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Synthesis of *N*-aryl and -heteroaryl γ -, δ - and ϵ -lactams using Deprotometalation-iodination and *N*-arylation, and Properties Thereof

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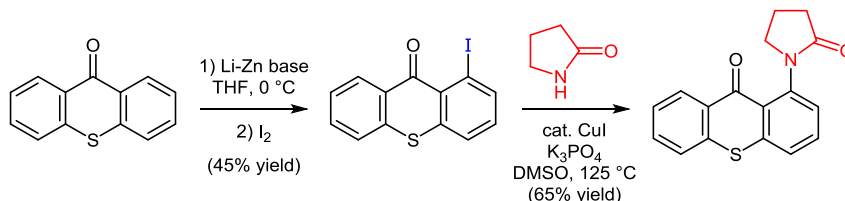
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Abstract Xanthone, thioxanthone, fluorenone, benzophenone, 2-benzoylpyridine, dibenzofuran and dibenzothiophene were deprotonated using a base prepared *in situ* from MCl_2 -TMEDA ($\text{M} = \text{Zn}$ or Cd ; TMEDA = *N,N,N',N'*-tetramethylethylenediamine) and lithium 2,2,6,6-tetramethylpiperidide in a 1:3 ratio, as demonstrated by subsequent iodolysis. The different aryl halides were involved as partners in the *N*-arylation of 2-pyrrolidinone. In the presence of copper(I) iodide and tripotassium phosphate, and using dimethylsulfoxide as solvent, the reactions could be performed in yields ranging from 40 to 70%. Most of the products were tested for their antimicrobial, antifungal, antioxidant and cytotoxic (MCF-7) activity.

Key words C-N bond formation, deprotonative metalation, lactam, aromatic compound, antimicrobial and antifungal activity

Due to their presence in molecules of biological importance or in organic materials for various applications, aromatic compounds and notably heterocycles are essential, as well as the development of methods to functionalize them.

To regioselectively introduce substituents, deprotometalation has imposed itself as a powerful tool.² If alkylolithiums and hindered lithium dialkylamides have been largely employed, alternative approaches using lithium-metal combinations based on 2,2,6,6-tetramethylpiperidide (TMP) have recently emerged for performing reactions with sensitive substrates.³ The 1:1 mixture of the homometallic amides LiTMP and Zn(TMP)_2 , generated from LiTMP and ZnCl_2 -TMEDA

(TMEDA = *N,N,N',N'*-tetramethylethylenediamine) in a 3:1 ratio, falls into this category.⁴ With LiTMP -mediated deprotonation and *in situ* Zn(TMP)_2 -induced transmetalation, this 'trans-metal trapping'⁵ approach ensures both chemoselective and high-yielding reactions.⁶

Whereas secondary carboxamides are hardly compatible with the conditions required for their palladium-catalyzed *N*-arylation and *N*-heteroarylation (Goldberg reaction),⁷ the corresponding copper-catalyzed reactions have benefited from the development of catalyst-base systems.⁸ Copper(I) iodide is often used in the presence of a diamine (e.g. *trans*-1,2-cyclohexanediamines or other 1,2-ethylenediamines, either *N*-alkylated or not) as ligand, and in combination with either a base (K_3PO_4 , K_2CO_3 or Cs_2CO_3) or CsF .^{7,9} Ligand-free catalysis is also possible at moderate reaction temperatures provided that DMSO (DMSO = dimethylsulfoxide) is used as solvent.¹⁰

We here describe the use of the lithium-zinc combination developed in the group to access aromatic iodides, as well as their conversion to *N*-arylated amides based on 2-pyrrolidinones, -piperidinones and -hexahydroazepinones. The antimicrobial, antifungal, antioxidant and cytotoxic activities of some of the prepared compounds were evaluated.

Synthesis

To subsequently access new *N*-aryl and -heteroaryl lactams, we first involved xanthone (**1a**), thioxanthone (**2a**), fluorenone (**3a**), benzophenone (**4a**) and 2-benzoylpyridine (**5a**) in the reaction using mixed lithium-metal bases before

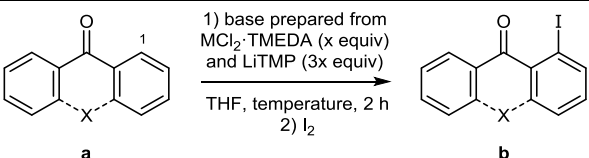
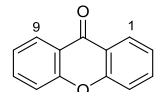
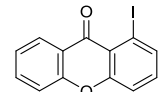
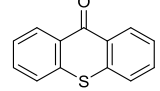
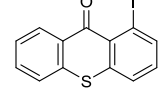
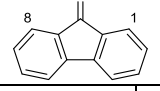
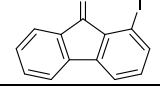
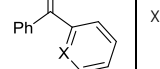
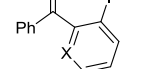
interception with iodine (Table 1). Achieving the deprotometalation of such aromatic ketones represents a challenge due to their low compatibility toward lithium species.¹¹ Indeed, the method has so far been restricted to a few carbonyl-containing five-membered¹² and six-membered¹³ aromatic compounds.

First, xanthone (**1a**) was reacted with the 1:1 mixture of LiTMP and Zn(TMP)₂ amides obtained by mixing ZnCl₂·TMEDA (0.5 equiv) and LiTMP (1.5 equiv).^{4a} Conducting the reaction in tetrahydrofuran (THF) at 0 °C for 2 h provided, after interception with iodine, the 1-iodo derivative **1b** in 43% yield; a small amount (5% yield) of 1,9-diiodoxanthone (**1b'**) was also isolated (entry 1) and identified unambiguously (Figure

1). Increasing either the amount of base to 1 equiv of ZnCl₂·TMEDA and 3 equiv of LiTMP, or the reaction temperature to 20–25 °C, led to extended degradation due to the high reactivity of the ketone. In addition, replacing ZnCl₂·TMEDA (0.5 equiv) by CdCl₂·TMEDA^{3d} (0.5 equiv) in the preparation of the base did not improve this result since a complex mixture was obtained.

Starting from thioxanthone (**2a**), a similar behavior was observed; using the 1:1 mixture of amides LiTMP and Zn(TMP)₂, this time obtained by mixing ZnCl₂·TMEDA (1 equiv) and LiTMP (3 equiv), furnished the 1-iodo derivative **2b** in 45% yield (entry 2, Figure 1).

Table 1 Deprotometalation-iodination of the ketones **1a–5a**

					
Entry	Ketone	M, x	Temperature	Iodoketone	Product, Yield (%) ^a
1	1a 	Zn, 0.5	0 °C		1b , 43 ^b
2	2a 	Zn, 1	0 °C		2b , 45
3	3a 	Zn, 0.5	rt		3b , ^c
4		Cd, 0.5			3b , 80
5	4a 	X = CH	rt		4b , 66 ^d
6		X = N Zn, 0.5 or 1	rt		5b , ^e

^a After purification by column chromatography. ^b 1,9-Diiodoxanthone (**1b'**) was also isolated in 5% yield. ^c The hydroxyketone **3b'** was obtained instead in 63% yield (see Scheme 1). ^d Using a protocol previously reported.¹³ ^e Complex mixtures were obtained under these conditions, and the ketone **5b** was prepared as described recently.¹⁴

In the case of fluorenone (**3a**), treatment by the base prepared from ZnCl₂·TMEDA (0.5 equiv) and LiTMP (1.5 equiv) in THF at room temperature for 2 h did not give any iodide; instead, the hydroxyketone **3b'** was isolated in 63% yield (entry 3). Even if we did not observe the expected iodide **3b**, this result is of interest because it confirms that an aryllithium is first formed by reaction using this basic mixture (Scheme 1).⁴ Indeed, trapping by the keto group would have been much more sluggish had an arylzinc (or zincate) been formed.^{6c} By decreasing the reaction temperature to 0 °C, a complex mixture was noticed.

To obtain the 1-iodo derivative **3b**, we efficiently turned to the corresponding lithium-cadmium base generated from CdCl₂·TMEDA (0.5 equiv) and LiTMP (1.5 equiv). After 2 h contact with **3a** in THF at room temperature and subsequent quenching with iodine, **3b** was this time obtained in 80% yield (Table 1, entry 4, Figure 1). This result (no detection of the hydroxyketone **3b'**) suggests a lithium cadmate-mediated deprotonation.^{3d,13,15} Otherwise, if deprotolithiation followed by transmetalation (Scheme 1) would rather happen as proposed,¹⁶ the latter could be considered as being quicker with cadmium compared with zinc. Unfortunately, due to the lack of studies concerning compared kinetics/mechanisms of

both lithium/zinc and lithium/cadmium transmetalations,¹⁷ it is not possible to come to a conclusion. Nevertheless, the superiority of the lithium-cadmium base over the lithium-zinc one to solve chemoselectivity issues is a general trend, and was for example used to convert benzophenone (**4a**) into the iodide **4b** (entry 5).¹³

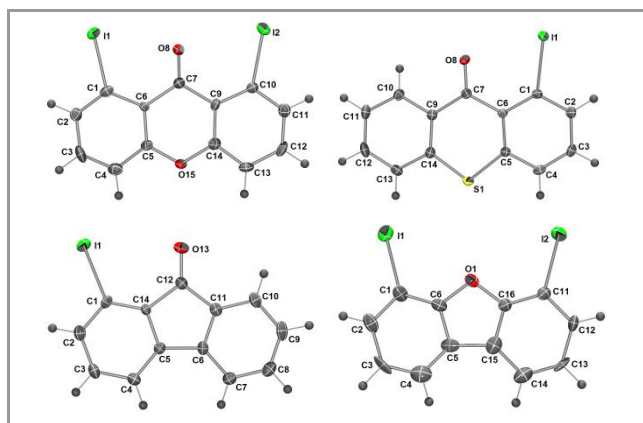
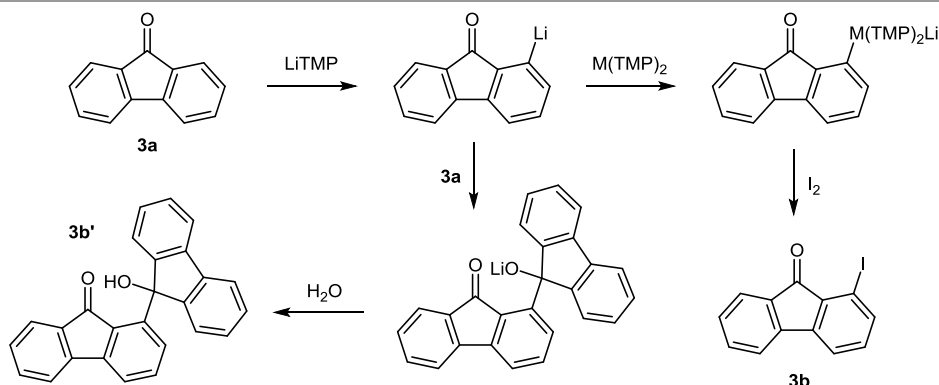


Figure 1 ORTEP diagrams (50% probability) of the compounds **1b'**, **2b**, **3b** and **6b'**

Scheme 1 Deprotometalation of fluorenone (**3a**)

Our attempts to use the lithium-zinc base as before from 2-benzoylpyridine (**5a**) failed (entry 6). In a recent communication,¹⁴ we showed it is possible to achieve its conversion to the 3-iodo derivative **5b** by using LiTMP in the presence of ZnCl₂·TMEDA, and used this protocol. These results suggest that the zinc chelate is a more efficient *in situ* trap than Zn(TMP)₂ to transmetalate the generated aryllithium.

We next turn to deprotometalation-iodolysis sequences starting from dibenzofuran (**6a**) and dibenzothiophene (**7a**) in order to generate either monoiodides or diiodides (Table 2). We chose the 1:1 mixture of amides LiTMP and Zn(TMP)₂ obtained by mixing ZnCl₂·TMEDA (*x* equiv) and LiTMP (3*x* equiv) because it has been efficiently used to either monofunctionalize or difunctionalize depending on the amount of base.^{6d,6e,18}

Dibenzofuran (**6a**) can be either mono-¹⁹ or dideprotonated²⁰ by using butyllithium, in the presence or not of TMEDA, at temperatures ranging from -75 °C to 60 °C. Using the base prepared from ZnCl₂·TMEDA (*x* equiv) and LiTMP (3*x* equiv) also led, at room temperature, to either the monometalated (*x* = 0.5) or the dimetalated (*x* = 1) derivatives in good yields, as evidenced by subsequent iodolysis (entries 1 and 2, Figure 1). Dibenzothiophene (**7a**) can be similarly mono-^{19d,21} or dideprotonated^{21c,22} using butyllithium. Surprisingly, whereas it was found possible to achieve its monometalation using the lithium-zinc base, an efficient dimetalation proved impossible under the conditions tried (entries 3-5).

Table 2 Deprotometalation-iodination of the substrates **6a** and **7a**

Entry	Substrate	<i>x</i>	Iodide/diiodide	Product, Yield (%) ^a	
1	6a 	0.5		6b , 90 ^b	
2	6a 	1		6b' , 79	
3	7a 	0.5		7b , 47 ^c	
4		1		7b , 66 ^c	
5		1.5		7b , 85	

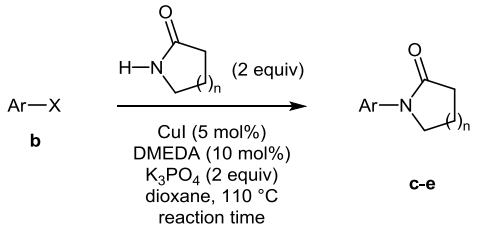

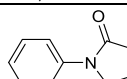

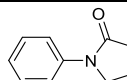

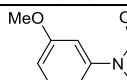

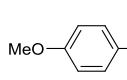

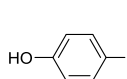

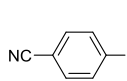

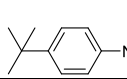

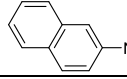

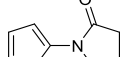

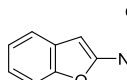

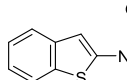

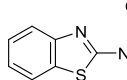
^a After purification by column chromatography. ^b 4,6-Diiododibenzofuran (**6b'**) was also identified in the crude. ^c The rest was starting material.

These iodides in hands, we considered their conversion to *N*-arylated amides. In search of an efficient method to achieve the C-N bond formation, we evaluated a protocol^{9a,9c,9d} using copper(I) iodide (5 mol%) as transition metal source, DMEDA (10 mol%) as ligand (DMEDA = *N,N'*-dimethylethylenediamine), K₃PO₄ (2 equiv) as base and dioxane as solvent at 110 °C on different aryl halides (Table 3, Figure 2).

The method works well with phenyl iodides provided that it is not substituted by a strong electron-donating group (entries 1-7). From phenyl bromides, these conditions are

more suitable in the presence of electron-withdrawing substituents compared with electron-donating (entries 8 and 9). Whereas a moderate yield is noticed from 2-iodonaphthalene (**15b**, entry 10), both 2-iodo- and 2-bromothiophene (**16b** and **16b'**, entries 11 and 12) are converted efficiently. This encouraged us to involve in the reaction iodinated benzoxazoles prepared by deprotometalation-iodolysis (entries 13-21).²³ The reactions proceed in correct to high yields from 2-iodobenzofuran and -thiophene (**17b** and **18b**) whereas 2-iodobenzothiazole (**19b**) is converted less efficiently.

Table 3 *N*-arylation of 2-pyrrolidinone, 2-piperidinone and hexahydro-2-azepinone with different aryl halides

					
Entry	Ar-X	Time	<i>N</i> -aryl amide	Product, Yield (%) ^a	
1	8b 	24 h		8c , 95	
2	9b 	24 h		9c , 99	
3	10b 	24 h		10c , 99	
4	11b 	24 h		<i>n</i> = 1	11c , 85
5		24 h		<i>n</i> = 2	11d , 73
6		24 h		<i>n</i> = 3	11e , 99
7	12b 	48 h		12c , 26 ^b , 20 ^c , 29 ^d	
8	13b' 	24 h		13c , 89	
9	14b' 	48 h		14c , 30	
10	15b 	72 h		15c , 45	
11	16b 	24 h		16c , 93	
12				16c , 99	
13	17b 	48 h		<i>n</i> = 1	17c , 84
14		48 h		<i>n</i> = 2	17d , 93
15		24 h		<i>n</i> = 3	17e , 65
16	18b 	48 h		<i>n</i> = 1	18c , 88
17				<i>n</i> = 2	18d , 81
18				<i>n</i> = 3	18e , 53
19	19b 	24 h		<i>n</i> = 1	19c , 66
20		48 h		<i>n</i> = 2	19d , 15
21		48 h		<i>n</i> = 3	19e , 50

^a After purification by column chromatography. ^b A similar result was obtained by using 3 equiv of K₃PO₄ (reaction time: 72 h). ^c Using DMSO instead of dioxane (48 h at 125 °C).

^d Using 10 mol% of CuI and DMSO instead of dioxane (48 h at 125 °C).

Inspired by the study published by Güell and Ribas in 2014,¹⁰ and in keeping with works recently developed in our group on azole *N*-arylation,²⁴ we next compared the previous protocol with a ligand-free one using DMSO as solvent. For this purpose, we employed 1-iodo-9-thioxanthone (**2b**) as substrate in the reaction with 2-pyrrolidinone, and demonstrated the superiority of the second protocol to arylate the lactam (Table 4).

These optimized conditions in hand, we first involved in the reaction the different aryl iodides **b** synthesized by

deprotometalation-iodolysis. The expected *N*-functionalized lactams were obtained in yields ranging from 40 to 70% (Table 5, Figure 3).

Unfortunately, the double C-N bond formation performed on the aryl diiodide **6b'** proved less obvious (Scheme 2, Figure 3). Double functionalization did not take place at all, the monoamides either deiodinated (**6c**, 55% yield) or not (**6c'**, detected) being the only reaction products. Reacting **6c'** under the same reaction conditions also failed, only leading to loss of iodine.

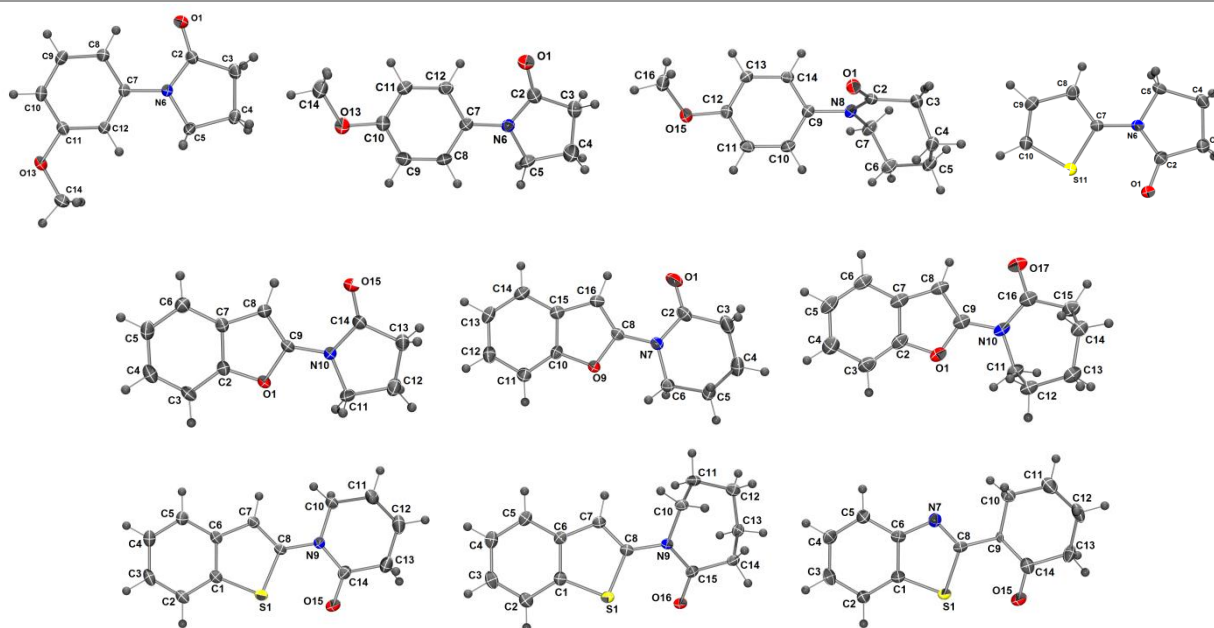


Figure 2 ORTEP diagrams (50% probability) of the compounds **10c**, **11c**, **11e**, **16c**, **17c-e**, **18d,e** and **19d**

Table 4 Comparison of both protocols for the *N*-arylation of 2-pyrrolidinone with 1-iodo-9-thioxanthone (**2b**)

Entry	x mol% CuI	y mol% DMEDA	Solvent	Temperature	Time	Yield (%) ^a
1	5	10	dioxane	110 °C	24 h	10
2	5	10	dioxane	110 °C	72 h	32
3	5	-	DMSO	125 °C	24 h	62
4	10	-	DMSO	125 °C	24 h	65

^a After purification by column chromatography.

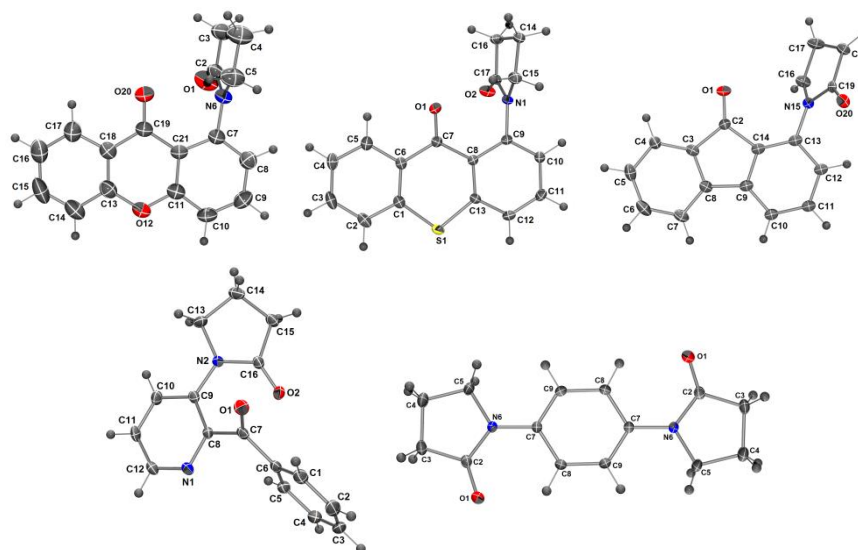
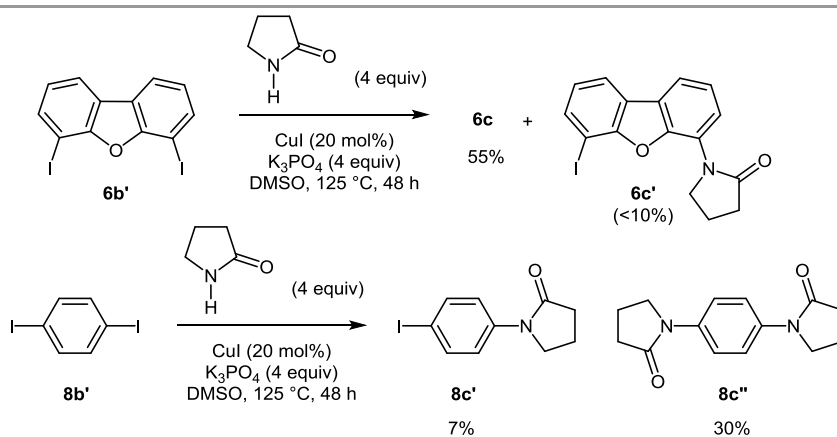


Figure 3 ORTEP diagrams (50% probability) of the compounds **1c**, **2c**, **3c**, **5c** and **8c'**

Table 5 *N*-arylation of 2-pyrrolidinone with different aryl monoiodides

Entry	Ar-I	Time	<i>N</i> -aryl amide	Product, Yield (%) ^a	
1	1b 	24 h		1c , 70	
2	3b 	24 h		3c , 62	
3	4b 	24 h		X = H	4c , 56
4		72 h		X = N	5c , 40
5	6b 	48 h		6c , 50	
6	7b 	48 h		7c , 54	

^a After purification by column chromatography.**Scheme 2** C-N bond formation from diiodides

This disappointing result led us to consider a more common substrate, 1,4-diiodobenzene (**8b'**), to attempt the same reaction. Even if more successful, the expected diamide **8c''** was isolated in a moderate 30% yield together with the iodinated amide **8c'** (7% yield). As already noticed for 4-iodophenol (**12b**) in Table 3 using similar conditions (entry 7, notes *c* and *d*), these results show that an electron-donating group (here, the introduced amide) tends to inhibit the reaction.

Biological evaluation

Because many pharmaceuticals are pyrrolidinone derivatives, e.g. cotinine (used to treat depression, Alzheimer's disease, post-traumatic stress disorder and schizophrenia),²⁵ doxapram (a respiratory stimulant)²⁶ and piracetam (a cyclic derivative of γ -aminobutyric acid mainly used to treat myoclonus),²⁷ some of the synthesized compounds were evaluated for their biological properties.

The compounds **1c**, **2c**, **3c**, **4c**, **5c**, **6c**, **7c**, **8c**, **8c''**, **10c**, **11c-e**, **13c**, **15c**, **16c**, **17c-e**, **18c-e** and **19-e** were screened for their antimicrobial activity against bacteria and for their antifungal

activity. An effect on the microbial growth of strains of bacteria was only noticed in the case of **4c**, **6c**, **7c** and **8c''**. 1-(2-Benzoylphenyl)-2-pyrrolidinone (**4c**) has no significant inhibition effect on *L. monocytogenes*; it inhibits *E. coli*, *P. aeruginosa* and *C. dubliniensis* at the same power while it strongly inhibits *S. aureus* and *E. faecium* compared to the

positive control. 1-(4-Dibenzofuryl)-2-pyrrolidinone (**6c**) inhibits *S. aureus*, but above all *C. albicans*. The behavior of 1-(4-dibenzothienyl)-2-piperidinone (**7c**) and 1,1'-(1,4-phenylene)bis-2-pyrrolidinone (**8c''**) is even more interesting since both selectively inhibit *C. albicans* with a strength comparable to that of nystatin (Table 6).

Table 6 Antimicrobial and antifungal activity of the compounds **4c**, **6c**, **7c** and **8c''**^a

Compound	Amount (μg) dissolved in DMSO	<i>Escherichia coli</i>	<i>Pseudomonas aeruginosa</i>	<i>Staphylococcus aureus</i>	<i>Enterococcus faecium</i>	<i>Listeria monocytogenes</i>	<i>Candida dubliniensis</i>	<i>Candida albicans</i>
4c ^b	500	8	8	10	9	±	8	-
6c ^c	150	0	0	4	0	0	-	14
7c ^c	150	0	0	0	0	0	-	14
8c'' ^c	150	0	0	0	0	0	-	15
DMSO	-	0	0	0	0	0	0	0
Reference compound		28	28	18	24	30	10	13
		Ceftazidime (30 μg)		Vancomycin (30 μg)		Ampicillin (25 μg)		Nystatin (416 UI)

^a The diameters of zones of inhibition are given in mm. ^b 10 μL/well. ^c 30 μL/well.

As shown in Table 7, various compounds showed an average antioxidant activity around 40-50%. A study was also carried out in order to investigate the cytotoxic potential of the derivatives **8c**, **10c**, **11c**, **12c**, **13c** and **16c** (Table 8). The antiproliferative activity of the derivatives was determined using breast cancer cell line MCF-7, which is an invasive differentiated mammary epithelial breast cancer cell line used worldwide to screen and compare the antiproliferative activity of new molecules vs standard anticancer compounds. None of the compounds synthesized can compete with the reference standard doxorubicin.

Table 7 Antioxidant activity of the compounds **1c**, **2c**, **3c**, **4c**, **5c**, **6c**, **7c**, **8c**, **8c''**, **10c**, **11c-e**, **13c**, **15c**, **16c**, **17c-e**, **18c-e** and **19c-e**

Compound	RSA (%) ^a at t = 0 min	RSA (%) ^a at t = 30 min
1c	49	52
2c	53	52
3c	72	50
4c	54	54
5c	58	61
6c	63	64
7c	60	61
8c	44	51
8c''	53	53
10c	12	50
11c	47	55
11d	46	46
11e	42	42
13c	41.5	49
15c	45	47
16c	43.5	49
17c	48	53
17d	50	55
17e	45.5	46
18c	44	47
18d	40	41
18e	41	42.5
19c	47	49
19d	51	53
19e	42	42

^a Percentage of the Radical Scavenger Activity.

Thus, by combining deprotonation-iodination of aromatic ketones with *N*-arylation of cyclic amides, we could

access a large range of *N*-aryl and -heteroaryl γ-, δ- and ε-lactams. Whereas **4c** shows promising activity as antimicrobial and antifungal, compounds **6c** and, above all, **7c** and **8c''** exhibit interesting selective antifungal activity against *C. albicans*.

Table 8 Cytotoxic activity on MCF-7 of the compounds **8c**, **10c**, **11c**, **12c**, **13c** and **16c**

Compound	IC ₅₀ (μg mL ⁻¹) ^a
8c	12.7
10c	12.4
11c	12.2
12c	11.9
13c	15.7
16c	13.0
doxorubicin	3.5

^a IC₅₀ is defined as the concentration which results in a 50% decrease in the cell number as compared with that of the control structures in the absence of an inhibitor.

All the reactions were performed under an argon atmosphere. THF was distilled over sodium/benzophenone. Column chromatography separations were achieved on silica gel (40-63 μm). Melting points were measured on a Kofler apparatus. IR spectra were taken on a Perkin-Elmer Spectrum 100 spectrometer. ¹H and ¹³C Nuclear Magnetic Resonance (NMR) spectra were recorded on a Bruker Avance III spectrometer at 300 MHz and 75 MHz, respectively. ¹H chemical shifts (δ) are given in ppm relative to the solvent residual peak and ¹³C chemical shifts are relative to the central peak of the solvent signal.²⁸ The structure of the new compounds was confirmed either by X-ray diffraction (see data below) or through microanalysis.

Crystallography. The samples were studied with graphite monochromatized Mo-Kα radiation (λ = 0.71073 Å). For compounds **1b'**, **2b**, **10c**, **11c**, **16c**, **17c-e**, **18d,e** and **19d**, the X-ray diffraction data were collected at *T* = 150 K using APEXII Bruker-AXS diffractometer. The structure was solved by direct methods using the SIR97 program,²⁹ and then refined with full-matrix least-square methods based on *F*² (SHELX-97)³⁰ with the aid of the WINGX program.³¹ All non-hydrogen atoms were refined with anisotropic atomic displacement parameters. H atoms were finally included in their calculated positions. For **3b**, **6b'**, **11e**, **1c**, **2c**, **3c**, **5c** and **8c''**, the X-ray diffraction data were collected using D8 VENTURE Bruker AXS diffractometer at the temperature given in the crystal data. The structure was solved by dual-space algorithm using the SHELXT program,³² and then refined with full-matrix least-square methods based on *F*² (SHELXL-2014).³³ All non-hydrogen atoms were refined with anisotropic atomic displacement parameters. H atoms were finally included in their calculated positions. The molecular diagrams were generated by ORTEP-3 (version 2.02).³⁴

1-Iodo-9-xanthone (1b). To a stirred, cooled (0 °C) solution of 2,2,6,6-tetramethylpiperidine (0.25 mL, 1.5 mmol) in THF (2–3 mL) were successively added BuLi (about 1.6 M hexanes solution, 1.5 mmol) and, 5 min later, ZnCl₂·TMEDA³⁵ (0.13 g, 0.50 mmol). The mixture was stirred for 15 min at 0 °C before introduction of xanthone (**1a**, 0.20 g, 1.0 mmol). After 2 h at this temperature, a solution of I₂ (0.38 g, 1.5 mmol) in THF (4 mL) was added. The mixture was stirred overnight before addition of an aqueous saturated solution of Na₂S₂O₃ (4 mL) and extraction with AcOEt (3 x 20 mL). The combined organic layers were dried over MgSO₄, filtered and concentrated under reduced pressure. Purification was performed by chromatography on silica gel (eluent: heptane-CH₂Cl₂ 100:0 to 80:20) to afford **1b** in 43% yield as a pale yellow powder: mp 176 °C (lit.³⁶ 172–173.5 °C); IR (ATR): 663, 752, 777, 849, 903, 931, 1108, 1147, 1161, 1234, 1255, 1297, 1328, 1346, 1421, 1443, 1466, 1554, 1590, 1612, 1661, 3065 cm⁻¹; ¹H NMR (CDCl₃) δ 7.27 (dd, 1H, *J* = 8.4 and 7.8 Hz), 7.36 (ddd, 1H, *J* = 8.1, 7.2 and 0.9 Hz), 7.41 (dm, 1H, *J* = 9.0 Hz), 7.48 (dd, 1H, *J* = 8.4 and 1.2 Hz), 7.70 (ddd, 1H, *J* = 8.7, 7.2 and 1.8 Hz), 8.00 (dd, 1H, *J* = 7.6 and 1.1 Hz), 8.31 (ddd, 1H, *J* = 8.1, 1.8 and 0.5 Hz); ¹³C NMR (CDCl₃) δ 91.3 (C), 117.7 (CH), 119.1 (CH), 120.1 (C), 121.3 (C), 124.3 (CH), 127.3 (CH), 134.7 (CH), 135.0 (CH), 138.6 (CH), 154.9 (C), 156.8 (C), 175.4 (C). These data are similar to those reported previously.³⁶ **1,8-Diiodo-9-xanthone (1b')** was also isolated in 5% yield as a yellow powder: mp 252 °C; IR (ATR): 658, 777, 804, 868, 906, 1159, 1276, 1354, 1448, 1578, 1659, 2927 cm⁻¹; ¹H NMR (CDCl₃) δ 7.26 (dd, 2H, *J* = 8.1 and 7.8 Hz), 7.42 (dd, 2H, *J* = 8.3 and 1.1 Hz), 8.01 (dd, 2H, *J* = 7.5 and 1.2 Hz); ¹³C NMR (CDCl₃) δ 92.1 (C), 118.7 (CH), 120.3 (C), 124.8 (C), 134.6 (CH), 138.9 (CH), 155.6 (C). **Crystal data for 1b'.** 2(C₁₃H₆I₂O₂), *M* = 895.96, triclinic, *P* -1, *a* = 8.2003(2), *b* = 10.2204(2), *c* = 15.1904(3) Å, α = 86.8230(10), β = 74.5930(10), γ = 75.9650(10)°, *V* = 1190.67(4) Å³, *Z* = 2, *d* = 2.499 g cm⁻³, μ = 5.267 mm⁻¹. A final refinement on *F*² with 5418 unique intensities and 307 parameters converged at ω(*R*²) = 0.0725 (*R*(*F*) = 0.0402) for 4325 observed reflections with *I* > 2σ(*I*). CCDC 1544822.

1-Iodo-9-thioxanthone (2b).³⁷ To a stirred, cooled (0 °C) solution of 2,2,6,6-tetramethylpiperidine (0.25 mL, 1.5 mmol) in THF (2–3 mL) were successively added BuLi (about 1.6 M hexanes solution, 1.5 mmol) and, 5 min later, ZnCl₂·TMEDA³⁵ (0.13 g, 0.50 mmol). The mixture was stirred for 15 min at 0 °C before introduction of thioxanthone (**2a**, 0.11 g, 0.50 mmol). After 2 h at this temperature, a solution of I₂ (0.38 g, 1.5 mmol) in THF (4 mL) was added. The mixture was stirred overnight before addition of an aqueous saturated solution of Na₂S₂O₃ (4 mL) and extraction with AcOEt (3 x 20 mL). The combined organic layers were dried over MgSO₄, filtered and concentrated under reduced pressure. Purification was performed by chromatography on silica gel (eluent: heptane-CH₂Cl₂ 100:0 to 80:20) to afford **2b** in 45% yield as a greenish powder: mp 156–158 °C; IR (ATR): 664, 711, 745, 777, 923, 1080, 1159, 1241, 1300, 1425, 1537, 1573, 1589, 1641, 3062 cm⁻¹; ¹H NMR (CDCl₃) δ 7.10 (t, 1H, *J* = 7.8 Hz), 7.41–7.47 (m, 2H), 7.52–7.60 (m, 2H), 8.14 (dd, 1H, *J* = 7.5 and 1.2 Hz), 8.47 (dm, 1H, *J* = 8.1 Hz); ¹³C NMR (CDCl₃) δ 94.8 (C), 125.5 (CH), 126.7 (CH), 126.8 (CH), 127.7 (C), 129.6 (C), 130.2 (CH), 131.8 (CH), 132.3 (CH), 135.0 (C), 138.7 (C), 141.8 (CH), 179.5 (C). **Crystal data for 2b.** C₁₃H₇IOS, *M* = 338.15, monoclinic, *C* 2/*c*, *a* = 13.5793(4), *b* = 8.3628(3), *c* = 19.5623(6) Å, β = 101.6770(10)°, *V* = 2175.54(12) Å³, *Z* = 8, *d* = 2.065 g cm⁻³, μ = 3.107 mm⁻¹. A final refinement on *F*² with 2491 unique intensities and 145 parameters converged at ω(*R*²) = 0.0537 (*R*(*F*) = 0.0249) for 2207 observed reflections with *I* > 2σ(*I*). CCDC 1544824.

9'-Hydroxy-1,9'-bi-9-fluorenone (3b'). To a stirred, cooled (0 °C) solution of 2,2,6,6-tetramethylpiperidine (0.25 mL, 1.5 mmol) in THF (2–3 mL) were successively added BuLi (about 1.6 M hexanes solution, 1.5 mmol) and, 5 min later, ZnCl₂·TMEDA³⁵ (0.13 g, 0.50 mmol). The mixture was stirred for 15 min at 0 °C before introduction of 9-fluorenone (**3a**, 0.18 g, 1.0 mmol) at 0–10 °C. After 2 h at room temperature, a solution of I₂ (0.38 g, 1.5 mmol) in THF (4 mL) was added. The mixture was stirred overnight before addition of an aqueous saturated solution of Na₂S₂O₃ (4 mL) and extraction with AcOEt (3 x 20 mL). The combined organic layers were dried over MgSO₄, filtered and concentrated under reduced pressure. Purification was performed by chromatography on silica gel (eluent: heptane-CH₂Cl₂ 80:20) to afford **3b'** in 63% yield as a beige

powder: mp 222–224 °C (lit.³⁸ 222–224 °C); IR (ATR): 686, 728, 753, 771, 803, 909, 958, 1066, 1102, 1139, 1195, 1265, 1284, 1427, 1451, 1469, 1572, 1592, 1607, 1683, 2245, 3060, 3302 cm⁻¹; ¹H NMR (CDCl₃) δ 6.47 (dd, 1H, *J* = 8.1 and 0.9 Hz), 7.11 (dd, 1H, *J* = 8.1 and 7.5 Hz), 7.28 (td, 2H, *J* = 7.5 and 0.9 Hz), 7.33–7.42 (m, 4H), 7.47–7.57 (m, 4H), 7.70 (d, 2H, *J* = 7.2 Hz), 7.78 (d, 1H, *J* = 7.2 Hz), 7.94 (s, 1H); ¹³C NMR (CDCl₃) δ 85.5 (C), 119.9 (CH), 120.3 (2CH), 120.3 (CH), 124.7 (2CH), 125.3 (CH), 128.4 (CH), 128.4 (2CH), 129.2 (2CH), 129.6 (CH), 132.1 (C), 133.4 (C), 135.5 (CH), 136.0 (CH), 139.9 (2C), 144.3 (C), 146.8 (C), 148.8 (C), 149.5 (2C), 198.2 (C). These data are as described previously.¹⁴

1-Iodo-9-fluorenone (3b). To a stirred, cooled (0 °C) solution of 2,2,6,6-tetramethylpiperidine (0.25 mL, 1.5 mmol) in THF (2–3 mL) were successively added BuLi (about 1.6 M hexanes solution, 1.5 mmol) and, 5 min later, CdCl₂·TMEDA¹³ (0.15 g, 0.50 mmol). The mixture was stirred for 15 min at 0 °C before introduction of 9-fluorenone (**3a**, 0.18 g, 1.0 mmol) at 0–10 °C. After 2 h at room temperature, a solution of I₂ (0.38 g, 1.5 mmol) in THF (4 mL) was added. The mixture was stirred overnight before addition of an aqueous saturated solution of Na₂S₂O₃ (4 mL) and extraction with AcOEt (3 x 20 mL). The combined organic layers were dried over MgSO₄, filtered and concentrated under reduced pressure. Purification was performed by chromatography on silica gel (eluent: heptane) to afford **3b** in 80% yield as a yellow powder: mp 148 °C (lit.³⁹ 144–145 °C); IR (ATR): 733, 747, 784, 792, 918, 1056, 1085, 1126, 1149, 1186, 1257, 1281, 1295, 1437, 1563, 1588, 1606, 1715, 3048 cm⁻¹; ¹H NMR (CDCl₃) δ 7.15 (dd, 1H, *J* = 8.1 and 7.5 Hz), 7.33 (ddd, 1H, *J* = 10.2, 7.5 and 4.8 Hz), 7.49–7.56 (m, 3H), 7.68–7.74 (m, 2H); ¹³C NMR (CDCl₃) δ 91.6 (C), 120.1 (CH), 120.2 (CH), 124.7 (CH), 129.8 (CH), 134.0 (C), 134.1 (C), 135.0 (CH), 135.1 (CH), 140.6 (CH), 142.0 (C), 147.2 (C), 191.8 (C). These data are as described previously.¹⁴ **Crystal data for 3b.** C₁₃H₇IO, *M* = 306.09, *T* = 150 K, monoclinic, *P* 2₁, *a* = 7.5211(7), *b* = 18.9683(18), *c* = 7.6189(7) Å, β = 108.620(3)°, *V* = 1030.04(17) Å³, *Z* = 4, *d* = 1.974 g cm⁻³, μ = 3.074 mm⁻¹. A final refinement on *F*² with 2426 unique intensities and 272 parameters converged at ω(*R*²) = 0.0597 (*R*(*F*) = 0.0248) for 2370 observed reflections with *I* > 2σ(*I*). CCDC 1544826.

4-Iododibenzofuran (6b). To a stirred, cooled (0 °C) solution of 2,2,6,6-tetramethylpiperidine (0.25 mL, 1.5 mmol) in THF (2–3 mL) were successively added BuLi (about 1.6 M hexanes solution, 1.5 mmol) and, 5 min later, ZnCl₂·TMEDA³⁵ (0.13 g, 0.50 mmol). The mixture was stirred for 15 min at 0 °C before introduction of dibenzofuran (**6a**, 0.17 g, 1.0 mmol). After 2 h at room temperature, a solution of I₂ (0.38 g, 1.5 mmol) in THF (4 mL) was added. The mixture was stirred overnight before addition of an aqueous saturated solution of Na₂S₂O₃ (4 mL) and extraction with AcOEt (3 x 20 mL). The combined organic layers were dried over MgSO₄, filtered and concentrated under reduced pressure. Purification was performed by chromatography on silica gel (eluent: heptane) to afford **6b** in 90% yield as a pale yellow powder: mp 72 °C (lit.⁴⁰ 71–72 °C); IR (ATR): 704, 722, 744, 785, 842, 851, 1022, 1100, 1192, 1303, 1382, 1432, 1444, 1470, 1539, 1570, 1788, 3048 cm⁻¹; ¹H NMR (CDCl₃) δ 7.09 (t, 1H, *J* = 7.7 Hz), 7.36 (td, 1H, *J* = 7.5 and 0.9 Hz), 7.49 (ddd, 1H, *J* = 8.1, 7.2 and 1.2 Hz), 7.65 (d, 1H, *J* = 8.1 Hz), 7.81 (dd, 1H, *J* = 7.8 and 1.2 Hz), 7.86–7.92 (m, 2H); ¹³C NMR (CDCl₃) δ 75.5 (C), 112.2 (CH), 120.6 (CH), 121.2 (CH), 123.3 (CH), 124.5 (CH), 124.6 (C), 124.7 (C), 127.8 (CH), 136.0 (CH), 155.8 (C), 156.5 (C). These data are similar to those reported previously.⁴¹

4,6-Diiododibenzofuran (6b'). To a stirred, cooled (0 °C) solution of 2,2,6,6-tetramethylpiperidine (0.50 mL, 3.0 mmol) in THF (4 mL) were successively added BuLi (about 1.6 M hexanes solution, 3.0 mmol) and, 5 min later, ZnCl₂·TMEDA³⁵ (0.26 g, 1.0 mmol). The mixture was stirred for 15 min at 0 °C before introduction of dibenzofuran (**6a**, 0.17 g, 1.0 mmol). After 2 h at room temperature, a solution of I₂ (0.76 g, 3.0 mmol) in THF (7 mL) was added. The mixture was stirred overnight before addition of an aqueous saturated solution of Na₂S₂O₃ (4 mL) and extraction with AcOEt (3 x 20 mL). The combined organic layers were dried over MgSO₄, filtered and concentrated under reduced pressure. Purification was performed by chromatography on silica gel (eluent: heptane) to afford **6b'** in 79% yield as a pale yellow powder: mp 155 °C (lit.⁴² 160 °C); IR (ATR): 663, 672, 724, 749, 763, 853, 1024, 1051, 1174, 1403, 1413, 1458, 1570, 2852, 2922, 2953, 3061 cm⁻¹; ¹H NMR (CDCl₃) δ 7.12 (t, 2H, *J* = 7.8 Hz), 7.83–7.89 (m, 4H); ¹³C NMR (CDCl₃) δ 75.7 (2C),

121.1 (2CH), 124.9 (2CH), 125.0 (2C), 136.7 (2CH), 156.2 (2C). These data are similar to those reported previously.⁴³ **Crystal data for 6b'**. $C_{12}H_{16}I_2O$, $M = 419.97$, $T = 150$ K, monoclinic, $P 2_1$, $a = 4.6869(8)$, $b = 13.973(3)$, $c = 17.703(3)$ Å, $\beta = 92.702(7)^\circ$, $V = 1158.1(4)$ Å³, $Z = 4$, $d = 2.409$ g cm⁻³, $\mu = 5.400$ mm⁻¹. A final refinement on F^2 with 4835 unique intensities and 266 parameters converged at $\omega R(F^2) = 0.1172$ ($R(F) = 0.0477$) for 4447 observed reflections with $I > 2\sigma(I)$. CCDC 1544830.

4-Iododibenzothiophene (7b). To a stirred, cooled (0 °C) solution of 2,2,6,6-tetramethylpiperidine (0.75 mL, 4.5 mmol) in THF (5 mL) were successively added BuLi (about 1.6 M hexanes solution, 4.5 mmol) and, 5 min later, ZnCl₂·TMEDA³⁵ (0.39 g, 1.5 mmol). The mixture was stirred for 15 min at 0 °C before introduction of dibenzothiophene (**7a**, 0.18 g, 1.0 mmol). After 2 h at room temperature, a solution of I₂ (1.1 g, 4.5 mmol) in THF (10 mL) was added. The mixture was stirred overnight before addition of an aqueous saturated solution of Na₂S₂O₃ (10 mL) and extraction with AcOEt (3 x 20 mL). The combined organic layers were dried over MgSO₄, filtered and concentrated under reduced pressure. Purification was performed by chromatography on silica gel (eluent: heptane) to afford **7b** in 85% yield as a pale yellow powder: mp 95–96 °C; IR (ATR): 703, 729, 745, 785, 1010, 1022, 1100, 1302, 1382, 1432, 1539, 1789, 3047 cm⁻¹; ¹H NMR (CDCl₃) δ 7.18 (t, 1H, $J = 7.8$ Hz), 7.47–7.50 (m, 2H), 7.81 (dd, 1H, $J = 7.5$ and 0.9 Hz), 7.86–7.89 (m, 1H), 8.06–8.09 (m, 1H), 8.13 (dd, 1H, $J = 7.8$ and 0.9 Hz); ¹³C NMR (CDCl₃) δ 88.3 (C), 121.2 (CH), 122.5 (CH), 122.9 (CH), 124.8 (CH), 125.8 (CH), 127.3 (CH), 135.8 (C), 136.0 (CH), 136.7 (C), 138.8 (C), 146.3 (C). These data are similar to those reported previously.⁴⁴

General procedure 1: A mixture of CuI (0.10 g, 0.50 mmol), the required lactam (12 mmol), K₃PO₄ (4.4 g, 20 mmol), the required halide (10 mmol) and *N,N'*-dimethylethylenediamine (0.11 mL, 1.0 mmol) in dioxane (5 mL) was degassed and heated under argon at 110 °C (the reaction time is given in the product description). After filtration over celite (washing using AcOEt) and removal of the solvents, the crude product is purified by chromatography over silica gel (the eluent is given in the product description).

1-Phenyl-2-pyrrolidinone (8c). The general procedure 1 (reaction time: 24 h) using iodobenzene (**8b**, 1.1 mL) and 2-pyrrolidinone (1.0 g) gave **8c** (eluent: hexane-AcOEt 50:50) in 95% yield as a white powder: mp 67–68 °C (lit.⁴⁵ 68–69 °C); ¹H NMR (CDCl₃) δ 2.16 (quint, 2H, $J = 7.6$ Hz), 2.61 (t, 2H, $J = 8.1$ Hz), 3.86 (t, 2H, $J = 7.1$ Hz), 7.14 (tt, 1H, $J = 7.6$ and 1.2 Hz), 7.34–7.40 (m, 2H), 7.59–7.63 (m, 2H); ¹³C NMR (CDCl₃) δ 18.2 (CH₂), 32.9 (CH₂), 48.9 (CH₂), 120.1 (2CH), 124.6 (CH), 128.9 (2CH), 139.5 (C), 174.4 (C).

1-(2-Methoxyphenyl)-2-pyrrolidinone (9c). The general procedure 1 (reaction time: 24 h) using 2-iodoanisole (**9b**, 2.3 g) and 2-pyrrolidinone (1.0 g) gave **9c** (eluent: hexane-AcOEt 40:60) in 99% yield as a pale yellow oil: ¹H NMR (CDCl₃) δ 2.17 (quint, 2H, $J = 7.6$ Hz), 2.55 (t, 2H, $J = 8.1$ Hz), 3.74 (t, 2H, $J = 7.1$ Hz), 3.82 (s, 3H), 6.93–7.00 (m, 2H), 7.21–7.29 (m, 2H); ¹³C NMR (CDCl₃) δ 19.0 (CH₂), 31.2 (CH₂), 50.1 (CH₂), 55.6 (CH₃), 112.0 (CH), 120.9 (CH), 127.1 (C), 128.7 (CH), 128.8 (CH), 154.8 (C), 175.5 (C). The spectral data are analogous to those described previously.⁴⁶

1-(3-Methoxyphenyl)-2-pyrrolidinone (10c). The general procedure 1 (reaction time: 24 h) using 3-iodoanisole (**10b**, 2.3 g) and 2-pyrrolidinone (1.0 g) gave **10c** (eluent: hexane-AcOEt 50:50) in 99% yield as a pale yellow powder: mp 62–63 °C (lit.⁴⁷ 56 °C); ¹H NMR (CDCl₃) δ 2.12 (quint, 2H, $J = 7.7$ Hz), 2.59 (t, 2H, $J = 8.1$ Hz), 3.80 (s, 3H), 3.82 (t, 2H, $J = 6.9$ Hz), 6.68 (ddd, 1H, $J = 8.1$, 2.4 and 0.9 Hz), 7.10 (dt, 1H, $J = 8.1$ and 0.9 Hz), 7.24 (t, 1H, $J = 8.1$ Hz), 7.33 (t, 1H, $J = 2.3$ Hz); ¹³C NMR (CDCl₃) δ 18.0 (CH₂), 33.0 (CH₂), 48.9 (CH₂), 55.4 (CH₃), 106.0 (CH), 110.0 (CH), 112.0 (CH), 129.5 (CH), 140.6 (C), 159.9 (C), 174.4 (C). **Crystal data for 10c.** $C_{11}H_{13}NO_2$, $M = 191.22$, monoclinic, $P 2_1/c$, $a = 9.5486(8)$, $b = 7.4520(8)$, $c = 13.6565(14)$ Å, $\beta = 103.073(3)^\circ$, $V = 946.56(16)$ Å³, $Z = 4$, $d = 1.342$ g cm⁻³, $\mu = 0.093$ mm⁻¹. A final refinement on F^2 with 2162 unique intensities and 128 parameters converged at $\omega R(F^2) = 0.1097$ ($R(F) = 0.0414$) for 1834 observed reflections with $I > 2\sigma(I)$. CCDC 1544832.

1-(4-Methoxyphenyl)-2-pyrrolidinone (11c). The general procedure 1 (reaction time: 24 h) using 4-iodoanisole (**11b**, 2.3 g) and 2-pyrrolidinone (1.0 g) gave **11c** (eluent: hexane-AcOEt 40:60) in 85% yield as a white powder: mp 119–120 °C (lit.⁴⁸ 113–114 °C); ¹H NMR (CDCl₃) δ 2.13 (quint, 2H, $J = 7.7$ Hz), 2.57 (t, 2H, $J = 8.0$ Hz), 3.78 (s, 3H), 3.81 (t, 2H, $J = 6.9$ Hz), 6.89 (m, 2H), 7.48 (m, 2H); ¹³C NMR (CDCl₃) δ 18.1 (CH₂), 32.6 (CH₂), 49.3 (CH₂), 55.5 (CH₃), 114.1 (2CH), 121.9 (2CH), 132.6 (C), 156.6 (C), 174.0 (C). **Crystal data for 11c.** $C_{11}H_{13}NO_2$, $M = 191.22$, orthorhombic, $P c a b$, $a = 6.4531(9)$, $b = 7.2771(11)$, $c = 40.841(6)$ Å, $V = 1917.9(5)$ Å³, $Z = 8$, $d = 1.325$ g cm⁻³, $\mu = 0.091$ mm⁻¹. A final refinement on F^2 with 2206 unique intensities and 128 parameters converged at $\omega R(F^2) = 0.1947$ ($R(F) = 0.0887$) for 1434 observed reflections with $I > 2\sigma(I)$. CCDC 1544827.

1-(4-Methoxyphenyl)-2-piperidinone (11d). The general procedure 1 (reaction time: 24 h) using 4-iodoanisole (**11b**, 2.3 g) and 2-piperidinone (1.2 g) gave **11d** (eluent: heptane-AcOEt 40:60) in 73% yield as a pale yellow powder: mp 72 °C; ¹H NMR (CDCl₃) δ 1.92 (quint, 4H, $J = 3.2$ Hz), 2.51–2.57 (m, 2H), 3.56–3.61 (m, 2H), 3.79 (s, 3H), 6.90 (d, 2H, $J = 9.0$ Hz), 7.14 (d, 2H, $J = 9.0$ Hz); ¹³C NMR (CDCl₃) δ 21.1 (CH₂), 23.1 (CH₂), 32.4 (CH₂), 51.6 (CH₂), 55.0 (CH₃), 114.0 (2CH), 127.0 (2CH), 135.9 (C), 157.6 (C), 169.7 (C). The spectral data are analogous to those described previously.⁴⁹

1-(4-Methoxyphenyl)hexahydro-2H-2-azepinone (11e).⁵⁰ The general procedure 1 (reaction time: 24 h) using 4-iodoanisole (**11b**, 2.3 g) and hexahydro-2H-2-azepinone (1.4 g) gave **11e** (eluent: heptane-AcOEt 40:60) in 99% yield as a pale yellow powder: mp 66 °C; ¹H NMR (CDCl₃) δ 1.76–1.85 (m, 6H), 2.67–2.70 (m, 2H), 3.69–3.72 (m, 2H), 3.78 (s, 3H), 6.88 (d, 2H, $J = 9.0$ Hz), 7.11 (d, 2H, $J = 9.0$ Hz); ¹³C NMR (CDCl₃) δ 23.2 (CH₂), 28.5 (CH₂), 29.5 (CH₂), 37.2 (CH₂), 53.0 (CH₂), 55.1 (CH₃), 114.0 (2CH), 127.0 (2CH), 137.2 (C), 157.5 (C), 175.6 (C). **Crystal data for 11e.** $C_{13}H_{17}NO_2$, $M = 219.27$, monoclinic, $P 2_1/c$, $a = 6.0345(3)$, $b = 19.2831(7)$, $c = 10.1665(4)$ Å, $\beta = 105.317(2)^\circ$, $V = 1140.99(8)$ Å³, $Z = 4$, $d = 1.276$ g cm⁻³, $\mu = 0.086$ mm⁻¹. A final refinement on F^2 with 2618 unique intensities and 147 parameters converged at $\omega R(F^2) = 0.0986$ ($R(F) = 0.0387$) for 2269 observed reflections with $I > 2\sigma(I)$. CCDC 1544833.

1-(4-Hydroxyphenyl)-2-pyrrolidinone (12c). The general procedure 1 (reaction time: 48 h) using 4-iodophenol (**12b**, 2.2 g) and 2-pyrrolidinone (1.0 g) gave **12c** (eluent: hexane-AcOEt 40:60) in 26% yield as a whitish powder: mp 168 °C (lit.⁵¹ 167 °C); ¹H NMR (CDCl₃) δ 2.16 (quint, 2H, $J = 7.6$ Hz), 2.61 (t, 2H, $J = 8.1$ Hz), 3.82 (t, 2H, $J = 7.1$ Hz), 6.19 (br s, 1H), 6.78 (d, 2H, $J = 9.0$ Hz), 7.32 (d, 2H, $J = 9.0$ Hz); ¹³C NMR (CDCl₃) δ 18.2 (CH₂), 32.5 (CH₂), 49.9 (CH₂), 115.9 (2CH), 122.9 (2CH), 132.0 (C), 153.7 (C), 173.9 (C). These data are analogous to those described previously.⁵¹

1-(4-Cyanophenyl)-2-pyrrolidinone (13c).⁵² The general procedure 1 (reaction time: 24 h) using 4-bromobenzonitrile (**13b'**, 1.8 g) and 2-pyrrolidinone (1.0 g) gave **13c** (eluent: hexane-AcOEt 70:30) in 89% yield as a white powder: mp 115–116 °C; IR (ATR): 748, 772, 984, 1007, 1029, 1091, 1220, 1257, 1308, 1334, 1407, 1455, 1589, 1703, 2911, 3332 cm⁻¹; ¹H NMR (CDCl₃) δ 2.19 (quint, 2H, $J = 7.6$ Hz), 2.63 (t, 2H, $J = 8.1$ Hz), 3.86 (t, 2H, $J = 7.1$ Hz), 7.61 (d, 2H, $J = 9.0$ Hz), 7.77 (d, 2H, $J = 9.0$ Hz); ¹³C NMR (CDCl₃) δ 17.8 (CH₂), 32.9 (CH₂), 48.3 (CH₂), 107.0 (C), 119.0 (C), 119.3 (2CH), 133.0 (2CH), 143.2 (C), 175.0 (C).

1-(4-tert-Butylphenyl)-2-pyrrolidinone (14c).⁵³ The general procedure 1 (reaction time: 48 h) using 1-bromo-4-(tert-butyl)benzene (**14b'**, 2.1 g) and 2-pyrrolidinone (1.0 g) gave **14c** (eluent: hexane-AcOEt 50:50) in 30% yield as a pale yellow oil; ¹H NMR (CDCl₃) δ 1.31 (s, 9H), 2.15 (quint, 2H, $J = 7.5$ Hz), 2.60 (t, 2H, $J = 8.1$ Hz), 3.85 (t, 2H, $J = 7.1$ Hz), 7.38 (d, 2H, $J = 9.0$ Hz), 7.51 (d, 1H, $J = 9.0$ Hz); ¹³C NMR (CDCl₃) δ 18.3 (CH₂), 29.8 (CH₂), 31.5 (3CH₃), 32.8 (C), 49.0 (CH₂), 120.0 (2CH), 125.8 (2CH), 136.9 (C), 147.6 (C), 174.2 (C).

1-(2-Naphthyl)-2-pyrrolidinone (15c). The general procedure 1 (reaction time: 72 h) using 2-iodonaphthalene (**15b**, 2.5 g) and 2-pyrrolidinone (1.0 g) gave **15c** (eluent: hexane-AcOEt 50:50) in 45% yield as a yellow powder: mp 120 °C (lit.⁵⁴ 125 °C); ¹H NMR (CDCl₃) δ 2.27 (quint, 2H, $J = 7.5$ Hz), 2.68 (t, 2H, $J = 8.1$ Hz), 3.81 (t, 2H, $J = 6.9$ Hz),

7.36 (dd, 1H, $J = 7.2$ and 1.2 Hz), 7.45–7.56 (m, 3H), 7.74–7.90 (m, 3H); ^{13}C NMR (CDCl_3) δ 19.1 (CH_2), 31.4 (CH_2), 51.7 (CH_2), 122.6 (CH), 124.5 (CH), 125.5 (CH), 126.2 (CH), 126.6 (CH), 128.2 (CH), 128.4 (CH), 129.5 (C), 134.4 (C), 135.4 (C), 175.3 (C).

1-(2-Thienyl)-2-pyrrolidinone (16c). The general procedure 1 (reaction time: 24 h) using 2-iodothiophene (**16b**, 1.1 mL) (or 2-bromothiophene (**16b'**, 0.97 mL)) and 2-pyrrolidinone (1.0 g) gave **16c** (eluent: hexane-AcOEt 50:50) in 93% (or 99%) yield as a whitish powder: mp 118–119 °C (lit.^{9d} 116–117 °C); ^1H NMR (CDCl_3) δ 2.22 (quint, 2H, $J = 7.7$ Hz), 2.59 (t, 2H, $J = 8.3$ Hz), 3.86 (t, 2H, $J = 7.2$ Hz), 6.51 (dd, 1H, $J = 3.6$ and 1.5 Hz), 6.84–6.92 (m, 2H); ^{13}C NMR (CDCl_3) δ 17.9 (CH_2), 31.3 (CH_2), 48.8 (CH_2), 110.6 (CH), 118.0 (CH), 123.8 (CH), 140.5 (C), 172.1 (C). **Crystal data for 16c.** $\text{C}_8\text{H}_9\text{NOS}$, $M = 167.22$, monoclinic, $P 2_1/n$, $a = 7.6305(14)$, $b = 8.928(2)$, $c = 11.712(2)$ Å, $\beta = 107.493(10)^\circ$, $V = 761.0(3)$ Å³, $Z = 4$, $d = 1.46$ g cm⁻³, $\mu = 0.358$ mm⁻¹. A final refinement on F^2 with 1732 unique intensities and 100 parameters converged at $\omega R(F^2) = 0.1199$ ($R(F) = 0.0435$) for 1379 observed reflections with $I > 2\sigma(I)$. CCDC 1544834.

1-(2-Benzofuryl)-2-pyrrolidinone (17c). The general procedure 1 (reaction time: 48 h) using 2-iodobenzofuran (**17b**, 2.4 g) and 2-pyrrolidinone (1.0 g) gave **17c** (eluent: heptane-AcOEt 40:60) in 84% yield as a white powder: mp 138 °C; IR (ATR): 748, 772, 931, 984, 1007, 1029, 1091, 1220, 1308, 1334, 1407, 1455, 1589, 1703, 2911, 3332 cm⁻¹; ^1H NMR (CDCl_3) δ 2.24 (quint, 2H, $J = 7.6$ Hz), 2.63 (t, 2H, $J = 8.0$ Hz), 4.08 (t, 2H, $J = 7.2$ Hz), 6.85 (d, 1H, $J = 0.9$ Hz), 7.14–7.24 (m, 2H), 7.36–7.40 (m, 1H), 7.47–7.51 (m, 1H); ^{13}C NMR (CDCl_3) δ 18.4 (CH_2), 31.9 (CH_2), 46.8 (CH_2), 90.2 (CH), 110.5 (CH), 120.5 (CH), 122.8 (CH), 123.4 (CH), 129.5 (C), 148.9 (C), 150.0 (C), 172.9 (C). **Crystal data for 17c.** $\text{C}_{12}\text{H}_{11}\text{NO}_2$, $M = 201.22$, triclinic, $P -1$, $a = 7.0061(4)$, $b = 10.3157(7)$, $c = 14.2592(9)$ Å, $\alpha = 70.602(3)$, $\beta = 86.907(3)$, $\gamma = 86.026(3)^\circ$, $V = 969.19(11)$ Å³, $Z = 4$, $d = 1.379$ g cm⁻³, $\mu = 0.095$ mm⁻¹. A final refinement on F^2 with 4400 unique intensities and 271 parameters converged at $\omega R(F^2) = 0.1157$ ($R(F) = 0.0469$) for 2847 observed reflections with $I > 2\sigma(I)$. CCDC 1544835.

1-(2-Benzofuryl)-2-piperidinone (17d). The general procedure 1 (reaction time: 48 h) using 2-iodobenzofuran (**17b**, 2.4 g) and 2-piperidinone (1.2 g) gave **17d** (eluent: heptane-AcOEt 60:40) in 93% yield as a white powder: mp 114–115 °C; IR (ATR): 754, 774, 932, 985, 1008, 1092, 1182, 1221, 1335, 1408, 1455, 1489, 1567, 1591, 1668, 1704, 2955 cm⁻¹; ^1H NMR (CDCl_3) δ 1.87–1.98 (m, 4H), 2.61 (t, 2H, $J = 6.0$ Hz), 3.92 (t, 2H, $J = 6.0$ Hz), 6.87 (d, 1H, $J = 0.9$ Hz), 7.17–7.23 (m, 2H), 7.35–7.40 (m, 1H), 7.48–7.54 (m, 1H); ^{13}C NMR (CDCl_3) δ 20.7 (CH_2), 22.8 (CH_2), 33.3 (CH_2), 47.9 (CH_2), 95.0 (CH), 110.5 (CH), 120.7 (CH), 123.0 (CH), 123.1 (CH), 129.2 (C), 150.2 (C), 150.3 (C), 169.1 (C). **Crystal data for 17d.** $\text{C}_{13}\text{H}_{13}\text{NO}_2$, $M = 215.24$, monoclinic, $P 2_1/n$, $a = 6.2043(6)$, $b = 13.6566(11)$, $c = 12.3273(9)$ Å, $\beta = 95.109(3)^\circ$, $V = 1040.34(15)$ Å³, $Z = 4$, $d = 1.374$ g cm⁻³, $\mu = 0.093$ mm⁻¹. A final refinement on F^2 with 2374 unique intensities and 145 parameters converged at $\omega R(F^2) = 0.1113$ ($R(F) = 0.0437$) for 1943 observed reflections with $I > 2\sigma(I)$. CCDC 1544855.

1-(2-Benzofuryl)hexahydro-2H-2-azepinone (17e). The general procedure 1 (reaction time: 24 h) using 2-iodobenzofuran (**17b**, 2.4 g) and hexahydro-2H-2-azepinone (1.4 g) gave **17e** (eluent: heptane-AcOEt 60:40) in 65% yield as a white powder: mp 76 °C; IR (ATR): 746, 786, 806, 945, 970, 983, 1148, 1165, 1187, 1247, 1352, 1364, 1401, 1437, 1454, 1571, 1678, 2858, 2931 cm⁻¹; ^1H NMR (CDCl_3) δ 1.81–1.91 (m, 6H), 2.73–2.77 (m, 2H), 3.96–3.99 (m, 2H), 6.73 (d, 1H, $J = 0.9$ Hz), 7.17–7.23 (m, 2H), 7.34–7.41 (m, 1H), 7.46–7.53 (m, 1H); ^{13}C NMR (CDCl_3) δ 23.6 (CH_2), 28.8 (CH_2), 29.7 (CH_2), 38.0 (CH_2), 49.1 (CH_2), 95.5 (CH), 110.6 (CH), 120.7 (CH), 123.1 (CH), 123.2 (CH), 129.3 (C), 150.4 (C), 150.5 (C), 174.9 (C). **Crystal data for 17e.** $\text{C}_{14}\text{H}_{15}\text{NO}_2$, $M = 229.27$, monoclinic, $C 2/c$, $a = 15.2276(19)$, $b = 10.4953(13)$, $c = 14.7612(19)$ Å, $\beta = 108.973(4)^\circ$, $V = 2230.9(5)$ Å³, $Z = 8$, $d = 1.365$ g cm⁻³, $\mu = 0.091$ mm⁻¹. A final refinement on F^2 with 2496 unique intensities and 154 parameters converged at $\omega R(F^2) = 0.1127$ ($R(F) = 0.0465$) for 1881 observed reflections with $I > 2\sigma(I)$. CCDC 1544836.

1-(2-Benzothienyl)-2-pyrrolidinone (18c). The general procedure 1 (reaction time: 48 h) using 2-iodobenzothienophene (**18b**, 2.6 g) and 2-pyrrolidinone (1.0 g) gave **18c** (eluent: heptane-AcOEt 40:60) in 88%

yield as a white powder: mp 210 °C; ^1H NMR (CDCl_3) δ 2.23 (quint, 2H, $J = 7.7$ Hz), 2.64 (t, 2H, $J = 8.1$ Hz), 3.91 (t, 2H, $J = 7.2$ Hz), 6.65 (d, 1H, $J = 0.6$ Hz), 7.22–7.35 (m, 2H), 7.63 (dm, 1H, $J = 7.8$ Hz), 7.76 (dm, 1H, $J = 7.8$ Hz); ^{13}C NMR (CDCl_3) δ 17.8 (CH_2), 31.5 (CH_2), 48.8 (CH_2), 106.1 (CH), 122.0 (CH), 122.2 (CH), 123.3 (CH), 124.5 (CH), 135.6 (C), 137.0 (C), 140.4 (C), 172.9 (C). The spectral data are analogous to those described previously.⁵⁵

1-(2-Benzothienyl)-2-piperidinone (18d). The general procedure 1 (reaction time: 48 h) using 2-iodobenzothienophene (**18b**, 2.6 g) and 2-piperidinone (1.2 g) gave **18d** (eluent: heptane-AcOEt 60:40) in 81% yield as a yellow powder: mp 180 °C; IR (ATR): 728, 741, 799, 1167, 1238, 1266, 1296, 1353, 1410, 1437, 1485, 1515, 1637, 2953, 3053 cm⁻¹; ^1H NMR (CDCl_3) δ 1.86–1.95 (m, 2H), 1.99–2.08 (m, 2H), 2.66 (t, 2H, $J = 6.6$ Hz), 3.88 (t, 2H, $J = 6.3$ Hz), 6.81 (s, 1H), 7.25 (td, 1H, $J = 7.2$ and 1.5 Hz), 7.31 (td, 1H, $J = 7.2$ and 1.2 Hz), 7.65 (dm, 1H, $J = 7.2$ Hz), 7.76 (dm, 1H, $J = 7.8$ Hz); ^{13}C NMR (CDCl_3) δ 20.5 (CH_2), 23.2 (CH_2), 33.2 (CH_2), 49.6 (CH_2), 107.0 (CH), 121.7 (CH), 122.2 (CH), 123.4 (CH), 124.3 (CH), 136.6 (C), 136.8 (C), 143.5 (C), 168.6 (C). **Crystal data for 18d.** $\text{C}_{13}\text{H}_{13}\text{NOS}$, $M = 231.30$, monoclinic, $P 2_1/n$, $a = 6.2311(4)$, $b = 13.6241(8)$, $c = 12.9733(7)$ Å, $\beta = 97.711(2)^\circ$, $V = 1091.39(11)$ Å³, $Z = 4$, $d = 1.408$ g cm⁻³, $\mu = 0.272$ mm⁻¹. A final refinement on F^2 with 2493 unique intensities and 145 parameters converged at $\omega R(F^2) = 0.1091$ ($R(F) = 0.0438$) for 1983 observed reflections with $I > 2\sigma(I)$. CCDC 1544837.

1-(2-Benzothienyl)hexahydro-2H-2-azepinone (18e). The general procedure 1 (reaction time: 48 h) using 2-iodobenzothienophene (**18b**, 2.6 g) and hexahydro-2H-2-azepinone (1.4 g) gave **18e** (eluent: heptane-AcOEt 70:30) in 53% yield as a white powder: mp 143 °C; IR (ATR): 744, 793, 979, 1195, 1217, 1242, 1267, 1303, 1397, 1439, 1522, 1659, 2857, 2930 cm⁻¹; ^1H NMR (CDCl_3) δ 1.81–1.92 (m, 6H), 2.78–2.82 (m, 2H), 4.00–4.03 (m, 2H), 6.87 (d, 1H, $J = 0.3$ Hz), 7.24 (td, 1H, $J = 7.5$ and 1.3 Hz), 7.31 (td, 1H, $J = 7.5$ and 1.3 Hz), 7.64 (dm, 1H, $J = 7.2$ Hz), 7.74 (dm, 1H, $J = 7.5$ Hz); ^{13}C NMR (CDCl_3) δ 23.4 (CH_2), 27.5 (CH_2), 29.3 (CH_2), 37.6 (CH_2), 51.4 (CH_2), 109.0 (CH), 121.7 (CH), 122.3 (CH), 123.4 (CH), 124.3 (CH), 136.7 (C), 136.9 (C), 144.5 (C), 174.4 (C). **Crystal data for 18e.** $\text{C}_{14}\text{H}_{15}\text{NOS}$, $M = 245.33$, orthorhombic, $P b n 2_1$, $a = 6.2621(7)$, $b = 9.9132(10)$, $c = 19.3294(15)$ Å, $V = 1199.9(2)$ Å³, $Z = 4$, $d = 1.358$ g cm⁻³, $\mu = 0.252$ mm⁻¹. A final refinement on F^2 with 2458 unique intensities and 154 parameters converged at $\omega R(F^2) = 0.0788$ ($R(F) = 0.0355$) for 2294 observed reflections with $I > 2\sigma(I)$. CCDC 1544838.

1-(2-Benzothiazolyl)-2-pyrrolidinone (19c). The general procedure 1 (reaction time: 24 h) using 2-iodobenzothiazole (**19b**, 2.5 g) and 2-pyrrolidinone (1.0 g) gave **19c** (eluent: heptane-AcOEt 60:40) in 66% yield as a white powder: mp 180 °C; ^1H NMR (CDCl_3) δ 2.30 (quint, 2H, $J = 8.4$ Hz), 2.75 (t, 2H, $J = 8.1$ Hz), 4.29 (t, 2H, $J = 7.2$ Hz), 7.31 (ddd, 1H, $J = 7.8$, 7.2 and 1.2 Hz), 7.44 (ddd, 1H, $J = 8.1$, 7.5 and 1.5 Hz), 7.80–7.87 (m, 2H); ^{13}C NMR (CDCl_3) δ 18.1 (CH_2), 31.9 (CH_2), 48.2 (CH_2), 121.3 (CH), 121.4 (CH), 124.0 (CH), 126.1 (CH), 132.3 (C), 148.5 (C), 157.1 (C), 174.3 (C). The spectral data are analogous to those described previously.⁵⁶

1-(2-Benzothiazolyl)-2-piperidinone (19d). The general procedure 1 (reaction time: 48 h) using 2-iodobenzothiazole (**19b**, 2.5 g) and 2-piperidinone (1.2 g) gave **19d** (eluent: heptane-AcOEt 70:30) in 15% yield as a beige powder: mp 143 °C; ^1H NMR (CDCl_3) δ 1.92–2.06 (m, 4H), 2.72 (t, 2H, $J = 6.8$ Hz), 4.28 (t, 2H, $J = 6.2$ Hz), 7.30 (td, 1H, $J = 7.6$ and 1.2 Hz), 7.42 (td, 1H, $J = 7.8$ and 1.4 Hz), 7.82 (t, 1H, $J = 7.7$ Hz); ^{13}C NMR (CDCl_3) δ 20.3 (CH_2), 22.8 (CH_2), 33.2 (CH_2), 48.7 (CH_2), 121.2 (CH), 121.4 (CH), 124.0 (CH), 126.0 (CH), 133.5 (C), 148.2 (C), 159.4 (C), 170.5 (C). The spectral data are analogous to those described previously.⁵⁵ **Crystal data for 19d.** $2(\text{C}_{13}\text{H}_{12}\text{NOS})$, $M = 460.59$, tetragonal, $P -4 2_1/c$, $a = 14.2662(9)$, $c = 21.0404(18)$ Å, $V = 4282.2(5)$ Å³, $Z = 8$, $d = 1.429$ g cm⁻³, $\mu = 0.277$ mm⁻¹. A final refinement on F^2 with 4894 unique intensities and 289 parameters converged at $\omega R(F^2) = 0.2382$ ($R(F) = 0.1$) for 3133 observed reflections with $I > 2\sigma(I)$. CCDC 1544839.

1-(2-Benzothiazolyl)hexahydro-2H-2-azepinone (19e). The general procedure 1 (reaction time: 48 h) using 2-iodobenzothiazole (**19b**, 2.5 g) and hexahydro-2H-2-azepinone (1.4 g) gave **19e** (eluent: heptane-AcOEt 60:40) in 50% yield as a pale yellow powder: mp 130 °C; ^1H NMR (CDCl_3) δ 1.83–1.90 (m, 6H), 2.85–2.89 (m, 2H), 4.57–4.61 (m, 2H), 7.29 (ddd, 1H, $J = 8.4$, 7.4 and 1.4 Hz), 7.42 (ddd, 1H, $J = 8.1$, 6.9 and 1.2 Hz), 7.78–7.83 (m,

2H); ^{13}C NMR (CDCl_3) δ 23.5 (CH_2), 28.0 (CH_2), 29.4 (CH_2), 37.9 (CH_2), 47.8 (CH_2), 121.0 (CH), 121.1 (CH), 123.7 (CH), 125.9 (CH), 133.6 (C), 147.9 (C), 159.7 (C), 175.6 (C). The spectral data are analogous to those described previously.⁵⁵

General procedure 2: A mixture of CuI (19 mg, 0.10 mmol), K_3PO_4 (0.42 g, 2.0 mmol), 2-pyrrolidinone (0.17 g, 2.0 mmol) and the required iodide (1.0 mmol) in DMSO (2 mL) was degassed and stirred under argon at 125 °C (the reaction time is given in the product description). After cooling to room temperature, the mixture was filtered over celite®. Addition of H_2O (25 mL) to the filtrate, extraction with Et_2O (3x10 mL), drying over Na_2SO_4 , removal of the solvent and purification by chromatography on silica gel (the eluent is given in the product description) led to the expected compound.

1-[1-(9-Xanthyl)]-2-pyrrolidinone (1c). The general procedure 2 (reaction time: 24 h) using 1-iodo-9-xanthone (**1b**, 0.32 g) gave **1c** (eluent: AcOEt) in 70% yield as a yellow powder: mp 236 °C; IR (ATR): 671, 727, 767, 797, 925, 1139, 1233, 1252, 1306, 1333, 1351, 1416, 1438, 1470, 1604, 1615, 1653, 1683, 2974 cm^{-1} ; ^1H NMR (CDCl_3) δ 2.33 (br s, 2H), 2.68 (br s, 2H), 3.82 (br s, 2H), 7.19 (dd, 1H, J = 7.8 and 1.2 Hz), 7.35 (ddd, 1H, J = 8.1, 7.2 and 1.2 Hz), 7.45 (dd, 1H, J = 8.4 and 0.6 Hz), 7.51 (dd, 1H, J = 8.7 and 1.2 Hz), 7.70 (ddd, 1H, J = 8.4, 7.2 and 1.5 Hz), 7.72 (dd, 1H, J = 8.4 and 7.5 Hz), 8.24 (dd, 1H, J = 8.0 and 1.4 Hz); ^{13}C NMR (CDCl_3) δ 19.4 (CH_2), 31.6 (CH_2), 51.5 (CH_2), 117.7 (CH), 118.4 (C), 118.8 (CH), 122.6 (C), 124.2 (CH), 125.1 (CH), 126.8 (CH), 134.6 (CH), 134.9 (CH), 138.8 (C), 155.3 (C), 157.9 (C), 176.3 (C), 176.3 (C). **Crystal data for 1c.** $\text{C}_{17}\text{H}_{13}\text{NO}_3$, M = 279.28, T = 295 K, orthorhombic, $Pn a 2_1$, a = 18.9134(17), b = 5.5288(5), c = 12.5988(9) Å, V = 1317.44(19) Å³, Z = 4, d = 1.408 g cm^{-3} , μ = 0.097 mm^{-1} . A final refinement on F^2 with 2959 unique intensities and 190 parameters converged at $\omega R(F^2)$ = 0.1398 ($R(F)$ = 0.0628) for 2150 observed reflections with $I > 2\sigma(I)$. CCDC 1544823.

1-[1-(9-Thioxanthyl)]-2-pyrrolidinone (2c). The general procedure 2 (reaction time: 24 h) using 1-iodo-9-thioxanthone (**2b**, 0.34 g) gave **2c** (eluent: AcOEt) in 65% yield as a yellow powder: mp 192 °C; IR (ATR): 673, 728, 755, 791, 918, 1079, 1122, 1160, 1249, 1308, 1409, 1449, 1591, 1641, 1691, 2975 cm^{-1} ; ^1H NMR (CDCl_3) δ 2.33 (quint, 2H, J = 7.5 Hz), 2.64 (t, 2H, J = 8.1 Hz), 3.90 (t, 2H, J = 6.8 Hz), 7.26 (dd, 1H, J = 6.9 and 1.8 Hz), 7.44 (ddd, 1H, J = 8.4, 6.9 and 1.5 Hz), 7.49-7.63 (m, 4H), 8.40 (ddd, 1H, J = 8.7, 1.5 and 0.6 Hz); ^{13}C NMR (CDCl_3) δ 19.4 (CH_2), 31.9 (CH_2), 51.6 (CH_2), 125.4 (CH), 126.0 (C), 126.3 (CH), 122.6 (CH), 127.4 (CH), 129.9 (CH), 131.3 (C), 132.1 (CH), 132.3 (CH), 135.7 (C), 139.5 (C), 140.5 (C), 175.8 (C), 180.8 (C). **Crystal data for 2c.** $\text{C}_{17}\text{H}_{13}\text{NO}_2\text{S}$, M = 295.34, T = 150 K, monoclinic, $P 2_1/c$, a = 13.3409(9), b = 5.4022(5), c = 18.5865(15) Å, β = 100.595(3) °, V = 1316.70(18) Å³, Z = 4, d = 1.490 g cm^{-3} , μ = 0.249 mm^{-1} . A final refinement on F^2 with 2988 unique intensities and 190 parameters converged at $\omega R(F^2)$ = 0.0889 ($R(F)$ = 0.0394) for 2290 observed reflections with $I > 2\sigma(I)$. CCDC 1544825.

1-[1-(9-Fluorenyl)]-2-pyrrolidinone (3c). The general procedure 2 (reaction time: 24 h) using 1-iodo-9-fluorenone (**3b**, 0.31 g) gave **3c** (eluent: AcOEt) in 62% yield as a yellow powder: mp 124 °C; IR (ATR): 676, 757, 802, 911, 1148, 1188, 1239, 1308, 1398, 1455, 1484, 1591, 1607, 1700, 2973 cm^{-1} ; ^1H NMR (CDCl_3) δ 2.27 (quint, 2H, J = 7.4 Hz), 2.63 (t, 2H, J = 8.0 Hz), 3.90 (t, 2H, J = 6.9 Hz), 7.22 (dd, 1H, J = 7.7 and 1.1 Hz), 7.29 (td, 1H, J = 7.2 and 1.2 Hz), 7.43-7.54 (m, 4H), 7.61 (dt, 1H, J = 7.5 and 1.7 Hz); ^{13}C NMR (CDCl_3) δ 19.3 (CH_2), 31.7 (CH_2), 50.4 (CH_2), 119.2 (CH), 120.4 (CH), 124.4 (CH), 127.9 (C), 128.2 (CH), 129.5 (CH), 134.2 (C), 134.7 (CH), 135.7 (CH), 137.1 (C), 143.7 (C), 146.2 (C), 175.4 (C), 191.7 (C). **Crystal data for 3c.** $2(\text{C}_{17}\text{H}_{10}\text{NO}_2)$, M = 520.52, monoclinic, $P 2_1/c$, a = 7.0380(3), b = 22.3046(13), c = 16.6958(9) Å, β = 104.886(2) °, V = 2532.9(2) Å³, Z = 4, d = 1.365 g cm^{-3} , μ = 0.090 mm^{-1} . A final refinement on F^2 with 5301 unique intensities and 331 parameters converged at $\omega R(F^2)$ = 0.3050 ($R(F)$ = 0.1373) for 4131 observed reflections with $I > 2\sigma(I)$. CCDC 1544828.

1-(2-Benzoylphenyl)-2-pyrrolidinone (4c). The general procedure 2 (reaction time: 24 h) using 2-iodobenzophenone (**4b**, 0.31 g) gave **4c** (eluent: AcOEt -heptane 80:20) in 56% yield as a yellow oil: IR (ATR): 701, 756, 921, 1137, 1236, 1316, 1397, 1454, 1484, 1599, 1664, 1698, 2961 cm^{-1} ; ^1H NMR (CDCl_3) δ 1.88 (quint, 2H, J = 7.4 Hz), 2.21 (t, 2H, J =

8.0 Hz), 3.77 (t, 2H, J = 6.9 Hz), 7.29 (dd, 1H, J = 8.0 and 0.7 Hz), 7.34 (td, 1H, J = 7.8 and 1.2 Hz), 7.40-7.47 (m, 2H), 7.49-7.58 (m, 3H), 7.78-7.83 (m, 2H); ^{13}C NMR (CDCl_3) δ 18.7 (CH_2), 31.4 (CH_2), 50.8 (CH_2), 125.4 (CH), 126.5 (CH), 128.3 (2CH), 129.9 (2CH), 130.2 (CH), 131.7 (CH), 132.9 (CH), 135.7 (C), 137.4 (C), 137.5 (C), 174.6 (C), 195.9 (C). The spectral data are analogous to those described previously.⁵⁷

1-(2-Benzoyl-3-pyridyl)-2-pyrrolidinone (5c). The general procedure 2 (reaction time: 72 h) using 2-benzoyl-3-iodopyridine¹⁴ (**5b**, 0.31 g) gave **5c** (eluent: AcOEt -heptane 60:40) in 40% yield as a pale yellow powder: mp 132 °C; IR (ATR): 664, 693, 711, 781, 804, 815, 920, 946, 1022, 1066, 1151, 1225, 1241, 1296, 1315, 1328, 1397, 1457, 1666, 1692, 2888, 2923, 2968, 3063 cm^{-1} ; ^1H NMR (CDCl_3) δ 2.14 (quint, 2H, J = 7.2 Hz), 2.39 (t, 2H, J = 8.0 Hz), 3.88 (t, 2H, J = 6.9 Hz), 7.42-7.49 (m, 3H), 7.55 (td, 1H, J = 7.4 and 1.2 Hz), 7.67 (d, 1H, J = 8.1 Hz), 7.92-7.96 (m, 2H), 8.53 (d, 1H, J = 4.5 Hz); ^{13}C NMR (CDCl_3) δ 18.8 (CH_2), 31.4 (CH_2), 50.2 (CH_2), 125.4 (CH), 128.3 (2CH), 130.7 (2CH), 132.9 (CH), 133.2 (CH), 134.1 (C), 135.8 (C), 146.0 (CH), 152.4 (C), 174.6 (C), 193.1 (C). **Crystal data for 5c.** $\text{C}_{16}\text{H}_{14}\text{N}_2\text{O}_2$, M = 266.29, T = 150 K, monoclinic, $P 2_1/c$, a = 10.8301(10), b = 8.2056(6), c = 14.9205(14) Å, β = 91.168(4) °, V = 1325.7(2) Å³, Z = 4, d = 1.334 g cm^{-3} , μ = 0.090 mm^{-1} . A final refinement on F^2 with 3012 unique intensities and 181 parameters converged at $\omega R(F^2)$ = 0.1349 ($R(F)$ = 0.0550) for 2432 observed reflections with $I > 2\sigma(I)$. CCDC 1544829.

1-(4-Dibenzofuryl)-2-pyrrolidinone (6c). The general procedure 2 (reaction time: 48 h) using 4-iododibenzofuran (**6b**, 0.29 g) gave **6c** (eluent: heptane- AcOEt 60:40) in 50% yield as a beige powder: mp 85 °C; IR (ATR): 675, 740, 753, 832, 1019, 1192, 1250, 1265, 1299, 1318, 1392, 1424, 1451, 1503, 1602, 1688, 2895, 2924, 2985 cm^{-1} ; ^1H NMR (CDCl_3) δ 2.27 (quint, 2H, J = 7.6 Hz), 2.65 (t, 2H, J = 8.0 Hz), 4.12 (t, 2H, J = 6.9 Hz), 7.31-7.38 (m, 2H), 7.45 (td, 1H, J = 7.8 and 1.4 Hz), 7.57 (d, 1H, J = 8.1 Hz), 7.67 (dd, 1H, J = 8.0 and 1.1 Hz), 7.81 (dd, 1H, J = 7.8 and 1.2 Hz), 7.93 (dd, 1H, J = 7.5 and 0.6 Hz); ^{13}C NMR (CDCl_3) δ 19.0 (CH_2), 31.5 (CH_2), 49.9 (CH_2), 111.8 (CH), 118.7 (CH), 120.8 (CH), 123.1 (CH), 123.1 (CH), 123.7 (C), 123.9 (CH), 124.0 (C), 126.0 (C), 127.5 (CH), 149.5 (C), 156.0 (C), 174.8 (C).

1-(4-Dibenzothiényl)-2-pyrrolidinone (7c). The general procedure 2 (reaction time: 48 h) using 4-iododibenzothiophene (**7b**, 0.31 g) gave **7c** (eluent: heptane- AcOEt 60:40) in 54% yield as a beige powder: mp 98 °C; IR (ATR): 704, 744, 837, 848, 888, 1067, 1120, 1206, 1229, 1243, 1270, 1305, 1410, 1443, 1466, 1569, 1606, 1682, 1729, 2901, 2972, 2988, 3675 cm^{-1} ; ^1H NMR (CDCl_3) δ 2.25 (quint, 2H, J = 7.5 Hz), 2.64 (t, 2H, J = 8.1 Hz), 3.90 (t, 2H, J = 6.9 Hz), 7.36-7.50 (m, 4H), 7.79-7.83 (m, 1H), 8.06 (dd, 1H, J = 7.8 and 1.2 Hz), 8.09-8.13 (m, 1H); ^{13}C NMR (CDCl_3) δ 19.4 (CH_2), 31.5 (CH_2), 49.8 (CH_2), 120.5 (CH), 121.9 (CH), 122.8 (CH), 124.2 (CH), 124.6 (CH), 125.3 (CH), 127.2 (CH), 133.8 (C), 135.6 (C), 136.1 (C), 137.6 (C), 139.3 (C), 174.4 (C).

General procedure 3: A mixture of CuI (38 mg, 0.20 mmol), K_3PO_4 (0.84 g, 4.0 mmol), 2-pyrrolidinone (0.34 g, 4.0 mmol) and the required iodide (1.0 mmol) in DMSO (2 mL) was degassed and stirred under argon at 125 °C (the reaction time is given in the product description). After cooling to room temperature, the mixture was filtered over celite®. Addition of H_2O (25 mL) to the filtrate, extraction with Et_2O (3x10 mL), drying over Na_2SO_4 , removal of the solvent and purification by chromatography on silica gel (the eluent is given in the product description) led to the expected compound.

1-(6-Iodo-4-dibenzofuryl)-2-pyrrolidinone (6c'). The general procedure 3 (reaction time: 48 h) using 4,6-diiododibenzofuran (**6b'**, 0.42 g) gave **6c'** (eluent: heptane- AcOEt 60:40) in 55% yield. **1-(6-Iodo-4-dibenzofuryl)-2-pyrrolidinone (6c')** was also detected in the crude, and identified by NMR: ^1H NMR (CDCl_3) δ 2.32 (quint, 2H, J = 7.5 Hz), 2.68 (t, 2H, J = 8.0 Hz), 4.28 (t, 2H, J = 7.1 Hz), 7.13 (t, 1H, J = 7.7 Hz), 7.39 (t, 1H, J = 7.8 Hz), 7.78 (dd, 1H, J = 7.8 and 1.2 Hz), 7.79-7.84 (m, 2H), 7.90 (dd, 1H, J = 7.7 and 1.1 Hz); ^{13}C NMR (CDCl_3) δ 19.3 (CH_2), 31.7 (CH_2), 50.0 (CH_2), 75.5 (C), 118.8 (CH), 120.8 (CH), 123.8 (CH), 124.2 (CH), 124.2 (C), 124.4 (C), 124.9 (CH), 126.3 (C), 136.2 (CH), 148.4 (C), 156.4 (C), 175.1 (C).

1,1'-(1,4-Phenylene)bis-2-pyrrolidinone (8c''). The general procedure 3 (reaction time: 24 h) using 1,4-diiodobenzene (**8b'**, 0.33 g) gave **8c''** (eluent: AcOEt-MeOH 90:10) in 30% yield as a beige powder: mp 255 °C (lit.⁵⁸ 251–253 °C); IR (ATR): 832, 1223, 1300, 1387, 1425, 1456, 1512, 1674, 2340, 2894 cm⁻¹; ¹H NMR (CDCl₃) δ 2.14 (quint, 4H, *J* = 7.5 Hz), 2.59 (t, 4H, *J* = 8.1 Hz), 3.83 (t, 4H, *J* = 6.9 Hz), 7.59 (s, 4H); ¹³C NMR (CDCl₃) δ 18.0 (2CH₂), 32.7 (2CH₂), 48.8 (2CH₂), 120.3 (4CH), 135.9 (2C), 174.2 (2C). **Crystal data for 8c''.** C₁₄H₁₆N₂O₂, *M* = 244.29, *T* = 150 K, monoclinic, *P* 2₁/*c*, *a* = 12.2154(6), *b* = 7.2772(3), *c* = 6.5169(3) Å, β = 91.436(2)°, *V* = 579.13(5) Å³, *Z* = 2, *d* = 1.401 g cm⁻³, μ = 0.095 mm⁻¹. A final refinement on *F*² with 1315 unique intensities and 82 parameters converged at ω*R*(*F*²) = 0.1134 (*R*(*F*) = 0.0425) for 1202 observed reflections with *I* > 2σ(*I*). CCDC 1544831. **1-(4-Iodophenyl)-2-pyrrolidinone (8c')** was also isolated in 7% yield as a white powder: mp 140 °C (lit.⁵⁹ 140–142 °C); IR (ATR): 694, 735, 765, 812, 836, 1001, 1034, 1068, 1126, 1189, 1224, 1303, 1386, 1403, 1484, 1583, 1598, 1678, 2854, 2924, 2955, 3101, 3349 cm⁻¹; ¹H NMR (CDCl₃) δ 2.15 (quint, 2H, *J* = 7.5 Hz), 2.59 (t, 2H, *J* = 8.1 Hz), 3.81 (t, 2H, *J* = 7.1 Hz), 7.37–7.42 (m, 2H), 7.62–7.67 (s, 2H); ¹³C NMR (CDCl₃) δ 18.0 (CH₂), 32.8 (CH₂), 48.6 (CH₂), 88.0 (C), 121.6 (2CH), 128.9 (C), 137.8 (2CH), 174.4 (C). The spectral data are analogous to those described previously.⁵⁹

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Supporting Information

YES (this text will be updated with links prior to publication)

Primary Data

NO (this text will be deleted prior to publication)

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