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ORIGINAL PAPER

Novel synthesis of 2*H*-1,5-benzoxathiepin-3(4*H*)-one and 5*H*-4,1-benzoxathiepin-3(2*H*)-one derivatives and chemical properties evaluation

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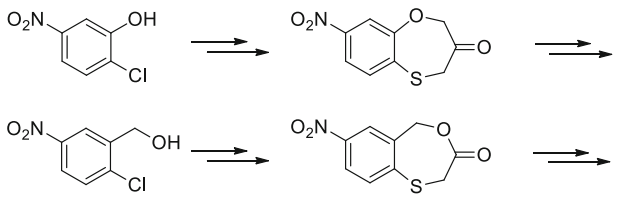
Abstract New methods for the synthesis of 2*H*-1,5-benzoxathiepin-3(4*H*)-one and 5*H*-4,1-benzoxathiepin-3(2*H*)-one derivatives have been developed. Carbonyl group of 2*H*-1,5-benzoxathiepin-3(4*H*)-one has been protected by cyclic and acyclic ketals. Interaction of 2*H*-1,5-benzoxathiepin-3(4*H*)-one with $NaBH_4$, hydroxylamine, hydrazines, and Br_2 has been investigated. Strecker reaction has been carried out for the synthesis of corresponding α-amino acid. Combination of Horner–Wadsworth–Emmons and Michael reactions allowed to obtain derivatives of β-substituted carboxylic acid. Also, 2*H*-1,5-benzoxathiepin-3(4*H*)-one have been involved in Johnson–Corey–Chaykovsky reaction.

Graphical abstract



Keywords Nucleophilic substitution · Dieckmann condensation · Benzoxathiepine · Johnson–Corey–Chaykovsky epoxidation · Strecker reaction · Horner–Wadsworth–Emmons reaction

Introduction

Seven-membered heterocycles, as known, attract attention of chemists and pharmacists due to wide spectrum of their biological activity. Rigid non-planar scaffold of heptatomic cycles fixed by heteroatoms are objects of physico-chemical, spectral, and structural researches [1–4].

Sulfur-containing compounds are important chemical entities, many of which show unique bioactivity [5–7]. For example, 1,5-benzoxathiepine derivatives exhibit serotonin S_2-receptor-blocking activity, calcium antagonism, actions to relieve cerebral vasospasm and to improve renal circulation, and diuretic and antithrombotic activities, and are of value as a prophylactic and therapeutic agent for ischemic cardiopathies, thrombosis, hypertension, and cerebral circulatory disorders [8]; can be used for the treatment of glaucoma [9]; and show anticancer activity [10, 11]. A number of patents on synthesis and using in medicine were published recently [12, 13].

Ring system of 1,5-benzoxathiepine is actively being studied as analogous of benzodiazepines [2–4, 14]. Moreover, 2*H*-1,5-benzoxathiepin-3(4*H*)-one is an isoster of calone (watermelon ketone) that was isolated from watermelon rind and is a valuable fragrance for preparing fresh, marine, and ozone aromas [15].

Synthesis of 2*H*-1,5-benzoxathiepin-3(4*H*)-one from alkylated 2-mercaptophenol via regioselective Dieckmann cyclization (71 % yield), hydrolysis, and decarboxylation (79 %) was reported in 1987 [16]. Surprisingly,

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transformations of 2*H*-1,5-benzoxathiepin-3(4*H*)-one are scarcely reported in the literature [17]. It was an interesting fact that isomeric 5*H*-4,1-benzoxathiepin-3(2*H*)-one cycle has not been described in literature. Only the syntheses of similar structures are reported [18, 19].

We resolved to amend this situation and introduce simple methods for the synthesis of 2*H*-1,5-benzoxathiepin-3(4*H*)-one and 5*H*-4,1-benzoxathiepin-3(2*H*)-one in high yields. In addition, we consider some of the chemical properties of these compounds. The more interesting and useful functional groups for medicinal chemistry are known to be amino and carboxyl groups. Previously, we have reported the synthesis of seven-member cycles with amino acid fragment [20]. The priority part of this work was synthesis of amino and carboxyl derivatives.

Results and discussion

In this article, we describe new approach for the synthesis of 2*H*-1,5-benzoxathiepin-3(4*H*)-one starting from 2-chloro-5-nitrophenol (**1**). Phenol **1** was alkylated by methyl chloroacetate in acetonitrile in the presence of potassium carbonate as a base in 93 % yield (Scheme 1). Nucleophilic substitution of chlorine in position 2 of compound **2** with methyl thioglycolate in DMSO with Et_3N led to diester **3** in 95 % yield. The treatment of THF solution of compound **3** with solution of 1.2 equivalent of MeONa in MeOH and subsequent refluxing during 15 h gave the product of regioselective Dieckmann cyclization **4** in 94 % yield. Hydrolysis and decarboxylation of ester **4** were carried out in mixture of H_2SO_4 and AcOH using modified described procedure [16].

The structure of ketone **5** is confirmed by singlets of methylene groups in the positions 2 and 4 of cycle at 4.81 and 4.14 ppm in ^{1}H NMR spectrum, respectively. Moreover, we observed an intensive band of carbonyl group at 1718 cm^{-1} in IR spectrum. Finally, the structure of ketone **5** was proved by X-ray diffraction study (Fig. 1). The seven-membered ring of compound **5** in crystal phase adopts a boat conformation with deviation of the C7 and C8 atoms from mean plane of remaining atoms of ring by 1.197(4) and 1.148(4) Å, respectively.

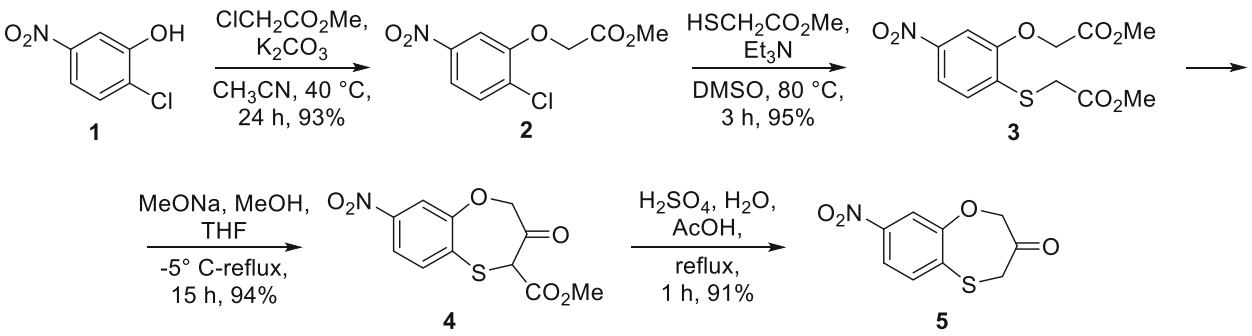
The next step of the work was protection of carbonyl group of ketone **5** (Scheme 2). Refluxing of oxathiepine **5** with 1,2-diols in benzene with Dean–Stark trap in the presence of catalytic amount of *p*–TSA led to dioxolanes **6a**–**6c**. As expected, the presence of oxolane protection lead to upfield shift of the signals of methylene groups in ^{1}H NMR spectra of compounds **6a**–**6c** in comparison with ketone **5**.

The structure of compound **6c** was confirmed by X-ray diffraction study (Fig. 2). The asymmetric part of unit cell contains two molecules (A and B) of compound **6c**. The seven-membered rings of both molecules adopt a distorted half-chair conformation with deviation of the C7, C8, C9 atoms from mean planes of remaining atoms of rings by −0.877(5), −0.170(6), 0.764(5) and −0.981(4), −0.326(5), 0.666(4) Å for molecules A and B, respectively. Molecules A and B differ in conformation of the five-membered ring. It adopts an envelope conformation in molecule A (deviation of the C12A atom from mean plane of remaining atoms of ring is −0.448(6) Å) and a twist conformation in molecule B (deviations of the C10B and C12B atoms from mean plane of remaining atoms of ring are −0.158(7) and 0.371(7) Å, respectively). The molecules of **6c** contain three chirality centers at C8, C10, and C12 atoms, and they exist in crystals as racemic mixture.

Acyclic dimethyl ketal **7** was obtained from compound **5** and MeOH in the presence of concentrated H_2SO_4 as a catalyst. The structure of ketal **7** was proved by characteristic signals in ^{1}H NMR spectrum: singlets of 2-CH_2 and 4-CH_2 at 4.38 and 3.30 ppm and singlet of two methoxy groups at 3.25 ppm.

The interaction of compound **5** with Br_2 led to unexpected results. Such attempts of bromination of ketone **5** in AcOH, CCl_4, and MeOH with excess of bromine failed. In

Scheme 1



the first and second cases, we observed starting material, but in the third sulfoxide **8** with carbonyl group protected by dimethyl ketal. Under reaction condition, bromine is a catalyst of oxidation of sulfide fragment and molecular oxygen is an oxidant [21, 22]. The process of ketalization was caused by catalytic amount of HBr in reaction mixture. It is a new condition for selective oxidation of sulfide fragment to sulfoxide.

The presence of chiral center in compound **8** caused the complexity of ^{1}H NMR spectrum of this compound in comparison with spectrum of ketal **7**. The characteristic signals in ^{1}H NMR are singlets of OMe at 3.24 and 3.32 ppm, two doublets (J = 12.4 Hz) of 4-CH_2 at 3.43 and 4.43 ppm, and multiplet of 2-CH_2 at 3.77 ppm. Finally, the structure of compound **8** was proved by X-ray diffraction study (Fig. 3). The seven-membered ring of compound **8** in crystal phase adopts a chair conformation with deviation of the C1, C6, and C8 atoms from mean plane of remaining atoms of the ring by −1.296(2), −1.102(2), and 0.704(2) Å, respectively.

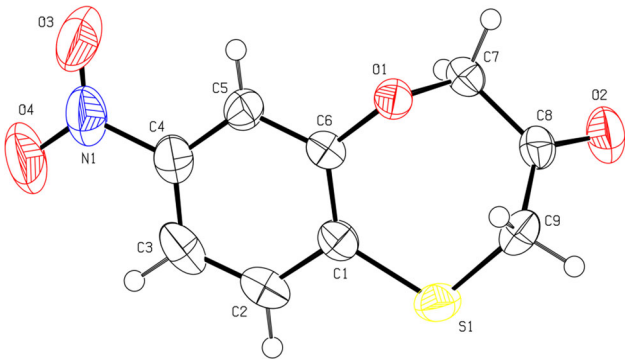


Fig. 1 Molecular structure of ketone **5** according to X-ray diffraction data

Reduction of benzoxathiepine **5** with $NaBH_4$ in MeOH led to corresponding alcohol **9** in 89 % yield. As in the case of compound **8**, the presence of chiral center is the cause of nonequivalence of the protons of methylene groups in ^{1}H NMR spectrum.

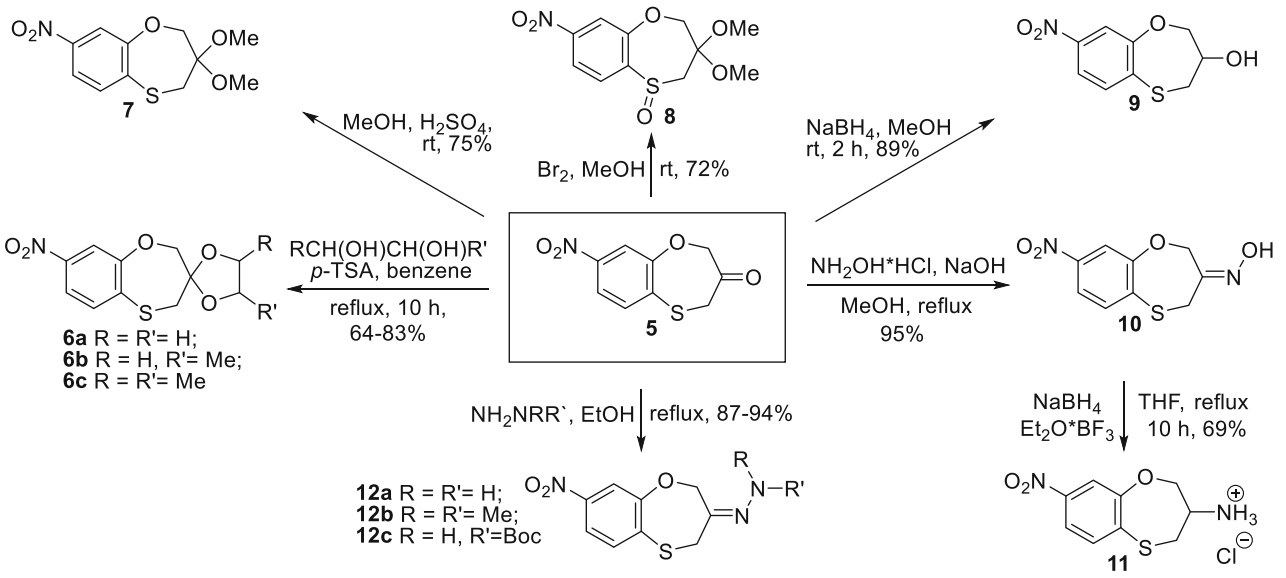
Refluxing of ketone **5** with hydroxylamine in MeOH led to oxime **10** in 95 % yield. The characteristic signals of compounds **10** in ^{1}H NMR are singlets of 2-CH_2 and 4-CH_2 at 5.05 and 4.05 ppm, respectively, and D_2O-exchangeable singlet of hydroxyl group at 11.08 ppm. Unfortunately, all attempts at the Beckmann rearrangement of oxime **10** into the corresponding benzothiazolinone were unsuccessful. Oxime **10** was reduced by in situ-generated borane from $Et_2O{\cdot}BF_3$ and $NaBH_4$ to amine **11** in 69 % yield. Methylene groups of compound **11** revealed as multiplets in ^{1}H NMR spectrum.

The treatment of ketone **5** with hydrazines in polar solvent (EtOH, *i*-PrOH) led to the products of condensation–hydrazones **12a–12c** in 87–94 % yields.

The Johnson–Corey–Chaykovsky reaction of ketone **5** was complete in 61 % yield of epoxide **13** (after column chromatography). ^{1}H NMR of compound **13** revealed the presence of nonequivalent protons of the methylene groups in both three-and seven-membered cycles.

Treatment of suspension of oxathiepine **5** in MeOH with aqueous ammonia, KCN, and NH_4Cl led to Strecker product **14** (Scheme 3). The next step of the work was the

Scheme 2



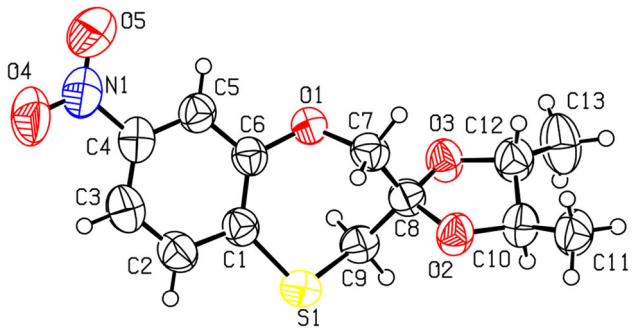


Fig. 2 Molecular structure of compound **6c** according to X-ray diffraction data

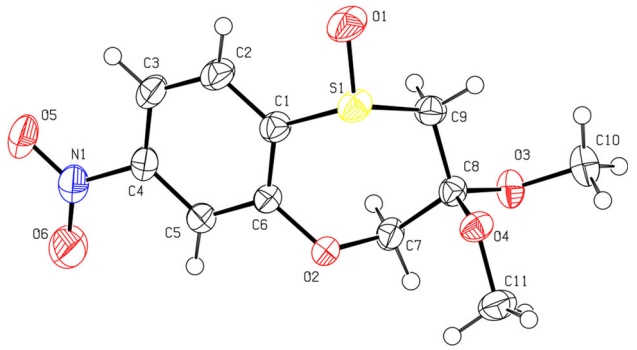


Fig. 3 Molecular structure of compound **8** according to X-ray diffraction data

protection of amino groups of compounds **14** by acylation with Ac_2O. Subsequent acidic hydrolysis of compound **15** afforded to α-amino acid **16**. The methylene groups in position 2 and 4 of compounds **14**–**16** appear in ^{1}H NMR spectra as two pairs of doublets between 3.10 and 3.80 ppm. The IR spectra of compounds **14** and **15** show band of nitrile group at 2242 cm^{-1}.

Using the combination of Horner–Wadsworth–Emmons and Michael reactions, we want to obtain corresponding derivatives of β-substituted acid. Under condition of Horner–Wadsworth–Emmons reaction, ketone **5** was transformed into alkene **17**. Ethyl ester **17** was transformed into methyl ester **18** by the treatment of catalytic amount of MeONa in MeOH. Treatment of compound **18** with 1.5 equivalent of MeONa at 50 °C gave product of Michael **19**. The characteristic signals of esters **17** and **18** are singlets of methylene groups in the position 2 and 4 at 4.97–5.37 and 4.18–4.50 ppm and CH at 6.01–6.06 ppm. The IR spectra of esters **17** and **18** revealed intensive bands of conjugate ester groups at 1697 and 1710 cm^{-1}, respectively. NOE experiments confirmed that both alkenes **17** and **18** exist as *Z* isomer.

A similar method has been proposed for the synthesis of isomeric 5*H*-4,1-benzoxathiepin-3(2*H*)-one **22** (Scheme 4). The first step was nucleophilic substitution of chlorine by residue of thioglycolic acid in 2-chloro-5-nitrobenzyl alcohol (**20**) synthesized from 2-chloro-5-nitrobenzaldehyde [17]. Cyclization of acid **21** at refluxing in Ac_2O led to lactone **22**.

The presence of lactone fragment caused downfield shift signals of methylene groups in ^{1}H NMR in comparison with acyclic molecules. Methylene groups in the position 2 and 5 of compound **22** appear at 4.34 and 5.56 ppm, respectively. The structure of compound **22** was confirmed by X-ray diffraction study (Fig. 4). In contrast to isomeric molecule **5,** the seven-membered ring of lactone **22** in crystal phase adopts a distorted half-chair conformation with deviation of the C9, C8, O1 atoms from mean plane of remaining atoms of ring by 0.262(4), −0.878(5), and −1.063(4) Å, respectively.

Having tried to involve lactone **22** in reactions, we understood the reasons why synthesis and chemical properties of 4,1-benzoxathiepin-3(2*H*)-one are not investigated and described. Attempts of reduction of nitro and carbonyl group, oxidation of sulfide fragment, bromination, and formylation of methylene group failed. We obtained the complex mixture of starting materials, ring-opening, and other side products.

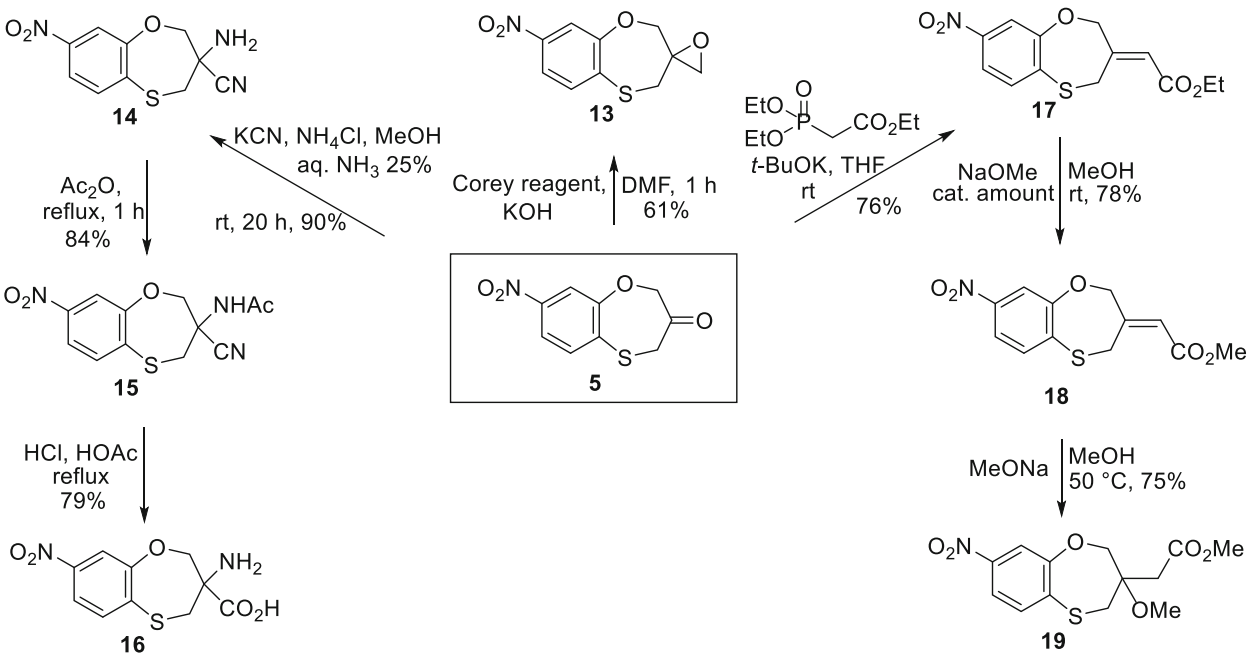
In summary, we have developed new methods for the synthesis of 2*H*-1,5-benzoxathiepin-3(4*H*)-and 5*H*-4,1-benzoxathiepin-3(2*H*)-ones in high yields from easily accessible reagents. We have carried out a number of transformation of carbonyl function in 1,5-benzoxathiepine-3(4*H*)-one and shown a synthetic potential of this cyclic system.

Experimental

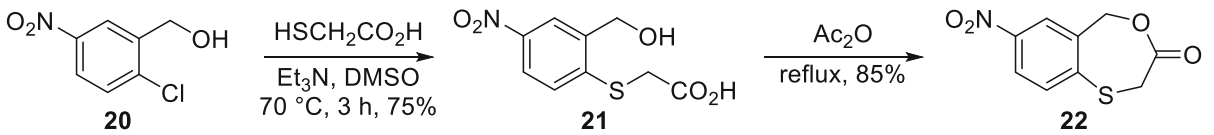
All commercially available chemicals were purchased from Aldrich (St. Louis, MO, USA) and Merck (Darmstadt, Germany). IR spectra were obtained on a Perkin Elmer BX II spectrometer in KBr tablets and are reported in cm^{-1}. ^{1}H and ^{13}C NMR spectra were recorded on a Varian Mercury 400 spectrometer at 400.45 and 100.61 MHz, respectively, using DMSO-d_6 as solvent and TMS as internal standards. Elemental analyses were determined on a Vario MICRO cube elemental analyzer. Melting points were measured with a small Boetius apparatus equipped with a VEB Analytic RNMK apparatus. Purity of the compounds synthesized was monitored by TLC on Silufol UV-254 plates with 9:1 chloroform–methanol as eluent.

Methyl (2-chloro-5-nitrophenoxy)acetate
(**2**, $C_9H_8ClNO_5$)
A mixture of 23.7 cm^3 methyl chloroacetate (0.27 mol), 43.4 g 2-chloro-5-nitrophenol (**1**, 0.25 mol), 41.4 g K_2CO_3

Scheme 3



Scheme 4



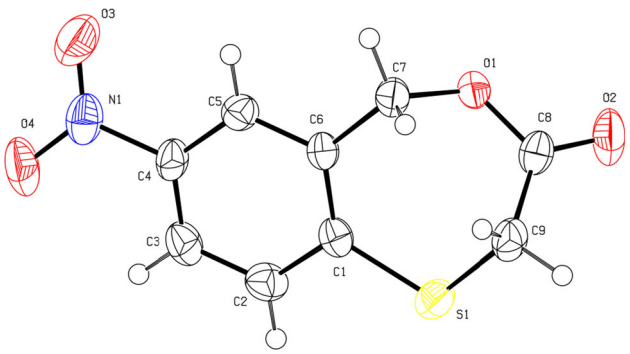


Fig. 4 Molecular structure of lactone **22** according to X-ray diffraction data

(0.30 mol), and 500 cm^3 CH_3CN was stirred at 30 °C for 20 h. The inorganic precipitate was filtered off, washed with CH_3CN and organic solvent was evaporated under reduced pressure. The solid residue was quenched with water, filtered, and dried to give the title compound **2** (93 %, 57.0 g). White solid; m.p.: 98–99 °C (*i*-PrOH); ^{1}H NMR (DMSO-d_6, 400 MHz): δ = 7.89 (s, 1H, H-6), 7.86 (d, J = 8.4 Hz, 1H, H-4), 7.69 (d, J = 8.4 Hz, 1H, H-3), 5.07 (s, 2H, CH_2), 3.76 (s, 3H, CH_3) ppm; ^{13}C NMR (DMSO-d_6, 100 MHz): δ = 168.5, 153.5, 147.1, 131.0, 129.0, 117.2, 108.7, 65.7, 52.2 ppm; IR (KBr): $\bar{\nu}$ = 1728 (C=O), 1525 (NO_2), 1344 (NO_2) cm^{-1}.

Methyl [[2-(2-methoxy-2-oxoethoxy)-4-nitrophenyl]thio]acetate (**3**, $C_{12}H_{13}NO_7S$)

A mixture of 24.1 cm^3 methyl thioglycolate (0.27 mol), 61.4 g ester **2** (0.25 mol), 51.7 cm^3 Et_3N (0.37 mol), and 150 cm^3 DMSO was stirred at 80 °C for 4 h. The reaction mixture was cooled to 20 °C and poured into water. The precipitate was filtered, washed with water and dried to afford diester **3** (95 %, 74.8 g). White solid; m.p.: 131–132 °C (*i*-PrOH); ^{1}H NMR (DMSO-d_6, 400 MHz): δ = 7.83 (dd, J = 8.4, 2.0 Hz, 1H, H-5), 7.68 (d, J = 2.0 Hz, 1H, H-3), 7.41 (d, J = 8.4 Hz, 1H, H-6), 4.99 (s, 2H, O-CH_2), 3.96 (s, 2H, S-CH_2), 3.78 (s, 3H,

CH_3), 3.70 (s, 3H, CH_3) ppm; ^{13}C NMR (DMSO-d_6, 100 MHz): δ = 169.2, 168.6, 153.4, 145.3, 135.5, 125.6, 117.1, 106.0, 65.6, 52.6, 52.1, 32.1 ppm; IR (KBr): $\bar{\nu}$ = 1732 (C=O), 1519 (NO_2), 1345 (NO_2) cm^{-1}.

Methyl 8-nitro-3-oxo-3,4-dihydro-2H-1,5-benzoxathiepine-4-carboxylate (**4**, $C_{11}H_9NO_6S$)
To a stirred solution of 47.25 g **3** (0.15 mol) in 400 cm^3 THF at 0 °C, a solution of MeONa (0.18 mol) in 100 cm^3 MeOH was added dropwise. The reaction mixture was stirred at 0 °C for 1 h and boiled for 10 h. Solvent was evaporated in vacuo, residue was quenched with cold water and acidified HCl (pH = 6). The precipitate was filtered, washed, and dried to give ketoester **4** (94 %, 40.0 g). White solid; m.p.: 171–172 °C (CH_3CN); ^{1}H NMR (DMSO-d_6, 400 MHz): δ = 7.94 (dd, J = 8.4, 2.4 Hz, 1H, H-7), 7.82 (d, J = 2.4 Hz, 1H, H-9), 7.63 (d, J = 8.4 Hz, 1H, H-6), 5.51 (s, 1H, CH), 4.98 (s, 2H, 2-CH_2), 3.74 (s, 3H, CH_3) ppm; ^{13}C NMR (DMSO-d_6, 100 MHz): δ = 198.5, 165.8, 155.5, 146.1, 134.8, 129.2, 120.4, 118.4, 78.2, 54.2, 54.0 ppm; IR (KBr): $\bar{\nu}$ = 1728 (C=O), 1514 (NO_2), 1351 (NO_2) cm^{-1}.

8-Nitro-2H-1,5-benzoxathiepin-3(4H)-one (**5**, $C_9H_7NO_4S$)
A mixture of 28.3 g of the ketoester **4** (0.1 mol), 200 cm^3 AcOH, 35 cm^3 98 % H_2SO_4, and 35 cm^3 water was refluxed for 1 h. The reaction mixture was poured into ice-H_2O, and the precipitate was filtered and dried. Recrystallization from CH_3CN afforded ketone **5** as white solid (91 %, 20.5 g). M.p.: 172–173 °C; ^{1}H NMR (DMSO-d_6, 400 MHz): δ = 7.89 (dd, J = 8.4, 2.4 Hz, 1H, H-7), 7.82 (d, J = 2.4 Hz, 1H, H-9), 7.48 (d, J = 8.4 Hz, 1H, H-6), 4.81 (s, 2H, 2-CH_2), 4.14 (s, 2H, 4-CH_2) ppm; ^{13}C NMR (DMSO-d_6, 100 MHz): δ = 202.5, 155.9, 145.6, 136.1, 129.1, 119.6, 118.0, 78.2, 36.7 ppm; IR (KBr): $\bar{\nu}$ = 1718 (C=O), 1508 (NO_2), 1335 (NO_2) cm^{-1}.

General procedure for preparation of compounds 6a–6c

A solution of 0.23 g ketone **5** (1 mmol), corresponding 1,2-diol (1.2 mmol), and *p*-toluenesulfonic acid (catalytic amount) in 20 cm^3 benzene was refluxed in a Dean–Stark apparatus for 6 h. The reaction mixture was evaporated in vacuo, quenched with aqueous solution of sodium hydrogen carbonate, filtered off, and washed with water. The precipitate was crystalized from *i*-PrOH to give oxolane **6a–6c** in 64–83 % yields.

8-Nitrospiro[1,5-benzoxathiepine-3,2′-[1,3]dioxolane] (**6a**, $C_{11}H_{11}NO_5S$)
White solid; yield 83 %; m.p.: 137–138 °C (*i*-PrOH); ^{1}H NMR (DMSO-d_6, 400 MHz): δ = 7.78 (d, J = 8.0 Hz, 1H, H-7), 7.66 (s, 1H, H-9), 7.47 (d, J = 8.0 Hz, 1H, H-6), 4.31 (s, 2H, 2-CH_2), 3.96 (s, 4H, CH_2CH_2), 3.33 (s, 2H, 4-CH_2) ppm; ^{13}C NMR (DMSO-d_6, 100 MHz): δ = 157.3, 146.2, 135.2, 131.0, 118.1, 116.3, 108.3, 74.3, 65.0, 36.7 ppm; IR (KBr): $\bar{\nu}$ = 1513 (NO_2), 1348 (NO_2) cm^{-1}.

4′-Methyl-8-nitrospiro[1,5-benzoxathiepine-3,2′-[1,3]-dioxolane] (**6b**, $C_{12}H_{13}NO_5S$)
White solid; yield 64 %; m.p.: 101–102 °C (*i*-PrOH); ^{1}H NMR (DMSO-d_6, 400 MHz): δ = 7.77 (d, J = 8.4 Hz, 1H, H-7), 7.66 (s, 1H, H-9), 7.46 (d, J = 8.4 Hz, 1H, H-6), 4.39 (d, J = 13.2 Hz, 1H, 2-C*H*H), 4.23 (m, 2H, 2-CH*H* + OC*H*H), 4.10 (m, 1H, CH), 3.45 (m, 2H, 4-CH_2), 3.19 (m, 1H, O-CH*H*), 1.21 (m, 3H, CH_3) ppm; ^{13}C NMR (DMSO-d_6, 100 MHz): δ = 157.1, 145.9, 135.1, 130.7, 117.9, 116.1, 108.2, 74.9, 72.4, 70.5, 36.6, 17.6 ppm; IR (KBr): $\bar{\nu}$ = 1505 (NO_2), 1339 (NO_2) cm^{-1}.

4′,5′-Dimethyl-8-nitrospiro[1,5-benzoxathiepine-3,2′-[1,3]-dioxolane] (**6c**, $C_{13}H_{15}NO_5S$)
White solid; yield 76 %; m.p.: 99–100 °C (*i*-PrOH); ^{1}H NMR (DMSO-d_6, 400 MHz): δ = 7.77 (d, J = 8.8 Hz, 1H, H-7), 7.66 (s, 1H, H-9), 7.48 (d, J = 8.8 Hz, 1H, H-6), 4.45 (d, J = 12.8 Hz, 1H, 2-C*H*H), 4.17 (d, J = 12.8 Hz, 1H, 2-CH*H*), 3.68 (br s, 2H, CHCH), 3.55 (d, J = 14.4 Hz, 1H, 4-C*H*H), 3.13 (d, J = 14.4 Hz, 1H, 4-CH*H*), 1.20 (br s, 6H, 2CH_3) ppm; ^{13}C NMR (DMSO-d_6, 100 MHz): δ = 157.1, 145.9, 134.9, 130.7, 117.8, 116.0, 107.0, 78.5, 77.8, 74.6, 37.4, 16.0, 15.9 ppm; IR (KBr): $\bar{\nu}$ = 1513 (NO_2), 1338 (NO_2) cm^{-1}.

3,3-Dimethoxy-8-nitro-3,4-dihydro-2H-1,5-benzoxathiepine (**7**, $C_{11}H_{13}NO_5S$)
To a solution of 0.23 g ketone **5** (1 mmol) in 10 cm^3 methanol was added 0.15 cm^3 H_2SO_4 (3 mmol), the mixture was left at room temperature for 2 days. The precipitate was filtered off, washed with MeOH, and dried. White solid; yield 75 %; m.p.: 120–121 °C (MeOH); ^{1}H NMR (DMSO-d_6, 400 MHz): δ = 7.76 (d, J = 8.4 Hz, 1H, H-7), 7.64 (s, 1H, H-9), 7.40 (d, J = 8.4 Hz, 1H, H-6), 4.38 (s, 2H, 2-CH_2), 3.30 (s, 2H, 4-CH_2), 3.25 (s, 6H, 2CH_3) ppm; ^{13}C NMR (DMSO-d_6, 100 MHz): δ = 157.8, 146.6, 135.8, 131.3, 118.4, 116.6, 101.6, 72.8, 49.2, 35.1 ppm; IR (KBr): $\bar{\nu}$ = 1524 (NO_2), 1341 (NO_2) cm^{-1}.

3,3-Dimethoxy-8-nitro-3,4-dihydro-2H-1,5-benzoxathiepine 5-oxide (**8**, $C_{11}H_{13}NO_6S$)
To a solution of 0.23 g ketone **5** (1 mmol) in 10 cm^3 methanol was added 0.25 cm^3 Br_2 (5 mmol), the mixture was left at room temperature for 5 days. The crystals were filtered off, washed with MeOH, and dried. Colorless crystals; yield 72 %; m.p.: 192–193 °C (MeOH); ^{1}H NMR (DMSO-d_6, 400 MHz): δ = 8.26 (d, J = 8.4 Hz, 1H, H-7), 7.96 (s, 1H, H-9), 7.82 (d, J = 8.4 Hz, 1H, H-6), 4.43 (d, J = 12.4 Hz, 1H, 4-C*H*H), 3.77 (m, 2H, 2-CH_2), 3.43 (d,

$J = 12.4$ Hz, 1H, 4-CH*H*), 3.32 (s, 3H, OCH_3), 3.24 (s, 3H, OCH_3) ppm; ^{13}C NMR (DMSO-d_6, 100 MHz): $\delta = 155.4$, 150.1, 147.3, 127.2, 120.5, 117.5, 98.1, 72.8, 58.5, 49.0, 48.5 ppm; IR (KBr): $\bar{\nu} = 1533$ (NO_2), 1352 (NO_2), 1052 (S=O) cm^{-1}.

8-Nitro-3,4-dihydro-2H-1,5-benzoxathiepin-3-ol (**9**, $C_9H_9NO_4S$)

To a stirred solution of 2.25 g ketone **5** (10 mmol) in 25 cm^3 MeOH at 0 °C was added 0.38 g $NaBH_4$ (10 mmol) by portions. The reaction mixture was stirred for 2 h at room temperature, evaporated in vacuo, quenched with water, filtered, washed with water, and dried. The precipitate was crystalized from *i*-PrOH to give title compound **9** as yellow solid (2.20 g, 89 %). M.p.: 96–97 °C (*i*-PrOH); ^1H NMR (DMSO-d_6, 400 MHz): $\delta = 7.76$ (d, $J = 8.0$ Hz, 1H, H-7), 7.65 (s, 1H, H-9), 7.48 (d, $J = 8.0$ Hz, 1H, H-6), 5.48 (br s, 1H, OH), 4.47 (d, $J = 11.2$ Hz, 1H, 2-C*H*H), 4.18 (m, 1H, CH), 4.05 (dd, $J = 11.2$, 4.8 Hz, 1H, 2-CH*H*), 3.26 (d, $J = 14.4$ Hz, 1H, 4-C*H*H), 3.06 (dd, $J = 14.4$, 7.2 Hz, 1H, 4-CH*H*) ppm; ^{13}C NMR (DMSO-d_6, 100 MHz): $\delta = 158.2$, 146.2, 136.3, 131.3, 117.7, 116.1, 75.8, 68.5, 36.0 ppm; IR (KBr): $\bar{\nu} = 3287$ (OH), 1508 (NO_2), 1338 (NO_2) cm^{-1}.

8-Nitro-2H-1,5-benzoxathiepin-3(4H)-one oxime (**10**, $C_9H_8N_2O_4S$)

To a solution of 0.45 g ketone **5** (2 mmol) in 10 cm^3 MeOH was added solution of hydroxylamine in 10 cm^3 MeOH obtained from 0.18 g $NH_2OH{\cdot}HCl$ (0.25 mmol) and 0.12 g NaOH (3 mmol). The mixture was refluxed for 3 h and cooled to room temperature; the precipitate was filtered and dried. White solid; yield 95 %; m.p.: 232–233 °C (MeOH); ^1H NMR (DMSO-d_6, 400 MHz): $\delta = 11.08$ (s, 1H, OH), 7.83 (d, $J = 8.8$ Hz, 1H, H-7), 7.76 (s, 1H, H-9), 7.37 (d, $J = 8.8$ Hz, 1H, H-6), 5.05 (s, 2H, 2-CH_2), 4.05 (s, 2H, 4-CH_2) ppm; ^{13}C NMR (DMSO-d_6, 100 MHz): $\delta = 156.3$, 154.8, 145.5, 138.0, 129.3, 119.6, 118.4, 70.5, 31.1 ppm; IR (KBr): $\bar{\nu} = 3273$ (OH), 1509 (NO_2), 1346 (NO_2) cm^{-1}.

8-Nitro-3,4-dihydro-2H-1,5-benzoxathiepin-3-amine hydrochloride (**11**, $C_9H_{11}ClN_2O_3S$)

To a magnetically stirred suspension of 0.96 g oxime **10** (4 mmol) and 0.79 g $NaBH_4$ (20 mmol) in 40 cm^3 dry THF at 0 °C was added dropwise 2.54 cm^3 boron trifluoride etherate (20 mmol). The resultant mixture was stirred at room temperature for 1 h, refluxed for 24 h, and concentrated in vacuo. Then, 50 cm^3 water was added. Aqueous solution was extracted with CH_2Cl_2. The extract was washed with brine, dried over $MgSO_4$, and evaporated in vacuo. To residue was added 10 cm^3 *i*-PrOH and calculated amount of hydrochloric acid. The precipitate was collected by filtration and washed with Et_2O. White solid; yield 69 %; m.p.: 210–212 °C (dec) (*i*-PrOH); ^1H NMR (DMSO-d_6, 400 MHz): $\delta = 8.82$ (br s, 3H, N^+H_3), 7.86 (d, $J = 8.4$ Hz, 1H, H-7), 7.81 (s, 1H, H-9), 7.64 (d, $J = 8.4$ Hz, 1H, H-6), 4.49 (m, 2H, 2-CH_2), 3.90 (m, 1H, 3-CH), 3.40 (m, 2H, 4-CH_2) ppm; ^{13}C NMR (DMSO-d_6, 100 MHz): $\delta = 159.4$, 147.5, 136.9, 132.8, 119.3, 117.5, 72.5, 50.8, 32.9 ppm; IR (KBr): $\bar{\nu} = 2905$ (N^+H_3), 1516 (NO_2), 1353 (NO_2) cm^{-1}.

General procedure for preparation of compounds 12a–12c

To the solution of 0.45 g ketone **5** (2 mmol) in 20 cm^3 EtOH or *i*–PrOH was added hydrazine hydrate, *N*,*N*-dimethylhydrazine, or *tert*-butoxycarbonyl hydrazide (2.4 mmol). The mixture refluxed for 2–4 h, then cooled to room temperature, the precipitate was filtered off and dried. The compounds **12a**–**12c** were obtained in 87–94 % yield.

8-Nitro-2H-1,5-benzoxathiepin-3(4H)-one hydrazone (**12a**, $C_9H_9N_3O_3S$)

White solid; yield 87 %; m.p.: 134–135 °C (EtOH); ^1H NMR (DMSO-d_6, 400 MHz): $\delta = 7.80$ (d, $J = 8.0$ Hz, 1H, H-7), 7.74 (s, 1H, H-9), 7.44 (d, $J = 8.0$ Hz, 1H, H-6), 6.44 (br s, 2H, NH_2), 4.74 (s, 2H, 2-CH_2), 3.96 (s, 2H, 4-CH_2) ppm; ^{13}C NMR (DMSO-d_6, 100 MHz): $\delta = 156.4$, 146.5, 138.2, 137.8, 130.6, 118.7, 117.7, 78.0, 26.1 ppm; IR (KBr): $\bar{\nu} = 3395(NH_2)$, 1507 (NO_2), 1341 (NO_2) cm^{-1}.

8-Nitro-2H-1,5-benzoxathiepin-3(4H)-one dimethylhydrazone (**12b**, $C_{11}H_{13}N_3O_3S$)

White solid; yield 90 %; m.p.: 113–114 °C (EtOH); ^1H NMR (DMSO-d_6, 400 MHz): $\delta = 7.85$ (d, $J = 8.0$ Hz, 1H, H-7), 7.75 (s, 1H, H-9), 7.40 (d, $J = 8.0$ Hz, 1H, H-6), 5.09 (s, 2H, 2-CH_2), 4.03 (s, 2H, 4-CH_2), 2.41 (s, 6H, NMe_2); ^{13}C NMR (DMSO-d_6, 100 MHz): $\delta = 163.2$, 156.8, 145.9, 137.9, 129.7, 119.7, 118.3, 72.0, 47.9, 34.1 ppm; IR (KBr): $\bar{\nu} = 1505$ (NO_2), 1345 (NO_2) cm^{-1}.

tert. Butyl 2-(8-nitro-2H-1,5-benzoxathiepin-3(4H)-ylidene)hydrazinecarboxylate (**12c**, $C_{14}H_{17}N_3O_5S$)

White solid; yield 94 %; m.p.: 204–205 °C (EtOH); ^1H NMR (DMSO-d_6, 400 MHz): $\delta = 10.07$ (br s, 1H, NH), 7.84 (d, $J = 8.0$ Hz, 1H, H-7), 7.80 (s, 1H, H-9), 7.44 (d, $J = 8.0$ Hz, 1H, H-6), 4.83 (s, 2H, 2-CH_2), 4.15 (s, 2H, 4-CH_2), 1.48 (s, 9H, 3 CH_3) ppm; ^{13}C NMR (DMSO-d_6, 100 MHz): $\delta = 156.6$, 153.3, 146.7, 145.7, 138.6, 130.7, 119.8, 118.6, 80.6, 78.1, 28.7, 26.9 ppm; IR (KBr): $\bar{\nu} = 3277$ (NH), 1709 (C=O), 1527 (NO_2), 1338 (NO_2) cm^{-1}.

8-Nitrospiro[1,5-benzoxathiepine-3,2′-oxirane] (**13**, $C_{10}H_9NO_4S$)

To a stirred solution of 0.22 g trimethylsulfoxonium iodide (1 mmol) in 3 cm^3 DMF was added 0.06 g KOH (1 mmol).

After stirring for 15 min, the solution of 0.23 g ketone **5** (1 mmol) in 2 cm^3 DMF was added. The reaction mixture was stirred for 1 h, quenched with water, acidified by HCl (pH = 6), and extracted CH_2Cl_2. Organic layer was washed with brine, dried over $MgSO_4$, filtered, and evaporated under reduced pressure. The crude residue was directly subjected to silica gel column chromatography (60–120 mesh, chloroform) to afford pure epoxide **13**. Pale yellow solid; yield 61 %; m.p.: 127–128 °C ($CHCl_3$); ^{1}H NMR (DMSO-d_6, 400 MHz): δ = 7.84 (d, J = 8.4 Hz, 1H, H-7), 7.76 (s, 1H, H-9), 7.59 (d, J = 8.4 Hz, 1H, H-6), 4.53 (d, J = 13.2 Hz, 1H, 2-C*H*H), 4.11 (d, J = 13.2 Hz, 1H, 2-CH*H*), 3.31 (s, 2H, 4-CH_2), 2.94 (m, 2H, CH_2) ppm; ^{13}C NMR (DMSO-d_6, 100 MHz): δ = 158.3, 146.5, 136.7, 131.7, 118.4, 116.8, 75.9, 58.4, 51.9, 35.1 ppm; IR (KBr): $\bar{\nu}$ = 1519 (NO_2), 1349 (NO_2) cm^{-1}.

3-Amino-8-nitro-3,4-dihydro-2H-1,5-benzoxathiepine-3-carbonitrile (**14**, $C_{10}H_9N_3O_3S$)

To a stirred solution of 2.25 g ketone **5** (10 mmol) in 20 cm^3 MeOH was added 20 cm^3 aqueous solution of NH_3 and NH_4Cl (20 mmol). After 15 min stirring, 0.85 g KCN (13 mmol) was added. The reaction mixture was stirred for 20 h. The precipitate was filtered, washed with MeOH, and dried. White solid; yield 90 %; m.p.: 138–139 °C (MeOH); ^{1}H NMR (DMSO-d_6, 400 MHz): δ = 7.85 (dd, J = 2.0, 8.4 Hz, 1H, H-7), 7.79 (d, J = 2.0 Hz, 1H, H-9), 7.55 (d, J = 8.4 Hz, 1H, H-6), 4.53 (d, J = 12.4 Hz, 1H, 2-C*H*H), 4.02 (d, J = 12.4 Hz, 1H, 2-CH*H*), 3.49 (d, J = 14.8 Hz, 1H, 4-C*H*H), 3.13 (d, J = 14.8 Hz, 1H, 4-CH*H*), 2.83 (br s, 2H, NH_2) ppm; ^{13}C NMR (DMSO-d_6, 100 MHz): δ = 158.6, 146.9, 136.2, 132.2, 122.1, 118.7, 116.9, 76.4, 56.1, 39.4 ppm; IR (KBr): $\bar{\nu}$ = 3570 (NH_2), 3395 (NH_2), 2244 (CN), 1513 (NO_2), 1344 (NO_2) cm^{-1}.

N-(3-Cyano-8-nitro-3,4-dihydro-2H-1,5-benzoxathiepin-3-yl)acetamide (**15**, $C_{12}H_{11}N_3O_4S$)

A solution of 2.51 g compound **14** (10 mmol) in 20 cm^3 Ac_2O was stirred at 80 °C for 5 h. The solvent was evaporated under reduced pressure and residue was quenched with water. The precipitate was filtered, dried, and crystalized. White solid; yield 84 %; m.p.: 221–222 °C (AcOH); ^{1}H NMR (DMSO-d_6, 400 MHz): δ = 8.92 (s, 1H, NH), 7.86 (d, J = 8.8 Hz, 1H, H-7), 7.78 (s, 1H, H-9), 7.58 (d, J = 8.8 Hz, 1H, H-6), 4.80 (d, J = 12.4 Hz, 1H, 2-C*H*H), 4.52 (d, J = 12.4 Hz, 1H, 2-CH*H*), 3.88 (d, J = 15.2 Hz, 1H, 4-C*H*H), 3.58 (d, J = 15.2 Hz, 1H, 4-CH*H*), 1.94 (s, 3H, CH_3) ppm; ^{13}C NMR (DMSO-d_6, 100 MHz): δ = 170.1, 157.4, 146.6, 134.7, 131.4, 118.6, 118.0, 116.5, 73.5, 54.3, 36.7, 22.6 ppm; IR (KBr): $\bar{\nu}$ = 3246 (NH), 2241 (CN), 1658 (CO), 1520 (NO_2), 1341 (NO_2) cm^{-1}.

3-Amino-8-nitro-3,4-dihydro-2H-1,5-benzoxathiepine-3-carboxylic acid (**16**, $C_{10}H_{10}N_2O_5S$)

A solution of 0.54 g amide **15** (2 mmol) in 8 cm^3 AcOH and 2 cm^3 concentrated HCl was refluxed for 10 h. The solvent was evaporated under reduced pressure and residue was quenched with water. The residue was filtered and dried. White solid; yield 79 %; m.p.: 203–204 °C (dec.) (AcOH-H_2O); ^{1}H NMR (DMSO-d_6, 400 MHz): δ = 9.27 (br s, 2H, NH_2), 7.90 (d, J = 7.6 Hz, 1H, H7), 7.86 (s, 1H, H9), 7.65 (d, J = 7.6 Hz, 1H, H6), 4.63 (s, 2H, 2-CH_2), 3.59 (s, 2H, 4-CH_2) ppm; ^{13}C NMR (DMSO-d_6, 100 MHz): δ = 168.3, 158.2, 146.9, 135.6, 131.9, 118.9, 116.9, 72.7, 61.5, 35.3 ppm; IR (KBr): $\bar{\nu}$ = 3032 (N^+H_3), 1648 (CO_2^-), 1523 (NO_2), 1354 (NO_2) cm^{-1}.

Ethyl (2Z)-(8-nitro-2H-1,5-benzoxathiepin-3(4H)-ylidene)ethanoate (**17**, $C_{13}H_{13}NO_5S$)

To a stirred solution of 0.3 g *t*-BuOK (2.6 mmol) in 15 cm^3 THF at 0 °C was added 0.44 cm^3 triethylphosphonoacetate (2.2 mmol). After stirring for 15 min, a solution of 0.45 g ketone **5** (2 mmol) in 10 cm^3 THF was added dropwise. The reaction mixture was stirred at 30 °C for 1 h, quenched with saturated aqueous solution of sodium bicarbonate and extracted with EtOAc. The extract was washed with brine, dried over $MgSO_4$, filtered, and evaporated. The residue was crystalized from EtOH, filtered, and dried. Yellow solid; yield 76 %; m.p.: 105–106 °C (EtOH); ^{1}H NMR (DMSO-d_6, 400 MHz): δ = 7.85 (d, J = 8.4 Hz, 1H, H-7), 7.77 (s, 1H, H-9), 7.45 (d, J = 8.4 Hz, 1H, H-6), 6.06 (s, 1H, CH), 5.37 (s, 2H, 2-CH_2), 4.18 (s, 2H, 4-CH_2), 4.10 (q, J = 6.8 Hz, 2H, CH_2CH_3), 1.20 (t, J = 6.8 Hz, 3H, CH_2CH_3) ppm; ^{13}C NMR (DMSO-d_6, 100 MHz): δ = 165.7, 157.1, 156.8, 146.0, 137.9, 129.5, 119.7, 118.2, 116.8, 74.0, 60.8, 34.7, 14.7 ppm; IR (KBr): $\bar{\nu}$ = 1697 (CO), 1521 (NO_2), 1341 (NO_2) cm^{-1}.

Methyl (2Z)-(8-nitro-2H-1,5-benzoxathiepin-3(4H)-ylidene)ethanoate (**18**, $C_{12}H_{11}NO_5S$)

To a suspension of 0.59 g ester **17** (2 mmol) in 10 cm^3 MeOH was added catalytic amount of MeONa. The mixture was stirred at room temperature for 20 h. The precipitate was filtered and dried. Yellow solid; yield 78 %; m.p.: 169–170 °C (MeOH); ^{1}H NMR (DMSO-d_6, 400 MHz): δ = 7.86 (d, J = 8.4 Hz, 1H, H-7), 7.78 (s, 1H, H-9), 7.50 (d, J = 8.4 Hz, 1H, H-6), 6.01 (s, 1H, CH), 4.97 (s, 2H, 2-CH_2), 4.51 (s, 2H, 4-CH_2), 3.68 (s, 3H, CH_3) ppm; ^{13}C NMR (DMSO-d_6, 100 MHz): δ = 166.0, 157.2, 153.8, 138.1, 130.8, 119.5, 117.8, 117.3, 77.3, 52.1, 29.7, 17.3 ppm; IR (KBr): $\bar{\nu}$ = 1711 (CO), 1516 (NO_2), 1341 (NO_2) cm^{-1}.

Methyl (3-methoxy-8-nitro-3,4-dihydro-2H-1,5-benzoxathiepin-3-yl)acetate (**19**, $C_{13}H_{15}NO_6S$)

To a suspension of 0.59 g ester **17** (2 mmol) in 10 cm^3 MeOH was added 0.16 g MeONa (3 mmol). The mixture was stirred at 50 °C for 10 h. The solution was evaporated and quenched with water. The precipitate was filtered and dried. White solid; yield 75 %; m.p.: 74–75 °C (MeOH); ^{1}H NMR (DMSO-d_6, 400 MHz): $\delta = 7.71$ (d, $J = 8.0$ Hz, 1H, H-7), 7.60 (s, 1H, H-9), 7.32 (d, $J = 8.0$ Hz, 1H, H-6), 4.41 (m, 2H, 2-CH_2), 3.62 (s, 3H, CH_3), 3.49 (d, $J = 14.0$ Hz, 1H, 4-C*H*H), 3.30 (s, 3H, CH_3), 3.23 (d, $J = 14.0$ Hz, 1H, 4-CH*H*), 2.76 (s, 2H, CH_2) ppm; ^{13}C NMR (DMSO-d_6, 100 MHz): $\delta = 170.6$, 157.9, 146.5, 135.7, 131.2, 118.4, 116.5, 78.8, 75.8, 52.3, 51.0, 37.8, 36.0 ppm; IR (KBr): $\bar{\nu} = 1724$ (CO), 1522 (NO_2), 1345 (NO_2) cm^{-1}.

[[2-(Hydroxymethyl)-4-nitrophenyl]thio]acetic acid (**21**, $C_9H_9NO_5S$)

To a stirred solution of 9.38 g 2-chloro-5-nitrobenzyl alcohol (**20**, 0.05 mol) and 20.9 cm^3 triethylamine (0.15 mol) in 25 cm^3 DMSO was added 3.55 cm^3 thioglycolic acid (0.05 mol). After being stirred at 50 °C for 5 h, the reaction mixture was cooled to room temperature, quenched with 250 cm^3 water, and acidified with HCl to pH = 5. The precipitate was filtered off, washed with water, and solubilized in aqueous solution of NaOH. Then, the solution was stirred with activated carbon, filtered, and acidified with HCl to pH = 5. The precipitate was filtered, washed with water, and dried. White solid; yield 74 %; m.p.: 139–140 °C (H_2O); ^{1}H NMR (DMSO-d_6, 400 MHz): $\delta = 8.27$ (s, 1H, H-3), 8.04 (d, $J = 8.4$ Hz, 1H, H-5), 7.45 (d, $J = 8.4$ Hz, 1H, H-6), 5.55 (br s, 1H, OH), 4.53 (s, 2H, CH_2-O), 3.93 (s, 2H, CH_2-S) ppm; ^{13}C NMR (DMSO-d_6, 100 MHz): $\delta = 169.9$, 144.8, 143.5, 130.3, 125.5, 122.1, 120.2, 59.7, 33.7 ppm; IR (KBr): $\bar{\nu} = 3371$ (OH), 1720 (CO), 1526 (NO_2), 1343 (NO_2) cm^{-1}.

7-Nitro-5H-4,1-benzoxathiepin-3(2H)-one (**22**, $C_9H_7NO_4S$)

A solution of acid 2.43 g **21** (10 mmol) in 20 cm^3 Ac_2O was refluxed for 3 h. The reaction mixture was cooled to room temperature and the precipitate filtered off, washed with AcOH, and dried to give title compound. White solid; yield 79 % (1.78 g); m.p.: 231–232 °C (AcOH); ^{1}H NMR (DMSO-d_6, 400 MHz): $\delta = 8.26$ (s, 1H, H-6), 8.07 (d, $J = 8.4$ Hz, 1H, H-8), 7.44 (d, $J = 8.4$ Hz, 1H, H-9), 5.56 (s, 2H, 5-CH_2), 4.34 (s, 2H, 2-CH_2) ppm; ^{13}C NMR (DMSO-d_6, 100 MHz): $\delta = 169.3$, 144.6, 144.3, 132.2, 127.7, 125.7, 123.9, 68.2, 29.2 ppm; IR (KBr): $\bar{\nu} = 1745$ (CO), 1519 (NO_2), 1340 (NO_2) cm^{-1}.

X-ray diffraction studies

Intensities of reflections were measured on an automatic Xcalibur 3 diffractometer (graphite monochromated Mo Kα radiation, CCD-detector ω scanning). All structures were solved by direct method using SHELX97 package [23]. Positions of the hydrogen atoms were located from electron density difference maps and refined by "riding" model with $U_{iso} = nU_{eq}$ of carrier non-hydrogen atom ($n = 1.5$ for methyl group and $n = 1.2$ for other hydrogen atoms). Structures were refined by full-matrix least-squares method against F^2 in anisotropic approximation for non-hydrogen atoms. Final atomic coordinates, geometrical parameters and crystallographic data have been deposited with the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB2 1EZ, UK (fax: +44 1223 336033; e-mail: deposit@ccdc.cam.ac.uk). CCDC deposition numbers for structures **5**, **6c**, **8**, and **22** are 997689, 999877, 997688, and 1013342, respectively. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/products/csd/request/.

Crystal data for **5** at 295 K: $C_9H_7NO_4S$, $M_r = 225.22$, $a = 9.8390(8)$ Å, $b = 23.1706(15)$ Å, $c = 4.1094(4)$ Å, $V = 936.83(13)$ Å^3, space group $Pna2_1$, $Z = 4$, $D_c = 1.597$ g/cm^{-3}, μ(MoKα) = 0.337 mm^{-1}, F(000) = 464. 7497 reflections measured up to $2\theta_{max} = 55.0°$, 2154 unique ($R_{int} = 0.0542$) which were used in all calculations. Refinement was converged at $wR_2 = 0.0838$ (all data), $R_1 = 0.0468$ (1557 reflections with $I > 2\sigma(I)$), GoF = 1.01.

Crystal data for **6c** at 295 K: $C_{13}H_{15}NO_5S$, $M_r = 297.32$, $a = 10.7816(6)$ Å, $b = 11.4384(8)$ Å, $c = 12.6744(12)$ Å, $\alpha = 101.569(7)°$, $\beta = 112.201(7)°$, $\gamma = 91.979(5)°$, $V = 1407.3(2)$ Å^3, space group P-1, $Z = 4$, $D_c = 1.403$ g/cm^{-3}, μ(MoKα) = 0.248 mm^{-1}, F(000) = 624. 11804 reflections measured up to $2\theta_{max} = 55.0°$, 6442 unique ($R_{int} = 0.0336$) which were used in all calculations. Refinement was converged at $wR_2 = 0.1570$ (all data), $R_1 = 0.0559$ (2918 reflections with $I > 2\sigma(I)$), GoF = 0.93.

Crystal data for **8** at 293 K: $C_{11}H_{13}NO_6S$, $M_r = 287.28$, $a = 6.6041(4)$ Å, $b = 8.7493(8)$ Å, $c = 11.3201(8)$ Å, $\alpha = 112.136(8)°$, $\beta = 92.121(6)°$, $\gamma = 95.031(6)°$, $V = 601.80(8)$ Å^3, space group P-1, $Z = 2$, $D_c = 1.585$ g/cm^{-3}, μ(MoKα) = 0.293 mm^{-1}, F(000) = 300. 5993 reflections measured up to $2\theta_{max} = 60.0°$, 3509 unique ($R_{int} = 0.0192$) which were used in all calculations. Refinement was converged at $wR_2 = 0.1173$ (all data), $R_1 = 0.0434$ (2726 reflections with $I > 2\sigma(I)$), GoF = 1.05.

Crystal data for **22** at 295 K: $C_9H_7NO_4S$, $M_r = 225.22$, $a = 6.2501(4)$ Å, $b = 18.1259(9)$ Å, $c = 8.0632(7)$ Å, $\beta = 90.712(7)°$, $V = 913.40(11)$ Å^3, space group $P2_1/n$, $Z = 4$, $D_c = 1.638$ g/cm^{-3}, $\mu(\text{MoK}\alpha) = 0.346$ mm^{-1}, $F(000) = 464$. 4637 reflections measured up to $2\theta_{max} = 50.0°$, 1546 unique ($R_{int} = 0.0502$) which were used in all calculations. Refinement was converged at $wR_2 = 0.0885$ (all data), $R_1 = 0.0445$ (1083 reflections with $I > 2\sigma(I)$), GoF = 1.01.

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