

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.

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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 multicompon-

ent 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 spiroannulated 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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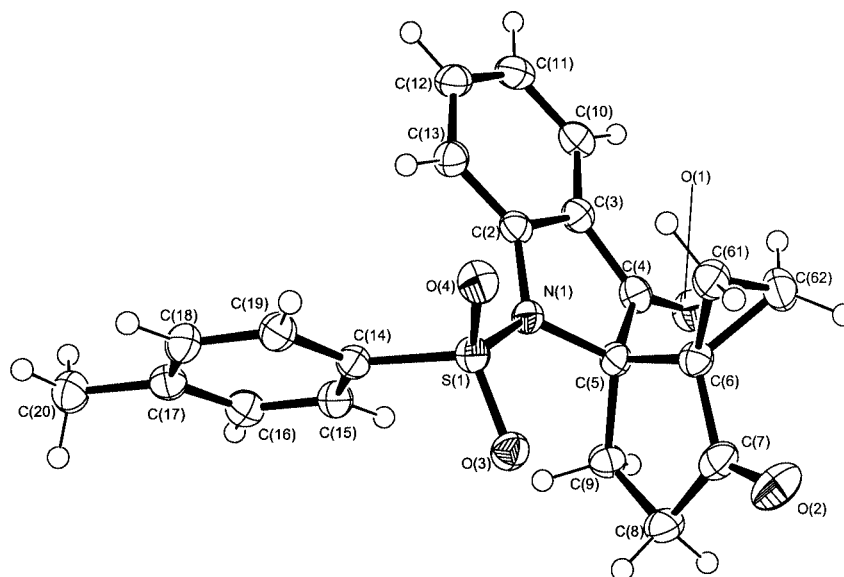
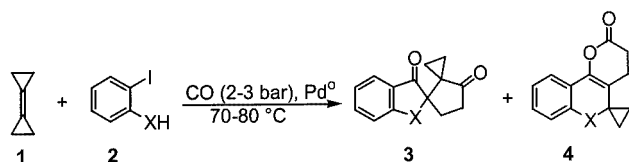


Figure 1. Structure of **3-NTs** in the crystal;^[5] selected bond lengths [Å] and angles [°]: N(1)–C(2) 1.414(2), C(2)–C(3) 1.396(2), C(3)–C(4) 1.457(2), C(4)–C(5) 1.536(2), C(4)–O(1) 1.218(2), C(5)–N(1) 1.503(2), C(5)–C(6) 1.538(2), C(6)–C(61) 1.509(2), C(6)–C(62) 1.530(2), C(61)–C(62) 1.482(3), C(6)–C(7) 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 bicyclopopylidene (**1**), aryl iodide **2** and carbon monoxide; for details see Table 1

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

Entry	X	Conditions ^[a]	Base	<i>t</i> [h]	3 (%)	4 (%)
1	NTs	A	K ₂ CO ₃	48	trace ^[b]	—
2	NTs	B	K ₂ CO ₃	72	40 ^[b]	—
3	NTs	B	Ag ₂ CO ₃	48	trace ^[b]	—
4	NTs	C	K ₂ CO ₃	20	61	—
5	O	B	K ₂ CO ₃	15	20	11
6	O	B	Cs ₂ CO ₃	16	1.8	—
7	O	B ^[c]	K ₂ CO ₃	62	trace	trace
8	O	D	K ₂ CO ₃	40	15	13
9	O	C	K ₂ CO ₃	24	11	24
10	O	E	K ₂ CO ₃	20	—	—
11	O	B	DABCO	48	—	—
12	OTMS	B	K ₂ CO ₃	18	29	trace

^[a] A: 10 mol % [Pd(OAc)₂], 20 mol % TFP, 100 mol % NBu₄Br, CO (2–3 bar), DMF. B: 4 mol % [Pd(PPh₃)₄], MeCN. C: as in B, 150 mol % NBu₄Br. D: 3 mol % [Pd₂dba₃], 12 mol % TFP. E: as in D, 150 mol % NBu₄Br. ^[b] Along with *N*-(2-iodophenyl)-4-methylbenzenesulfonamide (**2-NTs**). ^[c] 1 atm. CO.

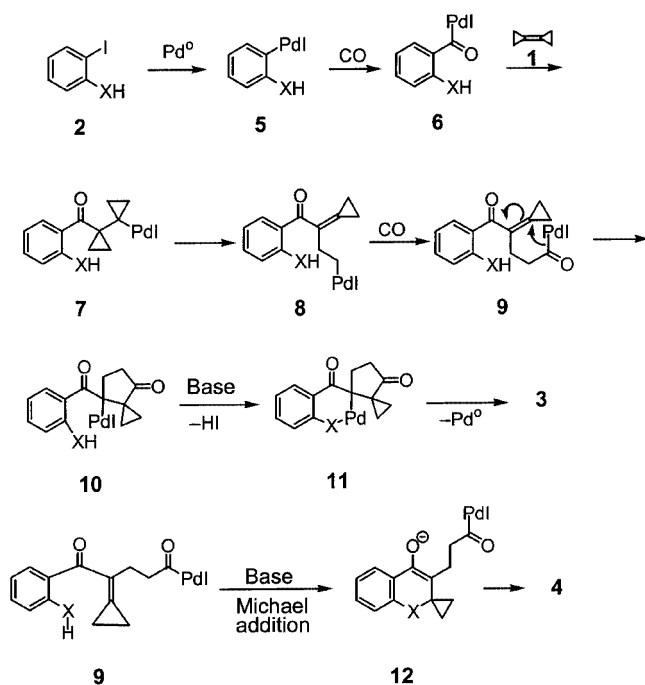
2-NTs (Entry 1). However, [Pd(PPh₃)₄] as catalyst in MeCN gave **3-NTs** as the sole product in 40% yield (Entry 2). Changing the base from K₂CO₃ to Ag₂CO₃ led to recovery of starting material **2-NTs** along with traces of **3-NTs** (Entry 3). The best result was obtained employing

[Pd(PPh₃)₄], K₂CO₃ and NBu₄Br 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, K₂CO₃ was the best base for this transformation (Entry 5), while the employment of Cs₂CO₃ or DABCO as bases led to complex mixtures (Entries 6 and 11). The catalytic system involving [Pd₂dba₃] and TFP (tris-2-furylphosphane) was also active (Entry 8), but in this case the addition of NBu₄Br led to decomposition products (Entry 10). However, NBu₄Br together with [Pd(PPh₃)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).

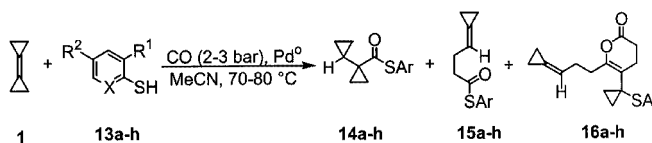
It is believed that both **3** and **4** arise via a tetramolecular queuing cascade^[7] involving a common intermediate **9**, which is derived from **2** via a sequence of elementary steps (Scheme 2). Two of these steps are carbonylations involving an aryl- (**5**) and an alkyl- (**8**) palladium intermediate. 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 bicyclopopylidene (**1**) reacts with various thiophenols



Scheme 2. Proposed mechanism of the tetramolecular queuing cascade involving bicyclopropylylidene (**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 bicyclopropylylidene (**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 [Pd₂dba₃]/TFP and with [Pd(PPh₃)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]

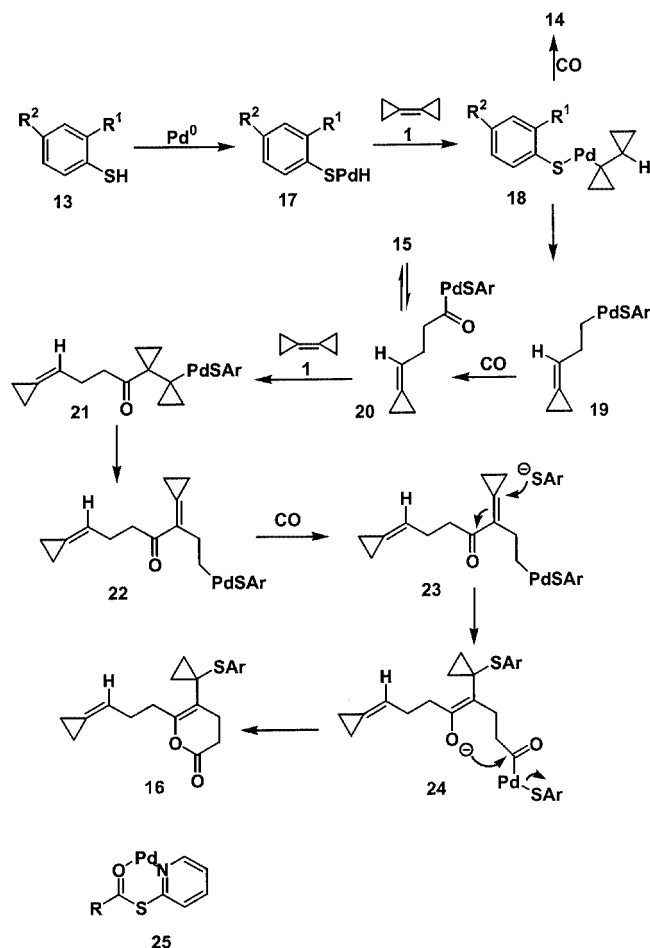
Possible mechanisms for the formation of **14–16** are shown in Scheme 4. Pd⁰ inserts oxidatively into the S–H bond to afford **17**, which adds to the very reactive electron rich C=C double bond of **1** to afford **18**. The palladium atom in intermediate **18** may be coordinated to the *ortho*-bromine or chlorine atoms (R¹ = 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 R¹ = H and R² = 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 Pd⁰ 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 bicyclopropylylidene (**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]	<i>t</i> [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>i</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

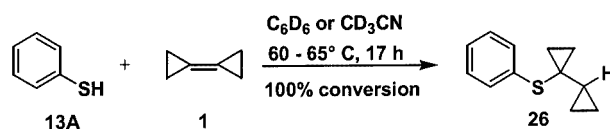
^[a] Conditions: 2.00 equiv. **1**, 1.00 equiv. **13a–h**, 2.00 equiv. K₂CO₃, 4 mol % [Pd(PPh₃)₄], CO (2–3 bar), MeCN, 70–80 °C. ^[b] pK_a values calculated using the software provided by ACD/I-Lab Web service (ACD/pK_a 5.0). ^[c] Ratio of **14:15** determined by ¹H NMR analysis of the crude product. ^[d] Performed without K₂CO₃ 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(PPh₃)₄]. ^[i] 2 mol % [Pd₂dba₃], 8 mol % TFP. ^[j] 2 mol % [Pd₂dba₃], 8 mol % P(*o*-tolyl)₃. ^[k] A significant amount of **14h** was observed in the ¹H NMR spectrum of the crude product.



Scheme 4. Mechanism of the five-component queuing cascade

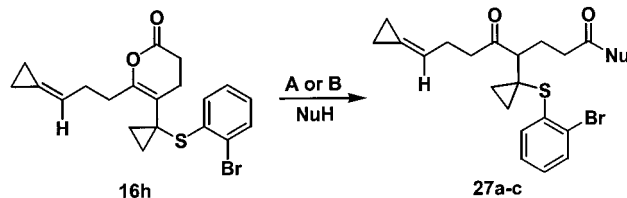
reactions described above (Scheme 3 and Table 2). However, in the reactions reported in this paper acetonitrile was the solvent. Therefore, the possible influence of the solvent was investigated.

Thiophenol (**13a**) reacted readily with **1** both in C₆D₆, as published,^[12] and in CD₃CN 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 CH₃CN in the presence of K₂CO₃, CO and a Pd catalyst only traces of **26** were detected, whilst in the absence of K₂CO₃ **26** was isolated in 20% yield indicating that both the Pd catalyst and K₂CO₃ 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 = H₂O, 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 bicyclopentyl 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: ^1H and ^{13}C NMR spectra were recorded at 300 or 500 MHz (^1H) 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 F₂₅₄) 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 Bicyclopentylidene (1) with Aryl Iodides or Thiols: K_2CO_3 (276 mg, 2.00 mmol), $[\text{Pd}(\text{PPh}_3)_4]$ (46.2 mg, 40.0 μmol), anhydrous MeCN (10 mL), bicyclopentylidene (1) (188 μL , 2.00 mmol, $d = 0.854 \text{ g/mL}$) 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 bicyclopentylidene (1) (188 μL , 2.00 mmol, $d = 0.854 \text{ g/mL}$), NBu_4Br (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 $\text{Et}_2\text{O}/\text{EtOAc}$ (1:1 v/v). ^1H NMR: $\delta = 0.91$ – 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, $J = 8.4 \text{ Hz}$, 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, $J = 8.4 \text{ Hz}$, 2 H, Ar-H)

ppm. ^{13}C NMR: $\delta = 18.1$ (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): $\tilde{\nu}_{\text{max}} = 1715$, 1593 , 1464 , 1343 , 1300 , 1210 , 1123 , 1071 , 1019 , 995 , 818 , 762 , 681 cm^{-1} . MS (ESI): m/z (%) = 404 (100) [$\text{M} + \text{Na}^+$], 333 (96) [$2 \times \text{C}_7\text{H}_7\text{SO}_2 + \text{Na}^+$]. MS (EI): m/z (%) = 381 (8) [M^+], 227/226 (16/100) [$\text{M}^+ - \text{C}_7\text{H}_7\text{SO}_2$], 198 (15), 184 (9), 183 (13), 155 (6) [$\text{C}_7\text{H}_7\text{SO}_2^+$]. $\text{C}_{21}\text{H}_{19}\text{NO}_4\text{S}$ (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-2H,5H-pyrano[3,2-c]chromen-2-one (4-O): Prepared over 15 h from bicyclopentylidene (1) (188 μL , 2.00 mmol, $d = 0.854 \text{ g/mL}$) and *ortho*-iodophenol (2-O) (220 mg, 1.00 mmol) according to the GP. After column chromatography (hexane/ Et_2O 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. ^1H NMR: $\delta = 0.83$ – 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: $\delta = 14.6$ (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): $\tilde{\nu}_{\text{max}} = 1732$, 1703 , 1617 , 1483 , 1092 , 893 , 754 cm^{-1} . MS (ESI): m/z (%) = 251 (100) [$\text{M} + \text{Na}^+$], 229 (8) [$\text{M} + \text{H}^+$]. MS (EI): m/z (%) = 228 (48) [M^+], 200 (100) [$\text{M}^+ - \text{CO}$], 185 (26), 172 (38), 121 (39). $\text{C}_{14}\text{H}_{12}\text{O}_3$ (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. ^1H NMR: $\delta = 0.86$, 1.19 (2 m, AA'BB', 4 H, cy-Pr), 2.20 , 2.76 (2 t, $J = 7.6 \text{ Hz}$, 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: $\delta = 12.3$ (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): $\tilde{\nu}_{\text{max}} = 1763$, 1489 , 1387 , 1253 , 1192 , 1169 , 1143 , 1103 , 766 cm^{-1} . MS (FAB): m/z (%) = 245 (7) [$\text{M} + \text{Na}^+$], 229 (50) [$\text{M} + \text{H}^+$], 228 (100) [M^+], 227 (38), 200 (74) [$\text{M}^+ - \text{CO}$], 199 (28), 185 (33), 147 (21). $\text{C}_{14}\text{H}_{12}\text{O}_3$ (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 bicyclopentylidene (1) (188 μL , 2.00 mmol, $d = 0.854 \text{ g/mL}$) and thiophenol (13a) (102 μL , $d = 1.075 \text{ g/mL}$, 1.00 mmol) according to the GP. After column chromatography (hexane/ Et_2O 20:1) a 1:1.6 mixture of 14a/15a (156 mg, 71%) was obtained as a colourless oil; $R_f = 0.20$.

14a: ^1H NMR: $\delta = 0.25$, 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: $\delta = 4.76$ (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: ^1H NMR: $\delta = 1.04$ – 1.05 (m, 4 H, cy-Pr), 2.58 (virt. q, $J = 7.2 \text{ Hz}$, 2 H, CH_2), 2.83 (t, $J = 7.2 \text{ Hz}$, 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: $\delta = 2.6$ (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) [$\text{M}^+ - \text{C}_6\text{H}_5\text{S}$], 81 (76) [$\text{M}^+ - \text{C}_6\text{H}_5\text{S} - \text{CO}$], 79 (41), 65 (34), 53 (39). $\text{C}_{13}\text{H}_{14}\text{OS}$ (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 μ L, 2.00 mmol, $d = 0.854$ g/ml) and *ortho*-methoxythiophenol (**13b**) (122 μ L, $d = 1.152$ g/ml, 1.00 mmol). After column chromatography (hexane/Et₂O 2:1) a 3.6:1 mixture of **14b/15b** (171 mg, 69%) was obtained as a pale yellow oil.

14b: $R_f = 0.35$. ¹H NMR: $\delta = 0.26, 0.66$ (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, CH₃), 6.93–7.00 (m, 2 H, Ar-H), 7.36–7.41 (m, 2 H, Ar-H) ppm. ¹³C NMR: $\delta = 4.74$ (2 C, CH₂), 11.50 (CH), 16.06 (2 C, CH₂), 33.85 (C), 56.43 (CH₃), 111.91 (CH), 117.10 (C), 121.43, 131.76, 137.51 (CH), 159.94, 200.33 (C) ppm.

15b: $R_f = 0.41$. ¹H NMR: $\delta = 1.04$ –1.05 (m, 4 H, cy-Pr), 2.58 (virt. q, $J = 7.5$ Hz, 2 H, CH₂), 2.84 (t, $J = 7.5$ Hz, 2 H, CH₂), 3.84 (s, 3 H, CH₃), 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. ¹³C NMR: $\delta = 2.5$ (2 C, CH₂, cy-Pr), 28.1, 43.3 (CH₂), 56.4 (CH₃), 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⁺ – C₇H₇OS], 81 (50) [M⁺ – C₇H₇OS – CO]. C₁₄H₁₆O₂S (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 μ L, 2.00 mmol, $d = 0.854$ g/ml) and *ortho*-isopropylthiophenol (**13c**) (152 μ L, $d = 1.005$ g/ml, 1.00 mmol, tech. 90%). After column chromatography (hexane/Et₂O 10:1) a 1:2 mixture of **14c/15c** (157 mg, 67% based on tech. **13c**) was obtained as a pale yellow oil.

14c: $R_f = 0.39$. ¹H NMR: $\delta = 0.25, 0.67$ (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 CH₃), 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. ¹³C NMR: $\delta = 4.8$ (2 C, CH₂), 11.6 (CH, cy-Pr), 16.0 (2 C, CH₂), 24.0 (2 C, CH₃), 31.5 (CH), 33.9 (C), 126.5, 126.7, 130.6, 137.2 (CH), 152.5, 201.2 (C) ppm.

15c: $R_f = 0.43$. ¹H NMR: $\delta = 1.05$ (virt. s, 4 H, cy-Pr), 1.19 (d, $J = 6.9$ Hz, 6 H, 2 CH₃), 2.59 (virt. q, $J = 7.0$ Hz, 2 H, CH₂), 2.84 (t, $J = 7.0$ Hz, 2 H, CH₂), 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. ¹³C NMR: $\delta = 2.5, 2.6$ (CH₂, cy-Pr), 24.0 (2 C, CH₃), 28.3 (CH₂), 31.5 (CH), 43.6 (CH₂), 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⁺ – C₉H₁₁S], 81 (76) [M⁺ – C₉H₁₁S – CO]. C₁₆H₂₀OS (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 K₂CO₃) from bicyclopropylidene (**1**) (188 μ L, 2.00 mmol, $d = 0.854$ g/ml) and 2-mercaptopyridine (**13d**) (111 mg, 1.00 mmol). After column chromatography (Et₂O/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. ¹H NMR: $\delta = 0.27, 0.69$ (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. ¹³C NMR: $\delta = 4.9$ (2 C, CH₂), 11.2 (CH), 16.6 (2 C, CH₂), 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⁺]. C₁₂H₁₃NOS (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-2H-pyran-2-one (16e): Prepared over 48 h by the GP from bicyclopropylidene (**1**) (188 μ L, 2.00 mmol, $d = 0.854$ g/ml) and *ortho*-fluorothiophenol (**13e**) (107 μ L, $d = 1.203$ g/ml, 1.00 mmol). After column chromatography (hexane/Et₂O 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. ¹H NMR: $\delta = 0.96$ (virt. s, 6 H, cy-Pr), 1.25–1.31 (m, 2 H, cy-Pr), 1.90–1.95 (m, 2 H, CH₂), 2.00–2.07 (m, 2 H, CH₂), 2.42–2.46 (m, 2 H, CH₂), 2.52–2.57 (m, 2 H, CH₂), 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. ¹³C NMR: $\delta = 2.0$ (2 CH₂, cy-Pr), 16.6 (2 C, CH₂, cy-Pr), 22.9, 28.3, 28.6, 28.8 (CH₂), 29.9 (C, cy-Pr), 113.8 (C), 116.1 (d, ² $J_{C,F} = 24.2$ Hz, CH), 116.5 (CH), 120.3 (d, ² $J_{C,F} = 19.6$ Hz, C), 121.9 (C), 124.6 (d, ³ $J_{C,F} = 3.8$ Hz, CH), 131.6 (d, ³ $J_{C,F} = 7.5$ Hz, CH), 138.3 (CH), 152.1 (C), 163.6 (d, ¹ $J_{C,F} = 246.8$ 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⁺]. C₂₀H₂₁FO₂S (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-2H-pyran-2-one (16f): Prepared over 48 h by the GP from bicyclopropylidene (**1**) (188 μ L, 2.00 mmol, $d = 0.854$ g/ml) and *ortho*-chlorothiophenol (**13f**) (113 μ L, $d = 1.277$ g/ml, 1.00 mmol). After column chromatography (hexane/Et₂O 3:2) **16f** (180 mg, 50%) was obtained as a colourless oil; $R_f = 0.28$. ¹H NMR: $\delta = 0.97$ (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 CH₂), 2.43–2.49 (m, 2 H, CH₂), 2.52–2.58 (m, 2 H, CH₂), 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. ¹³C NMR: $\delta = 2.0, 2.0$ (CH₂, cy-Pr), 16.6 (2 C, CH₂, cy-Pr), 23.1, 28.3, 28.8, 28.9 (CH₂), 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⁺]. C₂₀H₂₁ClO₂S (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-2H-pyran-2-one (16g): Prepared over 44 h by the GP from bicyclopropylidene (**1**) (188 μ L, 2.00 mmol, $d = 0.854$ g/ml), [Pd(PPh₃)₄] (92.4 mg, 80.0 μ mol) and *para*-chlorothiophenol (**13g**) (145 mg, 1.00 mmol). After column chromatography (gradient hexane/Et₂O 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/Et₂O 9:1; R_f (**16g**) = 0.32 hexane/Et₂O 2:1.

14g: ¹H NMR: $\delta = 0.25, 0.67$ (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. ¹³C NMR: $\delta = 4.8$ (2 C, CH₂), 11.3 (CH), 16.5 (2 C, CH₂), 33.9, 127.56 (C), 129.7 (2 CH), 135.9 (C), 136.5 (2 CH), 200.9 (C) ppm.

15g: ¹H NMR: $\delta = 1.04$ –1.05 (m, 4 H, cy-Pr), 2.57 (virt. q, $J = 7.6$ Hz, 2 H, CH₂), 2.83 (t, $J = 7.6$ Hz, 2 H, CH₂), 5.75–5.81 (m, 1 H, =CH), 7.28–7.40 (m, 4 H, Ar-H) ppm. ¹³C NMR: $\delta = 2.6, 2.6$ (CH₂, cy-Pr), 28.1 (CH₂), 43.6 (CH₂), 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: 1H 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, CH₂), 2.08–2.16 (m, 2 H, CH₂), 2.35–2.43 (m, 2 H, CH₂), 2.46–2.54 (m, 2 H, CH₂), 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 CH₂, cy-Pr), 16.6 (2 C, CH₂, cy-Pr), 23.2, 28.4, 28.88, 28.93 (CH₂), 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) $[2 \times M + Na^+]$, 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-(2-Bromophenyl)thio]cyclopropyl}-6-(3-cyclopropylidene-propyl)-3,4-dihydro-2H-pyran-2-one (16h): Prepared over 48 h by the GP from bicyclopropylidene (**1**) (188 μ L, 2.00 mmol, d = 0.854 g/ml) and *ortho*-bromothiophenol (**13g**) (118 μ L, d = 1.604 g/ml, 1.00 mmol). After column chromatography (hexane/Et₂O 2:1) **16h** (223 mg, 55%) was obtained as a colourless oil; R_f = 0.29. 1H 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 CH₂), 2.45–2.49 (m, 2 H, CH₂), 2.53–2.57 (m, 2 H, CH₂), 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 (CH₂, cy-Pr), 16.7 (2 C, CH₂, cy-Pr), 23.3, 28.4, 28.9, 29.1 (CH₂), 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-(2-bromophenyl)thio]cyclopropyl}-8-cyclopropylidene-5-oxooctanamide (27a): A solution of **16h** (52.0 mg, 128 μ mol) and benzylamine (28.0 μ L, d = 0.981 g/ml, 256 μ mol) 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 (Et₂O) to give **27a** (54.0 mg, 82%) as a colourless oil; R_f = 0.34. 1H 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, NCH₂), 4.38 (dd, J = 8.8, 3.4 Hz, 1 H, NCH₂), 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 (CH₂, cy-Pr), 25.5, 25.7 (CH₂), 26.5 (C, cy-Pr), 34.2, 43.5, 43.6 (CH₂), 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-(2-Bromophenyl)thio]cyclopropyl}-8-cyclopropylidene-5-oxo-N-phenyloctanohydrazide (27b): A solution of **16h** (91.0 mg, 225 μ mol) and phenylhydrazine (66.0 μ L, d = 1.099 g/ml, 675 μ mol) 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 (Et₂O) to give **27b** (91.0 mg, 79%) as a pale yellow oil, which comprised a 2:1 rotamer mixture; R_f = 0.30. 1H 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 (CH₂, cy-Pr), 25.5, 25.57 (CH₂), 26.7 (C, cy-Pr), 31.9, 43.4 (CH₂), 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 (CH₂, cy-Pr), 24.6, 25.5 (CH₂), 26.5 (C, cy-Pr), 30.3, 43.5 (CH₂), 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-(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 (Et₂O/hexane 3:1) to afford **27c** as a colourless oil; R_f = 0.32. 1H 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, CO₂ H) ppm. ^{13}C NMR: δ = 2.0, 2.1, 13.4, 14.3 (CH₂, cy-Pr), 24.6, 25.5 (CH₂), 26.5 (C, cy-Pr), 31.8, 43.9 (CH₂), 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 Et₂O/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 × 0.42 × 0.31 mm size). The structure was solved by direct methods (SHELXS-97) and refined by full-matrix least-squares on F² (SHELXL-97). All non-hydrogen atoms were refined anisotropically and all hydrogen atoms were located on the difference Fourier maps and refined isotropically. C₂₁H₁₉NO₄S (381.43), monoclinic, *a* = 7.27750(10), *b* = 8.17050(10), *c* = 15.6703(3) Å, β = 102.5370(6)°, *V* = 909.55(2) Å³, *Z* = 2, space group *P*2₁, *T* = 100(2) K, ρ = 1.393 g cm⁻³, *F*(000) = 400, μ = 0.206 mm⁻¹, intensities measured: 15935 (2.87° ≤ θ ≤ 25.99°), independent reflections: 3486 (*R*_{int} = 0.0455), observed reflections: 3451 [*I* > 2σ(*I*)], *R*₁ = 0.0306, *wR*₂ {final [*I* > 2σ(*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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