ChemInform Abstract: Reactions of o-Quinone Methides with Pyridinium Methylides: A Diastereoselective Synthesis of 1,2-Dihydronaphtho[2,1-b]furans and 2,3-Dihydrobenzofurans.

ARTICLE *in* THE JOURNAL OF ORGANIC CHEMISTRY · MAY 2013

Impact Factor: 4.72 · DOI: 10.1021/jo400621r · Source: PubMed

3 AUTHORS:

V. A. Osyanin
Samara State Technical University
53 PUBLICATIONS **119** CITATIONS
SEE PROFILE

Dmitry Osipov
Samara State Technical University
20 PUBLICATIONS **71** CITATIONS
SEE PROFILE

Yuri Klimochkin
Samara State Technical University
146 PUBLICATIONS **199** CITATIONS
SEE PROFILE

JOC The Journal of Organic Chemistry

Article

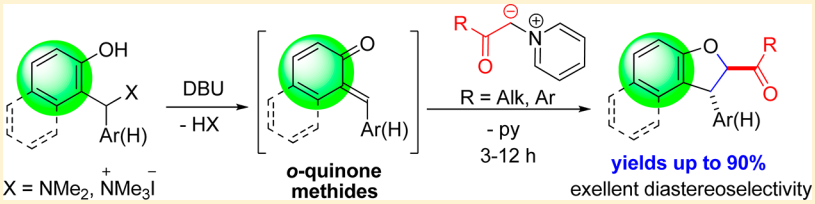
pubs.acs.org/joc

Reactions of *o*-Quinone Methides with Pyridinium Methylides: A Diastereoselective Synthesis of 1,2-Dihydronaphtho[2,1-*b*]furans and 2,3-Dihydrobenzofurans

Vitaly A. Osyanin,* Dmitry V. Osipov, and Yuri N. Klimochkin

Department of Organic Chemistry, Samara State Technical University, 244 Molodogvardeiskaya Street, 443100 Samara, Russian Federation

Supporting Information



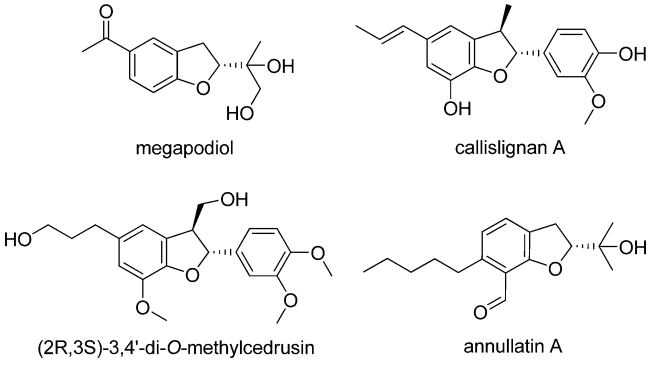
ABSTRACT: A simple, general route to the 1,2-dihydronaphtho[2,1-*b*]furans and 2,3-dihydrobenzofurans substituted at C-2 by an acyl or aryl group, starting from phenolic Mannich bases and pyridinium ylides, has been developed. The mechanism of the reaction is believed to involve the formation of the *o*-quinone methide intermediate, Michael-type addition of the ylide to the *o*-quinone methide, followed by intramolecular nucleophilic substitution.

INTRODUCTION

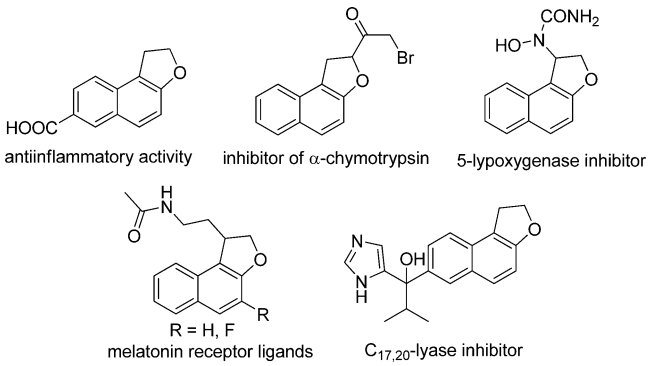
The dihydrobenzo(naphtho)furans belong to an important class of heterocycles, principally because this ring-system constitutes the core skeleton of an increasing number of pharmaceuticals and biologically active natural products. Remarkable examples of this class are the antileukemic agent megapodiol,[1] neolignan callislignan A, which exhibits antibacterial activity against *Staphylococcus aureus*,[2] the antitumor neolignan (2*R*,3*S*)-3,4′-di-*O*-methylcedrusin,[3] as well as isolated from *Cordyceps annullata* annullatin A, which exhibits potent agonistic activity toward the cannabinoid receptors CB1 and CB2 (Scheme 1).[4]

In addition, 1,2-dihydronaphtho[2,1-*b*]furans occupy a prominent place in medicinal chemistry due to their diverse pharmacological activities (Scheme 2).[5−9] Thus, the development of new and efficient methods for the synthesis of dihydrobenzo(naphtho)furans remains an area of current interest.

Scheme 1. Selection of Natural Products Containing 2,3-Dihydrobenzofuran Rings



Scheme 2. Biologically Relevant 1,2-Dihydronaphtho[2,1-*b*]furans



Although various methods for the preparation of 2,3-dihydrobenzofurans have been reported,[10] there are few reports about the synthesis of 1,2-dihydronaphtho[2,1-*b*]furans. Claisen rearrangement of allyl 2-naphthyl ethers in 1-allyl-2-naphthols followed by cyclization is the most frequently used to prepare 1,2-dihydro[2,1-*b*]naphthofurans.[11−15] Another synthetic path includes rearrangement of dihydronaphtho[1,2]-dioxines (prepared from 1-vinylnaphthalenes) to 1-(β-keto)-2-

Received: March 25, 2013
Published: May 13, 2013

   dx.doi.org/10.1021/jo400621r | *J. Org. Chem.* 2013, 78, 5505−5520

naphthols, which reacted with methyl(triphenylphosphoranylidene)acetate to afford 2,2-disubstituted 1,2-dihydronaphtho[2,1-*b*]furans.[16] $PdCl_2$-catalyzed cleavage of the cyclopropane ring in 1-(2-ethylcyclopropyl)naphthalen-2-ol resulted in formation of 2-ethyl-2-methyl-1,2-dihydronaphtho[2,1-*b*]furan.[17] Treatment of 2-naphthols with ethyl 2,3-dibromopropanoate in the presence of potassium carbonate gave the ethyl 1,2-dihydronaphtho[2,1-*b*]furan-2-carboxylates.[18] Reaction of 2,2-dialkylacetaldehydes with 2-naphthols in the presence of *p*-TSA under microwave irradiation conditions resulted in formation of 2,2-dialkyl-1,2-dihydronaphtho[2,1-*b*]furans.[11] Unsubstituted 1,2-dihydronaphtho[2,1-*b*]furan was prepared by reaction of 2-naphthol Mannich bases or their quaternized derivatives with dimethylsulfoxonium methylide or diazomethane.[19,20] 7-Bromo-1,2-dihydronaphtho[2,1-*b*]furan was produced by *o*-allylation of 6-bromo-2-naphthol followed by ozonolysis, reduction cleavage and finally ring closure under the action of acid.[9] Besides, 1-methyl-1,2-dihydronaphtho[2,1-*b*]furan was prepared from allyl 1-bromo-2-naphthyl ether by $S_{RN}1$ photostimulated cyclization[21] and 2-(1-hydroxy-1-methylethyl)-1,2-dihydronaphtho[2,1-*b*]furan-1-ol from corresponding *β*-hydroxy-*α*-tosyloxy ester.[22] Regarding the synthesis 2-acyl-1,2-dihydronaphtho[2,1-*b*]furans, to date only three reports can be found. Known approaches involve the Friedel–Crafts alkylation/annulation cascade reaction between chalcone epoxides and 2-naphthols,[23] the reaction of dimethylsulfonium ylides with quaternary salt on the base of 1-dimethylaminomethyl-2-naphthol,[24] and the condensation of 2-naphthol with 3,4-dibromobutan-2-one in the presence of potassium carbonate.[18]

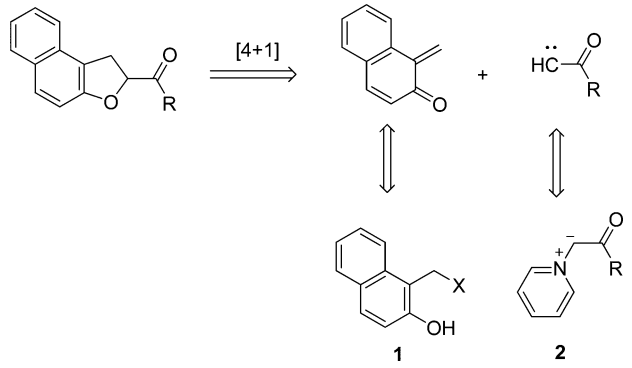
Cascade reactions have attracted considerable attention in organic synthesis as they can produce target products from readily available starting materials in a single operation without isolating the intermediates, thus reducing reaction times, labor, cost.[25] Compared to stepwise reactions, cascade processes minimize waste since the amounts of solvents, reagents, adsorbents and energy are decreased. As part of an overall synthetic program directed toward the development of new cascade transformations utilizing *o*-quinone methides (*o*-QMs),[26] we have focused attention on the synthesis of 1,2-dihydronaphtho[2,1-*b*]furans.

RESULTS AND DISCUSSION

A retrosynthetic analysis of the 2-acyl-1,2-dihydronaphtho[2,1-*b*]furans shows that they can be obtained starting from *o*-QMs and acyl carbenes as a result of the formal [4 + 1]-cycloaddition (Scheme 3). As synthetic equivalents of acyl carbenes the pyridinium ylides **2** can be used. Pyridinium ylides have a rich chemistry that can be used for rapid preparation of highly functionalized compounds from relatively simple compounds.[27]

The *o*-QM moiety is known to be a powerful synthon for preparation of various fused pyran and furan derivatives.[28] They are highly reactive, short-lived intermediates used in organic synthesis, acting as electrophilic enones toward nucleophiles. The high reactivities of *o*-QMs are due mainly to the tendency of their quinoid system of bonds to convert to a more stable aromatic system. There are many strategies, which have been established in order to generate *o*-QMs in situ in the past years.[29] In our work, *o*-QMs have been generated from different *o*-hydroxybenzyl derivatives, basically, from 2-naphtholic Mannich bases **1** via base-induced desamination. It is interesting to note that in solutions a number of Mannich bases of type **1** exhibited thermochromic properties due to their

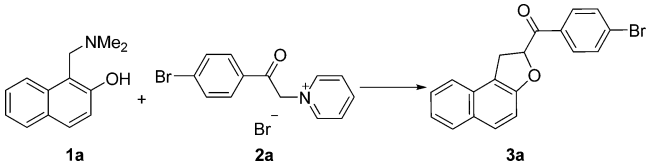
Scheme 3. Retrosynthetic Approach to 1,2-Dihydronaphtho[2,1-*b*]furans



reversible dissociation into dimethylamine and *o*-QMs. In organic solvents, solutions of **1**, colorless at first, gradually became yellow as a result of the establishment of an equilibrium. Heating of the solutions resulted in deepening of the color because of a shift of the equilibrium toward formation of *o*-QMs.

Using 1-[(dimethylamino)methyl]-2-naphthol **1a** and *N*-(4-bromophenacyl)pyridinium bromide **2a** (pK_a 9.4[30]) in equimolar amounts as a model system, a comprehensive review of reaction conditions for the synthesis of 1,2-dihydronaphtho[2,1-*b*]furan **3a** is presented in Table 1. The reaction was

Table 1. Optimization of Reaction Conditions for the Synthesis of 3a



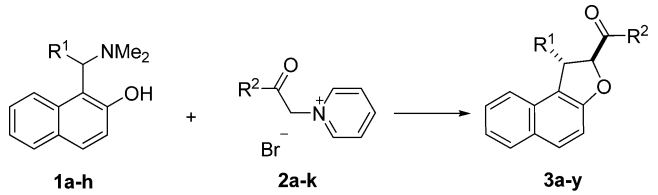
entry	solvent/*T* (°C)	base/quantity (equiv)	time (h)	yield[a] (%)
1	CH_3CN/81	–	5	82
2	CH_3CN/81	DBU/0.1	3	82
		DBU/0.5	3	80
		DBU/1	3	79
3	CH_3CN/81	TMG/1	3	80
4	CH_3CN/81	TEA/1	3	79
5	EtOH/78	–	3	85
6	EtOH/78	DBU/1	3	84
7	dioxane/101	DBU/1	10	75
8	DMF/80	DBU/1	3	83
9	$C_2H_4Cl_2$/84	DBU/1	10	73

[a]Isolated yield.

completed within 5 h in the absence of base at reflux temperature in acetonitrile (entry 1). However, under the same reaction conditions, by employing 0.1 equiv of DBU (pK_a 12), the reaction afforded expected product in up to 82% yield within 3 h of reaction time (entry 2). Increasing the catalyst to 0.5 and 1 equiv results in slight decrease of the reaction yields. When this reaction was repeated at room temperature, no desired product was formed. We also used different bases for this reaction. Replacement of DBU with 1,1,3,3-tetramethylguanidine (pK_a 13.6) or triethylamine (pK_a 10.75) also led to similar reaction yields (entries 3, 4), indicating a slight effect on the nature of the base on this process. Further, the effect of

dx.doi.org/10.1021/jo400621r | J. Org. Chem. 2013, 78, 5505–5520

Table 2. Synthesis of 1,2-Dihydronaphtho[2,1-*b*]furans



1a-h **2a-k** **3a-y**

entry	R^1 (Mannich base)	R^2 (pyridinium salt)	product	solvent	base	time (h)	yield[a] (%)
1	H (**1a**)	4-Br-C_6H_4 (**2a**)	**3a**	CH_3CN	–	3	82
				CH_3CN	DBU	3	74[b]
2	H (**1a**)	4-NO_2-C_6H_4 (**2b**)	**3b**	CH_3CN	–	3	34
3	H (**1a**)	4-F-C_6H_4 (**2c**)	**3c**	CH_3CN	–	3	79
4	H (**1a**)	4-CH_3-C_6H_4 (**2d**)	**3d**	CH_3CN	–	8	81
5	H (**1a**)	1-naphthyl (**2e**)	**3e**	CH_3CN	–	3	72
6	H (**1b**)	1-Ad (**2f**)	**3f**	EtOH	TMG	5	77
7	Ph (**1b**)	Ph (**2g**)	**3g**	CH_3CN	TMG	5	71
				EtOH	TMG	5	54
8	Ph (**1b**)	4-Br-C_6H_4 (**2a**)	**3h**	CH_3CN	DBU	3	89
				CH_3CN	–	10	67
9	Ph (**1b**)	1-naphthyl (**2e**)	**3i**	CH_3CN	DBU	4	62
				CH_3CN	–	4	90
10	Ph (**1b**)	$(CH_3)_3C$ (**2h**)	**3j**	CH_3CN	TMG	4	80
11	Ph (**1b**)	cyclopropyl (**2i**)	**3k**	CH_3CN	TMG	5	75
12	Ph (**1b**)	1-Ad (**2f**)	**3l**	EtOH	TMG	4	84
13	4-CH_3O-C_6H_4 (**1c**)	4-Cl-C_6H_4 (**2j**)	**3m**	CH_3CN	DBU	4	72
14	4-CH_3O-C_6H_4 (**1c**)	1-Ad (**2f**)	**3n**	EtOH	TMG	4	63
15	4-Cl-C_6H_4 (**1d**)	4-Cl-C_6H_4 (**2j**)	**3o**	CH_3CN	DBU	4	88
16	4-Cl-C_6H_4 (**1d**)	$(CH_3)_3C$ (**2h**)	**3p**	CH_3CN	DBU	3	72
17	4-Cl-C_6H_4 (**1d**)	1-Ad (**2f**)	**3q**	EtOH	DBU	3	78
18	4-Cl-C_6H_4 (**1d**)	4-F-C_6H_4 (**2c**)	**3r**	CH_3CN	–	4	84
19	4-Cl-C_6H_4 (**1d**)	4-CH_3-C_6H_4 (**2d**)	**3s**	CH_3CN	–	8	71
20	2-thienyl (**1e**)	$(CH_3)_3C$ (**2h**)	**3t**	CH_3CN	TMG	5	84
21	2-thienyl (**1e**)	1-Ad (**2f**)	**3u**	EtOH	TMG	5	80
22	3-NO_2-C_6H_4 (**1f**)	1-Ad (**2f**)	**3v**	EtOH	TMG	5	61
23	2-F-C_6H_4 (**1g**)	1-Ad (**2f**)	**3w**	EtOH	TMG	12	64
24	4-pyridyl (**1h**)	1-Ad (**2f**)	**3x**	EtOH	TMG	5	81
25	H (**1a**)	NH_2 (**2k**)	**3y**	CH_3CN	TMG	8	69[c]

[a]Isolated yield. [b]Methiodide of **1a** is used instead of Mannich base **1a**. [c]1-(2-Amino-2-oxoethyl)pyridinium chloride **2k** was used.

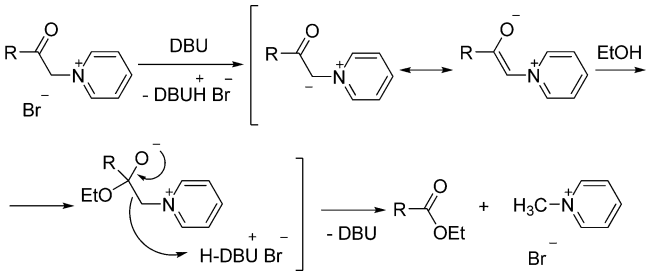
different solvents, such as EtOH, 1,4-dioxane, dichloroethane, and DMF was also investigated in the presence of 1 equiv of DBU. EtOH and DMF also gave good results (entries 5, 6, 8). 1,4-Dioxane and dichloroethane gave less satisfactory results because of the poor solubility of the pyridinium salt **2a** (entries 7, 9). In the case of EtOH and CH_3CN the product **3a** precipitated from the reaction mixture and was isolated by filtration. Conventional chromatographic purification was not required. The reaction was repeated on several different scales (up to 20 mmol), all with comparable yields.

Under the optimized reaction conditions, the scope and generality of this new one-pot process were then explored. As shown in Table 2, the cascade reaction proceed without any problems for a wide range of substrates bearing electron-donating or electron-withdrawing substituents on the aryl ring, providing 1,2-dihydronaphtho[2,1-*b*]furans in good yields and excellent diastereoselectivity. In particular, the sterically hindered adamantyl-substituted 1,2-dihydronaphtho[2,1-*b*]-furans were obtained in good yields, indicating that steric hindrance had no obvious influence on the efficiency of our method. Formation of *cis*-isomers was not noticed according to ^{1}H NMR data. 1-Unsubstituted 1,2-dihydronaphtho[2,1-*b*]-furans can be prepared in good yields without any base (entries 1−6, Table 2). Moreover, in the case of 4-nitrophenacylpyridinium bromide **2b**, the corresponding 1,2-dihydronaphtho-[2,1-*b*]furan **3b** cannot be isolated in the presence of 1 equiv of DBU or TMG. The deep colored unidentifiable products were noticed. In the absence of any base, dimethylamine (pK_a 10.7) released during the thermal decomposition of Mannich base acts as a base deprotonating the pyridinium salt. However, in the case of the pyridinium salts with poor solubility, the addition of a base not only decreases the reaction time but also increases the product yields.

It is known that in the *N*-phenacylpyridinium salts the reactivity of *N*-methylene group is comparable with that of the methylene group of *β*-keto esters.[31] In particular, the action of base rapidly generates ylides and further action results in cleavage to an acid and an alkylpyridinium salt (acid splitting) by a mechanism similar to that involved in the fission of *β*-dicarbonyl compounds. Protic solvents promote acid splitting of reactive ylides (Scheme 4).[32] For this reason, in the case of reactivity ylides acetonitrile should be used as a solvent instead of ethanol.

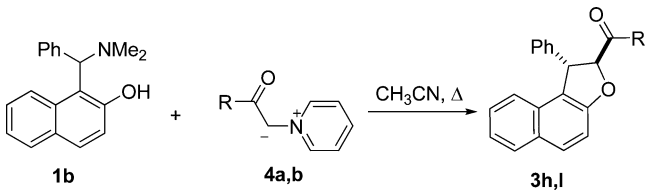
dx.doi.org/10.1021/jo400621r | J. Org. Chem. 2013, 78, 5505−5520

Scheme 4. Base-Catalysed Decomposition of *N*-Phenacylpyridinium Salts



Many carbonyl-stabilized pyridinium ylides are stable under normal conditions and thus can be both used in the individual state and generated from the appropriate pyridinium salts under the action of bases. When the pyridinium ylides **4a** and **4b**, instead of pyridinium salts **2a** and **2f**, were directly used without base, products **3h** and **3l** were also obtained in 77 and 79% yields, respectively (Scheme 5).

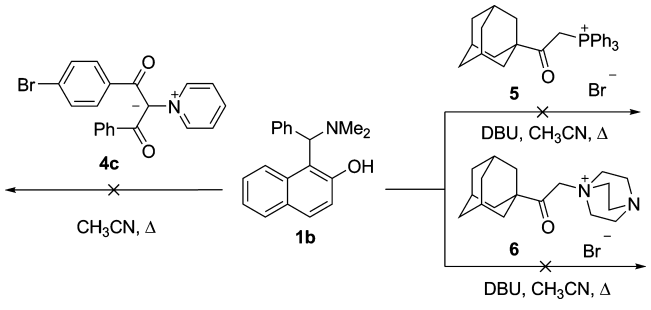
Scheme 5. Synthesis of 3h and 3l from Pyridinium Acylmethylides



Pyridinium salts bearing other functional groups (CO_2Et, CN, $CONH_2$ instead of RCO) were also investigated under the reaction conditions. However, the reaction was very sluggish, and a complicated mixture of products, including the expected dihydronaphthofuran, was obtained, which was difficult to separate. Nevertheless, we have succeeded in preparing the amide **3y** (entry 25, Table 2) in 69% yield. The highly stabilized ylide **4c**, phosphonic **5** and ammonium **6** salts in the presence of DBU also failed to effect addition even after 12 h at reflux temperature (Scheme 6).

It is interesting to note that 2-bromopyridinium salt **7** in the presence of TEA or DBU did not react with 1,2-naphthoquinone-1-methide generated from Mannich base **1b** but underwent cyclization in oxazolo[3,2-*a*]pyridinium salt **8** (Scheme 7).

Scheme 6. Studying the Possibility of Interaction of Mannich Base 1b with Other Ylides



Instead of carbonyl-stabilized pyridinium ylides, arylmethylides can also be used in this cascade reaction (Scheme 8). The pyridinium salts **9a,b** gave lower yields than **1** in the few examples investigated, but this result may well be due to failure to find the best experimental and isolation procedures. In this way 2-aryl-1,2-dihydronaphtho[2,1-*b*]furans **10a–c** were synthesized from Mannich bases **1a,b**. This reaction was then extended to heterocyclic precursors of *o*-QMs. From Mannich bases **1i,j** heterocyclic systems 7,8-dihydrofurano[3,2-*e*][1]-benzofuran **10d** and 1,6-dihydro-2*H*-furo[3,2-*e*]indole **10e** were prepared in moderate yields.

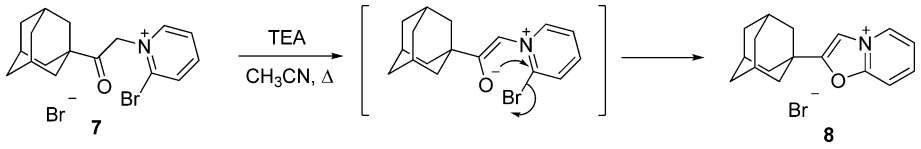
The 1,2-dihydronaphtho[2,1-*b*]furans can be easily aromatized to the corresponding naphtho[2,1-*b*]furans by oxidation with DDQ in refluxing toluene. For example, the heating of 1,2-dihydronaphtho[2,1-*b*]furans **3i,r,s,v** with 1.1 equiv of DDQ gives naphtho[2,1-*b*]furans **11a–d** in 65–81% yields (Scheme 9). In some cases, the reaction of 2-naphthol Mannich bases with *N*-phenacylpyridinium bromides gave the aromatization products as an impurity with the 1,2-dihydronaphtho[2,1-*b*]furans. The high tendency toward oxidation is related to the extension of the conjugation involving the benzene ring.

Structural assignment was based on elemental analyses and absence of an OH-band in the IR and of the phenolic proton signal in the ^{1}H NMR spectra of the dihydroarenofuran derivatives. The IR spectra of compounds **3a–x** show the presence of a carbonyl group (υ_{max} 1670–1717 cm^{-1}). The structure of 1,2-disubstituted dihydronaphtho[2,1-*b*]furans are clearly assigned as *trans* by the analysis of the vicinal coupling constant of the two methine protons. These protons at 1- and 2-positions of dihydronaphtho[2,1-*b*]furan ring display two doublets at 5.13–6.02 ppm with the vicinal coupling constant J = 4.9–5.6 Hz. It has been established that in *cis*-1,2-dihydronaphtho[2,1-*b*]furans the vicinal coupling constant of the two methine protons is 9.5–10.0 Hz, while in *trans*-isomers vicinal coupling constant is 5.3–5.7 Hz.[23] In the ^{1}H NMR spectra of 1-unsubstituted 1,2-dihydronaphtho[2,1-*b*]furans the H-2 proton signal of the dihydrofuran ring is seen in the 5.41–6.53 ppm region as a doublet of doublets due to a vicinal splitting by the methylene group protons. The latter also appear as doublets of doublets at 3.13–3.90 ppm. In the ^{13}C NMR spectra of the 1,2-disubstituted dihydronaphtho[2,1-*b*]furans, the carbonyl carbon signals are found in the region of 193.6–211.4 ppm, and the signals of carbon atoms in the 1- and 2-positions of the dihydrofuran fragment appear at 42.9–51.3 and 88.6–94.4 ppm, respectively.

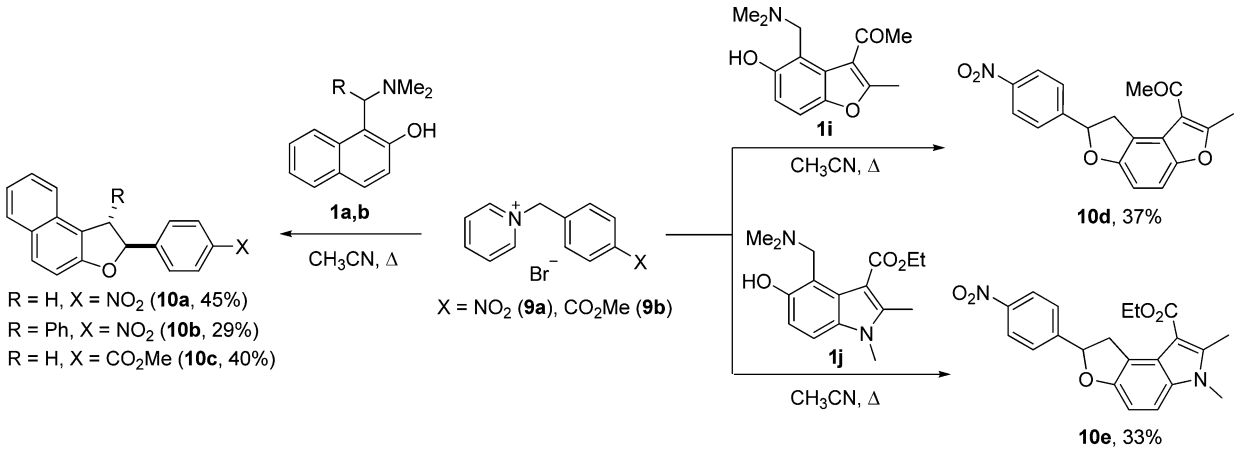
A mechanistic rationale portraying the probable sequence of events is given in Scheme 10. The first step is the formation of the two reaction intermediates. *o*-QM **A** is formed by the thermal decomposition of the Mannich base and deprotonation of the pyridinium salt gives ylide **B**. The second step is a Michael-type addition of a pyridinium ylide to the electron-deficient *o*-QM to afford the zwitterion intermediate **C**, which might react further according to three different paths to give three different products. In the first path, the three-membered ring C-cyclization could give the cyclopropane derivative,[27b] which is not observed here. The 1,3-dipolar character of the ylides, normally observed with a wide variety of electron-poor olefins,[33] is in this case not expressed (path 2). Probably, cyclopropanation and 1,3-dipolar cycloaddition are highly disfavored energetically because of the necessity for loss of aromaticity. In the third path, phenolate form **C** undergoes a five-membered ring *O*-cyclization to produce the final product 1,2-dihydronaphtho[2,1-*b*]furan (5-*exo*-*tet* ring closure). The

dx.doi.org/10.1021/jo400621r | J. Org. Chem. 2013, 78, 5505–5520

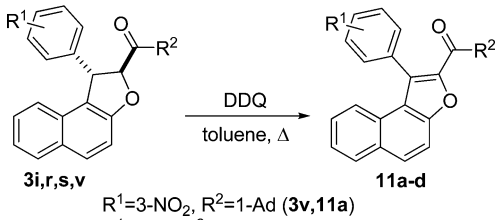
Scheme 7. Synthesis of Oxazolo[3,2-*a*]pyridinium Salt 8



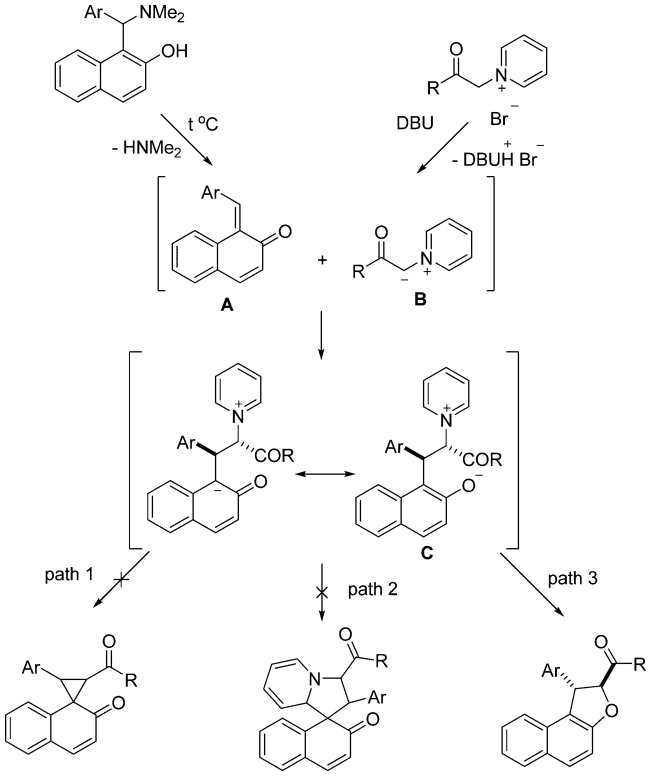
Scheme 8



Scheme 9. Aromatization of 1,2-Dihydronaphtho[2,1-*b*]furans



Scheme 10. Proposed Mechanism for the Formation of 1,2-Dihydronaphtho[2,1-*b*]furans



driving force of the reaction is the resulting rearomatization of the naphthalene fragment.

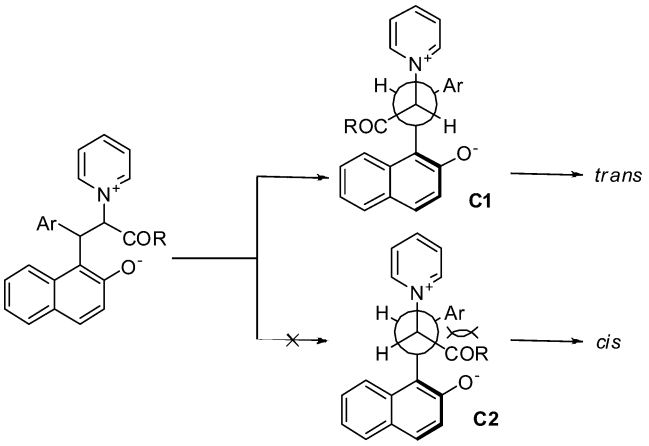
The last step is a typical intramolecular S_N2 substitution reaction. The stereochemistry of the S_N2 reaction requires phenolate attack from the back side of the electrophilic carbon atom bearing the leaving pyridyl group, which subsequently assumes two steric larger 2-acyl and 1-aryl groups in an opposite position for the sake of stereohindrance in the transition state. As shown in Newman projections **C1** and **C2**, intermediate **C1** is the favored one, followed by S_N substitution to give the thermodynamically more stable 1,2-disubstituted dihydronaphtho[2,1-*b*]furan with *trans*-configuration (Scheme 11).

Thus, the combination of ylides and electron-deficient *o*-QMs with the Michael-initiated ring closure strategy is a very useful methodology for preparing highly substituted dihydronaphthofurans. As Mannich bases **1** can easily be synthesized by the Mannich reaction from naphthols and pyridinium salts **2** are readily accessible from pyridines and α-bromoketones, the reaction described herein represents a convenient synthesis of dihydronaphthofurans.

Having successfully applied the "Mannich route" to the synthesis based on the naphthoquinone methides, it was of interest to see if we might be successful in applying the synthesis to benzoquinone methides. Attempts to extend this reaction to the Mannich bases of phenols, however, gave less satisfactory results to furnish the expected products. The reason may be due to the relatively greater thermal stability of these phenolic Mannich bases compared to that of the 2-naphthol series and consequent difficulty in generating the *o*-QMs under the conditions mentioned in this paper.

dx.doi.org/10.1021/jo400621r | J. Org. Chem. 2013, 78, 5505−5520

Scheme 11. Newman Projections of Intermediate C



Mannich base **12** did not react with *N*-(1-adamantylcarbonyl)methylpyridinium bromide **2f** in ethanol under reflux. At a higher temperature (boiling in DMF), however, 2,3-dihydrobenzofuran **13a** was obtained in 58% yield (Scheme 12).

In the reaction of pyridinium salt **2f** with 2,4-dihydroxy-3-morpholin-4-yl-methylacetophenone **14** only 2,3-dihydrobenzo[*b*]furan **13b** was isolated (Scheme 13). The structure of the product was determined on the basis of a sharp, low field chemical shift (12.70 ppm) of the unreacted phenolic proton due to intramolecular hydrogen bond. Thus, only one *o*-QM **D** is generated from Mannich base **14**.

Attempts to extend this reaction to the 2-dimethylaminomethyl-4-nitrophenol, however, failed, maybe because of the relatively greater thermal stability of this phenolic Mannich base. Nevertheless, in the reaction with ammoniophenolate **15**,[34] which is more reactivity precursor of *o*-QM, 2,3-dihydrobenzofurans **13c** and **13d** were prepared in 46 and 52% yields, respectively (Scheme 14).

We have also studied reaction of quaternary ammonium salt **16a** with pyridinium salt **2f** in the presence of DBU. Two products were isolated. One of these appears to be a 2,3-dihydrobenzofuran, assigned the structure **13e**. The other product appears to be a pyridinium salt, assigned the structure **17a** (Scheme 15). The NMR ^{1}H spectrum of **17a** shows two two-proton triplets at 3.05 and 4.82 ppm (J = 6.5 Hz), assigned to methylene protons and one two-proton doublet (J = 6.0 Hz) at low field (δ = 8.81 ppm) corresponding to the α hydrogen atoms of the pyridine ring, which can be explained by a positive charge on an adjacent nitrogen atom. The salt **17a** was not converted to dihydrobenzofuran **13e** during chromatography on silica gel, a possible acidic catalyst. The possible formation of dihydrobenzofuran **13e** from the thermal rearrangement of pyridinium salt **17a** was also investigated by refluxing the pure salt **17a** in CH_3CN in the presence of DBU. No dihydrobenzofuran **13e** was observed. It is likely that the salt **17a** is formed as a result of migration of an acyl group to the phenolic hydroxy group in the intermediate **E**. From the reaction of the quaternary ammonium salt **16a** with phenacylpyridinium bromides **2a** and **2d**, pyridinium salts **17b** and **17c** were isolated as major products.

In the case of other quaternary ammonium salts **16b–g** in the reaction with pyridinium acylmethylides, only 2,3-dihydrobenzofurans **13f–k** were isolated with moderate to good yields (Scheme 16, Table 3).

Thus, in the reaction with pyridinium salts, the better results obtained with the Mannich bases in the 2-naphthol series probably reflect the ease of formation of a *o*-QM adjacent to an aromatic ring as compared with the benzene series in which formation of the *o*-QM implies the disappearance of the only aromatic ring.

Instead of Mannich bases, other *o*-QM precursors can be used in this reaction including salicylic alcohols and 2-acetoxybenzyl acetates. 1-Adamantyl-2,3-dihydrobenzofuran-2-ylmethanone **13l** was prepared from salicylic alcohol **18** and pyridinium salt **2f** in 37% yield. The reaction was performed in refluxing DMF, at sufficiently high temperature to ensure the thermal decomposition of the *o*-QM precursor. When 2-acetoxybenzyl acetate **19a** and pyridinium salt **2f** were heated in ethanolic solution in the presence of DBU, the 2,3-dihydrobenzofuran **13l** was obtained in 23% yield only. Besides, undesired 2-(ethoxymethyl)phenol **20** and ethyl adamantane-1-carboxylate **21** were identified in reaction mixture. The first product is formed by 1,4-addition of ethanol to *o*-QM, the second as a result of acid splitting of pyridinium ylide. When acetonitrile was used in this reaction, the desired product **13l** was isolated in 73% yield. The diacetates **19b,c** also react with pyridinium salt **2f** under these conditions to afford the corresponding 2,3-dihydrobenzofurans **13m** and **13n** in 73 and 82% yields, respectively (Scheme 17).

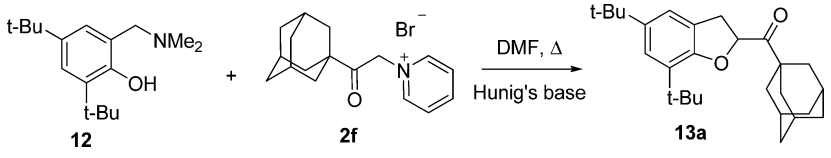
The proposed mechanism for the generation of *o*-QMs from 2-acethoxybenzyl acetates in the presence of DBU is shown in Scheme 18.

We have also applied our method to the synthesis of methyl (±)-7-methoxyanodendroate, which was first isolated in 2008 from *Zanthoxylum wutaiense*.[35] This compound was shown to possess antitubercular activity against *Mycobacterium tuberculosis* H37Rv with a minimum inhibitory concentration of 35 μg/mL. The first synthesis of methyl (+)-7-methoxyanodendroate was achieved in 2011 utilizing a Claisen rearrangement, a Grubbs cross-methathesis, and a Shi epoxidation–cyclization sequence.[36] We have prepared dihydrobenzofuran **13p** in two steps from quaternary ammonium salt **16d** and pyridinium salt **2l** with an overall yield 54% (Scheme 19).

CONCLUSION

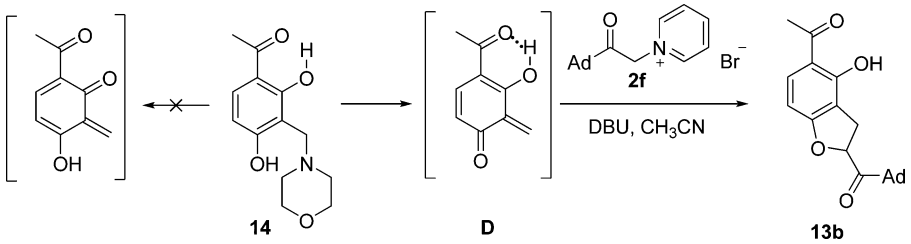
A new method for the synthesis of 1,2-dihydronaphtho[2,1-*b*]furans from Mannich bases and pyridinium salts has been developed. The reaction proceeds via Michael-type addition between *o*-QMs and pyridinium ylides formed in situ followed by intramolecular nucleophilic substitution. This protocol can

Scheme 12

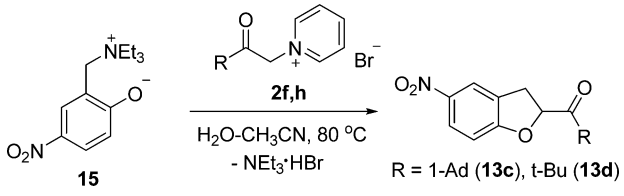


dx.doi.org/10.1021/jo400621r | J. Org. Chem. 2013, 78, 5505–5520

Scheme 13. Regioselective Synthesis of 2,3-Dihydrobenzo[*b*]furan 13b



Scheme 14



provide a novel and efficient methodology for the preparation of 2-acyl-1,2-dihydronaphtho[2,1-*b*]furans in a diastereoselective fashion. ^{1}H NMR spectroscopy indicates that the products are formed exclusively as the *trans* isomers. The reaction is applicable to a range of Mannich bases and pyridinium salts with a variety of versatile functional groups. Some of the prepared products may be useful intermediates for the obtaining of highly functionalized 1,2-dihydronaphtho[2,1-*b*]furans and 2,3-dihydrobenzofurans. The advantages of this approach include the use of readily available starting materials, simple experimental steps and product isolation, and chromatographic purification is not usually required.

EXPERIMENTAL SECTION

General Information. FTIR spectra were taken in KBr pellets. ^{1}H, ^{13}C, and DEPT NMR spectra were recorded using a 400 MHz NMR spectrometer in CD_3CN, $CDCl_3$ or DMSO-d_6 solutions with TMS as internal standard. Chemical shifts and coupling constants were recorded in units of ppm and Hz, respectively. The melting points were uncorrected. Elemental analysis was carried out on an automatic CHNS-analyzer. Mass spectra were recorded with 70 eV electron ionization energy. Thin-layer chromatography was carried out on aluminum-backed silica gel plates with visualization of components by UV light (254 nm) or exposure to I_2. Known Mannich bases and their quaternary ammonium salts were prepared according to the literature procedures.[20,37−39] Pyridinium 4-bromobenzoylmethylide **4a** was obtained by deprotonation of *N*-(4-bromophenacyl)pyridinium bromide **2a** under the action of potassium carbonate.[40] Phosphonic **5** and ammonium **6** salts were prepared from 1-(1-adamantyl)-2-bromoethanone and triphenylphosphine or DABCO in acetonitrile.[41]

*N-(1-Adamantylcarbonyl)methylpyridinium bromide (**2f**).* Pyridine (10 mL, 0.124 mol) was added to 1-(1-adamantyl)-2-bromoethanone (25 g, 0.097 mol) in diethyl ether (150 mL). After stirring overnight at room temperature, a precipitate that formed was filtered off and recrystallized from acetonitrile. Yield 24.5 g (75%). Colorless crystals: mp 226−227 °C (decomp.); IR ν_{max} (KBr) 3500−3300 (H_2O), 3028 (CH Ar), 2909, 2851 (CH Ad), 1713 (C=O), 1636, 1489, 1366, 1335, 1312, 1196, 1165, 1011, 745, 687 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ: 1.65−1.73 (m, 6H), 1.88−1.91 (m,

Scheme 16

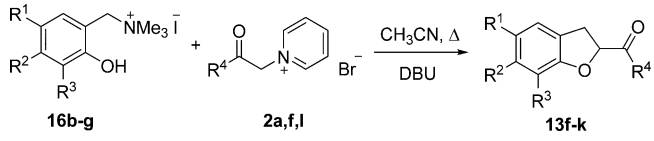
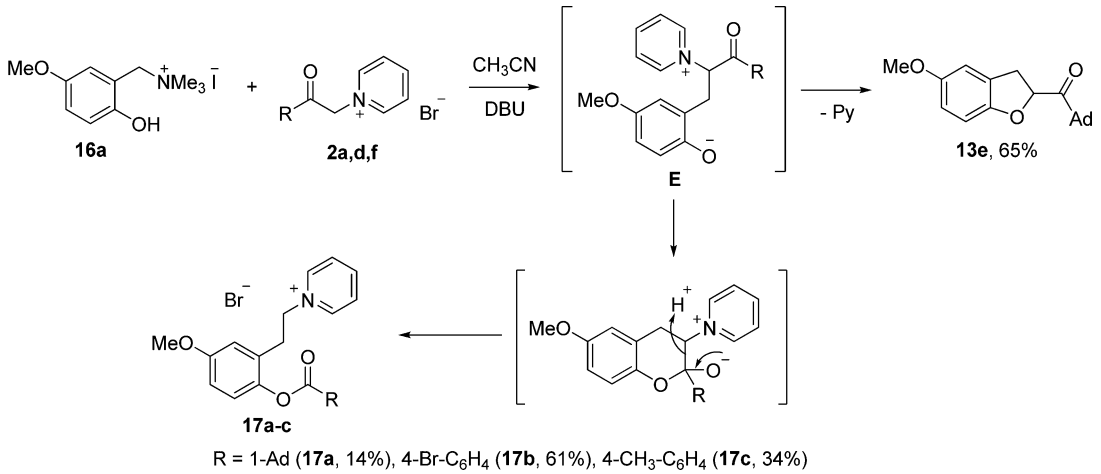


Table 3. Synthesis of 2,3-Dihydrobenzofurans 13f−k

entry	R^1	R^2	R^3	R^4	product	yield[a] (%)
1	CHO	H	OCH_3	4-BrC_6H_4	**13f**	71
2	NO_2	H	H	4-BrC_6H_4	**13g**	51
3	CO_2CH_3	H	OCH_3	4-BrC_6H_4	**13h**	69
4	H	CO_2CH_3	H	CH_3	**13i**	52
5	CH_3CO	H	H	CH_3	**13j**	61
6	CH_3	CH_3	H	1-Ad	**13k**	81

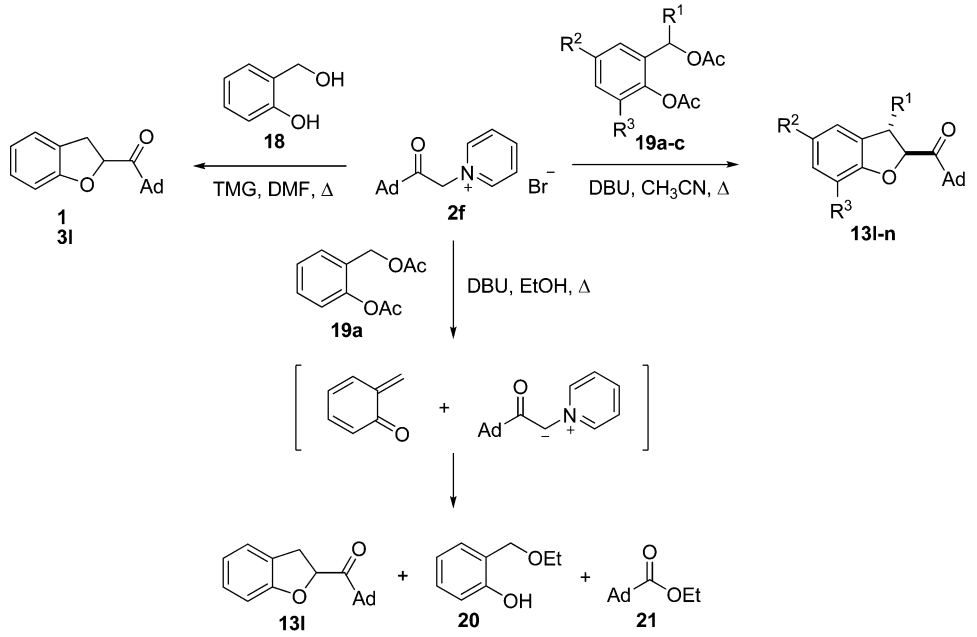
[a]Isolated yield.

Scheme 15



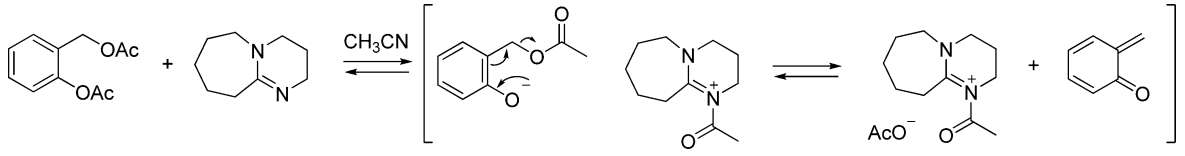
dx.doi.org/10.1021/jo400621r | J. Org. Chem. 2013, 78, 5505−5520

Scheme 17. Synthesis of 2,3-Dihydrobenzofurans 13l–n from Salicylic Alcohol and 2-Acethoxybenzyl Acetates

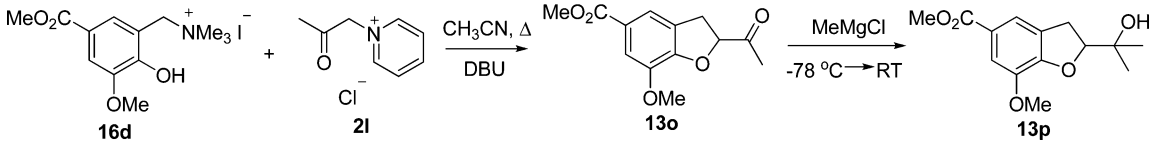


R^1=R^2=R^3=H (**13l,19a**); R^1=Ph, R^2=R^3=H (**13m,19b**); R^1=H, R^2=R^3=Br (**13n,19c**)

Scheme 18. Proposed Mechanism for the Generation of *o*-QMs from 2-Acetoxybenzyl Acetates



Scheme 19. Synthesis of Methyl (±)-7-Methoxyanodendroate



6H), 2.02 (br s, 3H), 6.03 (s, 2H), 8.19 (dd, 2H, J = 7.8, 6.6 Hz), 8.67 (tt, 1H, J = 8.0, 1.4 Hz), 8.87 (d, 2H, J = 5.5 Hz) ppm; ^{13}C NMR (100 MHz, DMSO-d_6) δ 27.7 (3CH), 36.4 ($3CH_2$), 37.6 ($3CH_2$), 45.6 (C), 65.5 (CH_2), 128.3 (2CH), 146.6 (2CH), 146.7 (CH), 206.5 (C) ppm. Anal. Calcd (%) for $C_{17}H_{22}BrNO{\cdot}0.35H_2O$: C, 59.60; H, 6.68; N, 4.09. Found (%): C, 59.42; H, 6.66; N, 4.11.

*Pyridinium (1-adamantylcarbonyl)methylide (**4b**).* DBU (4.5 mL, 0.03 mol) was added with stirring at room temperature to a solution of pyridinium salt **2f** (10 g, 0.03 mol) in water (100 mL). The mixture was strirred for 5 min and then extracted with dichloromethane. The extract was dried (Na_2SO_4) and evaporated as rapidly as possible under reduced pressure at room temperature. The residue was dissolved in CH_2Cl_2 and precipitated by hexane. *N*-Pyridinium ylide began to darken after a few hours; therefore, was stored in refrigerator. Yield 6.91 g (91%). Bright yellow powder: mp 155–157 °C (decomp.); IR ν_{max} (KBr) 3063 (CH Ar), 2905, 2849 (CH Ad), 1551, 1524, 1485, 1466, 1423, 1342, 1288, 1177, 1150, 1007, 976, 914, 864, 760, 671 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.68 (br s, 6H), 1.84 (br s, 6H), 1.98 (br s, 3H, CH Ad), 6.01 (br s, 1H), 7.23–7.26 (m, 3H), 9.42 (d, J = 6.0 Hz, 2H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 28.8 (3CH), 37.2 ($3CH_2$), 40.2 ($3CH_2$), 42.1 (C), 96.6 (CH), 125.8 (2CH), 128.5 (CH), 132.5 (2CH), 184.7 (C) ppm. Anal. Calcd (%) for $C_{17}H_{21}NO$: C, 79.96; H, 8.29; N, 5.49. Found: C (%), 80.12; H, 8.26; N, 5.50.

*[2-Hydroxy-3-methoxy-5-(methoxycarbonyl)benzyl]-trimethylammonium iodide (**16d**).* Dimethylamine (3 mL of 33% aqueous solution, 0.02 mol) and formaldehyde (1.5 mL of 37% aqueous solution, 0.02 mol) were added to a solution of methyl 4-hydroxy-3-methoxybenzoate (3.28 g, 0.018 mol) in methanol (20 mL). The reaction mixture was stirred at room temperature for 20 h. The solvent was evaporated in vacuo, and the residue was dissolved in acetonitrile (50 mL) and treated with CH_3I (5 mL). The resulting solution was stirred at room temperature for 12 h, the solvent was evaporated in vacuo, and the residue was recrystallized from acetonitrile. Yield 5.07 g (74%). Colorless solid: mp > 210 °C (decomp.); IR ν_{max} (KBr) 3275, 3001, 2940, 1705 (C=O), 1605, 1462, 1427, 1385, 1312, 1234, 1180, 1111, 1088, 953, 883, 760 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ 3.03 (9H, s), 3.79 (3H, s), 3.87 (3H, s), 4.52 (2H, s), 7.52 (1H, d, J = 1.8 Hz), 7.68 (1H, d, J = 1.8 Hz), 10.52 (1H, br s) ppm; ^{13}C NMR (100 MHz, DMSO-d_6) δ 52.6 (CH_3), 52.7 ($3CH_3$), 56.7 (CH_3), 63.1 (CH_2), 113.9 (CH), 115.6 (C), 120.8 (C), 128.6 (CH), 148.3 (C), 152.1 (C), 166.2 (C) ppm. Anal. Calcd (%) for $C_{13}H_{20}INO_4$: C, 40.96; H, 5.29; N, 3.67. Found: C (%), 41.03; H, 5.31; N, 3.63.

General Experimental Procedure for the Synthesis of 1,2-Dihydronaphtho[2,1-*b*]furans. A mixture of 2-naphthol Mannich base (3 mmol), pyridinium salt (3 mmol), base (3 mmol, TMG or DBU, if required) in CH_3CN or EtOH (20 mL) under an Ar atmosphere was heated at reflux temperature for 3–12 h. After the

dx.doi.org/10.1021/jo400621r | J. Org. Chem. 2013, 78, 5505–5520

indicated time period (see Table 2), the solvent was removed by evaporation under reduced pressure. The crude product was purified by recrystallization. The reaction conditions and yields of **3a**−**y** were summarized in Table 2.

Characterization Data of 1,2-Dihydronaphtho[2,1-*b*]furans. *(4-Bromophenyl)(1,2-dihydronaphtho[2,1-b]furan-2-yl)methanone (**3a**).* Yield 82%; 0.87 g. Colorless crystals: mp 173−175 °C (from CH_3CN); IR ν_{max} (KBr) 3059 (CH Ar), 2970, 2940, 1686 (C═O), 1628, 1582, 1516, 1447, 1396, 1366, 1312, 1219, 1161, 1069, 1049, 988, 964, 895, 845, 802, 748 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 3.79 (dd, 1H, J = 15.6, 11.0 Hz), 3.89 (dd, 1H, J = 15.6, 7.3 Hz), 6.03 (dd, 1H, J = 11.0, 7.3 Hz), 7.16 (d, 1H, J = 8.7 Hz), 3.33 (td, 1H, J = 8.2, 1.4 Hz), 7.48 (td, 1H, J = 8.2, 0.9 Hz), 7.59 (d, 1H, J = 8.2 Hz), 7.66 (d, 2H, J = 8.7 Hz), 7.71 (d, 1H, J = 8.7 Hz), 7.81 (d, 1H, J = 8.2 Hz), 7.95 (d, 2H, J = 8.7 Hz) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 31.4 (CH_2), 83.6 (CH), 112.1 (CH), 117.1 (C), 122.8 (CH), 123.5 (CH), 127.1 (CH), 128.9 (CH), 129.1 (C), 129.6 (CH), 129.7 (C), 130.6 (C), 130.8 (2CH), 132.2 (2CH), 133.4 (C), 156.5 (C), 194.8 (C) ppm; MS (EI) m/z (%) 353 (M^+, 5), 335 (6), 197 (8), 183 (BrC_6H_4CO, 22), 169 (62), 168 (43), 155 (BrC_6H_4, 24), 141 (100), 139 (63), 115 (58). Anal. Calcd (%) for $C_{19}H_{13}BrO_2$: C, 64.61; H, 3.71. Found (%): C, 64.75; H, 3.68.

*1,2-Dihydronaphtho[2,1-b]furan-2-yl(4-nitrophenyl)methanone (**3b**).* Yield 34%; 0.27 g. Yellow crystals: mp 194−196 °C (decomp., from EtOH/DMF); IR ν_{max} (KBr) 3051 (CH Ar), 2932, 1697 (C═O), 1628, 1601, 1520 (NO_2), 1466, 1350 (NO_2), 1323, 1265, 1246, 1219, 1161, 968, 903, 856, 810, 772, 714 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 3.67 (dd, 1H, J = 15.9, 6.5 Hz), 3.88 (dd, 1H, J = 15.9, 11.1 Hz), 6.53 (dd, 1H, J = 11.1, 6.5 Hz), 7.19 (d, 1H, J = 8.7 Hz), 7.31 and 7.46 (t, 2H, J = 7.4 Hz), 7.63 (d, 1H, J = 8.2 Hz), 7.76 (d, 1H, J = 8.7 Hz), 7.85 (d, 1H, J = 8.2 Hz), 8.28 (d, 2H, J = 8.7 Hz), 8.38 (d, 2H, J = 8.7 Hz) ppm; ^{13}C NMR (100 MHz, DMSO-d_6) δ 31.3 (CH_2), 83.4 (CH), 112.3 (CH), 117.7 (C), 123.4 (CH), 123.8 (CH), 124.5 (2CH), 127.5 (CH), 129.1 (CH), 129.6 (C), 129.8 (CH), 130.6 (C), 130.9 (2CH), 139.5 (C), 150.8 (C), 156.7 (C), 195.2 (C) ppm. Anal. Calcd (%) for $C_{19}H_{13}NO_4$: C, 71.47; H, 4.10; N, 4.39. Found (%): C, 71.58; H, 4.13; N, 4.37.

*1,2-Dihydronaphtho[2,1-b]furan-2-yl(4-fluorophenyl)methanone (**3c**).* Yield 79%; 0.69 g. Colorless crystals: mp 161−162 °C (from CH_3CN); IR ν_{max} (KBr) 3074 (CH Ar), 2913, 1694 (C═O), 1597, 1504, 1466, 1412, 1366, 1227, 1157, 1053, 991, 964, 914, 849, 806, 764, 741 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 3.79 (dd, 1H, J = 15.6, 10.8 Hz), 3.90 (dd, 1H, J = 15.6, 7.4 Hz), 6.04 (dd, 1H, J = 10.8, 7.4 Hz), 7.16−7.22 (m, 3H), 7.34 (ddd, 1H, J = 8.0, 6.9, 1.2 Hz), 7.48 (ddd, 1H, J = 8.2, 6.9, 1.2 Hz), 7.60 (d, 1H, J = 8.2 Hz), 7.71 (d, 1H, J = 9.0 Hz), 7.81 (d, 1H, J = 8.2 Hz), 8.10−8.15 (m, 2H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 31.5 (CH_2), 83.6 (CH), 112.1 (CH), 116.1 (d, 2CH, J_{CF} = 21.9 Hz), 117.2 (C), 122.8 (CH), 123.5 (CH), 127.0 (CH), 128.8 (CH), 129.6 (CH), 129.7 (C), 130.6 (C), 131.0 (d, C, J_{CF} = 2.9 Hz), 132.1 (d, 2CH, J_{CF} = 9.5 Hz), 156.5 (C), 166.2 (d, C, J_{CF} = 255.5 Hz), 194.1 (C) ppm. Anal. Calcd (%) for $C_{19}H_{13}FO_2$: C, 78.07; H, 4.48. Found (%): C, 77.89; H, 4.51.

*1,2-Dihydronaphtho[2,1-b]furan-2-yl(4-methylphenyl)-methanone (**3d**).* Yield 81%; 0.70 g. Colorless crystals: mp 143−144 °C (from EtOH); IR ν_{max} (KBr) 3028, 2922, 1699 (C═O), 1628, 1603, 1574, 1520, 1464, 1445, 1408, 1371, 1260, 1244, 1231, 1209, 1180, 1152, 1053, 995, 970, 908, 827, 818, 760, 729 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 2.44 (s, 3H), 3.79 (dd, 1H, J = 15.6, 10.3 Hz), 3.84 (dd, 1H, J = 15.6, 8.0 Hz), 6.10 (dd, 1H, J = 10.3, 8.0 Hz), 7.20 (d, 1H, J = 8.7 Hz), 7.31−7.35 (m, 3H), 7.47 (td, 1H, J = 7.0, 1.2 Hz), 7.58 (d, 1H, J = 8.0 Hz), 7.71 (d, 1H, J = 8.7 Hz), 7.81 (d, 1H, J = 8.2 Hz), 7.98 (d, 2H, J = 8.2 Hz) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.9 (CH_3), 32.0 (CH_2), 83.5 (CH), 112.2 (CH), 117.2 (C), 122.8 (CH), 123.3 (CH), 127.0 (CH), 128.8 (CH), 129.4 (2CH), 129.5 (CH), 129.6 (2CH, C), 130.7 (C), 132.0 (C), 144.8 (C), 156.8 (C), 195.1 (C) ppm. Anal. Calcd (%) for $C_{20}H_{16}O_2$: C, 83.31; H, 5.59. Found (%): C, 83.42; H, 5.54.

*1,2-Dihydronaphtho[2,1-b]furan-2-yl(1-naphthyl)methanone (**3e**).* Yield 72%; 0.70 g. Colorless crystals: mp 120−122 °C (from DMF/MeOH); IR ν_{max} (KBr) 3048 (CH Ar), 2920, 1682 (C═O), 1628, 1570, 1508, 1462, 1439, 1362, 1261, 1234, 1177, 1161, 1096, 964, 899, 818, 775, 756 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 3.78 (dd, 1H, J = 15.6, 10.3 Hz), 3.84 (dd, 1H, J = 15.6, 7.8 Hz), 6.20 (dd, 1H, J = 10.3, 7.8 Hz), 7.18 (d, 1H, J = 8.7 Hz), 7.33 (t, 1H, J = 7.3 Hz), 7.46 (t, 1H, J = 7.8 Hz), 7.52−7.59 (m, 4H), 7.71 (d, 1H, J = 8.7 Hz), 7.82 (d, 1H, J = 8.2 Hz), 7.89 (d, 1H, J = 8.7 Hz), 8.00 (d, 1H, J = 7.1 Hz), 8.05 (d, 1H, J = 8.0 Hz), 8.57 (d, 1H, J = 7.8 Hz) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 32.2 (CH_2), 84.6 (CH), 112.2 (CH), 117.0 (C), 122.8 (CH), 123.4 (CH), 124.4 (CH), 125.7 (CH), 126.8 (CH), 127.0 (CH), 128.4 (CH), 128.7 (2CH), 128.9 (CH), 129.6 (CH), 129.7 (C), 130.6 (C), 131.0 (C), 132.9 (C), 133.5 (CH), 134.1 (C), 156.9 (C), 199.7 (C) ppm. Anal. Calcd (%) for $C_{23}H_{16}O_2$: C, 85.16; H, 4.97. Found (%): C, 85.26; H, 4.95.

*1-Adamantyl-1,2-dihydronaphtho[2,1-b]furan-2-ylmethanone (**3f**).* Yield 77%; 0.77 g. Colorless crystals: mp 116−117 °C (from EtOH); IR ν_{max} (KBr) 2901, 2847 (CH Ad), 1701 (C═O), 1628, 1582, 1520, 1443, 1381, 1312, 1242, 1049, 976, 810, 752 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.74−1.82 (m, 6H), 1.93−2.03 (m, 6H), 2.10 (br s, 3H), 3.52 (dd, 1H, J = 15.3, 8.0 Hz), 3.63 (dd, 1H, J = 15.3, 10.5 Hz), 5.65 (dd, 1H, J = 10.5, 8.0 Hz), 7.17 (d, 1H, J = 8.7 Hz), 7.32 (dd, 1H, J = 8.2, 7.0 Hz), 7.47 (dd, 1H, J = 8.2, 7.0 Hz), 7.55 (d, 1H, J = 8.2 Hz), 7.69 (d, 1H, J = 8.7 Hz), 7.80 (d, 1H, J = 8.2 Hz) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 27.9 (3CH), 32.4 (CH_2), 36.6 ($3CH_2$), 38.0 ($3CH_2$), 46.0 (C), 81.8 (CH), 112.0 (CH), 117.0 (C), 122.7 (CH), 123.2 (CH), 126.9 (CH), 128.8 (CH), 129.5 (CH), 129.6 (C), 130.6 (CH), 156.9 (C), 210.7 (C) ppm; MS (EI) m/z (%) 332 (M^+, 8), 197 (M^+ − Ad, 92), 196 (M^+ − Ad − H, 65), 169 (M^+ − AdCO, 35), 168 (M^+ − AdCO − H, 56), 141 (51), 135 (Ad^+, 100). Anal. Calcd (%) for $C_{23}H_{24}O_2$: C, 83.10; H, 7.28. Found (%): C, 83.22; H, 7.31.

*trans-Phenyl-1-phenyl-1,2-dihydronaphtho[2,1-b]furan-2-ylmethanone (**3g**).* Yield 71%; 0.75 g. Colorless crystals: mp 137−138 °C (from EtOH); IR ν_{max} (KBr) 3059, 3028, 2920, 1690 (C═O), 1632, 1597, 1578, 1520, 1462, 1447, 1377, 1234, 984, 810, 744, 702 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.32 and 5.95 (d, 2H, J = 5.1 Hz), 7.23−7.33 (m, 9H), 7.49 (dd, 2H, J = 7.8, 7.3 Hz), 7.63 (t, 1H, J = 7.3 Hz), 7.80 (d, 2H, J = 8.7 Hz), 7.99 (d, 2H, J = 8.3 Hz) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 50.8 (CH), 91.7 (CH), 112.2 (CH), 120.0 (C), 122.9 (CH), 123.3 (CH), 127.0 (CH), 127.6 (CH), 128.1 (2CH), 128.9 (2CH), 128.9 (CH), 129.2 (2CH), 129.5 (2CH), 130.2 (C), 130.4 (C), 130.6 (CH), 134.0 (CH), 134.4 (C), 142.4 (C), 157.3 (C), 194.7 (C) ppm; MS (EI) m/z (%) 350 (M^+, 30), 333 (M^+ − OH, 10), 273 (M^+ − Ph, 4), 245 (M^+ − PhCO, 49), 217 (32), 215 (36), 202 ($C_{16}H_{10}$, 33), 168 (M^+ − Ph − PhCO, 7), 139 (11), 105 (PhCO, 100), 77 (Ph, 39). Anal. Calcd (%) for $C_{25}H_{18}O_2$: C, 85.69; H, 5.18. Found (%): C, 85.78; H, 5.15.

*trans-4-Bromophenyl-1-phenyl-1,2-dihydronaphtho[2,1-b]furan-2-ylmethanone (**3h**).* Yield 89%; 1.15 g. Colorless crystals: mp 184−186 °C (from EtOH); IR ν_{max} (KBr) 3059, 2905, 1697 (C═O), 1628, 1582, 1516, 1458, 1396, 1231, 1177, 1065, 984, 841, 814, 752, 702 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.35 and 5.87 (d, 2H, J = 5.5 Hz, H-1,2), 7.25−7.36 (m, 9H), 7.63 (d, 2H, J = 8.7 Hz), 7.80 (d, 2H, J = 8.7 Hz), 7.86 (d, 2H, J = 8.3 Hz) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 50.6 (CH), 91.7 (CH), 112.2 (CH), 119.9 (C), 123.0 (CH), 123.5 (CH), 127.1 (CH), 127.7 (CH), 128.1 (2CH), 128.9 (CH), 129.3 (2CH), 130.2 (C), 130.4 (C), 130.7 (CH), 131.0 (2CH), 132.2 (2CH), 133.2 (C), 142.3 (C), 157.0 (C), 194.0 (C) ppm; MS (EI) m/z (%) 428 (M^+, 6), 273 (M^+ − C_6H_4Br, 5), 245 (M^+ − C_7H_4BrO, 100), 226 (13), 215 (82), 202 ($C_{16}H_{10}$, 75), 183 (C_7H_4BrO, 54), 168 (25), 155 (C_6H_4Br, 28), 139 (35). Anal. Calcd (%) for $C_{25}H_{17}BrO_2$: C, 69.94; H, 3.99. Found (%): C, 70.09; H, 4.02.

*trans-1-Naphthyl(1-phenyl-1,2-dihydronaphtho[2,1-b]furan-2-yl)methanone (**3i**).* Yield 90%; 1.08 g. Colorless crystals: mp 161−163 °C (from EtOH); IR ν_{max} (KBr) 3055, 3024 (CH Ar), 1670 (C═O), 1628, 1597, 1574, 1508, 1458, 1231, 976, 806, 779, 755, 706 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.27 and 6.02 (d, 2H, J = 5.3 Hz), 7.08−7.11 (m, 2H), 7.22−7.27 (m, 6H), 7.30 (d, 1H, J = 8.2 Hz), 7.48 (dd, 1H, J = 8.2, 7.3 Hz), 7.54−7.60 (m, 2H), 7.78−7.85 (m, 3H), 7.90−7.92 (m, 1H), 8.06 (d, J = 8.2 Hz, 1H), 8.58−8.61 (m, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 51.2 (CH), 92.9 (CH), 112.3 (CH),

dx.doi.org/10.1021/jo400621r | J. Org. Chem. 2013, 78, 5505−5520

119.6 (C), 122.9 (CH), 123.3 (CH), 124.3 (CH), 125.7 (CH), 126.9 (CH), 127.0 (CH), 127.5 (CH), 127.9 (2CH), 128.5 (CH), 128.7 (CH), 128.9 (CH), 129.1 (2CH), 129.2 (CH), 130.2 (C), 130.4 (C), 130.7 (CH), 131.1 (C), 132.5 (C), 133.7 (CH), 134.1 (C), 142.5 (C), 157.5 (C), 198.7 (C) ppm. Anal. Calcd (%) for $C_{29}H_{20}O_2$: C, 86.98; H, 5.03. Found (%): C, 87.12; H, 4.99.

*trans-2,2-Dimethyl-1-(1-phenyl)-1,2-dihydronaphtho[2,1-b]-furan-2-yl)-1-propanone (**3j**).* Yield 80%; 0.79 g. Colorless crystals: mp 92−93 °C (from EtOH); IR ν_{max} (KBr) 3059 (CH Ar), 2974, 1717 (C═O), 1632, 1601, 1578, 1520, 1466, 1369, 1250, 1227, 1076, 964, 818, 748, 733, 698 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.27 (s, 9H), 5.25 and 5.42 (d, 2H, J = 5.5 Hz), 7.25−7.29 (m, 9H), 7.78−7.81 (m, 2H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 26.3 ($3CH_3$), 44.1 (C), 51.3 (CH), 91.4 (CH), 112.0 (CH), 120.2 (C), 123.0 (CH), 123.3 (CH), 127.0 (CH), 127.4 (CH), 128.1 (2CH), 128.9 (CH), 129.1 (2CH), 130.2 (C), 130.5 (CH, C), 142.7 (C), 157.1 (C), 211.4 (C). Anal. Calcd (%) for $C_{23}H_{22}O_2$: C, 83.61; H, 6.71. Found (%): C, 83.54; H, 6.74.

*trans-Cyclopropyl-1-phenyl-1,2-dihydronaphtho[2,1-b]furan-2-ylmethanone (**3k**).* Yield 75%; 0.71 g. Colorless crystals: mp 129−130 °C (from EtOH); IR ν_{max} (KBr) 3051, 3024, 3005, 2947, 2897, 1713 (C═O), 1628, 1597, 1578, 1516, 1462, 1377, 1254, 1219, 1192, 1153, 984, 818, 729, 698 cm^{-1}; ^1H NMR (400 MHz, CD_3CN) δ 0.87−0.94 (m, 1H), 0.95−1.07 (m, 3H), 2.26−2.32 (m, 1H,), 5.16 and 5.21 (d, 2H, J = 5.0 Hz), 7.21−7.34 (m, 9H), 7.82−7.86 (m, 2H) ppm; ^{13}C NMR (100 MHz, CD_3CN) δ 11.1 (CH_2), 11.4 (CH_2), 16.5 (CH), 51.2 (CH), 94.4 (CH), 112.0 (CH), 120.3 (C), 122.7 (CH), 123.4 (CH), 127.0 (CH), 127.4 (CH), 127.7 (2CH), 128.9 (CH), 129.1 (2CH), 130.1 (C), 130.3 (C), 130.7 (CH), 143.1 (C), 157.3 (C), 207.9 (C) ppm. Anal. Calcd (%) for $C_{22}H_{18}O_2$: C, 84.05; H, 5.77. Found (%): C, 83.89; H, 5.80.

*trans-1-Adamantyl-1-phenyl-1,2-dihydronaphtho[2,1-b]furan-2-ylmethanone (**3l**).* Yield 84%; 1.03 g. Colorless crystals: mp 185−186 °C (from EtOH); IR ν_{max} (KBr) 3059 (CH Ar), 2912, 2851 (CH Ad), 1705 (C═O), 1632, 1577, 1520, 1450, 1373, 1261, 1227, 1120, 1157, 999, 976, 922, 814 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.71−1.80 (m, 6H), 1.91−2.01 (m, 6H), 2.08 (br s, 3H), 5.22 and 5.46 (d, 2H, J = 5.5 Hz), 7.23−7.37 (m, 9H), 7.78−7.82 (m, 2H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 27.9 (3CH), 36.6 ($3CH_2$), 37.8 ($3CH_2$), 46.4 (C), 50.8 (CH), 90.3 (CH), 112.0 (CH), 120.3 (C), 123.0 (CH), 123.2 (CH), 126.9 (CH), 127.4 (CH), 128.1 (2CH), 128.9 (CH), 129.1 (2CH), 130.1 (C), 130.5 (CH, C), 142.7 (C), 157.2 (C), 210.0 (C) ppm; MS (EI) m/z (%) 408 (M^+, 1), 273 (M^+ − Ad, 100), 245 (11), 217 (16), 202 ($C_{16}H_{10}$, 14), 168 (12), 135 (Ad^+, 100). Anal. Calcd (%) for $C_{29}H_{28}O_2$: C, 85.26; H, 6.91. Found (%): C, 85.40; H, 6.88.

*trans-(4-Chlorophenyl)-1-(4-methoxyphenyl)-1,2-dihydronaphtho[2,1-b]furan-2-ylmethanone (**3m**).* Yield 72%; 0.90 g. Colorless crystals: mp 165−166 °C (from EtOH); IR ν_{max} (KBr) 3047 (CH Ar), 2959, 2928, 2905, 2835, 1690 (C═O), 1632, 1612, 1585, 1512, 1462, 1377, 1231, 1177, 1088, 1034, 980, 810, 748 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 3.78 (s, 3H), 5.27 and 5.83 (d, 2H, J = 5.5 Hz), 6.86 (d, 2H J = 8.7 Hz), 7.18 (d, 2H, J = 8.7 Hz), 7.22−7.32 (m, 4H), 7.46 (d, 2H, J = 8.7 Hz), 7.76−7.81 (m, 2H), 7.94 (d, 2H, J = 8.7 Hz) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 50.1 (CH), 55.4 (CH_3), 91.9 (CH), 112.1 (CH), 114.6 (2CH), 120.0 (C), 122.9 (CH), 123.4 (CH), 127.0 (CH), 128.9 (CH), 129.1 (2CH), 129.2 (2CH), 130.2 (C), 130.4 (C), 130.6 (CH), 130.9 (2CH), 132.8 (C), 134.4 (C), 140.4 (C), 156.9 (C), 159.0 (C), 193.9 (C) ppm. Anal. Calcd (%) for $C_{26}H_{19}ClO_3$: C, 75.27; H, 4.62. Found (%): C, 75.34; H, 4.58.

*trans-1-Adamantyl-1-(4-methoxyphenyl)-1,2-dihydronaphtho-[2,1-b]furan-2-ylmethanone (**3n**).* Yield 63%; 0.83 g. Colorless crystals: mp 179−180 °C (from EtOH); IR ν_{max} (KBr) 3063 (CH Ar), 2908, 2847 (CH Ad), 1709 (C═O), 1628, 1612, 1512, 1462, 1246, 1223, 1177, 1034, 1007, 984, 968, 841, 814, 752 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.70−1.78 (m, 6H), 1.89−1.99 (m, 6H), 2.06 (br s, 3H), 3.77 (s, 3H), 5.13 and 5.41 (d, 2H, J = 5.5 Hz), 6.84 (d, 2H, J = 8.7 Hz), 7.17 (d, 2H, J = 8.7 Hz), 7.22−7.33 (m, 4H), 7.76−7.80 (m, 2H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 27.9 (3CH), 36.6 ($3CH_2$), 37.8 ($3CH_2$), 46.3 (C), 50.2 (CH), 55.3 (CH_3), 90.3 (CH), 112.0 (CH), 114.4 (2CH), 120.4 (C), 123.0 (CH), 123.2 (CH), 126.8 (CH), 128.9 (CH), 129.1 (2CH), 130.1 (C), 130.4 (CH), 130.5 (C), 134.7 (C), 157.1 (C), 158.8 (C), 210.1 (C) ppm; MS (EI) m/z (%) 438 (M^+, 2), 303 (M^+ − Ad, 100), 275 (M^+ − AdCO, 7), 247 (14), 215 (12), 207 (7), 168 (M^+ − AdCO − $C_6H_4OCH_3$, 8), 135 (Ad^+, 33). Anal. Calcd (%) for $C_{30}H_{30}O_3$: C, 82.16; H, 6.89. Found (%): C, 82.30; H, 6.86.

*trans-(4-Chlorophenyl)-1-(4-chlorophenyl)-1,2-dihydronaphtho-[2,1-b]furan-2-ylmethanone (**3o**).* Yield 88%; 1.11 g. Colorless crystals: mp 123−125 °C (from EtOH); IR ν_{max} (KBr) 3067 (CH Ar), 2963, 2820, 2778, 1690 (C═O), 1620, 1597, 1582, 1520, 1489, 1466, 1408, 1373, 1265, 1234, 1092, 1007, 949, 814, 745 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.38 and 5.78 (d, 2H, J = 5.5 Hz), 7.20 (d, 2H, J = 8.5 Hz), 7.23−7.32 (6H, m), 7.47 (d, 2H, J = 8.7 Hz), 7.77−7.81 (m, 2H), 7.95 (d, 2H, J = 8.5 Hz) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 49.7 (CH), 91.6 (CH), 112.1 (CH), 119.4 (C), 122.8 (CH), 123.6 (CH), 127.2 (CH), 129.0 (CH), 129.2 (2CH), 129.4 (2CH), 129.5 (2CH), 130.2 (C), 130.3 (C), 130.9 (2CH), 130.9 (CH), 132.8 (C), 133.5 (C), 140.6 (C), 140.8 (C), 157.0 (C), 193.6 (C) ppm. Anal. Calcd (%) for $C_{25}H_{16}Cl_2O_2$: C, 71.61; H, 3.85. Found (%): C, 71.75; H, 3.90.

*trans-(2,2-Dimethyl-1-[1-(4-chlorophenyl)-1,2-dihydronaphtho-[2,1-b]furan-2-yl]-1-propanone (**3p**).* Yield 72%; 0.79 g. Colorless crystals: mp 108−110 °C (from EtOH); IR ν_{max} (KBr) 3059 (CH Ar), 2982, 2940, 2901, 2874, 1713 (C═O), 1632, 1578, 1516, 1485, 1466, 1369, 1246, 1215, 1246, 1215, 1088, 991, 972, 934, 829, 802, 741 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.26 (s, 9H), 5.24 and 5.31 (d, 2H, J = 5.5 Hz), 7.18−7.30 (m, 8H), 7.78−7.82 (m, 2H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 26.3 ($3CH_3$), 44.1 (C), 50.5 (CH), 91.4 (CH), 111.9 (CH), 119.6 (C), 122.9 (CH), 123.4 (CH), 127.1 (CH), 129.0 (CH), 129.3 (2CH), 129.4 (2CH), 130.2 (C), 130.3 (C), 130.8 (CH), 133.2 (C), 141.2 (C), 157.0 (C), 211.3 (C) ppm. Anal. Calcd (%) for $C_{23}H_{21}ClO_2$: C, 75.71; H, 5.80. Found (%): C, 75.81; H, 5.77.

*trans-1-Adamantyl-1-(4-chlorophenyl)-1,2-dihydronaphtho[2,1-b]furan-2-ylmethanone (**3q**).* Yield 78%; 1.04 g. Colorless crystals: mp 166−167 °C (from EtOH); IR ν_{max} (KBr) 3063 (CH Ar), 2926, 2903, 2849 (CH Ad), 1707 (C═O), 1632, 1578, 1489, 1464, 1450, 1375, 1252, 1223, 1092, 984, 961, 922, 833, 806, 754 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.71−1.78 (m, 6H), 1.89−1.98 (m, 6H), 2.06 (br s, 3H), 5.19 and 5.34 (d, 2H, J = 5.5 Hz), 7.17−7.27 (m, 8H), 7.77−7.80 (m, 2H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 27.9 (3CH), 36.6 ($3CH_2$), 37.8 ($3CH_2$), 46.4 (C), 50.1 (CH), 90.3 (CH), 112.0 (CH), 119.7 (C), 122.8 (CH), 123.3 (CH), 127.0 (CH), 129.0 (CH), 129.3 (2CH), 129.4 (2CH), 130.2 (C), 130.3 (C), 130.7 (CH), 133.1 (C), 141.1 (C), 157.1 (C), 209.8 (C) ppm; MS (EI) m/z (%) 442 (M^+, 4), 307(M^+ − Ad, 67), 306 (M^+ − Ad − H, 84), 216 (64), 215 (100), 168 (46), 135 (Ad^+, 76), 93 (40), 79 (27). Anal. Calcd (%) for $C_{29}H_{27}ClO_2$: C, 78.63; H, 6.14. Found (%): C, 78.78; H, 6.16.

*trans-[1-(4-Chlorophenyl)-1,2-dihydronaphtho[2,1-b]furan-2-yl](4-fluorophenyl)methanone (**3r**).* Yield 84%; 1.01 g. Colorless crystals: mp 173−174 °C (from EtOH); IR ν_{max} (KBr) 3067, 2926, 1690 (C═O), 1632, 1595, 1578, 1506, 1491, 1464, 1412, 1379, 1234, 1159, 1090, 1015, 984, 849, 812, 785, 752 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.40 and 5.79 (d, 2H, J = 5.5 Hz), 7.14−7.22 (m, 4H), 7.25−7.31 (m, 6H), 7.78−7.82 (m, 2H), 8.06 (dd, 2H, J = 9.2, 5.5 Hz) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 49.7 (CH), 91.6 (CH), 112.1 (CH), 116.1 (d, 2CH, J_{CF} = 21.9 Hz), 119.4 (C), 122.8 (CH), 123.6 (CH), 127.2 (CH), 129.0 (CH), 129.4 (2CH), 129.5 (2CH), 130.3 (2C), 130.8 (C), 130.9 (CH), 132.3 (d, 2CH, J_{CF} = 9.5 Hz), 133.4 (C), 140.9 (C), 157.0 (C), 166.3 (d, C, J_{CF} = 255.5 Hz), 193.1 (C) ppm. Anal. Calcd (%) for $C_{25}H_{16}ClFO_2$: C, 74.54; H, 4.00. Found (%): C, 74.62; H, 3.99.

*trans-[1-(4-Chlorophenyl)-1,2-dihydronaphtho[2,1-b]furan-2-yl](4-methylphenyl)methanone (**3s**).* Yield 71%; 0.85 g. Colorless crystals: mp 177−178 °C (from EtOH/DMF); IR ν_{max} (KBr) 3065 (CH Ar), 2920, 1686 (C═O), 1632, 1607, 1578, 1520, 1489, 1464, 1410, 1379, 1234, 1207, 1186, 1088, 1015, 984, 835, 812, 777, 748 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 2.45 (s, 3H), 5.33 and 5.86 (d, 2H, J = 5.5 Hz), 7.20−7.31 (m, 10H), 7.78−7.82 (m, 2H), 7.90 (d, 2H, J = 8.2 Hz) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.9 (CH_3),

dx.doi.org/10.1021/jo400621r | J. Org. Chem. 2013, 78, 5505−5520

50.1 (CH), 91.5 (CH), 112.2 (CH), 118.7 (C), 122.8 (CH), 123.4 (CH), 127.1 (CH), 129.0 (CH), 129.4 (2CH), 129.5 (2CH), 129.6 (4CH), 130.2 (C), 130.3 (C), 130.8 (CH), 131.8 (C), 133.3 (C), 141.0 (C), 145.1 (C), 157.3 (C), 194.1 (C) ppm. Anal. Calcd (%) for $C_{26}H_{19}ClO_2$: C, 78.29; H, 4.80. Found (%): C, 78.40; H, 4.78.

*trans-(2,2-Dimethyl-1-[1-(2-thienyl)-1,2-dihydronaphtho[2,1-b]furan-2-yl]-1-propanone (**3t**).* Yield 84%; 0.85 g. Creamy crystals: mp 75−76 °C (from EtOH); IR ν_{max} (KBr) 3055 (CH Ar), 2962, 2928, 1717 (C═O), 1628, 1520, 1462, 1366, 1242, 968, 822, 748, 702 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.29 (s, 9H), 5.45 and 5.58 (d, 2H, J = 5.1 Hz), 6.93−6.95 (m, 2H), 7.20 (dd, 1H, J = 4.6, 1.4 Hz), 7.22 (d, 1H, J = 8.7 Hz), 7.28 (td, 1H, J = 6.8, 0.9 Hz), 7.34 (td, 1H, J = 6.8, 0.9 Hz), 7.47 (d, 1H, J = 8.3 Hz), 7.79 (d, 1H, J = 8.7 Hz), 7.82 (d, 1H, J = 7.8 Hz) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 26.2 ($3CH_3$), 44.1 (C), 46.0 (CH), 91.0 (CH), 112.0 (CH), 119.6 (C), 122.8 (CH), 123.4 (CH), 125.1 (CH), 125.5 (CH), 127.1 (CH), 127.1 (CH), 128.9 (CH), 130.2 (C), 130.5 (C), 130.9 (CH), 146.1 (C), 156.7 (C), 211.0 (C) ppm. Anal. Calcd (%) for $C_{21}H_{20}O_2S$: C, 74.97; H, 5.99; S, 9.53. Found (%): C, 75.12; H, 6.02; S, 9.48.

*trans-1-Adamantyl-1-(2-thienyl)-1,2-dihydronaphtho[2,1-b]furan-2-ylmethanone (**3u**).* Yield 80%; 0.99 g. Colorless crystals: mp 154−155 °C (from hexane/ethylacetate); IR ν_{max} (KBr) 3101, 3063 (CH Ar), 2901, 2851 (CH Ad), 1701 (C═O), 1632, 1578, 1516, 1462, 1447, 1373, 1346, 1242, 1223, 964, 818 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.73−1.81 (m, 6H), 1.94−2.03 (m, 6H), 2.09 (br s, 3H), 5.49 and 5.54 (d, 2H, J = 5.0 Hz), 6.91−6.96 (m, 2H), 7.20 (dd, 1H, J = 5.0, 1.4 Hz), 7.23 (d, 1H, J = 8.7 Hz), 7.26−7.36 (m, 2H), 7.46 (d, 1H, J = 8.2 Hz), 7.78−7.82 (m, 2H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 27.9 (3CH), 36.6 ($3CH_2$), 37.8 ($3CH_2$), 45.6 (CH), 46.4 (C), 89.9 (CH), 112.0 (CH), 119.6 (C), 122.8 (CH), 123.4 (CH), 125.1 (CH), 125.5 (CH), 127.1 (CH), 127.1 (CH), 128.9 (CH), 130.1 (C), 130.5 (C), 130.9 (CH), 146.0 (C), 156.8 (C), 209.5 (C) ppm; MS (EI) m/z (%) 414 (M^+, 4), 279 (M^+ − Ad, 100), 250 (M^+ − AdCO − H, 14), 223 (17), 221 (22), 189 (14), 135 (Ad^+, 42), 93 (20), 79 (21). Anal. Calcd (%) for $C_{27}H_{26}O_2S$: C, 78.23; H, 6.32; S, 7.73. Found (%): C, 78.10; H, 6.34; S, 7.75.

*trans-1-Adamantyl-1-(3-nitrophenyl)-1,2-dihydronaphtho[2,1-b]furan-2-ylmethanone (**3v**).* Yield 61%; 0.83 g. Light yellow crystals: mp 205−206 °C (from EtOH); IR ν_{max} (KBr) 3070 (CH Ar), 2905, 2851 (CH Ad), 1705 (C═O), 1632, 1528 (NO_2), 1458, 1350 (NO_2), 1238, 1200, 987, 814, 748, 733, 687 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.70−1.79 (m, 6H), 1.91−2.01 (m, 6H), 2.07 (br s, 3H), 5.37 and 5.39 (d, 2H, J = 5.3 Hz), 7.20−7.29 (m, 4H), 7.47 (dd, 1H, J = 8.0, 7.8 Hz), 7.58 (d, 1H, J = 7.8 Hz), 7.81 (d, 2H, J = 8.9 Hz), 8.09−8.14 (m, 2H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 27.9 (3CH), 36.5 ($3CH_2$), 37.8 ($3CH_2$), 46.6 (C), 50.0 (CH), 90.5 (CH), 112.1 (CH), 119.0 (C), 122.5 (CH), 122.6 (CH), 122.9 (CH), 123.6 (CH), 127.3 (CH), 129.2 (CH), 130.1 (C), 130.2 (CH), 130.2 (C), 131.2 (CH), 134.3 (CH), 144.9 (C), 148.8 (C), 157.2 (C), 209.5 (C) ppm; MS (EI) m/z (%) 453 (M^+, 1), 318 (M^+ − Ad, 55), 317 (30), 215 (20), 168 (15), 135 (Ad^+, 100). Anal. Calcd (%) for $C_{29}H_{27}NO_4$: C, 76.80; H, 6.00; N, 3.09. Found (%): C, 76.95; H, 5.97; N, 3.07.

*trans-1-Adamantyl-1-(2-fluorophenyl)-1,2-dihydronaphtho[2,1-b]furan-2-ylmethanone (**3w**).* The crude product was purified by column chromatography over silica gel using toluene as eluent, followed by recrystallization from EtOH. Yield 64%; 0.82 g. Colorless crystals: mp 192−193 °C; IR ν_{max} (KBr) 3059 (CH Ar), 2912, 2851 (CH Ad), 1701 (C═O), 1632, 1485, 1450, 1223, 1200, 1161, 999, 954, 918, 814, 764 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.71−1.79 (m, 6H), 1.91−2.01 (m, 6H), 2.07 (br s, 3H), 5.48 and 5.50 (d, 2H, J = 4.9 Hz), 6.98−7.14 (m, 3H), 7.20−7.36 (m, 5H), 7.77−7.81 (m, 2H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 27.9 (3CH), 36.6 ($3CH_2$), 37.8 ($3CH_2$), 42.9 (d, CH, J_{CF} = 2.9 Hz), 46.1 (C), 88.6 (CH), 112.0 (CH), 115.7 (d, CH, J_{CF} = 21.9 Hz), 119.4 (C), 122.6 (CH), 123.3 (CH), 125.0 (d, CH, J_{CF} = 3.8 Hz), 127.1 (CH), 128.9 (CH), 129.0 (d, CH, J_{CF} = 7.6 Hz), 129.4 (d, C, J_{CF} = 14.3 Hz), 129.8 (d, CH, J_{CF} = 3.8 Hz), 130.0 (C), 130.4 (C), 130.6 (CH), 157.3 (C), 160.0 (C, J_{CF} = 245 Hz), 209.0 (C) ppm; MS (EI) m/z (%) 426 (M^+, 2), 291 (M^+ − Ad, 100), 290 (M^+ − Ad − H, 37), 263 (M^+ − AdCO, 11), 262 (M^+ − AdCO − H, 9), 235 (10), 233 (10), 215 (12), 168 (13), 135 (Ad^+, 54). Anal. Calcd (%) for $C_{29}H_{27}FO_2$: C, 81.66; H, 6.38. Found (%): C, 81.76; H, 6.36.

*trans-1-Adamantyl-1-(4-pyridyl)-1,2-dihydronaphtho[2,1-b]furan-2-ylmethanone (**3x**).* Yield 81%; 0.99 g. Colorless crystals: mp 195−196 °C (from EtOH); IR ν_{max} (KBr) 3063 (CH Ar), 2903, 2849 (CH Ad), 1707 (C═O), 1630, 1599, 1520, 1466, 1450, 1414, 1250, 1219, 1161, 1003, 978, 964, 922, 818, 752 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.69−1.78 (m, 6H), 1.88−1.98 (m, 6H), 2.06 (br s, 3H), 5.22 and 5.32 (d, 2H, J = 5.5 Hz), 7.15−7.31 (m, 6H), 7.78−7.82 (m, 2H), 8.53 (d, 2H, J = 6.0 Hz) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 27.8 (3CH), 36.5 ($3CH_2$), 37.7 ($3CH_2$), 46.5 (C), 49.7 (CH), 90.1 (CH), 112.0 (CH), 118.6 (C), 122.7 (CH), 123.2 (2CH), 123.5 (CH), 127.2 (CH), 129.0 (CH), 130.1 (C), 130.2 (C), 131.0 (CH), 150.6 (2CH), 151.3 (C), 157.3 (C), 209.4 (C) ppm; MS (EI) m/z (%) 409 (M^+, 6), 273 ((M^+ − Ad − H, 73), 246 (M^+ − AdCO, 35), 217 (58), 168 (46), 135 (Ad^+, 100), 93 (42), 79 (38). Anal. Calcd (%) for $C_{28}H_{27}NO_2$: C, 82.12; H, 6.65; N, 3.42. Found (%): C, 82.20; H, 6.59; N, 3.41.

*1,2-Dihydronaphtho[2,1-b]furan-2-carboxamide (**3y**).* Yield 69%; 0.44 g. Colorless crystals: mp 195−196 °C (from EtOH); IR ν_{max} (KBr) 3410, 3283, 3210 (NH_2), 3063 (CH Ar), 1632 (C═O), 1597, 1520, 1466, 1447, 1373, 1250, 1234, 1169, 1088, 1015, 995, 964, 810, 737, 721, 656 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 3.49 (dd, 1H, J = 16.0, 6.4 Hz), 3.71 (dd, 1H, J = 16.0, 10.9 Hz), 5.26 (dd, 1H, J = 10.9, 6.4 Hz), 7.18 (d, 1H, J = 8.7 Hz), 7.31 (t, 1H, J = 7.1 Hz), 7.42 (br s, 1H), 7.46 (t, 1H, J = 7.1 Hz), 7.62 (d, 1H, J = 8.2 Hz), 7.63 (br s, 1H), 7.75 (d, 1H, J = 8.7 Hz), 7.85 (d, 1H, J = 8.0 Hz) ppm; ^{13}C NMR (100 MHz, DMSO-d_6) δ 32.9 (CH_2), 81.2 (CH), 112.6 (CH), 118.1 (C), 123.5 (CH), 123.7 (CH), 127.4 (CH), 129.0 (CH), 129.4 (CH), 129.5 (C), 130.6 (C), 156.7 (C), 173.7 (C) ppm. Anal. Calcd (%) for $C_{13}H_{11}NO_2$: C, 73.22; H, 5.20; N, 6.57. Found (%): C, 73.35; H, 5.18; N, 6.60.

*2-(1-Adamantyl)[1,3]oxazolo[3,2-a]pyridin-4-ium bromide (**8**).* When using **7** instead of **2**, only oxazolo[3,2-*a*]pyridinium salt **8** was isolated under the conditions mentioned in this paper. Yield 56%; 0.56 g. Light beige crystals: mp > 300 °C; IR ν_{max} (KBr) 3098, 3024, 2997, 2928, 2905, 2851, 1639, 1562, 1493, 1450, 1204, 1173, 1153, 1026, 976, 937, 795 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 1.74 (br s, 6H), 1.97 (br s, 6H), 2.07 (br s, 3H), 7.88 (t, 1H, J = 6.6 Hz), 8.37−8.45 (m, 2H), 8.71 (s, 1H), 9.11 (d, 1H, J = 6.4 Hz) ppm; ^{13}C NMR (100 MHz, DMSO-d_6) δ 27.5 (3CH), 34.0 (C), 36.2 ($3CH_2$), 39.7 ($3CH_2$), 111.6 (CH), 112.2 (CH), 121.8 (CH), 132.5 (CH), 141.5 (CH), 153.3 (C), 163.1 (C) ppm. Anal. Calcd (%) for $C_{17}H_{20}BrNO$: C, 61.09; H, 6.03; N, 4.19. Found (%): C, 61.25; H, 5.99; N, 4.24.

*2-(4-Nitrophenyl)-1,2-dihydronaphtho[2,1-b]furan (**10a**).* A mixture of 1-[(dimethylamino)methyl]-2-naphthol **1a** (0.42 g, 2.1 mmol) and (2-nitrophenyl)metylpyridinium bromide **9a** (0.6 g, 2.1 mmol) in DMF (10 mL) was refluxed for 5 h under an Ar atmosphere. The resulting solution was cooled to room temperature and then poured into 50 mL of rapidly stirred saturated water solution of sodium chloride to yield a solid product, which was filtered, washed with water, dried and recrystallized from ethanol. Yield 45%, 0.28 g. Colorless crystals: mp 152−153 °C; IR ν_{max} (KBr) 3059 (CH Ar), 2920, 2889, 1632, 1601, 1512 (NO_2), 1346 (NO_2), 1238, 1165, 1107, 1065, 972, 853, 813, 752, 698 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 3.41 (dd, 1H, J = 15.3, 7.6 Hz), 4.02 (dd, 1H, J = 15.3, 10.3 Hz), 6.04 (dd, 1H, J = 10.3, 7.6 Hz), 7.23 (d, 1H, J = 8.7 Hz), 7.34 and 7.48 (t, 2H, J = 7.2 Hz), 7.55 (d, 1H, J = 8.2 Hz), 7.61 (d, 2H, J = 8.7 Hz), 7.76 (d, 1H, J = 9.0 Hz), 7.83 (d, 1H, J = 8.0 Hz), 8.23 (d, 2H, J = 8.7 Hz) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 37.6 (CH_2), 83.3 (CH-2), 111.9 (CH), 117.2 (C), 122.7 (CH), 123.4 (CH), 124.1 (2CH), 126.5 (2CH), 127.1 (CH), 128.9 (CH), 129.7 (C), 129.8 (CH), 130.7 (C), 147.7 (C), 149.8 (C), 156.9 (C) ppm. Anal. Calcd (%) for $C_{18}H_{13}NO_3$: C, 74.22; H, 4.50; N, 4.81. Found (%): C, 74.36; H, 4.47; N, 4.85.

*trans-2-(4-Nitrophenyl)-1-phenyl-1,2-dihydronaphtho[2,1-b]furan (**10b**).* Title compound was prepared similarly to compound **10a** from 1-[(dimethylamino)(phenyl)methyl]-2-naphthol **1b** and pyridinium salt **9a**. Yield 29%, 0.22g. Light yellow crystals: mp 209−210 °C (from EtOH/DMF); IR ν_{max} (KBr) 3061 (CH Ar), 2926,

dx.doi.org/10.1021/jo400621r | J. Org. Chem. 2013, 78, 5505−5520

1632, 1599, 1522 (NO_2), 1491, 1464, 1348 (NO_2), 1263, 1256, 1233, 1007, 995, 808, 746 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 4.83 (d, 1H, J = 6.6 Hz), 5.77 (d, 1H, J = 6.6 Hz), 7.17−7.20 (m, 1H), 7.22−7.27 (m, 4H), 7.31−7.37 (m, 4H), 7.52 (d, 2H, J = 8.5 Hz), 7.84 (t, 2H, J = 8.5 Hz), 8.22 (d, 2H, J = 9.0 Hz) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 58.1 (CH), 92.3 (CH), 112.0 (CH), 119.6 (C), 122.9 (CH), 123.4 (CH), 124.2 (2CH), 126.3 (2CH), 127.1 (CH), 127.7 (CH), 128.0 (2CH), 129.0 (CH), 129.4 (2CH), 130.3 (C), 130.6 (C), 130.9 (CH), 142.2 (C), 147.8 (C), 148.9 (C), 157.5 (C) ppm. Anal. Calcd (%) for $C_{24}H_{17}NO_3$: C, 78.46; H, 4.66; N, 3.81. Found (%): C, 78.61; H, 4.68; N, 3.78.

*Methyl 4-(1,2-dihydronaphtho[2,1-b]furan-2-yl)benzoate (**10c**).* Title compound was prepared similarly to compound **10a** from Mannich base **1b** and 1-[4-(methoxycarbonyl)benzyl]pyridinium bromide **9b**. Yield 40%, 0.26 g. Colorless crystals: mp 139−140 °C (from EtOH/DMF); IR ν_{max} (KBr) 3055, 3011 (CH Ar), 2959, 2934, 1715 (C═O), 1632, 1612, 1599, 1518, 1466, 1447, 1433, 1279, 1261, 1248, 1115, 1105, 974, 962, 810, 764, 739, 704 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 3.44 (dd, 1H, J = 15.4, 7.8 Hz), 3.92 (s, 3H), 3.98 (dd, 1H, J = 15.4, 10.1 Hz), 6.01 (dd, 1H, J = 10.1, 7.8 Hz), 7.22 (d, 1H, J = 8.9 Hz), 7.33 (ddd, 1H, J = 8.2, 6.9, 1.2 Hz), 7.47 (ddd, 1H, J = 8.2, 6.9, 1.2 Hz), 7.52 (d, 2H, J = 8.2 Hz), 7.56 (d, 1H, J = 8.2 Hz), 7.75 (d, 1H, J = 8.9 Hz), 7.83 (d, 1H, J = 8.2 Hz), 8.05 (d, 2H, J = 8.2 Hz) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 37.6 (CH_2), 52.3 (CH_3), 84.1 (CH), 112.0 (CH), 117.7 (C), 122.8 (CH), 123.2 (CH), 125.7 (2CH), 127.0 (CH), 128.9 (CH), 129.5 (CH), 129.6 (C), 129.9 (C), 130.2 (2CH), 130.8 (C), 147.5 (C), 157.1 (C), 166.9 (C) ppm. Anal. Calcd (%) for $C_{20}H_{16}O_3$: C, 78.93; H, 5.30. Found (%): C, 79.10; H, 5.26.

*2-Methyl-7-(4-nitrophenyl)-7,8-dihydrofurano[3,2-e][1]-benzofuran-1-ethanone (**10d**).* A mixture of Mannich base **1i** (0.87 g, 3.5 mmol) and pyridinium salt **9a** (1 g, 3.5 mmol) in DMF (10 mL) was refluxed for 5 h under an Ar atmosphere. The resulting solution was cooled to room temperature and then poured into 50 mL of rapidly stirred saturated water solution of sodium chloride to yield a solid product, which was filtered, washed with water and dried. The crude product was purified by column chromatography over silica gel using CH_2Cl_2 as eluent, followed by recrystallization from EtOH. Yield 37%; 0.44 g. Yellow crystals: mp 173−174 °C; IR ν_{max} (KBr) 2924, 1659 (C═O), 1601, 1516 (NO_2), 1474, 1431, 1396, 1342 (NO_2), 1242, 1215, 1011, 856, 810 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 2.52 (s, 3H), 2.74 (s, 3H), 3.58 (dd, 1H, J = 17.0, 7.6 Hz), 4.22 (dd, 1H, J = 17.0, 9.9 Hz), 5.88 (dd, 1H, J = 9.9, 7.6 Hz), 6.87 and 7.21 (d, 2H, J = 8.7 Hz), 7.57 (d, 2H, J = 8.5 Hz), 8.19 (d, 2H, J = 8.5 Hz) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 16.2 (CH_3), 30.8 (CH_3), 40.7 (CH_2), 82.9 (CH), 106.8 (CH), 109.9 (CH), 117.7 (C), 119.1 (C), 123.7 (C), 123.9 (2CH), 126.4 (2CH), 147.5 (C), 149.6 (C), 150.1 (C), 156.6 (C), 162.6 (C), 193.3 (C) ppm. Anal. Calcd (%) for $C_{19}H_{15}NO_5$: C, 67.65; H, 4.48; N, 4.15. Found (%):C, 67.79; H, 4.46; N, 4.17.

*Ethyl 6,7-dimethyl-2-(4-nitrophenyl)-1,6-dihydro-2H-furo[3,2-e]-indole-8-carboxylate (**10e**).* Title compound was prepared similarly to compound **10d** from Mannich base **1j** and pyridinium salt **9a**. Yield 33%; 0.44 g. Yellow crystals: mp 169−171 °C (from EtOH); IR ν_{max} (KBr) 3075, 2986, 2909, 1690 (C═O), 1597, 1516 (NO_2), 1474, 1435, 1412, 1346 (NO_2), 1231, 1211, 1165, 1084, 1065, 856, 775 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.36 (t, 3H, J = 7.1 Hz), 2.71 (s, 3H), 3.63 (dd, 1H, J = 16.7, 7.6 Hz), 3.67 (s, 3H), 4.26 (dd, 1H, J = 16.7, 10.1 Hz), 4.30 (q, 2H, J = 7.1 Hz), 5.86 (dd, 1H, J = 10.1, 7.6 Hz), 6.88 and 7.10 (d, 2H, J = 8.7 Hz), 7.59 (d, 2H, J = 8.5 Hz), 8.19 (d, 2H, J = 8.5 Hz) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 12.5 (CH_3), 14.7 (CH_3), 30.2 (CH_3), 41.1 (CH_2), 59.5 (CH_2), 82.6 (CH), 103.4 (C), 105.1 (CH), 108.8 (CH), 115.5 (C), 123.8 (C), 123.9 (2CH), 126.4 (2CH), 133.1 (C), 145.8 (C), 147.4 (C), 150.7 (C), 155.4 (C), 165.5 (C) ppm. Anal. Calcd (%) for $C_{21}H_{20}N_2O_5$: C, 66.31; H, 5.30; N, 7.36. Found (%): C, 66.45; H, 5.27; N, 7.40.

*1-Adamantyl[1-(3-nitrophenyl)naphtho[2,1-b]furan-2-yl]-methanone (**11a**).* A mixture of 1,2-dihydronaphtho[2,1-*b*]furan **3v** (0.20 g, 0.44 mmol) and DDQ (0.11 g, 0.48 mmol) in toluene (6 mL) was refluxed for 6 h. After being cooled to room temperature, the mixture was filtered and concentrated in vacuo, and the residue was purified by recrystallization from ethanol. Yield 70%; 0.14 g. Light yellow crystals: mp 207−209 °C; IR ν_{max} (KBr) 3075, 3055 (CH Ar), 2901, 2851 (CH Ad), 1659 (C═O), 1551, 1524 (NO_2), 1477, 1447, 1339 (NO_2), 1277, 1223, 1142, 1099, 1026, 1007, 953, 806, 741 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.82 (br s, 6H), 2.13 (br s, 3H), 2.16 (br s, 6H), 7.29−7.37 (m, 2H), 7.47 (ddd, 1H, J = 8.2, 6.9, 1.4 Hz), 7.70−7.76 (m, 2H), 7.82 (d, 1H, J = 7.3 Hz), 7.94−7.97 (m, 2H), 8.34 (dd, 1H, J = 1.8, 1.4 Hz), 8.39 (ddd, 1H, J = 8.2, 2.3, 0.9 Hz) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 28.2 (3CH), 36.8 ($3CH_2$), 37.8 ($3CH_2$), 46.9 (C), 112.7 (CH), 121.4 (C), 122.8 (CH), 123.3 (CH), 124.7 (CH), 125.5 (CH), 127.4 (CH), 128.2 (C), 128.3 (C), 129.5 (CH), 129.8 (CH), 130.4 (CH), 131.1 (C), 135.9 (CH), 136.0 (C), 148.0 (C), 148.6 (C), 151.9 (C), 196.6 (C) ppm. Anal. Calcd (%) for $C_{29}H_{25}NO_4$: C, 77.14; H, 5.58; N, 3.10. Found (%): C, 77.23; H, 5.60; N, 3.08.

*[1-(4-Chlorophenyl)naphtho[2,1-b]furan-2-yl](4-methylphenyl)-methanone (**11b**).* Title compound was prepared similarly to compound **11a** from dihydronaphthofuran **3s**. Yield 63%; 0.11 g. Light yellow crystals: mp 150−151 °C (from EtOH); IR ν_{max} (KBr) 1643 (C═O), 1607, 1541, 1485, 1339, 1279, 1240, 1180, 1086, 1013, 930, 868, 831, 804, 754 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 2.35 (s, 3H), 7.28 (d, 2H, J = 8.2 Hz), 7.41−7.45 (m, 1H), 7.49−7.57 (m, 6H), 7.77 (d, 2H, J = 8.2 Hz), 7.92 (d, 1H, J = 8.7 Hz), 8.08−8.11 (m, 2H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.7 (CH_3), 113.5 (CH), 120.3 (C), 122.7 (CH), 126.0 (CH), 127.9 (CH), 129.2 (CH), 129.4 (C), 129.5 (CH), 129.6 (C), 130.1 (CH), 130.1 (CH), 131.0 (CH), 131.3 (C), 132.0 (C), 132.2 (CH), 133.7 (C), 134.9 (C), 143.8 (C), 148.0 (C), 152.8 (C), 184.1 (C) ppm. Anal. Calcd (%) for $C_{26}H_{17}ClO_2$: C, 78.69; H, 4.32. Found (%): C, 78.85; H, 4.30.

*1-Naphthyl(1-phenylnaphtho[2,1-b]furan-2-yl)methanone (**11c**).* Title compound was prepared similarly to compound **11a** from dihydronaphthofuran **3i**. Yield 80%; 0.14 g. Colorless crystals: mp 170−172 °C (from EtOH); IR ν_{max} (KBr) 3051 (CH Ar), 2922, 1655 (C═O), 1543, 1508, 1398, 1344, 1288, 1204, 1082, 1057, 1007, 978, 910, 804, 781, 752, 698 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.04−7.07 (m, 2H), 7.12−7.15 (m, 3H), 7.21−7.30 (m, 2H), 7.41−7.47 (m, 3H), 7.51 (d, 2H, J = 7.8 Hz), 7.72−7.76 (m, 3H), 7.92−7.95 (m, 2H), 8.04−8.07 (m, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 112.9 (CH), 122.2 (C), 123.2 (CH), 124.3 (CH), 125.2 (CH), 125.3 (CH), 126.2 (CH), 127.2 (2CH), 127.6 (CH), 128.0 (2CH), 128.1 (CH), 128.3 (CH), 129.0 (CH), 129.4 (CH), 129.5 (2CH), 130.7 (C), 131.0 (CH), 131.1 (C), 131.2 (CH), 132.2 (C), 132.6 (C), 133.3 (C), 135.9 (C), 148.6 (C), 153.6 (C), 187.1 (C) ppm. Anal. Calcd (%) for $C_{29}H_{18}O_2$: C, 87.42; H, 4.55. Found (%): C, 87.57; H, 4.54.

*[1-(4-Chlorophenyl)naphtho[2,1-b]furan-2-yl](4-fluorophenyl)-methanone (**11d**).* Title compound was prepared similarly to compound **11a** from dihydronaphthofuran **3r**. Yield 74%; 0.13 g. Light yellow crystals: mp 168−169 °C (from EtOH); IR ν_{max} (KBr) 1641 (C═O), 1597, 1543, 1489, 1410, 1344, 1275, 1238, 1155, 1086, 1013, 932, 870, 804, 766 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.26−7.30 (m, 2H), 7.41−7.45 (m, 1H), 7.49−7.53 (m, 6H), 7.91−7.95 (m, 3H), 8.08−8.12 (m, 2H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 113.5 (CH), 116.0 (d, 2CH, J_{CF}= 21.9 Hz), 121.5 (C), 122.7 (CH), 126.1 (CH), 128.0 (CH), 128.4 (C), 129.2 (2CH), 130.1 (C), 130.2 (CH), 131.3 (C), 131.3 (C), 131.9 (C), 132.2 (2CH), 132.9 (d, 2CH, J_{CF} = 9.5 Hz), 133.8 (C), 134.2 (d, CH, J_{CF} = 2.9 Hz), 147.7 (C), 153.0 (C), 165.2 (d, CH, J_{CF} = 250.0 Hz), 183.0 (C) ppm. Anal. Calcd (%) for $C_{25}H_{14}ClFO_2$: C, 74.91; H, 3.52. Found (%): C, 74.99; H, 3.50.

*1-Adamantyl(5,7-di-tert-butyl-2,3-dihydro-1-benzofuran-2-yl)-methanone (**13a**).* A mixture of 4,6-di-*tert*-butyl-2-dimethylaminomethylphenol **12** (0.78 g, 3 mmol), pyridinium salt **2f** (1 g, 3 mmol), and Hünig's base (0.6 mL, 3.5 mmol) in DMF (10 mL) was refluxed for 6 h under an Ar atmosphere. Afterward, the reaction mixture was cooled and poured into 50 mL of cold water to yield the solid, which was filtered, washed with water, dried and recrystallized from methanol. Yield 58%; 0.68 g. Colorless crystals: mp 117−118 °C; IR ν_{max} (KBr) 2955, 2909, 2851 (CH Ad), 1705 (C═O), 1477, 1454, 1412, 1362, 1312, 1285, 1231, 1200, 1157, 1099, 980, 918, 876, 825, 744 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.28 (s, 9H), 1.38 (s, 9H), 1.71−1.79 (m,

dx.doi.org/10.1021/jo400621r | J. Org. Chem. 2013, 78, 5505−5520

6H), 1.95−2.03 (m, 6H), 2.06−2.09 (m, 3H), 3.28 (d, 2H, J = 9.6 Hz), 5.41 (t, 1H, J = 9.6 Hz), 7.04 (d, 1H, J = 2.3 Hz), 7.10 (d, 1H, J = 2.3 Hz) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 27.9 (3CH), 29.6 ($3CH_3$), 31.9 ($3CH_3$), 33.0 (CH_2), 34.3 (C), 34.5 (C), 36.6 (CH_2), 38.0 (CH_2), 46.1 (C), 81.5 (CH), 119.3 (CH), 122.1 (CH), 125.2 (C), 132.1 (C), 143.6 (C), 154.8 (C), 210.7 (C) ppm; MS (EI) m/z (%) 394 (M^+, 48), 379 ($M^+ - CH_3$, 18), 259 (M^+ − Ad, 87), 231 (M^+ − AdCO, 30), 230 (M^+ − AdCO − H, 45), 215 (M^+ − AdCO − H − CH_3, 100), 201 (14), 135 (Ad, 61), 57 (C_4H_9, 58). Anal. Calcd (%) for $C_{27}H_{38}O_2$: C, 82.18; H, 9.71. Found (%): C, 82.37; H, 9.67.

*1-[2-(1-Adamantylcarbonyl)-4-hydroxy-2,3-dihydrobenzo[b]-furan-5-y]-1-ethanone (**13b**).* A mixture of 2,4-dihydroxy-3-morpholin-4-yl-methylacetophenone **14** (0.75 g, 3 mmol), pyridinium salt **2f** (1 g, 3 mmol), and DBU (0.45 mL, 3 mmol) in CH_3CN (15 mL) under an Ar atmosphere was heated at reflux temperature for 4 h. The solvent was removed by evaporation under reduced pressure. The crude product was purified by column chromatography over silica gel using CH_2Cl_2 as eluent, followed by recrystallization from EtOH. Yield 68%; 0.69 g. Colorless crystals: mp 154−155 °C (from EtOH); IR ν_{max} (KBr) 2905, 2851, 1709 (C═O), 1651 (C═O), 1612, 1489, 1447, 1366, 1331, 1300, 1265, 1204, 1165, 1061, 991, 918, 845, 799 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.70−1.79 (m, 6H), 1.84−1.97 (m, 6H), 2.08 (br s, 3H), 2.53 (s, 3H), 3.13 (dd, 1H, J = 15.6, 7.6 Hz), 3.38 (dd, 1H, J = 15.6, 10.5 Hz), 5.64 (dd, 1H, J = 10.5, 7.6 Hz), 6.43 (d, 1H, J = 8.6 Hz), 7.60 (d, 1H, J = 8.6 Hz), 12.72 (s, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 26.5 (CH_3), 27.8 (3CH), 30.1 (CH_2), 36.5 ($3CH_2$), 38.0 ($3CH_2$), 45.7 (C), 82.4 (CH), 102.1 (CH), 111.7 (C), 115.1 (C), 133.4 (CH), 160.3 (C), 166.6 (C), 202.9 (C), 209.5 (C) ppm. Anal. Calcd (%) for $C_{21}H_{24}O_4$: C, 74.09; H, 7.11. Found (%): C, 73.95; H, 7.13.

*1-Adamantyl-5-nitro-2,3-dihydrobenzo[b]furan-2-ylmethanone (**13c**).* A mixture of 4-nitro-2-[(triethylammonio)methyl]phenolate **15**[34] (0.6 g, 2.4 mmol), pyridinium salt **2f** (0.8 g, 2.4 mmol), TMG (0.3 mL, 2.4 mmol), water (2 mL) and acetonitrile (4 mL) was refluxed for 5 h. The solvent was removed by evaporation under reduced pressure. The crude product was purified by recrystallization from ethanol. Yield 46%; 0.36 g. Light yellow crystals: mp 102−103 °C; IR ν_{max} (KBr) 2908, 2847 (CH Ad), 1717 (C═O), 1597, 1512 (NO_2), 1485, 1435, 1331 (NO_2), 1250, 1204, 1072, 991, 922 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.71−1.80 (m, 6H), 1.86−1.96 (m, 6H), 2.09 (br s, 3H), 3.34 (dd, 1H, J = 16.0, 7.3 Hz), 3.43 (dd, 1H, J = 16.0, 10.1 Hz), 5.68 (dd, 1H, J = 10.1, 7.3 Hz), 6.87 (d, 1H, J = 8.7 Hz), 8.05 (d, 1H, J = 2.3 Hz), 8.10 (dd, 1H, J = 8.7, 2.3 Hz) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 27.8 (3CH), 32.2 (CH_2), 36.5 ($3CH_2$), 37.9 ($3CH_2$), 45.9 (C), 82.1 (CH), 109.4 (CH), 121.2 (CH), 126.1 (CH), 127.0 (C), 142.5 (C), 164.7 (C), 209.1 (C) ppm. Anal. Calcd (%) for $C_{19}H_{21}NO_4$: C, 69.71; H, 6.47; N, 4.28. Found (%): C, 69.60; H, 6.49; N, 4.30.

*2,2-Dimethyl-1-(5-nitro-2,3-dihydrobenzo[b]furan-2-yl)-1-propanone (**13d**).* Title compound was obtained similarly to compound **13c** from phenolate **15**, 1-(3,3-dimethyl-2-oxobutyl)pyridinium bromide **2h**, and TMG. Yield 52%; 0.31 g. Yellow crystals: mp 99−100 °C (from EtOH); IR ν_{max} (KBr) 3105 (CH Ar), 2967, 2874, 1705 (C═O), 1620, 1597, 1520 (NO_2), 1474, 1447, 1335 (NO_2), 1238, 1107, 1065, 984, 922, 833, 810, 748, 667 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.24 (s, 9H), 3.36 (dd, 1H, J = 16.0, 7.3 Hz), 3.46 (dd, 1H, J = 16.0, 10.1 Hz), 5.65 (dd, 1H, J = 10.1, 7.3 Hz), 6.87 (d, 1H, J = 8.7 Hz), 8.04 (d, 1H, J = 2.3 Hz), 8.06 (dd, 1H, J = 8.7, 2.3 Hz) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 26.2 ($3CH_3$), 32.4 (CH_2), 43.7 (C), 82.9 (CH), 109.4 (CH), 121.2 (CH), 126.0 (CH), 127.1 (C), 142.5 (C), 164.5 (C), 210.2 (C) ppm. Anal. Calcd (%) for $C_{13}H_{15}NO_4$: C, 62.64; H, 6.07; N, 5.62. Found (%): C, 62.75; H, 6.04; N, 5.65.

*1-Adamantyl-5-methoxy-2,3-dihydrobenzo[b]furan-2-ylmethanone (**13e**) and 1-[2-(1-Adamantylcarbonyloxy)-5-methoxyphenethyl]pyridinium bromide (**17a**).* A mixture of quaternary ammonium salt **16a** (1 g, 3.1 mmol), pyridinium bromide **2f** (1.04 g, 3.1 mmol) and DBU (0.46 mL, 3.1 mmol) in CH_3CN (20 mL) was refluxed for 3 h under an Ar atmosphere. The solvent was removed by evaporation under reduced pressure. The products were separated by column chromatography (silica gel, CH_2Cl_2 → CH_2Cl_2:MeOH/1:1) to give **13e** (0.63 g, 65%), **17a** (0.2 g, 14%).

13e: colorless crystals; mp 117−118 °C (from EtOH); IR ν_{max} (KBr) 2905, 2851 (CH Ad), 1713 (C═O), 1489, 1447, 1431, 1254, 1238, 1204, 1177, 1138, 1034, 995, 922, 798 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.70−1.79 (m, 6H), 1.88−1.97 (m, 6H), 2.06 (br s, 3H), 3.26 (dd, 1H, J = 15.8, 7.8 Hz), 3.34 (dd, 1H, J = 15.8, 9.9 Hz), 3.73 (s, 3H), 5.46 (dd, 1H, J = 9.9, 7.8 Hz), 6.65 (dd, 1H, J = 8.5, 2.8 Hz), 6.72−6.74 (m, 2H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 27.9 (3CH), 33.6 (CH_2), 36.6 ($3CH_2$), 37.9 ($3CH_2$), 46.0 (C), 56.1 (CH_3), 81.4 (CH), 109.5 (CH), 111.1 (CH), 113.2 (CH), 126.3 (C), 153.4 (C), 154.5 (C), 210.9 (C) ppm; MS (EI) m/z (%) 312 (M^+, 14), 177 (M^+ − Ad, 12), 176 (M^+ − Ad − H, 10), 149 (M^+ − AdCO, 52), 148 (M^+ − AdCO − H, 64), 135 (Ad^+, 100). Anal. Calcd (%) for $C_{20}H_{24}O_3$: C, 76.89; H, 7.74. Found (%): C, 77.07; H, 7.70.

17a: colorless crystals; mp 239−240 °C (decomp.) (from EtOH); IR ν_{max} (KBr) 3040 (CH Ar), 2901, 2851 (CH Ad), 1736 (C═O), 1632, 1609, 1501, 1454, 1323, 1254, 1184, 1049, 679 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ 1.69 (br s, 6H), 1.90 (br s, 6H), 2.00 (br s, 3H), 3.05 (t, 2H, J = 6.5 Hz), 3.67 (s, 3H), 4.82 (t, 2H, J = 6.5 Hz), 6.79−6.86 (m, 3H), 8.09 (t, 2H, J = 7.1 Hz), 8.57 (t, 1H, J = 7.8 Hz), 8.81 (d, 2H, J = 6.0 Hz) ppm; ^{13}C NMR (100 MHz, DMSO-d_6) δ 27.8 (3CH), 31.1 (CH_2), 36.3 ($3CH_2$), 38.7 ($3CH_2$), 40.9 (C), 56.0 (CH_3O), 61.2 (CH_2N), 114.5 (CH), 115.6 (CH), 124.0 (CH), 128.5 (2CH), 129.4 (C), 142.9 (C), 145.2 (2CH), 146.4 (CH), 157.4 (C), 176.2 (C) ppm. Anal. Calcd (%) for $C_{25}H_{30}BrNO_3$: C, 63.56; H, 6.40; N, 2.96. Found (%): C, 63.69; H, 6.37; N, 3.00.

*1-(2-{2-[(4-Bromobenzoyl)oxy]-5-methoxyphenyl}ethyl)-pyridinium bromide (**17b**).* A mixture of quaternary ammonium salt **16a** (1 g, 3.1 mmol), *N*-(4-bromophenacyl)pyridinium bromide **2a** (1.07 g, 3.1 mmol) and DBU (0.47 mL, 3.1 mmol) in CH_3CN (20 mL) was refluxed for 3 h under an Ar atmosphere. The solvent was removed by evaporation under reduced pressure. The crude product was washed with water and purified by recrystallization from EtOH. Yield 61%; 0.93 g. Light yellow crystals: mp 198−199 °C; IR ν_{max} (KBr) 3051, 3009, 2967, 2936, 1732 (C═O), 1632, 1605, 1585, 1497, 1246, 1200, 1173, 1069, 1034, 1007, 748, 679 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ 3.19 (t, 2H, J = 6.6 Hz), 3.71 (s, 3H), 4.86 (t, 2H, J = 6.6 Hz), 6.87 (dd, 1H, J = 8.9, 3.0 Hz), 6.93 (d, 1H, J = 3.0 Hz), 7.10 (d, 1H, J = 8.9 Hz), 7.81 (d, 2H, J = 8.5 Hz), 7.95 (d, 2H, J = 8.5 Hz), 8.08 (t, 2H, J = 7.0 Hz), 8.57 (t, 1H, J = 7.7 Hz), 8.88 (d, 2H, J = 5.5 Hz) ppm; ^{13}C NMR (100 MHz, DMSO-d_6) δ 31.3 (CH_2), 56.1 (CH_3O), 61.2 (CH_2N), 114.5 (CH), 115.9 (CH), 124.2 (CH), 128.3 (C), 128.5 (2CH), 128.8 (C), 129.6 (C), 132.4 (2CH), 132.7 (2CH), 142.8 (C), 145.3 (2CH), 146.4 (CH), 157.7 (C), 164.7 (C) ppm. Anal. Calcd (%) for $C_{21}H_{19}Br_2NO_3$: C, 51.14; H, 3.88; N, 2.84. Found (%): C, 51.20; H, 3.86; N, 2.88.

*1-(2-{2-[(4-Methylbenzoyl)oxy]-5-methoxyphenyl}ethyl)-pyridinium bromide (**17c**).* Title compound was obtained similarly to compound **17b** from quaternary ammonium salt **16a** and pyridinium salt **2d**. Yield 34%; 0.45 g. Light yellow crystals: mp 201−203 °C (from EtOH); IR ν_{max} (KBr) 3055, 3028, 1732 (C═O), 1632, 1609, 1501, 1466, 1258, 1200, 1177, 1065, 1030, 1015, 748, 683 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ 2.40 (s, 3H), 3.17 (t, 2H, J = 6.6 Hz), 3.70 (s, 3H), 4.87 (t, 2H, J = 6.6 Hz), 6.86 (dd, 1H, J = 8.7, 2.7 Hz), 6.91 (d, 1H, J = 2.7 Hz), 7.07 (d, 1H, J = 8.7 Hz), 7.39 (d, 2H, J = 8.2 Hz), 7.93 (d, 2H, J = 8.2 Hz), 8.06 (dd, 2H, J = 7.8, 6.9 Hz), 8.57 (t, 1H, J = 7.8 Hz), 8.87 (d, 2H, J = 6.0 Hz) ppm; ^{13}C NMR (100 MHz, DMSO-d_6) δ 21.9 (CH_3), 31.3 (CH_2), 56.1 (CH_3), 61.2 (CH_2), 114.5 (CH), 115.8 (CH), 124.2 (CH), 126.3 (C), 128.5 (2CH), 129.6 (C), 130.1 (2CH), 130.5 (2CH), 142.9 (C), 145.2 (C, 2CH), 146.3 (CH), 157.6 (C), 165.3 (C) ppm. Anal. Calcd (%) for $C_{22}H_{22}BrNO_3$: C, 61.69; H, 5.18; N, 3.27. Found (%): C, 61.77; H, 5.17; N, 3.31.

General Experimental Procedure for the Synthesis of 2,3-Dihydrobenzofurans 13f−k. A mixture of quaternary ammonium salt **16b−g** (3 mmol), pyridinium salt **2a,f,l** (3 mmol), DBU (3 mmol) in CH_3CN (20 mL) under an Ar atmosphere was heated at reflux temperature for 4 h. The solvent was removed by evaporation under reduced pressure. The crude product was washed with water and

dx.doi.org/10.1021/jo400621r | J. Org. Chem. 2013, 78, 5505−5520

purified by column chromatography (silica gel, CH_2Cl_2). The yields of **13f–k** were summarized in Table 3.

*2-(4-Bromobenzoyl)-7-methoxy-2,3-dihydro-1-benzofuran-5-carbaldehyde (**13f**).* Yield 71%; 0.77 g. Bright yellow crystals: mp 107–108 °C (from EtOH); IR ν_{max} (KBr) 3001, 2970, 2940, 2843, 2808, 2754, 1682 (C=O), 1585, 1489, 1462, 1396, 1323, 1227, 1204, 1134, 1076, 910 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 3.39 (dd, 1H, J = 16.3, 6.4 Hz), 3.68 (dd, 1H, J = 16.3, 11.0 Hz), 3.82 (s, 3H), 6.51 (dd, 1H, J = 11.0, 6.4 Hz), 7.35 and 7.40 (d, 2H, J = 1.2 Hz), 7.77 (d, 2H, J = 8.7 Hz), 7.93 (d, 2H, J = 8.7 Hz), 9.77 (s, 1H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6) δ 32.3 (CH_2), 56.3 (CH_3), 83.8 (CH), 113.0 (CH), 120.9 (CH), 128.2 (C), 128.8 (C), 131.4 (2CH), 131.9 (C), 132.6 (2CH), 133.3 (C), 144.9 (C), 153.2 (C), 191.5 (CH), 194.3 (C) ppm. Anal. Calcd (%) for $C_{17}H_{13}BrO_4$: C, 56.53; H, 3.63. Found (%): C, 56.65; H, 3.59.

*(4-Bromophenyl)(5-nitro-2,3-dihydro-1-benzofuran-2-yl)-methanone (**13g**).* Yield 51%; 0.53 g. Creamy crystals: mp 128–129 °C (from EtOH); IR ν_{max} (KBr) 3082, 2959, 2932, 1701 (C=O), 1597, 1585, 1508 (NO_2), 1481, 1400, 1335 (NO_2), 1250, 1219, 1072, 988, 918, 903, 837, 748 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 3.41 (dd, 1H, J = 16.7, 6.4 Hz), 3.73 (dd, 1H, J = 16.7, 11.0 Hz), 6.51 (dd, 1H, J = 11.0, 6.4 Hz), 7.04 (d, 1H, J = 8.7 Hz), 7.87 (d, 2H, J = 8.5 Hz), 7.93 (d, 2H, J = 8.5 Hz), 8.07 (d, 1H, J = 8.7 Hz), 8.10 (s, 1H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6) δ 32.0 (CH_2), 84.4 (CH), 110.0 (CH), 121.9 (CH), 126.3 (CH), 128.4 (C), 128.9 (C), 131.3 (2CH), 132.6 (2CH), 133.1 (C), 142.2 (C), 165.0 (C), 194.2 (C) ppm. Anal. Calcd (%) for $C_{15}H_{10}BrNO_4$: C, 51.75; H, 2.90; N, 4.02. Found (%): C, 51.87; H, 2.91; N, 3.98.

*Methyl 2-(4-bromobenzoyl)-7-methoxy-2,3-dihydro-1-benzofuran-5-carboxylate (**13h**).* Yield 69%; 0.81 g. Colorless crystals: mp 145–146 °C (from EtOH/CH_3CN); IR ν_{max} (KBr) 3005, 2982, 2947, 2835, 1713 (C=O), 1686 (C=O), 1616, 1585, 1493, 1450, 1423, 1396, 1335, 1246, 1227, 1196, 1169, 1099, 1069, 991, 914, 764 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 3.36 (dd, 1H, J = 16.0, 6.6 Hz), 3.65 (dd, 1H, J = 16.0, 11.0 Hz), 3.77 (s, 3H), 3.79 (s, 3H), 6.38 (dd, 1H, J = 11.0, 6.6 Hz), 7.36 and 7.44 (d, 2H, J = 1.4 Hz), 7.77 (d, 2H, J = 8.5 Hz), 7.92 (d, 2H, J = 8.5 Hz) ppm; ^{13}C NMR (100 MHz, DMSO-d_6) δ 32.4 (CH_2), 52.4 (CH_3), 56.3 (CH_3), 83.6 (CH), 113.4 (CH), 119.6 (CH), 123.7 (C), 127.7 (C), 128.8 (C), 131.3 (2CH), 132.6 (2CH), 133.4 (C), 144.1 (C), 152.0 (C), 166.4 (C), 194.5 (C) ppm. Anal. Calcd (%) for $C_{18}H_{15}BrO_5$: C, 55.26; H, 3.86. Found (%): C, 55.37; H, 3.84.

*Methyl 2-acetyl-2,3-dihydro-1-benzofuran-6-carboxylate (**13i**).* Yield 52%; 0.34 g. Colorless crystals: mp 60–62 °C (from Et_2O); IR ν_{max} (KBr) 3005, 2959, 1717 (C=O), 1589, 1493, 1443, 1292, 1265, 1219, 1173, 1111, 1080, 972, 764 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 2.29 (s, 3H), 3.35 (dd, 1H, J = 17.0, 6.4 Hz), 3.49 (dd, 1H, J = 17.0, 11.0 Hz), 3.89 (s, 3H), 5.08 (dd, 1H, J = 11.0, 6.4 Hz), 7.21 (d, 1H, J = 7.4 Hz), 7.50 (d, 1H, J = 1.4 Hz), 7.61 (dd, 1H, J = 7.4, 1.4 Hz) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 26.4 (CH_3), 32.7 (CH_2), 52.3 (CH_3), 86.0 (CH), 110.6 (CH), 123.4 (CH), 124.8 (CH), 130.9 (2C), 159.2 (C), 166.8 (C), 208.3 (C) ppm. Anal. Calcd (%) for $C_{12}H_{12}O_4$: C, 65.45; H, 5.49. Found (%): C, 65.57; H, 5.46.

*2,5-Diacetyl-2,3-dihydro-1-benzofuran (**13j**).* Yield 69%; 0.42 g. Colorless crystals: mp 79–80 °C (from EtOH); IR ν_{max} (KBr) 2970, 1724 (C=O), 1670 (C=O), 1605, 1485, 1435, 1350, 1281, 1242, 1177, 1115, 1018, 968, 810 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 2.27 (s, 3H), 2.51 (s, 3H), 3.31 (dd, 1H, J = 16.0, 6.7 Hz), 3.48 (dd, 1H, J = 16.0, 11.0 Hz), 5.12 (dd, 1H, J = 11.0, 6.9 Hz), 6.88 (d, 1H, J = 8.7 Hz), 7.79–7.82 (m, 2H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 26.4 (CH_3), 26.6 (CH_3), 32.0 (CH_2), 86.6 (CH-2), 109.4 (CH), 125.7 (CH), 126.0 (C), 130.7 (CH), 131.6 (C), 163.1 (C), 196.6 (C), 207.4 (C) ppm; MS (EI) m/z (%) 204 (M^+, 28), 189 ($M^+ - CH_3$, 43), 161 ($M^+ - CH_3CO$, 27), 145 (10), 89 (10), 43 (CH_3CO, 100). Anal. Calcd (%) for $C_{12}H_{12}O_3$: C, 70.57; H, 5.92. Found (%): C, 70.76; H, 5.88.

*1-Adamantyl-5,6-dimethyl-2,3-dihydrobenzo[b]furan-2-ylmethanone (**13k**).* Yield 81%; 0.79 g. Colorless crystals: mp 112–113 °C (from EtOH); IR ν_{max} (KBr) 2924, 2901, 2847 (CH Ad), 1705 (C=O), 1624, 1597, 1497, 1454, 1261, 1165, 1068, 1011, 995, 922, 852 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.70–1.78 (m, 6H), 1.88–1.97 (m, 6H), 2.06 (br s, 3H), 2.16 (s, 3H), 2.19 (s, 3H), 3.19 (dd, 1H, J = 15.4, 7.8 Hz), 3.31 (dd, 1H, J = 15.4, 10.1 Hz), 5.44 (dd, 1H, J = 10.1, 7.8 Hz), 6.65 (s, 1H), 6.90 (s, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 19.3 (CH_3), 20.2 (CH_3), 27.9 (3CH), 33.2 (CH_2), 36.6 ($3CH_2$), 38.0 ($3CH_2$), 45.9 (C), 81.3 (CH), 110.7 (CH), 122.2 (C), 125.7 (CH), 128.8 (C), 136.5 (C), 157.6 (C), 211.0 (C) ppm; MS (EI) m/z (%) 310 (M^+, 7), 175 ($M^+ - Ad$, 36), 174 ($M^+ - Ad - H$, 27), 147 ($M^+ - AdCO$, 62), 146 ($M^+ - AdCO - H$, 75), 135 (Ad^+, 100), 131 (27), 119 (61), 107 (16). Anal. Calcd (%) for $C_{21}H_{26}O_2$: C, 81.25; H, 8.44. Found (%): C, 81.38; H, 8.41.

*1-Adamantyl-2,3-dihydrobenzo[b]furan-2-ylmethanone (**13l**). Method A.* TMG (0.41 mL, 3.2 mmol) was added to a mixture of salicylic alcohol **18** (0.2 g, 1.6 mmol) and pyridinium bromide **2f** (0.5 g, 1.5 mmol) in DMF (5 mL). The solution formed was refluxed for 2 h under an Ar atmosphere, and then most of the solvent was removed by evaporation under reduced pressure. The crude product was washed with water and filtered off. Recrystallization from ethanol gave pure ketone. Yield 37%; 0.17 g. Colorless crystals: mp 145–146 °C; IR ν_{max} (KBr) 3048 (CH Ar), 2905, 2851 (CH Ad), 1705 (C=O), 1593, 1481, 1462, 1323, 1234, 1200, 1169, 1099, 995, 922, 860, 799, 745 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.71–1.79 (m, 6H), 1.89–1.98 (m, 6H), 2.08 (br s, 3H), 3.26 (dd, 1H, J = 15.6, 8.0 Hz), 3.38 (dd, 1H, J = 15.6, 10.1 Hz), 5.49 (dd, 1H, J = 10.1, 8.0 Hz), 6.83–6.87 (m, 2H), 7.10–7.15 (m, 2H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 27.9 (3CH), 33.3 (CH_2), 36.6 ($3CH_2$), 38.0 ($3CH_2$), 45.9 (C), 81.0 (CH), 109.6 (CH), 121.0 (CH), 124.8 (CH), 125.2 (C), 128.4 (CH_2), 159.3 (C), 210.8 (C) ppm; MS (EI) m/z (%) 282 (M^+, 6), 254 ($M^+ - CO$, 3), 163 ($M^+ - AdCO$, 1), 147 (14), 146 (12), 135 (Ad^+, 100), 119 (19), 118 (52). Anal. Calcd (%) for $C_{19}H_{22}O_2$: C, 80.82; H, 7.85. Found (%): C, 80.71; H, 7.86.

Method B. DBU (0.43 mL, 2.9 mmol) was added to a mixture of 2-(acethyloxy)benzyl acetate (0.6 g, 2.9 mmol) and pyridinium bromide **2f** (0.97 g, 2.9 mmol) in EtOH (10 mL). The solution obtained was refluxed for 3 h under an Ar atmosphere. The solvent was evaporated in vacuo, the residue was treated with MeOH (5 mL), and the mixture was held for 1 day at −20 °C. The precipitate was filtered off and washed with cold MeOH. Yield 23%; 0.19 g.

Method C. DBU (0.86 mL, 5.8 mmol) was added to a mixture of 2-(acetyloxy)benzyl acetate **19a** (0.6 g, 2.9 mmol) and pyridinium bromide **2f** (0.97 g, 2.9 mmol) in CH_3CN (15 mL). The solution obtained was refluxed for 5 h under an Ar atmosphere. The solvent was evaporated in vacuo, and the residue was purified by column chromatography over silica gel using CH_2Cl_2 as eluent, followed by recrystallization from EtOH. Yield 75%; 0.61 g.

*trans-1-Adamantyl(3-phenyl-2,3-dihydro-1-benzofuran-2-yl)-methanone (**13m**).* DBU (0.84 mL, 5.6 mmol) was added to a mixture of 2-[(acetyloxy)(phenyl)methyl]phenyl acetate **19b** (0.8 g, 2.8 mmol) and pyridinium bromide **2f** (0.95 g, 2.8 mmol) in CH_3CN (20 mL). The solution obtained was refluxed for 5 h under an Ar atmosphere. The solvent was evaporated in vacuo, the residue was treated with MeOH, and the mixture was held for 1 day at −20 °C. The precipitate was filtered off and washed with ice-cold MeOH. Yield 73%; 0.74 g. Colorless crystals: mp 97–98 °C (from EtOH); IR ν_{max} (KBr) 2907, 2851 (CH Ad), 1705 (C=O), 1597, 1479, 1462, 1452, 1229, 1198, 1161, 949, 926, 752, 702 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.68–1.76 (m, 6H), 1.84–1.92 (m, 6H), 2.03 (br s, 3H), 4.83 and 5.55 (d, 2H, J = 6.5 Hz), 6.85–6.98 (m, 3H), 7.17–7.35 (m, 6H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 27.8 (3CH), 36.5 ($3CH_2$), 37.7 ($3CH_2$), 46.3 (C), 51.1 (CH), 88.8 (CH), 109.7 (CH), 121.5 (CH), 125.3 (CH), 127.4 (CH), 128.1 (2CH), 128.8 (CH), 129.0 (2CH), 129.7 (C), 142.3 (C), 159.1 (C), 210.0 (C) ppm. Anal. Calcd (%) for $C_{25}H_{26}O_2$: C, 83.76; H, 7.31. Found (%): C, 83.91; H, 7.35.

*1-Adamantyl(5,7-dibromo-2,3-dihydro-1-benzofuran-2-yl)-methanone (**13n**).* Title compound was prepared similarly to compound **13m** from 2-(acetyloxy)-3,5-dibromobenzyl acetate **19c**, pyridinium bromide **2f** and DBU. Yield 82%; 1.01 g. Colorless crystals: mp 106–107 °C (from EtOH); IR ν_{max} (KBr) 3078 (CH Ar), 2909, 2851 (CH Ad), 1709 (C=O), 1578, 1458, 1408, 1346, 1200, 1161, 995, 926, 868, 737 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.71–1.79

dx.doi.org/10.1021/jo400621r | J. Org. Chem. 2013, 78, 5505–5520

(m, 6H), 1.90−1.98 (m, 6H), 2.07 (br s, 3H), 3.41 (dd, 1H, J = 16.2, 9.7 Hz), 3.46 (dd, 1H, J = 16.2, 7.4 Hz), 5.51 (dd, 1H, J = 9.7, 7.4 Hz), 7.18 (s, 1H), 7.40 (s, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 27.9 (3CH), 33.4 (CH_2-3), 36.5 ($3CH_2$), 37.8 ($3CH_2$), 46.3 (C), 82.2 (CH), 103.3 (C), 113.1 (C), 126.9 (CH), 128.8 (C), 133.5 (CH), 156.0 (C), 209.6 (C) ppm. Anal. Calcd (%) for $C_{19}H_{20}Br_2O_2$: C, 51.84; H, 4.58. Found (%): C, 51.96; H, 4.60.

*Methyl 2-acetyl-7-methoxy-2,3-dihydro-1-benzofuran-5-carboxylate (**13o**).* A mixture of of quaternary salt **16d**, 1 g (2.6 mmol), 1-(2-oxopropyl)pyridinium chloride **2l** (0.9 g, 5.2 mmol) and DBU (0.78 mL, 5.2 mmol) in CH_3CN (50 mL) under an Ar atmosphere was heated at reflux temperature for 6 h. The solvent was removed by evaporation under reduced pressure. The crude product was purified by column chromatography over silica gel using $CHCl_3$ as eluent. Yield 69%; 0.45 g. Colorless crystals: mp 71−72 °C (from MeOH); IR ν_{max} (KBr) 3005, 2955, 2928, 1717 (C═O), 1620, 1601, 1497, 1431, 1339, 1234, 1180, 1103, 999, 957, 760 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.31 (s, 3H), 3.34 (dd, 1H, J = 16.0, 6.9 Hz), 3.49 (dd, 1H, J = 16.0, 11.0 Hz), 3.86 (s, 3H), 3.92 (s, 3H), 5.15 (dd, 1H, J = 11.0, 6.9 Hz), 7.48 (s, 1H), 7.52 (s, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 26.3 (CH_3), 32.7 (CH_2), 52.2 (CH_3), 56.2 (CH_3), 87.1 (CH), 113.3 (CH), 119.4 (CH), 124.5 (C), 126.5 (C), 144.2 (C), 151.4 (C), 166.7 (C), 207.6 (C═O) ppm; MS (EI) m/z (%) 250 (M^+, 84), 235 ($M^+ - CH_3$, 19), 219 ($M^+ - CH_3O$, 31), 207 ($M^+ - CH_3CO$, 80), 175 (71), 148 (100), 135 (46), 105 (23), 77 (14), 43 (CH_3CO, 23). Anal. Calcd (%) for $C_{13}H_{14}O_5$: C, 62.39; H, 5.64. Found (%): C, 62.51; H, 5.60.

*Methyl (±)-7-methoxyanodendroate (**13p**).* To a solution of dihydrobenzofuran **13o** (0.3 g, 1.2 mmol) in dry diethyl ether (10 mL) cooled to −78 °C, methylmagnesium chloride (0.42 mL, 1.3 mmol, 22 wt % solution in THF) was added dropwise with efficient stirring under an Ar atmosphere.The reaction mixture was stirred at the same temperature for 30 min and allowed to warm to room temperature over 2 h. After treatment with excess aqueous ammonium chloride, the mixture was extracted with diethyl ether, and the combined organic layers were washed with brine and dried over anhydrous sodium sulfate. Evaporation of the solvent gave the crude product, which was purified by column chromatography over silica gel using $CHCl_3$ as eluent. Yield 78%; 0.32 g. Light yellow oil: IR ν_{max} (film) 3499, 2978, 2951, 2839, 1717 (C═O), 1616, 1601, 1497, 1435, 1335, 1246, 1200, 1180, 1107, 1003, 953 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.20 (s, 3H), 1.35 (s, 3H), 2.14 (br s, 1H), 3.17 (dd, 2H, J = 12.6, 9.0 Hz), 3.84 (s, 3H), 3.88 (s, 3H), 4.72 (t, 1H, J = 9.0 Hz), 7.41 (s, 1H), 7.49 (s, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 24.3 (CH_3), 26.2 (CH_3), 30.7 (CH_2), 52.1 (CH_3), 56.0 (CH_3), 71.7 (CH), 91.2 (C), 112.9 (CH), 119.5 (CH), 123.4 (C), 128.4 (C), 143.8 (C), 152.2 (C), 167.0 (C); MS (EI) m/z (%) 266 (M^+, 77), 235 ($M^+ - OCH_3$, 20), 208 (100), 207 ($M^+ - COOCH_3$, 84), 195(19), 177 (39), 175 (47), 149 (40), 148 (45), 59 (64). Anal. Calcd (%) for $C_{14}H_{18}O_5$: C, 63.15; H, 6.81. Found (%): C, 62.98; H, 6.85.

■ ASSOCIATED CONTENT

Supporting Information

Copies of ^{1}H and ^{13}C NMR spectra for **2f**, **4b**, **16d**, **3a−y**, **8**, **10a−e**, **11a−d**, **13a−p**, and **17a−c**. This material is available free of charge via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

Corresponding Author

*E-mail: vosyanin@mail.ru.

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

This work was supported by the Russian Ministry of Education and Science within Federal Target Program "Scientific and Scientific-Pedagogical Personnel of Innovative Russia in 2009−2013" (Project No. 14.B37.21.1924) with use of equipment of Multiple-Access Center "Investigation of the physicochemical properties of substances and materials" of Samara State Technical University (Project No. 16.552.11.7076).

■ REFERENCES

(1) Jarvis, B. B.; Pena, N. B.; Comezoglu, S. N.; Rao, M. M. *Phytochemistry* **1986**, *25*, 533.
(2) Rattanaburi, S.; Mahabusarakam, W.; Phongpaichit, S.; Carroll, A. R. *Phytochem. Lett.* **2012**, *5*, 18.
(3) Pieters, L.; Dyck, S.; Gao, M.; Bai, R.; Hamel, E.; Vlietinck, A.; Lemière, G. *J. Med. Chem.* **1999**, *42*, 5475.
(4) Asai, T.; Luo, D.; Obara, Y.; Taniguchi, T.; Monde, K.; Yamashita, K.; Oshima, Y. *Tetrahedron Lett.* **2012**, *53*, 2239.
(5) Tamagnone, G. F.; Marchi, F. US 4029811, 1977.
(6) Pattabiraman, T. N.; Lawson, W. B. *Biochem. Biophys. Acta* **1972**, *258*, 548.
(7) Adams, J. L.; Garigipati, R. S.; Sorenson, M.; Schmidt, S. J.; Brian, W. R.; Newton, J. F.; Tyrrell, K. A.; Garver, E.; Yodis, L. A.; Chabot-Fletcher, M.; Tzimas, M.; Webb, E. F.; Breton, J. J.; Griswold, D. E. *J. Med. Chem.* **1996**, *39*, 5035.
(8) North, P. C.; Ladlow, M. WO 95/29173, 1995.
(9) Matsunaga, N.; Kaku, T.; Ojida, A.; Tanaka, T.; Hara, T.; Yamaoka, M.; Kusaka, M.; Tasaka, A. *Bioorg. Med. Chem.* **2004**, *12*, 4313.
(10) (a) For a review on the recent progress in the synthesis of 2,3-dihydrobenzofurans, see: Bertolini, F.; Pineschi, M. *Org. Prep. Proced. Int.* **2009**, *41*, 385. (b) Chen, M.-W.; Cao, L.-L.; Ye, Z.-S.; Jiang, G.-F.; Zhou, Y.-G. *Chem. Commun.* **2013**, *49*, 1660. (c) Jiang, H.; Sugiyama, T.; Hamajima, A.; Hamada, Y. *Adv. Synth. Catal.* **2011**, *353*, 155. (d) Albrecht, L.; Ransborg, L. K.; Lauridsen, V.; Overgaard, M.; Zweifel, T.; Jørgensen, K. A. *Angew. Chem.* **2011**, *123*, 12704. (e) Zhao, G.; Wang, B.; Yang, W.; Ren, H. *Eur. J. Org. Chem.* **2012**, 6236. (f) Ortega, N.; Urban, S.; Beiring, B.; Glorius, F. *Angew. Chem., Int. Ed.* **2012**, *51*, 1710. (g) Chen, C.; Weisel, M. *Synlett* **2013**, 189. (h) Xie, P.; Wang, L.; Li, E.; Ma, J.; Huang, Y.; Chen, R. *J. Org. Chem.* **2011**, *76*, 7699. (i) Li, Q.-B.; Hu, X.-C. *Chem. Lett.* **2012**, *41*, 1633. (j) Li, Q.-B.; Zhou, F.-T.; Liu, Z.-G.; Li, X.-F.; Zhu, W.-D.; Xie, J.-W. *J. Org. Chem.* **2011**, *76*, 7222. (k) Lu, A.; Hu, K.; Wang, Y.; Song, H.; Zhou, Z.; Fang, J.; Tang, C. *J. Org. Chem.* **2012**, *77*, 6208. (l) Gwon, S. H.; Kim, S.-G. *Bull. Korean Chem. Soc.* **2012**, *33*, 2781.
(11) Vaughan, D.; Jha, A. *Tetrahedron Lett.* **2009**, *50*, 5709 and references therein.
(12) Wang, F.; Yang, G.; Zhang, Y. J.; Zhang, W. *Tetrahedron* **2008**, *64*, 9413.
(13) Reich, N. W.; Yang, C.-G.; Shi, Z.; He, C. *Synlett* **2006**, 1278.
(14) Pancote, C. G.; Carvalho, B. S.; Luchez, C. V.; Fernandes, J. P. S.; Politi, M. J.; Brandt, C. A. *Synthesis* **2009**, 3963.
(15) Yadav, A. K.; Singh, B. K.; Singh, N.; Tripathi, R. P. *Tetrahedron Lett.* **2007**, *48*, 6628.
(16) Haselgrove, T. D.; Jevric, M.; Taylor, D. K.; Tiekink, E. R. T. *Tetrahedron* **1999**, *55*, 14739.
(17) He, Z.; Yudin, A. K. *Org. Lett.* **2006**, *8*, 5829.
(18) Arrault, A.; Touzeau, F.; Guillaumet, G.; Mérour, J.-Y. *Synthesis* **1999**, 1241.
(19) Breuer, E.; Melumad, D. *Tetrahedron Lett.* **1969**, *10*, 1875.
(20) Bladé-Font, A.; Rocabayera, T. *J. Chem. Soc., Perkin Trans. 1* **1982**, 841.
(21) Vaillard, S. E.; Postigo, A.; Rossi, R. A. *J. Org. Chem.* **2002**, *67*, 8500.
(22) Das, S. K.; Panda, G. *Tetrahedron* **2008**, *64*, 4162.
(23) Huo, C.; Xu, X.; An, J.; Jia, X.; Wang, X.; Wang, C. *J. Org. Chem.* **2012**, *77*, 8310.
(24) Cadona, L.; Croce, P. D. *Synthesis* **1976**, 800.
(25) (a) Tietze, L. F.; Brasche, G.; Gericke, K. *Domino Reactions in Organic Synthesis*; Wiley-VCH: Weinheim, 2006. (b) Ho, T.-L. *Tandem Organic Reactions*; J. Wiley: New York, 1992. (c) Dömling, A. *Chem. Rev.* **2006**, *106*, 17. (d) Nicolaou, K. C.; Edmonds, D. J.; Bulger, P. G. *Angew. Chem., Int. Ed.* **2006**, *45*, 7134. (e) Ihara, M.

ARKIVOC **2006**, No. vii, 416. (f) Lu, L.-Q.; Chen, J.-R.; Xiao, W.-J. *Acc. Chem. Res.* **2012**, *45*, 1278. (g) Vlaar, T.; Ruijter, E.; Orru, R. V. A. *Adv. Synth. Catal.* **2011**, *353*, 809.
(26) (a) Osyanin, V. A.; Osipov, D. V.; Klimochkin, Y. N. *Tetrahedron* **2012**, *68*, 5612. (b) Osyanin, V. A.; Ivleva, E. A.; Klimochkin, Y. N. *Synth. Commun.* **2012**, *42*, 1832. (c) Osyanin, V. A.; Sidorina, N. E.; Klimochkin, Y. N. *Synth. Commun.* **2012**, *42*, 2639. (d) Osipov, D. V.; Osyanin, V. A.; Klimochkin, Y. N. *Synlett* **2012**, 917. (e) Osyanin, V. A.; Ivleva, E. A.; Klimochkin, Y. N. *Chem. Heterocycl. Compd.* **2012**, *48*, 795. (f) Osyanin, V. A.; Osipov, D. V.; Klimochkin, Y. N. *Chem. Heterocycl. Compd.* **2012**, *47*, 1607. (g) Osyanin, V. A.; Osipov, D. V.; Klimochkin, Y. N. *Chem. Heterocycl. Compd.* **2012**, *47*, 1601. (h) Osyanin, V. A.; Osipov, D. V.; Klimochkin, Y. N. *Chem. Heterocycl. Compd.* **2012**, *48*, 993. (i) Osyanin, V. A.; Osipov, D. V.; Klimochkin, Y. N. *Chem. Heterocycl. Compd.* **2012**, *47*, 1460. (j) Sidorina, N. E.; Osyanin, V. A. *Chem. Heterocycl. Compd.* **2007**, *43*, 1065. (k) Osyanin, V. A.; Sidorina, N. E. *Chem. Heterocycl. Compd.* **2006**, *42*, 1499. (l) Sidorina, N. E.; Osyanin, V. A. *Chem. Heterocycl. Compd.* **2005**, *41*, 1201.
(27) (a) Chuang, C.-P.; Chen, K.-P. *Tetrahedron* **2012**, *68*, 1401 and references therein. (b) Wang, Q.-F.; Song, X.-K.; Chen, J.; Yan, C.-G. *J. Comb. Chem.* **2009**, *11*, 1007. (c) Han, Y.; Chen, J.; Hui, L.; Yan, C.-G. *Tetrahedron* **2010**, *66*, 7743. (d) Han, Y.; Hou, H.; Yao, R.; Fu, Q.; Yan, C.-G. *Synthesis* **2010**, 4061. (e) Altieri, E.; Cordaro, M.; Grassi, G.; Risitano, F.; Scala, A. *Tetrahedron* **2010**, *66*, 9493.
(28) (a) Jha, A.; Huang, P.-J. J. *J. Heterocycl. Chem.* **2009**, *46*, 1098. (b) Ferreira, S. B.; da Silva, F. C.; Pinto, A. C.; Gonzaga, D. T. G.; Ferreira, V. F. *J. Heterocycl. Chem.* **2009**, *46*, 1080. (c) Li, X.; Xue, J.; Huang, C.; Li, Y. *Chem.—Asian J.* **2012**, *7*, 903. (d) Batsomboon, P.; Phakhodee, W.; Ruchirawat, S.; Ploypradith, P. *J. Org. Chem.* **2009**, *74*, 4009. (e) Sugimoto, H.; Nakamura, S.; Ohwada, T. *Adv. Synth. Catal.* **2007**, *349*, 669. (f) Vaughan, D.; Naidu, A. B.; Jha, A. *Curr. Org. Synth.* **2012**, *9*, 613. (g) Gabbut, C. D.; Mark Heron, B.; Kolla, S. B.; Kilner, C.; Coles, S. J.; Horton, P. N.; Hursthouse, M. B. *Org. Biomol. Chem.* **2008**, *6*, 3096.
(29) (a) De Water, R. W.; Pettus, T. R. R. *Tetrahedron* **2002**, *58*, 5367. (b) Rokita, S. E., Ed.; *Quinone Methides*; Wiley: Hoboken, 2009. (c) Veljković, J.; Uzelac, L.; Molčanov, K.; Mlinarić-Majerski, K.; Kralj, M.; Wan, P.; Basarić, N. *J. Org. Chem.* **2012**, *77*, 4596. (d) Shaikh, A.; Cobb, A. J. A.; Varvounis, G. *Org. Lett.* **2012**, *14*, 584 and references therein.
(30) Phillips, W. G.; Ratts, K. W. *J. Org. Chem.* **1970**, *35*, 3144.
(31) Henrick, C. A.; Ritchie, E.; Taylor, W. C. *Aust. J. Chem.* **1967**, *20*, 2441.
(32) Carey, A. R. E.; O'Ferrall, R. A. M.; Murray, B. A. *J. Chem. Soc., Perkin Trans. 2* **1983**, 2297.
(33) (a) Katritzky, A. R.; Grzeskowiak, N. E.; Alvarez-Builla, J. *J. Chem. Soc., Perkin Trans. 1* **1981**, 1180. (b) Stuckwisch, C. G. *Synthesis* **1973**, 469. (c) Uchida, T. *Synthesis* **1976**, 209.
(34) Fanghänel, E.; Böckelmann, J.; Grossman, N.; Pfeifer, D. *J. Prakt. Chem.* **1986**, *328*, 724.
(35) Huang, H.-Y.; Ishikawa, T.; Peng, C.-F.; Tsai, I.-L.; Chen, I.-S. *J. Nat. Prod.* **2008**, *71*, 1146.
(36) Aumann, K. M.; Hungerford, N. L.; Coster, M. J. *Tetrahedron Lett.* **2011**, *52*, 6988.
(37) Rokita, S. E. *J. Am. Chem. Soc.* **2006**, *128*, 11940.
(38) Tramontini, M. *Synthesis* **1973**, 703.
(39) Brode, W. R.; Littman, J. B. *J. Am. Chem. Soc.* **1931**, *53*, 1531.
(40) Henrick, C. A.; Ritchie, E.; Taylor, W. C. *Aust. J. Chem.* **1967**, *20*, 2455.
(41) Kuchař, M. *Collect. Czech. Chem. Commun.* **1968**, *33*, 880.