Electrophilic Cyclisation of Bis(4-methoxybenzylthio)acetylene – Competition Between Ar₂-6 and Ar₁-5 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 (Ar₂-6 cyclisation). In the case of **1**, however, the high electron density in the *ipso* position of the aromatic ring favours *ipso* attack (Ar₁-5 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**.

Introduction

We recently described an efficient synthesis of 1H-2benzo- and 1H-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, 2H-benzothiopyran derivatives were obtained.^[2] These Ar₂-6 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)-1Hbenzothiopyran (2a) was produced in good yield.^[1] In view of the known Ar₂-6/Ar₁-5 (ortholipso) competition in electrophilic cyclisation and substitution reactions of electronrich 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 1H-2-benzothiopyran pathway – there is indeed also an in-

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Beutenbergstrasse 11, 07745 Jena, Germany ^[b] Department of Chemistry Martin Luther In the presence of 3-methylbenzyl alcohol, the methoxy substituent of the 2-benzothiopyran ring is exchanged by the 3methylbenzyloxy 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.

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tramolecular *ipso* attack on the 4-methoxyphenyl ring in **1** by the intermediate vinyl cation (Ar₁-5 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(arylmethyl-thio)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 byproduct, traces of 1*H*-2-benzothiopyran **2a**' were formed by

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proton-induced cyclisation of 1. Compound 2a' was identified by ¹H 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*-2benzothiopyran 2b was formed (iii) from 3a by a protoncatalysed 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 ¹H NMR analysis

The structure of **3a** was deduced from its ¹H and ¹³C 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 $105.3(3)-112.1(3)^{\circ}$]. 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 [A]: 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 1H-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 ¹H 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)-1H-2benzothiopyran 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 1H-2benzothiopyrans 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 C₈H₉O (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 3methylbenzyl alcohol

the intermediate **3b** by the proton-catalysed rearrangement described above. As a second reaction product, the 6ethoxy-1*H*-2-benzothiopyran **2f** was chromatographically separated and identified by ¹H 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 $\rm H_2SO_4$ in $\rm C_2H_5OH/H_2O$

petition between Ar₁-5 and Ar₂-6 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).



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 3d 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. Ar₁-5 cyclisation competes successfully with the Ar₂-6 cyclisation under these reaction conditions. The formation of 3-methylbenzyloxy-substituted 1*H*-2-benzothiopyran **2d** by replacement of the methanol used for the Ar₂-6 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 (Ar₁-5 pathway). This σ complex is also the first intermediate in the





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

formation of 1H-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 benzyloxysubstituted 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 1H-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 3is high, due to their conversion into 1H-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 ¹³C 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 freezethaw cycles. The ESI mass spectra were performed with a Finnigan MAT LCO 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)-1H-2-benzothiopyran (2a) has already been described.[1]

3-Iodo-4-(4-methoxybenzylthio)-1H-2-benzothiopyran-6-ol (2b): Compound 3a (90 mg, 0.2 mmol) was dissolved in dry CH₃CN (3 mL), and CF₃COOH (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 NaHCO3 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 MgSO₄. The solvent was evaporated in vacuo and the residue was dissolved in CH₂Cl₂. Compound 2b (53 mg, 59%) precipitated upon addition of a fivefold volume of nhexane. TLC (cyclohexane/ethyl acetate, 4:1): $R_{\rm f}(3a) = 0.25$, $R_{\rm f}(2b) = 0.40$; slightly yellow crystals, m.p. 118–120 °C. ¹H NMR (300 MHz, CDCl₃, 25 °C): δ = 3.47 (s, 2 H, CH₂), 3.75 (s, 3 H, OCH₃), 3.79 (s, 2 H, CH₂), 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. ¹³C NMR (300 MHz, CDCl₃, 25 °C): δ = 35.35 (CH₂), 39.22 (CH₂), 55.29 (OCH₃), 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 (CH₃CN): $\lambda_{max} = 227$ (26900), 250 (sh, 14300), 319 (5660), 339 (sh, 5180) nm. IR (KBr): $\tilde{v} = 3355 \text{ cm}^{-1}$ (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 dropwise 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%), $R_{\rm f} = 0.64$. ¹H NMR (300 MHz, CDCl₃, 25 °C): $\delta = 1.41$ (t, J = 7 Hz, 3 H, CH₃-ethoxy), 3.48 (s, 2 H, CH₂-benzyl), 3.77 (s, 3 H, OCH₃), 3.80 (s, 2 H, CH₂-thiopyran), 4.04 (q, J = 7 Hz, 2 H, CH₂-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%), $R_{\rm f} = 0.40$.

3-Iodo-4-(4-methoxybenzylthio)-6-(3-methylbenzyloxy)-1H-2-benzothiopyran (2d): Compound 1 (100 mg, 0.3 mmol) was dissolved in CH₂Cl₂ (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 CH₂Cl₂ (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 ($R_{\rm f} = 0.63$) 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. ¹H NMR (300 MHz, CDCl₃, 25 °C): $\delta = 2.35$ (s, 3 H, CH₃-tolyl), 3.45 (s, 2 H, CH₂-thiopyran), 3.65 (s, 2 H, CH₂-benzyl), 3.74 (s, 3 H, OCH₃), 5.05 (s, 2 H, CH₂-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. ¹³C NMR (300 MHz, CDCl₃, 25 °C): $\delta = 22.32$ (CH₃-tolyl), 36.28 (CH₂-thiopyran), 39.99 (CH₂benzyl), 56.22 (CH₃O), 71.25 (CH₂O), 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 + Ph₃CBF₄): m/z (%) = 545 (100) [M]⁺, 418 (15) $[M^+ - I]$.

6-Ethoxy-4-(4-methoxybenzylthio)-1H-2-benzothiopyran (2f) and 4-(4-Methoxybenzylthio)-1H-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, H₂O (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 NaHCO₃ solution and H₂O, and then dried with MgSO₄. 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%); $R_{\rm f}$ = 0.82, colourless oil. ¹H NMR (300 MHz, CDCl₃, 25 °C): $\delta = 1.41$ 3 H, OCH₃), 3.79 (s, 2 H, CH₂-thiopyran), 4.04 (q, J = 7 Hz. 2 H, CH₂-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. ¹³C NMR (300 MHz, CDCl₃, 25 °C): $\delta = 14.82$ (CH₂-ethoxy), 30.31 (CH₂-benzyl), 38.37 (CH₂-thiopyran), 55.21 (OCH₃), 63.59 (CH₂-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. ¹H NMR (300 MHz, CDCl₃, 25 °C): δ = 3.62 (s, 2 H, CH₂), 3.76 (s, 3 H, OCH₃), 3.77 (s, 2 H, CH₂), 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. ¹³C NMR $(300 \text{ MHz}, \text{ CDCl}_3, 25 \text{ °C}): \delta = 30.29 \text{ (CH}_2), 38.43 \text{ (CH}_2), 55.27$

(CH₃O), 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 (CH₃CN): $\lambda_{max} = 226$ (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-8one (3a): Compound 1 (248 mg, 0.75 mmol) was dissolved in CH₂Cl₂ (4 mL), methanol (6 mL) and H₂O (1 mL). NaHCO₃ (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 CO₂/acetone. ICl (134 mg, 0.84 mmol) in CH₂Cl₂ (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; $R_{\rm f}(1) = 0.55$, $R_{\rm f}(3a) = 0.22 - 0.25$. The solvent was removed in vacuo (bath temperature 25 °C, p =150-50 mbar). The remaining solid was extracted with CH₂Cl₂ (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. ¹H NMR (300 MHz, CDCl₃, 25 °C): δ = 3.35 (s, 2 H, CH₂), 3.78 (s, 3 H, OCH_3), 3.80 (s, 2 H, CH₂), 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. ¹³C NMR (300 MHz, CDCl₃, 25 °C): $\delta = 39.75$ (CH₂), 43.86 (CH₂), 55.32 (OCH₃), 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 (CH₃CN): $\lambda_{\text{max}} = 280 \ (8100), \ 301 \ (\text{sh}) \ \text{nm. IR} \ (\text{KBr}): \ \tilde{\nu} = 1660 \ \text{cm}^{-1}. \ \text{MS}$ EI: m/z (%) = 442 (14) [M⁺], 316 (3) [C₁₇H₁₅S₂O₂⁺], 253 (6) $[C_5H_2IS_2^+]$, 227 (6) $[C_{15}H_{15}S_2^+]$, 215 (3) $[C_2IS_2^+]$, 149 (4) [C₈H₅SO⁺], 135 (3) [C₇H₃SO⁺], 127 (5) [I⁺], 121 (100) [C₈H₉O⁺], 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: C₁₇H₁₅IO₂S₂, $M_r = 442.34$, 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 ($\lambda = 0.71073$ Å) in ω / 20 scanning mode at T = 293 K, crystal size $0.49 \times 0.34 \times 0.30$ 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) Å³, Z = 4, $D_{calcd.} =$ 1.694 g cm⁻³, $\mu = 2.090$ mm⁻¹ (empirical absorption correction), F(000) = 872, 5833 measured reflections in the range $1.22^{\circ} \leq \theta$ \leq 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 F² (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)-2thiaspiro[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. ¹H NMR (300 MHz, CDCl₃, 25 °C): $\delta = 3.34$ (d, J = 3.0 Hz, 2 H, CH₂), 3.78 (s, 3 H, OCH₃), 3.84 (q, J = 12.4 Hz, 2 H, CH₂), 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. ¹³C NMR (300 MHz, CDCl₃, 25 °C): $\delta = 39.70$ (CH₂), 45.13 (CH₂), 55.31 (OCH₃), 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 (CH₂Cl₂): $\lambda_{max} = 392$ nm. C₂₃H₁₉IN₄O₅S₂ (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 2,4dinitrophenylhydrazine (200 mg, 1 mmol) in H₂SO₄ (1 mL), H₂O (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. ¹H NMR (300 MHz, CDCl₃, 25 °C): $\delta = 3.29$ (d, J = 4.9 Hz, 2 H, CH₂), 3.76 (s, 3 H, OCH₃), 3.83 (s, 2 H, CH₂), 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. ¹³C NMR (300 MHz, CDCl₃, 25 °C): $\delta =$ 38.68 (CH₂), 42.99 (CH₂), 55.22 (OCH₃), 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 (CH₂Cl₂): λ_{max} = 392 nm. C₂₃H₂₀N₄O₅S₂ (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 TrBF₄ (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. ¹H NMR (300 MHz, CD₃CN, 25 °C): δ = 3.68 (s, 3 H, OCH₃), 4.16 (s, 2 H, CH₂), 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. ¹³C NMR (300 MHz, CD₃CN, 25 °C): δ = 41.53 (CH₂), 55.98 (OCH₃), 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 (CH₃CN): $\lambda_{max} = 282$ (18800), 371 (8100), 422 (7100) nm. IR (KBr): $\tilde{v} = 1061$ cm⁻¹ (BF₄⁻). MS ESI: *m/z* (%) = 441 (100) [M⁺]. C₁₇H₁₄S₂O₂I⁺BF₄⁻ (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.). ¹H NMR (300 MHz, CD₃CN, 25 °C): $\delta = 3.76$ (s, 3 H, OCH₃), 4.33 (s, 2 H, CH₂), 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. ¹³C NMR (300 MHz, CD₃CN, 25 °C): δ = 38.20 (CH₂), 56.17 (OCH₃), 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): $\tilde{v} = 1062 \text{ cm}^{-1} (\text{BF}_4^{-})$, 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): $\lambda_{max} = 271$ (22800), 369 (8040), 538 (28700) nm. C₂₃H₁₉N₄O₅S₂⁺BF₄ (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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