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## CHEMISTRY OF POLYHALOGENATED NITROBUTADIENES, 12: SYNTHESIS OF NOVEL, HIGHLY SUBSTITUTED BI- AND TRICYCLIC 5,6,7,8-TETRAHYDRO-4H-CHROMEN-5-ONES

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Dedicated to Professor Ei-ichi Negishi on the occasion of his 77th birthday

**Abstract** - Knoevenagel condensation of 3,4-push-pull-substituted thiophene-2-carbaldehydes **4** with malononitrile gives the *gem*-dicyanovinylthiophenes **5**, followed by a Michael addition of dimedone and a subsequent cyclization to 4-(2-thienyl)-5,6,7,8-tetrahydro-4*H*-chromen-5-ones **6**. Protonolysis of the latter in methanol led to a mixture of four heterocycles **7-10**, the main product being the novel tricyclic 9-(2-thienyl)-6,7-dihydro-5*H*-thieno[3,2-*b*]chromen-8(9*H*)-one derivative **7**. A mechanism of the protonolysis reaction is proposed, the structures of the two products **7a/8a** have been confirmed by X-ray analysis.

## INTRODUCTION

Polyhalo-1,3-butadienes, carrying at least one nitro group, are valuable starting materials for the directed synthesis of highly functionalized heterocycles with a wide variety of synthetically and/or physiologically interesting properties,<sup>1-4</sup> with 2-nitropentachloro-1,3-butadiene (**1**) being one of the most attractive members of this rather new class of synthetic building units. Starting from **1**, the push-pull substituted thiophenes **3** are efficiently accessible in three steps *via* the aminodithiolanes **2** (Scheme 1).<sup>5</sup> To

interconnect these thiophenes, we have developed a new and unusual variant of the *ipso*-Vilsmeier reaction recently, in which a halogen is substituted by a formyl group under Vilsmeier-Haack conditions to give thiophene-2-carbaldehydes **4**.<sup>6</sup> This substitution reaction was first developed with electron-rich thiophenes such as **3**, featuring a unique substitution pattern.

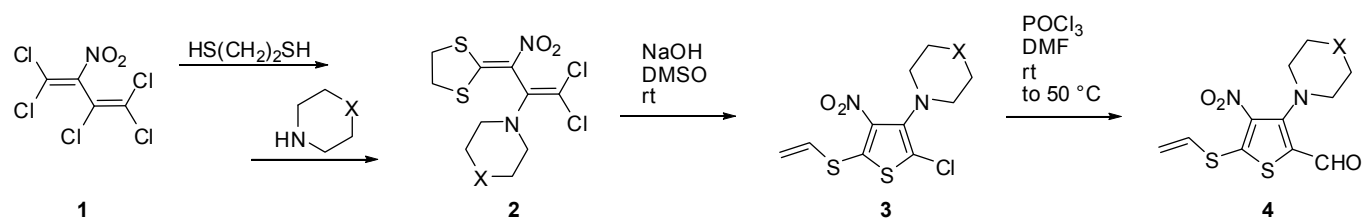
In the present paper, we mainly focus on recent progress in

a) the synthesis of substituted 2-thienyl-5,6,7,8-tetrahydro-4*H*-chromen-5-ones **6** by condensation of **4** with malononitrile and subsequent Michael addition/cyclization of dimedone with the Knoevenagel products **5**, and

b) the protonolysis products of **6** in methanol as a solvent under sulfuric acid catalysis.

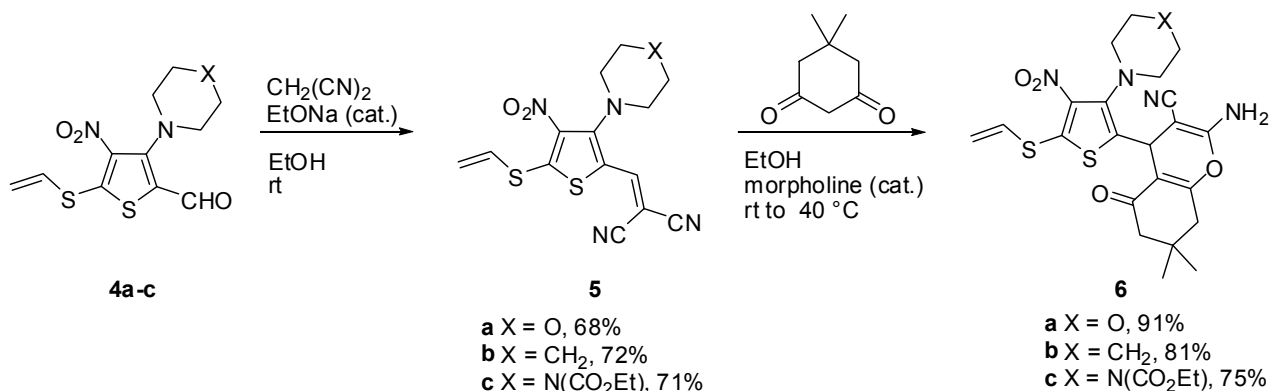
## RESULTS AND DISCUSSION

Starting from 2-nitroperchlorobutadiene (**1**),<sup>7</sup> 4-nitrothiophenes **3a-c** are accessible in very good yields (90-95%).<sup>5,6</sup> *Ips*o-formylation of **3a-c** under Vilsmeier-Haack conditions give the 4-nitrothiophene-2-carbaldehydes (**4a-c**) in good yields (70-79%).<sup>6</sup>



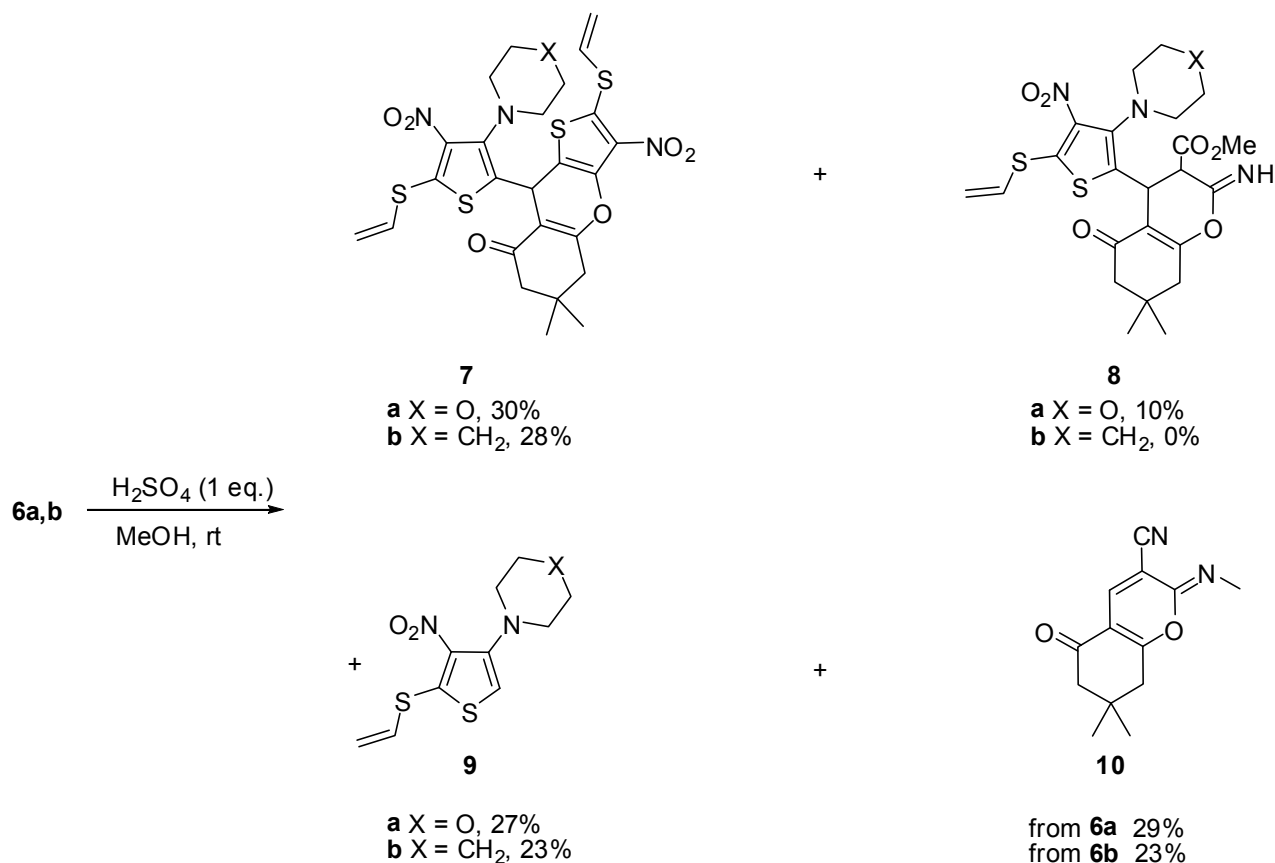
Scheme 1

In a Knoevenagel condensation of **4a-c** with malononitrile in ethanol at room temperature (rt) in the presence of catalytic amounts of sodium ethanolate 2-((4-nitro-3-(organylthio)-5-(vinylthio)thiophen-2-yl)methylene)malononitriles **5a-c** were formed in 68-72%. Treatment of these vinylthiophenes **5a-c** with dimedone led to the formation of the expected Michael adducts, followed by cyclization giving **6a-c**. Carrying out the reaction with 10% excess of dimedone in ethanol in the presence of catalytic amounts of morpholine first at rt, followed by 35-40 °C (TLC monitoring), the 4*H*-chromene-3-carbonitriles (**6**) were formed in 75-91% yield. These results are depicted in Scheme 2. The formation of 2-amino-5-oxo-7,7-dimethyl-5,6,7,8-tetrahydro-4*H*-chromene-3-carbonitriles by Michael addition of malononitrile derivatives with dimedone has been well studied.<sup>8</sup> These bicyclic heterocycles were synthesized from dimedone and the corresponding arylidenemalononitriles by a 6-*exo-dig* cyclization of  $\delta$ -oxonitriles.<sup>9</sup>



Scheme 2

2-Amino-5-oxo-5,6,7,8-tetrahydro-4*H*-chromene-3-carbonitriles are important synthetic building blocks with considerable pharmacological relevance. Their most important chemical transformations are (a) iodine-promoted domino reaction with various isocyanates to *N*-substituted 2-aminoquinoline-3-carbonitriles,<sup>10a</sup> (b) synthesis of substituted and annulated pyrano[2,3-*d*]pyrimidines consisting of an acylation of 2-amino-3-cyano-4*H*-pyrans with acetic anhydride,<sup>10b</sup> (c) simple and convenient approach to the Friedländer synthesis of pyrano[2,3-*b*]pyridines,<sup>10c-e</sup> (d) reaction with phenylisothiocyanate and ethyl orthoformate with formation of the chromenopyrimidine and the formimidate, respectively,<sup>8f</sup> (e) synthesis of 4-isopropyl-7,7-dimethyl-2,5-dioxo-1,2,3,4,5,6,7,8-octahydroquinoline-3-carboxamide by treatment of the corresponding 4*H*-chromene-3-carbonitrile derivatives with a solution of bromine in aqueous methanol,<sup>10f</sup> (f) opening of a substituted 2-amino-3-cyano-4*H*-pyrane ring, resulting in formation of methyl acrylate derivatives,<sup>10g</sup> (g) synthesis of 4-amino-6-aryl-2-phenylpyrimidine-5-carbonitriles under the action of benzamidine hydrochloride in the presence of sodium ethanolate,<sup>10h</sup> (h) utility of 2-aminochromene-3-carbonitriles in the synthesis of chromeno[3,2-*e*][1,2,4]triazolo[1,5-*c*]pyrimidine,<sup>10i</sup> (i) hydrolysis with hydrochloric acid under the formation of fused furo[2,3-*b*]furanones,<sup>10j</sup> (j) treatment of 2-aminochromene-3-carbonitriles with ammonium acetate, benzylidenemalononitrile, and ammonium thiocyanate/benzoyl chloride leads to 5-oxocyclohexanopyridin-3-carbonitriles, 3-azaacridin-4,6-diones and cyclohexano[*g*]-4*H*-pyrano[2,3-*d*]pyrimidin-7-ones, respectively.<sup>10k</sup>

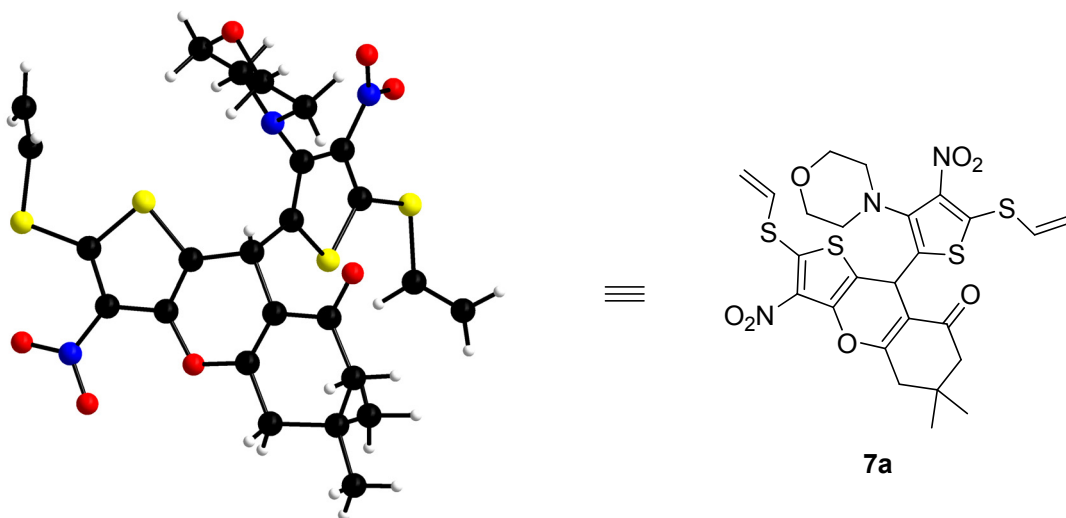


Scheme 3

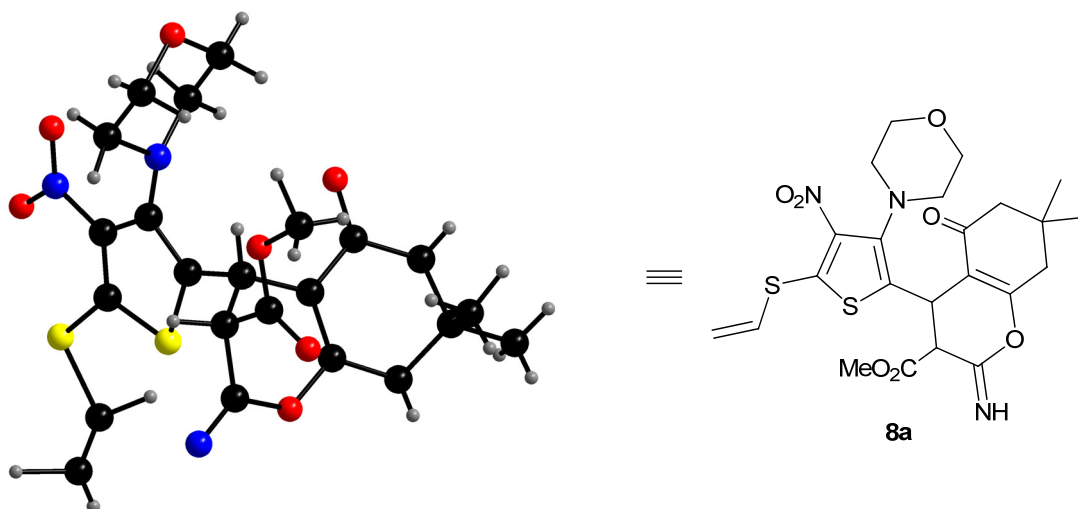
We first tested the hydrolytic behavior of the 4*H*-chromene-3-carbonitriles **6a,b** in aqueous methanol at rt in the presence of equimolar amounts of conc. sulfuric acid. The reaction led to the formation of a complex mixture of products, from which we could isolate four main compounds **7-10**. While both thieno[3,2-*b*]chromen-8-ones **7a,b** were obtained in 28-30% yield, a 2*H*-chromene-3-carboxylate **8a** could only be isolated in case of the morpholino derivative **6a** (10% yield). The trisubstituted thiophenes **9a,b** resulted in 27-23% yield, and finally, the tetrahydro-2*H*-chromene **10** was formed in 29-23% (Scheme 3).

In addition to the standard NMR, MS and IR spectroscopic investigations, X-ray analyses proved the structures of the thieno[3,2-*b*]chromen-8(9*H*)-one **7a** (see Figure 1) and the methyl hexahydro-2*H*-chromene-3-carboxylate **8a** (Figure 2).<sup>11,12</sup>

**Figure 1.** X-Ray crystal structure of 6,6-dimethyl-9-(3-morpholino-4-nitro-5-(vinylthio)thien-2-yl)-3-nitro-2-(vinylthio)-6,7-dihydro-5*H*-thieno[3,2-*b*]chromen-8(9*H*)-one (**7a**)

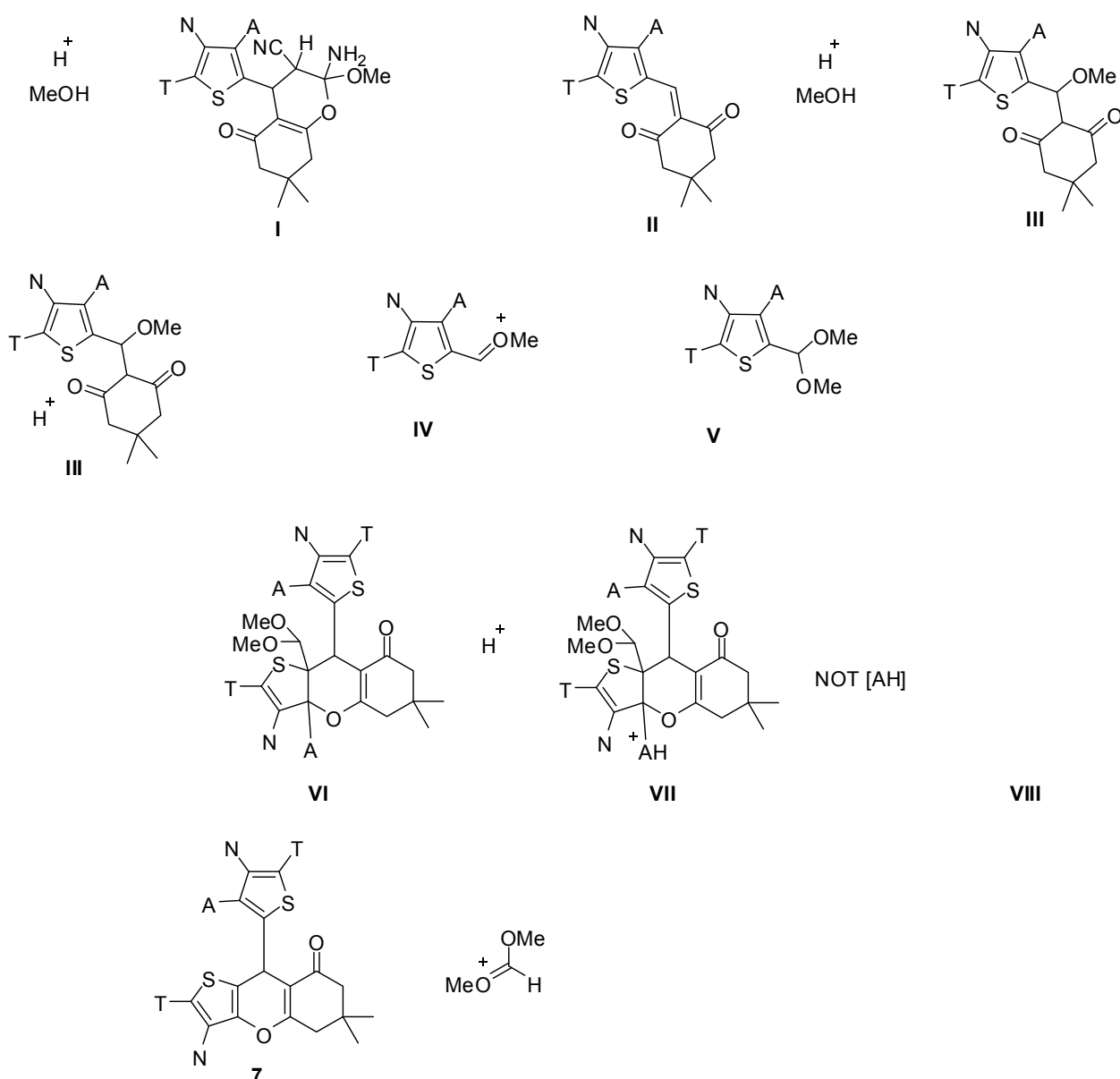


**Figure 2.** X-Ray crystal structure of methyl 2-imino-7,7-dimethyl-4-(3-morpholino-4-nitro-5-(vinylthio)thien-2-yl)-5-oxo-3,4,5,6,7,8-hexahydro-2*H*-chromene-3-carboxylate (**8a**)



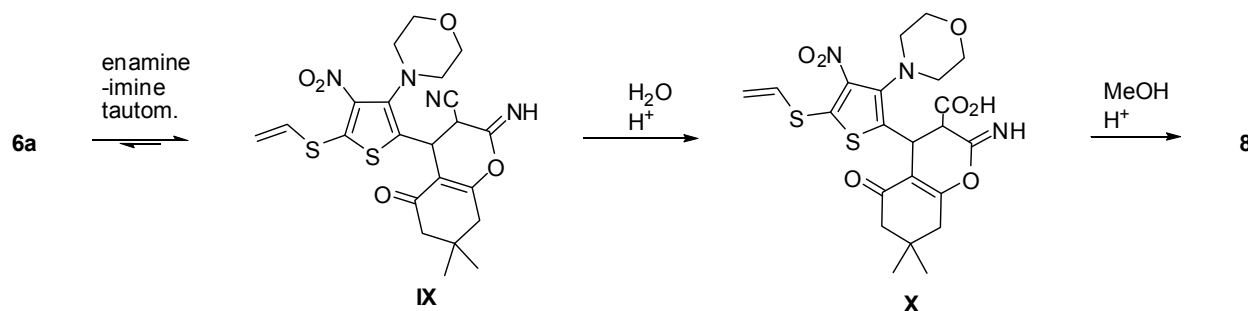
Conceivable mechanisms for the formation of the compounds **7-10** are presented in Scheme 4 (thieno[3,2-*b*]chromen-8-ones **7**), Scheme 5 (methyl 2*H*-chromene-3-carboxylate **8**), and Scheme 6 (thiophenes **9** and chromene **10**). In the cascade mechanism leading to **7** initially, the hemiaminal **I** is formed upon acid catalyzed addition of methanol to the push-pull substituted double bond in **6**. The combination of a retro cyclization/Michael addition then leads to the formal Knoevenagel condensation product **II** of **4** with dimedone, which adds methanol to form the ether **III** by acid catalysis. The proposed intermediate **II**

could not be isolated so far. Formally, it represents the diene part of a retro hetero-Diels-Alder reaction. Cycloreversion reactions of dihydropyrans are known, but occur at higher reaction temperatures.<sup>13</sup> Subsequent acid-catalyzed retro Knoevenagel condensation of **III** leads to oxonium salt **IV**, which is stabilized by acetalization to **V**. Hetero-Diels-Alder reaction of the electron-rich acetal **V** and **II** leads to the thieno[3,2-*b*]chromen-8-one **VI**, which is protonated exclusively at the condensed thieno unit to the ammonium salt **VII**. Subsequent elimination of morpholine (or piperidine) from the sterically demanding intermediate **VII** results in the salt **VIII**, which is stabilized upon elimination of (methoxymethylidene)(methyl)oxonium to form the stable tricyclic heterocycle **7** (Scheme 4).



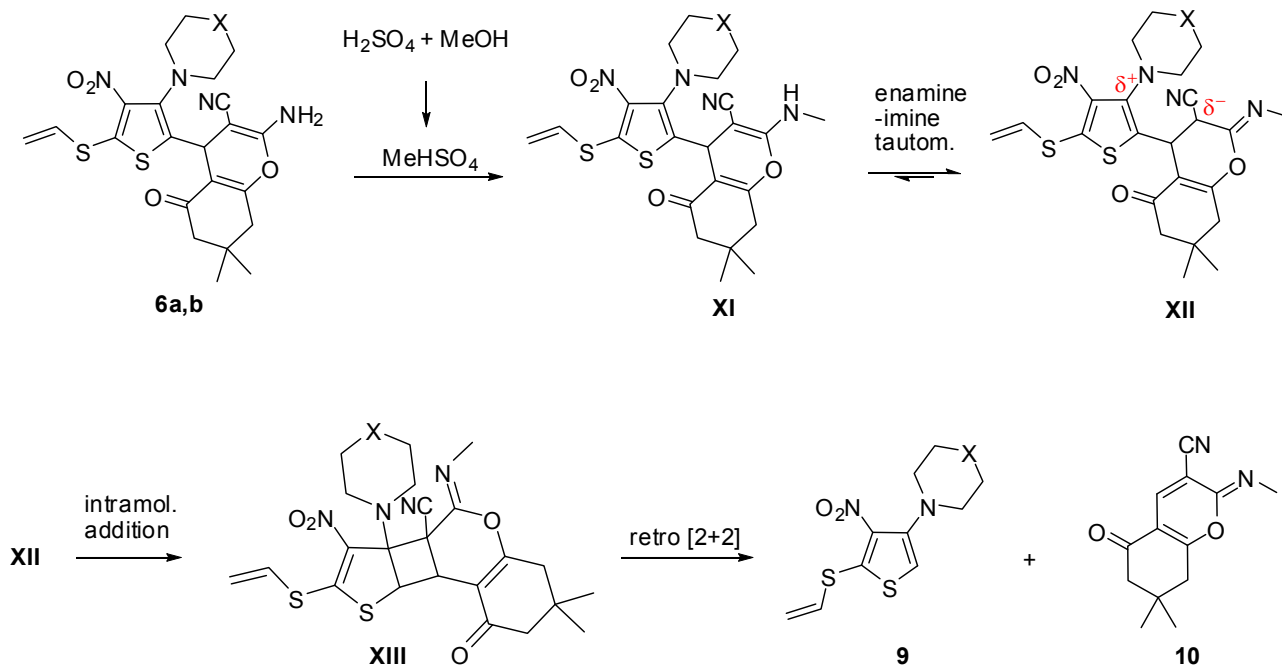
Scheme 4

In the mechanism to **8** first the starting material **6a** tautomerizes to the imine **IX**. Acid catalyzed hydrolysis of **IX** forms the acid **X**, then by esterification the stable methyl ester **8** is obtained (Scheme 5).



Scheme 5

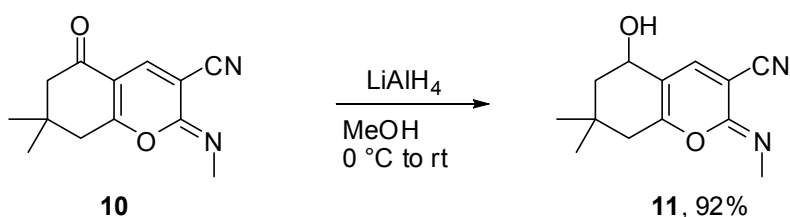
In the mechanism to **9** and **10** initially, the starting amines **6** were methylated with methyl sulfate, which forms *in situ* from sulfuric acid and methanol, to the methylamine derivative **XI**. This type of monomethylation of primary amines is known from the literature.<sup>14</sup> Subsequent enamine-imine tautomerization to the imin **XII** and intramolecular addition leads to the tetracyclic intermediate **XIII**. Finally, [2 + 2] cycloreversion results in thiophenes **9** and chromene **10** (Scheme 6).



Scheme 6

By treatment of tetrahydro-2*H*-chromene-3-carbonitrile (**10**) with lithium aluminium hydride in methanol at 0 °C to rt for 3 h only the carbonyl group in **10** is reduced by formation of 5-hydroxy-chromene **11** in

92% yield. The methylimino group in **10** remains unchanged under these reaction conditions (Scheme 7). To the best of our knowledge, tetrahydro-2*H*-chromene-3-carbonitriles of type **10** are very rare. Thus, 2-imino-7,7-dimethyl-4-methylsulfanyl-5-oxo-5,6,7,8-tetrahydro-2*H*-chromene-3-carbonitrile is formed in 85% yield by reaction of [bis(methylsulfanyl)methylidene]malononitrile with dimedone in refluxed 1,4-dioxane in the presence of equivalent amounts of KOH.<sup>15</sup>



**Scheme 7**

The starting thiophenes **3** have a unique substitution pattern and cannot be synthesized on any other way, so far, despite wrong assumptions in the recent patent literature.<sup>16</sup> They have proved to be interesting materials for varying applications, e.g. they can be used for prevention of retroviral infections due to their antiviral activity.<sup>16</sup> Derivatives of 2-(thien-2-ylmethylene)malononitrile are nonlinear optical (NLO) chromophores,<sup>17a</sup> near-infrared fluorophores,<sup>17b</sup> show anti-Trypanosoma cruzi activity<sup>17c</sup> and are possible epidermal growth factor receptor tyrosine kinase inhibitors.<sup>17d</sup> Dicyanovinyl-oligothiophenes are interesting for application as donor in solar cells.<sup>17e</sup> 2-Amino-3-cyanochromenes and its derivatives are known to possess molluscicidal,<sup>8f</sup> neuroprotective,<sup>10e</sup> antibacterial,<sup>18a-b</sup> and antimicrobial activity.<sup>18c</sup>

## CONCLUSION

By a Knoevenagel/Michael/cyclization sequence starting from 3-organylamino-4-nitro-5-(vinylthio)thiophene-2-carbaldehydes **4** potentially biologically active 2-amino-7,7-dimethyl-4-(3-organylamino-4-nitro-5-(vinylthio)thiophen-2-yl)-5-oxo-5,6,7,8-tetrahydro-4*H*-chromene-3-carbonitriles **6** were synthesized. Acidic hydrolysis of **6** in methanol at rt led to a mixture of heterocycles **7-10**, mainly the novel 9-(thien-2-yl)-6,7-dihydro-5*H*-thieno[3,2-*b*]chromen-8(9*H*)-one derivatives **7** were formed via a reaction cascade with an unexpected hetero-Diels-Alder reaction with inverse electron demand.

## EXPERIMENTAL

Melting points were determined with a Büchi apparatus 520 and are uncorrected. Thin layer chromatography (TLC) was performed on Merck TLC-plates (aluminum based) silica gel 60 F 254. FT-IR spectra were obtained in the range of 400 to 4000 cm<sup>-1</sup> with a Bruker Vector 22 FT-IR spectrometer

equipped with ALPHA's *Platinum ATR* single reflection diamond ATR module. Mass spectra were obtained on a Varian 320 MS Triple Quad GC/MS/MS instrument with a Varian 450-GC unit usually in direct mode with electron impact (70 eV). The elemental composition was confirmed by high-resolution EI and (+)-ESI mass spectrometry. All HRMS results were satisfactory in comparison to the calculated accurate masses of the molecular ions ( $\pm 2$  ppm,  $R \sim 10000$ ).  $^1\text{H}$  NMR (600 MHz),  $^{13}\text{C}$  NMR (150 MHz): Avance III 600 MHz FT-NMR spectrometer (Bruker, Rheinstetten, Germany);  $^1\text{H}$  NMR (400 MHz),  $^{13}\text{C}$  NMR (100 MHz): Avance 400 FT-NMR spectrometer (also Bruker).  $^1\text{H}$  NMR (200 MHz),  $^{13}\text{C}$  NMR (50 MHz): DPX 200 FT-NMR spectrometer (also Bruker).  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra were referenced to the residual solvent peak:  $\text{CDCl}_3$ :  $\delta = 7.26$  ( $^1\text{H}$ ),  $\delta = 77.0$  ( $^{13}\text{C}$ ) ppm;  $\text{DMSO}-d_6$ :  $\delta = 2.50$  ( $^1\text{H}$ ),  $\delta = 39.7$  ( $^{13}\text{C}$ ) ppm. Chemical shifts  $\delta$  are given in ppm. In most cases, peak assignments were accomplished by HSQC and HMBC NMR experiments. Separation of compounds (**7-10**) and purifications were carried out by means of column chromatography on silica gel 60 (Merck). Petroleum ether as eluent had the boiling range 60 – 70 °C.

**Starting Material.** 2-Nitropentachlorobuta-1,3-diene (**1**) was synthesized according to the literature<sup>19</sup> from 2*H*-pentachlorobuta-1,3-diene with a 10:1 solution of 63%  $\text{HNO}_3$  and 98%  $\text{H}_2\text{SO}_4$  in 53% yield (bp 69–71 °C, 1 mbar). Dithiolanes **2** and thiophenes **3** were prepared by previously reported procedure.<sup>5</sup> Thiophene-2-carbaldehydes **4** were synthesized according to the literature.<sup>6</sup> All other chemicals used in this study were commercially available.

### Typical Procedure for the Preparation of Products 5a-c.

#### 2-((3-Morpholino-4-nitro-5-(vinylthio)thien-2-yl)methylene)malononitrile (**5a**).

To a suspension of thiophene-2-carbaldehyde **4a** (3.00 g, 10.0 mmol) and malononitrile (0.99 g, 15 mmol) in 80 mL EtOH at 0 °C was added EtONa (0.068 g, 1.0 mmol) and the resulting mixture was stirred for 2 h at 0 °C and 18 h at rt. Subsequently, the supernatant liquid was concentrated *in vacuo* to a volume of about 30 mL, cooled to 10 °C and treated with 2 mL conc. HCl. The precipitate was isolated, washed with  $\text{H}_2\text{O}$  (2 x 20 mL), cold EtOH (1 x 5 mL), and finally dried under reduced pressure. Purification if necessary was carried out by means of column chromatography, eluent petroleum ether : EtOAc = 3 : 1. Yield 2.37 g (68%); red solid; mp 167-169 °C; IR 3107, 2960, 2923, 2869, 2214 (CN), 1546, 1522 ( $\text{NO}_2$ ), 1440, 1327 ( $\text{NO}_2$ ), 1185, 1113, 994, 949, 864, 776, 642, 602  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR (200 MHz,  $\text{CDCl}_3$ )  $\delta$  3.16-3.34 (m, 4H), 3.74-3.93 (m, 4H), 6.05 (d,  $J = 9.1$  Hz, 1H), 6.06 (d,  $J = 16.4$  Hz, 1H), 6.66 (dd,  $J = 16.4, 9.1$  Hz, 1H), 7.88 (s, 1H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ )  $\delta$  52.09 (NCH<sub>2</sub>), 67.05 (OCH<sub>2</sub>), 75.57 ( $\underline{\text{C}}\text{CN}$ ), 113.43 (CN), 114.20 (CN), 120.66 (SC), 124.76 (SCH), 130.04 (CH<sub>2</sub>), 136.52 (CNO<sub>2</sub>), 146.32 (CH), 152.88, 158.17 (SCS); MS  $m/z$  347 ( $\text{M}^+ - \text{H}$ , 25), 330 ( $\text{M}^+ - \text{H}_2\text{O}$ , 9), 271 ( $\text{M}^+ - \text{CH}=\text{C}(\text{CN})_2$ , 15); HRMS

(EI) calcd for  $C_{14}H_{12}N_4O_3S_2$  348.0351, found:  $m/z$  348.0349.

**2-((3-Piperidino-4-nitro-5-(vinylthio)thien-2-yl)methylene)malononitrile (5b).** Reaction time: 15 h at rt. Yield 72%; reddish brown solid; mp 133-134 °C; IR 2942, 2885, 2215 (CN), 1540, 1525 (NO<sub>2</sub>), 1444, 1379, 1332 (NO<sub>2</sub>), 1257, 1190, 1101, 991, 956, 858, 774, 643, 601 cm<sup>-1</sup>; <sup>1</sup>H NMR (200 MHz, CDCl<sub>3</sub>) δ 1.55-1.88 (m, 6H), 3.06-3.38 (m, 4H), 6.01 (d,  $J = 8.9$  Hz, 1H), 6.03 (d,  $J = 16.3$  Hz, 1H), 6.65 (dd,  $J = 16.3, 8.9$  Hz, 1H), 7.75 (s, 1H); <sup>13</sup>C NMR (CDCl<sub>3</sub>) δ 23.53 (CH<sub>2</sub>), 26.41 (2CH<sub>2</sub>), 54.08 (NCH<sub>2</sub>), 73.06 (C<sub>CCN</sub>), 113.88 (CN), 114.75 (CN), 117.70 (SC), 124.79 (SCH), 129.50 (CH<sub>2</sub>), 137.92 (CNO<sub>2</sub>), 146.53 (CH), 154.73, 157.84 (SCS); MS  $m/z$  346 (M<sup>+</sup>, 45), 330 (M<sup>+</sup>-OH, 68), 312 (38), 298 (M<sup>+</sup>-HNO<sub>2</sub>, 25), 285 (30); HRMS (EI) calcd for  $C_{15}H_{14}N_4O_3S_2$  346.0558, found:  $m/z$  346.0551.

**Ethyl 4-(2-(2,2-dicyanovinyl)-4-nitro-5-(vinylthio)thien-3-yl)piperazine-1-carboxylate (5c).** Reaction time: 12 h at rt. Yield 71%; red solid; mp 151-152 °C; IR 2861, 2221 (CN), 1698 (CO), 1572, 1520 (NO<sub>2</sub>), 1470, 1434, 1386, 1333 (NO<sub>2</sub>), 1243, 1128, 1116, 990, 957, 837, 763, 611 cm<sup>-1</sup>; <sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>) δ 1.21 (t,  $J = 7.1$  Hz, 3H), 3.27-3.37 (m, 4H), 3.51-3.59 (m, 4H), 4.08 (q,  $J = 7.1$  Hz, 2H), 6.15 (d,  $J = 9.0$  Hz, 1H), 6.16 (d,  $J = 16.3$  Hz, 1H), 6.88 (dd,  $J = 16.3, 9.1$  Hz, 1H), 8.29 (s, 1H); <sup>13</sup>C NMR (DMSO-*d*<sub>6</sub>) δ 14.75 (Me), 43.85 (NCH<sub>2</sub>), 52.03 (NCH<sub>2</sub>), 61.10 (OCH<sub>2</sub>), 72.64 (C<sub>CCN</sub>), 114.71 (CN), 115.13 (CN), 117.62 (SC), 125.27 (SCH), 130.88 (CH<sub>2</sub>), 137.50 (CNO<sub>2</sub>), 148.86 (CH), 153.34 (CO), 154.87, 157.77 (SCS); MS  $m/z$  419 (M<sup>+</sup>, 95), 403 (M<sup>+</sup>-O, 27), 374 (M<sup>+</sup>-OEt, 18), 275 (48), 259 (52); HRMS (EI) calcd for  $C_{17}H_{17}N_5O_4S_2$  419.0722, found:  $m/z$  419.0722.

### Typical Procedure for the Preparation of Products 6a-c.

**2-Amino-7,7-dimethyl-4-(3-morpholino-4-nitro-5-(vinylthio)thien-2-yl)-5-oxo-5,6,7,8-tetrahydro-4H-chromene-3-carbonitrile (6a).** To a suspension of thiophene **5a** (3.48 g, 10.0 mmol) in 80 mL EtOH was added dimedone (1.54 g, 11.0 mmol) and morpholine (0.09 g, 1.0 mmol) at rt. The resulting mixture was stirred 8 h at rt and 6 h at 35-40 °C. Subsequently, the supernatant liquid was concentrated *in vacuo* to a volume of about 30 mL, cooled to 10 °C and treated with 2 mL conc. HCl. The precipitate was isolated, washed with H<sub>2</sub>O (2 x 20 mL), cold EtOH (1 x 5 mL), and finally dried under reduced pressure. Purification if necessary was carried out by means of column chromatography, eluent petroleum ether: EtOAc = 3 :1. Yield 4.45 g (91%); yellow solid; mp 203-205 °C; IR 3378, 3326, 3191, 2943, 2857, 2194 (CN), 1678, 1650, 1546 (NO<sub>2</sub>), 1495, 1365 (NO<sub>2</sub>), 1322, 1218, 1104, 977, 853, 657, 561 cm<sup>-1</sup>; <sup>1</sup>H NMR (200 MHz, DMSO-*d*<sub>6</sub>) δ 1.02 (s, 3H, Me), 1.05 (s, 3H, Me), 2.15 (d,  $J = 16.1$  Hz, 1H, CH<sub>2</sub>), 2.30 (d,  $J = 16.1$  Hz, 1H, CH<sub>2</sub>), 2.40-2.60 (m, 2H, CH<sub>2</sub>), 3.03-3.17 (m, 2H, NCH<sub>2</sub>), 3.18-3.33 (m, 2H, NCH<sub>2</sub>), 3.60-3.86 (m, 4H, OCH<sub>2</sub>), 5.03 (s, 1H, CH), 5.89 (d,  $J = 9.2$  Hz, 1H), 5.93 (d,  $J = 16.3$  Hz, 1H), 6.78 (dd,  $J =$

16.3, 9.2 Hz, 1H), 7.23 (br. s, 2H, NH<sub>2</sub>); <sup>13</sup>C NMR (DMSO-*d*<sub>6</sub>) δ 26.99 (CH), 28.63 (Me), 28.68 (Me), 32.01 (Cq), 39.61 (CH<sub>2</sub>), 49.60 (NCH<sub>2</sub>), 50.07 (CH<sub>2</sub>), 57.09 (C<sub>≡</sub>CN), 67.09 (OCH<sub>2</sub>), 111.28 (Cq), 119.49 (CN), 127.08 (CH<sub>2</sub>), 127.15 (SCH), 139.15 (SC), 139.48 (CNO<sub>2</sub>), 143.74 (Cq), 144.26 (Cq), 158.61 (Cq), 164.01 (Cq), 195.97 (CO); MS *m/z* 488 (M<sup>+</sup>, 17), 471 (M<sup>+</sup>-OH, 14), 271 (thienyl unit, 10), 217 (chromene unit, 100); HRMS (EI) calcd for C<sub>22</sub>H<sub>24</sub>N<sub>4</sub>O<sub>5</sub>S<sub>2</sub> 488.1188, found: *m/z* 488.1187.

**2-Amino-7,7-dimethyl-4-(3-piperidino-4-nitro-5-(vinylthio)thien-2-yl)-5-oxo-5,6,7,8-tetrahydro-4H-chromene-3-carbonitrile (6b).** Reaction time: 5 h at 35-40 °C. Yield 89%; dark orange solid; mp 157-159 °C; IR 3331, 3171, 2937, 2850, 2200 (CN), 1681, 1654, 1542 (NO<sub>2</sub>), 1500, 1364 (NO<sub>2</sub>), 1330, 1215, 1142, 1037, 962, 855, 723, 560 cm<sup>-1</sup>; <sup>1</sup>H NMR (200 MHz, DMSO-*d*<sub>6</sub>) δ 1.03 (s, 3H, Me), 1.05 (s, 3H, Me), 1.40-1.72 (m, 6H), 2.14 (d, *J* = 16.1 Hz, 1H, CH<sub>2</sub>), 2.30 (d, *J* = 16.1 Hz, 1H, CH<sub>2</sub>), 2.46 (d, *J* = 16.4 Hz, 1H, CH<sub>2</sub>), 2.57 (d, *J* = 16.4 Hz, 1H, CH<sub>2</sub>), 2.91-3.07 (m, 2H, NCH<sub>2</sub>), 3.11-3.26 (m, 2H, NCH<sub>2</sub>), 4.94 (s, 1H, CH), 5.85 (d, *J* = 9.0 Hz, 1H), 5.87 (d, *J* = 16.6 Hz, 1H), 6.75 (dd, *J* = 16.6, 9.0 Hz, 1H), 7.20 (br. s, 2H, NH<sub>2</sub>); <sup>13</sup>C NMR (DMSO-*d*<sub>6</sub>) δ 23.91 (CH<sub>2</sub>), 26.30 (2CH<sub>2</sub>), 26.95 (CH), 28.63 (Me), 28.64 (Me), 31.95 (Cq), 39.65 (CH<sub>2</sub>), 50.10 (CH<sub>2</sub>), 50.51 (NCH<sub>2</sub>), 57.29 (C<sub>≡</sub>CN), 111.43 (Cq), 119.18 (CN), 126.28 (CH<sub>2</sub>), 127.37 (SCH), 140.17 (SC), 140.70 (Cq), 142.32 (CNO<sub>2</sub>), 142.74 (Cq), 158.65 (Cq), 163.85 (Cq), 195.83 (CO); MS *m/z* 486 (M<sup>+</sup>, 12), 469 (M<sup>+</sup>-OH, 12), 269 (thienyl unit, 3), 217 (chromene unit, 18); HRMS (EI) calcd for C<sub>23</sub>H<sub>26</sub>N<sub>4</sub>O<sub>4</sub>S<sub>2</sub> 486.1396, found: *m/z* 486.1398.

**Ethyl 4-(2-(2-amino-3-cyano-7,7-dimethyl-5-oxo-5,6,7,8-tetrahydro-4H-chromen-4-yl)-4-nitro-5-(vinylthio)thien-3-yl)piperazine-1-carboxylate (6c).** Reaction time: 3 h at 35-40 °C. Yield 75%; a yellow solid; mp 189-190 °C; IR 3392, 3326, 3195, 2959, 2193 (CN), 1673 (CO), 1607, 1549 (NO<sub>2</sub>), 1504, 1486, 1362 (NO<sub>2</sub>), 1330, 1246, 1215, 1142, 1071, 992, 720 cm<sup>-1</sup>; <sup>1</sup>H NMR (200 MHz, DMSO-*d*<sub>6</sub>) δ 1.03 (s, 3H, Me), 1.05 (s, 3H, Me), 1.20 (t, *J* = 7.1 Hz, 3H, Me), 2.16 (d, *J* = 16.1 Hz, 1H, CH<sub>2</sub>), 2.29 (d, *J* = 16.1 Hz, 1H, CH<sub>2</sub>), 2.49 (d, *J* = 17.6 Hz, 1H, CH<sub>2</sub>), 2.56 (d, *J* = 17.6 Hz, 1H, CH<sub>2</sub>), 2.90-3.08 (m, 2H, NCH<sub>2</sub>), 3.15-3.26 (m, 2H, NCH<sub>2</sub>), 3.33-3.40 (m, 1H, NCH<sub>2</sub>), 3.40-3.48 (m, 1H, NCH<sub>2</sub>), 3.48-3.70 (m, 2H, NCH<sub>2</sub>), 4.06 (q, *J* = 7.1 Hz, 2H, OCH<sub>2</sub>), 5.01 (s, 1H, CH), 5.89 (d, *J* = 9.2 Hz, 1H), 5.93 (d, *J* = 16.4 Hz, 1H), 6.77 (dd, *J* = 16.4, 9.2 Hz, 1H), 7.24 (br s, 2H, NH<sub>2</sub>); <sup>13</sup>C NMR (DMSO-*d*<sub>6</sub>) δ 14.7 (Me), 27.02 (CH), 28.64 (Me), 28.70 (Me), 32.05 (Cq), 39.83 (CH<sub>2</sub>), 44.32 (CH<sub>2</sub>), 49.21 (CH<sub>2</sub>), 50.05 (CH<sub>2</sub>), 57.12 (C<sub>≡</sub>CN), 61.04 (OCH<sub>2</sub>), 111.32 (Cq), 119.48 (CN), 127.09 (SCH), 127.24 (CH<sub>2</sub>), 139.15 (SC), 139.30 (CNO<sub>2</sub>), 143.55 (Cq), 144.54 (Cq), 154.90 (CO), 158.58 (Cq), 163.91 (Cq), 195.88 (CO); MS *m/z* 559 (M<sup>+</sup>, 20), 542 (M<sup>+</sup>-OH, 8), 342 (thienyl unit, 10), 217 (chromene unit, 100); HRMS (ESI) calcd for C<sub>25</sub>H<sub>30</sub>N<sub>5</sub>O<sub>6</sub>S<sub>2</sub> 560.1638 (M<sup>+</sup>+H), found: *m/z* 560.1615.

## Typical Procedure for Protonolysis of 2-Amino-4*H*-chromene-3-carbonitriles (6a,b) to Compounds 7-10.

### Protonolysis of Chromene (6a) to 7a-9a and 10.

To a suspension of chromene **6a** (2.44 g, 5.0 mmol) in 150 mL MeOH at rt was added 0.49 g (5.0 mmol) conc. H<sub>2</sub>SO<sub>4</sub> and the resulting mixture was stirred at this temperature. After disappearance of starting material (about 7 d, TLC control) the supernatant liquid was concentrated *in vacuo* at rt to a volume of about 30 mL. The precipitated solid was filtered, washed with cold MeOH (1 x 5 mL), H<sub>2</sub>O (2 x 10 mL), Et<sub>2</sub>O (1 x 5 mL), and finally dried under reduced pressure to afford **7a**. To the combined mother liquor and wash fractions cold H<sub>2</sub>O (200 mL) was added at 0 to 5 °C under vigorous stirring. The resulting mixture was extracted with CHCl<sub>3</sub> (3 x 70 mL), and then the organic phase was washed with H<sub>2</sub>O (2 x 100 mL) and dried with CaCl<sub>2</sub>. After evaporation of the solvent and separation *via* column chromatography the products **8a**, **9a**, **10** were obtained (first petroleum ether : EtOAc mixture 5:1 was used as eluent for separation of **9a** and **10**, then petroleum ether : EtOAc 1:1 for isolation of **8a**).

**6,6-Dimethyl-9-(3-morpholino-4-nitro-5-(vinylthio)thien-2-yl)-3-nitro-2-(vinylthio)-6,7-dihydro-5*H*-thieno[3,2-*b*]chromen-8(9*H*)-one (7a).** R<sub>f</sub> (petroleum ether : EtOAc = 1: 1) = 0.85; Yield 0.91 g (30%) of **7a**; yellow solid; mp 183-184 °C; IR 2951, 2859, 1639, 1575, 1543 (NO<sub>2</sub>), 1508 (NO<sub>2</sub>), 1363 (NO<sub>2</sub>), 1325 (NO<sub>2</sub>), 1262, 1209, 1112, 1038, 995, 859, 774, 659, 525 cm<sup>-1</sup>; <sup>1</sup>H NMR (200 MHz, CDCl<sub>3</sub>) δ 1.17 (s, 3H, Me), 1.19 (s, 3H, Me), 2.32 (s, 2H, CH<sub>2</sub>), 2.66 (d, *J* = 17.8 Hz, 1H, CH<sub>2</sub>), 2.77 (d, *J* = 17.8 Hz, 1H, CH<sub>2</sub>), 3.05-3.26 (m, 2H, NCH<sub>2</sub>), 3.40-3.58 (m, 2H, NCH<sub>2</sub>), 3.81-3.98 (m, 4H, OCH<sub>2</sub>), 5.71 (s, 1H, CH), 5.78 (d, *J* = 9.0 Hz, 1H), 5.84 (d, *J* = 16.2 Hz, 1H), 5.91 (d, *J* = 9.1 Hz, 1H), 5.96 (d, *J* = 16.4 Hz, 1H), 6.48 (dd, *J* = 16.4, 9.1 Hz, 1H), 6.52 (dd, *J* = 16.2, 9.0 Hz, 1H); <sup>13</sup>C NMR (CDCl<sub>3</sub>) δ 27.74 (Me), 28.85 (Me), 29.29 (CH), 32.22 (Cq), 41.36 (CH<sub>2</sub>), 49.88 (NCH<sub>2</sub>), 50.77 (CH<sub>2</sub>), 67.78 (OCH<sub>2</sub>), 109.47 (Cq), 116.51 (Cq), 125.51 (SCH), 126.21 (CH<sub>2</sub>), 126.98 (SCH), 128.30 (CH<sub>2</sub>), 138.41 (Cq), 139.38 (Cq), 139.92 (Cq), 141.69 (Cq), 143.55 (Cq), 145.20 (Cq), 147.43 (Cq), 166.05 (Cq), 196.33 (CO); MS *m/z* 606 (M<sup>+</sup>-H, 8), 589 (M<sup>+</sup>-H<sub>2</sub>O, 8), 335 (thienochromenone unit-H, 100), 271 (thiophene unit, 4); HRMS (ESI) calcd for C<sub>25</sub>H<sub>26</sub>N<sub>3</sub>O<sub>7</sub>S<sub>4</sub> 608.0654 (M<sup>+</sup>+H), found: *m/z* 608.0648.

**Methyl 2-imino-7,7-dimethyl-4-(3-morpholino-4-nitro-5-(vinylthio)thiophen-2-yl)-5-oxo-3,4,5,6,7,8-hexahydro-2*H*-chromene-3-carboxylate (8a).** R<sub>f</sub> (petroleum ether : EtOAc = 1: 1) = 0.38; Yield 0.26 g (10%); orange solid; mp 220-222 °C; IR 2957, 2873, 1744 (CO), 1717 (CO), 1652, 1629, 1539 (NO<sub>2</sub>), 1500, 1370, 1328 (NO<sub>2</sub>), 1261, 1169, 1103, 987, 847, 664, 555, 530 cm<sup>-1</sup>; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 1.12 (s, 3H, Me), 1.14 (s, 3H, Me), 2.27 (d, *J* = 16.4 Hz, 1H, CH<sub>2</sub>), 2.33 (d, *J* = 16.4 Hz, 1H, CH<sub>2</sub>), 2.40 (d, *J* = 17.3 Hz, 1H, CH<sub>2</sub>), 2.50 (d, *J* = 17.3 Hz, 1H, CH<sub>2</sub>), 3.01-3.18 (m, 2H, NCH<sub>2</sub>), 3.26-3.38 (m, 2H,

NCH<sub>2</sub>), 3.66 (br s, 1H, CHCO<sub>2</sub>), 3.80 (s, 3H, OMe), 3.80-3.94 (m, 4H, OCH<sub>2</sub>), 5.26 (br s, 1H, CH), 5.73 (d, *J* = 9.2 Hz, 1H), 5.81 (d, *J* = 16.5 Hz, 1H), 6.48 (dd, *J* = 16.5, 9.2 Hz, 1H), 8.49 (br s, 1H, NH); <sup>13</sup>C NMR (CDCl<sub>3</sub>) δ 28.03 (Me), 28.55 (Me), 32.12 (CH), 33.04 (Cq), 40.88 (CH<sub>2</sub>), 49.86 (NCH<sub>2</sub>), 50.23 (CH<sub>2</sub>), 53.4 (OMe), 54.2 (CHCO<sub>2</sub>), 67.77 (OCH<sub>2</sub>), 111.57 (Cq), 125.23 (CH<sub>2</sub>), 127.29 (SCH), 136.87 (Cq), 140.60 (Cq), 141.02 (Cq), 142.78 (CNO<sub>2</sub>), 151.82 (C=NH), 166.37 (Cq), 167.65 (Cq), 194.44 (CO); MS *m/z* 520 (M<sup>+</sup>-H, 1), 504 (M<sup>+</sup>-OH, 4), 462 (M<sup>+</sup>-CO<sub>2</sub>Me, 3), 272 (thiophene unit+H, 5), 250 (chromenone unit, 8); HRMS (ESI) calcd for C<sub>23</sub>H<sub>28</sub>N<sub>3</sub>O<sub>7</sub>S<sub>2</sub> 522.1387 (M<sup>+</sup>+H), found: *m/z* 522.1363.

**4-(4-Nitro-5-(vinylthio)thiophen-3-yl)morpholine (9a).** R<sub>f</sub> (petroleum ether : EtOAc = 5 : 1) = 0.14; Yield 0.37 g (27%); orange solid; mp 122-123 °C; IR 2973, 2923, 2862, 1536 (NO<sub>2</sub>), 1475, 1380, 1301 (NO<sub>2</sub>), 1184, 1110, 996, 920, 858, 765, 661, 609, 588 cm<sup>-1</sup>; <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>) δ 2.96-2.98 (m, 4 H), 3.84-3.86 (m, 4 H), 5.81 (d, *J* = 9.2 Hz, 1 H), 5.90 (d, *J* = 16.4 Hz, 1 H), 6.37 (s, 1 H), 6.62 (dd, *J* = 16.4, 9.2 Hz, 1 H); <sup>13</sup>C NMR (CDCl<sub>3</sub>) δ 52.62 (2 CH<sub>2</sub>), 66.60 (2 CH<sub>2</sub>), 104.58 (CH), 125.71 (CH<sub>2</sub>), 127.28 (SCH), 137.02 (CNO<sub>2</sub>), 147.48 (Cq), 148.59 (Cq); MS *m/z* 272 (M<sup>+</sup>, 74), 255 (M<sup>+</sup>-OH, 27), 238 (30), 227 (16); HRMS (EI) calcd for C<sub>10</sub>H<sub>12</sub>N<sub>2</sub>O<sub>3</sub>S<sub>2</sub> 272.0289 found: *m/z* 272.0290.

**7,7-Dimethyl-2-(methylimino)-5-oxo-5,6,7,8-tetrahydro-2H-chromene-3-carbonitrile (10).** R<sub>f</sub> (petroleum ether : EtOAc = 5 : 1) = 0.28; Yield 0.33 g (29%); a white solid; mp 125-126 °C; IR 3050, 2947, 2871, 2230 (CN), 1689 (CO), 1591, 1558, 1482, 1429, 1400, 1319, 1236, 1121, 1042, 978, 770, 565, 458 cm<sup>-1</sup>; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 1.10 (s, 6H, Me), 2.51 (s, 2H, CH<sub>2</sub>), 2.95 (s, 2H, CH<sub>2</sub>), 4.41 (s, 3H, NMe), 8.43 (s, 1H, CH); <sup>13</sup>C NMR (CDCl<sub>3</sub>) δ 28.22 (2 Me), 32.78 (Cq), 46.54 (CH<sub>2</sub>), 51.40 (CH<sub>2</sub>), 55.23 (NMe), 95.88 (CCN), 114.52 (CN), 121.57 (Cq), 142.11 (CH), 165.54 (C=N), 166.41 (Cq), 195.12 (C=O); MS *m/z* 230 (M<sup>+</sup>, 70), 215 (M<sup>+</sup>-Me, 10), 201 (M<sup>+</sup>-CO-H, 12), 174 (M<sup>+</sup>-(MeN=C-O)+H, 100); HRMS (EI) calcd for C<sub>13</sub>H<sub>14</sub>N<sub>2</sub>O<sub>2</sub> 230.1055 found: *m/z* 230.1054.

**Protonolysis of Chromene (6b) to Compounds 7b, 9b and 10.** Reaction time: 7 d at rt (TLC control) with using of 0.49 g (1.0 mmol) of **6b** and 0.10 g (1.0 mmol) conc. H<sub>2</sub>SO<sub>4</sub> in 30 mL MeOH. Workup see protonolysis of **6a**.

**6,6-Dimethyl-3-nitro-9-(4-nitro-3-piperidino-5-(vinylthio)thien-2-yl)-2-(vinylthio)-6,7-dihydro-5H-thieno[3,2-*b*]chromen-8(9H)-one (7b).** R<sub>f</sub> (petroleum ether : EtOAc = 5 : 1) = 0.42; Yield 0.17 g (28%); orange solid; mp 191-193 °C; IR 3030, 2938, 2850, 1711, 1665, 1643, 1574, 1544 (NO<sub>2</sub>), 1510 (NO<sub>2</sub>), 1362 (NO<sub>2</sub>), 1325 (NO<sub>2</sub>), 1273, 1209, 1180, 1115, 1036, 997, 966, 855, 773, 656, 538 cm<sup>-1</sup>; <sup>1</sup>H NMR (200 MHz, CDCl<sub>3</sub>) δ 1.17 (s, 3H, Me), 1.20 (s, 3H, Me), 1.55-1.78 (m, 6H, CH<sub>2</sub>), 2.34 (br s, 2H, CH<sub>2</sub>), 2.64 (d, *J* = 17.9 Hz, 1H, CH<sub>2</sub>), 2.76 (d, *J* = 17.9 Hz, 1H, CH<sub>2</sub>), 2.89-3.24 (m, 2H, NCH<sub>2</sub>), 3.28-3.41 (m,

2H, NCH<sub>2</sub>), 5.62 (s, 1H, CH), 5.66 (d,  $J = 9.0$  Hz, 1H), 5.72 (d,  $J = 16.4$  Hz, 1H), 5.89 (d,  $J = 9.0$  Hz, 1H), 5.95 (d,  $J = 16.4$  Hz, 1H), 6.46 (dd,  $J = 16.4, 9.0$  Hz, 1H), 6.53 (dd,  $J = 16.4, 9.0$  Hz, 1H); <sup>13</sup>C NMR (CDCl<sub>3</sub>) δ 23.92 (CH<sub>2</sub>), 26.71 (2CH<sub>2</sub>), 27.79 (Me), 28.87 (Me), 29.27 (CH), 32.21 (Cq), 41.41 (CH<sub>2</sub>), 50.70 (CH<sub>2</sub>), 50.80 (NCH<sub>2</sub>), 109.45 (Cq), 116.84 (Cq), 125.20 (CH<sub>2</sub>), 125.66 (SCH), 127.41 (SCH), 128.06 (CH<sub>2</sub>), 138.28 (Cq), 140.86 (Cq), 141.05 (Cq), 142.82 (Cq), 144.12 (Cq), 146.25 (Cq), 147.57 (Cq), 166.13 (Cq), 196.29 (CO); MS  $m/z$  605 (M<sup>+</sup>, 22), 588 (M<sup>+</sup>-OH, 20), 336 (thienochromenone unit-H, 100), 269 (thiophene unit, 10); HRMS (ESI) calcd for C<sub>26</sub>H<sub>28</sub>N<sub>3</sub>O<sub>6</sub>S<sub>4</sub> 606.0861 (M<sup>+</sup>+H), found:  $m/z$  606.0855.

**1-(4-Nitro-5-(vinylthio)thien-3-yl)piperidine (9b).** R<sub>f</sub> (petroleum ether : EtOAc = 5 : 1) = 0.55; Yield 0.062 g (23%); orange solid; mp 82-83 °C; IR 3114, 2928, 2807, 1541 (NO<sub>2</sub>), 1472, 1385, 1305 (NO<sub>2</sub>), 1191, 1112, 991, 955, 921, 857, 799, 667, 619, 589 cm<sup>-1</sup>; <sup>1</sup>H NMR (200 MHz, CDCl<sub>3</sub>) δ 1.47-1.60 (m, 2H, CH<sub>2</sub>), 1.70-1.82 (m, 4H, CH<sub>2</sub>), 2.84-2.94 (m, 4H, NCH<sub>2</sub>), 5.79 (d,  $J = 9.2$  Hz, 1H), 5.88 (d,  $J = 16.4$  Hz, 1H), 6.35 (s, 1H, CH), 6.64 (dd,  $J = 16.4, 9.2$  Hz, 1H); <sup>13</sup>C NMR (CDCl<sub>3</sub>) δ 23.85 (CH<sub>2</sub>), 25.65 (2 CH<sub>2</sub>), 53.68 (NCH<sub>2</sub>), 104.06 (CH), 125.15 (CH<sub>2</sub>), 127.56 (SCH), 137.05 (CNO<sub>2</sub>), 147.66 (Cq), 148.40 (Cq); MS  $m/z$  270 (M<sup>+</sup>, 77), 253 (M<sup>+</sup>-OH, 95), 236 (72), 222 (10); HRMS (EI) calcd for C<sub>11</sub>H<sub>14</sub>N<sub>2</sub>O<sub>2</sub>S<sub>2</sub> 270.0497, found:  $m/z$  270.0505.

**7,7-Dimethyl-2-(methylimino)-5-oxo-5,6,7,8-tetrahydro-2H-chromene-3-carbonitrile (10).** Yield 0.053 g (23%).

**5-Hydroxy-7,7-dimethyl-2-(methylimino)-5,6,7,8-tetrahydro-2H-chromene-3-carbonitrile (11).** To a solution of 0.23 g (1.0 mmol) of chromen-5-one **10** in 10 mL MeOH was added at 0 °C 0.076 g (2.0 mmol) LiAlH<sub>4</sub> and the resulting mixture was stirred 1 h at 0 °C and 2 h at rt. The supernatant liquid was concentrated *in vacuo* at rt to a volume of about 1 mL, cooled down to 0 °C, and then treated with 5 % aqueous HCl (10 mL). After 20 min stirring, the precipitate was filtered off, washed with H<sub>2</sub>O (2 x 5 mL), and then dried under reduced pressure to give 0.214 g (92%) of alcohol **11**; bright yellow solid; mp 104-105 °C; IR 3428 (OH), 2951, 2920, 2226 (CN), 1596, 1564, 1475, 1422, 1395, 1308, 1254, 1109, 1072, 978, 762, 562, 462 cm<sup>-1</sup>; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 0.97 (s, 3H, Me), 1.12 (s, 3H, Me), 1.53 (dd,  $J = 12.8, 13.0$  Hz, 1H, CH<sub>2</sub>), 2.02 (ddd,  $J = 12.8, 6.3, 2.0$  Hz, 1H, CH<sub>2</sub>), 2.04 (br s, 1H, OH), 2.61 (dd,  $J = 18.1, 2.0$  Hz, 1H, CH<sub>2</sub>), 2.70 (d,  $J = 18.1$  Hz, 1H, CH<sub>2</sub>), 4.00 (s, 3H, NMe), 4.77 (dd,  $J = 13.0, 6.3$  Hz, 1H, CH(OH)), 8.06 (s, 1H, =CH); <sup>13</sup>C NMR (CDCl<sub>3</sub>) δ 26.12 (Me), 30.83 (Cq), 31.01 (Me), 45.74 (CH<sub>2</sub>), 46.52 (CH<sub>2</sub>), 54.28 (NMe), 66.13 (CH(OH)), 94.27 (C<sub>≡</sub>CN), 115.68 (CN), 126.59 (Cq), 142.56 (=CH), 159.38 (Cq), 162.57 (Cq); MS  $m/z$  232 (M<sup>+</sup>, 78), 217 (M<sup>+</sup>-Me, 34), 214 (M<sup>+</sup>-H<sub>2</sub>O, 42), 199 (M<sup>+</sup>-H<sub>2</sub>O-Me,

95), 176 ( $M^+-(MeN=C-O)+H$ , 100); HRMS (EI) calcd for  $C_{13}H_{16}N_2O_2$  232.1211, found:  $m/z$  232.1212.

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11. **X-Ray structure analysis for 7a and 8a:** Suitable single crystals of the title compounds were selected under a polarization microscope and mounted in a glass capillary ( $d = 0.3$  mm). The crystal structures were determined by X-ray diffraction analysis using graphite monochromated Mo- $K_{\alpha}$  radiation ( $0.71073 \text{ \AA}$ ) [ $T = 223(2) \text{ K}$ ], whereas the scattering intensities were collected with a single crystal diffractometer (STOE IPDS II). The crystal structures were solved by Direct Methods using SHELXS-97 and refined using alternating cycles of least squares refinements against  $F^2$  (SHELXL-97). All non-H atoms were located in Difference Fourier maps and were refined with anisotropic displacement parameters. In **7a** the H positions were determined by a final Difference Fourier Synthesis, but the hydrogen positions in C24 and C25 were calculated using the riding model. In compound **8a** the hydrogen position of N1 couldn't be located.
- 7a** crystallized in the monoclinic space group  $C2/c$  (no. 15), lattice parameters  $a = 22.069(7)$ ,  $b = 11.584(2)$ ,  $c = 26.900(6) \text{ \AA}$ ,  $\beta = 101.60(2)^\circ$ ,  $V = 6737(3) \text{ \AA}^3$ ,  $Z = 4$ ,  $d_{calc.} = 1.370 \text{ g cm}^{-3}$ ,  $F(000) = 2912$  using 6040 independent reflections and 521 parameters.  $R1 = 0.0537$ ,  $wR2 = 0.1068$  [ $I > 2\sigma(I)$ ], goodness of fit on  $F^2 = 0.974$ , residual electron density = 0.353 and  $-0.289 \text{ e \AA}^{-3}$ . **8a** crystallized in the triclinic space group  $P1$  (no. 2), lattice parameters  $a = 9.959(3)$ ,  $b = 10.455(3)$ ,  $c = 13.185(4) \text{ \AA}$ ,  $\alpha = 69.76(2)$ ,  $\beta = 89.34(2)$ ,  $\gamma = 75.91(2)^\circ$ ,  $\bar{V} = 1245.3(6) \text{ \AA}^3$ ,  $Z = 1$ ,  $d_{calc.} = 1.388 \text{ g cm}^{-3}$ ,  $F(000) = 546$  using 4446 independent reflections and 410 parameters.  $R1 = 0.0804$ ,  $wR2 = 0.1815$  [ $I > 2\sigma(I)$ ], goodness of fit on  $F^2 = 1.034$ , residual electron density = 0.472 and  $-0.4990 \text{ e \AA}^{-3}$ . Further details of the crystal structure investigations have been deposited with the Cambridge Crystallographic Data Center, CCDC 886707 for **7a** and CCDC 886706 for **8a**. Copies of this information may be obtained free of charge from The Director, CCDC, 12 Union Road, Cambridge, CB2 1EZ, UK (Fax: +44(1223)-336 033; e-mail: [fileserv@ccdc.ac.uk](mailto:fileserv@ccdc.ac.uk) or <http://www.ccdc.cam.ac.uk>).
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