Synthesis of Benzo[*b*]furans by Palladium–NHC Catalyzed Ring Closure of *o*-Bromobenzyl Ketones

János Faragó,[1] András Kotschy*[2]

Institute of Chemistry, Eötvös Loránd University, Pázmány Péter sétány 1/A, 1117 Budapest, Hungary
Fax +36(1)8812011; E-mail: andras.kotschy@hu.netgrs.com

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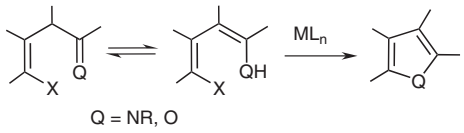
Abstract: The palladium-catalyzed ring closure of aryl *o*-bromobenzyl ketones, easily accessible from aromatic aldehydes and 2-bromobenzyl bromide, provides a straightforward route to 2-arylbenzofurans. A study of the ring closure revealed that a heterocyclic carbene based catalyst provides the best results.

Key words: ring closure, palladium, catalysis, benzofurans

In nature's collection of biologically active heterocycles, benzo[*b*]furan derivatives[3] constitute a major group. Their broad range of biological activities and significant pharmacological potentials have generated extensive and enduring efforts toward the synthesis of this important heterocyclic compound class[4] and its representatives in nature.[5] It is not surprising therefore that there is an ever increasing number of synthetic approaches toward the construction of the benzofuran core. The major synthetic strategies involve the cyclization of *o*-ethynylphenols,[5c,6] the oxidative cyclization of *o*-vinylphenols,[5a,7] the cyclization of phenoxy ketones,[8] and cyclizations through olefin formation.[9]

A more recent approach is based on aromatic nucleophilic substitution as the ring-forming process. δ-Halogenated carbonyl compounds and their imine analogs (e.g., *ortho*-halobenzyl ketones and imines) are in equilibrium with their enol and enamine forms, respectively, which are ideally suited for cyclization through a transition-metal-catalyzed C–O or C–N coupling (Scheme 1). Copper[10] catalysts were successfully applied to the synthesis of benzofurans in such an approach, and the analogous palladium-catalyzed ring closure of 1-(*o*-bromobenzyl)-3,4-dihydroisoquinolines to form the dibenzopyrrocoline skeleton has also been published.[11] Willis and co-workers studied the palladium-catalyzed synthesis of benzofurans and reported[12] that the palladium–DPEphos {bis[2-(diphenylphosphino)phenyl] ether} system in toluene catalyzes the ring closure. Interestingly, the analogous Xantphos-based [Xantphos = 4,5-bis(diphenylphosphino)-9,9-dimethylxanthene] system was found to be ineffective.

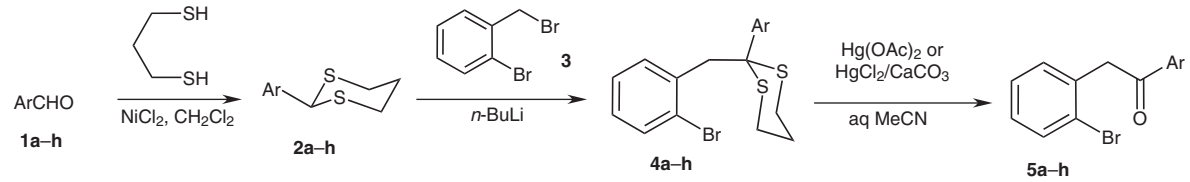


Scheme 1 A general strategy for the synthesis of five-membered heterocycles through tautomeric equilibrium and nucleophilic substitution

Our present work was aimed at establishing if there are any other palladium-based catalysts that lead to the efficient formation of benzofurans from *o*-bromobenzyl ketones. From the several routes leading to our key intermediates (e.g., hydration of alkynes,[10c] arylation of ketones[12]) we envisaged the synthesis of the aryl *o*-bromobenzyl ketones through a sequence of well-established transformations utilizing aromatic aldehydes and 2-bromobenzyl bromide as building blocks.

A literature procedure[13] was followed to convert a series of aromatic aldehydes **1a–h** into their thioketal derivatives **2a–h** by use of propane-1,3-dithiol in the presence of a catalytic amount of nickel(II) chloride (Scheme 2) in dichloromethane. As expected, all reactions worked well and gave the desired 2-aryldithianes **2a–h** in excellent yields (Table 1).

We utilized the thus prepared dithianes **2a–h** as acyl anion equivalents (Scheme 2). Their deprotonation with butyllithium proceeded readily and the anions that formed were quenched by reaction with 2-bromobenzyl bromide (**3**) (Scheme 2). After workup, we isolated the desired products **4a–h** in good yield (Scheme 2, Table 1). The efficiency of the reactions was in agreement with literature



Scheme 2 The synthesis of aryl 2-bromobenzyl ketones **5a–h** from aromatic aldehydes **1a–h** and 2-bromobenzyl bromide (**3**)

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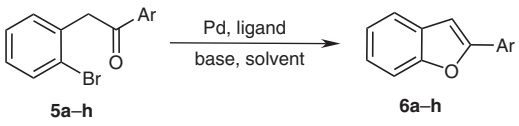
Table 1 The Yields of Aryl 2-Bromobenzyl Ketones **5a–h** and the 2-Aryl-1,3-dithiane Intermediates **2a–h** and the 2-Aryl-2-(2-bromobenzyl)-1,3-dithiane Intermediates **4a–h**

	a	**b**	**c**	**d**	**e**	**f**	**g**	**h**
Ar	Ph	PMP	4-ClC_6H_4	4-FC_6H_4	3-$MeOC_6H_4$	Naph	4-$Me_2NC_6H_4$	Tol
2	87%	99%	87%	90%	99%	87%	65%	99%
4	69%	75%	72%	94%	62%	83%	45%	85%
5	50%	82%	72%	60%	65%	60%	40%	64%

precedence.[14] Our attempts to improve the yield of the process by utilizing other bases (LDA, LiHMDS) were unsuccessful.

The concluding step in the preparation of the key intermediate aryl *o*-bromobenzyl ketones **5a–h** was the removal of the dithiane protecting group (Scheme 2). From the series of deprotection methods (heavy metal salts, oxidative treatment), only the use of mercury(II) salts gave satisfactory results. Mercury(II) acetate[15] or a mixture of mercury(II) chloride and calcium carbonate[16] were equally effective in removing the propanedithiol moiety and giving the aryl *o*-bromobenzyl ketones **5a–h**[10a,c,12b,17] in moderate to good yields (Scheme 2, Table 1). For practical reasons, we used the former reagent in our case.

With the bromobenzyl ketones in hand, we set out to identify the optimal conditions for the ring-closure reaction. The model reaction was the conversion of **5a** into 2-phenylbenzofuran (**6a**; Scheme 3). The screening of a selection of phosphine ligands (Table 2, entries 1–4) revealed that under the applied conditions [$Pd_2(dba)_3$, Cs_2CO_3, DMF, 100 °C, 4 h] significant conversion occurred only in the presence of Xantphos (entry 4). It is interesting to note that the change of the solvent to *o*-xylene diminished the catalytic activity of the system (Table 2, entry 5), in line with the report of Willis et al. who described a similar 'inefficiency' for Xantphos in toluene.[12] The use of palladium(II) acetate as palladium source (Table 2, entry 6) was equally successful, while other salts [allylpalladium(II) chloride, palladium(II) chloride or $Pd(PPh_3)_2Cl_2$] led to a significant drop in conversion. The transformation is sensitive to the applied temperature too, since at 80 °C we observed no conversion, while at 120 °C we started to see decomposition products.



5a–h **6a–h**

Scheme 3 The synthesis of 2-arylbenzofurans **6a–h** by the ring closure of aryl 2-bromobenzyl ketones **5a–h**

We also tested a series of heterocyclic carbenes as ligands in the transformation (Table 2, entries 7–11). In the presence of these ligands the ring closure was slower in general, and its efficiency depended greatly both on the structure of the carbene and the applied solvent. We obtained the best results with 1,3-bis(2,6-diisopropylphenyl)imidazolium tetrafluoroborate (IPr), which gave nearly full conversion in *o*-xylene (Table 2, entry 8). Partial saturation of the ligand led to decreased activity. Interestingly, the change of the solvent to the more polar *N*,*N*-dimethylformamide resulted in a significant drop in the efficiency of the catalyst (SIPr and IMes giving 5% and 2% conversion in 24 hours, respectively). We also tested a series of other bases (K_2CO_3, Et_3N, *t*-BuONa) for the conditions of entries 4 and 8, but, in general, we did not observe any conversion except for decomposition.

Using the optimized conditions, we were able to convert all the aryl *o*-bromobenzyl ketones **5a–h** into the corresponding 2-arylbenzofuran derivatives **6a–h** (Scheme 3). The yield of the process varied greatly with the nature of the aryl group (Table 3), and we were unable to establish a clear trend in reactivity. In certain cases we obtained good yields (**6a–d**), while in other cases (**6e–h**) the efficiency of the process was only mediocre, e.g., the reaction

Table 2 The Optimization of the Reaction Conditions for the Ring Closure of 2-Bromobenzyl Phenyl Ketone (**5a**)[a]

Entry	Pd source	Ligand	Base	Solvent	Conversion[b] (%)
1	$Pd_2(dba)_3$	(*o*-Tol)$_3$P	Cs_2CO_3	DMF	10
2	$Pd_2(dba)_3$	Cy_3P	Cs_2CO_3	DMF	0
3	$Pd_2(dba)_3$	*t*-Bu_3P	Cs_2CO_3	DMF	8[c]
4	$Pd_2(dba)_3$	Xantphos	Cs_2CO_3	DMF	90
5	$Pd_2(dba)_3$	Xantphos	Cs_2CO_3	*o*-xylene	5[c]
6	$Pd(OAc)_2$	Xantphos	Cs_2CO_3	DMF	88
7	$Pd_2(dba)_3$	IPr[d]	Cs_2CO_3	DMF	18[c]
8	$Pd_2(dba)_3$	IPr[d]	Cs_2CO_3	*o*-xylene	95[c]
9	$Pd_2(dba)_3$	SIPr[d]	Cs_2CO_3	*o*-xylene	45[c]
10	$Pd_2(dba)_3$	IMes[d]	Cs_2CO_3	*o*-xylene	13[c]
11	$Pd_2(dba)_3$	SIMes[d]	Cs_2CO_3	*o*-xylene	0[c]

[a] Reagents and conditions: **5a**, Pd cat. (5 mol%), ligand (10 mol%), base (2 equiv), solvent (containing tridecane as internal standard), 100 °C, 4 h.

[b] The conversions were determined by GC analysis.

[c] The reaction was run for 24 h.

[d] IMes = 1,3-dimesitylimidazolium tetrafluoroborate; SIMes = 1,3-dimesitylimidazolinium tetrafluoroborate; IPr = 1,3-bis(2,6-diisopropylphenyl)imidazolium tetrafluoroborate; SIPr = 1,3-bis(2,6-diisopropylphenyl)imidazolinium tetrafluoroborate.

Table 3 The Yields of 2-Arylbenzofurans **6a–h** Prepared by the Ring Closure of Aryl *o*-Bromobenzyl Ketones **5a–h**

Compound **6**	Ar	Yield (%)
6a	Ph	94
6b	PMP	82
6c	4-ClC_6H_4	72
6d	4-FC_6H_4	76
6e	3-$MeOC_6H_4$	36
6f	Naph	40
6g	4-$Me_2NC_6H_4$	20
6h	Tol	38

of the dimethylaminophenyl derivative **6g** giving only very poor results. In comparison with the analogous copper-catalyzed[10] ring-closure reactions, the ring closure catalyzed by palladium–N-heterocyclic carbene complexes might serve only as a second choice for systems where the copper-catalyzed processes fail.

In summary, we have developed a synthetic approach to benzofuran derivatives starting from aromatic aldehydes and 2-bromobenzyl bromide. The key step of the process is the palladium-catalyzed ring closure of aryl *o*-bromobenzyl ketones. Studying this transformation, we established and demonstrated that the heterocyclic carbene ligand derived from 1,3-bis(2,6-diisopropylphenyl)imidazolium tetrafluoroborate (IPr) gives an efficient catalyst. We also established that the transformation is very sensitive to the applied solvent, and in polar solvents a Xantphos-based catalyst is also able to initiate ring closure.

Unless otherwise indicated, all starting materials were obtained from commercial suppliers (Aldrich, Fisher, Merck) and were used without further purification. Analytical TLC was performed on Polygram SIL G/ UV 254 precoated plastic TLC plates with 0.25 mm silica gel (Macherey-Nagel Co.). Silica gel column chromatography was carried out with flash silica gel (0.040–0.063 mm) from Merck. When a hexane–EtOAc mixture was used as chromatography eluent, the column was prepared with hexane and the EtOAc content of the eluent was increased gradually during chromatography. Melting points were determined on a Büchi B-540 melting point apparatus. The ^1H and ^{13}C NMR spectra of samples in $CDCl_3$ or DMSO-d_6 were recorded on a Bruker DRX-250 spectrometer. Chemical shifts (δ) are expressed relative to residual solvent protons as internal standards ($CDCl_3$: δ = 7.26 for ^1H, δ = 77 for ^{13}C; DMSO-d_6: δ = 2.50 for ^1H, δ = 39.43 for ^{13}C). The following compounds were prepared according to literature procedures: 2-phenyl-1,3-dithiane (**2a**),[13] 2-anisyl-1,3-dithiane (**2b**),[13] 2-(4-chlorophenyl)-1,3-dithiane (**2c**), 2-(4-fluorophenyl)-1,3-dithiane (**2d**), 2-(3-methoxyphenyl)-1,3-dithiane (**2e**), 2-(2-naphthyl)-1,3-dithiane (**2f**),[13] 2-[4-(dimethylamino)phenyl]-1,3-dithiane (**2g**), 2-(*p*-tolyl)-1,3-dithiane (**2h**).[13]

2-Aryl-2-(2-bromobenzyl)-1,3-dithianes 4a–h; General Procedure

The appropriate 2-aryl-1,3-dithiane **2** (10 mmol) was dissolved in freshly distilled THF (40 mL) under argon. After the mixture had been cooled to –50 °C, 1.6 M *n*-BuLi in hexane (6.9 mL, 11 mmol) was added dropwise to the stirring soln. After the mixture had stirred for 90 min, a soln of 2-bromobenzyl bromide (**3**; 2.749 g, 11 mmol) in absolute THF (20 mL) was added dropwise, and after stirring for 1 h, the mixture was left to warm to r.t. Following the careful quenching of the reaction by H_2O, the THF was removed under reduced pressure and the remaining aqueous phase was extracted with CH_2Cl_2 (3 × 50 mL). The combined organic phase was dried ($MgSO_4$). After evaporation of the solvent under reduced pressure, the residue was purified by column chromatography.

2-(2-Bromobenzyl)-2-phenyl-1,3-dithiane (4a)

Obtained from 2-phenyl-1,3-dithiane (**2a**); white crystals; yield: 2.52 g (69%); mp 128–130 °C.

^1H NMR (250 MHz, $CDCl_3$): δ = 7.73–7.68 (m, 2 H), 7.37–7.33 (m, 1 H), 7.24–7.18 (m, 3 H), 7.03–6.91 (m, 2 H), 6.83–6.80 (m, 1 H), 3.43 (s, 2 H), 2.62–2.52 (m, 4 H), 1.89–1.79 (m, 2 H).

^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 140.2, 134.5, 133.0, 132.5, 129.6, 128.5, 128.4, 127.1, 126.6, 126.2, 60.4, 49.5, 27.6, 24.7.

HRMS (EI): *m*/*z* calcd for $C_{17}H_{17}BrS_2$: 363.9955; found: 363.9949.

2-Anisyl-2-(2-bromobenzyl)-1,3-dithiane (4b)

Obtained from 2-anisyl-1,3-dithiane (**2b**); white crystals; yield: 2.97 g (75%); mp 72–73 °C.

^1H NMR (250 MHz, $CDCl_3$): δ = 7.61–7.55 (m, 2 H), 7.36–7.32 (m, 1 H), 7.02–6.89 (m, 2 H), 6.82–6.79 (m, 1 H), 6.77–6.71 (m, 2 H), 3.73 (s, 3 H), 3.41 (s, 2 H), 2.67–2.48 (m, 4 H), 1.87–1.77 (m, 2 H).

^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 158.5, 134.5, 132.9, 132.5, 132.0, 130.9, 128.3, 126.5, 126.1, 113.4, 59.9, 55.2, 49.5, 27.5, 24.8.

HRMS (EI): *m*/*z* calcd for $C_{18}H_{19}BrOS_2$: 394.0061; found: 394.0054.

2-(2-Bromobenzyl)-2-(4-chlorophenyl)-1,3-dithiane (4c)

Obtained from 2-(4-chlorophenyl)-1,3-dithiane (**2c**); white crystals; yield: 2.88 g (72%); mp 113–114 °C.

^1H NMR (250 MHz, $CDCl_3$): δ = 7.74–7.68 (m, 2 H), 7.43 (d, *J* = 8.3 Hz, 1 H), 7.29–7.23 (m, 2 H), 7.15–7.00 (m, 3 H), 3.50 (s, 2 H), 2.67–2.63 (m, 4 H), 1.98–1.88 (m, 2 H).

^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 138.9, 134.1, 133.2, 133.0, 132.7, 131.3, 128.6, 128.4, 126.6, 126.3, 59.7, 49.4, 27.6, 24.7.

HRMS (EI): *m*/*z* calcd for $C_{17}H_{16}BrClS_2$: 397.9565; found: 397.9556.

2-(2-Bromobenzyl)-2-(4-fluorophenyl)-1,3-dithiane (4d)

Obtained from 2-(4-fluorophenyl)-1,3-dithiane (**2d**); white crystals; yield: 3.60 g (94%); mp 103–104 °C.

^1H NMR (250 MHz, $CDCl_3$): δ = 7.76–7.68 (m, 2 H), 7.40 (dd, *J* = 7.7, 1.4 Hz, 1 H), 7.13–6.91 (m, 5 H), 3.48 (s, 2 H), 2.68–2.59 (m, 4 H), 1.99–1.86 (m, 2 H).

^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 161.8 (d, *J* = 247.3 Hz), 135.6 (d, *J* = 3.3 Hz), 134.1, 132.9, 132.5, 131.5 (d, *J* = 7.8 Hz), 128.5, 126.5, 126.1, 114.9 (d, *J* = 21.2 Hz), 59.5, 49.4, 27.4, 24.6.

HRMS (EI): *m*/*z* calcd for $C_{17}H_{16}BrFS_2$: 381.9861; found: 381.9857.

2-(2-Bromobenzyl)-2-(3-methoxyphenyl)-1,3-dithiane (4e)

Obtained from 2-(3-methoxyphenyl)-1,3-dithiane (**2e**); white crystals; yield: 2.45 g (62%); mp 85–86 °C.

^{1}H NMR (250 MHz, $CDCl_3$): δ = 7.36–7.32 (m, 2 H), 7.28 (m, 1 H), 7.09 (t, *J* = 7.7 Hz, 1 H), 6.98–6.95 (m, 2 H), 6.90–6.84 (m, 2 H), 3.70 (s, 3 H), 3.40 (s, 2 H), 2.66–2.46 (m, 4 H), 1.86–1.75 (m, 2 H).

^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 154.8, 137.0, 135.3, 133.4, 133.1, 131.0, 128.5, 126.5, 126.1, 120.5, 119.5, 112.2, 61.1, 55.0, 49.9, 27.5, 24.8.

HRMS (EI): *m*/*z* calcd for $C_{18}H_{19}BrOS_2$: 394.0061; found: 394.0051.

2-(2-Bromobenzyl)-2-(2-naphthyl)-1,3-dithiane (4f)
Obtained from 2-(2-naphthyl)-1,3-dithiane (**2f**); white crystals; yield: 3.45 g (83%); mp 116–117 °C.

^{1}H NMR (250 MHz, $CDCl_3$): δ = 8.15 (d, *J* = 1.7 Hz, 1 H), 7.83 (dd, *J* = 8.8, 2.0 Hz, 1 H), 7.75–7.66 (m, 3 H), 7.39–7.35 (m, 2 H), 7.33–7.26 (m, 1 H), 6.92–6.85 (m, 2 H), 6.78–6.72 (m, 1 H), 3.49 (s, 2 H), 2.60–2.53 (m, 4 H), 1.86–1.70 (m, 2 H).

^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 137.7, 134.3, 133.1, 132.8, 132.5, 132.2, 129.4, 128.5, 128.3, 128.1, 127.2, 126.9, 126.4, 126.2, 126.1, 125.9, 60.3, 49.2, 27.6, 24.6.

HRMS (EI): *m*/*z* calcd for $C_{21}H_{19}BrS_2$: 414.0112; found: 414.0109.

2-(2-Bromobenzyl)-2-[4-(dimethylamino)phenyl]-1,3-dithiane (4g)
Obtained from 2-[4-(dimethylamino)phenyl]-1,3-dithiane (**2g**); white crystals; yield: 1.82 g (45%); mp 128–130 °C.

^{1}H NMR (250 MHz, $CDCl_3$): δ = 7.60–7.53 (m, 2 H), 7.35–7.30 (m, 1 H), 7.00–6.90 (m, 3 H), 3. 6.56–6.52 (m, 2 H), 3.44 (s, 2 H), 2.86 (s, 6 H), 2.72–2.51 (m, 4 H), 1.88–1.77 (m, 2 H).

^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 150.1, 132.1, 130.4, 130.0, 129.5, 128.1, 126.6, 124.0, 123.4, 112.0, 59.7, 49.4, 40.3, 27.5, 24.8.

HRMS (EI): *m*/*z* calcd for $C_{19}H_{22}BrNS_2$: 407.0377; found: 407.0371.

2-(2-Bromobenzyl)-2-(*p*-tolyl)-1,3-dithiane (4h)
Obtained from 2-(*p*-tolyl)-1,3-dithiane (**2h**); white crystals; yield: 3.22 g (85%); mp 70–71 °C.

^{1}H NMR (250 MHz, $CDCl_3$): δ = 7.59–7.54 (m, 2 H), 7.49–7.46 (m, 1 H), 7.19–7.15 (m, 2 H), 7.14–7.12 (m, 1 H), 7.10 (d, *J* = 2.0 Hz, 1 H), 6.90 (dd, *J* = 7.4, 2.0 Hz, 1 H), 3.45 (s, 2 H), 2.73–2.53 (m, 4 H), 2.30 (s, 3 H), 1.86–1.74 (m, 2 H).

^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 137.5, 136.3, 134.4, 132.8, 132.3, 129.0, 128.8, 128.0, 126.5, 125.9, 59.3, 48.6, 27.0, 24.2, 20.5.

HRMS (EI): *m*/*z* calcd for $C_{18}H_{19}BrS_2$: 378.0112; found: 378.0105.

Aryl 2-Bromobenzyl Ketones 5a–h; General Procedure
$Hg(OAc)_2$ (1.59 g, 5 mmol) was added to a slurry of the appropriate 2-aryl-2-(2-bromobenzyl)-1,3-dithiane **4** (2 mmol) in a mixture of MeCN (4.4 mL) and H_2O (1.1 mL), and the resulting slurry was stirred at r.t. for 25 min. The reaction mixture was filtered through Celite and the Celite was washed with EtOAc. The combined organic phase was dried ($MgSO_4$). After evaporation of the solvent under reduced pressure, the residue was purified by column chromatography.

Phenyl 2-Bromobenzyl Ketone (5a)
Obtained from 2-(2-bromobenzyl)-2-phenyl-1,3-dithiane (**4a**); white crystals; yield: 0.28 g (50%); mp 71–72 °C.

^{1}H NMR (250 MHz, $CDCl_3$): δ = 7.97 (d, *J* = 7.4 Hz, 2 H), 7.50–7.43 (m, 2 H), 7.35 (t, *J* = 7.7 Hz, 2 H), 7.16–7.12 (m, 2 H), 7.05–6.98 (m, 1 H), 4.34 (s, 2 H).

^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 195.6, 136.1, 134.7, 132.8, 132.2, 131.4, 128.3, 128.2, 127.8, 127.1, 124.7, 45.3.

HRMS (EI): *m*/*z* calcd for $C_{14}H_{11}BrO$: 273.9993; found: 273.9990.

Anisyl 2-Bromobenzyl Ketone (5b)
Obtained from 2-anisyl-2-(2-bromobenzyl)-1,3-dithiane (**4b**); white crystals; yield: 0.50 g (82%); mp 51–53 °C.

^{1}H NMR (250 MHz, $CDCl_3$): δ = 7.89–7.83 (m, 2 H), 7.41 (d, *J* = 7.8 Hz, 1 H), 7.10–7.06 (m, 2 H), 6.99–6.92 (m, 1 H), 6.81–6.75 (m, 2 H), 4.22 (s, 2 H), 3.66 (s, 3 H).

^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 194.5, 163.3, 135.1, 132.4, 131.5, 130.3, 129.3, 128.3, 127.2, 124.8, 113.6, 55.2, 45.1.

HRMS (EI): *m*/*z* calcd for $C_{15}H_{13}BrO_2$: 304.0099; found: 304.0095.

2-Bromobenzyl 4-Chlorophenyl Ketone (5c)
Obtained from 2-(2-bromobenzyl)-2-(4-chlorophenyl)-1,3-dithiane (**4c**); white crystals; yield: 0.45 g (72%); mp 76–77 °C.

^{1}H NMR (250 MHz, $CDCl_3$): δ = 7.98 (d, *J* = 8.5 Hz, 2 H), 7.59 (d, *J* = 7.9 Hz, 1 H), 7.45 (d, *J* = 8.5 Hz, 2 H), 7.32–7.12 (m, 3 H), 4.41 (s, 2 H).

^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 195.1, 139.7, 134.8, 134.6, 132.8, 131.6, 129.7, 129.0, 128.8, 127.5, 125.0, 45.7.

HRMS (EI): *m*/*z* calcd for $C_{14}H_{10}BrClO$: 307.9604; found: 307.9598.

2-Bromobenzyl 4-Fluorophenyl Ketone (5d)
Obtained from 2-(2-bromobenzyl)-2-(4-fluorophenyl)-1,3-dithiane (**4d**); white crystals; yield: 0.35 g (60%); mp 65.5–66 °C.

^{1}H NMR (250 MHz, $CDCl_3$): δ = 8.11–8.03 (m, 2 H), 7.59 (dd, *J* = 7.9, 0.9 Hz, 1 H), 7.32–7.21 (m, 2 H), 7.19–7.11 (m, 3 H), 4.42 (s, 2 H).

^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 194.7, 165.8 (d, *J* = 255.1 Hz), 134.7, 132.9 (d, *J* = 3.2 Hz), 132.8, 131.6, 131.0 (d, *J* = 9.4 Hz), 128.8, 127.5, 125.0, 115.8 (d, *J* = 22.1 Hz), 45.6.

HRMS (EI): *m*/*z* calcd for $C_{14}H_{10}BrFO$: 291.9899; found: 291.9891.

2-Bromobenzyl 3-Methoxyphenyl Ketone (5e)
Obtained from 2-(2-bromobenzyl)-2-(3-methoxyphenyl)-1,3-dithiane (**4e**); white crystals; yield: 0.40 g (65%); mp 67–68 °C.

^{1}H NMR (250 MHz, $CDCl_3$): δ = 7.46 (d, *J* = 7.8 Hz, 1 H), 7.41–7.38 (m, 2 H), 7.19 (t, *J* = 7.7 Hz, 1 H), 7.11–7.03 (m, 2 H), 6.97–6.91 (m, 2 H), 4.24 (s, 2 H), 3.62 (s, 3 H).

^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 196.4, 160.3, 138.4, 135.5, 133.1, 132.2, 130.1, 129.2, 128.0, 125.6, 121.3, 120.1, 113.1, 55.8, 46.3.

HRMS (EI): *m*/*z* calcd for $C_{15}H_{13}BrO_2$: 304.0099; found: 304.0090.

2-Bromobenzyl 2-Naphthyl Ketone (5f)
Obtained from 2-(2-bromobenzyl)-2-(2-naphthyl)-1,3-dithiane (**4f**); white crystals; yield: 0.39 g (60%); mp 121–122 °C.

^{1}H NMR (250 MHz, $CDCl_3$): δ = 8.58 (s, 1 H), 8.08 (dd, *J* = 8.6, 1.8 Hz, 1 H), 7.97 (d, *J* = 8.2 Hz, 1 H), 7.91–7.84 (m, 2 H), 7.63–7.51 (m, 3 H), 7.32–7.23 (m, 2 H), 7.19–7.09 (m, 1 H), 4.57 (s, 2 H).

^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 196.2, 135.6, 135.0, 133.8, 132.8, 132.4, 131.7, 130.0, 129.6, 128.7, 128.5, 128.5, 127.7, 127.5, 126.8, 125.1, 124.0, 45.8.

HRMS (EI): *m*/*z* calcd for $C_{18}H_{13}BrO$: 324.0150; found: 324.0139.

2-Bromobenzyl 4-(Dimethylamino)phenyl Ketone (5g)
Obtained from 2-(2-bromobenzyl)-2-(4-dimethylaminophenyl)-1,3-dithiane (**4g**); white crystals; yield: 0.26 g (40%); mp 113–114 °C.

^{1}H NMR (250 MHz, $CDCl_3$): δ = 7.97–7.91 (m, 2 H), 7.56 (d, *J* = 7.8 Hz, 1 H), 7.25–7.23 (m, 2 H), 7.14–7.06 (m, 1 H), 6.67–6.61 (m, 2 H), 4.34 (s, 2 H), 3.03 (s, 6 H).

^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 194.3, 153.4, 135.9, 132.6, 131.5, 130.5, 128.2, 127.3, 125.0, 124.5, 110.6, 44.9, 39.9.

HRMS (EI): *m*/*z* calcd for $C_{16}H_{16}BrNO$: 317.0415; found: 317.0407.

2-Bromobenzyl *p*-Tolyl Ketone (5h)
Obtained from 2-(2-bromobenzyl)-2-(*p*-tolyl)-1,3-dithiane (**4h**); white crystals; yield: 0.37 g (64%); mp 48–49 °C.

^{1}H NMR (250 MHz, $CDCl_3$): δ = 7.93 (d, *J* = 8.2 Hz, 2 H), 7.55 (d, *J* = 8.2 Hz, 1 H), 7.28–7.19 (m, 4 H), 7.13–7.06 (m, 1 H), 4.39 (s, 2 H), 2.38 (s, 3 H).

^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 195.7, 143.9, 135.0, 134.0, 132.5, 131.5, 129.2, 128.4, 128.3, 127.3, 124.9, 45.4, 21.5.

HRMS (EI): *m*/*z* calcd for $C_{15}H_{13}BrO$: 288.0150; found: 288.0148.

2-Arylbenzofurans 6a–h; General Procedure
A flame-dried vial was charged with the appropriate aryl 2-bromobenzyl ketone **5** (1.5 mmol), $Pd_2(dba)_3$ (69 mg, 0.075 mmol), 1,3-bis(diisopropylphenyl)imidazolinium tetrafluoroborate (IPr; 71.6 mg, 0.15 mmol), Cs_2CO_3 (980 mg, 3 mmol), and anhyd xylene (5 mL). After the vial had been purged with argon, it was closed and heated under argon in a 110 °C oil bath for 24 h. After cooling to r.t. and evaporation of the volatiles, the residue was purified by column chromatography [alumina (neutral, Brockmann II grade), hexane–EtOAc, 10:0 to 10:2].

2-Phenylbenzofuran (6a)[17a]
Obtained from 2-bromobenzyl phenyl ketone (**5a**); white crystals; yield: 0.274 g (94%).

^{1}H NMR (250 MHz, $CDCl_3$): δ = 7.92 (d, *J* = 7.4 Hz, 2 H), 7.59 (d, *J* = 7.6 Hz, 1 H), 7.52 (d, *J* = 7.5 Hz, 1 H), 7.45 (t, *J* = 7.2 Hz, 2 H), 7.38 (t, *J* = 7.2 Hz, 1 H), 7.31 (t, *J* = 7.3 Hz, 1 H), 7.25 (t, *J* = 7.2 Hz, 1 H), 7.03 (s, 1 H).

^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 155.9, 154.9, 130.5, 129.2, 128.8, 128.5, 124.9, 124.2, 122.9, 120.9, 111.2, 101.3.

HRMS (EI): *m*/*z* calcd for $C_{14}H_{10}O$: 194.0732; found: 194.0728.

2-Anisylbenzofuran (6b)[10a]
Obtained from anisyl 2-bromobenzyl ketone (**5b**); white crystals; yield: 0.276 g (82%).

^{1}H NMR (250 MHz, $CDCl_3$): δ = 7.81 (dt, *J* = 9.0, 2.2 Hz, 2 H), 7.57–7.47 (m, 3 H), 7.22 (dt, *J* = 6.7, 2.2 Hz, 2 H), 7.00–6.97 (m, 2 H), 3.87 (s, 3 H).

^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 156.0, 154.7, 128.0, 126.4, 123.7, 123.3, 122.8, 120.5, 116.0, 114.2, 111.0, 99.7, 55.4.

HRMS (EI): *m*/*z* calcd for $C_{15}H_{12}O_2$: 224.0837; found: 224.0834.

2-(4-Chlorophenyl)benzofuran (6c)[7]
Obtained from 2-bromobenzyl 4-chlorophenyl ketone (**5c**); white crystals; yield: 0.247 g (72%).

^{1}H NMR (250 MHz, $CDCl_3$): δ = 7.83–7.77 (m, 2 H), 7.61–7.50 (m, 2 H), 7.45–7.40 (m, 2 H), 7.34–7.23 (m, 2 H), 7.02 (s, 1 H).

^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 133.1, 132.4, 132.1, 130.9, 128.8, 127.6, 127.4, 126.8, 125.2, 124.7, 124.7, 120.5.

HRMS (EI): *m*/*z* calcd for $C_{14}H_9ClO$: 228.0342; found: 228.0336.

2-(4-Fluorophenyl)benzofuran (6d)[18]
Obtained from 2-bromobenzyl 4-fluorophenyl ketone (**5d**); white crystals; yield: 0.242 g (76%).

^{1}H NMR (250 MHz, $CDCl_3$): δ = 7.87–7.79 (m, 2 H), 7.59–7.49 (m, 2 H), 7.32–7.20 (m, 2 H), 7.18–7.09 (m, 2 H), 6.95 (s, 1 H).

^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 162.8 (d, *J* = 248.6 Hz), 155.0, 154.8, 129.1, 126.7, 126.7 (d, *J* = 8.3 Hz), 124.2, 123.0, 120.9, 115.9 (d, *J* = 22.0 Hz), 111.1, 101.0 (d, *J* = 1.8 Hz).

HRMS (EI): *m*/*z* calcd for $C_{14}H_9FO$: 212.0637; found: 212.0630.

2-(3-Methoxyphenyl)benzofuran (6e)[19]
Obtained from 2-bromobenzyl 3-methoxyphenyl ketone (**5e**); white crystals; yield: 0.121 g (36%).

^{1}H NMR (250 MHz, $CDCl_3$): δ = 8.73 (d, *J* = 8.7 Hz, 1 H), 7.70–7.59 (m, 2 H), 7.45 (t, *J* = 7.7 Hz, 1 H), 7.31 (s, 1 H), 7.21–7.11 (m, 3 H), 7.00 (dt, *J* = 7.7, 1.6 Hz, 1 H), 3.69 (s, 3 H).

^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 198.0, 159.7, 138.9, 135.3, 130.5, 129.5, 128.5, 128.0, 127.4, 127.3, 123.9, 122.98, 120.8, 113.0, 55.4.

HRMS (EI): *m*/*z* calcd for $C_{15}H_{12}O_2$: 224.0837; found: 224.0832.

2-(2-Naphthyl)benzofuran (6f)[20]
Obtained from 2-bromobenzyl β-naphthyl ketone (**5f**); white crystals; yield: 0.147 g (40%).

^{1}H NMR (250 MHz, $CDCl_3$): δ = 8.30 (s, 1 H), 7.86–7.74 (m, 4 H), 7.55–7.37 (m, 4 H), 7.27–7.14 (m, 2 H), 7.06 (d, *J* = 0.6 Hz, 1 H).

^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 155.9, 155.0, 133.4, 133.3, 129.3, 128.5, 128.4, 127.8, 127.7, 126.6, 126.5, 124.4, 123.8, 123.0, 122.8, 120.9, 111.2, 101.9.

HRMS (EI): *m*/*z* calcd for $C_{18}H_{12}O$: 244.0888; found: 244.0886.

2-[4-(Dimethylamino)phenyl]benzofuran (6g)[21]
Obtained from 2-bromobenzyl 4-(dimethylamino)phenyl ketone (**5g**); white crystals; yield: 0.071 g (20%).

^{1}H NMR (250 MHz, $CDCl_3$): δ = 7.66 (dt, *J* = 9.0, 2.1 Hz, 2 H), 7.47–7.37 (m, 2 H), 7.17–7.10 (m, 2 H), 6.72 (d, *J* = 0.8 Hz, 1 H), 6.69 (dt, *J* = 9.0, 2.1 Hz, 2 H), 2.94 (s, 6 H).

^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 157.0, 154.5, 150.6, 129.9, 126.1, 123.1, 122.6, 120.1, 118.6, 112.1, 110.8, 98.1, 40.3.

HRMS (EI): *m*/*z* calcd for $C_{16}H_{15}NO$: 237.1154; found: 237.1149.

2-(*p*-Tolyl)benzofuran (6h)[10a]
Obtained from 2-bromobenzyl *p*-tolyl ketone (**5h**); white crystals; yield: 0.119 g (38%).

^{1}H NMR (250 MHz, $CDCl_3$): δ = 7.76 (dt, *J* = 8.5, 1.9 Hz, 2 H), 7.59–7.55 (m, 1 H), 7.54–7.49 (m, 1 H), 7.31–7.18 (m, 4 H), 6.97 (d, *J* = 1.0 Hz, 1 H), 2.40 (s, 3 H).

^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 156.2, 151.3, 138.6, 135.7, 129.5, 129.3, 124.9, 124.0, 122.8, 120.7, 111.1, 100.5, 21.4.

HRMS (EI): *m*/*z* calcd for $C_{15}H_{12}O$: 208.0888; found: 208.0885.

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(1) New address: J. Faragó, Gedeon Richter Chemical Works, Gyömröi út 19–21, Budapest, Hungary.

(2) New address: A. Kotschy, Servier Research Institute of Medicinal Chemistry, Záhony u. 7, 1031 Budapest, Hungary.

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