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Acid Catalyzed Ring Transformation of Benzofurans to Tri- and Tetrasubstituted Furans†

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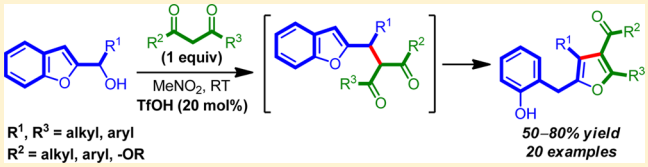
Supporting Information

ABSTRACT: An unusual Brønsted acid catalyzed benzofuran ring opening and furan ring closure sequence for the formation of tri- and tetrasubstituted furans is presented. Benzofuranyl carbinols and 1,3-dicarbonyls in the presence of a catalytic amount of an acid generated functionalized, polysubstituted furans in good to excellent yields via an unusual benzofuran ring opening and furan recyclization process. This reaction is found to be general even on furyl carbinols; however, it generates the rearranged polysubstituted furans in moderate yields.



INTRODUCTION

The majority of important discoveries in chemical science occurred out of accident or serendipity. This phenomenon is responsible for the development of several fundamental synthetic transformations.[1] On the other hand, domino reactions[2] have attracted wide attention from the synthetic community, as they display high atom economy and efficiently build complex molecular architectures in a single step while skipping the need for several workup and time-consuming purification steps. In this account, we describe a serendipitous outcome of a pseudo ring transformation reaction[3] that generates tri- and tetrasubstituted furans from readily available precursors under operationally simple conditions. In an unprecedented event, a rigid benzofuran core sacrifices itself to facilitate the formation of a polysubstituted furan.

Furans represent an important class of five-membered heterocycles which are components of many bioactive natural products as well as primary structural motifs in several pharmaceuticals, macromolecules (such as porphyrins and calixarenes), and functional polymers.[4] Polysubstituted furans especially display significant biological activity profiles and are employed as therapeutics.[5] Furans also represent versatile building blocks for the synthesis of more complex carbocycles and heterocycles.[6] As the latest development with tremendous potential, a rich source of biomass-derived furans can be converted into biodiesel and jet fuels.[7] Furan and benzofuran (coumarone) cores have been recognized as privileged structures in drug discovery.[8] For these reasons, a myriad of impressive approaches have been developed over the years to access polysubstituted furans.[9] While the most frequently used methods for furan synthesis include the versatile Paal–Knorr synthesis[10] and the classical Feist–Benary synthesis,[11] Kanematsu's famous furan ring transfer (FRT) reactions of furanyl propargyl ethers,[12] Butin's versatile furan ring opening–ring closures,[13] the novel propargylation–cycloisomerization strategy,[14] and Yin's recent attractive approaches to furans[15] are considered some of the excellent alternatives to the synthesis of polysubstituted furans that have attracted great attention from the synthetic community.

However, the design, execution, and outcome of many of these approaches are rather predictive and some of the limitations of the existing methods are (i) they lack selectivity, (ii) they lack flexibility regarding their substitution pattern, (iii) they are not economical and scalable, (iv) it is difficult to access starting materials, (v) they are environmentally unfriendly, and (vi) they require harsh reaction conditions that lack functional group tolerance. For these reasons, the development of general and more efficient methods for the synthesis of functionalized and polysubstituted furans by inexpensive, atom-economical, mild, and readily accessible methods still remains an area of intense research.

RESULTS AND DISCUSSION

As part of our interest in the development of novel strategies to form furan derivatives, we have recently reported[16] the Lewis acid catalyzed generation of furfuryl cations (furylcarbenium ions) from 2- and 3-furylcarbinols and inter- and intramolecular furfurylations with a broad range of nucleophiles.

During this study, we investigated the influence of several Lewis acids and Brønsted acids on the furfurylation of 1,3-dicarbonyls (Table 1). No product formation was observed in the absence of an acid (entry 1). Catalytic amounts of Lewis acids such as $BiCl_3$ and $InCl_3$ and Brønsted acids such as *p*-toluenesulfonic acid (PTSA) and phosphoric acid (H_3PO_4) generated only the acetylacetone adduct **2**,[16a] as expected. Most other acids initially furnished the product **2**; however, contrary to our expectation, the concentration of acetylacetone adduct **2** started diminishing while accumulation of the unanticipated product **3** was observed.[17] Thus, we have drawn the conclusion

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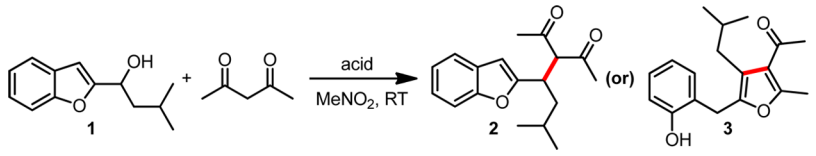
Table 1. Optimization of Acid for the Conversion of the Alcohol 1 to the Tetrasubstituted Furan 3[a,b]



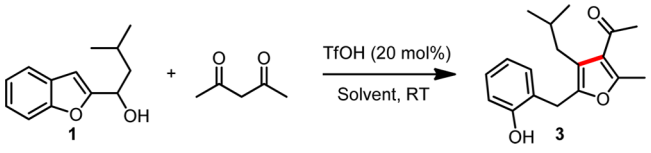
entry	acid	% yield (%) (time (h)) for 2[c]	% yield (%) (time (h)) for 3[c]	% yield (%) (time (h)) for 3[d]	% yield (%) (time (h)) for 3[e]	% yield (%) (time (h)) for 3[f]
1		NP[g] (250)				
2	**$BiCl_3$**	**84 (1)**				
3	$Bi(OTf)_3$	83 (0.5)	60 (12)[h]	64 (6)	57 (2)	56 (0.5)
4	$FeCl_3$	84 (0.5)	56 (72)		53 (8)	
5	$InCl_3$	71 (1)	<5 (48)			
6	$In(OTf)_3$	72 (1)	30 (70)		57 (2)	
7	TMSOTf	71 (0.5)	56 (10)		66 (3)	
8	PTSA	75 (1)	<5 (48)			<5 (48)
9	TFA	72 (1)	NP (72)		NP (48)	
10	$HClO_4$	78 (0.5)	61 (22)	54 (12)	53 (10)	51 (0.5)
11	H_3PO_4	74 (1)	NP (70)			
12	H_2SO_4	78 (1)	51 (9)[h]		42 (3)	
13[i]	**TfOH**	**84 (5 min)**	**74 (6)**[h]	**71 (1.5)**	**72 (1)**	**66 (0.5)**
14	Amberlyst-15	78 (1)[j]	NP (48)[j]		46 (7)[k]	

[a]A mixture of alcohol **1** (0.1 mmol), acetylacetone (0.11 mmol), and an acid in 1 mL of nitromethane was stirred at room temperature (30−35 °C) for an appropriate time. [b]Isolated yields after silica gel column chromatography. [c]20 mol % of acid was employed. [d]50 mol % of acid was employed. [e]1 equiv of acid was employed. [f]5 equiv of acid was employed. [g]NP = no product; no trace of product was observed by crude ^1H NMR. [h]Only traces of rearranged product (**3**) were observed at less than 25 °C (most remained as the acetylacetone adduct **2**). [i]With 10 mol % TfOH, only about 80% conversion was observed, even after 72 h. [j]20 wt % of Amberlyst-15 was employed. [k]At 100 °C, 1 wt equiv of Amberlyst-15 was employed.

that at this stage that the unexpected product **3** formed via the intermediacy of **2**. The reaction can be interrupted at the mentioned times (column 3, Table 1) in order to obtain the acetylacetone adduct **2** and/or can be transformed to the tetrasubstituted furan **3** (column 4, Table 1). The structure of the unexpected product **3** was deduced from ^1H and ^{13}C NMR data and was further confirmed by single-crystal X-ray diffraction analysis (see the Supporting Information for details). No significant improvement in the yield of **3** was observed by increasing the acid loading; in fact a marginal drop in yield was realized (entries 3, 10, and 13). As is evident from Table 1, in terms of yield and reaction time, a substoichiometric amount of triflic acid is conducive for the domino transformation of the alcohol **1** to the tetrasubstituted furan **3**. To the best of our knowledge, a rigid benzofuran moiety sacrificing itself *for the formation of a furan* is unprecedented.[18] An interesting temperature dependence is observed for the conversion of **1** to **3** (entries 3, 12, and 13), but a similar trend is not observed for the conversion of **1** to **2**. The reaction generates only traces of the rearranged product **3** and stalls as acetylacetone adduct **2**, when it is conducted at less than 25 °C, irrespective of the acid employed. Overall, $BiCl_3$ is found to be effective in the formation of acetylacetone adduct **2** and triflic acid for the domino product **3**.[19]

Solvent screening was adopted on the basis of our earlier experience with the successful transformation of **1** to **2**,[16a] delivering no significant improvement in the yield or reaction time (Table 2). It is observed that only those Lewis or Brønsted acids that yielded better results in generating **2** furnished the tetrasubstituted furan **3** in good yields. It is interesting to note that, during the entire study, we never observed any side product originating from nitromethane as the nucleophile. Our efforts to develop a reaction in water were unsuccessful (entry 7).

Table 2. Solvent Screening Results[a,b]



entry	solvent[c]	time (h)	yield of **3** (%)
1	dichloromethane	18	42
2	toluene	48	32
3	dichloroethane	10	43
4	acetonitrile	48	NR[d]
5	nitroethane	1	56
6	nitropropane	4	62
7[e]	water	72	NR

[a]A mixture of alcohol **1** (0.1 mmol), acetylacetone (0.11 mmol), and TfOH (20 mol %) in 1 mL of solvent was stirred for an appropriate time at room temperature (30−35 °C). [b]Isolated yields after silica gel column chromatography. [c]Solvent screening was not done in acetone, ethyl acetate,or tetrahydrofuran, as they are known to be ineffective, even to convert **1** to **2**.[16a] [d]NR = no reaction. [e]In the presence of 20 mol % sodium dodecyl sulfate (SDS).

In order to further evaluate the generality of this one-pot domino process, a range of benzofuranyl carbinols, which were prepared according to literature methods,[16a] were subjected to optimized reaction conditions. Some of the noteworthy features of this methodology are (i) it is a 100% atom-economical reaction and water is the only side product, (ii) it is simple and effective and the reaction conditions are easily executable, (iii) it is insensitive to air and moisture, (iv) most of the 1,3-dicarbonyls are commercially available and furfuryl alcohols can be easily prepared via costless synthesis, (v) it is a one-pot process where two C−O bond breaking and two bond forming events occur (one C−O, one C−C), apart from several O−H

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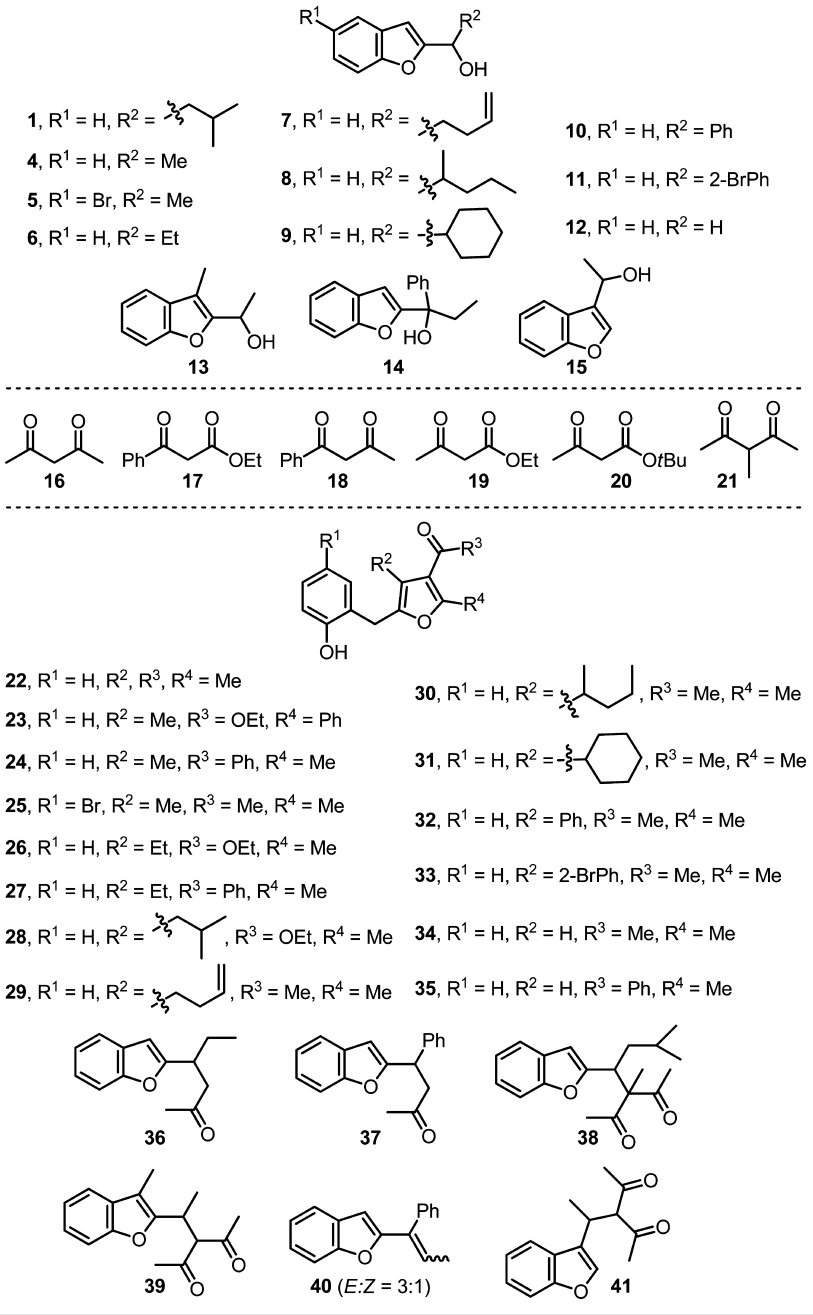
Table 3. Scope of Benzofuranyl Carbinols and 1,3-Dicarbonyls



entry	alcohol	1,3-dicarbonyl	time (h)	yield (%)	product
1	**4**	**16**	8	78	**22**
2	**4**	**17**	15	69	**23**
3	**4**	**18**	18	71	**24**
4[a]	**5**	**16**	16	77	**25**
5	**6**	**19**	14	74	**26**
6	**6**	**18**	6	73	**27**
7	**1**	**19**	16	72	**28**
8	**7**	**16**	16	64	**29**
9	**8**	**16**	10	74	**30**
10	**9**	**16**	18	68	**31**
11	**10**	**16**	14	62	**32**
12	**11**	**16**	15	64	**33**
13	**12**	**16**	6	57	**34**
14	**12**	**18**	8	49	**35**
15	**6**	**20**	1	73	**36**
16	**10**	**20**	13	72	**37**

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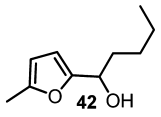
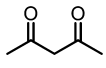
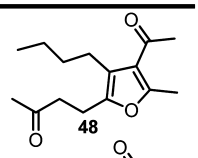
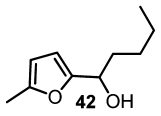
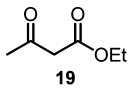
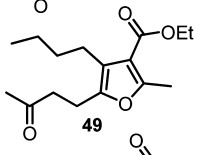
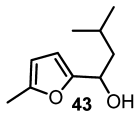
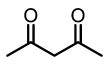
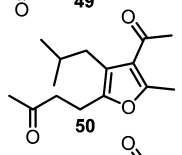
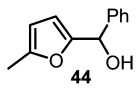
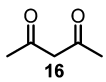
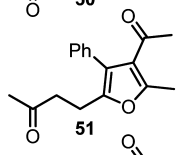
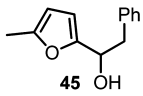
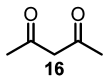
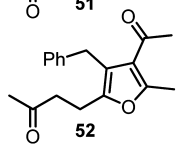
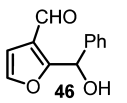
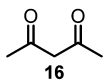
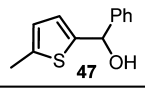
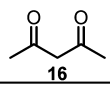
Table 3. continued

entry	alcohol	1,3-dicarbonyl	time (h)	yield (%)	product
17	**1**	**21**	12	73	**38**
18	**13**	**16**	24	78	**39**
19[b]	**14**	**16**	6	81	**40**
20	**15**	**16**	24	74	**41**

[a]An additional 20 mol % of TfOH was added after 12 h. [b]*E*/*Z* ratio from crude ^{1}H NMR.

Table 4. Substrate Scope with Furfuryl and Thiophenyl Alcohols

Entry	Furfuryl alcohol	1,3-Dicarbonyl	Time (h)	Yield (%)	Product
1	 **42**	 **16**	2	34	 **48**
2	 **42**	 **19**	2	33	 **49**
3	 **43**	 **16**	2	37	 **50**
4	 **44**	 **16**	2	51	 **51**
5	 **45**	 **16**	2	46	 **52**
6	 **46**	 **16**	24	-	Complex mixture
7	 **47**	 **16**	9	-	Complex mixture

and C−H bond breaking or bond forming events, and (vi) it is a unique approach to access functionalized and tri- and tetrasubstituted furans in very good yields.

A variety of alkyl and aryl benzofuranyl carbinols (**1**, **4**−**11**) react with 1,3-diketones and *β*-keto esters efficiently in generating 3-acetyl and 3-alkoxycarbonyl furan derivatives (**22**−**33**), respectively, in very good yields (Table 3). With the proper choice of substituents, these tetrasubstituted furans are amenable to further elaborations. Though marginally less efficient, reaction of the benzofuranyl carbinol **12** with 1,3-diketones **16** and **18** indeed resulted in the formation of trisubstituted furans **34** and **35**, respectively. In the case of *tert*-butyl acetoacetate **20** as reactant, the acid treatment leads to an in situ decarboxylation leading to the formation of *β*-branched 4-(2-benzofuranyl)-2-butanones (furans **36** and **37**), which are otherwise difficult to access. Reactions of 2-substituted 1,3-dicarbonyls failed to furnish the desired domino product; rather, furfurylation went smoothly (entry 17). Despite several efforts, surprisingly, the benzofuranyl carbinol **13** bearing a methyl group at C-3 failed to furnish the expected rearranged product, generating only the acetylacetone adduct **39**. Even adding excess TfOH or conducting the reaction at elevated temperatures could not promote formation of the rearranged product from alcohol **13**. Further studies are required to ascertain the role of the substituent at C-3 of benzofuran in the formation of the rearranged product. Tertiary alcohol **14** underwent elimination under the influence of acid to the trisubstituted olefin **40** in a 3/1 *E*/*Z* ratio, while the benzofuranyl carbinol **15** afforded only the acetylacetone adduct **41**.

Having established successfully a general methodology for the synthesis of tri- and tetrasubstituted furans from benzofuranyl carbinols, we turned our attention to the curious case of furfuryl and thiophenyl alcohols. Accordingly, the alcohols **42**−**47** were subjected to the optimized reaction conditions. The results are summarized in Table 4. Moderate to good yields of 4-(3,5-alkyl/aryl-4-acetyl-2-furanyl)butanones (**48**−**52**) were obtained. Both aliphatic and aromatic furyl carbinols generated the anticipated tetrasubstituted furans. 3-Formyl-2-furyl carbinol **46**, having no substitution at C-5, and the thiophenyl alcohol **47** generated initially the respective acetylacetone adducts, which eventually transformed into a

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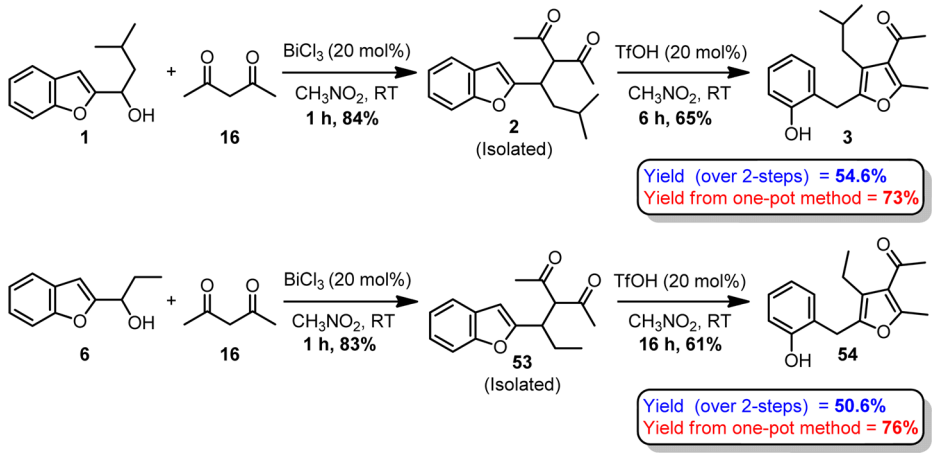
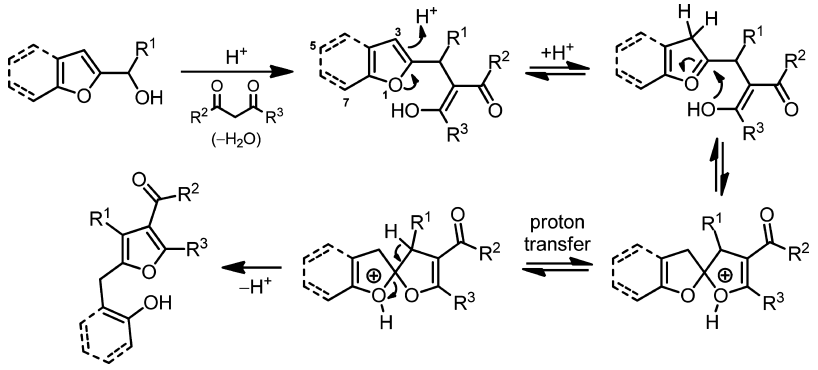
Scheme 1. Comparison between the Efficiencies of the One-Pot Process and the Two-Step Approach To Synthesize the Same End Product



Scheme 2. Proposed Mechanism for the Pseudo Ring Transformation of Benzofurans to Tri- and Tetrasubstituted Furans



complex mixture of products. Our efforts to obtain the desired rearranged product of the thiophenyl alcohol **47** with TMSOTf, $Bi(OTf)_3$, or $BiCl_3$ were also unsuccessful.

It is interesting to note that the stepwise process leading to the formation of tetrasubstituted furans is found to be far less efficient than the one-pot process (Scheme 1). In a separate reaction, acetylacetone adducts **2** and **53** were prepared via $BiCl_3$ catalysis[16a] and were individually subjected to TfOH catalysis. Furans **3** and **54** were obtained in 54% and 50% overall yields from the respective alcohols **1** and **6**, while the same products were obtained in 73% and 76% yields from alcohols **1** and **6**, respectively, highlighting the distinct advantage of the one-pot domino process. X-ray analysis unequivocally confirmed the structures of furans **3** and **54** (see the Supporting Information for details).

A general and straightforward mechanism is proposed[20] as shown in Scheme 2, which rationalizes the transformation of furyl and benzofuranyl carbinols to tri- and tetrasubstituted furans under acidic conditions. The reaction commences with an initial reversible protonation of the benzofuran ring at C-3, which prompts reversible attack of the enol oxygen at the positively charged C-2. Protonation and subsequent ring opening deliver the product. This reversibility could explain why the transformation of **2** and its analogues into 2-(2-hydroxybenzyl)furans proceeds slowly. It also explains the observed thermodynamic control of the rearrangement reaction and, further, is consistent with the failure of benzofuran ring opening in the case of **15** as substrate, delivering **41** as the only product.

CONCLUSIONS

We have described an unprecedented chemistry of sacrificial benzofurans facilitating the formation of tri- and tetrasubstituted furans under simple, effective, air- and moisture-insensitive conditions. The new methodology provides a direct and facile access to the preparation of synthetically useful and medicinally important polysubstituted furan derivatives. We believe that this study will be helpful for a thorough understanding of the cationic furfurylation reactions and subsequent domino processes involving benzofurans. We anticipate that the current strategy has the potential for elaboration to the synthesis of other heterocycles as well. Further investigation of the application of this method to the synthesis of biologically interesting molecules is underway and will be communicated shortly.

EXPERIMENTAL SECTION

General Experimental Methods. The starting compounds 5-methylfuran, 5-methylfurfural, benzofuran, 3-methylbenzofuran, 5-methylthiophene, 5-methyl-2-thiophenecarboxaldehyde, nitromethane, Lewis acids, Brønsted acids, and solvents were used as such without further purification. For thin-layer chromatography (TLC), silica aluminum foils with a fluorescent indicator (254 nm) were used and compounds were visualized by irradiation with UV light and/or by treatment with a solution of *p*-anisaldehyde (23 mL), concentrated H_2SO_4 (35 mL), and acetic acid (10 mL) in ethanol (900 mL) followed by heating. Column chromatography was performed using silica gel 100–200 mesh (approximately 15–20 g per 1 g of the crude product). Dry THF was obtained by distillation over sodium and

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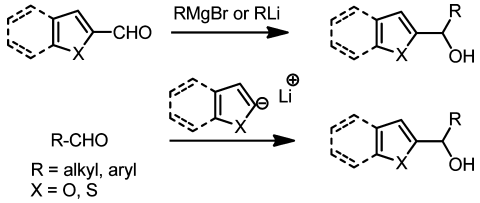
stored over sodium wire. IR spectra were recorded on a FT-IR system as thin films or KBr pellets, as indicated, with ν_{max} values given in reciprocal centimeters. Melting points were recorded on a digital melting point apparatus and were uncorrected. ^{1}H NMR and ^{13}C NMR spectra were recorded on a 400 MHz FT-NMR spectrometer. NMR shifts are reported as delta (δ) units in parts per million (ppm), and coupling constants (J) are reported in hertz (Hz). The following abbreviations are utilized to describe peak patterns when appropriate: br = broad, s = singlet, d = doublet, t = triplet, q = quartet, quin = quintet, and m = multiplet. Proton chemical shifts are given in δ relative to tetramethylsilane (δ 0.00 ppm) in $CDCl_3$ or to the residual proton signals of the deuterated solvent in $(CD_3)_2CO$ (δ 2.05 ppm). Carbon chemical shifts are internally referenced to the deuterated solvent signals in $CDCl_3$ (δ 77.1 ppm) or $(CD_3)_2CO$ (δ 29.9 and 206.7 ppm). High-resolution mass spectra were recorded on Q-TOF mass spectrometers.

Synthesis of Furfuryl and Thiophenyl Alcohols. Furfuryl and thiophenyl alcohols were prepared according to literature procedures,[16a] either by the addition of organolithium reagents or organomagnesium reagents to aldehydes (for example, 5-methylfuran-2-carboxaldehyde, 5-methylthiophene-2-carboxaldehyde, benzofuran-3-carboxaldehyde, etc.) or by the generation of furyllithium/thiophenyllithium/benzofuranyllithium and addition to aldehydes (for example, isovaleraldehyde, 2-methylpentanal, benzaldehyde, acetaldehyde, etc.) as in the general scheme



Note: most of the furfuryl alcohols employed in this study are found to be unstable and decompose upon storage; some of them decomposed on silica gel and even in deuterated chloroform. However, benzofuranyl carbinols and thiophenyl alcohols are found to be reasonably stable upon cold storage.

Complete characterization data of the alcohols **1**, **4**−**6**, **8**, **10**−**15**, **42**−**44**, and **46** have already been reported,[16a] the spectroscopic data of the newly synthesized alcohols are presented below.

*1-(Benzofuran-2-yl)pent-4-en-1-ol (**7**).* This compound was obtained as a pale yellow oil (350 mg, 81%). R_f = 0.5 (hexane/EtOAc = 4/1). IR (thin film, neat): ν_{max}/cm^{-1} 3423, 1651, 1556, 1455, 1265, 1233, 754. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.56 (d, J = 7.2 Hz, 1H), 7.49 (d, J = 7.32 Hz, 1H), 7.32−7.22 (m, 2H), 6.63 (s, 1H), 5.94−5.82 (m, 1H), 5.07 (m, 2H), 4.86 (t, J = 6.4 Hz, 1H), 2.44 (br s, 1H), 2.32−2.16 (m, 2H), 2.14−1.98 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.2, 154.7, 137.7, 128.1, 124.1, 122.8, 121.0, 115.4, 111.2, 102.6, 67.7, 34.5, 29.6. HRMS (ESI-TOF): m/z calcd for $C_{13}H_{13}O$ (M − OH)$^+$ 185.0966, found 185.0964.

*(Benzofuran-2-yl)(cyclohexyl)methanol (**9**).* This compound was obtained as a pale yellow oil (550 mg, 92%). R_f = 0.5 (hexane/EtOAc = 4/1). IR (thin film, neat): ν_{max}/cm^{-1} 3567, 2929, 2853, 1454, 1264, 1253, 739. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.56 (d, J = 7.2 Hz, 1H), 7.48 (d, J = 7.2 Hz, 1H), 7.31−7.21 (m, 2H), 6.63 (s, 1H), 4.56 (d, J = 7.0 Hz, 1H), 3.50 (s, 1H), 2.11−1.47 (m, 5H), 1.35−1.01 (m, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 158.6, 154.6, 128.1, 123.9, 122.7, 120.9, 111.2, 103.4, 73.1, 42.7, 29.1, 28.4, 26.3, 25.9, 25.9. HRMS (ESI-TOF): m/z calcd for $C_{15}H_{17}O$ (M − OH)$^+$ 213.1263, found 213.1279.

*1-(5-Methylfuran-2-yl)-2-phenylethanol (**45**).* This compound was obtained as a colorless oil (642 mg, 73%). R_f = 0.5 (hexane/EtOAc = 9/1). IR (thin film, neat): ν_{max}/cm^{-1} 3324, 1456, 1123, 1043, 743. ^{1}H NMR (400 MHz, CD_3OD): δ 7.26−7.13 (m, 5H), 6.06 (s, 1H), 5.90 (s, 1H), 4.74 (t, J = 7.1 Hz, 1H), 3.14 (dd, J = 13.4 and 6.8 Hz, 1H), 3.10 (dd, J = 13.4 and 7.8 Hz, 1H), 2.28 (s, 3H). ^{13}C NMR (100 MHz, CD_3OD): δ 154.4, 151.0, 138.1, 129.0 (2CH), 127.7 (2CH), 125.8, 106.8, 105.5, 68.3, 41.7, 12.0. HRMS (ESI-TOF): m/z calcd for $C_{13}H_{13}O_2$ (M−H)$^+$: 201.0916, found 201.0914.

*(5-Methylthiophen-2-yl)(phenyl)methanol (**47**).* This compound was obtained as a colorless solid (695 mg, 84%). Mp: 54−56 °C. R_f = 0.5 (hexane/EtOAc = 9/1). IR (thin film, neat): ν_{max}/cm^{-1} 3324, 1446, 1190, 1043, 763. ^{1}H NMR (400 MHz, $CDCl_3$): 7.52−7.25 (m, 5H), 6.64 (s, 1H), 6.60 (s, 1H), 5.62 (s, 1H), 2.47 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): 143.5, 141.3, 140.4, 128.4 (2CH), 127.8, 127.1 (2CH), 125.8, 124.3, 76.2, 15.5. HRMS (ESI-TOF): m/z calcd for $C_{12}H_{11}OS$ (M − H)$^+$ 203.0531, found 203.0538.

General Procedure for Catalyst Screening (Table 1). To a solution of furfuryl alcohol **1** (0.1 mmol, 1 equiv) in nitromethane (1 mL) was added acetylacetone (0.11 mmol, 1.1 equiv) followed by an acid (0.02 mmol, 0.2 equiv) at room temperature (30−35 °C). The reaction mixture was stirred until the alcohol was consumed, as monitored by TLC. The reaction mixture was quenched with aqueous saturated sodium bicarbonate solution (1−2 mL) and diluted with ethyl acetate (1−2 mL), and the layers were separated. The aqueous layer was further extracted with ethyl acetate (1−2 mL). The organic layers were combined, dried over Na_2SO_4, concentrated, and purified by silica gel column chromatography (hexanes/ethyl acetate as eluent) to afford the product (either **2** or **3**, depending on the acid employed).

General Procedure for Solvent Screening (Table 2). To a solution of furfuryl alcohol **1** (0.1 mmol, 1 equiv) in an appropriate solvent (1 mL) was added acetylacetone (0.11 mmol, 1.1 equiv) followed by triflic acid (0.02 mmol, 0.2 equiv) at room temperature (30−35 °C). The reaction mixture was stirred until the alcohol was consumed ,as monitored by TLC, and the reaction mixture was quenched with aqueous saturated sodium bicarbonate solution (1−2 mL). The reaction mixture was diluted with ethyl acetate (1−2 mL), and the layers were separated. The aqueous layer was further extracted with ethyl acetate (1−2 mL). The organic layers were combined, dried over Na_2SO_4, concentrated, and purified by silica gel column chromatography (hexanes/ethyl acetate as eluent) to afford product **3**.

General Procedure for Triflic Acid Catalyzed Reactions of Furyl and Benzofuranyl Carbinols with Different 1,3-Dicarbonyls (Tables 3 and 4). To a solution of an alcohol (0.25 mmol, 1 equiv) in nitromethane (2 mL) was added an appropriate 1,3-dicarbonyl (0.27 mmol, 1.1 equiv) followed by triflic acid (0.05 mmol, 0.2 equiv) at room temperature (30−35 °C). The reaction mixture was stirred at room temperature until the alcohol was consumed, as monitored by TLC. The reaction mixture was quenched with aqueous saturated sodium bicarbonate solution (1−2 mL) and diluted with ethyl acetate (1−2 mL), and the layers were separated. The aqueous layer was further extracted with ethyl acetate (1−2 mL). The organic layers were combined, dried over Na_2SO_4, concentrated, and purified by silica gel column chromatography (hexanes/ethyl acetate) to afford the product.

*1-(5-(2-Hydroxybenzyl)-4-isobutyl-2-methylfuran-3-yl)ethanone (**3**).* This compound was obtained as a colorless solid (33 mg, 72%). Mp: 98−112 °C. R_f = 0.5 (hexane/EtOAc = 7/3). IR (thin film, neat): ν_{max}/cm^{-1} 3372, 2966, 1643, 1595, 1455, 1070, 752. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.02 (t, J = 7.5 Hz, 1H), 6.96 (d, J = 7.1 Hz, 1H), 6.80−6.73 (m, 2H), 6.08 (br s, 1H), 3.83 (s, 2H), 2.44 (s, 3H), 2.42 (d, J = 7.1 Hz, 2H), 2.35 (s, 3H), 1.75−1.62 (m, 1H), 0.81 (d, J = 6.4 Hz, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 195.5, 157.2, 153.8, 148.3, 130.1, 127.8, 124.5, 122.8, 120.6, 119.8, 115.6, 33.2, 30.7, 29.3, 26.2, 24.4, 15.6. HRMS (ESI-TOF): m/z calcd for $C_{18}H_{22}O_3Na$ (M + Na)$^+$ 309.1467, found 309.1459.

*1-(5-(2-Hydroxybenzyl)-2,4-dimethylfuran-3-yl)ethanone (**22**).* This compound was obtained as a pale yellow oil (135 mg, 78%). R_f = 0.5 (hexane/EtOAc = 7/3). IR (thin film, neat): ν_{max}/cm^{-1} 3354, 2925, 2851, 1650, 1455, 1253, 751. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.13 (dt, J = 7.7 and 1.4 Hz, 1H), 7.07 (dd, J = 7.4 and 1.3 Hz, 1H), 6.86 (m, 2H), 6.19 (br s, 1H), 3.92 (s, 2H), 2.59 (s, 3H), 2.45 (s, 3H), 2.21 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 195.8, 157.4, 153.8, 147.7, 130.0, 127.8, 124.5, 123.1, 120.6, 115.6, 115.4, 30.8, 26.0, 15.4, 10.6. HRMS (ESI-TOF): m/z calcd for $C_{15}H_{17}O_3$ (M + H)$^+$ 245.1178, found 245.1175.

*Ethyl 5-(2-Hydroxybenzyl)-4-methyl-2-phenylfuran-3-carboxylate (**23**).* This compound was obtained as a colorless oil (157 mg, 69%). R_f = 0.4 (hexane/EtOAc = 7/3). IR (thin film, neat): ν_{max}/cm^{-1}

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3227, 2967, 2931, 1717, 1459, 1292, 724. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.77−7.73 (m, 2H), 7.43−7.34 (m, 3H), 7.15−7.10 (m, 2H), 6.89 (dt, J = 7.6 and 1.0 Hz, 1H), 6.81 (dd, J = 8.3 and 1.0 Hz, 1H), 5.70 (br s, 1H), 4.31 (q, J = 7.1 Hz, 2H), 4.01 (s, 2H), 2.25 (s, 3H), 1.31 (t, J = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 164.8, 155.7, 153.5, 149.0, 130.3, 130.1, 128.8, 128.3 (2CH), 127.9 (3CH), 124.4, 120.9, 117.5, 115.6, 114.6, 60.4, 26.4, 14.1, 10.0. HRMS (ESI-TOF): m/z calcd for $C_{21}H_{20}O_4Na$ $(M + Na)^+$ 359.1259, found 359.1261.

*(5-(2-Hydroxybenzyl)-2,4-dimethylfuran-3-yl)(phenyl)methanone (**24**).* This compound was obtained as a colorless oil (137 mg, 71%). R_f = 0.5 (hexane/EtOAc = 7/3). IR (thin film, neat): ν_{max}/cm^{-1} 3342, 2958, 2871, 1644, 1455, 1235, 964, 739. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.78 (dd, J = 8.1 and 1.2 Hz, 2H), 7.52 (tt, J = 7.8 and 1.2 Hz, 1H), 7.47 (dt, J = 8.1 and 1.2 Hz, 2H), 7.13 (d, J = 7.4 Hz, 2H), 6.90 (dt, J = 7.4 and 1.0 Hz, 1H), 6.85 (dd, J = 8.3 and 1.0 Hz, 1H), 5.90 (br s, 1H), 3.95 (s, 2H), 2.14 (s, 3H), 2.02 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 193.6, 155.5, 153.8, 147.9, 139.4, 132.5, 130.2, 129.2 (2CH), 128.4 (2CH), 127.9, 124.5, 122.6, 120.7, 115.9, 115.7, 26.3, 14.3, 9.4. HRMS (ESI-TOF): m/z calcd for $C_{20}H_{19}O_3$ $(M + H)^+$ 307.1334, found 307.1337.

*1-(5-(5-Bromo-2-hydroxybenzyl)-2,4-dimethylfuran-3-yl)-ethanone (**25**).* This compound was obtained as a colorless solid (72 mg, 77%). Mp: 132−122 °C. R_f = 0.5 (hexane/EtOAc = 7/3). IR (thin film, neat): ν_{max}/cm^{-1} 3216, 1651, 1556, 1453, 1092, 739. ^{1}H NMR (400 MHz, 1:4 $CDCl_3$ + $(CD_3)_2CO$): δ 7.19 (d, J = 8.5 Hz, 1H), 7.10 (s, 1H), 6.83 (d, J = 8.5, 1H), 3.86 (s, 2H), 2.51 (s, 3H), 2.40 (s, 3H), 2.18 (s, 3H). ^{13}C NMR (100 MHz, 1:4 $CDCl_3$ + $(CD_3)_2CO$): δ 193.9, 156.6, 154.2, 147.1, 132.0, 130.1, 127.5, 122.9, 116.6, 115.6, 110.8, 30.1, 24.9, 14.4, 9.0. HRMS (ESI-TOF): m/z calcd for $C_{15}H_{14}BrO_3$ $(M + H)^+$ 321.0127, found 321.0121.

*Ethyl 5-(2-Hydroxybenzyl)-4-ethyl-2-methylfuran-3-carboxylate (**26**).* This compound was obtained as a colorless oil (143 mg, 74%). R_f = 0.4 (hexane/EtOAc = 7/3). IR (thin film, neat): ν_{max}/cm^{-1} 3227, 2957, 2931, 1713, 1455, 1292, 724. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.13 (dt, J = 7.7 and 1.6 Hz, 1H), 7.07 (dd, J = 7.4 and 1.4 Hz, 1H), 6.89 (dt, J = 7.4 and 1.0 Hz, 1H), 6.83 (dd, J = 7.9 and 1.0 Hz, 1H), 5.47 (br s, 1H), 4.3 (q, J = 7.1 Hz, 2H), 3.91 (s, 2H), 2.64 (q, J = 7.4 Hz, 2H), 2.52 (s, 3H), 1.37 (t, J = 7.1 Hz, 3H), 1.14 (t, J = 7.4 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 164.7, 158.4, 153.6, 146.8, 130.1, 127.9, 124.7, 122.5, 120.9, 115.8, 113.1, 59.8, 26.3, 17.6, 15.3, 14.4, 14.2. HRMS (ESI-TOF): m/z calcd for $C_{17}H_{19}O_4$ $(M - H)^+$ 287.1283, found 287.1286.

*(4-Ethyl-5-(2-hydroxybenzyl)-2-methylfuran-3-yl)(phenyl)-methanone (**27**).* This compound was obtained as a colorless oil (134 mg, 73%). R_f = 0.4 (hexane/EtOAc = 7/3). IR (thin film, neat): ν_{max}/cm^{-1} 3346, 2952, 2871, 1644, 1455, 1235, 964, 739. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.80 (d, J = 7.8 Hz, 2H), 7.58 (t, J = 7.8 Hz, 1H), 7.53−7.44 (m, 2H), 7.14 (t, J = 8.8 Hz, 2H), 6.91 (t, J = 7.4 Hz, 1H), 6.85 (d, J = 7.8 Hz, 1H), 5.74 (s, 1H), 3.96 (s, 2H), 2.54 (q, J = 7.4 Hz, 2H), 2.10 (s, 3H), 1.00 (t, J = 7.4 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 193.6, 155.1, 153.1, 147.4, 139.3, 132.6, 130.2, 129.2 (2CH), 128.5 (2CH), 127.9, 124.6, 122.8, 121.8, 120.8, 115.8, 26.4, 17.0, 15.3, 14.2. HRMS (ESI-TOF): m/z calcd for $C_{21}H_{20}O_3Na$ $(M + Na)^+$ 343.1310, found 343.1313.

*Ethyl 5-(2-Hydroxybenzyl)-4-isobutyl-2-methylfuran-3-carboxylate (**28**).* This compound was obtained as a colorless solid (39 mg, 72%). Mp: 98−102 °C. R_f = 0.4 (hexane/EtOAc = 7/3). IR (thin film, neat): ν_{max}/cm^{-1} 3224, 2957, 2931, 1713, 1454, 1292, 724. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.14 (dt, J = 7.5 and 1.6 Hz, 1H), 7.07 (dd, J = 7.5 and 1.6 Hz, 1H), 6.88 (dt, J = 7.4 and 1.1 Hz, 1H), 6.83 (dd, J = 7.6 and 1.0 Hz, 1H), 5.45 (br s, 1H), 4.29 (q, J = 7.1 Hz, 2H), 3.91 (s, 2H), 2.53 (s, 3H), 2.49 (d, J = 7.0 Hz, 2H), 1.91−1.79 (m, 1H), 1.37 (t, J = 7.1 Hz, 3H), 0.91 (d, J = 6.6 Hz, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 164.9, 158.5, 153.6, 147.7, 130.2, 127.9, 124.5, 120.8, 119.9, 115.8, 113.5, 59.8, 33.2, 29.2, 26.5, 22.4 ($2CH_3$), 14.4, 14.3. HRMS (ESI-TOF): m/z calcd for $C_{19}H_{24}O_4Na$ $(M + Na)^+$ 339.1572, found 339.1573.

*1-(4-(But-3-en-1-yl)-5-(2-hydroxybenzyl)-2-methylfuran-3-yl)-ethanone (**29**).* This compound was obtained as a colorless solid (104 mg, 64%). Mp: 159−162 °C. R_f = 0.4 (hexane/EtOAc = 7/3). IR (thin film, neat): ν_{max}/cm^{-1} 3423, 1651, 1556, 1455, 1265, 1233, 754. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.14 (dt, J = 7.8 and 1.3 Hz, 1H), 7.08 (dd, J = 7.4 and 1.3 Hz, 1H), 6.89 (dt, J = 7.4 and 1.1 Hz, 1H), 6.82 (dd, J = 7.8 and 1.1 Hz, 1H), 5.90−5.81(m, 1H), 5.53 (br s, 1H), 5.06−4.89 (m, 2H), 3.90 (s, 2H), 2.73 (t, J = 7.2 Hz, 2H), 2.55 (s, 3H), 2.45 (s, 3H), 2.21 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 194.9, 157.1, 153.6, 147.8, 138.3, 130.2, 128.0, 124.4, 122.7, 120.8, 120.1, 115.7, 114.9, 34.7, 30.7, 26.2, 24.0, 15.6. HRMS (ESI-TOF): m/z calcd for $C_{18}H_{20}O_3Na$ $(M + Na)^+$ 307.1310, found 307.1316.

*1-(5-(2-Hydroxybenzyl)-2-methyl-4-(pentan-2-yl)furan-3-yl)-ethanone (**30**).* This compound was obtained as a colorless oil (104 mg, 74%). R_f = 0.5 (hexane/EtOAc = 7/3). IR (thin film, neat): ν_{max}/cm^{-1} 3342, 2958, 2871, 1644, 1455, 1235, 964, 739. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.13 (dt, J = 7.5 and 1.5 Hz, 1H), 7.02 (dd, J = 7.5 and 1.5 Hz, 1H), 6.88 (dt, J = 7.4 and, 1.1 Hz, 1H), 6.83 (dd, J = 7.8 and 1.1 Hz, 1H), 3.96 (s, 2H), 3.12 (m, 1H), 2.52 (s, 3H), 2.45 (s, 3H), 1.71−1.49 (m, 4H), 1.23 (d, J = 7.1 Hz, 3H), 0.84 (t, J = 7.3 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 195.5, 156.1, 153.6, 147.0, 130.0, 127.8, 125.6, 124.6, 123.6, 120.8, 115.7, 38.3, 31.5, 29.6, 27.3, 21.3, 20.3, 15.7, 14.1. HRMS (ESI-TOF): m/z calcd for $C_{19}H_{24}O_3Na$ $(M + Na)^+$ 323.1623, found 323.1628.

*1-(5-(2-Hydroxybenzyl)-4-cyclohexyl-2-methylfuran-3-yl)-ethanone (**31**).* This compound was obtained as a colorless oil (100 mg, 68%). R_f = 0.5 (hexane/EtOAc = 7/3). IR (thin film, neat): ν_{max}/cm^{-1} 3354, 2925, 1644, 1455, 1217, 751. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.13 (dt, J = 7.6 and 1.4 Hz, 1H), 7.00 (dd, J = 7.6 and 1.4 Hz, 1H), 6.87 (dt, J = 7.1 and 1.1 Hz, 1H), 6.85 (dd, J = 7.8 and 1.1 Hz, 1H), 5.82 (br s, 1H), 4.02 (s, 2H), 2.96 (tt, J = 11.8 and 3.6 Hz, 1H), 2.51 (s, 3H), 2.47 (s, 3H), 1.87−1.58 (m, 6H), 1.42−1.12 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 196.0, 156.2, 153.6, 146.9, 129.9, 127.7, 125.9, 124.8, 123.3, 120.7, 115.6, 35.0, 32.3 ($2CH_2$), 31.4, 27.6, 27.1 ($2CH_2$), 26.0, 15.6. HRMS (ESI-TOF): m/z calcd for $C_{20}H_{24}O_3Na$ $(M + Na)^+$ 335.1623, found 335.1623.

*1-(5-(2-Hydroxybenzyl)-2-methyl-4-phenylfuran-3-yl)ethanone (**32**).* This compound was obtained as a colorless solid (48 mg, 62%). Mp: 175−179 °C. R_f = 0.5 (hexane/EtOAc = 7/3). IR (thin film, neat): ν_{max}/cm^{-1} 3216, 1651, 1556, 1453, 1092, 739, 696. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.46−7.34 (m, 3H), 7.34−7.26 (m, 2H), 7.12 (dt, J = 7.5 and 1.6 Hz, 1H), 6.99 (dd, J = 7.5 and 1.5 Hz, 1H), 6.87 (dt, J = 7.4 and 1.1 Hz, 1H), 6.81 (dd, J = 8.0 and 1.0 Hz, 1H), 5.72 (br s, 1H), 3.85 (s, 2H), 2.56 (s, 3H), 1.96 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 196.5, 157.4, 153.7, 148.3, 133.1, 130.0 (3CH), 128.6 (2CH), 128.0, 127.7, 124.3, 123.0, 122.0, 120.7, 115.7, 30.7, 26.4, 14.5. HRMS (ESI-TOF): m/z calcd for $C_{20}H_{18}O_3Na$ $(M + Na)^+$ 329.1154, found 329.1151.

*1-(5-(2-Hydroxybenzyl)-4-(2-bromophenyl)-2-methylfuran-3-yl)-ethanone (**33**).* This compound was obtained as a colorless solid (78 mg, 64%). Mp: 159−164 °C. R_f = 0.5 (hexane/EtOAc = 7/3). IR (thin film, neat): ν_{max}/cm^{-1} 3224, 1651, 1556, 1453, 1092, 739, 696. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.68 (dd, J = 8.0 and 1.0 Hz, 1H), 7.37 (dt, J = 7.4 and 1.2 Hz, 1H), 7.33−7.23 (m, 2H), 7.11 (dt, J = 7.6 and 1.6 Hz, 1H), 6.98 (dd, J = 7.6 and 1.6 Hz, 1H), 6.84 (dt, J = 7.6 and 1.0 Hz, 1H), 6.77 (dd, J = 8.0 and 1.0 Hz, 1H), 5.31 (br s, 1H), 3.76 (AB q, J = 16.2 Hz, 2H), 2.59 (s, 3H), 1.95 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 195.3, 157.7, 153.5, 148.6, 134.5, 132.8, 132.1, 130.3, 129.7, 128.0, 127.5, 125.5, 123.7, 122.5, 121.0, 120.8, 115.7, 29.9, 26.7, 14.8. HRMS (ESI-TOF): m/z calcd for $C_{20}H_{17}BrO_3Na$ $(M + Na)^+$ 407.0259, found 407.0257.

*1-(5-(2-Hydroxybenzyl)-2-methylfuran-3-yl)ethanone (**34**).* This compound was obtained as a pale yellow oil (63 mg, 57%). R_f = 0.5 (hexane/EtOAc = 4/1). IR (thin film, neat): ν_{max}/cm^{-1} 3359, 2925, 2881, 1643, 1455, 1253, 741. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.17 (d, J = 7.5 Hz, 2H), 6.93 (dt, J = 6.5 and 0.9 Hz, 1H), 6.84 (d, J = 7.8 Hz, 1H), 6.23 (s, 1H), 5.23 (br s, 1H), 3.95 (s, 2H), 2.57 (s, 3H), 2.36 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 194.4, 157.6, 153.6, 151.7, 130.7, 128.3, 123.6, 122.1, 121.0, 115.8, 106.7, 29.1, 28.6, 14.4. HRMS (ESI-TOF): m/z calcd for $C_{14}H_{15}O_3$ $(M + H)^+$ 231.1021, found 231.1011.

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*5-(2-Hydroxybenzyl)-2-methylfuran-3-yl(phenyl)methanone (**35**).* This compound was obtained as a colorless oil (56 mg, 49%). R_f = 0.5 (hexane/EtOAc = 4/1). IR (thin film, neat): ν_{max}/cm^{-1} 3359, 2935, 2881, 1643, 1423, 1253, 745. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.80−7.76 (m, 2H), 7.59−7.52 (m, 1H), 7.49−7.43 (m, 2H), 7.21−7.13 (m, 2H), 6.92 (dt, J = 7.4 and 1.1 Hz, 1H), 6.83 (d, J = 7.9 Hz, 1H), 6.25 (s, 1H), 3.98 (s, 2H), 2.49 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 191.5, 158.6, 153.6, 151.6, 139.2, 132.0, 130.6, 128.9 (2CH), 128.3 (2CH), 123.7, 121.2, 121.0, 115.8, 110.7, 108.1, 28.6, 14.6. HRMS (ESI-TOF): m/z calcd for $C_{19}H_{16}O_3Na$ (M + Na)$^+$ 315.0997, found 315.0995.

*4-(Benzofuran-2-yl)hexan-2-one (**36**).* This compound was obtained as a colorless oil (112 mg, 73%). R_f = 0.5 (hexane/EtOAc = 4/1). IR (thin film, neat): ν_{max}/cm^{-1} 2963, 1716, 1455, 1359, 1253, 751. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.50 (d, J = 7.2 Hz, 1H), 7.43 (d, J = 7.8 Hz, 1H), 7.26−7.15 (m, 2H), 6.44 (s, 1H), 3.36 (quin, J = 7.0 Hz, 1H), 2.95 (dd, J = 16.8 and 7.3 Hz, 1H), 2.77 (dd, J = 16.8 and 7.3 Hz, 1H), 2.14 (s, 3H), 1.75 (dq, J = 13.2 and 5.7 Hz, 2H), 0.90 (t, J = 7.4 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 207.1, 160.3, 154.5, 128.6, 123.3, 122.5, 120.4, 110.8, 102.5, 47.2, 36.2, 30.5, 26.6, 11.6. HRMS (ESI-TOF): m/z calcd for $C_{14}H_{17}O_2$ (M + H)$^+$ 217.1229, found 217.1227.

*4-(Benzofuran-2-yl)-4-phenylbutan-2-one (**37**).* This compound was obtained as a colorless oil (129 mg, 72%). R_f = 0.5 (hexane/EtOAc = 4/1). IR (thin film, neat): ν_{max}/cm^{-1} 2963, 1716, 1455, 1359, 1253, 751. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.50 (d, J = 7.6 Hz, 1H), 7.43 (d, J = 8.1 Hz, 1H), 7.37−71.7 (m, 7H), 6.43 (s, 1H), 4.78 (t, J = 7.3 Hz, 1H), 3.40 (dd, J = 17.0 and 7.3 Hz, 1H), 3.15 (dd, J = 17.0 and 7.3 Hz, 1H), 2.17 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 205.9, 159.6, 154.7, 140.9, 128.7, 128.5 (2CH), 127.9 (2CH), 127.1, 123.6, 122.6, 120.6, 111.0, 102.9, 48.0, 40.5, 30.5. HRMS (ESI-TOF): m/z calcd for $C_{18}H_{16}O_2Na$ (M + Na)$^+$: 287.1048, found 287.1046.

*3-(1-(Benzofuran-2-yl)-3-methylbutyl)-3-methylpentane-2,4-dione (**38**).* This compound was obtained as a pale yellow oil (134 mg, 73%). R_f = 0.7 (hexane/EtOAc = 4/1). IR (thin film, neat): ν_{max}/cm^{-1} 1732, 1698, 1454, 1373, 1094, 1046, 911, 736. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.40 (d, J = 7.3 Hz, 1H),7.32 (d, J = 7.5 Hz, 1H), 7.18−7.08 (m, 2H), 6.41 (s, 1H), 4.03 (dd, J = 12.1 and 2.3 Hz, 1H), 2.08 (s, 3H), 1.92 (s, 3H), 1.76 (m, 1H), 1.43 (s, 3H), 1.26 (m, 1H), 0.98 (m, 1H), 0.88 (d, J = 6.6 Hz, 3H), 0.75 (d, J = 6.6 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 206.0, 206.1, 157.1, 154.5, 128.1, 123.7, 122.7, 120.6, 111.0, 105.6, 71.1, 40.8, 37.9, 27.1, 26.9, 26.0, 23.9, 21.0, 14.9. HRMS (ESI-TOF): m/z calcd for $C_{19}H_{24}O_3Na$ (M + Na)$^+$ 323.1623, found 323.1623.

*3-(1-(3-Methylbenzofuran-2-yl)ethyl)pentane-2,4-dione (**39**).* This compound was obtained as a pale yellow oil (105 mg, 78%). R_f = 0.7 (hexane/EtOAc = 4/1). IR (thin film, neat): ν_{max}/cm^{-1} 2969, 1736, 1732, 1561, 1377, 1248, 1099, 1045, 743. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.43 (d, J = 7.4 Hz, 1H), 7.43 (d, J = 7.9 Hz, 1H), 7.17−7.09 (m, 2H), 4.30 (d, J = 12.7 Hz, 1H), 3.84, (dq, J = 12.7 and 7.0 Hz, 1H), 2.20 (s, 3H), 2.09 (s, 3H), 1.84 (s, 3H), 1.19 (d, J = 6.9 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 202.6, 202.4, 153.8, 153.2, 129.8, 123.7, 122.3, 119.2, 110.7, 110.5, 72.8, 31.8, 29.9, 29.7, 17.8, 7.7. HRMS (ESI-TOF): m/z calcd for $C_{16}H_{19}O_3$ (M + H)$^+$ 259.1334, found 259.1329.

*2-(1-Phenylprop-1-en-1-yl)benzofuran (**40**).* This compound was obtained as a pale yellow oil (98 mg, 81%). R_f = 0.5 (hexane/EtOAc = 9/1). IR (thin film, neat): ν_{max}/cm^{-1} 3057, 1556, 1494, 1471, 1452, 1303, 1279, 1256, 1007, 940, 801, 784, 762. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.45−7.01 (m, 9H), 6.60 (q, J = 7.2 Hz, 1H), 5.99 (s, 1H), 2.06 (d, J = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 157.5, 154.7, 132.7, 129.9, 128.2 (2CH), 128.1 (2CH), 127.6, 125.0, 124.2, 122.7, 120.8, 111.2, 107.3, 103.8, 15.0. HRMS (ESI-TOF): m/z calcd for $C_{17}H_{15}O$ (M + H)$^+$ 235.1123, found 235.1134.

*3-(1-(Benzofuran-3-yl)ethyl)pentane-2,4-dione (**41**).* This compound was obtained as a pale yellow oil (79 mg, 74%). R_f = 0.7 (hexane/EtOAc = 4/1). IR (thin film, neat): ν_{max}/cm^{-1} 2936, 2880, 1724, 1700, 1598, 1455, 1422, 1358, 1253, 1167, 1011, 942, 809, 752. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.61−7.06 (m, 5H), 4.12 (d, J = 11.2 Hz, 1H), 3.77 (m, 1H), 2.27 (s, 3H), 1.84 (s, 3H), 1.22 (d, J = 6.8 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 203.2, 203.2, 154.4, 142.2, 126.3, 124.6, 122.8, 122.0, 119.8, 111.0, 75.0, 30.4, 30.1, 29.0, 19.5. HRMS (ESI-TOF): m/z calcd for $C_{15}H_{16}O_3Na$ (M + Na)$^+$ 267.0997, found 267.0994.

*4-(4-Acetyl-3-butyl-5-methylfuran-2-yl)butan-2-one (**48**).* This compound was obtained as a pale yellow oil (26 mg, 34%). R_f = 0.5 (hexane/EtOAc = 9/1). IR (thin film, neat): ν_{max}/cm^{-1} 3055, 2959, 1715, 1665, 1359, 1265, 738. ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.82−2.71 (m, 4H), 2.51 (s, 3H), 2.42 (s, 3H), 2.18 (s, 3H), 1.45−1.21 (m, 6H), 0.98 (t, J = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 207.3, 194.8, 156.5, 148.2, 122.6, 119.9, 41.9, 33.1, 30.7, 29.9, 23.9, 22.6, 19.6, 15.4, 13.9. HRMS (ESI-TOF): m/z calcd for $C_{15}H_{22}O_3Na$ (M + Na)$^+$ 273.1467, found 273.1454.

*Ethyl 4-Butyl-2-methyl-5-(3-oxobutyl)furan-3-carboxylate (**49**).* This compound was obtained as a pale yellow oil (46 mg, 33%). R_f = 0.5 (hexane/EtOAc = 9/1). IR (thin film, neat): ν_{max}/cm^{-1} 2957, 2931, 1719, 1713, 1367, 1292, 1165, 754. ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.28 (q, J = 7.1 Hz, 2H), 2.84−2.67 (m, 4H), 2.51(t, J = 7.3 Hz, 2H), 2.50 (s, 3H), 2.18 (s, 3H), 1.47−1.22 (m, 4H), 1.35 (t, J = 7.1 Hz, 3H), 0.92 (t, J = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 207.5, 164.8, 158.0, 148.2, 119.7, 112.9, 59.7, 42.0, 32.1, 30.0, 23.9, 22.7 (2CH_2), 19.7, 14.3, 14.0. HRMS (ESI-TOF): m/z calcd for $C_{16}H_{23}O_4$ (M + H)$^+$ 279.1591, found 279.1596.

*4-(4-Acetyl-3-isobutyl-5-methylfuran-2-yl)butan-2-one (**50**).* This compound was obtained as a pale yellow oil (39 mg, 37%). R_f = 0.5 (hexane/EtOAc = 9/1). IR (thin film, neat): ν_{max}/cm^{-1} 3055, 2959, 1715, 1665, 1359, 1265, 738. ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.69 (m, 4H), 2.43 (s, 3H), 2.33 (s, 3H), 2.31 (d, J = 8.1 Hz, 2H), 2.15 (s, 3H), 1.63 (m, 1H), 0.79 (d, J = 6.6 Hz, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 207.3, 194.9, 156.4, 148.8, 122.8, 118.8, 41.7, 33.2, 30.7, 29.7, 29.2, 22.3 (2CH_3), 19.7, 15.4. HRMS (ESI-TOF): m/z calcd for $C_{15}H_{23}O_3$ (M + H)$^+$ 251.1647, found 251.1642.

*4-(4-Acetyl-5-methyl-3-phenylfuran-2-yl)butan-2-one (**51**).* This compound was obtained as a pale yellow oil (65 mg, 51%). R_f = 0.5 (hexane/EtOAc = 9/1). IR (thin film, neat): ν_{max}/cm^{-1} 1716, 1673, 1561, 1418, 1315, 952, 761. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.44−7.33 (m, 3H), 7.28 −7.23 (m, 2H), 2.80−2.69 (m, 4H), 2.54 (s, 3H), 2.12 (s, 3H), 1.91 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 207.0, 196.0, 156.5, 148.9, 133.2, 129.9 (2CH), 128.5 (2CH), 127.6, 123.0, 121.1, 41.6, 30.7, 29.8, 20.1, 14.3. HRMS (ESI-TOF): m/z calcd for $C_{17}H_{18}O_3Na$ (M + Na)$^+$ 293.1154, found 293.1163.

*4-(4-Acetyl-3-benzyl-5-methylfuran-2-yl)butan-2-one (**52**).* This compound was obtained as a pale yellow oil (61 mg, 46%). R_f = 0.5 (hexane/EtOAc = 9/1). IR (thin film, neat): ν_{max}/cm^{-1} 1720, 1675, 1561, 1428, 1323, 957, 768. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.32−7.33 (m, 3H), 7.21−7.10 (m, 2H), 4.00 (s, 2H), 2.84 (t, J = 7.6 Hz, 2H), 2.73 (t, J = 7.6 Hz, 2H), 2.55 (s, 3H), 2.30 (s, 3H), 2.15 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 207.1, 194.7, 157.0, 149.6, 140.5, 128.3 (2CH), 128.0 (2CH), 125.9, 122.5, 117.5, 41.6, 30.7, 29.9, 29.7, 19.7, 15.4. HRMS (ESI-TOF): m/z calcd for $C_{18}H_{20}O_3Na$ (M + Na)$^+$ 307.1310, found 307.1316.

*1-(5-(2-Hydroxybenzyl)-4-ethyl-2-methylfuran-3-yl)ethanone (**54**).* This compound was obtained as a colorless solid (127 mg, 76%). Mp: 165−170 °C. R_f = 0.5 (hexane/EtOAc = 7/3). IR (thin film, neat): ν_{max}/cm^{-1} 3354, 2925, 2851, 1667, 1455, 1234, 751. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.12 (dt, J = 7.7 and 1.6 Hz, 1H), 7.06 (dd, J = 7.4 and 1.4 Hz, 1H), 6.90−6.83 (m, 2H), 6.29 (br s, 1H), 3.93 (s, 2H), 2.67 (q, J = 7.4 Hz, 2H), 2.54 (s, 3H), 2.47 (s, 3H), 1.10 (t, J = 7.4 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 195.5, 157.3, 153.8, 147.4, 130.0, 127.8, 124.6, 122.5, 122.3, 120.6, 115.6, 30.6, 25.9, 17.7, 15.6, 15.3. HRMS (ESI-TOF): m/z calcd for $C_{16}H_{18}O_3Na$ (M + Na)$^+$ 281.1154, found 281.1157.

■ ASSOCIATED CONTENT

Supporting Information

Figures giving ^{1}H and ^{13}C NMR of all new compounds and figures, tables, and CIF files giving single-crystal X-ray diffraction analysis data for compounds **3** and **54**. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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DEDICATION

†This article is dedicated to Prof. Carlos F. Barbas III.

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(19) The reaction is found to be air and moisture insensitive. This reaction can be carried out using laboratory grade solvents and does not require any precautions such as working under a nitrogen atmosphere.

(20) We sincerely thank one of the reviewers for valuable suggestions on the mechanism of the rearrangement reaction.