd. C 46.16, H 3.42, S 14.50; found C 46.38, H 3.48, S 14.69.

Crystal Data and X-ray Structure Analysis of 3a: $C_{17}H_{15}IO_2S_2$, M_r = 442.34, yellow plates from diethyl ether, X-ray diffraction data collected with a Stoe STADI-4 four-circle diffractometer with graphite-monochromatized Mo-K_α radiation (λ = 0.71073 Å) in ω/2θ scanning mode at T = 293 K, crystal size 0.49 × 0.34 × 0.30 mm, orthorhombic, space group $P2_12_12_1$, a = 5.7013(6), b = 9.1416(10), c = 33.280(4) Å, V = 1734.5(3) Å^3, Z = 4, $D_{calcd.}$ = 1.694 g cm^{-3}, μ = 2.090 mm^{-1} (empirical absorption correction), F(000) = 872, 5833 measured reflections in the range 1.22° ≤ θ ≤ 30.00°, 5028 unique reflections (R_{int} = 0.0156), 3537 observed reflections [$I > 2\sigma(I)$]. Structure solved by direct methods (SHELXS-86)[16] and refined by full-matrix least-squares techniques against F^2 (SHELXL-93),[17] hydrogen atoms placed at calculated positions and treated according to the riding model, 199 parameters, $w = 1/[\sigma^2(F_o)^2 + (0.0451P)^2 + 0.16P]$ {with $P = [(F_o)^2 + 2(F_c)^2]/3$}, $R1_{obsd.}$ = 0.034, $wR2_{obsd.}$ = 0.078, $R1_{all}$ = 0.066, $wR2_{all}$ = 0.087, GOF = 1.039, Flack parameter = −0.01(2), max./min. electron density 1.052/−0.613 e Å^{-3}. Figures 1 and 2 were plotted using the program XP/PC.[18] CCDC-127357 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge at www.ccdc.cam.ac.uk/conts/retrieving.html or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK [Fax: (internat.) + 44-1223/336-033; E-mail: deposit@ccdc.cam.ac.uk].

2,4-Dinitrophenylhydrazone of 3-Iodo-4-(4-methoxybenzylthio)-2-thiaspiro[4.5]deca-3,6,9-trien-8-one (3c): Compound **3a** (85 mg, 0.2 mmol), dissolved in ethanol (25 mL), was poured into a solution of 2,4-dinitrophenylhydrazine (400 mg, 2 mmol) in H_2SO_4 (2 mL), H_2O (3 mL) and ethanol (10 mL), and the mixture was stirred for 1 h at room temperature. Red crystals started to precipitate almost instantaneously. Finally, they were suction-filtered,

washed twice with ethanol and recrystallised from ethanol (91 mg, 75%); m.p. 154−156 °C. ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 3.34 (d, *J* = 3.0 Hz, 2 H, CH_2), 3.78 (s, 3 H, OCH_3), 3.84 (q, *J* = 12.4 Hz, 2 H, CH_2), 6.01 (d, *J* = 9.4 Hz, 1 H), 6.21 (d, *J* = 9.8 Hz, 1 H), 6.45 (d, *J* = 9.7 Hz, 1 H), 6.59 (d, *J* = 10.0 Hz, 1 H), 6.82 (d, *J* = 8.1 Hz, 2 H), 7.14 (d, *J* = 8.1 Hz, 2 H), 8.03 (d, *J* = 9.5 Hz, 1 H), 8.34 (d, *J* = 9.2 Hz, 1 H), 9.13 (s, 1 H), 11.59 (s, 1 H, NH) ppm. ^{13}C NMR (300 MHz, $CDCl_3$, 25 °C): δ = 39.70 (CH_2), 45.13 (CH_2), 55.31 (OCH_3), 58.21, 101.26, 113.86, 114.96, 116.56, 123.40, 127.27, 129.15 129.73, 130.03, 130.49, 132.97, 135.96, 138.32, 141.81, 144.42, 144.92, 159.11 ppm. UV/Vis (CH_2Cl_2): λ_{max} = 392 nm. $C_{23}H_{19}IN_4O_5S_2$ (622.46): calcd. C 44.38, H 3.08, N 9.03, S 10.30; found C 43.94, H 3.20, N 8.64, S 10.07.

2,4-Dinitrophenylhydrazone of 4-(4-Methoxybenzylthio)-2-thiaspiro-[4.5]deca-3,6,9-trien-8-one (3d): Compound **1** (33 mg, 0.1 mmol), dissolved in ethanol (10 mL), was poured into a solution of 2,4-dinitrophenylhydrazine (200 mg, 1 mmol) in H_2SO_4 (1 mL), H_2O (1.5 mL) and ethanol (5 mL), and the mixture was stirred for 1 h at room temperature. Red-orange crystals started to precipitate after 1 min. Finally, they were suction-filtered, washed twice with ethanol and recrystallised from ethanol (44 mg, 89%); m.p. 153−154 °C. ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 3.29 (d, *J* = 4.9 Hz, 2 H, CH_2), 3.76 (s, 3 H, OCH_3), 3.83 (s, 2 H, CH_2), 6.01 (s, 1 H), 6.24 (d, *J* = 9.8 Hz, 1 H), 6.52 (d, *J* = 10.0 Hz, 2 H), 6.74 (d, *J* = 10.2 Hz, 1 H), 6.81 (d, *J* = 8.6 Hz, 2 H), 7.16 (d, *J* = 8.6 Hz, 2 H), 8.01 (d, *J* = 9.6 Hz, 1 H), 8.31 (d, *J* = 9.5 Hz, 1 H), 9.12 (s, 1 H), 11.62 (s, 1 H, NH) ppm. ^{13}C NMR (300 MHz, $CDCl_3$, 25 °C): δ = 38.68 (CH_2), 42.99 (CH_2), 55.22 (OCH_3), 58.63, 113.91, 115.04, 116.51, 123.32, 124.15, 127.32, 128.29, 129.42, 129.63, 129.94, 136.52, 138.21, 142.70, 144.42, 145.05, 158.95 ppm. UV/Vis (CH_2Cl_2): λ_{max} = 392 nm. $C_{23}H_{20}N_4O_5S_2$ (496.56): calcd. C 55.63, H 4.06, N 11.29, O 16.10, S 12.91; found C 55.27, H 4.26, N 10.90, O 16.45, S 12.92.

General Procedure for the Synthesis of the 2-Benzothiopyrylium Salts 4 by Hydride Abstraction with Tritylium Tetrafluoroborate from 3:[1] All steps were carried out under argon and exclusion of moisture. Compound **3** (0.2 mmol) was dissolved in dry CH_2Cl_2 (1.5 mL) and added in one portion to an ice-cold solution of $TrBF_4$ (185 mg; 0.56 mmol) in CH_2Cl_2 (1.5 mL). The resulting dark liquid was stirred for 30 min at 0 °C and for a further 30 min at room temperature. The solution was concentrated to 1 mL in vacuo, and poured into dry diethyl ether (10 mL) with vigorous stirring. The solid formed was collected, washed twice with diethyl ether and dried in a vacuum desiccator. If necessary, recrystallisation was possible in acetic anhydride with some loss of material (incomplete precipitation).

6-Hydroxy-4-iodo-4-(4-methoxybenzylthio)-2-benzothiopyrylium Tetrafluoroborate (4a): 35 mg (66%) of **4a** was obtained from 44 mg (0.1 mmol) of **3a**; yellow crystals, m.p. 154−155 °C. ^{1}H NMR (300 MHz, CD_3CN, 25 °C): δ = 3.68 (s, 3 H, OCH_3), 4.16 (s, 2 H, CH_2), 6.68 (d, *J* = 8.5 Hz, 2 H), 6.96 (d, *J* = 8.5 Hz, 2 H), 7.57 (dd, *J* = 9.0, 2.19 Hz, 1 H), 8.29 (d, *J* = 2.0 Hz, 1 H), 8.35 (d, *J* = 9.0 Hz, 1 H), 10.03 (s, 1 H, S^+=CH) ppm. ^{13}C NMR (300 MHz, CD_3CN, 25 °C): δ = 41.53 (CH_2), 55.98 (OCH_3), 113.20 (C−I), 114.89, 115.99, 118.31, 124.86, 128.81, 130.31, 131.47, 139.92, 145.16, 160.40, 168.43, 173.21 ppm. UV/Vis (CH_3CN): λ_{max} = 282 (18800), 371 (8100), 422 (7100) nm. IR (KBr): $\tilde{\nu}$ = 1061 cm^{-1} (BF_4^-). MS ESI: *m*/*z* (%) = 441 (100) [M^+]. $C_{17}H_{14}S_2O_2I^+BF_4^-$ (528.13): calcd. C 38.66, H 2.67, S 12.14; found C 38.98, H 2.84, S 12.06.

6-(2,4-Dinitrophenylhydrazino)-4-(4-methoxybenzylthio)benzothiopyrylium Tetrafluoroborate (4b): 110 mg (95%) from **3d** (100 mg, 0.2 mmol); m.p. > 145 °C (dec.). ^{1}H NMR (300 MHz, CD_3CN, 25 °C): δ = 3.76 (s, 3 H, OCH_3), 4.33 (s, 2 H, CH_2), 6.86 (d, *J* = 8.4 Hz, 2 H), 7.28 (d, *J* = 8.0 Hz, 2 H), 7.36 (d, *J* = 9.5 Hz, 1 H), 7.69 (d, *J* = 9.2 Hz, 1 H), 7.78 (s, 1 H), 8.30 (m, 3 H), 8.99 (s, NH), 9.03 (d, *J* = 2.3 Hz, 1 H), 9.79 (s, NH), 9.85 (d, *J* = 2.6 Hz, 1 H) ppm. ^{13}C NMR (300 MHz, CD_3CN, 25 °C): δ = 38.20 (CH_2), 56.17 (OCH_3), 99.18, 115.41, 116.30, 117.65, 118.24, 124.32, 127.43, 128.08, 128.81, 128.95, 129.46, 129.69, 130.31, 131.50 (2 C), 131.57 (2 C), 138.37, 144.27, 148.75, 156.89, 160.36, 160.77 ppm. IR (KBr): $\tilde{\nu}$ = 1062 cm^{-1} (BF_4^-), 3311 cm^{-1} (NH). MS EI: *m*/*z* (%) = 493 (20) [$M^+ - BF_4^-$], 183 (18) [$C_6H_4N_3O_4^+$], 121 (100) [$C_8H_9O^+$]. UV/Vis (DMSO): λ_{max} = 271 (22800), 369 (8040), 538 (28700) nm. $C_{23}H_{19}N_4O_5S_2^+BF_4$ (582.36): calcd. C 47.44, H 3.29, N 9.62, S 11.01; found C 47.56, H 3.46, N 9.34, S 11.90.

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