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An Efficient Synthesis of 2,3,5-Trisubstituted Furans from α,β-Unsaturated Ketones

Catherine D. Brown, J. Michael Chong,* and Lixin Shen

Guelph-Waterloo Centre for Graduate Work in Chemistry
Department of Chemistry, University of Waterloo, Waterloo, Ontario, Canada N2L 3G1

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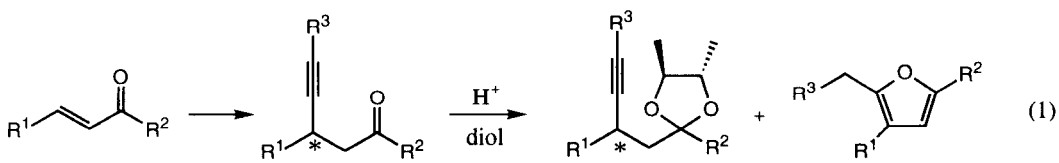
Abstract: A simple, regioselective synthesis of 2,3,5-trisubstituted furans is described. Conjugate addition of alkynylboronates to α,β-unsaturated ketones, followed by acid-catalyzed cyclization of the resulting γ-alkynyl ketones affords trisubstituted furans in 31-97% overall yields. © 1999 Elsevier Science Ltd. All rights reserved.

Keywords: Furans, alkynes, cyclization, regioselective

Introduction

Furans are important heterocycles in both natural products and pharmaceuticals, and are also useful intermediates in many syntheses.[1] Hence it is not surprising that a great many synthetic routes to furans have been developed.[2] While a plethora of routes already exist, new methods continue to be developed, particularly for the regioselective synthesis of multiply-substituted systems.[3] The unabated interest in furan synthesis stems from their importance and from limitations of the known methodology. For example, while it has been known for over 30 years[4-7] that γ-alkynyl ketones may be cyclized to furans under acidic or basic conditions, there seems to be renewed interest in this transformation.[8-12] It seems that this route to furans has been limited by ready access to γ-alkynyl ketones[13] and by moderate yields in the cyclization step. We now report an approach to furans from γ-alkynyl ketones which addresses both of these issues.

Our interest in furan synthesis arose from a seredipitous observation made during our work on the asymmetric conjugate addition of alkynyl groups to α,β-unsaturated ketones (Eq 1).[14] One approach to the determination of the enantiomeric purity of the addition products **2** involved the formation of a ketal with a chiral diol under acidic conditions.[15] While ketals were often formed, we occasionally noted the formation of a by-product which was eventually identified as a furan; in the absence of diol, the furan was the exclusive product formed.



1 **2** **3** **4** (1)

* E-mail: jmchong@uwaterloo.ca

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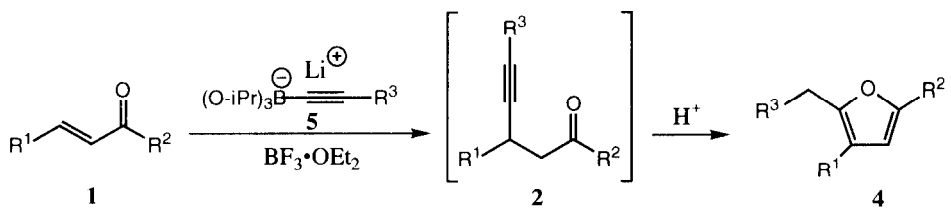
It became clear that this route to furans could be very efficient if appropriate conditions could be developed to make the conjugate addition and cyclization steps high yielding processes. Moreover, if the two steps could be carried out in one pot, this furan synthesis would be operationally very simple.

Results and Discussion

It has been reported that 1-alkynyldiisopropoxyboranes readily convert acyclic α,β-unsaturated ketones to γ-alkynylketones in the presence of BF_3•OEt_2.[16] For this work, we wanted to avoid isolation of the air-sensitive boranes. Thus we chose to use borates prepared from lithium acetylides and triisopropyl borate[17,18]; these salts are easily prepared and are very stable with no noticeable decomposition after several months at 4°C. We expected that treatment of these salts with BF_3•OEt_2 in the presence of enones would generate boronates *in situ* which, with BF_3•OEt_2 activation, would transfer alkynyl groups to the enones. We were delighted to find that this is, in fact, the case (Scheme).

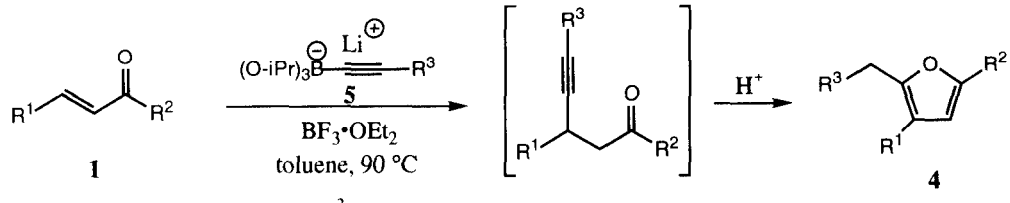
Scheme



Our initial studies were carried out using chalcone (**1a**, $R^1 = R^2 = Ph$) as substrate and borate **5a** ($R^3 = n\text{-}C_6H_{13}$) as the alkynylating reagent. With the solvent previously used, CH_2Cl_2, the conversion of chalcone to γ-alkynyl ketone **2a** (**2**: $R^1 = R^2 = Ph$, $R^3 = n\text{-}C_6H_{13}$) proceeded smoothly and reasonably efficiently (75-80% isolated yields) but was slow (16 to 24 h at 40°C). In order to increase the rate of the reaction and to allow for a possible one-pot addition-cyclization sequence, solvents with higher boiling points were considered. Of the solvents investigated, toluene proved to be the best: reaction at 90°C was complete within 1 h and ketone **2a** could be isolated in excellent (>95%) yield; at reflux temperature, the reaction was even faster but small amounts of side-products complicated isolation of ketone **2a**.

Cyclization could be carried out *in situ* by the addition of PTSA to the toluene solution and warming the reaction mixture to reflux. Quantitative (GC-MS) conversion of ketone **2a** to furan **4a** could be achieved within 2 hours. However, under the acidic reaction conditions, toluene underwent Friedel-Crafts alkylations and many isopropylated arenes (which interfered with isolation of the desired furan) were also formed. Presumably, the source of the isopropyl groups was the borate used. Therefore it was decided that the by-products of the addition step should be removed before cyclization. This was done by washing the reaction mixture with aqueous NaOH and H_2O before the addition of acid to effect cyclization. This procedure avoided formation of products derived from toluene and provided furan **4a** as the sole product (GC-MS). When PTSA was used as the acid catalyst, furan **4a** could be isolated in 72% yield; with oxalic acid, the isolated yield of **4a** increased to 97% (over two steps). With this very encouraging result in hand, we investigated other enones and borates to test the generality of this route to furans (Table).

Table. Preparation of Furans from Enones.



1a: $R^1 = R^2 = Ph$
1b: $R^1 = Me$, $R^2 = Ph$
1c: $R^1 = iPr$, $R^2 = Ph$
1d: $R^1 = Ph$, $R^2 = Me$
1e: $R^1 = 4\text{-}MeOC_6H_4$, $R^2 = 4\text{-}ClC_6H_4$
1f: $R^1 = R^2 = Me$

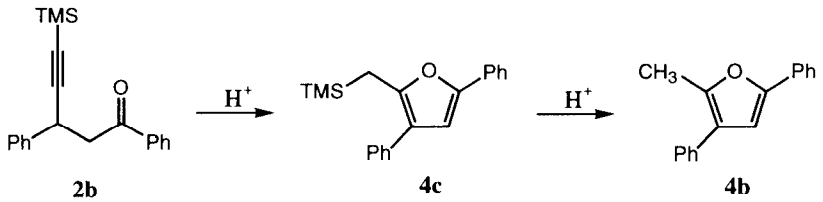
5a: $R^3 = n\text{-}C_6H_{13}$
5b: $R^3 = Me_3Si$
5c: $R^3 = Ph$

Entry	Enone	Borate	Furan				Yield (%)[a]
			#	R^1	R^2	R^3	
1	**1a**	**5a**	**4a**	Ph	Ph	$n\text{-}C_6H_{13}$	97
2	**1a**	**5b**	**4b**	Ph	Ph	H	97
3[b]	**1a**	**5b**	**4c**	Ph	Ph	Me_3Si	73
4	**1b**	**5a**	**4d**	Me	Ph	$n\text{-}C_6H_{13}$	62 (90)
5	**1b**	**5b**	**4e**	Me	Ph	H	47
6	**1c**	**5a**	**4f**	iPr	Ph	$n\text{-}C_6H_{13}$	44
7	**1c**	**5b**	**4g**	iPr	Ph	H	47 (80)
8	**1d**	**5a**	**4h**	Ph	Me	$n\text{-}C_6H_{13}$	82
9	**1e**	**5a**	**4i**	$4\text{-}MeOC_6H_4$	$4\text{-}ClC_6H_4$	$n\text{-}C_6H_{13}$	65
10	**1f**	**5a**	**4j**	Me	Me	$n\text{-}C_6H_{13}$	31
11	**1a**	**5c**	**4k**	Ph	Ph	Ph	12

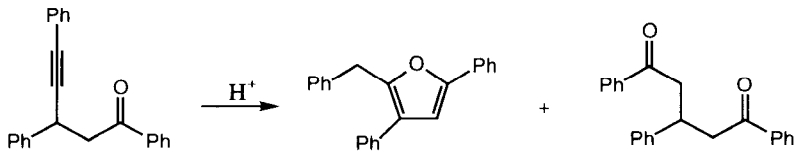
[a] Isolated, chromatographed yields from enones **1**. Values in parentheses are yields based on ^1H NMR analysis of crude reaction mixtures.
[b] Trifluoroacetic acid was used in place of oxalic acid.

In all of the cases examined, alkynylation of the enone proceeded smoothly to give the expected alkynyl ketone as the only product detected by GC-MS. In general, the subsequent cyclizations also proceeded cleanly to give the crude furan in good yield. However, high yields of chromatographed material were obtained only when an aryl group was present in the β-position of the enone. (This group becomes the C3-substituent of the furan.) With alkyl groups in the β-position, it seems that the furans are formed in high yields but only modest yields of purified furans could be obtained (see entires 4-7, 11), possibly due to the instability of these materials to chromatography.[19]

In the case of alkynyl ketone **2b** (**2**: $R^1 = R^2 = Ph$, $R^3 = Me_3Si$), oxalic acid effected cyclization to furan **4c** and subsequent protodesilylation to give furan **4b** in excellent yield; use of a weaker acid (TFA), allowed for the formation of **4c** as the major product which could be isolated in good yield (Eq 2). Treatment of alkynyl ketone **2c** (**2**: $R^1 = R^2 = R^3 = Ph$) with acid provided the desired furan **4k** as a minor product with dione **6** as the major product (Eq 3). This shift in reaction pathway is likely due to competitive formation of a vinyl cation stabilized by the phenyl group. Other than these special cases, the synthesis of furans from enones using this approach proceeded without incident.



2b **4c** **4b** (2)



2c **4k** **6** (3)

Conclusions

The route to furans described here represents a short, efficient access to these important compounds. The required starting materials and reagents are readily available, the reactions are clean and high yielding, and the protocol developed is operationally simple.

Experimental

All experiments involving air or moisture sensitive reagents were performed under an atmosphere of argon. The glassware was flame-dried under vacuum and flushed with argon. Toluene was freshly distilled from sodium. Boron trifluoride etherate was treated with a 10% by volume portion of diethyl ether to ensure an excess and distilled (60-62°C/20 Torr).[20] Enones were obtained from Aldrich Chemical Co. or prepared by literature methods.[21,22] Flash column chromatography was performed on Merck silica gel 60 (230-400 mesh) and analytical TLC on silica gel 60 F-254 plates. Nuclear magnetic resonance spectra were recorded in $CDCl_3$ using either a Bruker AM-250 or AC-300 spectrometer. Chemical shifts are given in parts per million downfield from tetramethylsilane. Infrared (IR) spectra were recorded on a Perkin Elmer Spectrum RX-1 FT-IR infrared spectrophotometer as neat liquids between sodium chloride plates or as KBr pellets. High resolution mass spectra were recorded using a VG 7070 mass spectrometer. Elemental

analyses were performed by M-H-W Laboratories, Phoenix, Arizona. Gas chromatographic analysis was done using a Hewlett Packard G1800A GCD system fitted with a 30 m x 0.25 mm HP5 column.

1-phenyl-2-buten-1-one (1b)

To a 300 mL round bottom flask fitted with a stir bar and an argon inlet was added THF (150 mL) and phenylmagnesium chloride (25 mL of a 2.0 M solution in THF, 50.0 mmol). The flask was cooled in an ice-water bath for 10 minutes, crotonaldehyde (4.1 mL, 50.0 mmol) was added dropwise to the flask over a period of 10 minutes and the reaction was stirred for 30 minutes at 0°C. The reaction was quenched with aqueous sat. NH_4Cl (20 mL), then THF was removed *in vacuo* to give an oil. The resulting oil was diluted with Et_2O (120 mL) and washed with 1 M HCl (40 mL), H_2O (2 x 40 mL), brine (30 mL), and dried over $MgSO_4$. The removal of ether *in vacuo* afforded 6.9 g of a yellow oil which was used without purification. The oil was added to pyridinium dichromate (23.5 g, 62.5 mmol) in DMF (40 mL) in a 100 mL round bottom flask at room temperature. The reaction was stirred at room temperature for one hour, then diluted with ether (1200 mL), washed with water (3 x 1000 mL), brine (500 mL) and dried over $MgSO_4$. Removal of solvent, followed by distillation under high vacuum gave 5.85 g of the target enone (80%). ^1H NMR (250 MHz): δ 8.10-7.70 (2H, m, aryl-H), 7.60-7.30 (3H, m, aryl-H), 7.08 (1H, dq, J = 15.3, 6.6 Hz, CH_3-HC=C), 6.91 (1H, dq, J = 15.3, 1.1 Hz, C=CH-CO), 2.00 (3H, dd, J = 6.6, 1.1 Hz, CH_3); ^{13}C NMR (63 MHz): δ 191.0, 155.7, 137.9, 132.5, 127.8, 123.0, 30.3; MS (EI): *m/z* 147 (M^++1, 5), 146 (M^+, 51), 145 (15), 131 (45), 117 (12), 105 (100), 77 (76), 69 (56), 41 (19), 39 (16); IR (neat): ν = 3061, 2973, 1669, 1623, 1578, 1446, 1296, 1222 cm^{-1}; Anal. Calcd for $C_{10}H_{10}O$: C, 82.16; H 6.89. Found: C, 82.10; H, 7.02.

***E*-4-Methyl-1-phenyl-2-penten-1-one (1c)**

Compound **1c** was prepared using a modification of a literature procedure.[21] From acetophenone (11.70 mL, 100.0 mmol) and isobutyraldehyde (10.0 mL, 110 mmol), there was obtained, after purification by column chromatography (EtOAc/hexane: 1:10), 14.10 g of **1c** (81%). IR (neat): 1676 cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.88-8.02 (2H, m), 7.43-7.62 (3H, m), 7.04 (1H, dd, J = 15.4, 6.6 Hz), 6.83 (1H, dd, J = 15.5; 1.3 Hz), 2.58 (1H, ddq, J = 1.3; 6.7; 6.6 Hz), 1.13 (6H, d, J = 6.7 Hz); ^{13}C NMR ($CDCl_3$): δ 191.1, 155.8, 138.0, 132.4, 128.3, 123.0, 31.3, 21.2; MS m/e (relative intensity): 174 (M^+, 30), 159 (18), 105 (100), 91 (7), 77 (56), 51 (17), 43 (9), 41 (15), 39 (7). Anal. Calcd for $C_{12}H_{14}O$: C, 82.72; H, 8.10. Found: C, 82.66; H, 8.12.

1-(*p*-Chlorophenyl)-3-(*p*-methoxyphenyl)-2-propen-1-one (1e)

4-Methoxybenzaldehyde (2.24 mL, 18.4 mmol), 4'-chloroacetophenone (2.84 g, 18.4 mmol), and NaOH (73.6 mg, 1.84 mmol) were mixed with water (20 mL) and MeOH (20 mL) in a 150 mL round bottom flask. The mixture was heated to reflux for 2 hours. After cooling to room temperature, 6 M HCl (0.32 mL, 1.92 mmol) was added to the flask to neutralize NaOH. The resulting mixture was extracted with CH_2Cl_2 (3 x 50 mL) and the organic solution was washed with saturated aqueous $NaHCO_3$ (50 mL), brine (50 mL), dried over Na_2SO_4, and concentrated to give a crude product. Subsequent purification by crystallization from MeOH/H_2O provided **1e** as a yellow solid (4.52 g, 90%). mp: 119-120 °C; ^1H NMR

(250 MHz): δ 8.20-7.90 (2H, m, aryl-H), 7.79 (1H, d, J = 15.6 Hz, aryl-HC=C), 7.77-7.36 (4H, m, aryl-H), 7.37 (1H, d, J = 15.6 Hz, HC=C-CO), 7.05-6.85 (2H, m, aryl-H), 3.87 (3H, s, OCH_3); ^{13}C NMR (63 MHz): δ 188.8, 161.7, 145.0, 138.7, 136.6, 130.2, 129.6, 128.7, 127.2, 118.9, 114.3, 55.2; MS (EI): *m/z* 274 (M^++1, 11), 273 (M^+, 12), 272 (32), 271 (21), 237 (35), 165 (11), 161 (30), 139 (19), 133 (16), 111 (25), 108 (18), 89 (12), 77 (10), 75 (15), 32 (45), 28 (100); IR (KBr): ν = 1657, 1594, 1511, 1425, 1296, 1258, 1211, 1109, 1010 cm^{-1}; Anal. Calcd for $C_{16}H_{13}ClO_2$: C, 70.46; H, 4.80. Found: C, 70.29; H, 5.03.

General Procedure for Synthesis of Alkynylborates

The procedure for the synthesis is a modification of a literature method.[17] A 100 mL, one neck flask was equipped with argon line, flame-dried under vacuum and cooled under argon. Dry ether (40 mL) and alkyne (30 mmol) were added by syringe and cooled to -78°C. After stirring for 10 minutes, *n*BuLi (30 mmol) was added and stirred at -78°C for thirty minutes. In a separate 200 mL flask, prepared as above, was added ether (100 mL) and triisopropylborate (30 mmol). After stirring at -78°C for ten minutes, the contents of the first flask were transferred via a double ended needle into the second flask. The white mixture was stirred with a strong stirrer for two hours at -78°C. The viscous, white solution was warmed to room temperature and then dried under vacuum for 48 hours to give a white solid which was used without characterization.

Lithium *B*-1-octynyltriisopropylborate (5a)

Using the above procedure, 1-octyne (4.43 mL, 30 mmol) in ether (40 mL) and *n*BuLi (20 mL of 1.49 M solution, 30 mmol) were reacted and added to triisopropylborate (6.92 mL, 30 mmol) in ether (100 mL) in the second flask.

Lithium *B*-1-trimethylsilylethynyltriisopropylborate (5b)

Using the above procedure, trimethylsilylacetylene (2.4 mL, 17.1 mmol) in ether (30 mL) and *n*BuLi (12 mL of 1.40 M solution, 17.1 mmol) were reacted and added to triisopropylborate (3.95 mL, 17.1 mmol) in ether (70 mL) in the second flask.

Lithium *B*-1-phenylethynyltriisopropylborate (5c)

Using the above procedure, ethynylbenzene (1.5 mL, 13.7 mmol) in ether (20 mL) and *n*BuLi (9.2 mL of 1.49 M solution, 13.7 mmol) were reacted and added to triisopropylborate (3.16 mL, 13.7 mmol) in ether (50 mL) in the second flask.

General Procedure for Synthesis of Furans 4 from Enones 1

A 50 mL, three neck round bottom flask was equipped with condenser and argon line, thermometer, and a stopcock valve with a septum. The system was flame-dried under vacuum and cooled under argon. The alkynylborate **5** (1.18 mmol) and ketone **1** (if solid, 0.786 mmol) were measured out and added quickly. The system was evacuated and flushed with argon twice more. Liquid ketones were added at this point in 5 mL of toluene. Dry toluene (20 mL total) was then added, followed by boron trifluoride etherate (0.34 mL,

2.75 mmol) via syringe. The reaction was then heated slowly to 90°C and monitored by TLC. When complete, the reaction was cooled to room temperature and quenched with aqueous 2 M NaOH (3 mL). The organic layer was washed twice with water (10 mL) and transferred to a two neck 50 mL flask. The flask was equipped with condenser, argon line, stopcock valve and septum. Oxalic acid (50 mg, 0.384 mmol) was added and the reaction was heated to reflux. When complete, the reaction was cooled to room temperature and quenched with aqueous 2 M NaOH (3 mL). The organic layer was washed twice with water (10 mL), dried over Na_2SO_4, filtered and concentrated to afford the crude product.

2-Heptyl-3,5-diphenylfuran (4a)

Using the above procedure, borate **5a** (359 mg, 1.18 mmol) and chalcone (**1a**, 164 mg, 0.786 mmol) were allowed to react for 1 h followed by cyclization for 1.5 h. The crude mixture was purified by column chromatography (10:1 hexane/CH_2Cl_2) to afford furan **4a** (242 mg, 97%) as a colorless oil. ^{1}H NMR (250 MHz): δ 7.69-7.66 (2H, d, J = 8.0 Hz, aryl-H), 7.41-7.19 (8H, m, aryl-H), 6.75 (1H, s, furyl-H), 2.82 (2H, t, J = 7.5 Hz, CH_2), 1.76 (2H, m, CH_2), 1.30 (8H, m, CH_2), 0.87 (3H, t, CH_3); ^{13}C NMR (63 MHz): δ 151.8, 131.0, 128.6, 128.5, 127.7, 126.9, 126.5, 123.5, 123.0, 106.6, 31.8, 29.3, 29.0, 28.6, 27.0, 22.6, 14.0; MS (EI): *m/z* 318 (M^+, 20), 233 (100), 105 (26), 77 (19); IR (neat): ν = 2940, 1473, 1212, 758, 697 cm^{-1}; HRMS(FAB) calcd for $C_{23}H_{27}O$ ($M+H^+$): 319.2062; found: 319.2090.

2-Methyl-3,5-diphenylfuran (4b)[23]

Using the above procedure, borate **5b** (345 mg, 1.18 mmol) and chalcone (**1a**, 164 mg, 0.786 mmol) were allowed to react for 1.25 h followed by cyclization for 1 h. The crude mixture was purified by column chromatography (10:1 hexane/CH_2Cl_2) to afford furan **4b** (178 mg, 97%) as a colorless oil. ^{1}H NMR (250 MHz): δ 7.70-7.66 (2H, dd, J = 8.8, 1.5 Hz, aryl-H), 7.46-7.21 (8H, m, aryl-H), 6.78 (1H, s, furyl-H), 2.52 (3H, s, CH_3); ^{13}C NMR (63 MHz): δ 151.5, 147.4, 133.9, 133.2, 130.8, 130.6, 129.1, 128.5, 127.4, 126.9, 126.3, 123.3, 123.0, 118.9, 106.4, 13.0; MS (EI): *m/z* 234 (M^+, 100), 233 (30), 191 (40), 105 (22), 77 (28).

2-Trimethylsilylmethyl-3,5-diphenylfuran (4c)

Using the above procedure, borate **5b** (345 mg, 1.18 mmol) and chalcone (**1a**, 164 mg, 0.786 mmol) were allowed to react for 1.25 h followed by cyclization for 21 h with the exception of changing the acid to trifluoroacetic acid (0.09 mL, 1.18 mmol). The crude mixture was purified by column chromatography (100% hexane) to afford furan **4c** (176 mg, 73%) along with furan **4b** (40 mg, 22%). ^{1}H NMR (300 MHz): δ 7.66-7.63 (2H, dd, J = 8.3, 1.3 Hz, aryl-H), 7.41- 7.34 (6H, m, aryl-H), 7.28-7.19 (2H, m, aryl-H), 6.76 (1H, s, furyl-H), 2.33 (2H, s, CH_2), 0.09 (9H, s, $Si(CH_3)_3$); ^{13}C NMR (75 MHz): δ 150.8, 134.7, 131.0, 128.7, 128.5, 127.6, 126.6, 126.2, 123.4, 123.1, 121.5, 106.8, 17.4, -1.1; MS (EI): *m/z* 306 (M^+, 46), 233 (34), 105 (14) 77 (19), 73 (100); IR (neat): ν = 2955, 1495, 1249, 849, 758, 698 cm^{-1}; Anal. Calcd for $C_{20}H_{22}OSi$: C, 78.38; H, 7.24. Found: C, 78.36; H, 7.13.

2-Heptyl-3-methyl-5-phenylfuran (4d)

Using the above procedure, borate **5a** (359 mg, 1.18 mmol) and enone **1b** (112 mg, 0.786 mmol) were allowed to react for 1 h followed by cyclization for 1 h. The crude mixture was purified by column chromatography (100% hexane) to afford furan **4d** (125 mg, 62%) as a colorless oil. ^{1}H NMR (250 MHz): δ 7.59 (2H, dd, J = 8.4, 1.5 Hz, aryl-H), 7.33 (2H, m, aryl-H), 7.15 (1H, m, aryl-H), 6.43 (1H, s, furyl-H), 2.60 (2H, t, J = 7.5 Hz, CH_2), 1.98 (3H, s, CH_3), 1.65 (2H, m, CH_2), 1.30 (8H, m, CH_2), 0.88 (3H, m, CH_3); ^{13}C NMR (63 MHz): δ 151.6, 150.9, 131.4, 128.5, 126.5, 123.2, 115.8, 108.3, 31.8, 29.2, 29.1, 28.6, 26.1, 22.6, 14.0, 9.9; MS (EI): *m/z* 256 (M^+, 13), 171 (100), 128 (14); IR (neat): ν = 2926, 1466, 758, 691 cm^{-1}; Anal. Calcd for $C_{18}H_{24}O$: C, 84.32; H, 9.44. Found: C, 84.48; H, 9.20.

2,3-Dimethyl-5-Phenylfuran (4e)[24]

Using the above procedure, borate **5b** (345 mg, 1.18 mmol) and enone **1b** (115 mg, 0.786 mmol) were allowed to react for 1 h followed by cyclization for 1 h. The crude mixture was purified by column chromatography (100% hexane) to afford furan **4h** (63 mg, 47%) as a colorless oil. ^{1}H NMR (250 MHz): δ 7.61-7.58 (2H, d, J = 8.0 Hz, aryl-H), 7.36-7.16 (3H, m, aryl-H), 6.43 (1H, s, furyl-H), 2.27 (3H, s, CH_3), 1.98 (3H, s, CH_3); MS (EI): *m/z* 172 (M^+, 100), 157 (26), 128 (36), 77 (21).

2-Heptyl-3-isopropyl-5-phenylfuran (4f)

Using the above procedure, borate **5a** (359 mg, 1.18 mmol) and enone **1c** (137 mg, 0.786 mmol) were allowed to react for 1 h followed by cyclization for 5.5 h. The crude mixture was purified by column chromatography (100:1 hexane/Et_3N) to afford furan **4i** (99 mg, 44%) as a colorless oil. ^{1}H NMR (250 MHz): δ 7.60 (2H, dd, J = 8.4, 1.1 Hz, aryl-H), 7.49-7.12 (3H, m, aryl-H), 6.51 (1H, s, furyl-H), 2.78 (1H, m, CH), 2.61 (2H, t, J = 7.5 Hz, CH_2), 1.65 (2H, m, CH_2), 1.29 (8H, m, CH_2), 1.17 (6H, d, J = 6.9 Hz, CH_3), 0.86 (3H, m, CH_3); ^{13}C NMR (63 MHz): δ 151.1, 150.0, 131.5, 128.5, 127.8, 126.4, 123.2, 104.4, 31.8, 29.3, 29.1, 28.9, 26.2, 24.6, 23.9, 22.7, 14.0; MS (EI): *m/z* 284 (M^+, 21), 199 (100), 105 (13); IR (neat): ν = 2935, 1475, 1194, 758, 691 cm^{-1}; Anal. Calcd for $C_{20}H_{28}O$: C, 84.45; H, 9.92. Found: C, 84.50; H, 9.70.

3-Isopropyl-2-methyl-5-phenylfuran (4g)

Using the above procedure, borate **5b** (345 mg, 1.18 mmol) and enone **1c** (137 mg, 0.786 mmol) were allowed to react for 1 h followed by cyclization for 4.5 h. The crude mixture was purified by column chromatography (100:1 hexane/Et_3N) to afford furan **4j** (73 mg, 47%) as a colorless oil. ^{1}H NMR (250 MHz): δ 7.61 (2H, m, aryl-H), 7.59-7.13 (3H, m, aryl-H), 6.51 (1H, s, furyl-H), 2.77 (1H, m, J = 6.9 Hz, CH), 2.28 (3H, s, CH_3), 1.17 (6H, d, J = 6.6 Hz, CH_3); ^{13}C NMR (63 MHz): δ 151.1, 145.7, 131.4, 128.5, 127.9, 126.5, 123.2, 104.7, 24.7, 23.5, 11.7; MS (EI): *m/z* 200 (M^+, 65), 185 (100), 141 (10), 128 (10), 115 (14), 77 (14); IR (neat): ν = 2940, 1469, 1092, 759, 693 cm^{-1}; HRMS(FAB) calcd for $C_{14}H_{17}O$ ($M+H^+$): 201.1274; found 201.1282.

2-Heptyl-5-methyl-3-phenylfuran (4h)

Using the above procedure, borate **5a** (359 mg, 1.18 mmol) and enone **1d** (115 mg, 0.786 mmol) were allowed to react for 3.5 h followed by cyclization for 2.5 h. The crude mixture was purified by column chromatography (6:1 hexane : EtOAc) to afford furan **4h** (170 mg, 82%) as a pale yellow oil. ^{1}H NMR (250 MHz): δ 7.29-7.13 (5H, m, aryl-H), 6.00 (1H, s, furyl-H), 2.63 (2H, t, J = 7.7 Hz, CH_2), 2.21 (3H, s, CH_3), 1.60 (2H, m, CH_2), 1.19 (8H, m, CH_2), 0.79 (3H, m, CH_3); ^{13}C NMR (63 MHz): δ 150.2, 149.7, 128.5, 128.1, 127.6, 126.5, 126.1, 107.1, 31.8, 29.4, 29.0, 28.8, 27.0, 22.7, 14.1, 13.4; MS (EI): *m/z* 256 (M^+, 14), 171 (100), 128 (12); IR (neat): ν = 2940, 1450, 763, 698 cm^{-1}; Anal. Calcd for $C_{18}H_{24}O$: C, 84.32; H, 9.44. Found: C, 84.44; H, 9.26.

2-Heptyl-5-*p*-chlorophenyl-3-*p*-methoxyphenylfuran (4i)

Using the above procedure, borate **5a** (359 mg, 1.18 mmol) and enone **1e** (214 mg, 0.786 mmol) were allowed to react for 1 h followed by cyclization for 21 h. The crude mixture was purified by column chromatography (1000:1 hexane/Et_3N) to afford furan **4i** (195 mg, 65%) as a yellow oil. ^{1}H NMR (250 MHz): δ 7.6-7.55 (2H, AA' of AA'XX', aryl-H of ArOMe), 7.33-7.29 (4H, m, aryl-H of ArCl), 6.97-6.91 (2H, XX' of AA'XX', aryl-H of ArOMe), 6.68 (1H, s, furyl-H), 3.82 (3H, s, OCH_3), 2.78 (2H, t, J = 7.5 Hz, CH_2), 1.73 (2H, m, CH_2), 1.28 (8H, m, CH_2), 0.87 (3H, m, CH_3); ^{13}C NMR (63 MHz): δ 158.5, 151.7, 150.4, 132.5, 129.6, 128.8, 126.5, 124.6, 122.7, 114.1, 107.2, 55.3, 31.8, 29.3, 29.0, 28.6, 27.0, 22.6, 14.0; MS (EI): *m/z* 382 (M^+, 2), 297 (10), 28 (100); IR (neat): ν = 2939, 1511, 1483, 1248, 834, 806 cm^{-1}; Anal. Calcd for $C_{24}H_{27}ClO_2$: C, 75.28; H, 7.11. Found: C, 75.26; H, 7.03.

2-Heptyl-3,5-dimethylfuran (4j):

Using the above procedure, borate **5a** (359 mg, 1.18 mmol) and 3-penten-2-one (66 mg, 0.786 mmol) were allowed to react for 1 h followed by cyclization for 3.5 h. The crude mixture was purified by column chromatography (100% hexane) to afford furan **4j** (47 mg, 31%) as an orange oil. ^{1}H NMR (300 MHz): δ 5.72 (1H, s, furyl-H), 2.48 (2H, t, J=7.5, CH_2), 2.20 (3H, s, CH_3), 1.88 (3H, s, CH_3), 1.56 (2H, m, CH_2), 1.28 (8H, m, CH_2), 0.88 (3H, m, CH_3); ^{13}C NMR (63 MHz): δ 149.6, 148.8, 114.1, 108.6, 31.9, 29.2, 29.1, 28.8, 25.9, 22.6, 14.0, 13.4, 9.8; MS (EI): *m/z* 194 (M^+, 6), 109 (100); IR (neat): ν = 2925, 1456, 1264, 794 cm^{-1}; HRMS(EI) calcd for $C_{13}H_{22}O$ (M^+): 194.1671; found 194.1655.

2-Benzyl-3,5-diphenylfuran (4k)

Using the above procedure, borate **5c** (349 mg, 1.18 mmol) and chalcone (**1a**, 164 mg, 0.786 mmol) were allowed to react for 1 h followed by cyclization for 21 h. The crude mixture was purified by column chromatography (10:1 hexane/CH_2Cl_2) to afford furan **4k**[10] (30 mg, 12%) as a colorless oil. ^{1}H NMR (250 MHz): δ 7.69-7.65 (2H, dd, J = 8.8, 1.5 Hz, aryl-H), 7.45-7.20 (13H, m, aryl-H), 6.82 (1H, s, furyl-H), 4.19 (2H, s, CH_2); ^{13}C NMR (63 MHz): δ 152.5, 149.0, 138.5, 133.8, 130.8, 128.6, 128.3, 127.7, 127.2, 126.8, 126.4, 124.5, 123.6, 106.7, 33.0; MS (EI): *m/z* 310 (M^+, 2), 205 (19), 105 (16), 77 (12). The major product was 1,3,5-triphenylpentan-1,5-dione (**6**)[25]: ^{1}H NMR (250 MHz): δ 7.97-7.93 (4H, m, aryl-H), 7.58-7.40

(7H, m, aryl-H), 7.30-7.26 (4H, m, aryl-H), 4.07 (1H, X of AABBX, $J_{AX} = J_{BX} = 7.2$ Hz, CH), 3.43 (4H, AABB of AABBX, $J_{AX} = J_{BX} = 7.2$, $J_{AB} = 16.8$ Hz, CH_2).

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References and Notes

1. Keay, B. A.; Dibble, P. W. In *Comprehensive Heterocyclic Chemistry II*, Ed. Bird, C. W. Elsevier: New York, 1996, Vol 2, pp. 395-436.
2. Hou, X. L.; Cheung, H. Y.; Hon, T. Y.; Kwan, P. L.; Lo, T. H.; Tong, S. Y.; Wong, H. N. C. *Tetrahedron* **1998**, *54*, 1955 and references therein.
3. Keay, B. A. *Chem. Soc. Rev.* **1999**, *28*, 209.
4. Schulte, K. E.; Reisch, J.; Mock, A. *Arch. Pharm. (Weinheim, Ger.)* **1962**, *295*, 627.
5. Schulte, K. E.; Reisch, J.; Bergenthal, D. *Chem. Ber.* **1968**, *101*, 1540.
6. Bicking, K. J.; Jones, J. H.; Holtz, W. J.; Robb, C. M.; Kuehl, F. A. Jr.; Minsker, D. H.; Cragoe, E. J. Jr. *J. Med. Chem.* **1978**, *21*, 1011.
7. Cook, S.; Henderson, D.; Richardson, K. A.; Taylor, R. J. K.; Saunders, J.; Strange, P. G. *J. Chem. Soc. Perkin Trans. I* **1987**, 1825.
8. Arcadi, A.; Cacchi, S.; Larock,R. C.; Marinelli, F. *Tetrahedron Lett.* **1993**, *34*, 2813.
9. Vieser, R.; Eberbach, W. *Tetrahedron Lett.* **1995**, *36*, 4405.
10. Arcadi, A.; Rossi, E. *Tetrahedron* **1998**, *54*, 15253.
11. MaGee, D. I.; Leach, J. D. *Tetrahedron Lett.* **1997**, *38*, 8129.
12. MaGee, D. I.; Leach, J. D.; Setiadji, S. *Tetrahedron* **1999**, *55*, 2847.
13. Alkynylalanes have been used to conjugately add alkynyl groups to enones (see References 10,12) but this reaction is often complicated by competing 1,2-addition: Hooz, J.; Layton, R. B. *Can. J. Chem.* **1973**, *51*, 2098. Alkynyl-9-BBN derivatives have also been used for this transformation: Sinclair, J. A.; Molander, G. A.; Brown, H. C. *J. Am. Chem. Soc.* **1977**, *99*, 954.
14. Chong, J. M.; Shen, L. 81st Canadian Society for Chemistry Conference and Exhibition, Whistler, BC, Canada, May 31-June 4, 1998, Abstract #297; Chong, J. M.; Shen, L.; Taylor, N. J. *J. Am. Chem. Soc.* submitted.
15. Lemière, G. L.; Dommisse, R. A.; Lepoivre, J. A.; Alderweireldt, F. C.; Hiemstra, H.; Wynberg, H.; Jones, J. B.; Toone, E. J. *J. Am. Chem. Soc.* **1987**, *109*, 1363.
16. Fujishima, H.; Takada, E.; Hara, S.; Suzuki, A. *Chem. Lett.* **1992**, 695.
17. Brown, H. C.; Cole, T. E. *Organometallics* **1983**, *2*, 1316.
18. Brown, H. C.; Bhat, N. G.; Srebnik, M. *Tetrahedron Lett.* **1988**, *29*, 2631.
19. We are not aware of other reports of the relative stabilities of C3-alkyl vs aryl-substituted furans but our experimental results suggest that the aryl substituted furans are more stable.
20. Perrin, D. D.; Armarego, W. L. F. *Purification of Laboratory Chemicals, 3rd ed.*, Pergamon: Oxford, 1988, p. 316.
21. Oare, A. D.; Henderson, M. A.; Sanner, M. A.; Heathcock, C. H. *J. Org. Chem.* **1990**, *55*, 132.
22. Chiu, P.; Wong, S. T. *Synth. Commun.* **1998**, *28*, 4513.
23. Rio, G.; Lecas-Nawrockaa, A. *Bull. Soc. Chim. Fr.* **1974**, *12*, 2824.
24. Seiller, B.; Bruneau, C.; Dixneuf, P. H. *Tetrahedron* **1995**, *51*, 13089.
25. Boyer, J; Corriu, R. J. P.; Perz, R.; Reye, C. *J. Organomet. Chem.* **1980**, *184*, 157.