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Reactions of Heteroaryl Substituted Propenones*

Lutz Greiner-Bechert, Thomas Sprang, and **Hans-Hartwig Otto**#

Department of Pharmaceutical/Medicinal Chemistry, Institute of Pharmacy,
University of Greifswald, D-17487 Greifswald, Germany

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Summary. Thienyl- and furylpropenones reacted with malonates, cyanoacetates, and malononitrile giving addition products which could be cyclized to heteroaryl substituted dihydropyranes, cyclohexanols, and piperidones. Heteroaryl substituted cyclopropyl ketones were prepared by reactions with Me_3SO^+ I^-, and by reaction with *Lewis* acids they were transformed into substituted dihydrobenzo[*b*]furanone or -thiophenone, or γ-hydroxy ketones. Cycloadditions with thiophene derivatives allowed the synthesis of substituted benzo[*b*]thiophene derivatives, but with poor yields. Structures and stereochemistry were established mainly by means of NMR spectroscopy.

Keywords. Benzo[*b*]thiophene; Cyclopropyl ketone; *Michael* addition; Thienyl propenone.

Introduction

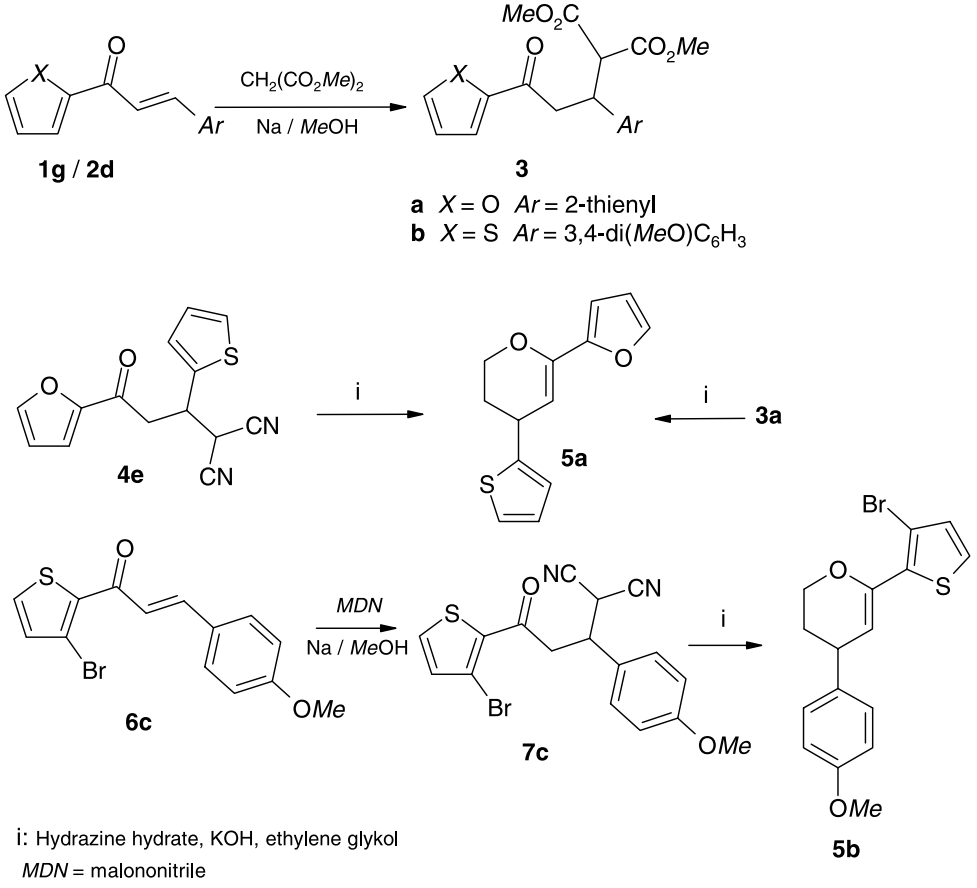
Substituted propenones are long known typical *Michael* acceptors, and the adducts allow a wide range of reactions depending on their substituents [1]. We have described the synthesis of 1,3-diaryl and heteroaryl substituted propenones, and their reaction with malononitrile opening an effective route to 4,6-diaryl/heteroaryl substituted pyridine-2-carbonitriles [2]. To explore further possibilities of using these propenones in (drug) synthesis, we here report about their reactions with activated methylene compounds, about their transformation into cyclopropyl ketones, and about some transformations of these ketones [3].

Results and Discussion

The furylthienylpropenone **1g** [4], and the thienylphenylpropenone **2d** [5] reacted with dimethyl malonate in the presence of *LDA* at $-78°$ yielding the oxovalerates **3a** and **3b** in satisfactory yields up to 83%. These adducts may be used as

* Dedicated to Prof. *F. Sauter*, Vienna, with cordial thanks for many valuable advices

Corresponding author. E-mail: ottohh@pharmazie.uni-greifswald.de

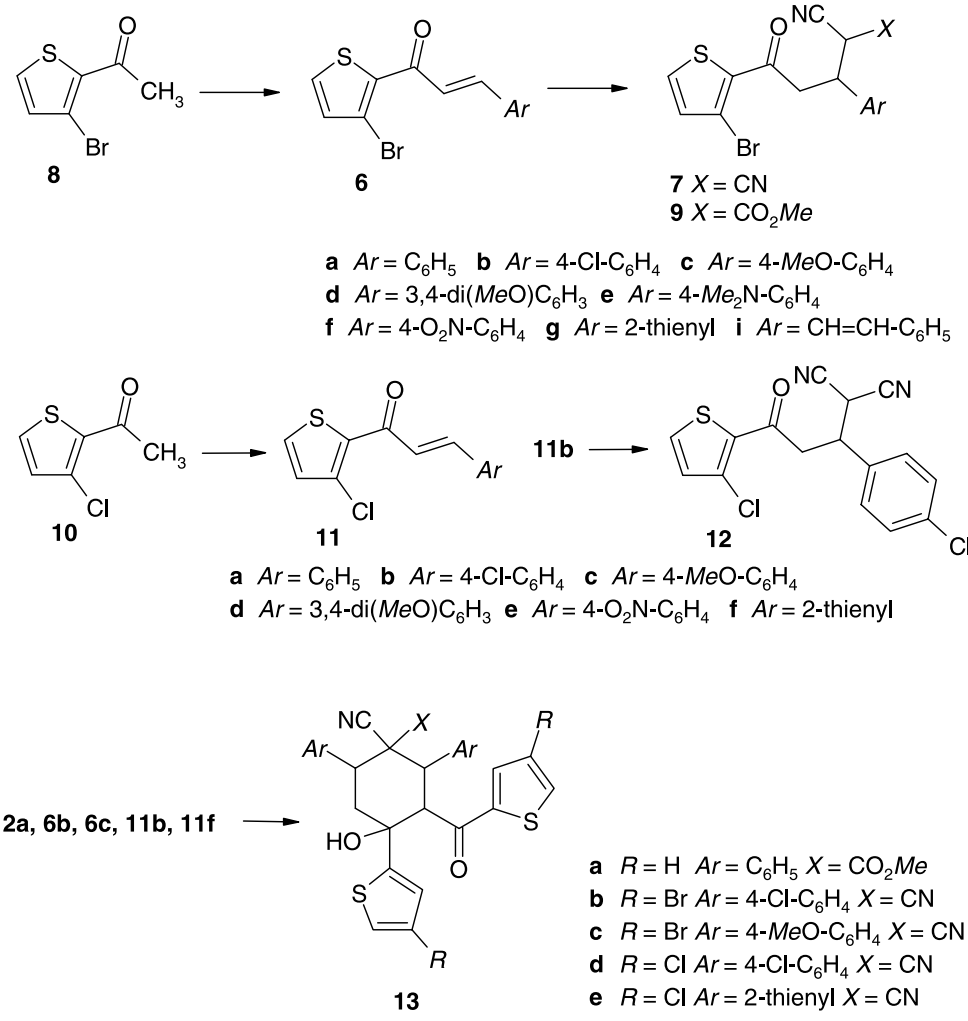


Scheme 1

building blocks for the synthesis of heterocyclic substituted dihydropyrane derivatives [3]. By cyclization under reductive conditions we obtained from **4e** [3] or from **3a** the dihydropyrane derivative **5a**, whereas **5b** was obtained from the bromothienyl propenone **6c** *via* the addition product **7c** by an analogous procedure (Scheme 1).

Starting from 2-acetyl-3-bromothiophene (**8**) [6] or 2-acetyl-3-chlorothiophene (**10**) [7] we prepared by basic condensation (NaOH, *Me*OH) with appropriate aldehydes the parent thienylpropenones **6** and **11**. These were excellent substrates for the addition of malononitrile, which was best done by reaction in *DMSO* in the presence of NaH at room temperature. Thereby, from **6a**–**6c** and **6f** the compounds **7a**–**7d**, and from **11b** compound **12** were obtained with yields of 60–90%. The adducts **9a** and **9b** were accessible with yields of 60–80% by an analogous reaction with methyl cyanoacetate.

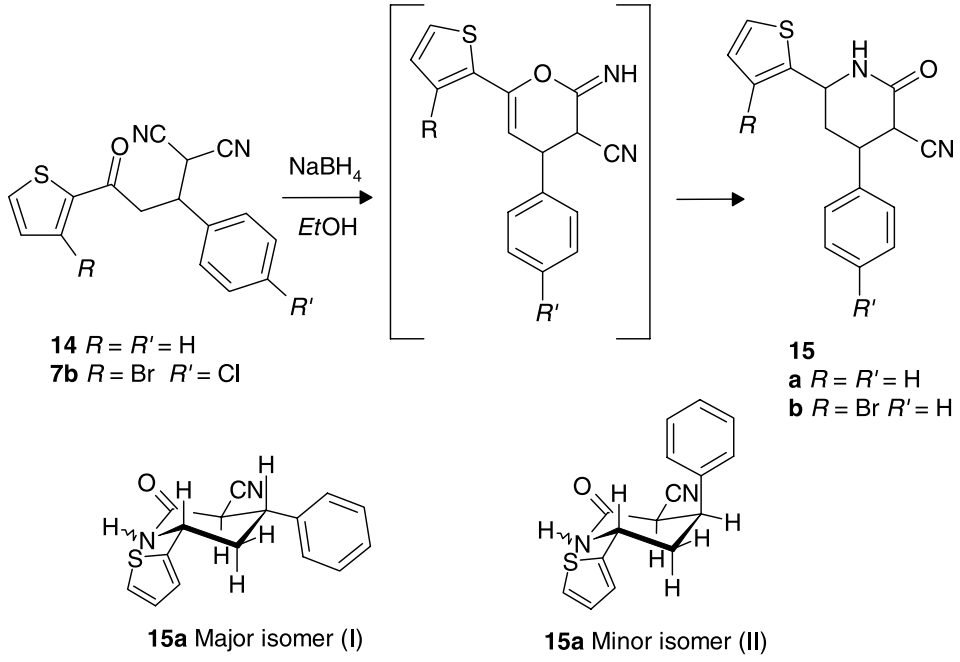
A remarkable observation was the formation of the compounds **13a**–**13e**. Compound **13a** was formed as a by-product, yield 10%, in the reaction between **2a** and methyl cyanoacetate, ratio 1:1, with Na in *Me*OH, reflux for 1 h, and acidic workup. Higher yields, and the analogous products were obtained from reactions between two equivalents of the propenone and one equivalent of malononitrile or



Scheme 2

methyl cyanoacetate (Scheme 2). Thus, the reaction between **11f** and malononitrile, ratio 2:1, gave **13e** with more than 70% yield when performed at room temperature in *Et*OH with some drops of piperidine. Elemental analyses and spectroscopic data established the structure with equatorial orientation of the aromatic groups and the acyl group. The stereochemistry of compounds **13** was deduced from the ^{1}H NMR data showing that the substituents in positions 2, 3, and 6 are orientated in the equatorial positions. The following coupling constants were found in the spectrum of **13b**. The coupling between 2-H and 3-H was $J = 12$ Hz, that between 5-H_{ax} and O–H $J = 2$ Hz, that between 5-H_{ax} and 6-H $J = 14$ Hz, and that between 5-H_{eq} and 6-H $J = 3$ Hz.

Similar reactions were described as sequences of nucleophilic additions [8], but the formation of **13** cannot be explained as a double *Michael* addition as known from reactions between malononitrile and 1,4-pentadiene-3-ones [9] or as a sequential *Michael* addition. Instead, structure **13** was formed by a sequence, whereby first two *Michael* additions of one reactive methylene group to two molecules of

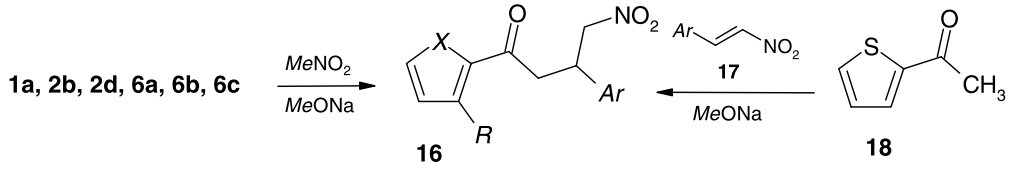


Scheme 3

the propenone occurred followed by an intramolecular aldol addition between one methylene group and one carbonyl group [10].

Another unusual cyclization was observed when we tried to reduce the propenones **14** [11] and **7b** with $NaBH_4$ in *Et*OH to the corresponding alcohols. Instead of the alcohols, we isolated the crystalline piperidone derivatives **15a** and **15b** with yields of 90% and higher (Scheme 3). Their IR spectra showed an amide I band at 1630 cm^{-1}, and an N–H band around 3300 cm^{-1}. Whereas the nitrile groups in the spectra of **14** and **7b** caused a weak band at 2250–2260 cm^{-1}, the spectra of compounds **15** exhibited a strong nitrile band at 2000 cm^{-1}. The piperidone structure was further established by the ^1H NMR data. The data of **15a** obtained from spectra in $CDCl_3$ and *DMSO*-d_6 showed that this compound was isolated as a mixture of two diastereoisomers with a ratio of 7:3. The coupling constants in the spectra of the major isomer (I) suggest all substituents in equatorial positions, whereas in the minor isomer (II) the phenyl group at C-4 was detected in the axial position. The signals at $\delta = 4.50$ and 4.55 ppm ($CDCl_3$) or $\delta = 6.45$ and 6.55 ppm (*DMSO*-d_6) disappeared after addition of D_2O demonstrating that these signals were caused by the acidic protons 1-H and 3-H. The formation of **15** might be explained by a reaction sequence starting with the reduction of the carbonyl group, followed by the addition of the newly formed hydroxyl group to one nitrile group with formation of a (not isolated) iminodihydropyrane which was finally transformed into the δ-lactam by a *Dimroth* rearrangement [12].

Similar to the addition of cyano derivatives, the addition of nitromethane was successful. Thus, the ω-nitro ketones **16a**, **16b**, and **16c** were prepared *via* reaction of **1a**, **2b**, and **2d** with nitromethane in the presence of Na in *Me*OH with yields of 60–66%. An alternative route was demonstrated by the reaction of 2-acetylthiophene



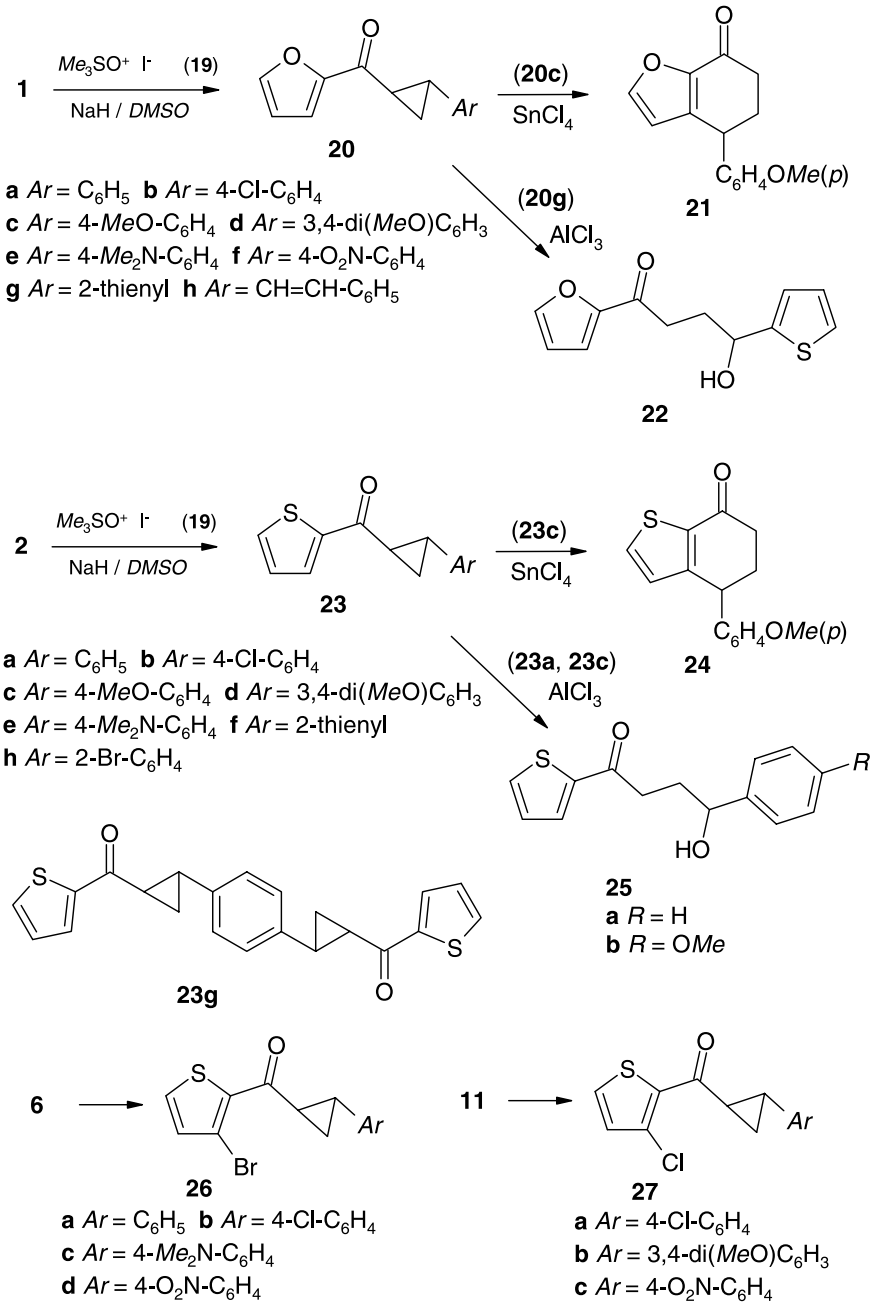
a $X = O$ $R = H$ $Ar = C_6H_5$
b $X = S$ $R = H$ $Ar = 4\text{-Cl-}C_6H_4$
c $X = S$ $R = H$ $Ar = 3,4\text{-di}(MeO)C_6H_3$
d $X = S$ $R = Br$ $Ar = C_6H_5$
e $X = S$ $R = Br$ $Ar = 4\text{-Cl-}C_6H_4$
f $X = S$ $R = Br$ $Ar = 4\text{-}MeO\text{-}C_6H_4$

Scheme 4

(**18**) with the nitro olefin **17** and *Me*ONa giving **16b** with 68% yield. The liquid compounds **16d**, **16e**, and **16f** were obtained by the analogous reaction of the 3-bromothienyl substituted propenones **6a**, **6b**, and **6c** with yields of 70–84% (Scheme 4).

Another possibility to use the propenones for further transformations was opened by their reaction with sulfur ylides yielding substituted cyclopropanes [13]. We used trimethylsulfoxonium iodide (**19**), as all reactions conveniently could be done at room temperature in *DMSO* in the presence of NaH, and we isolated from all reactions the cyclopropyl ketones with satisfactory to good yields. The furan derivatives **20a**–**20h** were obtained as waxy crystals with yields of 78–95%, whereas the analogue thiophene derivatives **23a**–**23h** were isolated as colorless to light yellow crystals with yields of 70–93%, and the halogeno substituted derivatives **26b**–**26d** and **27a**–**27c** were isolated as crystalline compounds with good yields, too. Only **26a** was obtained as a light liquid with 83% yield. The IR spectra of these cyclopropyl ketones were characterized by bands around 3100 ($H–C_{cyclopropyl}$), 1630 (C=O), 1010 ($C–C_{3\text{-ring}}$), and about 950 cm^{-1}. The last one was found in the same area as the band of *trans* substituted, conjugated double bonds, and therefore, could be used as an indicator for the *trans* substitution of the 3-membered ring. This was in agreement with the ^1H NMR data showing an ABCD system from the protons of the cyclopropyl moiety. Values from compound **20b** are $\delta = 2.75$ ppm (1-H, D), $\delta = 2.65$ ppm (2-H, C), $\delta = 1.80$ ppm (3-H, B), and $\delta = 1.40$ ppm (3′-H, A) with coupling constants $J_{AB} = 4$ Hz, $J_{AC} = 6.5$ Hz, $J_{BC} = 10$ Hz, $J_{AD} = 8$ Hz, and $J_{BD} = 5$ Hz. These values are in agreement with the 1,2-*trans* orientation at the cyclopropane ring.

4-Aryltetralones can be prepared *via* intramolecular *Friedel-Crafts* cyclization of substituted benzoyl aryl ketones with $SnCl_4$ in benzene [14]. To prove if this cyclization is possible even with our heteroaryl substituted cyclopropyl ketones we studied some reactions with *Lewis* acids. When the furan derivative **20c** or the thiophene derivative **23c** were reacted with $SnCl_4$ in C_6H_6 at room temperature, we isolated after acidic workup (HCl) the [*b*]annelated cyclohexenones **21** and **24** with yields of 94 (**21**) and 54% (**24**) after chromatographic work-up. But when the same reaction with $SnCl_4$ or $AlCl_3$ was done and worked-up under basic conditions (aq. NaOH), we isolated from the reactions of **20g**, **23a**, and **23c** the hydroxy



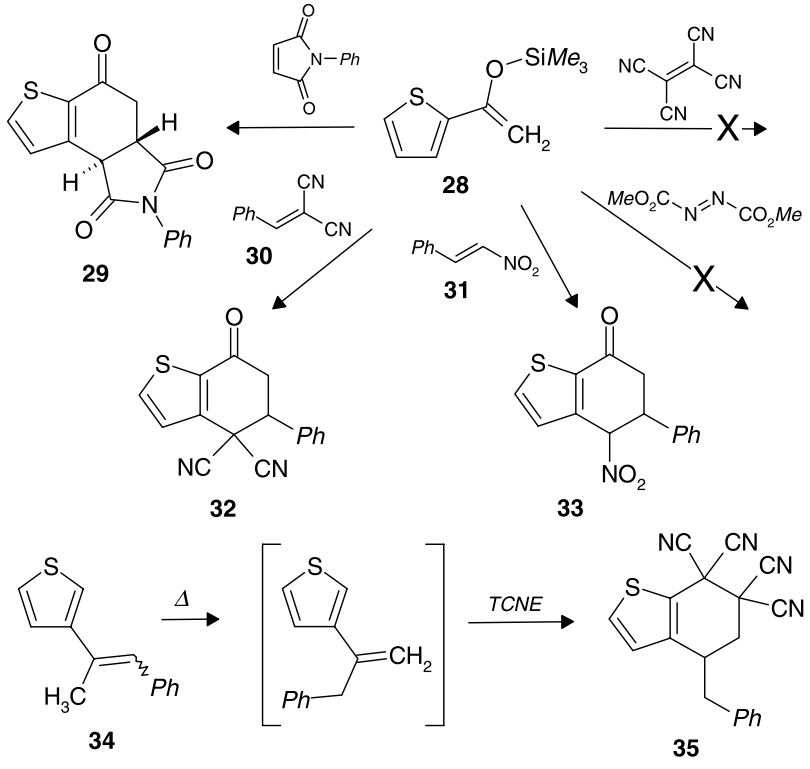
Scheme 5

compounds **22**, **25a**, and **25b** with yields of 40–70%, probably formed by a nucleophilic reaction between the base and C-2 of the cyclopropane ring, activated as complexed by the *Lewis* acid (Scheme 5).

The structures of the annelated ketones **21** and **24** and of the γ-hydroxy ketones **22** and **25** were established by spectroscopic data, from which the shift of the carbonyl bands in their IR spectra was significant. In the spectra of the cyclopropyl

ketones **20c**, **23a**, and **23c** this band was found at 1640 (**20c**) and 1625 cm^{-1} (**23a**, **23c**), whereas the annelated cyclohexenones **21** and **24** showed the carbonyl band shifted to 1675 and 1655 cm^{-1}. In the spectra of the γ-hydroxy ketones an intensive hydroxy band at 3400–3450 cm^{-1} and the carbonyl band at 1655 (**22**), 1650 (**25b**), and at 1635 cm^{-1} (**25a**) were found. Furthermore, the data from ^{1}H and ^{13}C NMR spectra were in full agreement with the postulated structures.

Another way to thieno annelated cyclohexenones should be the *Diels-Alder* reaction between an appropriate derivative of thiophene and a dienophile. Therefore, we prepared 2-(1-trimethylsiloxyvinyl)thiophene (**28**) [15] from 2-acetylthiophene and $ClSiMe_3$ in *THF* with *LDA*. When we performed the synthesis as described, we isolated **28** only in poor yields. But by strictly working at 0°C, and completing the synthesis within 20–30 minutes, we could improve the yield to 93%. It is known that the furan analogous compounds of **28** behave as suitable dienes for *Diels-Alder* reactions [16], and that vinylthiophene and derivatives usually are less reactive. Nevertheless, we checked reactions of **28** with activated double bonds (Scheme 6). Although we tried many different reaction conditions, solvents, and catalysts, we obtained only from three reactions defined compounds. From most other reactions, only 2-acetylthiophene and the dienophile were isolated. Thus, the reaction between **28** and *N*-phenylmaleinimide in CH_2Cl_2 in a sealed tube at 80°C for 24 h yielded the adduct **29** with yields about 17%. Using the acrylonitrile **30** or the nitroolefine **31** under similar conditions the yields were



Scheme 6

significantly lower. The annelated products **32** and **33** were isolated only with yields of 4–5%. A higher yield was obtained from the reaction between the thiophene derivative **34** and *TCNE*, whereby we obtained the benzyl substituted bicycle **35**. The structures of compounds **29**, **32**, **33**, and **35** were deduced from ^{1}H NMR data. The reaction of **34** forming **35** was remarkable, as it included in the first step a thermal isomerization of **34** to the substituted vinyl derivative (not isolated), which underwent the cycloaddition to **35**.

Experimental

Melting points: Linström apparatus (uncorrected); IR spectra (KBr): Perkin-Elmer IR 841, IR 1310, Beckmann IR 4240; NMR spectra: ^{1}H: Varian T 60 (60 MHz), Bruker WP 80 (80 MHz), ^{13}C: Bruker WH 90 (22.63 MHz), room temperature, internal *TMS*, $CDCl_3$, values from 80 MHz spectra, $CDCl_3$, if not otherwise noted; elemental analyses: Pharmazeutisches Institut, University of Freiburg or Pharmazeutisches Institut, University of Greifswald; the results agreed with the calculated values within experimental error. Column chromatography (CC) with silica gel 60 Merck Nr. 7734. Lithium diisopropylamide (*LDA*) was freshly prepared by mixing of equimolar amounts of diisopropylamine in *THF* and *n*-butyl lithium (*Bu*Li, 1.6 *M* in *n*-hexane) at −78°C. Abbreviations: *ar* = aromatic. For the syntheses of propenones **1** and **2** see Ref. [2], for 1-(2-furyl)-3-(2-thienyl)-2-propen-1-one (**1g**) see Ref. [4], for 3-(3,4-dimethoxyphenyl)-1-(2-thienyl)-2-propen-1-one (**2d**) see Ref. [5], for 2-cyano-5-(2-furyl)-5-oxo-3-(2-thienyl)valeronitrile (**4e**), 2-acetyl-3-bromothiophene (**8**), 1-(3-bromo-2-thienyl)-3-(4-chlorophenyl)-2-propen-1-one (**6b**), 2-acetyl-3-chlorothiophene (**10**), 3-(4-chlorophenyl)-1-(3-chloro-2-thienyl)-2-propen-1-one (**11b**), and 2-cyano-5-oxo-3-phenyl-5-(2-thienyl)valeronitrile (**14**) see Ref. [2], for 2-(4-chlorophenyl)-1-nitroethene (**17**), and 2-cyano-3-phenylacrylonitrile (**30**) see Ref. [17], and for 1-phenyl-2-(3-thienyl)propene (**34**) see Ref. [18]. Trimethylsulfoxonium iodide (**19**) was purchased from Janssen (Nr. 14.026.58), and 1-nitro-2-phenylethene (**31**) from Merck Schuchardt (Nr. 818165).

Methyl (RS)-5-(2-Furyl)-2-methoxycarbonyl-5-oxo-3-(2-thienyl)valerate (**3a**, $C_{16}H_{16}O_6S$)

Dimethyl malonate (1.32 g, 11 mmol) was added at room temperature to a solution of 0.25 g of Na (11 mmol) in 50 cm^3 of Et_2O with stirring, a solution of 2.04 g of **1g** (10 mmol) in Et_2O was added, the mixture was refluxed for 1 h, cooled, hydrolyzed with dil. HCl, extracted 3× with Et_2O, the organic layer was dried (Na_2SO_4), and evaporated. Yield 2.8 g (83%); colorless crystals; mp 69°C (*Me*OH); IR: $\bar{\nu}$ = 2950 (CH), 1730, 1665 (CO), 1560 (*ar*) cm^{-1}; ^{1}H NMR: δ = 3.40 (d, J = 7 Hz, CH_2), 3.60 (s, O*Me*), 3.75 (s, O*Me*), 3.90 (d, J = 8 Hz, 2-H), 4.50 (dd, J = 7, 8 Hz, 3-H), 6.45 (m, 1H, 4-H_{furyl}), 6.75–7.60 (m, 5 *ar* H) ppm.

Methyl (RS)-3-(3,4-Dimethoxyphenyl)-2-methoxycarbonyl-5-oxo-5-(2-thienyl)valerate (**3b**, $C_{20}H_{22}O_7S$)

From dimethyl malonate (3.2 g, 20 mmol) and 2.75 g of **2d** (10 mmol) as **3a**. Yield 2.2 g (55%); colorless crystals; mp 88°C (*Me*OH); IR: $\bar{\nu}$ = 1735, 1650 (CO), 1130, 860 (*ar*) cm^{-1}; ^{1}H NMR: δ = 3.25–4.20 (m, 16H, O*Me*, aliphat. H), 6.70–7.75 (m, 6 *ar* H) ppm.

(RS)-2-(2-Furyl)-4-(2-thienyl)-4H-5,6-dihydropyrane (**5a**, $C_{13}H_{12}O_2S$)

KOH (1.4 g, 25 mmol) was dissolved in 20 cm^3 of ethyleneglycol. Compound **4e** (1.35 g, 5 mmol) (a), or 1.68 g of **3a** (5 mmol) (b) and 1.0 g of hydrazine hydrate (98%, 20 mmol) were added with stirring.

Then the mixture was refluxed for 2 h. The following azeotropic distillation was finished at 180°C, the residue was poured into ice-H_2O, acidified with conc. HCl, and several times extracted with Et_2O. The combined organic layers were dried ($MgSO_4$), and evaporated *in vacuo*. The residue was purified by CC (Et_2O/*n*-pentane 1/1). Yield a) 0.87 g (75%), b) 0.84 g (72%); colorless liquid; IR (film): $\bar{\nu} = 3105$, 3075, 3000 (CH), 1600 (enolether), 845 (C=C) cm^{-1}; ^1H NMR: $\delta = 1.40$ (m, 3H, CH), 2.30 (m, 2H, CH), 5.75–7.35 (m, 7 *ar* H) ppm.

(RS)-2-(3-Bromo-2-thienyl)-4-(4-methoxyphenyl)-4H-5,6-dihydropyrane (**5b**, $C_{16}H_{15}BrO_2S$)

From **7c** (1.95 g, 5 mmol) as described for **5a**. Yield 1.2 g (68%); colorless liquid; IR (film): $\bar{\nu} = 2930$ (CH), 1610, 860 (*ar*), 820 (C=C) cm^{-1}; ^1H NMR: $\delta = 1.15$–2.85 (m, 5H, CH), 3.75 (s, O*Me*), 6.20–7.80 (m, 7 *ar* H) ppm.

General Procedure for the Synthesis of 3-Bromothienylpropenones ***6***

Compound **8** (10 mmol) and an equimolar amount of the aldehyde were dissolved with stirring in 20 cm^3 of *Me*OH, then some pellets of NaOH were added, and stirring was continued for 2 h. The precipitate was separated and purified by recrystallization.

1-(3-Bromo-2-thienyl)-3-phenyl-2-propen-1-one (**6a**, $C_{13}H_9BrOS$)

From **8** (2.04 g, 10 mmol) and 1.05 g of benzaldehyde (10 mmol). Yield 2.5 g (85%); colorless crystals; mp 42°C (*Me*OH); IR: $\bar{\nu} = 1640$ (CO), 1590 (*ar*), 975 (*trans* C=C), 760, 705 (*ar*) cm^{-1}; ^1H NMR (60 MHz): $\delta = 7.30$–8.15 (m, 9 *ar* H) ppm.

1-(3-Bromo-2-thienyl)-3-(4-methoxyphenyl)-2-propen-1-one (**6c**, $C_{14}H_{11}BrO_2S$)

From **8** (2.04 g, 10 mmol) and 1.36 g of 4-methoxybenzaldehyde (10 mmol), 1 h reflux. Yield 2.8 g (86%); yellow crystals; mp 73°C (*Me*OH); IR: $\bar{\nu} = 1635$ (CO), 1580 (*ar*), 1260, 980 (*trans* C=C), 820 (*ar*) cm^{-1}; ^1H NMR (60 MHz): $\delta = 3.95$ (s, O*Me*), 7.25–8.00 (m, 8 *ar* H) ppm.

1-(3-Bromo-2-thienyl)-3-(3,4-dimethoxyphenyl)-2-propen-1-one (**6d**, $C_{15}H_{13}BrO_3S$)

From **8** (2.04 g, 10 mmol) and 1.60 g of 3,4-dimethoxybenzaldehyde (10 mmol). Yield 2.75 g (78%); yellow crystals; mp 110°C (*Me*OH); IR: $\bar{\nu} = 1635$ (CO), 1580 (*ar*), 970 (*trans* C=C), 835 (*ar*) cm^{-1}; ^1H NMR: $\delta = 3.95$ (s, 2 O*Me*), 7.25–7.60 (m, 5 *ar* H), 7.55, 7.85 (AB, $J = 15$ Hz, 7-H, 8-H) ppm; ^1H NMR (benzene-d_6): $\delta = 3.30$ (s, O*Me*), 3.40 (s, O*Me*), 6.35–7.15 (m, 5 *ar* H), 7.65, 8.05 (AB, $J = 15$ Hz, 7-H, 8-H) ppm.

1-(3-Bromo-2-thienyl)-3-(4-dimethylaminophenyl)-2-propen-1-one (**6e**, $C_{15}H_{14}BrNOS$)

From **8** (2.04 g, 10 mmol) and 1.49 g of 4-dimethylaminobenzaldehyde (10 mmol). Yield 3.0 g (85%); red crystals; mp 92°C (*Me*OH); IR: $\bar{\nu} = 1625$ (CO), 1610 (*ar*), 980 (*trans* C=C), 875 (*ar*) cm^{-1}; ^1H NMR (60 MHz): $\delta = 3.10$ (s, 2 *Me*), 6.65–7.85 (m, 8 *ar* H) ppm.

1-(3-Bromo-2-thienyl)-3-(4-nitrophenyl)-2-propen-1-one (**6f**, $C_{13}H_8BrNO_3S$)

From **8** (2.04 g, 10 mmol) and 1.51 g of 4-nitrobenzaldehyde (10 mmol). Yield 3.1 g (92%); light yellow crystals; mp 128°C (*Me*OH); IR: $\bar{\nu} = 1645$ (CO), 1605 (*ar*), 1510, 1340 (NO_2), 840 (*ar*) cm^{-1}.

1-(3-Bromo-2-thienyl)-3-(2-thienyl)-2-propen-1-one (**6g**, $C_{11}H_7BrOS_2$)

From **8** (2.04 g, 10 mmol) and 1.12 g of thiophene-2-carbaldehyde (10 mmol, freshly distilled). Yield 2.2 g (75%); yellow crystals; mp 58°C (*Me*OH); IR: $\bar{\nu} = 1630$ (CO), 1580 (*ar*), 980 (*trans* C=C) cm^{-1}; ^1H NMR (60 MHz): $\delta = 7.30–8.45$ (m, 7 *ar* H) ppm.

1-(3-Bromo-2-thienyl)-5-phenylpenta-2,4-dien-1-one (**6i**, $C_{15}H_{11}BrOS$)

From **8** (2.04 g, 10 mmol) and 1.30 g of cinnamaldehyde (10 mmol). Yield 2.75 g (78%); yellow crystals; mp 93°C (*Me*OH); IR: $\bar{\nu} = 1630$ (CO), 1565 (*ar*), 990 (*trans* C=C), 735, 680 (*ar*) cm^{-1}; ^1H NMR (60 MHz): $\delta = 7.05–7.95$ (m, 11 *ar* H) ppm.

5-(3-Bromo-2-thienyl)-2-cyano-5-oxo-3-phenylvaleronitrile (**7a**, $C_{16}H_{11}BrN_2OS$)

At room temperature and with stirring 0.12 g of NaH (5 mmol) were added to a solution of 0.7 g of malononitrile (11 mmol) in 10 cm^3 of *DMSO*, then 2.94 g of **6a** (10 mmol) dissolved in 10 cm^3 of *DMSO* were dropwise added over 15 min. The mixture was stirred for 2 h, poured into 50 cm^3 of ice-H_2O, neutralized with dil. HCl, extracted with 3×30 cm^3 of $CHCl_3$, the combined organic layers were dried ($MgSO_4$), and evaporated *in vacuo*. Yield 2.9 g (82%); colorless crystals; mp 105°C (*Me*OH); IR: $\bar{\nu} = 2900$ (CH), 2250 (CN), 1660 (CO) cm^{-1}; ^1H NMR: $\delta = 3.60$ (d, $J = 6$ Hz, 2H, 4-H), 4.00 (m, 3-H), 4.65 (d, $J = 5$ Hz, 2-H), 7.00–8.00 (m, 7 *ar* H) ppm; ^{13}C NMR: $\delta = 28.89$ (C-2), 40.17 (C-4), 41.41 (C-3), 111.97 (CN), 124.41 ($C\text{-}3_{thienyl}$), 127.97, 129.97 (*ar* C), 131.71 ($C\text{-}4_{thienyl}$), 133.02 ($C\text{-}5_{thienyl}$), 136.33 ($C\text{-}1_{phenyl}$), 144.42 ($C\text{-}2_{thienyl}$), 188.24 (CO) ppm.

5-(3-Bromo-2-thienyl)-3-(4-chlorophenyl)-2-cyano-5-oxovaleronitrile (**7b**, $C_{16}H_{10}BrClN_2OS$)

From **6b** (3.28 g, 10 mmol) and 0.7 g of malononitrile (11 mmol) as **7a**, extraction with Et_2O. Yield 3.5 g (90%); yellow crystals; mp 110°C (Et_2O); IR: $\bar{\nu} = 2900$ (CH), 2250 (CN), 1650 (CO), 830 (*ar*) cm^{-1}; ^1H NMR: $\delta = 3.30–4.20$ (m, 3H, CH), 4.55 (d, $J = 4.5$ Hz, 2-H), 6.90–7.95 (m, 6 *ar* H) ppm.

5-(3-Bromo-2-thienyl)-2-cyano-3-(4-methoxyphenyl)-5-oxovaleronitrile (**7c**, $C_{17}H_{13}BrN_2O_2S$)

From **6c** (3.24 g, 10 mmol) and 0.7 g of malononitrile (11 mmol) as **7a**, extraction with CH_2Cl_2. Purification by CC (Et_2O/*n*-hexane 2/1). Yield 2.7 g (69%); yellow-orange liquid; IR (film): $\bar{\nu} = 2900$ (CH), 2210 (CN), 1650 (CO) 830 (*ar*) cm^{-1}; ^1H NMR (60 MHz): $\delta = 3.30–4.20$ (m, 3H, CH), 3.80 (s, O*Me*), 4.55 (d, 2-H), 6.90–7.95 (m, 6 *ar* H) ppm.

5-(3-Bromo-2-thienyl)-2-cyano-3-(4-nitrophenyl)-5-oxovaleronitrile (**7d**, $C_{16}H_{10}BrN_3O_3S$)

From **6f** (3.40 g, 10 mmol) and 0.7 g of malononitrile (11 mmol) as **7a**. Yield 2.5 g (63%); colorless crystals; mp 104°C (*Ac*OH/H_2O 2/1); IR: $\bar{\nu} = 2900$ (CH), 2250 (CN), 1650 (CO), 1515, 1350 (NO_2), 850 (*ar*) cm^{-1}; ^1H NMR: $\delta = 3.55$ (m, 2H, 4-H), 3.75 (m, 3-H), 4.55 (d, $J = 5$ Hz, 2-H), 6.90–7.75 (m, 6 *ar* H) ppm.

Methyl 5-(3-bromo-2-thienyl)-2-cyano-5-oxo-3-phenylvalerate (**9a**, $C_{17}H_{14}BrNO_3S$)

Methyl cyanoacetate (5.0 g, 50 mmol) was added at room temperature to a solution of 0.25 g of Na (11 mmol) in 10 cm^3 of *Me*OH with stirring, a solution of 2.94 g of **6a** (10 mmol) in *Me*OH was added, the mixture was stirred at room temperature for 3 h, hydrolyzed with dil. HCl, and concentrated *in vacuo*. H_2O (30 cm^3) was added to the residue, the mixture was extracted with 3×20 cm^3 of $CHCl_3$, the organic layer was dried (Na_2SO_4), and evaporated. Purification by CC (Et_2O/*n*-hexane 2/1). Yield 2.4 g (58%);

colorless crystals; mp 87°C (*Me*OH); IR: $\bar{\nu} = 3100$ (CH), 2220, 2210 (CN), 1745, 1655 (CO), 1600, 875 (*ar*) cm^{-1}; ^1H NMR: $\delta = 3.25–4.40$ (m, 7H, *Me*, CH_2, CH, CH), 7.00–7.55 (m, 7 *ar* H) ppm.

Methyl 5-(3-bromo-2-thienyl)-3-(4-chlorophenyl)-2-cyano-5-oxovalerate (**9b**, $C_{17}H_{13}BrClNO_3S$)

From **6b** (3.27 g, 10 mmol) as described for **9a**, 1 h stirring. Yield 6.9 g (81%); colorless crystals; mp 93°C (*Me*OH); IR: $\bar{\nu} = 2950$ (CH), 2250 (CN), 1750, 1655 (CO), 875 (*ar*) cm^{-1}; ^1H NMR: $\delta =$ 3.25–4.40 (m, 7H, *Me*, CH_2, CH, CH), 6.90–7.70 (m, 6 *ar* H) ppm.

*General Procedure for the Synthesis of 3-Chlorothienylpropenones **11***

Compound **10** (10 mmol) and an equimolar amount of the aldehyde were dissolved with stirring in 20 cm^3 of *Me*OH, then some pellets of NaOH were added, and stirring was continued for 2 h. The precipitate was separated and purified by recrystallization.

1-(3-Chloro-2-thienyl)-3-phenyl-2-propen-1-one (**11a**, $C_{13}H_9ClOS$)

From **10** (1.61 g, 10 mmol) and 1.05 g of benzaldehyde (10 mmol). Yield 2.0 g (82%); colorless crystals; mp 58°C (*Me*OH); IR: $\bar{\nu} = 1635$ (CO), 1585 (*ar*), 980 (*trans* C=C), 760, 700 (*ar*) cm^{-1}; ^1H NMR (60 MHz): $\delta = 7.25–8.10$ (m, 9 *ar* H) ppm.

1-(3-Chloro-2-thienyl)-3-(4-methoxyphenyl)-2-propen-1-one (**11c**, $C_{14}H_{11}ClO_2S$)

From **10** (1.61 g, 10 mmol) and 1.37 g of 4-methoxybenzaldehyde (10 mmol). Yield 2.45 g (88%); yellow crystals; mp 82°C (*Me*OH); IR: $\bar{\nu} = 1640$ (CO), 1585 (*ar*), 985 (*trans* C=C), 825 (*ar*) cm^{-1}; ^1H NMR (60 MHz): $\delta = 3.90$ (s, O*Me*), 7.05–8.30 (m, 8 *ar* H) ppm.

1-(3-Chloro-2-thienyl)-3-(3,4-dimethoxyphenyl)-2-propen-1-one (**11d**, $C_{15}H_{13}ClO_3S$)

From **10** (1.61 g, 10 mmol) and 1.60 g of 3,4-dimethoxybenzaldehyde (10 mmol). Yield 2.50 g (81%); yellow crystals; mp 125°C (*Me*OH); IR: $\bar{\nu} = 1635$ (CO), 1575 (*ar*), 970 (*trans* C=C), 835 (*ar*) cm^{-1}; ^1H NMR (60 MHz): $\delta = 3.95$ (s, 2 O*Me*), 7.25–8.00 (m, 7 *ar* H) ppm.

1-(3-Chloro-2-thienyl)-3-(4-nitrophenyl)-2-propen-1-one (**11e**, $C_{13}H_8ClNO_3S$)

From **10** (1.61 g, 10 mmol) and 1.51 g of 4-nitrobenzaldehyde (10 mmol). Yield 2.5 g (85%); light yellow crystals; mp 148°C (*Me*OH); IR: $\bar{\nu} = 1640$ (CO), 1580 (*ar*), 1510, 1340 (NO_2), 980 (*trans* C=C), 840 (*ar*) cm^{-1}; ^1H NMR (60 MHz): $\delta = 7.10–8.50$ (m, 8 *ar* H) ppm.

1-(3-Chloro-2-thienyl)-3-(2-thienyl)-2-propen-1-one (**11f**, $C_{11}H_7ClOS$)

From **10** (1.61 g, 10 mmol) and 1.12 g of thiophene-2-carbaldehyde (10 mmol). Yield 1.9 g (87%); yellow crystals; mp 74°C (*Me*OH); IR: $\bar{\nu} = 1630$ (CO), 1580 (*ar*), 990 (*trans* C=C) cm^{-1}; ^1H NMR (60 MHz): $\delta = 7.00–8.15$ (m, 7 *ar* H) ppm.

3-(4-Chlorophenyl)-1-(3-chloro-2-thienyl)-2-cyano-5-oxovaleronitrile (**12**, $C_{16}H_{10}Cl_2N_2OS$)

From **11b** (2.83 g, 10 mmol) and 0.7 g malononitrile (11 mmol) as described for **7a**, extraction with Et_2O. Yield 2.5 g (72%); yellow crystals; mp 195°C (CCl_4); IR: $\bar{\nu} = 2250$ (CN), 1650 (CO),

830 (*ar*) cm^{-1}; ^1H NMR: $\delta = 3.65$ (d, $J = 6$ Hz, CH_2), 3.95 (m, 3-H), 4.55 (d, $J = 5$ Hz, 2-H), 6.70–7.75 (m, 6 *ar* H) ppm.

Methyl 1-cyano-2,6-diphenyl-4-hydroxy-3-thienoyl-4-(2-thienyl)cyclohexane-1-carboxylate (**13a**, $C_{17}H_{15}NO_3S$)

As a by-product of the synthesis of methyl 2-cyano-5-oxo-3-phenyl-5-(2-thienyl)valerate [2], isolated from the mother liquor. Yield 0.3 g (10%); colorless crystals; mp 148°C (*Me*OH); IR: $\bar{\nu} = 3400$ (OH), 2220 (CN), 1740, 1630 (CO), 750, 700 (*ar*) cm^{-1}; ^1H NMR (200 MHz): $\delta = 2.40$ (dd, $J = 3.5$, 14 Hz, 5-H), 2.90 (dt, $J = 2.5$, 13 Hz, 3-H), 3.25 (s, O*Me*), 4.20 (dd, $J = 3$, 5, 13 Hz, 6-H), 4.45 (dd, $J = 13$, 14 Hz, CH_2), 5.45 (d, $J = 2$ Hz, OH), 6.60–7.50 (m, 16 *ar* H) ppm.

2,6-Bis(4-chlorophenyl)-3-(3-bromo-2-thienoyl)-4-(3-bromo-2-thienyl)-1-cyano-4-hydroxycyclohexane-1-carbonitrile (**13b**, $C_{29}H_{18}Br_2Cl_2N_2O_2S_2$)

From **6b** (3.28 g, 10 mmol) and 0.33 g of malononitrile (5 mmol) as described for **7a**, 2 h stirring at room temperature, extraction with $CHCl_3$. Yield 2.1 g (58%); colorless crystals; mp 180°C (*Et*OH); IR: $\bar{\nu} = 3400$ (OH), 3105 (CH), 1635 (CO), 1590, 830 (*ar*) cm^{-1}; ^1H NMR: $\delta = 2.20$ (dd, $J = 2$, 14 Hz, 3-H), 3.50–4.15 (m, CH_2), 4.05 (d, $J = 12$ Hz, 5-H), 4.90 (d, $J = 12$ Hz, 6-H), 5.85 (d, $J = 2$ Hz, OH), 6.75–7.60 (m, 12 *ar* H) ppm.

2,6-Bis(4-methoxyphenyl)-3-(3-bromo-2-thienoyl)-4-(3-bromo-2-thienyl)-1-cyano-4-hydroxycyclohexane-1-carbonitrile (**13c**, $C_{31}H_{24}Br_2N_2O_4S_2$)

As a by-product of the synthesis of **7c**, isolated from the mother liquor. Yield 0.75 g (20%); colorless crystals; mp 153°C (CCl_4); IR: $\bar{\nu} = 3400$ (OH), 3100 (CH), 1635 (CO), 1610, 830 (*ar*) cm^{-1}; ^1H NMR: $\delta = 2.85$ (dd, $J = 2$, 13 Hz, 3-H), 3.45–4.10 (m, 3H, CH), 3.60, 3.75 (2s, 2 O*Me*), 4.90 (d, $J = 12$ Hz, 6-H), 5.85 (d, $J = 2$ Hz, OH), 6.75–7.60 (m, 12 *ar* H) ppm.

2,6-Bis(4-chlorophenyl)-3-(3-chloro-2-thienoyl)-4-(3-chloro-2-thienyl)-4-hydroxy-1-cyanocyclohexane-1-carbonitrile (**13d**, $C_{29}H_{18}Cl_4N_2O_2S_2$)

As a by-product of the synthesis of **12**, isolated from the mother liquor. Yield 0.3 g (9%); colorless crystals; mp 198°C (CCl_4); IR: $\bar{\nu} = 3400$ (OH), 3105 (CH), 2220 (CN), 1630 (CO), 830 (*ar*) cm^{-1}; ^1H NMR: $\delta = 2.20$ (dd, $J = 3$, 14 Hz, 3-H), 3.30–4.10 (m, CH_2), 4.05 (d, $J = 12$ Hz, 5-H), 4.95 (d, $J = 12$ Hz, 6-H), 5.70 (d, $J = 2$ Hz, OH), 6.70–7.60 (m, 12 *ar* H) ppm.

2,6-Bis(2-thienyl)-3-(3-chloro-2-thienoyl)-4-(3-chloro-2-thienyl)-1-cyano-4-hydroxycyclohexane-1-carbonitrile (**13e**, $C_{25}H_{16}Cl_2N_2O_2S_4$)

Malononitrile (0.7 g, 11 mmol) was dissolved in 20 cm^3 of *Et*OH, 1.42 g of **11f** (5 mmol) and 5 drops piperidine were added, and the mixture was stirred at room temperature for 2 h. After 24 h, the precipitate was separated. Yield 2.1 g (73%); colorless crystals; mp 187°C (*Et*OH); IR: $\bar{\nu} = 3400$ (OH), 3105 (CH), 1635 (CO) cm^{-1}; ^1H NMR: $\delta = 2.35$ (dd, $J = 3$, 15 Hz, 5-H, 5′-H), 3.45 (m, 3-H), 4.35 (dd, $J = 3$, 13 Hz, 6-H), 4.65 (dd, $J = 12$ Hz, 2-H), 6.85 (d, $J = 2$ Hz, OH), 6.60–7.50 (m, 10 *ar* H) ppm.

3-Cyano-4-phenyl-6-(2-thienyl)piperidin-2-one (**15a**, $C_{16}H_{14}N_2OS$)

NaH (0.05 g, 1.3 mmol) was added with stirring to a solution of 0.7 g of **14** (2.5 mmol) in 10 cm^3 of *Et*OH, and after 3 h stirring at room temperature 50 cm^3 of H_2O were added and the mixture was

extracted with $3\times10\,cm^3$ of CH_2Cl_2. The combined organic layers were washed with $50\,cm^3$ of satd. NaCl solution, and dried ($MgSO_4$). After a few days at room temperature, the crystals were collected. Yield 0.65 g (92%); colorless crystals; mp 138°C (CH_2Cl_2); IR: $\bar{\nu} = 3300$ (NH), 3010 (CH), 2200 (CN), 1640 (CO), 1590, 760, 700 (*ar*) cm^{-1}; ^1H NMR (*DMSO*-d_6, 200 MHz): Isomer I: $\delta = 1.81$ (dt, $J = 13.4$, 11.3 Hz, 5-H_{ax}), 2.3–2.4 (m, 5-H_{eq}), 3.85 (dd, $J = 11.4$, 6.2 Hz, 4-H), 5.49 (dd, $J = 11.3$, 1.2 Hz, 6-H), 6.45, 6.55 (2s, 3-H, N–H), 6.80–7.65 (m, 8 *ar* H) ppm; Isomer II: $\delta = 1.96$–2.17 (m, 5-H_{ax}), 2.3–2.4 (m, 5-H_{eq}), 3.74 (dd, $J = 6.0$, 3.5 Hz, 4-H), 5.21 (dd, $J = 10.0$, 1.9 Hz, 6-H), 6.45, 6.55 (2s, 3-H, N–H), 6.80–7.65 (m, 8 *ar* H) ppm.

6-(3-Bromo-2-thienyl)-4-(4-chlorophenyl)-3-cyanopiperidin-2-one (**15b**, $C_{16}H_{12}BrClN_2OS$)

From **7b** (3.94 g, 10 mmol), and 0.19 g of NaH (5 mmol) as described for **15a**. The reaction mixture was concentrated *in vacuo*, $20\,cm^3$ H_2O were added to the residue, then it was extracted with Et_2O. Yield 3.5 g (90%); colorless crystals; mp 122°C (*Et*OH); IR: $\bar{\nu} = 3310$ (NH), 2940 (CH), 2190 (CN), 1630 (CO), 1590, 830 (*ar*) cm^{-1}; ^1H NMR: $\delta = 1.90$–2.65 (m, CH_2), 3.75–4.15 (m, 3-H), 4.75 (bs, N-H, 2-H), 5.15–5.70 (m, 5-H), 6.90–8.00 (m, 6 *ar* H) ppm.

1-(2-Furyl)-4-nitro-3-phenylbutan-1-one (**16a**, $C_{14}H_{13}NO_4$)

From nitromethane (3.0 g, 50 mmol) and 1.98 g of **1a** (10 mmol) as described for **9a**. Yield 1.7 g (66%); colorless crystals; mp 60°C (*Me*OH); IR: $\bar{\nu} = 1670$ (CO), 1565 (*ar*), 1540, 1360 (NO_2), 700, 760 (*ar*) cm^{-1}; ^1H NMR: $\delta = 3.25$ (d, $J = 6$ Hz, 2H, 2-H), 4.10 (m, 3-H), 4.70 (dd, $J = 3$, 6 Hz, 2H, 4-H), 6.50 (m, 1H, 4-H_{furyl}), 7.15–7.60 (m, 7 *ar* H) ppm.

3-(4-Chlorophenyl)-4-nitro-1-(2-thienyl)butan-1-one (**16b**, $C_{14}H_{12}ClNO_3S$)

a. From nitromethane (3.0 g, 50 mmol) and 2.49 g of **2b** (10 mmol) as described for **9a**, 1 h reflux. b. From **18** (1.3 g, 10 mmol) and 1.84 g of **17** (10 mmol) with *Me*ONa (5 mmol) in *Me*OH, 3 h reflux. The product was purified by Kugelrohr distillation. Yield a. 1.7 g (55%), b. 2.1 g (68%); light yellow liquid; bp 190°C/133 Pa; IR (film): $\bar{\nu} = 1660$ (CO), 1550, 1375 (NO_2), 830 (*ar*) cm^{-1}; ^1H NMR: $\delta = 3.35$ (d, $J = 7$ Hz, 2H, 2-H), 4.15 (m, 3-H), 4.75 (dd, $J = 4$, 4 Hz, 2H, 4-H), 7.00–7.75 (m, 7 *ar* H) ppm.

3-(3,4-Dimethoxyphenyl)-4-nitro-1-(2-thienyl)butan-1-one (**16c**, $C_{16}H_{15}NO_5S$)

From nitromethane (3.0 g, 50 mmol) and 2.49 g of **2d** (10 mmol) as described for **9a**, 1 h reflux. Yield 2.0 g (60%); colorless crystals; mp 91°C (*Me*OH); IR: $\bar{\nu} = 1650$ (CO), 1530, 1350 (NO_2), 810 (*ar*) cm^{-1}; ^1H NMR: $\delta = 3.35$ (d, $J = 7$ Hz, 2H, 2-H), 3.90 (s, 2 O*Me*), 4.10 (m, 3-H), 4.80 (dd, $J = 3$, 3 Hz, 2H, 4-H), 6.80–7.75 (m, 6 *ar* H) ppm.

1-(3-Bromo-2-thienyl)-4-nitro-3-phenylbutan-1-one (**16d**, $C_{14}H_{12}BrNO_3S$)

From nitromethane (3.0 g, 50 mmol) and 2.94 g of **6a** (10 mmol) as described for **9a**, 1 h reflux. Yield 2.5 g (71%); brownish liquid; IR (film): $\bar{\nu} = 3020$ (CH), 1655 (CO), 1550, 1380 (NO_2) cm^{-1}; ^1H NMR: $\delta = 3.40$ (dd, $J = 7$, 16 Hz, 2H, 2-H), 4.15 (m, 3-H), 4.70, (dd, $J = 4$, 7 Hz, 2H, 4-H), 6.90–7.50 (m, 7 *ar* H) ppm.

1-(3-Bromo-2-thienyl)-3-(4-chlorophenyl)-4-nitrobutan-1-one (**16e**, $C_{14}H_{11}BrClNO_3S$)

From **6b** (3.27 g, 10 mmol) as described **16d**. Yield 3.25 g (84%); brownish liquid; IR (film): $\bar{\nu} = 3020$ (CH), 1655 (CO), 1550, 1380 (NO_2) cm^{-1}; ^1H NMR: $\delta = 3.45$ (dd, $J = 7$, 16 Hz, 2H, 2-H), 4.15 (m, 3-H), 4.70 (dd, $J = 4$, 7 Hz, 2H, 4-H), 7.00–7.55 (m, 6 *ar* H) ppm.

1-(3-Bromo-2-thienyl)-3-(4-methoxyphenyl)-4-nitrobutan-1-one (**16f**, $C_{15}H_{14}BrNO_4S$)

From **6c** (3.24 g, 20 mmol) as described for **16d**. Yield 5.8 g (76%); brownish liquid; IR (film): $\bar{\nu} = 3010$ (CH), 1655 (CO), 1550, 1385 (NO_2) cm^{-1}; ^1H NMR: $\delta = 3.40$ (dd, $J = 7$, 18 Hz, 2H, 2-H), 3.70 (s, OCH_3), 4.10 (m, 3-H), 4.65 (dd, $J = 3$, 6 Hz, 2H, 4-H), 6.55–7.60 (m, 6 *ar* H) ppm.

General Procedure for the Synthesis of (2-Arylcyclopropyl) (2-Heteroaryl) Ketones

NaH (0.29 g, 11 mmol) was added to a suspension of 2.40 g of **19** (11 mmol) in 20 cm^3 of *DMSO*. After 30 min, a solution of **1** or **2** (10 mmol) in 10 cm^3 of *DMSO* was added dropwise, the mixture was stirred for 3 h, then poured into 50 cm^3 of H_2O, neutralized with conc. HCl, and extracted with 3×20 cm^3 of $CHCl_3$. The combined organic layers were washed with 5×50 cm^3 of H_2O, once with 30 cm^3 of satd. NaCl solution, dried (Na_2SO_4), and evaporated *in vacuo*.

2-Furyl 2-phenylcyclopropyl ketone (**20a**, $C_{14}H_{12}O_2$)

From **1a** (1.98 g, 10 mmol). Yield 2.0 g (94%); brown waxy crystals; mp 73°C (*Et*$_2$O); IR: $\bar{\nu} = 3100$ (H–$C_{cyclopropyl}$), 1640 (CO), 1560, 770, 695 (*ar*) cm^{-1}; ^1H NMR: $\delta = 1.50$, 1.80 (2m, each 1 H–$C_{cyclopropyl}$), 2.55 (m, CH_2), 6.50 (m, 4-H_{furyl}), 6.90–7.50 (m, 7 *ar* H) ppm.

2-(4-Chlorophenyl)cyclopropyl 2-furyl ketone (**20b**, $C_{14}H_{11}ClO_2$)

From **1b** (2.33 g, 10 mmol). Yield 2.35 g (95%); reddish waxy crystals; mp 77°C (*Et*$_2$O); IR: $\bar{\nu} = 3100$ (H–$C_{cyclopropyl}$), 1640 (CO), 1560, 810 (*ar*) cm^{-1}; ^1H NMR: $\delta = 1.40$ (m, $J = 4$, 6.5, 8 Hz, 3-H′$_{cyclopropyl}$), 1.80 (m, $J = 4$, 5, 10 Hz, 3-$H_{cyclopropyl}$), 2.65 (m, $J = 6.5$, 10 Hz, 2-$H_{cyclopropyl}$), 2.75 (m, $J = 5$, 8 Hz, 1-$H_{cyclopropyl}$), 6.50 (m, 4-H_{furyl}), 6.90–7.60 (m, 6 *ar* H) ppm.

2-Furyl 2-(4-methoxyphenyl)cyclopropyl ketone (**20c**, $C_{15}H_{14}O_3$)

From **1c** (2.33 g, 10 mmol). Yield 2.18 g (90%); reddish waxy crystals; mp 67°C (*Et*$_2$O); IR: $\bar{\nu} = 3100$ (H–$C_{cyclopropyl}$), 1640 (CO), 1560, 805 (*ar*) cm^{-1}; ^1H NMR: $\delta = 1.40$, 1.80 (2m, each 1 $H_{cyclopropyl}$), 2.70 (m, CH_2), 3.70 (s, O*Me*), 6.50 (m, 4-H_{furyl}), 6.70–7.60 (m, 6 *ar* H) ppm; ^{13}C NMR: $\delta = 18.68$ ($CH_{2(cyclopropyl)}$), 28.99 ($CH_{cyclopropyl}$), 55.37 (O*Me*), 112.38 (C-4$_{furyl}$), 114.15 (*ar* C), 116.69 (C-3$_{furyl}$), 127.58 (*ar* C), 132.42 (*ar* C), 146.46 (C-5$_{furyl}$), 153.41 (C-2$_{furyl}$), 158.66 (*ar* C), 187.33 (CO) ppm.

2-(3,4-Dimethoxyphenyl)cyclopropyl 2-furyl ketone (**20d**, $C_{16}H_{16}O_4$)

From **1d** (2.58 g, 10 mmol). Yield 2.23 g (82%); yellowish waxy crystals; mp 102°C (*Et*$_2$O); IR: $\bar{\nu} = 3110$ (H–$C_{cyclopropyl}$), 1640 (CO), 1590, 790 (*ar*) cm^{-1}; ^1H NMR: $\delta = 1.50$, 1.80 (2m, each 1$H_{cyclopropyl}$), 2.70 (m, CH_2), 3.80 (s, 2 O*Me*), 6.50–7.60 (m, 6 *ar* H) ppm.

2-(4-Dimethylaminophenyl)cyclopropyl 2-furyl ketone (**20e**, $C_{16}H_{17}NO_2$)

From **1e** (2.40 g, 10 mmol). Yield 2.1 g (82%); yellowish crystals; mp 122°C (*Et*$_2$O); IR: $\bar{\nu} = 2910$ (H–$C_{cyclopropyl}$), 1645 (CO), 1595, 810 (*ar*) cm^{-1}; ^1H NMR: $\delta = 2.60$ (m, 2$H_{cyclopropyl}$), 2.50–3.20 (m, 8H, $H_{cyclopropyl}$, *Me*), 6.45–7.90 (m, 7 *ar* H) ppm.

2-Furyl 2-(4-nitrophenyl)cyclopropyl ketone (**20f**, $C_{14}H_{11}NO_4$)

From **1f** (2.45 g, 10 mmol). Yield 2.0 g (78%); reddish waxy crystals; mp 139°C (*Et*$_2$O); IR: $\bar{\nu} = 3100$ (H–$C_{cyclopropyl}$), 1640 (CO), 1560 (*ar*), 1510, 1340 (NO_2), 795 (*ar*) cm^{-1}; ^1H NMR: $\delta = 1.60$, 1.95 (2m, each 1 $H_{cyclopropyl}$), 2.80 (m, CH_2), 6.55 (m, 4-H_{furyl}), 7.25–8.30 (m, 6 *ar* H) ppm.

2-Furyl 2-(2-thienyl)cyclopropyl ketone (**20g**, $C_{12}H_{10}O_2S$)

From **1g** (2.04 g, 10 mmol). Yield 1.9 g (90%); brown waxy crystals; mp 49°C (Et_2O); IR: $\bar{\nu} = 3105$ (H–$C_{cyclopropyl}$), 1650 (CO), 1570 (*ar*) cm^{-1}; ^1H NMR: $\delta = 1.40$, 1.80 (2 m, each $1H_{cyclopropyl}$), 2.80 (t, $J = 7$ Hz, CH_2), 6.40–7.55 (m, 6 *ar* H) ppm.

2-Furyl 2-styrylcyclopropyl ketone (**20h**, $C_{16}H_{14}O_2$)

From **1i** (2.24 g, 10 mmol). Yield 2.2 g (92%); yellow waxy crystals; mp 97°C (Et_2O); IR: $\bar{\nu} = 3100$ (H–$C_{cyclopropyl}$), 1640 (CO), 1560, 750, 690 cm^{-1} (*ar*) cm^{-1}; ^1H NMR: $\delta = 1.20$, 1.75 (2m, each $1H_{cyclopropyl}$), 2.50 (m, CH_2), 5.65–7.75 (m, 10 *ar* H) ppm.

(RS)-4-(4-Methoxyphenyl)-4,5-dihydrobenzo[b]furan-7(6H)-one (**21**, $C_{15}H_{14}O_3$)

At room temperature, $SnCl_4$ (3.9 g, 15 mmol) was added dropwise with stirring to a solution of 2.31 g of **20c** (10 mmol) in 20 cm^3 of C_6H_6. After stirring for 1 h, the mixture was poured into 50 cm^3 of dil. HCl, extracted with 3×30 cm^3 of $CHCl_3$, the combined organic layers were washed with 3×50 cm^3 of H_2O, dried ($MgSO_4$), and evaporated *in vacuo*. Yield 2.0 g (94%); reddish waxy crystals; mp 39°C (C_6H_6); IR: $\bar{\nu} = 3120$ (CH), 1675 (CO), 1615, 770 (*ar*) cm^{-1}; ^1H NMR: $\delta = 1.95$–2.65 (m, 4H, 5-H, 6-H), 3.75 (s, O*Me*), 4.15 (m, 4-H), 6.65–7.60 (m, 6 *ar* H) ppm; ^{13}C NMR: $\delta = 32.70$ (C-5), 36.52 (C-6), 40.16 (C-4), 55.31 (O*Me*), 106.57 (C-3), 114.34 (*ar* C), 122.05 (C-3′), 128.87 (*ar* C), 131.82 (*ar* C), 143.36 (C-2), 159.03 (*ar* C), 167.62 (C-7′), 194.52 (C-7) ppm.

(RS)-1-(2-Furyl)-4-hydroxy-4-(2-thienyl)butan-1-one (**22**, $C_{12}H_{12}O_3S$)

A solution of $SnCl_4$ (1.8 cm^3, 15 mmol) in 5 cm^3 of C_6H_6 was added dropwise with stirring to a solution of 2.18 g of **20g** (10 mmol) in 20 cm^3 of C_6H_6. After stirring for 1 h, the solution was poured into a solution of NaOH (10%, 50 cm^3), and extracted with 3×20 cm^3 of $CHCl_3$. The combined organic layers were washed with 3×50 cm^3 of H_2O, dried ($MgSO_4$), and evaporated *in vacuo*. Yield 1.35 g (57%); yellow crystals; mp 44°C (C_6H_6); IR: $\bar{\nu} = 3400$ (OH), 3110 (CH), 1655 (CO) cm^{-1}; ^1H NMR: $\delta = 2.20$ (m, CH_2), 2.95 (t, $J = 7$ Hz, CH_2), 3.20 (s, OH), 4.50 (t, $J = 7$ Hz, 4-H), 6.50 (m, 4-H_{furyl}), 6.80–7.60 (m, 5 *ar* H) ppm.

2-Phenylcyclopropyl 2-thienyl ketone (**23a**, $C_{14}H_{12}OS$)

From **2a** (2.14 g, 10 mmol). Yield 2.10 g (92%); yellow crystals; mp 72°C (Et_2O); IR: $\bar{\nu} = 3075$ (H–$C_{cyclopropyl}$), 1625 (CO), 1595 (*ar*), 730, 690 (*ar*) cm^{-1}; ^1H NMR: $\delta = 1.50$, 1.85 (2m, each $1H_{cyclopropyl}$), 2.70 (t, $J = 7$ Hz, CH_2), 6.90–7.75 (m, 8 *ar* H) ppm.

2-(4-Chlorophenyl)cyclopropyl 2-thienyl ketone (**23b**, $C_{14}H_{11}ClOS$)

From **2b** (2.48 g, 10 mmol). Yield 2.35 g (90%); yellow crystals; mp 78°C (Et_2O); IR: $\bar{\nu} = 3065$ (H–$C_{cyclopropyl}$), 1625 (CO), 720 (*ar*) cm^{-1}; ^1H NMR: $\delta = 1.45$, 1.80 (2m, each $1H_{cyclopropyl}$), 2.65 (t, $J = 7$ Hz, CH_2), 6.90–7.80 (m, 7 *ar* H) ppm.

2-(4-Methoxyphenyl)cyclopropyl 2-thienyl ketone (**23c**, $C_{15}H_{14}O_2S$)

From **2c** (2.44 g, 10 mmol). Yield 2.25 g (88%); light yellow crystals; mp 65°C (Et_2O); IR: $\bar{\nu} = 3070$ (H–$C_{cyclopropyl}$), 1625 (CO), 1580, 800 (*ar*) cm^{-1}; ^1H NMR: $\delta = 1.40$, 1.80 (2m, each $1H_{cyclopropyl}$), 2.65 (t, $J = 7$ Hz, CH_2), 3.65 (s, O*Me*), 6.65–7.75 (m, 7 *ar* H) ppm; ^{13}C NMR:

$\delta = 18.73$ ($CH_{2(cyclopropyl)}$), 29.19 ($CH_{cyclopropyl}$), 29.98 ($CH_{cyclopropyl}$), 55.48 (O*Me*), 114.27 (*ar* C), 127.72 (*ar* C), 128.31 (C-4), 131.79 (C-5), 132.53 (*ar* C), 133.51 (C-3), 145.2 (C-2), 158.79 (*ar* C), 191.03 (CO) ppm.

2-(3,4-Dimethoxyphenyl)cyclopropyl 2-thienyl ketone (**23d**, $C_{16}H_{16}O_3S$)

From **2d** (2.75 g, 10 mmol). Yield 2.65 g (93%); colorless crystals; mp 98°C (*Et*$_2$O); IR: $\bar{\nu} = 3080$ (H–$C_{cyclopropyl}$), 1630 (CO), 1590, 860 (*ar*) cm^{-1}; ^1H NMR: $\delta = 1.50$, 1.80 (2m, each $1H_{cyclopropyl}$), 2.55 (t, $J = 7$ Hz, CH_2), 3.65 (s, O*Me*), 6.90–8.10 (m, 6 *ar* H) ppm.

2-(4-Dimethylaminophenyl)cyclopropyl 2-thienyl ketone (**23e**, $C_{16}H_{17}NOS$)

From **2e** (2.57 g, 10 mmol). Yield 1.90 g (70%); colorless crystals; mp 137°C (*Et*$_2$O); IR: $\bar{\nu} = 3080$ (H–$C_{cyclopropyl}$), 1630 (CO), 810 (*ar*) cm^{-1}; ^1H NMR: $\delta = 1.65$ (m, 2 $H_{cyclopropyl}$), 2.70 (t, $J = 8$ Hz, CH_2), 2.95 (s, 2 *Me*), 6.65–7.95 (m, 7 *ar* H) ppm.

2-(2-Thienyl)cyclopropyl 2-thienyl ketone (**23f**, $C_{12}H_{10}O_2S$)

From **2g** (2.20 g, 10 mmol). Yield 2.15 g (92%); light yellow crystals; mp 63°C (*Et*$_2$O); IR: $\bar{\nu} = 3080$ (H–$C_{cyclopropyl}$), 1620 (CO) cm^{-1}; ^1H NMR: $\delta = 1.55$, 1.90 (2m, each 1 $H_{cyclopropyl}$), 2.80 (m, CH_2), 6.75–7.80 (m, 6 *ar* H) ppm.

2,2′-(1,4-Phenylene)bis[cyclopropyl 2-thienyl ketone] (**23g**, $C_{22}H_{18}O_2S_2$)

From **19** (4.80 g, 22 mmol) and 3.50 g of **2h** (10 mmol). Yield 2.75 g (73%); yellowish crystals; mp 150°C (*Et*$_2$O); IR: $\bar{\nu} = 3090$ (H–$C_{cyclopropyl}$), 1630 (CO), 840 (*ar*) cm^{-1}; ^1H NMR: $\delta = 1.50$, 1.85 (2m, each 1 $H_{cyclopropyl}$), (t, $J = 7$ Hz, CH_2), 7.00–7.90 (m, 10 *ar* H) ppm.

2-(2-Bromophenyl)cyclopropyl 2-thienyl ketone (**23h**, $C_{14}H_{11}BrOS$)

From **2k** (2.94 g, 10 mmol). Yield 2.8 g (91%); light red liquid; IR (film): $\bar{\nu} = 3010$ (H–$C_{cyclopropyl}$), 1645 (CO), 755, 725 (*ar*) cm^{-1}; ^1H NMR: $\delta = 1.55$, 1.80 (2m, each 1 $H_{cyclopropyl}$), 2.65 (m, CH_2), 6.90–7.85 (m, 7 *ar* H) ppm.

(RS)-4-(4-Methoxyphenyl)-4,5-dihydrobenzo[b]thiophen-7(6H)-one (**24**, $C_{15}H_{14}O_2S$)

From **23c** (2.47 g, 10 mmol) and 3.9 g of $SnCl_4$ (15 mmol) as described for **21**, stirring for 4 h, CC with *Et*$_2$O/*n*-hexane (1/1). Yield 1.4 g (54%); brown waxy crystals; mp 48°C (*Et*$_2$O); IR: $\bar{\nu} = 3100$ (CH), 1655 (CO), 1610, 770 (*ar*) cm^{-1}; ^1H NMR: $\delta = 1.85$–2.80 (m, 4H, 5-H, 6-H), 3.80 (s, O*Me*), 4.10 (m, 4-H), 7.55–8.60 (m, 6 *ar* H) ppm; ^{13}C NMR: $\delta = 33.90$ (C-5), 37.11 (C-6), 42.63 (C-4), 55.23 (O*Me*), 114.12 (*ar* C), 128.82 (C-3), 129.00 (*ar* C), 133.69 (C-2), 134.86 (*ar* C), 136.81 (C-3′), 155.14 (C-7′), 158.64 (*ar* C), 191.97 (C-7) ppm.

(RS)-4-Hydroxy-4-phenyl-1-(2-thienyl)butan-1-one (**25a**, $C_{14}H_{14}O_2S$)

From **23a** (2.14 g, 10 mmol) and 1.4 g of $AlCl_3$ (11 mmol) in CH_2Cl_2, as described for **22**, refluxing for 1 h. Yield 1.1 g (43%); brown liquid; IR (film): $\bar{\nu} = 3450$ (OH), 3100 (CH), 1635 (CO), 1610, 740, 705 (*ar*) cm^{-1}; ^1H NMR (60 MHz): $\delta = 2.15$ (m, CH_2), 3.00 (t, $J = 7$ Hz, CH_2, OH), 4.85 (t, $J = 6$ Hz, 4-H), 6.90–7.90 (m, 5 *ar* H) ppm.

(RS)-4-Hydroxy-4-(4-methoxyphenyl)-1-(2-thienyl)butan-1-one (**25b**, $C_{15}H_{16}O_3S$)

From **23c** (2.47 g, 10 mmol) and 1.8 cm^3 of $SnCl_4$ (15 mmol) in 20 cm^3 of C_6H_6, as described for **22**, 1 h stirring at room temperature. Yield 1.9 g (69%); light yellow liquid; IR (film): $\bar{\nu} = 3400$ (OH), 3100 (CH), 1650 (CO), 1610, 750 (*ar*) cm^{-1}; ^1H NMR: $\delta = 2.10$ (m, 2H, 5-H), 2.95 (t, $J = 7$ Hz, 2H, 6-H), 3.70 (s, O*Me*), 4.75 (t, $J = 7$ Hz, 4-H), 7.70–8.70 (m, 7 *ar* H) ppm.

3-Bromo-2-thienyl 2-phenylcyclopropyl ketone (**26a**, $C_{14}H_{10}BrClOS$)

From **19** (2.40 g, 11 mmol) and 2.93 g of **6a** (10 mmol) as described for **20a**. After evaporation of the solvent a light liquid was obtained. Yield 2.55 g (83%); IR (film): $\bar{\nu} = 3105$ ($H–C_{cyclopropyl}$), 1640 (CO), 740, 700 (*ar*) cm^{-1}; ^1H NMR: $\delta = 1.45$, 2.05, 2.70, 3.20 (4m, each 1 $H_{cyclopropyl}$), 6.65–7.95 (m, 6 *ar* H) ppm.

3-Bromo-2-thienyl 2-(4-chlorophenyl)cyclopropyl ketone (**26b**, $C_{14}H_{10}BrClOS$)

From **19** (2.40 g, 11 mmol) and 3.28 g of **6b** (10 mmol). Yield 2.30 g (75%); yellowish crystals; mp 53°C; IR: $\bar{\nu} = 3100$ ($H–C_{cyclopropyl}$), 1630 (CO), 800 (*ar*) cm^{-1}; ^1H NMR: $\delta = 1.50$, 1.90, 2.65, 3.15 (4m, each 1 $H_{cyclopropyl}$), 6.90–7.45 (m, 7 *ar* H) ppm.

3-Bromo-2-thienyl 2-(4-dimethylaminophenyl)cyclopropyl ketone (**26c**, $C_{16}H_{16}BrNOS$)

From **19** (2.40 g, 11 mmol) and 3.30 g of **6e** (10 mmol). Yield 2.80 g (80%); red crystals; mp 90°C (*Et*$_2$O/*n*-pentane 2/1); IR: $\bar{\nu} = 2910$ ($H–C_{cyclopropyl}$), 1630 (CO), 800 (*ar*) cm^{-1}; ^1H NMR: $\delta = 1.65$ (m, 2 $H_{cyclopropyl}$), 2.90 (m, 8H, *Me*, $H_{cyclopropyl}$), 6.60–7.60 (m, 6 *ar* H) ppm.

3-Bromo-2-thienyl 2-(4-nitrophenyl)cyclopropyl ketone (**26d**, $C_{14}H_{10}BrNO_3S$)

From **19** (2.40 g, 11 mmol) and 3.40 g of **6f** (10 mmol). After evaporation of the solvent, some drops of *Et*$_2$O were added to the residue for crystallization. Yield 2.6 g (73%); yellowish crystals; mp 75°C (*Et*$_2$O); IR: $\bar{\nu} = 3100$ ($H–C_{cyclopropyl}$), 1630 (CO), 1510, 1345 (NO_2), 855 (*ar*) cm^{-1}; ^1H NMR: $\delta = 1.55$, 1.95, 2.75, 3.05 (4m, each 1 $H_{cyclopropyl}$), 7.00–8.20 (m, 6 *ar* H) ppm.

2-(4-Chlorophenyl)cyclopropyl 3-chloro-2-thienyl ketone (**27a**, $C_{14}H_{10}Cl_2OS$)

From **19** (2.40 g, 11 mmol) and 2.83 g of **11b** (10 mmol). Yield 2.6 g (87%); colorless crystals; mp 54°C (*Et*$_2$O); IR: $\bar{\nu} = 3100$ ($H–C_{cyclopropyl}$), 1620 (CO), 805 (*ar*) cm^{-1}; ^1H NMR: $\delta = 1.50$, 1.95, 2.70, 3.10 (4m, each 1 $H_{cyclopropyl}$), 6.95–7.95 (m, 6 *ar* H) ppm.

3-Chloro-2-thienyl 2-(3,4-dimethoxyphenyl)cyclopropyl ketone (**27b**, $C_{16}H_{15}ClO_3S$)

From **19** (2.40 g, 11 mmol) and 3.20 g of **11d** (10 mmol). Yield 2.8 g (87%); colorless crystals; mp 67°C (*Et*$_2$O); IR: $\bar{\nu} = 3100$ ($H–C_{cyclopropyl}$), 1625 (CO), 825 (*ar*) cm^{-1}; ^1H NMR: $\delta = 1.45$, 1.85, 2.65, 3.05 (4m, each 1 $H_{cyclopropyl}$), 3.80 (s, 2 O*Me*), 6.50–7.70 (m, 6 *ar* H) ppm.

3-Chloro-2-thienyl 2-(4-nitrophenyl)cyclopropyl ketone (**27c**, $C_{14}H_{10}ClNO_3S$)

From **19** (2.40 g, 11 mmol) and 2.94 g of **11f** (10 mmol). Yield 2.5 g (81%); colorless crystals; mp 83°C (*Et*$_2$O); IR: $\bar{\nu} = 3095$ ($H–C_{cyclopropyl}$), 1620 (CO), 1510, 1340 (NO_2), 865 (*ar*) cm^{-1}; ^1H NMR:

$\delta = 1.60$, 2.05, 2.85, 3.30 (4m, each 1 $H_{cyclopropyl}$), 7.05 (d, $J = 5$ Hz, 4-H), 7.35 (d, $J = 8$ Hz, 2 *ar* H), 7.55 (d, $J = 5$ Hz, *ar* H), 8.20 (d, $J = 8$ Hz, 2 *ar* H) ppm.

2-(1-Trimethylsiloxyvinyl)thiophene (**28**, $C_9H_{14}OSSi$)

With stirring, under N_2, and at −78°C, **18** (5.4 cm^3, 50 mmol) was dropwise added to a solution of 55 mmol of *LDA* in 100 cm^3 of *THF* within 5 min. After stirring for 15–20 min 7.6 cm^3 of ClSi*Me*$_3$ (60 mmol) were added. After 4–5 min the mixture was diluted with 100 cm^3 of ice-cooled pentane, and poured into 150 cm^3 of an ice-cooled satd. solution of $NaHCO_3$, the organic layer was separated, twice washed with H_2O, and once with 50 cm^3 of a satd. solution of NaCl, dried ($MgSO_4$), and evaporated *in vacuo*. Yield 9.2 g (93%); colorless liquid; bp 120°C/2666 Pa (Ref. [15] 73°C/267 Pa); ^{1}H NMR: $\delta = 0.35$, 0.40 (2s, Si*Me*$_3$), 4.25, 4.75 (2d, $J = 2$ Hz, CH_2), 6.80–7.60 (m, 3 *ar* H) ppm.

4,5,6,7-Tetrahydro-7-oxo-N-phenylbenzo[b]thiophene-4,5-dicarboximide (**29**, $C_{16}H_{11}NO_3S$)

Compound **28** (2.0 g, 10 mmol, freshly prepared) and 1.7 g of *N*-phenylmaleinimide (10 mmol) dissolved in 10 cm^3 of CH_2Cl_2 were heated in a sealed tube to 80°C for 24 h. After cooling, the solvent was evaporated *in vacuo*, and the residue was purified by CC (*Et*$_2$O/*n*-hexane 1/1). Yield 0.5 g (17%); colorless crystals; mp 150°C (Ref. [19] 168°C); IR: $\bar{\nu} = 1710$, 1660 (CO), 1600, 740, 690 (*ar*) cm^{-1}; ^{1}H NMR: $\delta = 2.85$ (dd, $J = 8$, 18 Hz, 6-H_{eq}), 3.40 (dd, $J = 3$, 18 Hz, 6-H_{ax}), 3.75 (td, $J = 3$, 8 Hz, 5-H), 4.40 (d, $J = 8$ Hz, 4-H), 7.05–7.75 (m, 7 *ar* H) ppm.

4,4-Dicyano-5-phenyl-4,5-dihydrobenzo[b]thiophene-7(6H)-one (**32**, $C_{16}H_{10}N_2OS$)

From **28** (1.0 g, 5 mmol) and 0.75 g of **30** (5 mmol) as described for **29**. Yield 70 mg (5%); brownish crystals; mp 125°C (*Et*$_2$O/*n*-hexane 1/1); IR: $\bar{\nu} = 2900$ (CH), 2260 (CN), 1660 (CO), 730, 700 (*ar*) cm^{-1}; ^{1}H NMR (60 MHz): $\delta = 2.90$ (dd, $J = 4$, 16 Hz, 6-H_{eq}), 3.45 (dd, $J = 12$, 19 Hz, 6-H_{ax}), 4.10 (dd, $J = 4$, 12 Hz, 5-H), 7.20–7.90 (m, 7 *ar* H) ppm.

4-Nitro-5-phenyl-4,5-dihydrobenzo[b]thiophene-7(6H)-one (**33**, $C_{14}H_{11}NO_3S$)

From **28** (1.0 g, 5 mmol) and 0.75 g of **31** (5 mmol) as described for **29**. Yield 50 mg (4%); yellow liquid; IR (Film): $\bar{\nu} = 3100$, 2035 (CH), 1655 (CO), 1600, 730, 700 (*ar*) cm^{-1}; ^{1}H NMR (60 MHz): $\delta = 2.85$ (dd, $J = 8$, 18 Hz, 6-H_{eq}), 3.45 (dd, $J = 5$, 19 Hz, 6-H_{ax}), 4.10 (dd, $J = 4$, 12 Hz, 5-H), 7.00–7.80 (m, 7 *ar* H) ppm.

4-Benzyl-4,5,6,7-tetrahydro-6,6,7,7-tetracyanobenzo[b]thiophene (**35**, $C_{19}H_{12}N_4S$)

34 (2.0 g, 10 mmol), and 1.28 g of *TCNE* dissolved in 20 cm^3 of C_6H_6 were refluxed for 24 h. After cooling and evaporation of the solvent, the residue was purified by CC (*Et*$_2$O/*n*-pentane 2/1). Yield 0.65 g (20%); colorless crystals; mp 116°C (*Et*$_2$O); IR: $\bar{\nu} = 3080$, 3060 (CH), 2260 (CN), 1710, 1660 (CO), 1600 (*ar*) cm^{-1}; ^{1}H NMR: $\delta = 3.00$ (d, $J = 3$ Hz, $CH_{2(benzyl)}$), 3.45 (d(s), CH_2), 4.60 (m, 4-H), 6.80 (dd, $J = 2$, 6 Hz, 2-H), 6.65 (dd, $J = 2$, 6 Hz, 1H, 3-H), 7.05–7.50 (m, 5 *ar* H) ppm.

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