Base-Mediated Ring-Contraction of Pyran Systems Promoted by Palladium and Phase-Transfer Catalysis

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Abstract – A study of the ring-contraction of a model 3*H*-naphtho[2,1-*b*]pyran is described in order to elucidate and optimise the ring-contraction of naphthopyrans. Two efficient base-mediated protocols to access multiple naphthofurans, naphthodifurans and a benzo-fused indole in generally good yields are reported. Furthermore, a protocol to selectively prepare (hetero)aryl substituted naphthofurans via a Suzuki-coupling – ring-contraction process is presented. An additional protocol that allows Suzuki cross-coupling reactions to be performed on bromo-substituted naphthopyrans without the ring-contraction side reaction is reported.

Keywords: Ring-Contraction, Phase-Transfer Catalysis, Naphthofuran, Naphthodifuran, Benzindole.

Introduction

Naphthofurans are an important class of oxygen-containing heterocycle, consisting of a naphthalene moiety fused to a furan ring that occur naturally¹ and exhibit a wide range of biological activities (Figure 1).²

Figure 1. Isomeric naphthofurans

Several naphtho[2,1-*b*]furans have shown genotoxic activity against different bacteria,³ cytotoxicity^{4,5} and antiandrogen activity⁶ against human cancer lines, and more recently inhibition of the influenza A (H1N1) virus.⁷ Nitro-substituted naphtho[2,1-*b*]furans induce carcinogenic⁸ and regulatory⁹ effects in mammalian cells. A naphtho[2,3-*b*]furan-4,9-dione has shown the ability to suppress keratinocyte hyperproliferation.¹⁰

Naphthodifuran derivatives have garnered interest in the materials arena,¹¹ with a naphtho[1,2-*b*:5,6-*b'*]difuran based oligomer offering potential in photovoltaic applications,¹² and naphtho[2,1-*b*:4,3-*b'*]difurans being employed in organic light emitting diodes and in organic field-effect transistors.¹³ Naphtho[2,1-*b*:6,5-*b'*]difurans have been integrated in electronic inks in combination with organic semiconductors.¹⁴

Considering the extensive panoply of interesting properties that naphthofurans and naphthodifurans possess, it is extremely important to develop efficient methods for building naphtho(di)furan scaffolds. Recent syntheses of naphthodifurans have capitalised upon the cyclisation of *o*-hydroxyaryl substituted internal alkynes,¹⁵ Pd-mediated cyclisation of *o*-allyl hydroxynaphthalenes¹⁶ and a Pummerer annulation – cross-coupling strategy applied to ketene dithioacetal monoxide with hydroxynaphthalenes.¹⁷

A potential strategy for the synthesis of naphthofurans involves the ring-contraction of readily accessible naphthopyran systems.¹⁸ The ring-contraction of benzopyrans and naphthopyrans has been described almost invariably as unique serendipitous observations. For example, the oxidative ring-contraction of the 1,2-dihydrospiro[benzo[*f*]chroman-3,9'-xanthene] **4** afforded the 9-(naphtho[2,1-*b*]furan-2-yl)-9*H*-xanthene **5** in 34 – 57% yield upon thermolysis with sulfur (Scheme 1).¹⁹

Scheme 1. Thermal ring-contraction of 1,2-dihydrospiro[benzo[*f*]chroman-3,9'-xanthene] **4**

The action of base on the 3-bromo substituted 2*H*-naphtho[1,2-*b*]pyran **6** promoted an addition – dehydrobromination reaction leading to the corresponding naphtho[1,2-*b*]furan **7** (Scheme 2).²⁰ Conversely, heating aryl substituted naphthopyrans with 4-TsOH (20 mol %) effects the

destruction of the pyran ring via a ring-opening and Friedel-Crafts alkylation to afford inden-3-yl-naphthols.²¹

Scheme 2. Base mediated ring-contraction of 3-bromonaphthopyran 6

According to Gabbutt *et al.*, the presence of very strong electron-withdrawing groups at the saturated carbon of the pyran moiety favours the quantitative ring-contraction of the spiro(3*H*-naphtho[2,1-*b*]pyran-3,9'-thioxanthene-10,10-dioxide) **8** to generate the 9-(naphtho[2,1-*b*]furan-2-yl)-9*H*-thioxanthene-10,10-dioxide **9** (Scheme 3). The bis-sulfone **10** underwent an efficient photochemical ring-contraction to the naphtho[2,1-*b*]furan **11** in 85% yield.²²

Scheme 3. Photochemical and thermal ring-contraction of naphthopyrans 8 and 10

The synthesis of benzo- and naphtho- fused pyrans and furans may often be intertwined, for example Banwell *et al.*, have reported that the Au(I)-catalysed intramolecular hydroarylation reaction of terminal alkynes **12a, b** affords mixtures of benzopyrans (**13, 15**) and benzofurans (**14, 16**) in near equal amounts (Scheme 4).²³ According to the authors, the fragmentation of a late-stage aurylated intermediate generates the benzo- and naphtho- furans.

Scheme 4. Au(I)-catalysed intramolecular hydroarylation of propargyl ethers to afford benzopyrans and benzofurans

In an attempt to prepare a 6-styryl-2H[1]benzopyran from the 6-bromo-2,2-diaryl-2H-[1]benzopyran **17** and styrene, Gabbutt *et al.*, instead isolated the 2-(diarylmethyl)-5-styrylbenzofuran **18** in 30% yield resulting from a *tandem* Heck-coupling – ring-contraction sequence (Scheme 5).²⁴

Scheme 5. Heck-coupling – ring-contraction of bromobenzopyran 17

An undesirable ring-contraction of the 3*H*-naphtho[2,1-*b*]pyran **19** to afford the naphtho[2,1-*b*]furan **20** in 65% yield was observed instead of the postulated palladium-catalysed cyanation reaction (Scheme 6).²⁵

Scheme 6. Failed Pd-mediated cyanation of 2-bromonaphthopyran 19

Given the predisposition of the pyran unit to contract under a variety of reaction conditions, especially including in the presence of base and palladium, this present study aims to understand the ring-contraction mechanism of naphthopyrans. Furthermore, our investigations have revealed two efficient and robust ring-contraction protocols which have been successfully applied to the preparation of naphthofurans, naphthodifurans and a benzindole. Moreover, specific reaction conditions to effect either a Suzuki-coupling – ring-contraction or a selective Suzuki-coupling without ring-contraction, are described. The foregoing reaction conditions constitute the first effective protocol to selectively prepare naphthofurans *via* a sequential process.

Results and Discussion

Since ring-contraction may occur in pyran systems during palladium-promoted cross-coupling reactions, a kinetic study was developed to gather more information about the ring-contraction process and determine the ideal experimental conditions to effect the ring-contraction. The ring-contraction of 3,3-bis(4-methoxyphenyl)-3*H*-naphtho[2,1-*b*]pyran **21** to naphtho[2,1-*b*]furan **22** under different experimental conditions was analysed (Scheme 7).

Scheme 7. Ring-contraction of 3,3-bis(4-methoxyphenyl)-3*H*-naphtho[2,1-*b*]pyran **21**

First, a series of test reactions were performed in order to evaluate the overall stability of the naphthopyran **21** to various solvents and reactants. Thus, there was no ring-contraction after exposure of **21** to either DCM, PhMe, EtOH, DMAc or mixtures of PhMe:EtOH (1:1) at room temperature (rt) or reflux (Entries 1 – 5, Table 1). Additionally there was no ring-contraction when **21** was exposed to DCM with Pd(PPh₃)₄ (5 mol%) at rt (Entry 6, Table 1).

Table 1. Evaluation of the behavior of naphthopyran **21 to reactants and solvents**

Entry	Pd	Base	Solvent	Temp./ °C	Time / h	21:22 [†]	k /M.h ⁻¹
Catalyst							
1	No	No	DCM	rt	18	1.0:0	0
2	No	No	PhMe	rt	17	1.0:0	0
3	No	No	EtOH	rt	28	1.0:0	0
4	No	No	PhMe:EtOH	rt and/or	15 (rt)	1.0:0	0
			(1:1)	reflux	14 (reflux)	1.0:0	0

**Table 1. Evaluation of the behavior of naphthopyran 21 to reactants and solvents
(Continuation)**

Entry	Pd Catalyst	Base	Solvent	Temp./ °C	Time / h	21:22 [†]	k /M.h ⁻¹
5	No	No	DMAc	rt and/or	28 (rt)	1.0:0	0
				150	14 (150 °C)	1.0:0	0
6	Pd(PPh ₃) ₄ (5 mol%)	No	DCM	rt	23	1.0:0	0
7[‡]	Pd(PPh ₃) ₄ (5 mol%)	K ₂ CO ₃ (1.5 equiv)	PhMe:EtOH (1:1)	reflux	80	1.0:3.5	0.48
8[¥]	Pd(OAc) ₂ (10 mol%)	KOAc (1.9 equiv)	DMAc	150	5	1.0:1.1	N/A
9^{‡#}	No	K ₂ CO ₃ (1.5 equiv)	PhMe:EtOH (1:1)	reflux	80	1.0:2.0	0.44
10[‡]	No	K ₂ CO ₃ (3.0 equiv)	PhMe:EtOH (1:1)	reflux	74	0:1.0	0.62
11	Pd(PPh ₃) ₄ (5 mol%)	No	PhMe:EtOH (1:1)	reflux	48	1.0:0	0
12[#]	No	CS ₂ CO ₃ (1.5 equiv)	PhMe:EtOH (1:1)	reflux	80	1.0:2.0	0.41
13[#]	No	Li ₂ CO ₃ (1.5 equiv)	PhMe:EtOH (1:1)	reflux	80	1.8:1.0	0.21
14[#]	No	Na ₂ CO ₃ (1.5 equiv)	PhMe:EtOH (1:1)	reflux	80	1.1:1.0	0.31
15[¥]	No	K ₃ PO ₄ (1.5 equiv)	PhMe:EtOH (1:1)	reflux	14	1.7:1.0	N/A

[†] Relative proportion of **21:22** calculated based on the integral of the ¹H NMR spectrum of the reaction mixture.

[‡] Rate constant data presented in Figure 3. [#] Rate constant data presented in Figure 2. [¥] Relative proportion of **21:22** determined after reaction terminated; no kinetic data was recorded.

Two typical Pd-mediated cross-coupling reaction conditions²⁶ were employed to ring-contract 3*H*-naphtho[2,1-*b*]pyran **21** at a fairly slow rate. When using K₂CO₃ (1.5 equiv) and Pd(PPh₃)₄ (5 mol%) in PhMe:EtOH (1:1) at reflux, a 1.0:3.5 (**21:22**) mixture was obtained after 80 h (Entry 7, Table 1). When using KOAc (1.9 equiv) and Pd(OAc)₂ (10 mol%) in DMAc at 150 °C, a 1.0:1.1 (**21:22**) mixture was attained after 5 h (Entry 8, Table 1). Formation of the ring-contracted product **22** was determined by the presence in the ¹H NMR spectrum of a singlet at 6.76 ppm and at 5.63 ppm which corresponded to the resonance of H-1 and H-α, respectively.

A surprising finding was that the ring-contraction of the 3*H*-naphtho[2,1-*b*]pyran **21** occurred with zero order kinetics without the deliberate addition of a palladium catalyst. Thus, when employing K₂CO₃ (1.5 equiv) in PhMe:EtOH (1:1) at reflux, a 1:2 (**21:22**) mixture was produced after 80 h (Entry 9, Table 1). Palladium cross-contamination from laboratory equipment was ruled out after obtaining the same outcome with a virgin stirrer bar, condenser and reaction flask (Entry 9, Table 1).²⁷ On the other hand, considering the prior work from Leadbeater *et al.*,²⁸ it was determined by ICP-MS that Li₂CO₃, Na₂CO₃, K₂CO₃ and Cs₂CO₃ (supplied by Alfa Aesar) contained extremely low levels of palladium (0.35 – 2.65 ppb) – at the very limit of detection of these bases. Consequently, it was extremely unlikely that any significant palladium contamination had occurred and, therefore, it was safe to assume that the ring-contraction of the 3*H*-naphtho[2,1-*b*]pyran **21** did not require palladium to occur. Furthermore, it was determined that the rate of the ring-contraction of the 3*H*-naphtho[2,1-*b*]pyran **21** depended on the stoichiometry of K₂CO₃: by doubling the molar amount of K₂CO₃ (3 equiv), the rate constant of the reaction increased by 29% (Entry 10, Table 1). Thus, the ring-contraction of the 3*H*-naphtho[2,1-*b*]pyran **21** was complete after 74 h of reaction. Notably, in the absence of base, but employing Pd(PPh₃)₄ (5 mol%) in PhMe:EtOH (1:1) at

reflux, no ring-contraction of **21** was observed after 48 h of reaction, which strongly reaffirmed that the base played a pivotal role in the ring-contraction process (Entry 11, Table 1).

The kinetics of the ring-contraction of the 3*H*-naphtho[2,1-*b*]pyran **21** varied with the nature of the carbonate bases (Figure 2). A similar rate constant was observed between Cs₂CO₃ (Entry 12, Table 1) and K₂CO₃ (Entry 9, Table 1). On the other hand, when employing Li₂CO₃ (Entry 13, Table 1), the rate constant was two times smaller when compared to K₂CO₃. Hence, when using Na₂CO₃ (Entry 14, Table 1), the ring-contraction occurred faster than Li₂CO₃ yet slower than K₂CO₃ and Cs₂CO₃ – after 80 h only 48% of the 3*H*-naphtho[2,1-*b*]pyran **21** had ring-contracted. The differences in the kinetics of the ring-contraction of the 3*H*-naphtho[2,1-*b*]pyran **21** by employing different carbonate bases could be attributed to differences in solubility in PhMe:EtOH (1:1) – Li₂CO₃ is less soluble than Na₂CO₃ as lithium is a harder metal. Likewise, Na₂CO₃ is less soluble when compared to K₂CO₃ and Cs₂CO₃.

- ▲ Li₂CO₃ (1.5 equiv), PhMe:EtOH (1:1), reflux (Entry 13, Table 1)
- K₂CO₃ (1.5 equiv), PhMe:EtOH (1:1), reflux (Entry 9, Table 1)
- ◆ Na₂CO₃ (1.5 equiv), PhMe:EtOH (1:1), reflux (Entry 14, Table 1)
- Cs₂CO₃ (1.5 equiv), PhMe:EtOH (1:1), reflux (Entry 12, Table 1)

Figure 2. Rate Plots showing the influence of base upon the contraction of naphthopyran **21**

Bases with varying pK_b values were also tested: when using K₃PO₄ (1.5 equiv), which is a stronger base than K₂CO₃, in PhMe:EtOH (1:1) at reflux, 37% of the 3*H*-naphtho[2,1-*b*]pyran **21** had ring-contracted after 14 h of reaction (Entry 15, Table 1). By comparison, when employing K₂CO₃, only 13% of the ring-contracted product **22** was formed after 14 h. Therefore, the ring-contraction of the 3*H*-naphtho[2,1-*b*]pyran **21** when using the stronger base K₃PO₄ was 35% faster than K₂CO₃. An obvious problem concerning the ring-contraction of **21** was the relatively low rate of the reaction (Entry 1, Table 2). Consequently, the effect of 18-crown-6 was tested as it could act as a phase-transfer catalyst.²⁹ Thus, with 18-crown-6 (3 equiv) and K₂CO₃ (1.5 equiv) in toluene at reflux, the rate constant of the ring-contraction increased by one order of magnitude (Entry 2, Table 2). Consequently, in the presence of 18-crown-6, the 3*H*-naphtho[2,1-*b*]pyran **21** fully ring-contracted to the naphtho[2,1-*b*]furan **22**

with zero-order kinetics after only 10 h (Figure 3). No ring-contraction was observed in the absence of K₂CO₃ (Entry 3, Table 2). Another important finding was that ring-contraction of **21** occurred even with only 10 mol% of K₂CO₃, with 18-crown-6 (20 mol%) in toluene at reflux (Figure 3 and Entry 4, Table 2). Thus, the 3*H*-naphtho[2,1-*b*]pyran **21** fully ring-contracted to the naphtho[2,1-*b*]furan **22** after approximately 24 h. This result showed that the base, already established as pivotal for the ring-contraction process, was not consumed in the reaction and was instead being regenerated in a catalytic fashion.

Table 2. Influence of base, crown ether and Pd-catalyst on ring-contraction of naphthopyran 21

Entry	Base	Pd Catalyst	crown Ether	Solvent	Temp.	k/ M.h ⁻¹
1 [‡]	K ₂ CO ₃ (1.5 equiv)	No	No	PhMe	reflux	0.44
2 [‡]	K ₂ CO ₃ (1.5 equiv)	No	18-crown-6 (3.0 equiv)	PhMe	reflux	5.4
3	No	No	18-crown-6 (3.0 equiv)	PhMe	reflux	0
4 [‡]	K ₂ CO ₃ (10 mol%)	No	18-crown-6 (20 mol%)	PhMe	reflux	1.6
5 [‡]	K ₂ CO ₃ (1.5 equiv)	Pd(OAc) ₂ (4 mol%)	18-crown-6 (3.0 equiv)	PhMe	reflux	8.3

[‡] Rate constant data presented in Figure 3. [#] Rate constant data presented in Figure 2.

- K_2CO_3 (1.5 equiv), PhMe:EtOH (1:1), reflux (Entry 9, Table 1)
- ▲ $\text{Pd}(\text{PPh}_3)_4$ (5 mol%), K_2CO_3 (1.5 equiv), PhMe:EtOH (1:1), reflux (Entry 7, Table 1)
- K_2CO_3 (3 equiv), PhMe:EtOH (1:1), reflux (Entry 10, Table 1)
- ◆ K_2CO_3 (10 mol%), 18-crown-6 (20 mol%), PhMe, reflux (Entry 4, Table 2)
- ✚ K_2CO_3 (1.5 equiv), 18-crown-6 (3.0 equiv), PhMe, reflux (Entry 2, Table 2)

Figure 3. Rate Plot showing influence of base and crown ether concentration on rate of ring-contraction of naphthopyran **21**

Since the ring-contraction of 3*H*-naphtho[2,1-*b*]pyran **21** follows zero-order kinetics and operates under catalytic amounts of base, a mechanism for the ring-contraction of the 3*H*-naphtho[2,1-*b*]pyran **21** was proposed. An initial thermal 6π -electrocyclic ring-opening of the pyran unit of **21** led to the formation of the dienone;³⁰ this feature is supported by the reaction mixture taking on an intense orange hue upon heating (Scheme 8). It was rationalized that the non-solvated ‘naked’ carbonate anion would abstract a proton from **23** to generate the allenolate **24**. Considering previous reports of base mediated ring-closure of allenylphenols to benzofurans,³¹ it was proposed that the 5-*exo-dig* cyclization of the allenolate **24** led to the formation of the naphtho[2,1-*b*]furan **22** with regeneration of the base.

Scheme 8. Proposed base-mediated mechanism for the ring-contraction of naphthopyran **21**

Moreover, the influence of the palladium catalyst on the rate of the ring-contraction was also tested. Curiously, when employing Pd(OAc)₂ (4 mol%), 18-crown-6 (3 equiv) and K₂CO₃ (1.5 equiv) in toluene at reflux (Entry 5, Table 2 and Figure 4), the rate constant of the ring-contraction of **21** increased by 35%. This increased rate of the reaction implies that a parallel mechanism mediated by nanoparticulate palladium³² takes place. The oxidative addition of nanoparticulate Pd⁰ to C-1 led to the formation of the π -allyl complex **25** which reorganises to palladacycle **26** (Scheme 9). Hence, the reductive elimination promoted by the base afforded **24** and regenerated the nanoparticulate Pd⁰. In a final step, the 5-*exo-dig* cyclization of **24** led to the formation of the naphtho[2,1-*b*]furan **22** with regeneration of the base.

Scheme 9. Proposed mechanism for the ring-contraction of naphthopyran 21 involving base and Pd-catalyst

Figure 4. Comparative rate plots for the ring-contraction of naphthopyran 21 with and without Pd-catalyst

As a result of this study, an experimental protocol (**Protocol A**) was developed that allowed the complete efficient ring-contraction of 3*H*-naphtho[2,1-*b*]pyran **21** under 9 h of reaction in the absence of palladium, giving the naphtho[2,1-*b*]furan **22** in 80% yield after a simple crystallization from DCM/ hexane (Scheme 10).

Scheme 10. Optimised Pd-free reagent conditions for the ring-contraction of naphthopyran **21 (Protocol A)**

Considering the dramatic effect of the crown ether on the rate of the reaction, the use of the comparatively cheaper tetrabutylammonium bromide (TBAB) was also tested. Thus, by using Pd(OAc)₂ (10 mol%), KOAc (1.9 equiv), TBAB (1 equiv) in DMAc at 150 °C, the naphtho[2,1-*b*]furan **22** was formed as the only product after only 6 h and isolated in 78% yield albeit after column chromatography (Scheme 11). Thus, TBAB constituted an alternative to 18-crown-6 for the ring-contraction process (**Protocol B**). The addition of a catalytic amount of Pd(OAc)₂ was justified by the previously demonstrated enhancement of the rate of the reaction. Furthermore, the use of DMAc allowed the reactions to be performed at a higher temperature than toluene which also contributed to the enhanced kinetics.

Scheme 11. Optimised ring-contraction conditions for naphthopyran 21 in the presence of the Pd-catalyst (Protocol B)

To extend the scope of the ring-contraction to more complex systems and establish a comparison between **Protocols A** and **B**, a variety of substrates that were to hand were subjected to both the ring-contraction protocols (Scheme 12 and Table 3).

Scheme 12. Reagents and conditions for the optimised protocols for the ring-contraction of substituted 3*H*-naphtho[2,1-*b*]pyrans and a benzo-fused dihydroquinoline

Table 3. Selected examples of the ring-contraction of substituted 3*H*-naphtho[2,1-*b*]pyrans, naphthodipyrans and a benzo-fused dihydroquinoline (Ar = 4-MeOC₆H₄)

Entry	Starting Material	Product	NMR (δ)	Yield (%) [Method]
1			δ_H 5.63 (α -H)	
			δ_C 49.8 (α -H)	80 [A]
			δ_H 6.76 (1-H)	78 [B]
2			δ_H 5.42 (α -H)	
			δ_C 46.7 (α -H)	49 [A] 70 [B]
3			δ_H 5.58 (α -H)	
			δ_C 49.8 (α -H)	76 [A]
			δ_H 6.68 (1-H)	87 [B]
4			δ_H 5.87 (α -H)	
			δ_C 46.0 (α -H)	63 [B]
5			δ_H 5.61 (α , β -H)	
			δ_C 49.8 (α , β -H)	88 [A]
			δ_H 6.81 (1, 10-H)	96 [B]

Table 3. Selected examples of the ring-contraction of substituted 3*H*-naphtho[2,1-*b*]pyrans, naphthodipyrans and a benzo-fused dihydroquinoline (Continuation) (Ar = 4-MeOC₆H₄)

Entry	Starting Material	Product	NMR (δ)	Yield (%) [Method]
6	37	38	δ_H 5.60 (α , β -H)	48 [A] 22 [B]
			δ_C 49.8 (α , β -H) δ_H 6.75 (1, 6-H)	
7	39	40	δ_H 5.73 (α , β -H)	74 [A] δ_H 6.68 (1, 6-H)
			δ_C 49.2 (α , β -H)	
8	41	42	δ_H 5.27 (α -H)	80 [A] δ_H 6.56 (1-H)
			δ_C 48.1 (α -H)	

Protocols A and **B** were successfully applied to the electron-rich 3*H*-naphtho[2,1-*b*]pyran **31**, containing an electron-donating morpholino group at C-6, giving the corresponding naphtho[2,1-*b*]furan **32** (Entry 3, Table 3) in good yield (76%, **Protocol A**) and very good yield (87%, **Protocol B**). Furthermore, **Protocol B** was also effectively applied to the ring-contraction of 3*H*-naphtho[2,1-*b*]pyran **33** (Entry 4, Table 3), containing the electron-donating thienyl group at C-3, giving the naphtho[2,1-*b*]furan **34** in 63% yield. As stated before, both

Protocols A and **B** were employed to the more electronically neutral 3*H*-naphtho[2,1-*b*]pyran **21** (Entry 1, Table 3) in similar yield (78 – 80%). Moreover, both procedures (**A** and **B**) were used to ring-contrast bisnaphthopyrans **35** (Entry 5, Table 3) and **37** (Entry 6, Table 3) with comparable yields. Furthermore, **Protocol A** was applied to the synthesis of bisnaphthofuran **40** (Entry 7, Table 3) in good yield (74%). The slower rate of reaction and lower yield of the ring-contraction of the 3*H*-naphtho[2,1-*b*]pyran **29** (Entry 2, Table 3) was possibly due to the increased steric encumbrment of the phenyl at C-1. Furthermore, **Protocol A** was also employed to the ring-contraction of the benzo-1,2-dihydroisoquinoline **41** which afforded the corresponding benzindole **42** in 80% yield (Entry 8, Table 3).

The developed protocols (**A** and **B**) were also applied to the ring-contraction of the isomeric 2*H*-naphtho[1,2-*b*]pyrans **43**, affording the corresponding naphtho[1,2-*b*]furans and unsymmetrical naphthodifurans **44** though in diminished yield (19 – 47%) (Scheme 13 and Table 4). It is generally established that the 2*H*-naphtho[1,2-*b*]pyrans are more prone to degradation when compared to the isomeric 3*H*-naphtho[2,1-*b*]pyrans and this feature might have contributed to the lower yields.³³ Moreover, protocol **B**, with the higher reaction temperature, led to more decomposition when compared to protocol **A**.

Protocol A: K₂CO₃ (1.5 equiv), 18-crown-6 (3.0 equiv), PhMe, reflux, N₂; **Protocol B:** Pd(OAc)₂ (10 mol%), KOAc (2.0 equiv), TBAB (1 equiv), DMAc, 150 °C, N₂

Scheme 13. Reagents and conditions for the optimised protocols for the ring-contraction of substituted 2*H*-naphtho[1,2-*b*]pyrans

Table 4. Selected examples of the ring-contraction of substituted 2*H*-naphtho[1,2-*b*]pyrans (Ar = 4-MeOC₆H₄)

Entry	Starting Material	Product	NMR (δ)	Yield (%) [Method]
1			δ_{H} 5.59 (α -H) δ_{C} 49.8 (α -H) δ_{H} 6.31 (3-H)	19 [A]
2			δ_{H} 5.61 (α -H) δ_{C} 47.2 (α -H)	34 [A] 20 [B]
3			δ_{H} 5.66 (α -H) δ_{C} 49.9 (α -H)	44 [A] [‡] < 11 [B]
4			δ_{H} 5.41 (α -H) δ_{C} 46.7 (α -H)	47 [A] [‡] < 3 [B]

[‡] 4 mol% of Pd(OAc)₂ added.

In summary, **Protocols A** and **B** were similarly effective to perform the ring-contraction of 3*H*-naphtho[2,1-*b*]pyrans of different electronic and steric nature, however **Protocol A** proved to be more suitable for the ring-contraction of the more thermally sensitive 2*H*-naphtho[1,2-*b*]pyrans. Moreover, because the expensive palladium catalyst has a relatively small effect on the rate of ring-contraction of the naphthopyrans, its addition may be avoided.

Another interesting finding was that, by employing K_2CO_3 (1.5 equiv), $\text{Pd}(\text{PPh}_3)_4$ (5 mol%) and 18-crown-6 (3.1 equiv) in toluene at reflux for 19 h, the 8-bromo-3*H*-naphtho[2,1-*b*]pyran **53** was successfully coupled to 4-pyridineboronic acid pinacol ester **54** affording the 8-(4-pyridyl)-3*H*-naphtho[2,1-*b*]pyran that ring-contracted *in situ* to the corresponding naphtho[1,2-*b*]furan **55**. The latter was isolated as the single product of the reaction and was obtained in 47% yield after flash column chromatography (Scheme 14). The foregoing reaction conditions constitute an effective protocol to selectively prepare, in one step, (hetero)aryl substituted naphthofurans via a Suzuki-coupling – ring-contraction process .

Scheme 14. Reaction conditions illustrating selective Suzuki coupling – ring-contraction and selective Suzuki coupling

The ring-contraction of naphthopyrans in palladium-catalysed cross-coupling reactions is very often a nuisance. The formation of naphthofurans as by-products constitutes a very significant practical problem, as the purification by flash column chromatography is extremely difficult due to the similar R_f of the structural isomers in both a variety of mobile and stationary phases. With a view to accomplishing a Suzuki cross-coupling between naphthopyran **53** and boronic acid ester **54**, without the competing ring-contraction, we elected to employ monobasic KF, a weaker base than those employed in the kinetic experiments (Table 1), since KF had found success in Suzuki cross-coupling reactions.³⁴

Thus, when using KF (1.5 equiv) and $\text{Pd}(\text{PPh}_3)_4$ (5 mol%) in PhMe:EtOH (1:1) at reflux, 8-bromo-3*H*-naphtho[2,1-*b*]pyran **53** was successfully coupled to 4-pyridineboronic acid pinacol ester **54** affording the 8-(4-pyridyl)-3*H*-naphtho[2,1-*b*]pyran **56** in 67% yield, without the formation of the corresponding naphtho[2,1-*b*]furan **55** as a by-product (Scheme 14).

One implication of the Suzuki cross-coupling mechanism is that the base is effectively consumed during the catalytic cycle. Since the rate of the Suzuki cross-coupling reaction is generally faster than the rate of the ring-contraction, it was rationalized that employing only 1.5 equiv of KF, no base would be left available to promote the ring-contraction, as it had been consumed during the Suzuki cross-coupling process. However, it was deemed important to explore the likelihood of ring-contraction where excess KF was present. Thus, the use of excess KF (3.0 equiv) with the foregoing cross-coupling conditions again effected smooth conversion to **56** (59%) without any ring-contraction. This developed protocol (unoptimised) allows Suzuki cross-coupling reactions to be performed with naphthopyrans without the ring-contraction side reaction and strongly suggests that the ring-contraction is dependent upon the basicity of the base; thus for selective Suzuki coupling the use of KF is recommended.

Conclusions

The ring-contraction of the model 3,3-bis(4-methoxyphenyl) substituted 3*H*-naphtho[2,1-*b*]pyran **21** has been investigated and found to operate by two independent processes: one involving Pd-catalysis and the other mediated only by the carbonate base. Optimisation of these processes has enabled a series of novel diarylmethyl substituted naphthofurans and a series of symmetrical and unsymmetrical naphthodifurans to be efficiently isolated in good yield. The methodology has been further extended to provide the first example of a ring-contraction of a 3,4-dihydrobenzoquinoline ring to a benzoindole.

By judicious choice of the optimised reaction conditions either a Pd-mediated Suzuki cross-coupling – ring-contraction of a bromonaphthopyran to afford an (hetero)aryl substituted naphthofuran or a selective Pd-mediated Suzuki cross-coupling reaction to afford a (hetero)aryl substituted naphthopyran can be accomplished. Given the wide interest in synthesising complex photochromic naphthopyran containing materials³⁵ which rely upon Pd-mediated methodologies we believe that the latter optimised, selective protocol will be useful to materials scientists.

Experimental Section

Unless otherwise stated, reagents and solvents were purchased from major chemical catalogue companies and were used as supplied. For reactions requiring heating, DrySyn[®] aluminium heating blocks in conjunction with electrical stirrer hotplates were used as the heat source. Substrates for ring-contraction were to hand within the department. ¹H NMR (400 MHz) and ¹³C{¹H} NMR (100 MHz) spectra were recorded on a Bruker Avance DPX400 in either CDCl₃ or d₆-DMSO unless stated otherwise. Chemical shifts are provided in parts per million (ppm) using either the residual solvent peak or TMS as the internal reference. 2D NMR experiments (COSY, HSQC and HMBC) were performed on specific examples to unequivocally sign the

protons of the molecules. Coupling constants (*J*) are provided in Hz. FT-IR spectra were recorded on a Nicolet 380 FTIR spectrophotometer equipped with a diamond ATR attachment (neat sample). Flash column chromatography was performed on chromatography silica gel (either Sigma-Aldrich, 40-63 micron particle size distribution or Fluorochem Silica gel 40-63 micron particle size distribution). All final compounds were homogeneous by TLC using a range of eluent systems of differing polarity (either Merck TLC aluminium sheets silica gel 60 F254 (cat. No 105554) or Fluorochem cat. No. LC0927). Melting points were determined in capillary tubes, using a Stuart SMP10 melting point apparatus, and are uncorrected. Accurate mass measurements were obtained from the Innovative Physical Organic Solutions (IPOS) centre at the University of Huddersfield.

The following benzochromene (naphthopyran) substrates used in this study were prepared according to literature procedures and possessed physical and spectroscopic properties that were in excellent agreement with those previously reported in the literature for their preparation: 3,3-bis(4-methoxyphenyl)-3*H*-benzo[*f*]chromene **21**;³⁶ 4-(3,3-bis(4-methoxyphenyl)-3*H*-benzo[*f*]chromen-6-yl)morpholine **31**;³⁷ 3-(4-methoxyphenyl)-3-(thiophen-2-yl)-3*H*-benzo[*f*]chromene **33**;³⁸ 2,2,11,11-tetrakis(4-methoxyphenyl)-2,11-dihydrobenzo[*f*]pyrano[3,2-*h*]chromene **37**;³⁹ 2,2,8,8-tetrakis(4-methoxyphenyl)-2,8-dihydrochromeno[6,5-*f*]chromene **39**;⁴⁰ 6-methoxy-2,2-bis(4-methoxyphenyl)-2*H*-benzo[*h*]chromene **45**;⁴¹ 6-methoxy-2,2-bis(4-methoxyphenyl)-4-(*p*-tolyl)-2*H*-benzo[*h*]chromene **47**;⁴¹ (6,6-bis(4-methoxyphenyl)-6*H*-benzo[*h*]furo[3,2-*f*]chromen-3-yl)(phenyl)methanone **49**;⁴² (6,6-bis(4-methoxyphenyl)-4-(*p*-tolyl)-6*H*-benzo[*h*]furo[3,2-*f*]chromen-3-yl)(phenyl)methanone **51**⁴² and 8-bromo-3,3-bis(4-methoxyphenyl)-3*H*-benzo[*f*]chromene **53**.⁴⁰

Preparation of Novel Substrates

Synthesis of 3,3-Bis(4-methoxyphenyl)-1-(*p*-tolyl)-3*H*-benzo[*f*]chromene 29: a solution of 2-naphthol (1.01 g, 6.94 mmol), 1,1-bis(4-methoxyphenyl)-3-(*p*-tolyl)prop-2-yn-1-ol (2.55 g, 7.11 mmol), pyridinium *p*-toluenesulfonate (PPTS) (0.18 g, 0.69 mmol) and trimethyl orthoformate (1.52 mL, 13.9 mmol) in 1,2-dichloroethane (75 mL) was heated under reflux (250 mL, 2-neck RBF, 100 °C) until no propynol remained as indicated by TLC (30% EtOAc / hexane, 3 h). The solvent was removed from the cooled reaction mixture and the resulting solid triturated with hexane/EtOAc. The resulting pale solid was collected by vacuum filtration, rinsed with hexane and allowed to dry, giving a pale yellow solid. Purified via recrystallization from EtOAc/hexane to afford 3,3-bis(4-methoxyphenyl)-1-(*p*-tolyl)-3*H*-benzo[*f*]chromene (1.77 g, Yield = 53%). m.p. = 117–119 °C; ν_{max} (neat) 2961, 2834, 1738, 1607, 1507 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ_{H} 2.41 (3H, s, Tol-H), 3.75 (6H, s, An-H), 6.14 (1H, s, 2-H), 6.81 (4H, app. d, $J = 8.8$ Hz, 3', 3'', 5', 5''-H), 7.04 (1H, app. t, $J = 8.2$ Hz, Ar-H), 7.16 – 7.26 (6H, m, Ar-H), 7.31 (1H, d, $J = 8.8$ Hz, Ar-H), 7.44 (4H, app. d, $J = 8.8$ Hz, 2', 2'', 6', 6''-H), 7.67 – 7.71 (2H, m, Ar-H); $^{13}\text{C}\{^1\text{H}\}$ NMR (400 MHz, CDCl_3) δ_{C} 21.3; 55.2, 81.9, 113.3, 116.7, 118.8, 123.1, 124.9, 126.6, 127.9, 128.3, 128.5, 129.1, 129.4, 129.9, 130.2, 130.7, 136.7, 136.8, 137.3, 138.4, 152.6, 158.8; HRMS (ESI) m/z : $[\text{M}+\text{H}]^+$ Calcd for $\text{C}_{34}\text{H}_{29}\text{O}_3^+$ 485.2106; Found 485.2111.

Synthesis of 3,3,10,10-Tetrakis(4-methoxyphenyl)-3*H*,10*H*-chromeno[5,6-*f*]chromene 35: a solution of 2,7-dihydroxynaphthalene (1 mmol), 1,1-bis(4-methoxyphenyl)prop-2-yn-1-ol (2.1 mmol), pyridinium *p*-toluenesulfonate (PPTS) (10 mol%) and trimethyl orthoformate (4 mmol) in 1,2-dichloroethane (6 mL) was heated under reflux until no propynol remained as indicated by TLC (30% EtOAc / hexane) examination of the reaction mixture (*ca.* 2.5 h). The solvent was removed from the reaction mixture and the resulting solid triturated with

hexane/EtOAc. The resulting pale solid was collected by vacuum filtration, rinsed with hexane and allowed to dry, giving a pale yellow solid. Washings with hot EtOH and EtOAc afforded the desired product as an off-white powder (3.37 g, Yield = 82%); m.p. = 220–223 °C; ν_{max} (neat) 1608, 1509, 1298, 1251, 1172, 1034, 985, 954, 836, 729, 580 cm^{-1} ; Photomerocyanine λ_{max} = 448 nm (PhMe); ^1H NMR (400 MHz, CDCl_3) δ_{H} 3.77 (s, 12H, OMe), 6.00 (d, 2H, J = 9.6 Hz, 2, 11-H), 6.83 (app. d, 8H, J = 8.9 Hz, 3', 5', 3'', 5'', 3''', 5''', 3''', 5''''-H), 7.00 (d, 2H, J = 8.7 Hz, 5, 8-H), 7.11 (d, 2H, J = 9.6 Hz, 1, 12-H), 7.40 (app. d, 8H, J = 8.8 Hz, 2', 6', 2'', 6'', 2''', 6''', 2''', 6''''-H), 7.49 (d, 2H, J = 8.7 Hz, 6, 7-H) ppm; $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) δ_{C} 55.2, 81.8, 113.3, 114.7, 115.8, 124.4, 124.7, 125.6, 128.5, 128.5, 130.9, 137.0, 152.8, 158.9 ppm; HRMS (ESI) m/z : $[\text{M}+\text{H}]^+$ Calcd for $\text{C}_{44}\text{H}_{37}\text{O}_6^+$ 661.2585; Found 661.2585.

Synthesis of 4-(3,3,4-Tris(4-methoxyphenyl)-3,4-dihydrobenzo[*f*]quinolin-6-yl)morpholine 41: acidic alumina (3.0 g) was added in a single portion to a stirred warmed (*ca.* 40 °C) solution of 1,1-bis(4-methoxyphenyl)prop-2-yn-1-ol (0.81 g, 3.0 mmol) and *N*-(4-methoxyphenyl)-4-morpholinonaphthalen-2-amine (1.0 g, 3.0 mmol) in toluene (50 mL). The solution was heated to reflux for 3 h and then cooled to *ca.* 60 °C whereupon the mixture was filtered to remove the Al_2O_3 catalyst. The catalyst was washed with EtOAc (2 $\times$ 30 mL) and the combined filtrates evaporated to afford a brown gum which was subjected to flash column chromatography [Aldrich silica gel (60 Å, 230-400 mesh, 40-63 μm), eluent: EtOAc (20%) in hexanes, fraction 2] followed by crystallization from a mixture of DCM/hexane, providing the title product as a pale pink crystalline solid (0.77 g, 1.3 mmol, 44%); m.p. = 211–212 °C; ν_{max} (neat) 2947, 2839, 1607, 1583, 1505, 1441, 1246, 1173, 1116, 1027, 836, 737, 538 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ_{H} 2.87 (4H, bs, $\text{N}(\text{CH}_2)_2$), 3.71 (3H, s, OMe), 3.74 (6H, s, OMe), 3.87 (4H, t, J = 4.4 Hz, $\text{O}(\text{CH}_2)_2$), 5.98 (1H, d, J = 9.7 Hz, 2-H), 6.32 (1H, s, 5-H), 6.57 (2H, app. d, J = 8.8 Hz, Ar-H), 6.72 (4H, app. d, J = 8.7 Hz, Ar-H), 6.83 (2H, app. d, J = 8.8 Hz,

Ar-H), 7.15–7.22 (2H, m, Ar-H), 7.26–7.29 (5H, m, Ar-H), 7.37 (1H, t, $J = 7.6$ Hz, 9-H), 7.89 (1H, d, $J = 8.5$ Hz, 10-H), 8.01 (1H, d, $J = 8.4$ Hz, 7-H) ppm; $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) δ_{C} 53.2, 55.19, 55.24, 67.4, 70.3, 107.8, 109.3, 112.8, 113.8, 117.6, 121.6, 121.7, 122.6, 123.7, 126.6, 128.0, 130.0, 131.6, 131.7, 137.7, 138.0, 142.3, 149.8, 157.0, 158.2 ppm; HRMS (ESI) m/z : $[\text{M}+\text{H}]^+$ Calcd for $\text{C}_{38}\text{H}_{37}\text{N}_2\text{O}_4^+$ 585.2748; Found 585.2746.

Ring-Contraction Experiments

1. Kinetic Study of the Ring-Contraction of 3,3-Bis(4-methoxyphenyl)-3*H*-naphtho[2,1-*b*]pyran **21**

Entry 1, Table 1. 3,3-Bis(4-methoxyphenyl)-3*H*-naphtho[2,1-*b*]pyran **21** (0.01 g, 0.03 mmol) was dissolved in DCM and stirred in a sealed flask at room temperature. After 18 h, ^1H NMR analysis had shown no change in the reaction mixture.

Entry 2, Table 1. 3,3-Bis(4-methoxyphenyl)-3*H*-naphtho[2,1-*b*]pyran **21** (0.01 g, 0.03 mmol) was dissolved in PhMe and stirred in a sealed flask at room temperature. After 17 h, ^1H NMR analysis had shown no change in the reaction mixture.

Entry 3, Table 1. 3,3-Bis(4-methoxyphenyl)-3*H*-naphtho[2,1-*b*]pyran **21** (0.01 g, 0.03 mmol) was mixed in EtOH and stirred in a sealed flask at room temperature. After 28 h, ^1H NMR analysis had shown no change in the reaction mixture.

Entry 4, Table 1. 3,3-Bis(4-methoxyphenyl)-3*H*-naphtho[2,1-*b*]pyran **21** (0.01 g, 0.03 mmol) was dissolved in PhMe:EtOH (1:1) and stirred in a sealed flask at room temperature. After 15 h, ^1H NMR analysis had shown no change in the reaction mixture. 3,3-Bis(4-methoxyphenyl)-3*H*-naphtho[2,1-*b*]pyran **21** (0.01 g, 0.03 mmol) was dissolved in PhMe:EtOH (1:1) and stirred in a reaction vessel at reflux. After 14 h, ^1H NMR analysis had shown no change in the reaction mixture.

Entry 5, Table 1. 3,3-Bis(4-methoxyphenyl)-3*H*-naphtho[2,1-*b*]pyran **21** (0.01 g, 0.03 mmol) was dissolved in DMAc and stirred in a sealed flask at room temperature. After 28 h, ¹H NMR analysis had shown no change in the reaction mixture. 3,3-Bis(4-methoxyphenyl)-3*H*-naphtho[2,1-*b*]pyran **21** (0.01 g, 0.03 mmol) was dissolved in DMAc and stirred in a reaction vessel at 150 °C. After 14 h, ¹H NMR analysis had shown no change in the reaction mixture.

Entry 6, Table 1. 3,3-Bis(4-methoxyphenyl)-3*H*-naphtho[2,1-*b*]pyran **21** (0.01 g, 0.03 mmol) was dissolved in DCM and a catalytic amount of Pd(PPh₃)₄ was added, and stirred in a sealed flask at room temperature. After 23 h, ¹H NMR analysis had shown no change in the reaction mixture

Entry 7, Table 1. 3,3-Bis(4-methoxyphenyl)-3*H*-naphtho[2,1-*b*]pyran **21** (250.2 mg, 0.6343 mmol), K₂CO₃ (126.2 mg, 0.9131 mmol) and Pd(PPh₃)₄ (35.2 mg, 0.0305 mmol) were dissolved in PhMe (6 mL) and EtOH (6 mL), and refluxed under N₂ for 48 h. ¹H NMR analysis showed a 1.0:3.5 (**21:22**) mixture.

Entry 8, Table 1. 3,3-Bis(4-methoxyphenyl)-3*H*-naphtho[2,1-*b*]pyran **21** (0.51 g, 1.3 mmol) and KOAc (0.25 g, 2.5 mmol) were dissolved in DMAc (20 mL) and degassed with N₂ for 15 minutes at room temperature. Then Pd(OAc)₂ (0.0287 g, 0.127 mmol) was added and the mixture heated to 150 °C, and the reaction followed by TLC (25% EtOAc in hexanes). After 5 h, the reaction mixture was added to water (100 mL) and extracted with DCM (3 × 50 mL). The combined organic layers were washed with water (3 × 50 mL), the organic layer reduced, re-dissolved in EtOAc (50 mL) and filtered. The filtrate was washed with brine (8 × 50 mL) and the organic layer reduced to afford the crude product (0.35 g). ¹H NMR analysis showed a 1.0:1.1 (**21:22**) mixture.

Entry 9, Table 1. 3,3-Bis(4-methoxyphenyl)-3*H*-naphtho[2,1-*b*]pyran **21** (250.9 mg, 0.6360 mmol) and K₂CO₃ (125.7 mg, 0.9095 mmol) were dissolved in PhMe (6 mL) and EtOH (6 mL), and refluxed under N₂. ¹H NMR analysis showed a 1.0:2.0 (**21:22**) mixture after 80 h.

Entry 10, Table 1. 3,3-Bis(4-methoxyphenyl)-3*H*-naphtho[2,1-*b*]pyran (100.0 mg, 0.2535 mmol), K₂CO₃ (105.1 mg, 0.7605 mmol) in PhMe (3 mL) and ethanol (3 mL) was heated at reflux under N₂. ¹H NMR analysis showed full conversion to **22** after 74 h.

Entry 11, Table 1. 3,3-Bis(4-methoxyphenyl)-3*H*-naphtho[2,1-*b*]pyran **21** (250.2 mg, 0.6343 mmol) and Pd(PPh₃)₄ (35.3 mg, 0.0305 mmol) were dissolved in PhMe (6 mL) and EtOH (6 mL), and refluxed under N₂ for 48 h. ¹H NMR analysis had shown no change in the reaction mixture.

Entry 12, Table 1. 3,3-Bis(4-methoxyphenyl)-3*H*-naphtho[2,1-*b*]pyran (200.9 mg, 0.5093 mmol), Cs₂CO₃ (248.3 mg, 0.7621 mmol) were dissolved in PhMe (5 mL) and EtOH (5 mL), and refluxed under N₂. ¹H NMR analysis showed a 1.0:2.0 (**21:22**) mixture after 80 h.

Entry 13, Table 1. 3,3-Bis(4-methoxyphenyl)-3*H*-naphtho[2,1-*b*]pyran (200.9 mg, 0.5093 mmol), Li₂CO₃ (56.7 mg, 0.767 mmol) were dissolved in PhMe (5 mL) and EtOH (5 mL), and refluxed under N₂. ¹H NMR analysis showed a 1.8:1.0 (**21:22**) mixture after 80 h.

Entry 14, Table 1. 3,3-Bis(4-methoxyphenyl)-3*H*-naphtho[2,1-*b*]pyran (200.6 mg, 0.5085 mmol), Na₂CO₃ (80.7 mg, 0.761 mmol) were dissolved in PhMe (5 mL) and EtOH (5 mL), and refluxed under N₂. ¹H NMR analysis showed a 1.1:1.0 (**21:22**) mixture after 80 h.

Entry 15, Table 1. 3,3-Bis(4-methoxyphenyl)-3*H*-naphtho[2,1-*b*]pyran (199.8 mg, 0.5065 mmol), K₃PO₄ (161.4 mg, 0.7604 mmol) were dissolved in PhMe (5 mL) and EtOH (5 mL), and refluxed under N₂. ¹H NMR analysis showed a 1.7:1.0 (**21:22**) mixture after 14 h.

Entry 1, Table 2. 3,3-Bis(4-methoxyphenyl)-3*H*-naphtho[2,1-*b*]pyran **21** (250.9 mg, 0.6360 mmol) and K₂CO₃ (125.7 mg, 0.9095 mmol) were dissolved in PhMe (6 mL) and EtOH (6 mL), and refluxed under N₂. Several samples were obtained over time and subjected to ¹H NMR analysis.

Entry 2, Table 2. 3,3-Bis(4-methoxyphenyl)-3*H*-naphtho[2,1-*b*]pyran **21** (199.9 mg, 0.5068 mmol), K₂CO₃ (105.0 mg, 0.7597 mmol) and 18-crown-6 (415.3 mg, 1.571 mmol) were dissolved in PhMe (10 mL), and refluxed under N₂. Several samples were obtained over time and subjected to ¹H NMR analysis.

Entry 3, Table 2. 3,3-Bis(4-methoxyphenyl)-3*H*-naphtho[2,1-*b*]pyran **21** (152.8 mg, 0.3874 mmol) and 18-crown-6 (387.4 mg, 1.221 mmol) were dissolved in PhMe (7.4 mL), and refluxed under N₂. ¹H NMR analysis had shown no change in the reaction mixture.

Entry 4, Table 2. 3,3-Bis(4-methoxyphenyl)-3*H*-naphtho[2,1-*b*]pyran (427.7 mg, 1.084 mmol), K₂CO₃ (14.9 mg, 0.108 mmol) and 18-crown-6 (57.0 mg, 0.216 mmol) were dissolved in PhMe (28 mL), and refluxed under N₂. Several samples were obtained over time and subjected to ¹H NMR analysis.

Entry 5, Table 2. 3,3-Bis(4-methoxyphenyl)-3*H*-naphtho[2,1-*b*]pyran (120.5 mg, 0.3055 mmol), K₂CO₃ (62.7 mg, 0.454 mmol), 18-crown-6 (243.6 mg, 0.9216 mmol) and Pd(OAc)₂ (2.6 mg, 0.012 mmol) were dissolved in PhMe (6.0 mL), and refluxed under N₂. Several samples were obtained over time and subjected to ¹H NMR analysis.

2. General Experimental Procedure for the Pyran (Dihydroquinoline) Ring-Contraction

Protocol A: a mixture of naphthopyran (1.3 mmol), 18-crown-6 (3.93 mmol), K₂CO₃ (1.9 mmol) in PhMe (25.0 mL) was heated at reflux under N₂. After the completion of the reaction, the crude was evaporated to dryness. The residue was dissolved in DCM (150 mL), washed

with water (3×150 mL), the organic layer dried with anhydrous sodium sulfate and the solvent removed under reduced pressure, giving the corresponding product after purification if needed.

Note: Pd(OAc)₂ (4 mol%) was added to the reaction mixture when noted.

Protocol B: a mixture of naphthopyran (1.27 mmol), KOAc (2.54 mmol) and TBAB (1.27 mmol) in anhydrous *N,N*-dimethylacetamide (20 mL) was deaerated with N₂ for 20 min. Hence, Pd(OAc)₂ (10 mol %) was added and the mixture heated at 150 °C until TLC examination of the reaction mixture indicated that no naphthopyran remained. When the reaction was judged to be complete (4 – 8 h typical reaction time), the crude was cooled, diluted with EtOAc (150 mL) and filtered. The solution was washed with brine (6×50 mL) and water (2×50 mL), before drying with anhydrous sodium sulfate and removal of the solvent. The residue was subjected to flash column chromatography to afford the title compound.

Entry 1, Table 3. 2-(Bis(4-methoxyphenyl)methyl)naphtho[2,1-*b*]furan 22. Protocol A: from 3,3-bis(4-methoxyphenyl)-3*H*-naphtho[2,1-*b*]pyran **21** (0.50 g, 1.3 mmol) after 9 h of reaction; crystallization from a mixture of DCM/hexane gave the corresponding product as a yellow crystalline solid (0.40 g, 80%). **Protocol B:** from 3,3-bis(4-methoxyphenyl)-3*H*-naphtho[2,1-*b*]pyran **21** (0.50 g, 1.3 mmol) after elution from silica gel with EtOAc (25%) in hexanes as off-white microcrystals (0.39 g, 78%). m.p. = 172–173 °C; ν_{max} (neat) 1607, 1581, 1505, 1440, 1243, 1176, 1027, 807, 746, 584 cm⁻¹; NMR (400 MHz, CDCl₃) δ_{H} 3.81 (6H, s, OMe), 5.59 (1H, s, α -H), 6.73 (1H, s, 1-H), 6.88 (4H, app. d, J = 8.6 Hz, 3', 5', 3'', 5''-H), 7.17 (4H, app. d, J = 8.6 Hz, 2', 6', 2'', 6''-H), 7.44 (1H, app. t, J = 7.5 Hz, 8-H), 7.52 (1H, app. t, J = 7.5 Hz, 7-H), 7.58 (1H, d, J = 9.0 Hz, 5-H), 7.66 (1H, d, J = 9.0 Hz, 4-H), 7.91 (1H, d, J = 8.1 Hz, 9-H), 8.01 (1H, d, J = 8.2 Hz, 6-H) ppm; ¹³C{¹H} NMR (100 MHz, CDCl₃) δ_{C} 49.8, 55.3, 104.4, 112.4, 114.0, 123.4, 123.6, 124.3, 124.5, 126.1, 127.5, 128.7, 129.8, 130.2, 133.7,

152.4, 158.5, 160.0 ppm; HRMS (ESI) m/z : $[M+H]^+$ Calcd for $C_{27}H_{23}O_3^+$ 395.1642; Found 395.1634.

Entry 2, Table 3. 2-(Bis(4-methoxyphenyl)methyl)-1-(*p*-tolyl)naphtho[2,1-*b*]furan 30.

Protocol A: from 3,3-bis(4-methoxyphenyl)-1-(*p*-tolyl)-3*H*-naphtho[2,1-*b*]pyran **29** (75.6 mg, 0.156 mmol) after 64 h of reaction; Purification by preparative TLC [Merck Silica gel 60 F₂₅₄, EtOAc (10%) in hexanes, fraction 2] led to the corresponding product as an off-white powder (38.6 mg, 49%). **Protocol B:** from 3,3-bis(4-methoxyphenyl)-1-(*p*-tolyl)-3*H*-naphtho[2,1-*b*]pyran **29** (0.50 g, 1.0 mmol) after elution from silica gel with DCM (50%) in hexanes as colourless microcrystals (0.35 g, 70%). m.p.= 164–165 °C; $\nu_{\max}$ (neat) 2929, 2833, 1608, 1582, 1507, 1461, 1244, 1175, 1033, 1004, 822, 746, 569 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ_{H} 2.49 (3H, s, Me), 3.77 (6H, s, OMe), 5.38 (1H, s, α -H), 6.82 (4H, app. d, J = 8.7 Hz, 3', 5', 3'', 5''-H), 7.15 (4H, app. d, J = 8.7 Hz, 2', 6', 2'', 6''-H), 7.25–7.38 (6H, m, Ar-H), 7.64 (1H, d, J = 8.9 Hz, 4-H), 7.69 (1H, d, J = 8.9 Hz, 5-H), 7.74 (1H, d, J = 8.3 Hz, 9-H), 7.89 (1H, d, J = 8.0 Hz, 6-H) ppm; $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) δ_{C} 21.4, 46.6, 55.2, 112.6, 113.3, 113.8, 120.0, 122.2, 123.3, 124.1, 124.9, 125.7, 128.2, 128.5, 128.8, 129.5, 129.9, 130.4, 130.71, 130.74, 134.3, 137.5, 151.9, 154.5, 158.2 ppm; HRMS (ESI) m/z : $[M+H]^+$ Calcd for $C_{34}H_{29}O_3^+$ 485.2111; Found 485.2105.

Entry 3, Table 3. 4-(2-(Bis(4-methoxyphenyl)methyl)naphtho[2,1-*b*]furan-5-yl)morpholine 32. Protocol A: from 3,3-bis(4-methoxyphenyl)-6-morpholino-3*H*-

naphtho[2,1-*b*]pyran **31** (0.17 g, 0.35 mmol) after 9 h of reaction; Flash column chromatography [Aldrich silica gel (60 Å, 40-63 μm), eluent: EtOAc (25%) in petroleum ether, fraction 1] led to the corresponding product as a white powder (0.13 g, 76%). **Protocol B:** from 3,3-bis(4-methoxyphenyl)-6-morpholino-3*H*-naphtho[2,1-*b*]pyran **31** (1.0 g, 2.1 mmol) after elution from silica gel with EtOAc (20%) in hexanes as an off-white powder (0.87 g, 87%);

Flash column chromatography [Aldrich silica gel (60 Å, 40-63 µm), eluent: EtOAc (25%) in petroleum ether, fraction 1] led to the corresponding product as a white powder (0.13 g, 76%). m.p. = 178–180 °C; ν_{max} (neat) 2963, 1606, 1507, 1301, 1241, 1145, 1129, 1029, 801, 579, 564 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ_{H} 3.02 (4H, bs, $\text{N}(\text{CH}_2)_2$), 3.73 (6H, s, OMe), 3.92 (4H, t, $J = 4.5$ Hz, $\text{O}(\text{CH}_2)_2$), 5.49 (1H, s, α -H), 6.59 (1H, s, 1-H), 6.80 (4H, app. d, $J = 8.7$ Hz, 3', 5', 3'', 5''-H), 7.10 (4H, app. d, $J = 8.7$ Hz, 2', 6', 2'', 6''-H), 7.22 (1H, s, 4-H), 7.38–7.44 (2H, m, Ar-H), 7.93 (1H, d, $J = 7.6$ Hz, 9-H), 8.22 (1H, d, $J = 8.1$ Hz, 6-H) ppm; $^{13}\text{C}\{^1\text{H}\}$ NMR (CDCl_3) δ_{C} 48.8, 52.8, 54.2, 66.4, 101.5, 103.1, 112.9, 118.7, 123.0, 123.4, 125.0, 125.3, 127.2, 128.8, 132.7, 146.1, 151.5, 157.5, 158.2 ppm; HRMS (ESI) m/z : $[\text{M}+\text{H}]^+$ Calcd for $\text{C}_{31}\text{H}_{30}\text{NO}_4^+$ 480.2169; Found 480.2169.

Entry 4, Table 3. 2-((4-Methoxyphenyl)(thiophen-2-yl)methyl)naphtho[2,1-*b*]furan 34.

Protocol B: from 3-(4-methoxyphenyl)-3-(thiophen-2-yl)-3*H*-naphtho[2,1-*b*]pyran **33** (1.0 g, 2.7 mmol) after elution from SiO_2 with EtOAc (20 %) in hexanes as an off-white powder (0.63 g, 63%). m.p. = 158–160 °C; ν_{max} (neat) 2955, 2930, 2834, 1608, 1586, 1509, 1463, 1441, 1383, 1249, 1109, 1030, 991, 954, 854, 804, 774, 744, 718, 559, 530.0 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ_{H} 3.83 (3H, s, OMe), 5.87 (1H, s, α -H), 6.92 – 6.95 (4H, m, Ar-H), 7.02 (1H, app. t, $J = 3.7$ Hz, Ar-H), 7.28 – 7.34 (3H, m, Ar-H), 7.49 (1H, app. t, $J = 7.6$ Hz, Ar-H), 7.57 (1H, app. t, $J = 7.2$ Hz, Ar-H), 7.62 (1H, d, $J = 8.9$ Hz, 4-H), 7.70 (1H, d, $J = 8.9$ Hz, 5-H), 7.95 (1H, d, $J = 8.0$ Hz, 6-H), 8.07 (1H, d, $J = 8.1$ Hz, 9-H); $^{13}\text{C}\{^1\text{H}\}$ NMR (400 MHz, CDCl_3) δ_{C} 46.0, 55.3, 104.0, 112.4, 114.1, 123.49, 123.51, 124.4, 124.8, 124.9, 126.2, 126.8, 127.6, 128.8, 129.6, 130.3, 133.2, 145.1, 152.5, 158.86, 158.90; HRMS (ESI) m/z : $[\text{M}+\text{H}]^+$ Calcd for $\text{C}_{24}\text{H}_{19}\text{O}_2\text{S}^+$ 371.1100; Found 371.1104.

Entry 5, Table 3. 2,9-Bis(bis(4-methoxyphenyl)methyl)naphtho[2,1-*b*:7,8-*b'*]difuran 36.

Protocol A: from 3,3,10,10-tetrakis(4-methoxyphenyl)-3,10-dihydrochromeno[5,6-

f]chromene **35** (0.50 g, 0.76 mmol) after 9 h of reaction; brown powder (0.44 g, 88%). **Protocol B:** from 3,3,10,10-tetrakis(4-methoxyphenyl)-3,10-dihydrochromeno[5,6-*f*]chromene **35** (0.5 g, 0.8 mmol) after elution from SiO₂ with EtOAc (25%) in hexanes as an off-white powder (0.48 g, 96%). m.p. = 160–162 °C; ν_{max} (neat) 2927, 2833, 1609, 1507, 1301, 1248, 1173, 1024, 810, 770, 567 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ_{H} 3.79 (12H, s, OMe), 5.59 (2H, s, α , β -H), 6.79 (2H, s, 1, 10-H), 6.86 (8H, app. d, J = 8.7 Hz, 3', 5', 3'', 5'', 3''', 5''', 3''', 5''''-H), 7.17 (8H, app. d, J = 8.7 Hz, 2', 6', 2'', 6'', 2''', 6''', 2''', 6''''-H), 7.55 (2H, d, J = 8.9 Hz, 5, 6-H), 7.74 (2H, d, J = 8.9 Hz, 4, 7-H) ppm; ¹³C{¹H} NMR (100 MHz, CDCl₃) δ_{C} 49.8, 55.3, 105.3, 110.5, 114.0, 121.5, 122.0, 125.4, 127.0, 129.8, 133.8, 153.2, 158.5, 159.5 ppm; HRMS (ESI) m/z : [M+H]⁺ Calcd for C₄₄H₃₇O₆⁺ 661.2585; Found 661.2553.

Entry 6, Table 3. 2,9-Bis(bis(4-methoxyphenyl)methyl)naphtho[2,1-*b*:3,4-*b'*]difuran **38.**

Protocol A: from 2,2,11,11-tetrakis(4-methoxyphenyl)-2,11-dihydrobenzo[*f*]pyrano[3,2-*h*]chromene **37** (0.50 g, 0.76 mmol) after 9 h of reaction; Crystallization from a mixture of DCM/hexane led to the corresponding product as a brown crystalline powder (0.24 g, 48%).

Protocol B: from 2,2,11,11-tetrakis(4-methoxyphenyl)-2,11-dihydrobenzo[*f*]pyrano[3,2-*h*]chromene **37** (0.5 g, 0.8 mmol) after elution from SiO₂ with EtOAc (20 %) in hexanes as an off-white powder (0.10 g, 20%). m.p. = 184–188 °C (darkened at 141 °C); ν_{max} (neat) 2930, 2833, 1606, 1582, 1508, 1440, 1238, 1175, 1110, 1028, 815, 760, 556 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ_{H} 3.80 (12H, s, OMe), 5.60 (2H, s, α , β -H), 6.75 (2H, s, 3, 8-H), 6.86 (8H, app. d, J = 8.6 Hz, 3', 5', 3'', 5'', 3''', 5''', 3''', 5''''-H), 7.16 (8H, app. d, J = 8.6 Hz, 2', 6', 2'', 6'', 2''', 6''', 2''', 6''''-H), 7.46–7.49 (2H, m, 5, 6-H), 8.03–8.05 (2H, m, 4, 7-H) ppm; ¹³C{¹H} NMR (100 MHz, CDCl₃) δ_{C} 49.8, 55.3, 105.2, 114.0, 122.2, 124.1, 124.7, 124.9, 129.8, 133.7, 139.5, 158.5, 159.4 ppm; HRMS (ESI) m/z : [M+K]⁺ Calcd for C₄₄H₃₆O₆K⁺ 699.2143; Found 699.2135.

Entry 7, Table 3. 2,7-Bis(bis(4-methoxyphenyl)methyl)naphtho[2,1-*b*:6,5-*b'*]difuran 40.

Protocol A: from 2,2,8,8-tetrakis(4-methoxyphenyl)-2,8-dihydrochromeno[6,5-*f*]chromene **39** (0.50 g, 0.76 mmol) after 21 h of reaction; After the reaction was completed, the crude was evaporated to dryness. Afterwards, PhMe (200 mL) was added and the resulting mixture filtered hot. The resulting filtrand was poured into water (50 mL), filtered off, rinsed with water (100 mL), cold PhMe (15 mL) and cold Et₂O (5 mL) giving the corresponding product as an off-white powder (0.16 g, 32%). The former filtrate was reduced and the solid filtered off, rinsed with water (100 mL), cold PhMe (15 mL) and cold Et₂O (5 mL) giving the corresponding product as an off-white powder (0.21 g, 42%). m.p. = 279–282 °C (darkened at 264 °C); $\nu_{\max}$ (neat) 2834, 1606, 1508, 1239, 1175, 1156, 1033, 816, 571 cm⁻¹; ¹H NMR (400 MHz, DMSO-*d*₆) δ_{H} 3.74 (12H, s, OMe), 5.7 (2H, s, α , β -H), 6.93 (8H, app. d, J = 8.7 Hz, Ar-H), 7.08 (2H, s, 1, 6-H), 7.22 (8H, app. d, J = 8.7 Hz, Ar-H), 7.74 (2H, d, J = 9.0 Hz, Ar-H), 8.08 (2H, d, J = 9.0 Hz, Ar-H) ppm; ¹³C{¹H} NMR (100 MHz, DMSO-*d*₆)[‡] δ_{C} 49.2, 55.5, 104.5, 112.5, 114.4, 120.6, 124.2, 124.6, 130.0, 134.0, 151.4, 158.4, 160.5 ppm; HRMS (ESI) m/z : [M+K]⁺ Calcd for C₄₄H₃₆O₆K⁺ 699.2143; Found 699.2144.

[‡]Due to the low solubility of the compound, the ¹³C NMR peaks were inferred from HSQC and HMBC analysis.

Entry 8, Table 3. 4-(2-(Bis(4-methoxyphenyl)methyl)-3-phenyl-3*H*-benzo[*e*]indol-5-

yl)morpholine 42. Protocol A: from 4-(3,3,4-tris(4-methoxyphenyl)-3,4-dihydrobenzo[*f*]quinolin-6-yl)morpholine **41** (0.50 g, 0.86 mmol) after 9 days of reaction; The residue was crystallized from a mixture of DCM/hexane giving the corresponding product as an off-white crystalline solid (0.28 g, 56%); The resulting mother-liquor was purified by flash column chromatography [Aldrich silica gel (60 Å, 40-63 μ m), eluent: EtOAc (25%) in hexanes, fraction 2] giving the corresponding product as a beige powder (0.12 g, 24%); m.p. = 215–217

°C; $\nu_{\max}$ (neat) 2969, 1508, 1457, 1358, 1244, 1174, 1114, 1035, 842, 760 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ_{H} 2.98 (4H, bs, $\text{N}(\text{CH}_2)_2$), 3.78 (6H, s, OMe), 3.86 (3H, s, 4'''-OMe), 3.92 (4H, t, $J = 4.5$ Hz, $\text{O}(\text{CH}_2)_2$), 5.27 (1H, s, α -H), 6.56 (1H, s, 1-H), 6.76–6.79 (5H, m, Ar-H), 6.88–6.90 (2H, m, Ar-H), 6.99 (6H, app. d, $J = 8.6$ Hz, Ar-H), 7.37–7.41 (1H, m, 7-H), 7.46–7.50 (1H, m, 8-H), 8.13 (1H, app. d, $J = 7.7$ Hz, 9-H), 8.26 (1H, app. d, $J = 8.3$ Hz, 6-H) ppm; $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) δ_{C} 48.1, 53.9, 55.3, 55.5, 67.6, 101.7, 101.9, 113.6, 114.4, 119.1, 123.0, 123.6, 124.2, 125.3, 125.8, 128.6, 129.9, 130.0, 130.1, 134.9, 135.1, 142.2, 145.2, 158.1, 159.2 ppm; HRMS (ESI) m/z : $[\text{M}+\text{H}]^+$ Calcd for $\text{C}_{38}\text{H}_{37}\text{N}_2\text{O}_4^+$ 585.2748; Found 585.2748.

Entry 1, Table 4. 2-(Bis(4-methoxyphenyl)methyl)-5-methoxynaphtho[1,2-*b*]furan 46.

Protocol A: from 6-methoxy-2,2-bis(4-methoxyphenyl)-2*H*-naphtho[1,2-*b*]pyran **45** (185.5 mg, 0.4370 mmol) after 9 h of reaction; Purification by preparative TLC [Merck Silica gel 60 F₂₅₄, eluent: EtOAc (10%) in hexanes, fraction 1] led to the corresponding product as an off-white powder (34.9 mg, 19%). m.p. = 115–118 °C; $\nu_{\max}$ (neat) 2926, 2834, 1607, 1588, 1508, 1456, 1378, 1240, 1176, 1032, 830, 770, 549 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ_{H} 3.79 (6H, s, OMe), 3.98 (3H, s, 5-OMe), 5.59 (1H, s, α -H), 6.31 (1H, d, $J = 0.9$ Hz, 3-H), 6.83–6.87 (5H, m, Ar-H), 7.14–7.17 (4H, m, Ar-H), 7.41–7.45 (1H, m, 7-H), 7.51–7.55 (1H, m, 8-H), 8.13 (1H, app. d, $J = 7.9$ Hz, 9-H), 8.28 (1H, app. d, $J = 8.3$ Hz, 6-H) ppm; $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) δ_{C} 49.8, 55.3, 55.9, 96.9, 106.6, 113.9, 119.8, 121.7, 122.9, 123.2, 123.6, 124.2, 126.7, 129.8, 134.1, 145.3, 152.0, 158.4, 159.7 ppm; HRMS (ESI) m/z : $[\text{M}+\text{H}]^+$ Calcd for $\text{C}_{28}\text{H}_{25}\text{O}_4^+$ 425.1747; Found 425.1749.

Entry 2, Table 4. 2-(Bis(4-methoxyphenyl)methyl)-5-methoxy-3-(*p*-tolyl)naphtho[1,2-*b*]furan 48. Protocol A: from 6-methoxy-2,2-bis(4-methoxyphenyl)-4-(*p*-tolyl)-2*H*-naphtho[1,2-*b*]pyran **47** (0.50 g, 0.97 mmol) after 25 h of reaction; Purification by flash column

chromatography [Aldrich silica gel (60 Å, 40-63 µm), eluent: EtOAc (10%) in hexanes, fraction 1] gave the corresponding product as an off-white powder (0.17 g, 34%). **Protocol B:** from 6-methoxy-2,2-bis(4-methoxyphenyl)-4-(*p*-tolyl)-2*H*-naphtho[1,2-*b*]pyran **47** (0.50 g, 0.97 mmol) after 22 h of reaction; The residue was purified by flash column chromatography [Aldrich silica gel (60 Å, 40-63 µm), eluent: EtOAc (10%) in hexanes, fraction 1] giving the corresponding product as an off-white powder (0.10 g, 20%). m.p. = 196–200 °C; ν_{max} (neat) 2926, 2832, 1610, 1585, 1507, 1459, 1376, 1247, 1173, 1034, 831, 765, 515 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ_{H} 2.45 (3H, s, CH₃), 3.77 (6H, s, OMe), 3.97 (3H, s, OMe), 5.61 (1H, s, α -H), 6.83 (4H, app. d, J = 8.7 Hz, 3', 3'', 5', 5''-H), 6.91 (1H, s, 4-H), 7.23 (4H, app. d, J = 8.7 Hz, 2', 6', 2'', 6''-H), 7.32 (2H, app. d, J = 7.9 Hz, Ar-H), 7.40 (2H, app. d, J = 7.9 Hz, Ar-H), 7.43–7.47 (1H, m, Ar-H), 7.54–7.58 (1H, m, Ar-H), 8.19 (1H, app. d, J = 7.9 Hz, 9-H), 8.29 (1H, app. d, J = 8.3 Hz, 6-H) ppm; ¹³C{¹H} NMR (76 MHz, CDCl₃) δ_{C} 21.3, 47.2, 55.3, 56.0, 95.9, 113.8, 119.6, 119.9, 121.7, 123.0, 123.2, 123.9, 124.4, 126.8, 129.2, 129.6, 129.8, 130.0, 134.6, 137.1, 144.8, 152.3, 153.5, 158.3 ppm; HRMS (ESI) m/z : [M+H]⁺ Calcd for C₃₅H₃₁O₄⁺ 515.2217; Found 515.2207.

Entry 3, Table 4. (5-(Bis(4-methoxyphenyl)methyl)naphtho[1,2-*b*:4,3-*b'*]difuran-3-yl)(phenyl)methanone 50. **Protocol A:** from (6,6-bis(4-methoxyphenyl)-6*H*-benzo[*h*]furo[3,2-*f*]chromen-3-yl)(phenyl)methanone **49** (208.0 mg, 0.3862 mmol) after 14 h of reaction – Pd(OAc)₂ (4 mol%) was added to the reaction mixture. Purification by flash column chromatography [Aldrich silica gel (60 Å, 40-63 µm), eluent: EtOAc (10%) in hexanes, fraction 1], followed by trituration from hexanes, gave the corresponding product as an off-white powder (92.1 mg, 44%). **Protocol B:** from (6,6-bis(4-methoxyphenyl)-6*H*-benzo[*h*]furo[3,2-*f*]chromen-3-yl)(phenyl)methanone **49** (139.5 mg, 0.2590 mmol) after 14 h of reaction. Flash column chromatography [Aldrich silica gel (60 Å, 40-63 µm), eluent: EtOAc

(10%) in petroleum ether, fraction 1] led to the corresponding product as a not entirely pure pale-yellow powder (15.5 mg, < 11%). m.p. = 188–190 °C; ν_{max} (neat) 1653, 1508, 1244, 1180, 1171, 1148, 1107, 1034, 880, 771, 674, 560 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ_{H} 3.80 (6H, s, OMe), 5.66 (1H, s, α -H), 6.86 (4H, app. d, J = 8.6 Hz, 3', 3'', 5', 5''-H), 7.07 (1H, s, 3-H), 7.20 (4H, app. d, J = 8.6 Hz, 2', 2'', 6', 6''-H), 7.50 – 7.64 (5H, m, Ar-H), 7.92 (2H, d, J = 7.2 Hz, Ar-H), 8.20 (1H, s, 5-H), 8.30 – 8.36 (2H, m, Ar-H) ppm; $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) δ_{C} 49.9, 55.3, 107.8, 113.9, 115.1, 118.0, 118.3, 119.9, 120.7, 120.9, 123.3, 125.5, 126.2, 128.7, 129.0, 129.8, 132.6, 134.0, 139.3, 148.3, 148.7, 151.1, 158.4, 159.6, 190.3 ppm; HRMS (ESI) m/z : $[\text{M}+\text{H}]^+$ Calcd for $\text{C}_{36}\text{H}_{27}\text{O}_5^+$ 539.1858; Found 539.1851.

Entry 4, Table 4. (5-(Bis(4-methoxyphenyl)methyl)-4-(*p*-tolyl)naphtho[1,2-*b*:4,3-*b'*]difuran-3-yl)(phenyl)methanone 52. Protocol A: from (6,6-bis(4-methoxyphenyl)-4-(*p*-tolyl)-6*H*-benzo[*h*]furo[3,2-*f*]chromen-3-yl)(phenyl)methanone **51** (0.30 g, 0.48 mmol) after 14 h of reaction – $\text{Pd}(\text{OAc})_2$ (4 mol%) was added to the reaction mixture. Purification by flash column chromatography [Aldrich silica gel (60 Å, 40–63 μm), eluent: EtOAc (10%) in petroleum ether, fraction 1], followed by crystallization from EtOAc (10%) in petroleum ether, led to the corresponding product as an off-white powder (0.14 g, 47%). **Protocol B:** from (6,6-bis(4-methoxyphenyl)-4-(*p*-tolyl)-6*H*-benzo[*h*]furo[3,2-*f*]chromen-3-yl)(phenyl)methanone **51** (0.30 g, 0.48 mmol) after 14 h of reaction. Purification by flash column chromatography [Aldrich silica gel (60 Å, 40–63 μm), eluent: EtOAc (10%) in petroleum ether, fraction 1], followed by crystallization from EtOAc (10%) in petroleum ether, led to the corresponding product as a not entirely pure pale-yellow powder (0.01 g, < 3%). m.p. = 195–197 °C; ν_{max} (neat) 1654, 1601, 1506, 1455, 1245, 1231, 1174, 1029, 886, 767, 689, 557 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ_{H} 2.30 (3H, s, CH_3), 3.78 (6H, s, OMe), 5.41 (1H, s, α -H), 6.79 – 6.86 (8H, m, Ar-H), 7.15 – 7.21 (6H, m, Ar-H), 7.39 (1H, t, J = 7.4 Hz, Ar-H), 7.45 (1H, d, J = 7.5 Hz, Ar-

H), 7.60 – 7.64 (2H, m, Ar-H), 8.02 (1H, s, 5-H), 8.33 – 8.36 (1H, m, Ar-H), 8.38 – 8.41 (1H, m, Ar-H) ppm; $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) δ_{C} 21.2, 46.7, 55.2, 113.8, 114.5, 117.2, 118.8, 119.8, 120.1, 120.9, 123.8, 125.7, 126.2, 127.7, 128.7, 129.5, 129.6, 129.8, 129.9, 132.7, 134.4, 136.6, 136.9, 146.1, 147.6, 148.6, 154.3, 158.3, 189.4 ppm; HRMS (ESI) m/z : $[\text{M}+\text{H}]^+$ Calcd for $\text{C}_{43}\text{H}_{33}\text{O}_5^+$ 629.2328; Found 629.2331.

Experimental Procedure for the Synthesis of 4-(2-(bis(4-methoxyphenyl)methyl)naphtho[2,1-*b*]furan-7-yl)pyridine 55: a mixture of 8-bromo-3,3-bis(4-methoxyphenyl)-3*H*-naphtho[2,1-*b*]pyran **53** (200.1 mg, 0.4227 mmol), 4-pyridineboronic acid pinacol ester **54** (129.9 mg, 0.6335 mmol), K_2CO_3 (87.6 mg, 0.634 mmol), 18-crown-6 (347.0 mg, 1.313 mmol) and $\text{Pd}(\text{PPh}_3)_4$ (24.8 mg, 0.0215 mmol) in PhMe (10.0 mL) was heated at reflux under N_2 for 19 h. After this time, the mixture was cooled and poured into water (100 mL). Afterwards, the residue was extracted with DCM (3×100 mL), washed with water (3×150 mL), the organic layer dried over anhydrous sodium sulphate and the solvent removed under reduced pressure. Flash column chromatography [Fluorochem silica gel (60 Å, 40-63 µm), eluent: MeOH (4%) in DCM, fraction 5], followed by trituration with ethylic ether, led to the corresponding product as a yellow powder.

2-(Bis(4-methoxyphenyl)methyl)-7-(4-pyridyl)naphtho[2,1-*b*]furan 55. Yellow powder (93.8 mg, 47%); m.p. = 168–172 °C; ν_{max} (neat) 1594, 1507, 1462, 1301, 1244, 1174, 1031, 994, 805, 727, 586 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ_{H} 3.81 (s, 6H, OMe), 5.61 (s, 1H, α -H), 6.75 (s, 1H, 1-H), 6.90 (app. d, 4H, $J = 8.6$ Hz, 3', 5', 3'', 5''-H), 7.18 (app. d, 4H, $J = 8.6$ Hz, 2', 6', 2'', 6''-H), 7.63–7.66 (m, 3H, 4, 2''', 6'''-H), 7.74 (d, 1H, $J = 8.9$ Hz, 5-H), 7.79 (dd, 1H, $J = 8.5, 1.5$ Hz, 8-H), 8.12 (d, 1H, $J = 8.5$ Hz, 9-H), 8.20 (app. s, 1H, 6-H), 8.69 (d, 2H, $J = 4.7$ Hz, 3''', 5'''-H) ppm; $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) δ_{C} 49.9, 55.3, 104.4, 113.3, 114.0, 121.8, 123.6, 124.57, 124.64, 124.9, 127.3, 127.7, 129.8, 130.4, 133.5, 133.8, 148.6, 150.1,

153.0, 158.6, 160.6 ppm; HRMS (ESI) m/z: [M+H]⁺ Calcd for C₃₂H₂₆NO₃⁺ 472.1907; Found 472.1908.

Experimental Procedure for the Synthesis of 3,3-Bis(4-methoxyphenyl)-8-(4-pyridyl)-3*H*-naphtho[2,1-*b*]pyran **56 using KF (1.5 equiv):** a mixture of 8-bromo-3,3-bis(4-methoxyphenyl)-3*H*-naphtho[2,1-*b*]pyran **53** (200.0 mg, 0.4225 mmol), 4-pyridineboronic acid pinacol ester **54** (129.7 mg, 0.6325 mmol), KF (37.0 mg, 0.637 mmol) and Pd(PPh₃)₄ (24.5 mg, 0.0212 mmol) in PhMe (5.0 mL) and ethanol (5.0 mL) was heated at reflux under N₂ for 15h. After this time, the mixture was evaporated to dryness. Afterwards, the residue was extracted with DCM (3 × 100 mL), washed with water (3 × 150 mL), the organic layer dried over anhydrous sodium sulphate and the solvent removed under reduced pressure. Flash column chromatography [Fluorochem silica gel (60 Å, 40-63 µm), MeOH (4%) in DCM, fraction 2], followed by trituration with diethyl ether, led to the corresponding product as a white powder.

Experimental Procedure for the Synthesis of 3,3-Bis(4-methoxyphenyl)-8-(4-pyridyl)-3*H*-naphtho[2,1-*b*]pyran **56 using KF (3.0 equiv):** a mixture of 8-bromo-3,3-bis(4-methoxyphenyl)-3*H*-naphtho[2,1-*b*]pyran **53** (101.3 mg, 0.2140 mmol), 4-pyridineboronic acid pinacol ester **54** (64.6 mg, 0.315 mmol), KF (36.8 mg, 0.633 mmol) and Pd(PPh₃)₄ (12.6 mg, 0.0109 mmol) in PhMe (2.0 mL) and ethanol (2.0 mL) was heated at reflux under N₂ for 13h. After this time, the mixture was evaporated to dryness. Afterwards, the residue was dissolved in EtOAc (40 mL), washed with water (2 × 40 mL), the organic layer dried with anhydrous sodium sulphate and the solvent removed under reduced pressure. Flash column chromatography [Fluorochem silica gel (60 Å, 40-63 µm), MeOH (4%) in DCM, fraction 2], followed by trituration with diethyl ether, led to the corresponding product as a white powder.

3,3-Bis(4-methoxyphenyl)-8-(4-pyridyl)-3*H*-naphtho[2,1-*b*]pyran 56. White powder [(132.8 mg, 67% using KF 1.5 equiv); (59.1 mg, 59% using KF 3.0 equiv)]; m.p. = 180–184 °C; ν_{max} (neat) 1581, 1505, 1462, 1303, 1250, 1173, 1032, 999, 955, 810, 787, 725, 552 cm^{-1} ; Photomerocyanine λ_{max} = 482 nm (PhMe); ^1H NMR (400 MHz, CDCl_3) δ_{H} 3.77 (s, 6H, OMe), 6.25 (d, 1H, J = 10.0 Hz, 2-H), 6.85 (app. d, 4H, J = 8.8 Hz, 3', 5', 3'', 5''-H), 7.22 (d, 1H, J = 8.8 Hz, 5-H), 7.29 (d, 1H, J = 10.0 Hz, 1-H), 7.39 (app. d, 4H, J = 8.8 Hz, 2', 6', 2'', 6''-H), 7.59 (d, 2H, J = 5.3 Hz, 2''', 6'''-H), 7.71–7.75 (m, 2H, 6, 9-H), 7.99 (app. s, 1H, 7-H), 8.05 (d, 1H, J = 8.8 Hz, 10-H), 8.67 (d, 2H, J = 5.3 Hz, 3''', 5'''-H) ppm; $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) δ_{C} 55.3, 82.5, 113.4, 114.0, 118.9, 119.3, 121.5, 122.5, 125.1, 127.0, 128.4, 128.5, 129.3, 129.9, 130.3, 133.0, 137.0, 148.1, 150.3, 151.4, 159.0 ppm; HRMS (ESI) m/z : $[\text{M}+\text{H}]^+$ Calcd for $\text{C}_{32}\text{H}_{20}\text{NO}_3^+$ 472.1907; Found 472.1900.

Associated Content

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.xxxxxxx.

Description of Kinetics Experiments, ^1H and $^{13}\text{C}\{^1\text{H}\}$ NMR Spectra, Mass Spectral Data for compounds 22, 29, 30, 32, 34, 35, 36, 38, 40, 41, 42, 46, 48, 50, 52, 55 and 56. Selected 2D NMR Spectra for compound 40 (PDF)

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Notes

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