Multicomponent Queuing Cascades of Bicyclopropylidene, Carbon Monoxide and Aryl Iodides or Aryl Thiols[‡]

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Bicyclopropylidene (**1**) reacts with *N*-(2-iodophenyl)-4-methylbenzenesulfonamide (**2**-NTs) and carbon monoxide (2–3 bar) under mild conditions in a novel palladium-catalysed tetramolecular cascade to give the dispiro compound **3**-NTs (61%). The structure of **3**-NTs was determined by X-ray analysis. With *ortho*-iodophenol (**2**-OH) replacing **2**-NTs a mixture of **3**-O (20%) and 3,4-dihydro-2*H*,5*H*-pyrano[3,2-c]chromen-2-one (**4**-O; 11%) was obtained. Mechanistically this cascade is interpreted in terms of the acylation of **1** followed by a cyclopropylcarbinyl-homoallyl rearrangement, carbon monoxide insertion and intramolecular trapping of a nucleophile. Various thiophenols reacted with **1** and CO (2–3 bar) to give the thiocarbonylated products **14a–d,g** and **15a–c,g** (33–77% yield). With *ortho*- or *para*-halo-substituted thiophenols as substrates the vinyl lactones **16e–h** (31–55% yield) were obtained in a novel palladium-catalysed five-component cascade. The outcome of this cascade is discussed in terms of the electronic and steric properties of the thiophenols.

Introduction

Organic synthesis is concerned with developing viable processes to useful materials by methods that minimise waste, maximise molecular complexity and are highly selective (regio-, stereo-, chiro- and chemospecific). One of the most elegant ways to achieve this is by cascade reactions,[1] defined as multicomponent "one-pot" sequences, in which the first reaction creates the functionality to trigger the second reaction and so on. Cascade reactions are also termed tandem or domino processes by some authors. Bicyclopropylidene (**1**) is a unique tetrasubstituted alkene readily available in preparative quantities.[2] It has been incorporated by the de Meijere group in cascade Heck−Diels−Alder reactions[3] and in nucleophilic trapping of π-allylpalladium intermediates generated by carbopalladation of **1**.[4] Herein we present new multicomponent palladium-catalysed cascade reactions combining bicyclopropylidene (**1**) with carbon monoxide and aryl iodides or aryl thiols.

Results and Discussion

The palladium-catalysed cross-coupling reaction of bicyclopropylidene (**1**) with *N*-(2-iodophenyl)-4-methylbenzenesulfonamide (**2**-NTs) employing 2−3 bar of carbon monoxide gave the unusual 5-azadispiro[2.0.4.3]undecane-8,11-dione (**3**-NTs) as the sole product. With *ortho*-iodophenol (**2**-OH) as starting material a mixture of **3**-O and 3,4-dihydro-2*H*,5*H*-pyrano[3,2-c]chromen-2-one (**4**-O) was obtained (Scheme 1). The constitution of **3**-NTs was determined by an X-ray crystal structure analysis (Figure 1).[5]

The two spiroannelated cyclopentane moieties of **3**-NTs are perpendicular to each other and make up a central spiro[4.4]nonane unit. The bond lengths in the spirocyclopropane moiety display the expected features arising from the unique ability of the cyclopropane group to function as an electron donating moiety:[6] conjugation of the cyclopropane unit with the perfectly *syn*-periplanar oriented carbonyl group in the α-position makes the two proximal bonds longer [1.509(2) and 1.530(2) Å, respectively] and shortens the distal bond [1.482(3) Å].

Various catalytic systems were used in attempts to optimise the yields of **3** and **4** (Table 1). The cross-coupling reaction of **1**,**2**-NTs and carbon monoxide under typical Heck conditions furnished only traces of **3**-NTs along with polymeric material and a significant amount of starting material

[‡] Palladium-Catalysed Queuing Processes, Part 3. Part 2: U. Anwar, A. Casaschi, R. Grigg, J. M. Sansano, *Tetrahedron* **2001**, *57*, 1361−1367. Cyclopropyl Building Blocks for Organic Synthesis, 80. Part 79: A. de Meijere, C. M. Williams, A. Kourdioukov, S. V. Sviridov, V. Chaplinski, M. Kordes, A. Savtchenko, C. Stratmann, M. Noltemeyer, *Chem. Eur. J.* **2002**, *8*, 3789−3801.

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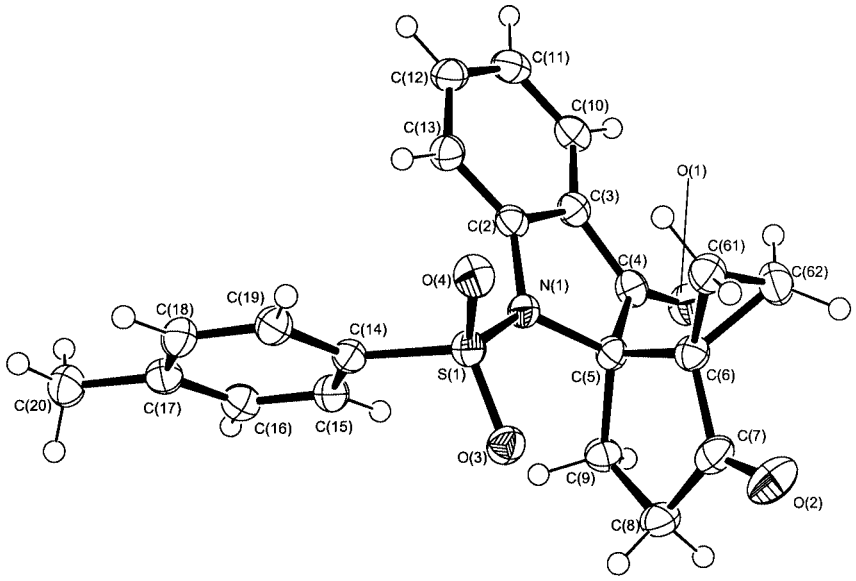
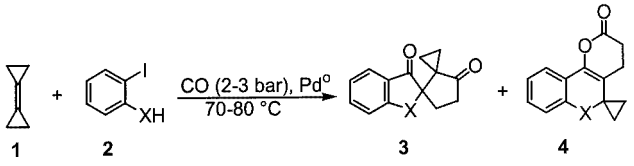


Figure 1. Structure of **3**-NTs in the crystal;[5] selected bond lengths [Å] and angles [°]: N(1)−C(2) 1.414(2), C(2)−C(3) 1.396(2), C(3)−C(4) 1.457(2), C(4)−C(5) 1.536(2), C(4)−O(1) 1.218(2), C(5)-N(1) 1.503(2), C(5)−C(6) 1.538(2), C(6)−C(61) 1.509(2), C(6)−C(62) 1.530(2), C(61)−C(62) 1.482(3), C(6)−C(7) 1.488(2), C(7)−C(8) 1.508(3), C(7)−O(2) 1.217(2), C(8)−C(9) 1.541(3), C(9)−C(5) 1.555(2); N(1)−C(5)−C(4) 101.26(13), C(6)−C(5)−C(9) 105.11(14), C(5)−C(6)−C(7) 108.67(14), C(61)−C(6)−C(7) 118.56(14), C(62)−C(6)−C(7) 116.18(14), C(61)−C(6)−C(62) 58.33(11), C(6)−C(61)−C(62) 61.55(11), C(6)−C(62)−C(61) 60.12(11)



Scheme 1. Four-component reaction involving bicyclopropylidene (**1**), aryl iodide **2** and carbon monoxide; for details see Table 1

Table 1. Four-component reactions of bicyclopropylidene (**1**), aryl iodide **2** and carbon monoxide

Entry	X	Conditions[a]	Base	*t* [h]	**3** (%)	**4** (%)
1	NTs	A	K_2CO_3	48	trace[b]	–
2	NTs	B	K_2CO_3	72	40[b]	–
3	NTs	B	Ag_2CO_3	48	trace[b]	–
4	NTs	C	K_2CO_3	20	61	–
5	O	B	K_2CO_3	15	20	11
6	O	B	Cs_2CO_3	16	1.8	–
7	O	B[c]	K_2CO_3	62	trace	trace
8	O	D	K_2CO_3	40	15	13
9	O	C	K_2CO_3	24	11	24
10	O	E	K_2CO_3	20	–	–
11	O	B	DABCO	48	–	–
12	OTMS	B	K_2CO_3	18	29	trace

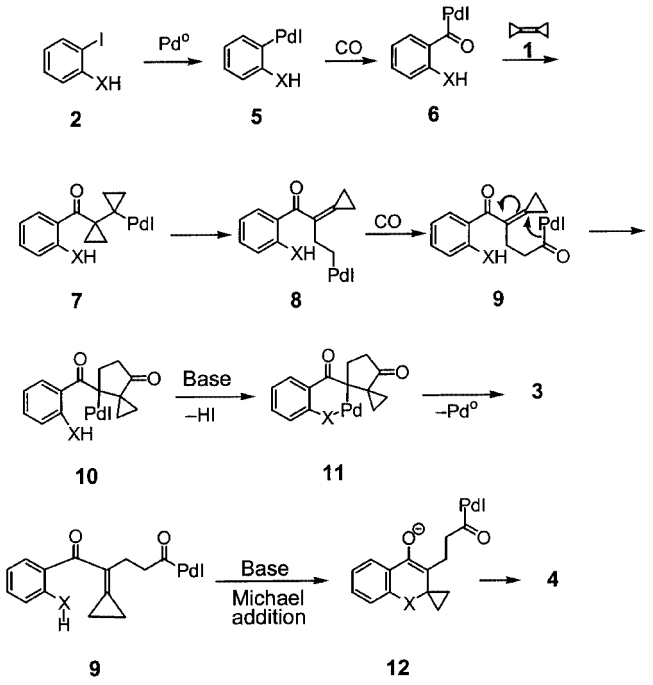
[a] **A**: 10 mol % $[Pd(OAc)_2]$, 20 mol % TFP, 100 mol % NBu_4Br, CO (2−3 bar), DMF. **B**: 4 mol % $[Pd(PPh_3)_4]$, MeCN. **C**: as in **B**, 150 mol % NBu_4Br. **D**: 3 mol % $[Pd_2dba_3]$, 12 mol % TFP. **E**: as in **D**, 150 mol % NBu_4Br. [b] Along with *N*-(2-iodophenyl)-4-methylbenzenesulfonamide (**2**-NTs). [c] 1 atm. CO.

2-NTs (Entry 1). However, $[Pd(PPh_3)_4]$ as catalyst in MeCN gave **3**-NTs as the sole product in 40% yield (Entry 2). Changing the base from K_2CO_3 to Ag_2CO_3 led to recovery of starting material **2**-NTs along with traces of **3**-NTs (Entry 3). The best result was obtained employing $[Pd(PPh_3)_4]$, K_2CO_3 and NBu_4Br as additive which afforded **3**-NTs in 61% yield (Entry 4).

The four-component cascade with *ortho*-iodophenol (**2**-OH) furnished a mixture of **3**-O and **4**-O (Entries 5, 8 and 9). Again, K_2CO_3 was the best base for this transformation (Entry 5), while the employment of Cs_2CO_3 or DABCO as bases led to complex mixtures (Entries 6 and 11). The catalytic system involving $[Pd_2dba_3]$ and TFP (tris-2-furylphosphane) was also active (Entry 8), but in this case the addition of NBu_4Br led to decomposition products (Entry 10). However, NBu_4Br together with $[Pd(PPh_3)_4]$ favoured the formation of **4**-O (24% yield) over **3**-O (11% yield) (Entry 9); normally **3**-O is the main product. The reaction under 1 bar pressure of carbon monoxide gave only a trace of products along with polymeric material (Entry 7). Using **2**-OTMS as starting material with TMS as a temporary protecting group provided **3**-O in 29% yield whilst traces of **4**-O were observed by HPLC analysis (Entry 12).

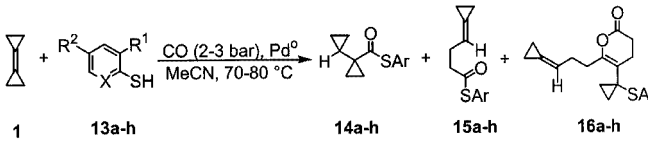
It is believed that both **3** and **4** arise via a tetramolecular queuing cascade[7] involving a common intermediate **9**, which is derived from **2** via a sequence of elementary steps (Scheme 2). Two of these steps are carbonylations involving an aryl- (**5**) and an alkyl- (**8**) palladium intermediate. Depending on the nucleophilicity of the deprotonated X−H fragment, the intermediate **9** may undergo a 5-*endo*-*trig*-cyclisation (X = NTs) to **10** followed by capture by the deprotonated internal nucleophile **10** to give **11** and reductive elimination to **3**. The potentially competitive route to **4** involves an intramolecular Michael addition **9**→**12** followed by lactonisation to yield **4** (Scheme 2).

The thiocarbonylation of various unsaturated substrates at high pressure has been reported previously.[8] We observe that bicyclopropylidene (**1**) reacts with various thiophenols



Scheme 2. Proposed mechanism of the tetramolecular queuing cascade involving bicyclopropylidene (**1**), aryl iodide **2** and CO

and CO under mild pressure (2−3 bar) to give the thiocarbonylated products **14a−h**, **15a−h** or **16a−h**, respectively (Scheme 3)



Scheme 3. Thiocarbonylation of bicyclopropylidene (**1**); for details see Table 2

The reaction between **1** and thiophenols **13a** or **13c** furnished a mixture of **14a/15a** or **14c/15c**, respectively, favouring **15**, in which ring opening of one of the cyclopropanes has occurred (Entries 1 and 3). However, with a methoxy group *ortho* to the thiol moiety (**13b**) the major product is **14b** (Entry 2). Interestingly, 2-mercaptopyridine (**13d**) afforded the bicyclopropyl derivative **14d** as the sole product (Entry 4). Only a few other examples are known in which **1** reacts under palladium catalysis with retention of both three-membered rings.[9] With *ortho*-halothiophenols the unusual vinyl lactones **16e**, **16f** and **16h**, respectively, were obtained and products of type **14** and **15** were only observed in trace amounts (Entries 5, 6, 9 and 10). The best yield (55%) was obtained with **13h**, which afforded **16h**. Therefore, the soft and more nucleophilic bromine atom in **13h** apparently stabilises one or more of the reactive intermediates better than the harder, more electronegative fluorine or chlorine substituents. This *ortho*-effect was investigated using *para*-chlorothiophenol (**13g**), which reacted with **1** to afford a mixture of all three products **14g/15g** (29%) and **16g** (20%) (Entry 7). Therefore, an electronic effect is operative and a simple buttressing effect can be discounted (compare Entries 2 and 3 with Entries 6 and 10). Doubling the amount of Pd catalyst improved the yield of **16g** from 20% to 31% (Entry 8), whereas a reduction of the reaction time led only to the formation of **14g** and **15g** (Entry 7). Different catalytic systems were also investigated. Thus **13h** gives almost the same yield of **16h** with both $[Pd_2dba_3]$/TFP and with $[Pd(PPh_3)_4]$ as catalysts (Entries 9 and 11), while P(*o*-tolyl)$_3$ as ligand suppressed the formation of **16h** (Entry 12) and a significant amount of **14h** and polymeric material were formed. Interestingly the type of product formed from **1** and **13a−h** correlates quite well with the calculated pK_a's of the thiols (Table 2). Thiols with a calculated pK_a of 6.5−7.2 give rise to mixtures of **14** and **15** only (Table 2, Entries 1−3), whilst thiols with a calculated pK_a of 5.5−6.4 give rise to only **16** (Table 2, Entries 5, 6, 9−12), except for *para*-chlorothiophenol, which gives mixtures of all three products (Table 2, Entries 7 and 8). The role of the *ortho*-halogen in the thiophenols may be a combination of an iodide effect together with coordination to Pd via a halogen lone pair. In the case of *ortho*-fluorothiophenol the iodide effect is dominant, whilst progressing from *ortho*-chloro to *ortho*-bromo would be marked by increasing lone pair coordination. The effect of *ortho*-bromo substituents has also been noted in ruthenium metathesis by the Grigg group.[10]

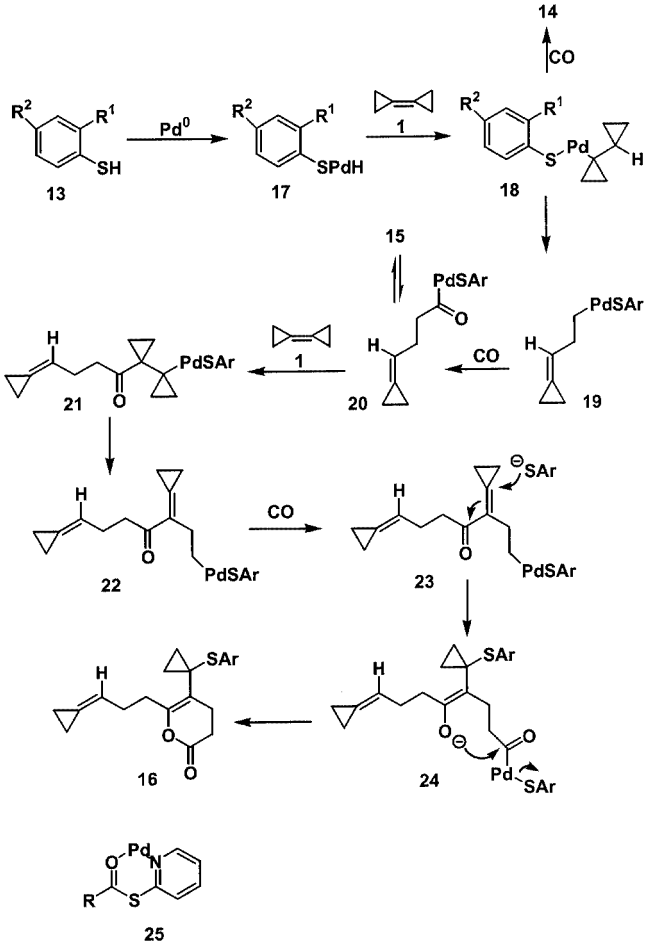
Possible mechanisms for the formation of **14−16** are shown in Scheme 4. Pd^0 inserts oxidatively into the S−H bond to afford **17**, which adds to the very reactive electron rich C=C double bond of **1** to afford **18**. The palladium atom in intermediate **18** may be coordinated to the *ortho*-bromine or chlorine atoms (R^1 = Br, Cl). The cyclopropylcarbinyl-homoallyl rearrangement of **18** to **19** appears to be competitive with carbonylation-reductive elimination to give **14**, while carbonylation-reductive elimination of **19** leads via **20** to **15**. However, if R^1 = H and R^2 = Cl (**13g**) the reaction leads exclusively to **14g** and **15g** after 18 h, although after 41 h the product comprised a 3:2 mixture of **14g/15g** and **16g** (Entry 7). One way to account for this result is to postulate the interconversion of **20** and **15**. Palladium insertion into S-acyl bonds has been reported recently by several groups.[11] Addition of **20** to **1** furnishes **21** and subsequent cyclopropylcarbinyl-homoallyl rearrangement affords **22**. Finally, Michael addition of thiolate anion to **23** furnishes **24**, which undergoes ring closure to **16**. The correlation of product selectivity with the pK_a of the thiophenol would agree with an increasing ease of Pd^0 insertion into the S-acyl bond of **15** (and possibly **14**) as the pK_a of the thiophenol decreases. Such a tendency would promote the conversion of **15** (and **14**) into **16**. The selectivity of pyridine-2(1*H*)-thione for **14d** reflects the high pK_a of the thione tautomer but additionally suggests chelation of Pd. Compound **25** may suppress oxidative addition into the S-acyl bond.

de Meijere et al. reported that thiols add easily to bicyclopropylidene (**1**) in benzene solution and proposed a radical mechanism.[12] They also reported that the addition is suppressed in the presence of $[Pd(OAc)_2]$. This could explain why only traces of thioethers like **26** were observed in the

Table 2. Thiocarbonylation of bicyclopropylidene (**1**)[a]

Entry	Thiol	R^1	R^2	X	pK_a [b]	*t* [h]	**14** and **15** (%) (**14**:**15**)[c]	**16** (%)
1	13a	H	H	CH	6.6 ± 0.1	42	71 (1:1.6)	–
2	13b	OMe	H	CH	6.6 ± 0.4	22	69 (3.6:1)	–
3	13c	*i*Pr	H	CH	6.8 ± 0.4	20	67 (1:2)	–
4[d]	13d	H	H	N	10.1 ± 0.2[e]	24	77 (>96:4)	–
5	13e	F	H	CH	6.0 ± 0.4	48	–	37
6	13f	Cl	H	CH	5.9 ± 0.4	48	–	50 (27)[f]
7	13g	H	Cl	CH	6.1 ± 0.1	41	29 (1.5:1)	20[g]
8[h]	13g	H	Cl	CH		44	33 (1.5:1)	31
9	13h	Br	H	CH	5.9 ± 0.4	19	–	45
10	13h	Br	H	CH		48	–	55
11[i]	13h	Br	H	CH		18	–[k]	44
12[j]	13h	Br	H	CH		16	–[k]	27

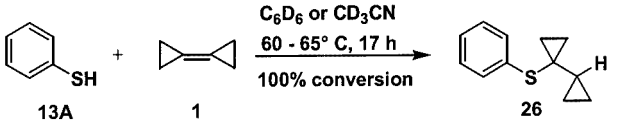
[a] Conditions: 2.00 equiv. **1**, 1.00 equiv. **13a**–**h**, 2.00 equiv. K_2CO_3, 4 mol % [$Pd(PPh_3)_4$], CO (2–3 bar), MeCN, 70–80 °C. [b] p*K*a values calculated using the software provided by ACD/I-Lab Web service (ACD/pK_a 5.0). [c] Ratio of **14**:**15** determined by ^{1}H NMR analysis of the crude product. [d] Performed without K_2CO_3 as additional base. [e] pK_a of the stable tautomer pyridine-2(1*H*)-thione. [f] 25 h. [g] After 18 h 40% conversion and only **14**:**15** (1:1.7) were observed. [h] 8 mol % [$Pd(PPh_3)_4$]. [i] 2 mol % [Pd_2dba_3], 8 mol % TFP. [j] 2 mol % [Pd_2dba_3], 8 mol % P(*o*-tolyl)$_3$. [k] A significant amount of **14h** was observed in the ^{1}H NMR spectrum of the crude product.



Scheme 4. Mechanism of the five-component queuing cascade

reactions described above (Scheme 3 and Table 2). However, in the reactions reported in this paper acetonitrile was the solvent. Therefore, the possible influence of the solvent was investigated.

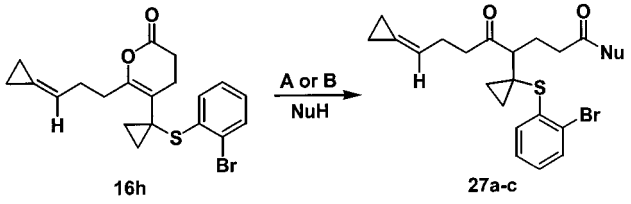
Thiophenol (**13a**) reacted readily with **1** both in C_6D_6, as published,[12] and in CD_3CN to afford **26** quantitatively



Scheme 5. Radical addition of thiophenol (**13a**) to **1** in benzene[12] or acetonitrile

(Scheme 5). However, when the same reaction was performed in CH_3CN in the presence of K_2CO_3, CO and a Pd catalyst only traces of **26** were detected, whilst in the absence of K_2CO_3 **26** was isolated in 20% yield indicating that both the Pd catalyst and K_2CO_3 are important for the outcome of the cascade reaction.

The highly reactive lactone **16h** undergoes ring opening with nucleophiles. Benzylamine and phenylhydrazine give **27a** and **27b** in 82% and 79% yield, respectively, and **16h** was quantitatively converted into the carboxylic acid **27c** upon keeping in a closed flask for 30 days (Scheme 6).



Scheme 6. Ester cleavage in **16h** with various nucleophiles (NuH); **A**: NuH = benzylamine, THF, 20 °C, 20 h, **27a** (82%); NuH = phenylhydrazine, THF, 20 °C, 45 h, **27b** (79%); **B**: NuH = H_2O, 30 days, >90% conversion.

Conclusion

The novel tetramolecular cascade process with bicyclopropylidene (**1**), *N*-(2-iodophenyl)-4-methylbenzenesulfona-

mide (**2**-NTs) or *ortho*-iodophenol (**2**-OH) and CO (2−3 bar) constitutes a straightforward approach to highly substituted 5-aza- or 5-oxadispiro[2.0.4.3]undecanes **3**-NTs and **3**-O. Under similar reaction conditions **1**, CO (2−3 bar) and thiophenols **13a−h** afford both thiocarbonylated bicyclopropyl derivatives **14a−d,g** and ring-opening products **15a−c,g**. The reaction with halogen-substituted thiophenols **13e−h** proceeds via a novel five-component cascade resulting in highly reactive lactones **16e−h**, which can be opened with various nucleophiles to give the products **27a−c**.

Experimental Section

General Remarks: ^{1}H and ^{13}C NMR spectra were recorded at 300 or 500 MHz (^{1}H) and 75.5 or 125.8 MHz [^{13}C, DEPT (Distortionless Enhancement by Polarization Transfer)] with Bruker DPX 300 or DRX 500 spectrometers, respectively, in $CDCl_3$ with TMS (0.03%) as internal standard. Mass spectra (EI and FAB): VG Autospec. (70 eV); (ESI): LCT Micromass (TOF). The mass spectra of isomers **14** and **15** were essentially identical in all cases and hence a single set of data is reported. IR: Midac M-2000 FT-IR, measured as KBr pellets or as oils between KBr plates. Elemental analysis: Carlo Erba MOD 11016 instrument. R_f values refer to TLC on 0.25 mm precoated silica gel plates (Merck F_{254}) with the same eluent as used for the separation of the compound by flash column chromatography employing silica gel 60 (Merck 9385). Melting points (m.p.): Reichert microscope with a Reichert heating mantle, values uncorrected. Anhydrous MeCN and all other chemicals were used as commercially available (Merck, Lancaster and Aldrich).

General Procedure (GP) for the Palladium Carbonylation or Thiocarbonylation of Bicyclopropylidene (1) with Aryl Iodides or Thiols: K_2CO_3 (276 mg, 2.00 mmol), [Pd(PPh$_3$)$_4$] (46.2 mg, 40.0 μmol), anhydrous MeCN (10 mL), bicyclopropylidene (**1**) (188 μL, 2.00 mmol, d = 0.854 g/ml) and aryl iodide (**2**-NTs or **2**-O, 1.00 mmol) or thiol (**13a−h**, 1.00 mmol) were added under a nitrogen atmosphere to a 100 mL oven dried Schlenk tube with a stirring bar. The mixture was frozen with liquid nitrogen and left under vacuum ($< 10^{-1}$ mbar) for around 2 min. The Schlenk tube was then charged with CO (1 bar), the mixture allowed to reach room temperature, placed in an oil bath pre-heated to 80 °C and stirred for an appropriate time. After cooling, the excess CO was vented, the reaction mixture filtered through silica gel, and the solvent removed by rotary evaporation. The residue was purified by flash column chromatography on silica gel.

6,7-Benzo-5-[(4-methylphenyl)sulfonyl]-5-azadispiro[2.0.4.3]-undecane-8,11-dione (3-NTs): Prepared from bicyclopropylidene (**1**) (188 μL, 2.00 mmol, d = 0.854 g/ml), NBu$_4$Br (484 mg, 1.50 mmol) and *N*-(2-iodophenyl)-4-methylbenzenesulfonamide (**2**-NTs) (373 mg, 1.00 mmol) over 20 h by the GP. Column chromatography (hexane/EtOAc 2:1) afforded **3**-NTs (233 mg, 61%) as a pale-orange solid; R_f = 0.20; m.p. 221−222 °C. Suitable pale yellow prisms for X-ray analysis were obtained by crystallisation from Et$_2$O/EtOAc (1:1 v/v). ^{1}H NMR: δ = 0.91−1.04 (m, 2 H, cy-Pr), 1.26−1.33 (m, 1 H, cy-Pr), 1.43−1.50 (m, 1 H, cy-Pr), 2.42 (s, 3 H, CH_3), 2.56−2.81 (m, 3 H, CH_2), 2.96−3.09 (m, 1 H, CH_2), 7.13−7.26 (m, 1 H, Ar-H), 7.33 (d, J = 8.4 Hz, 2 H, Ar-H), 7.61−7.70 (m, 2 H, Ar-H), 7.76−7.80 (m, 1 H, Ar-H), 7.82 (d, J = 8.4 Hz, 2 H, Ar-H) ppm. ^{13}C NMR: δ = 18.1 (CH_2, cy-Pr), 21.6 (CH_3), 22.4 (CH_2, cy-Pr), 29.9 (CH_2), 36.1 (CH_2), 37.7 (C, cy-Pr), 79.8 (C), 114.5 (CH), 121.7 (C), 123.6, 124.8 (CH), 126.8, 130.1 (2 CH), 137.6 (C), 137.8 (CH), 144.9, 152.5, 199.2, 214.6 (C) ppm. IR (KBr): $\tilde{\nu}_{max}$ = 1715, 1593, 1464, 1343, 1300, 1210, 1123, 1071, 1019, 995, 818, 762, 681 cm^{-1}. MS (ESI): m/z (%) = 404 (100) [M + Na$^+$], 333 (96) [2 × $C_7H_7SO_2$ + Na$^+$]. MS (EI): m/z (%) = 381 (8) [M$^+$], 227/226 (16/100) [M$^+$ − $C_7H_7SO_2$], 198 (15), 184 (9), 183 (13), 155 (6) [$C_7H_7SO_2^+$]. $C_{21}H_{19}NO_4S$ (381.4): calcd. C 66.13, H 5.02, N 3.67; found C 66.35, H 5.10, N 3.80.

6,7-Benzo-5-oxadispiro[2.0.4.3]undecane-8,11-dione (3-O) and 3,4-Dihydro-5,1′-spirocyclopropane-2*H*,5*H*-pyrano[3,2-*c*]chromen-2-one (4-O): Prepared over 15 h from bicyclopropylidene (**1**) (188 μL, 2.00 mmol, d = 0.854 g/ml) and *ortho*-iodophenol (**2**-O) (220 mg, 1.00 mmol) according to the GP. After column chromatography (hexane/Et$_2$O 1:1) **3**-O (46 mg, 20%) and **4**-O (26 mg, 11%) were obtained as pale yellow solids.

3-O: R_f = 0.23, m.p. 107−108 °C. ^{1}H NMR: δ = 0.83−0.90 (m, 1 H, cy-Pr), 1.24−1.39 (m, 3 H, cy-Pr), 2.32−2.41 (m, 1 H, CH_2), 2.48−2.59 (m, 1 H, CH_2), 2.65−2.87 (m, 2 H, CH_2), 7.07−7.12 (m, 2 H, Ar-H), 7.62−7.68 (m, 2 H, Ar-H) ppm. ^{13}C NMR: δ = 14.6 (CH_2, cy-Pr), 18.44 (CH_2, cy-Pr), 31.9 (CH_2), 35.8 (C, cy-Pr), 36.1 (CH_2), 94.7 (C), 113.3 (CH), 120.4 (C), 122.2, 124.5, 138.7 (CH), 171.5, 200.6, 214.3 (C) ppm. IR (KBr): $\tilde{\nu}_{max}$ = 1732, 1703, 1617, 1483, 1092, 893, 754 cm^{-1}. MS (ESI): m/z (%) = 251 (100) [M + Na$^+$], 229 (8) [M + H$^+$]. MS (EI): m/z (%) = 228 (48) [M$^+$], 200 (100) [M$^+$ − CO], 185 (26), 172 (38), 121 (39). $C_{14}H_{12}O_3$ (228.2): calcd. C 73.67, H 5.30; found C 73.40, H 5.55.

4-O: R_f = 0.17, m.p. 88−90 °C. ^{1}H NMR: δ = 0.86, 1.19 (2 m, AA′BB′, 4 H, cy-Pr), 2.20, 2.76 (2 t, J = 7.6 Hz, 4 H, CH_2), 6.73 (dd, J = 7.7, 1.0 Hz, 1 H, Ar-H), 6.95 (dt, J = 7.7, 1.0 Hz, 1 H, Ar-H), 7.17 (dt, J = 7.7, 1.6 Hz, 1 H, Ar-H), 7.38 (dd, J = 7.7, 1.6 Hz, 1 H, Ar-H) ppm. ^{13}C NMR: δ = 12.3 (2 C, CH_2, cy-Pr), 19.6, 28.9 (CH_2), 61.2, 109.2 (C), 116.1 (CH), 118.3 (C), 121.4, 122.1, 130.3 (CH), 142.2, 153.9, 167.8 (C) ppm. IR (KBr): $\tilde{\nu}_{max}$ = 1763, 1489, 1387, 1253, 1192, 1169, 1143, 1103, 766 cm^{-1}. MS (FAB): m/z (%) = 245 (7) [M + Na$^+$], 229 (50) [M + H$^+$], 228 (100) [M$^+$], 227 (38), 200 (74) [M$^+$ − CO], 199 (28), 185 (33), 147 (21). $C_{14}H_{12}O_3$ (228.2): calcd. C 73.67, H 5.30; found C 73.40, H 5.50.

***S*-Phenyl 1,1′-Bi(cyclopropyl)-1-carbothioate (14a) and *S*-Phenyl 4-Cyclopropylidenebutanethioate (15a):** Prepared over 42 h from bicyclopropylidene (**1**) (188 μL, 2.00 mmol, d = 0.854 g/ml) and thiophenol (**13a**) (102 μL, d = 1.075 g/ml, 1.00 mmol) according to the GP. After column chromatography (hexane/Et$_2$O 20:1) a 1:1.6 mixture of **14a**/**15a** (156 mg, 71%) was obtained as a colourless oil; R_f = 0.20.

14a: ^{1}H NMR: δ = 0.25, 0.66 (2 m, AA′BB′, 4 H, cy-Pr), 0.72, 1.23 (2 m, CC′DD′, 4 H, cy-Pr), 1.53−1.62 (m, 1 H, cy-Pr), 7.37−7.44 (m, 5 H, Ar-H) ppm. ^{13}C NMR: δ = 4.76 (2 C, CH_2), 11.35 (CH), 16.32 (2 C, CH_2), 33.87 (C), 129.00 (C), 129.46 (2 C, CH), 129.52 (CH), 135.31 (2 C, CH), 201.38 (C) ppm.

15a: ^{1}H NMR: δ = 1.04−1.05 (m, 4 H, cy-Pr), 2.58 (virt. q, J = 7.2 Hz, 2 H, CH_2), 2.83 (t, J = 7.2 Hz, 2 H, CH_2), 5.77−5.82 (m, 1 H, =CH), 7.39−7.40 (m, 5 H, Ar-H) ppm. ^{13}C NMR: δ = 2.6 (2 C, CH_2, cy-Pr), 28.1, 43.5 (CH_2), 115.9 (CH), 123.4 (C), 128.3 (C), 129.6 (2 C, CH), 129.7 (CH), 134.9 (2 C, CH), 197.6 (C) ppm.

14a/15a: MS (EI): m/z (%) = 218 (2) [M$^+$], 190 (9), 123 (14), 110 (26), 109 (100) [M$^+$ − C_6H_5S], 81 (76) [M$^+$ − C_6H_5S − CO], 79 (41), 65 (34), 53 (39). $C_{13}H_{14}OS$ (218.3): calcd. C 71.52, H 6.46, S 14.69; found C 71.55, H 6.50, S 14.45.

***S*-(2-Methoxyphenyl) 1,1′-Bi(cyclopropyl)-1-carbothioate (14b) and *S*-(2-Methoxyphenyl) 4-Cyclopropylidenebutanethioate (15b):** Prepared over 22 h by the GP from bicyclopropylidene (**1**) (188 μL, 2.00 mmol, d = 0.854 g/ml) and *ortho*-methoxythiophenol (**13b**) (122 μL, d = 1.152 g/ml, 1.00 mmol). After column chromatography (hexane/Et_2O 2:1) a 3.6:1 mixture of **14b/15b** (171 mg, 69%) was obtained as a pale yellow oil.

14b: R_f = 0.35. ^{1}H NMR: δ = 0.26, 0.66 (2 m, AA′BB′, 4 H, cy-Pr), 0.69, 1.21 (2 m, CC′DD′, 4 H, cy-Pr), 1.59−1.66 (m, 1 H, cy-Pr), 3.83 (s, 3 H, CH_3), 6.93−7.00 (m, 2 H, Ar-H), 7.36−7.41 (m, 2 H, Ar-H) ppm. ^{13}C NMR: δ = 4.74 (2 C, CH_2), 11.50 (CH), 16.06 (2 C, CH_2), 33.85 (C), 56.43 (CH_3), 111.91 (CH), 117.10 (C), 121.43, 131.76, 137.51 (CH), 159.94, 200.33 (C) ppm.

15b: R_f = 0.41. ^{1}H NMR: δ = 1.04−1.05 (m, 4 H, cy-Pr), 2.58 (virt. q, J = 7.5 Hz, 2 H, CH_2), 2.84 (t, J = 7.5 Hz, 2 H, CH_2), 3.84 (s, 3 H, CH_3), 5.77−5.83 (m, 1 H, =CH), 6.95−7.01 (m, 2 H, Ar-H), 7.36−7.44 (m, 2 H, Ar-H) ppm. ^{13}C NMR: δ = 2.5 (2 C, CH_2, cy-Pr), 28.1, 43.3 (CH_2), 56.4 (CH_3), 111.9 (CH), 116.1 (CH), 116.4 (C), 121.5 (CH), 123.2 (C), 132.0, 137.2 (CH), 159.6, 196.9 (C) ppm.

14b/15b: MS (FAB): m/z (%) = 249 (41) [M + H$^+$], 109 (100) [M$^+$ − C_7H_7OS], 81 (50) [M$^+$ − C_7H_7OS − CO]. $C_{14}H_{16}O_2S$ (248.3): calcd. C 67.71, H 6.49, S 12.91; found C 67.45, H 6.55, S 12.85.

***S*-(2-Isopropylphenyl) 1,1′-Bi(cyclopropyl)-1-carbothioate (14c) and *S*-(2-Isopropylphenyl) 4-Cyclopropylidenebutanethioate (15c):** Prepared over 20 h by the GP from bicyclopropylidene (**1**) (188 μL, 2.00 mmol, d = 0.854 g/ml) and *ortho*-isopropylthiophenol (**13c**) (152 μL, d = 1.005 g/ml, 1.00 mmol, tech. 90%). After column chromatography (hexane/Et_2O 10:1) a 1:2 mixture of **14c/15c** (157 mg, 67% based on tech. **13c**) was obtained as a pale yellow oil.

14c: R_f = 0.39. ^{1}H NMR: δ = 0.25, 0.67 (2 m, AA′BB′, 4 H, cy-Pr), 0.69 (m, CC′DD′, 2 H, cy-Pr), 1.19 (d, J = 6.8 Hz, 6 H, 2 CH_3), 1.23 (m, CC′DD′, 2 H, cy-Pr), 1.58−1.63 (m, 1 H, cy-Pr), 3.30 (sept, J = 6.8 Hz, 1 H, CH), 7.16−7.22 (m, 1 H, Ar-H), 7.31−7.40 (m, 3 H, Ar-H) ppm. ^{13}C NMR: δ = 4.8 (2 C, CH_2), 11.6 (CH, cy-Pr), 16.0 (2 C, CH_2), 24.0 (2 C, CH_3), 31.5 (CH), 33.9 (C), 126.5, 126.7, 130.6, 137.2 (CH), 152.5, 201.2 (C) ppm.

15c: R_f = 0.43. ^{1}H NMR: δ = 1.05 (virt. s, 4 H, cy-Pr), 1.19 (d, J = 6.9 Hz, 6 H, 2 CH_3), 2.59 (virt. q, J = 7.0 Hz, 2 H, CH_2), 2.84 (t, J = 7.0 Hz, 2 H, CH_2), 3.30 (sept, J = 6.9 Hz, 1 H, CH), 5.77−5.82 (m, 1 H, =CH), 7.17−7.25 (m, 1 H, Ar-H), 7.35−7.43 (m, 3 H, Ar-H) ppm. ^{13}C NMR: δ = 2.5, 2.6 (CH_2, cy-Pr), 24.0 (2 C, CH_3), 28.3 (CH_2), 31.5 (CH), 43.6 (CH_2), 116.0 (CH), 123.4 (C), 126.6, 126.8, 130.8, 136.9 (CH), 152.2, 197.7 (C) ppm.

14c/15c: MS (FAB): m/z (%) = 261 (100) [M + H$^+$], 109 (75) [M$^+$ − $C_9H_{11}S$], 81 (76) [M$^+$ − $C_9H_{11}S$ − CO]. $C_{16}H_{20}OS$ (260.4): calcd. C 73.80, H 7.74, S 12.31; found C 73.60, H 7.65, S 12.35.

***S*-(2-Pyridyl) 1,1′-Bi(cyclopropyl)-1-carbothioate (14d):** Prepared over 24 h by the GP (without K_2CO_3) from bicyclopropylidene (**1**) (188 μL, 2.00 mmol, d = 0.854 g/ml) and 2-mercaptopyridine (**13d**) (111 mg, 1.00 mmol). After column chromatography (Et_2O/hexane 5:1) **14d** (169 mg, 77%) was obtained as a pale yellow oil. After storage for a few days at −20 °C **14d** was obtained as a colourless solid; (R_f = 0.43); m.p. 32−34 °C. ^{1}H NMR: δ = 0.27, 0.69 (2 m, AA′BB′, 4 H, cy-Pr), 0.75, 1.25 (2 m, CC′DD′, 4 H, cy-Pr), 1.52−1.61 (m, 1 H, cy-Pr), 7.24−7.31 (m, 1 H, Py-H), 7.56−7.62 (m, 1 H, Py-H), 7.68−7.76 (m, 1 H, Py-H), 8.62−8.66 (m, 1 H, Py-H) ppm. ^{13}C NMR: δ = 4.9 (2 C, CH_2), 11.2 (CH), 16.6 (2 C, CH_2), 34.2 (C), 123.8, 131.2, 137.4, 150.8 (CH), 152.7, 200.7 (C) ppm. IR (film): $\tilde{\nu}_{max}$ = 3003, 1682, 1574, 1565, 1449, 1424, 1290, 1248, 1038, 986, 957, 830 cm^{-1}. MS (FAB): m/z (%) = 221/220 (13/100) [M + H$^+$]. $C_{12}H_{13}NOS$ (219.3): calcd. C 65.73, H 5.97, N 6.38, S 14.62; found C 65.55, H 6.05, N 6.35, S 14.35.

6-(3-Cyclopropylidenepropyl)-5-{1-[(2-fluorophenyl)thio]-cyclopropyl}-3,4-dihydro-2*H*-pyran-2-one (16e): Prepared over 48 h by the GP from bicyclopropylidene (**1**) (188 μL, 2.00 mmol, d = 0.854 g/ml) and *ortho*-fluorothiophenol (**13e**) (107 μL, d = 1.203 g/ml, 1.00 mmol). After column chromatography (hexane/Et_2O 3:1) **16e** (126 mg, 37%) was obtained as a pale yellow oil. After storage for a few days at −20 °C **16e** was obtained as a colourless solid; R_f = 0.22; m.p. 45 °C. ^{1}H NMR: δ = 0.96 (virt. s, 6 H, cy-Pr), 1.25−1.31 (m, 2 H, cy-Pr), 1.90−1.95 (m, 2 H, CH_2), 2.00−2.07 (m, 2 H, CH_2), 2.42−2.46 (m, 2 H, CH_2), 2.52−2.57 (m, 2 H, CH_2), 5.52−5.56 (m, 1 H, =CH), 7.08−7.14 (m, 2 H, Ar-H), 7.34−7.43 (m, 1 H, Ar-H), 7.45−7.52 (m, 1 H, Ar-H) ppm. ^{13}C NMR: δ = 2.0 (2 CH_2, cy-Pr), 16.6 (2 C, CH_2, cy-Pr), 22.9, 28.3, 28.6, 28.8 (CH_2), 29.9 (C, cy-Pr), 113.8 (C), 116.1 (d, $^2J_{C,F}$ = 24.2 Hz, CH), 116.5 (CH), 120.3 (d, $^2J_{C,F}$ = 19.6 Hz, C), 121.9 (C), 124.6 (d, $^3J_{C,F}$ = 3.8 Hz, CH), 131.6 (d, $^3J_{C,F}$ = 7.5 Hz, CH), 138.3 (CH), 152.1 (C), 163.6 (d, $^1J_{C,F}$ = 246.8 Hz, C), 168.9 (C) ppm. IR (KBr): $\tilde{\nu}_{max}$ = 3056, 2982, 2903, 1765, 1688, 1472, 1445, 1256, 1219, 1171, 1136, 1046, 1011, 961, 936, 903, 768 cm^{-1}. MS (ESI): m/z (%) = 689 (15) [2 × M + H$^+$], 345 (100) [M + H$^+$]. $C_{20}H_{21}FO_2S$ (344.4): calcd. C 69.74, H 6.14, S 9.31; found C 69.45, H 6.30, S 9.35.

5-{1-[(2-Chlorophenyl)thio]cyclopropyl}-6-(3-cyclopropylidenepropyl)-3,4-dihydro-2*H*-pyran-2-one (16f): Prepared over 48 h by the GP from bicyclopropylidene (**1**) (188 μL, 2.00 mmol, d = 0.854 g/ml) and *ortho*-chlorothiophenol (**13f**) (113 μL, d = 1.277 g/ml, 1.00 mmol). After column chromatography (hexane/Et_2O 3:2) **16f** (180 mg, 50%) was obtained as a colourless oil; R_f = 0.28. ^{1}H NMR: δ = 0.97 (virt. s, 4 H, cy-Pr), 1.00, 1.36 (2 m, AA′BB′, 4 H, cy-Pr), 1.99−2.09 (m, 4 H, 2 CH_2), 2.43−2.49 (m, 2 H, CH_2), 2.52−2.58 (m, 2 H, CH_2), 5.54−5.57 (m, 1 H, =CH), 7.19−7.32 (m, 2 H, Ar-H), 7.43−7.47 (m, 1 H, Ar-H), 7.60−7.63 (m, 1 H, Ar-H) ppm. ^{13}C NMR: δ = 2.0, 2.0 (CH_2, cy-Pr), 16.6 (2 C, CH_2, cy-Pr), 23.1, 28.3, 28.8, 28.9 (CH_2), 29.9 (C, cy-Pr), 113.7 (C), 116.5 (CH), 121.9 (C), 127.1, 130.2, 130.2 (CH), 132.9 (C), 137.5 (CH), 139.1, 152.2, 168.8 (C) ppm. IR (film): $\tilde{\nu}_{max}$ = 2979, 2913, 1765, 1678, 1449, 1424, 1254, 1188, 1140, 1113, 1036, 901, 756 cm^{-1}. MS (ESI): m/z (%) = 725/723/721 (2/18/28) [2 × M + H$^+$], 363/361 (28/100) [M + H$^+$]. $C_{20}H_{21}ClO_2S$ (360.9): calcd. C 66.56, H 5.86, Cl 9.82, S 8.88; found C 66.30, H 6.05, Cl 9.90, S 9.00.

***S*-(4-Chlorophenyl) 1,1′-Bi(cyclopropyl)-1-carbothioate (14g), *S*-(4-Chlorophenyl) 4-Cyclopropylidenebutanethioate (15g) and 5-{1-[(4-Chlorophenyl)thio]cyclopropyl}-6-(3-cyclopropylidenepropyl)-3,4-dihydro-2*H*-pyran-2-one (16g):** Prepared over 44 h by the GP from bicyclopropylidene (**1**) (188 μL, 2.00 mmol, d = 0.854 g/ml), [Pd(PPh_3)$_4$] (92.4 mg, 80.0 μmol) and *para*-chlorothiophenol (**13g**) (145 mg, 1.00 mmol). After column chromatography (gradient hexane/Et_2O 10:1 to 2:1) a 1.5:1 mixture of **14g/15g** (83 mg, 33%) and **16g** (111 mg, 31%) were obtained as colourless oils; R_f (**14g/15g**) = 0.36 hexane/Et_2O 9:1; R_f (**16g**) = 0.32 hexane/Et_2O 2:1.

14g: ^{1}H NMR: δ = 0.25, 0.67 (2 m, AA′BB′, 4 H, cy-Pr), 0.73, 1.22 (2 m, CC′DD′, 4 H, cy-Pr), 1.50−1.59 (m, 1 H, cy-Pr), 7.28−7.40 (m, 4 H, Ar-H) ppm. ^{13}C NMR: δ = 4.8 (2 C, CH_2), 11.3 (CH), 16.5 (2 C, CH_2), 33.9, 127.56 (C), 129.7 (2 CH), 135.9 (C), 136.5 (2 CH), 200.9 (C) ppm.

15g: ^{1}H NMR: δ = 1.04−1.05 (m, 4 H, cy-Pr), 2.57 (virt. q, J = 7.6 Hz, 2 H, CH_2), 2.83 (t, J = 7.6 Hz, 2 H, CH_2), 5.75−5.81 (m, 1 H, =CH), 7.28−7.40 (m, 4 H, Ar-H) ppm. ^{13}C NMR: δ = 2.6, 2.6 (CH_2, cy-Pr), 28.1 (CH_2), 43.6 (CH_2), 115.8 (CH), 123.5, 129.6 (C), 129.8 (2 CH), 136.1 (2 CH, C), 196.9 (C) ppm.

14g/15g: MS (ESI): *m/z* (%) = 255/253 (23/100) [M + H$^+$]. $C_{13}H_{13}ClOS$ (252.8): calcd. C 61.78, H 5.18, Cl 14.03, S 12.68; found C 62.00, H 5.20, Cl 13.95, S 12.55.

16g: ^{1}H NMR: δ = 0.96−1.01 (m, 6 H, cy-Pr), 1.25 (m, AA′BB′, 2 H, cy-Pr), 1.97−2.02 (m, 2 H, CH_2), 2.08−2.16 (m, 2 H, CH_2), 2.35−2.43 (m, 2 H, CH_2), 2.46−2.54 (m, 2 H, CH_2), 5.57−5.62 (m, 1 H, =CH), 7.30 (d, *J* = 8.5 Hz, 2 H, Ar-H), 7.42 (d, *J* = 8.5 Hz, 2 H, Ar-H) ppm. ^{13}C NMR: δ = 2.0 (2 CH_2, cy-Pr), 16.6 (2 C, CH_2, cy-Pr), 23.2, 28.4, 28.88, 28.93 (CH_2), 30.4 (C, cy-Pr), 113.8 (C), 116.4 (CH), 122.0 (C), 129.1 (2 CH), 132.2, 135.4 (C), 136.4 (2 CH), 152.3, 168.7 (C) ppm. IR (film): $\tilde{\nu}_{max}$ = 2979, 1759, 1678, 1476, 1443, 1418, 1256, 1223, 1188, 1130, 1096, 1042, 1015, 901, 824, 747 cm^{-1}. MS (EI): *m/z* (%) = 747/745/743 (2/19/34) [2 × M +Na$^+$], 385/383 (21/100) [M + Na$^+$]. $C_{20}H_{21}ClO_2S$ (360.9): calcd. C 66.56, H 5.86, Cl 9.82, S 8.88; found C 66.30, H 5.95, Cl 9.90, S 9.00.

5-{1-[(2-Bromophenyl)thio]cyclopropyl}-6-(3-cyclopropylidenepropyl)-3,4-dihydro-2*H*-pyran-2-one (16h): Prepared over 48 h by the GP from bicyclopropylidene (**1**) (188 µL, 2.00 mmol, *d* = 0.854 g/ml) and *ortho*-bromothiophenol (**13g**) (118 µL, *d* = 1.604 g/ml, 1.00 mmol). After column chromatography (hexane/Et$_2$O 2:1) **16h** (223 mg, 55%) was obtained as a colourless oil; R_f = 0.29. ^{1}H NMR: δ = 0.94−0.99 (m, 4 H, cy-Pr), 1.01, 1.38 (2 m, AA′BB′, 4 H, cy-Pr), 2.05−2.12 (m, 4 H, 2 CH_2), 2.45−2.49 (m, 2 H, CH_2), 2.53−2.57 (m, 2 H, CH_2), 5.56−5.60 (m, 1 H, =CH), 7.16−7.20 (m, 1 H, Ar-H), 7.25−7.29 (m, 1 H, Ar-H), 7.62−7.65 (m, 2 H, Ar-H) ppm. ^{13}C NMR: δ = 2.0, 2.1 (CH_2, cy-Pr), 16.7 (2 C, CH_2, cy-Pr), 23.3, 28.4, 28.9, 29.1 (CH_2), 30.2 (C, cy-Pr), 113.7 (C), 116.6 (CH), 122.1 (C), 127.8 (CH), 129.8 (C), 130.1, 133.6 (CH), 135.4 (C), 136.9 (CH), 152.4, 168.7 (C) ppm. IR (film): $\tilde{\nu}_{max}$ = 1765, 1445, 1134, 1042, 1021, 754 cm^{-1}. MS (EI): *m/z* (%) = 406/404 (1/1) [M$^+$], 378/376 (21/21) [M$^+$ − CO], 326/325/324/323 (16/99/16/100) [M$^+$ − C_6H_9], 297/295 (9/9), 283/281 (6/6). $C_{20}H_{21}BrO_2S$ (405.3): calcd. C 59.26, H 5.21, Br 19.71, S 7.91; found C 59.35, H 4.95, Br 19.65, S 7.60.

***N*-Benzyl-4-{1-[(2-bromophenyl)thio]cyclopropyl}-8-cyclopropylidene-5-oxooctanamide (27a):** A solution of **16h** (52.0 mg, 128 µmol) and benzylamine (28.0 µL, *d* = 0.981 g/ml, 256 µmol) in anhydrous THF (2 mL) was stirred at room temperature for 20 h. The solvent was removed by rotary evaporation and the residue purified by flash column chromatography on silica gel (Et$_2$O) to give **27a** (54.0 mg, 82%) as a colourless oil; R_f = 0.34. ^{1}H NMR: δ = 0.99−1.02 (m, 4 H, cy-Pr), 1.02−1.10 (m, 2 H, cy-Pr), 1.23−1.33 (m, 2 H, cy-Pr), 1.90−2.00 (m, 2 H), 2.01−2.06 (m, 1 H), 2.11−2.18 (m, 1 H), 2.33−2.41 (m, 2 H), 2.54−2.61 (m, 1 H), 2.79−2.86 (m, 2 H), 4.32 (dd, *J* = 8.8, 3.4 Hz, 1 H, NCH_2), 4.38 (dd, *J* = 8.8, 3.4 Hz, 1 H, NCH_2), 5.69−5.74 (m, 1 H, =CH), 5.81 (s, 1 H, NH), 7.01−7.05 (m, 1 H, Ar-H), 7.19−7.31 (m, 6 H, Ar-H), 7.50−7.54 (m, 2 H, Ar-H) ppm. ^{13}C NMR: δ = 1.9, 2.1, 13.8, 14.2 (CH_2, cy-Pr), 25.5, 25.7 (CH_2), 26.5 (C, cy-Pr), 34.2, 43.5, 43.6 (CH_2), 54.2 (CH), 116.5 (CH), 122.3, 122.6 (C), 126.8, 127.5, 127.6 (CH), 127.8 (2 CH), 128.3 (CH), 128.7 (2 CH), 133.3 (CH), 137.5, 138.1, 171.7, 210.5 (C) ppm. MS (FAB): *m/z* (%) = 514/512 (14/14) [M + H$^+$], 406/404 (6/6), 324 (19), 216 (8), 109 (21), 91 (100). MS (ESI): *m/z* (%) = 536/534 (12/39) [M + Na$^+$], 514/512 (99/100) [M + H$^+$]. MS (HR-ESI): 512.1278 ($C_{27}H_{31}BrNO_2S$, calcd. 512.1259). MS (HR-ESI): 534.1075 ($C_{27}H_{30}BrNO_2SNa$, calcd. 534.1078).

4-{1-[(2-Bromophenyl)thio]cyclopropyl}-8-cyclopropylidene-5-oxo-*N*-phenyloctanohydrazide (27b): A solution of **16h** (91.0 mg, 225 µmol) and phenylhydrazine (66.0 µL, *d* = 1.099 g/ml, 675 µmol) in anhydrous THF (2 mL) was stirred at room temperature for 45 h. The solvent was removed by rotary evaporation and the residue purified by flash column chromatography on silica gel (Et$_2$O) to give **27b** (91.0 mg, 79%) as a pale yellow oil, which comprised a 2:1 rotamer mixture; R_f = 0.30. ^{1}H NMR: δ = 0.95−1.12 (m, 6 H, cy-Pr), 1.22−1.30 (m, 2 H, cy-Pr), 1.91−2.02 (m, 2 H), 2.03−2.10 (m, 1 H), 2.16−2.28 (m, 1 H), 2.29−2.43 (m, 2 H), 2.46−2.64 (m, 1 H), 2.74−2.87 (m, 2 H), 5.64−5.76 (m, 1 H, =CH), 5.79 (s, 1 H, NH), 6.69−6.78 (m, 2 H, Ar-H), 6.84−6.91 (m, 1 H, Ar-H), 6.96−7.05 (m, 1 H, Ar-H), 7.14−7.29 (m, 3 H, Ar-H), 7.50−7.53 (m, 2 H, Ar-H), 7.82 (s, 1 H, NH) ppm. ^{13}C NMR (**rotamer A**): δ = 2.0, 2.2, 13.9, 14.5 (CH_2, cy-Pr), 25.5, 25.57 (CH_2), 26.7 (C, cy-Pr), 31.9, 43.4 (CH_2), 54.5 (CH), 113.2 (2 CH), 116.4, 121.2 (CH), 122.4, 122.8 (C), 126.9, 127.7, 128.6 (CH), 129.2 (2 CH), 133.3 (CH), 137.4, 147.8, 172.2, 210.5 (C) ppm. ^{13}C NMR (**rotamer B**): δ = 1.9, 2.1, 13.5, 14.2 (CH_2, cy-Pr), 24.6, 25.5 (CH_2), 26.5 (C, cy-Pr), 30.3, 43.5 (CH_2), 54.1 (CH), 112.4 (2 CH), 116.5, 121.3 (CH), 122.1, 122.5 (C), 126.7, 127.6, 128.3 (CH), 129.5 (2 CH), 133.3 (CH), 137.7, 146.9, 178.0, 210.6 (C) ppm. MS (FAB): *m/z* (%) = 515/513 (39/39) [M + H$^+$], 325 (17), 217 (33), 109 (72), 97 (61), 85 (46), 83 (78), 81 (99), 71 (61), 69 (100). MS (HR-ESI): 535.1017 ($C_{26}H_{29}BrN_2O_2SNa$, calcd. 535.1031).

4-{1-[(2-Bromophenyl)thio]cyclopropyl}-8-cyclopropylidene-5-oxooctanoic Acid (27c): Vinyl lactone **16h** was hydrolysed with > 90% conversion into **27c** after storage in a closed but not sealed flask at room temperature for 1 month, and purified by column chromatography (Et$_2$O/hexane 3:1) to afford **27c** as a colourless oil; R_f = 0.32. ^{1}H NMR: δ = 1.01−1.10 (m, 6 H, cy-Pr), 1.26−1.29 (m, 2 H, cy-Pr), 1.91−2.03 (m, 2 H), 2.14−2.21 (m, 1 H), 2.26−2.33 (m, 1 H), 2.35−2.41 (m, 2 H), 2.53−2.60 (m, 1 H), 2.79−2.87 (m, 2 H), 5.71−5.75 (m, 1 H, =CH), 7.03−7.07 (m, 1 H, Ar-H), 7.28−7.31 (m, 1 H, Ar-H), 7.52−7.55 (m, 2 H, Ar-H), 8.00−11.50 (br. s, 1 H, CO_2 H) ppm. ^{13}C NMR: δ = 2.0, 2.1, 13.4, 14.3 (CH_2, cy-Pr), 24.6, 25.5 (CH_2), 26.5 (C, cy-Pr), 31.8, 43.9 (CH_2), 53.6 (CH), 116.3 (CH), 122.4, 122.8 (C), 126.9, 127.6, 128.4, 133.3 (CH), 137.5, 179.0, 210.2 (C) ppm. MS (ESI): *m/z* (%) = 447/445 (99/100) [M + Na$^+$]. $C_{20}H_{23}BrO_3S$ (423.4): calcd. C 56.74, H 5.48, Br 18.87, S 7.57; found C 56.60, H 5.70, Br 18.60, S 7.30.

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[5] **Crystal Structure of 3-NTs**: Crystals (prisms) of **3**-NTs were grown from a solution of Et_2O/EtOAc (1:1) and measured on a Nonius Kappa CCD area-detector diffractometer using graphite-monochromated Mo-K_α radiation. A correction was applied for the prismatic shape of the crystals ($0.56 \times 0.42 \times 0.31$ mm size). The structure was solved by direct methods (SHELXS-97) and refined by full-matrix least-squares on F^2 (SHELXL-97). All non-hydrogen atoms were refined anisotropically and all hydrogen atoms were located on the difference Fourier maps and refined isotropically. $C_{21}H_{19}NO_4S$ (381.43), monoclinic, a = 7.27750(10), b = 8.17050(10), c = 15.6703(3) Å, β = 102.5370(6)°, V = 909.55(2) Å^3, Z = 2, space group $P2_1$, T = 100(2) K, ρ = 1.393 g cm^{-3}, $F(000)$ = 400, μ = 0.206 mm^{-1}, intensities measured: 15935 ($2.87° \leq \theta \leq 25.99°$), independent reflections: 3486 (R_{int} = 0.0455), observed reflections: 3451 [$I > 2\sigma(I)$], R_1 = 0.0306, wR_2 {final [$I > 2\sigma(I)$]} = 0.0805, Goodness of fit = 1.064, maximum residual electron density 0.327 and −0.284 e Å^{-3}. CCDC-180833 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge at www.ccdc.cam.ac.uk/conts/retrieving.html [or from the Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge CB2 1EZ, UK; Fax: (internat.) +44-1223/336-033; E-mail: deposit@ccdc.cam.ac.uk].

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