6110 *J. Org. Chem.* **1994,** *59,* 6110−6113

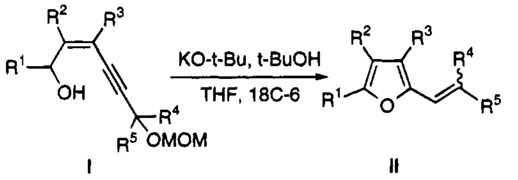
Synthesis of Furans by S_N2' Cyclization of γ-Alkynyl Allylic Alcohol Derivatives

James A. Marshall* and Chad E. Bennett[†]

Department of Chemistry and Biochemistry, University of South Carolina, Columbia, South Carolina 29208

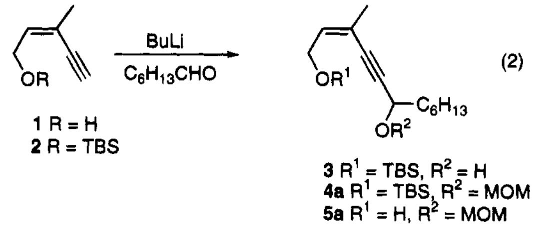
Received June 28, 1994

We recently described novel routes to furans through base-catalyzed isomerization of β- and γ-alkynyl allylic alcohols.[1] A particularly interesting variant of the methodology entailed the use of a propargylic OMOM substituent as a leaving group (eq 1).



(1)

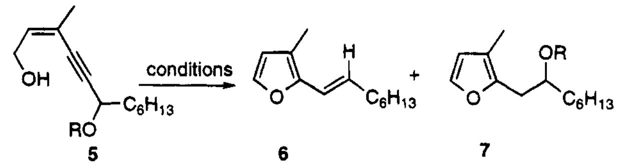
The present study was undertaken to explore this S_N2'-type vinylfuran synthesis in greater detail and to devise milder and more convenient reaction conditions.[2] As a starting point we examined a prototype system, the propargylic OMOM allylic alcohol **5a**. This was prepared as previously reported from the available enynol **1** (eq 2).[1,3]



Our first modification was to replace the 18-crown-6 cosolvent with the less toxic and less expensive additive 1,3-dimethyl-3,4,5,6-tetrahydro-2(1*H*)-pyrimidinone (dimethyl-1,3-propanediylurea, DMPU). As can be seen in Table 1 (compare entries 1 and 2), the reaction proceeds readily to afford a *ca.* 2:1 mixture of (*E*) and (*Z*) vinylfurans **6E** and **6Z** along with a small amount of the MOM ether **7** resulting from cyclization and subsequent isomerization without elimination.[1] When the reaction time was extended to 72 h, a 95:5 mixture of **6E** and **6Z** was obtained in comparable yield. Interestingly, with KH as the base in the absence of *t*-BuOH the reaction was appreciably slower and allene intermediate **8** could be isolated (entry 3).[4] Evidently, isomerization of this initial S_N2' cyclization product to furan **6** is relatively slow under these conditions (eq 3).

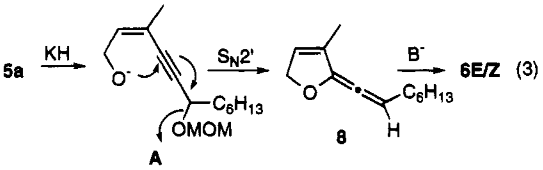
We next examined the effect of replacing the OMOM substituent with a carboxylate leaving group. The benzoate **5b** was rapidly converted to furans **6E/6Z** with KO-*t*-Bu and DMPU, but in only 39% yield (entry 4). The remaining material isolated was the diol **5d** resulting from saponification. This problem was solved through use of the hindered 2,6-dimethoxybenzoate **5c**. This ester gave rise to 2:1 mixture of vinylfurans **6E/6Z** in 80% yield (entry 5). In neither case was the ester analogue of furan **7** detected.

Table 1



entry	series	R	conditions[a]	time, h	yield, %	6E:6Z:7
1	a	MOM	A	0.1	84	75:15:10[b]
2	a	MOM	B	0.7	86	63:31:6[c]
3	a	MOM	C	2.25	69	56:19:3[d]
4	b	PhCO	B	0.5	39[e]	70:30:0
5	c	DMB[b]	B	0.2	80	67:33:0
6	c	DMB[f]	D	3.25	77	91:9:0
7	a	MOM	D	7.3	34	25:1:74
8	d	H	D	4.1	21	94:6:0
9	c	DMB[f]	E	24.0	85	95:5:0

[a] A = KO-*t*-Bu, 18-C-6, *t*-BuOH, THF; B = KO-*t*-Bu, DMPU, *t*-BuOH, THF; C = KH, DMPU, THF; D = KOH/Aliquot 336, CH_2Cl_2, H_2O; E = IRA-400 OH resin, EtOH, H_2O. [b] Reference 1. [c] Ratio of **6E**:**6Z** of 95:5 after prolonged exposure to reaction conditions. [d] Remaining material was allene dihydrofuran **8** (see text). [e] Remaining material was diol **5d** (see text). [f] DMB = 2,6-dimethoxybenzoyl.



Ester **5c** also gave excellent results under phase-transfer conditions with KOH−Aliquot 336 as the base (entry 6). Furans **6E/6Z** were formed as a 91:9 mixture in 77% yield, albeit more slowly than with the KO-*t*-Bu system. In contrast, the MOM derivative **5a** afforded a 25:1:74 mixture of furans **6E/6Z**, and **7** in only 34% yield after 7 h under phase-transfer conditions (entry 7). In this case, protonolysis of the developing vinylic anion from intermediate **A** (eq 3) effectively competes with elimination. Interestingly, diol **5d** afforded furans **6E/6Z** (94:6) and none of the protonolysis product **7** under these conditions (entry 8). As expected the reaction was slow, affording only 21% of products after 4 h. Finally, when the basic ion exchange resin IRA-400[3] was employed in aqueous ethanol, furan **6** was obtained in 85% yield from the DMB derivative **5c** as a 95:5 mixture of (*E*) and (*Z*) isomers (entry 9).

The optimized reaction conditions from Table 1 were applied to two other representative systems: enynols **11a** and **11b**, featuring primary leaving groups; and enynols **13a** and **13b**, with tertiary leaving groups. The former were prepared along previously established lines from propargylic alcohol **9**, as shown in eq 4.[1,5] Enynol **13a**

[‡] Undergraduate research participant, 1993−1994.

(1) Marshall, J. A.; DuBay, W. J. *J. Org. Chem.* **1993**, *58*, 3435.

(2) For an application of this methodology to natural product synthesis, see Marshall, J. A.; DuBay, W. J. *J. Org. Chem.* **1994** *59*, 1703.

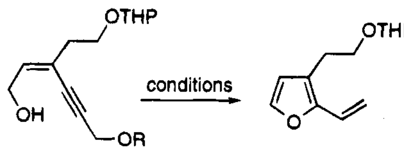
(3) Aldrich Chemical Co., Milwaukee, WI.

(4) cf. Pompes, J. A.; Hoff, S.; Montijir, P. O.; Brandsma, L.; Arens, J. F. *Rec. Trav. Chim.* **1969**, *88*, 119. Hoff, S.; Brandsma, L.; Arens, J. F. *Rec. Trav. Chim.* **1969**, *88*, 609.

(5) Sonogashira, K.; Tohda, Y.; Hagihara, N. *Tetrahedron Lett.* **1975**, 4467.

0022-3263/94/1959-6110$04.50/0

Table 2



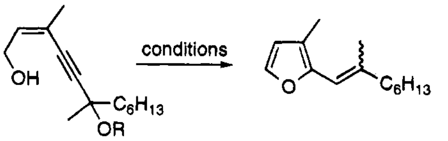
11a R = MOM
11b R = DMB

12

entry	R	conditions[a]	time, h	yield, %
1	MOM	B	1.1	78
2	DMB[a]	B	0.2	81
3	DMB[a]	D	1.0	76
4	DMB[a]	E	12.0	49

[a] See Table 1.

Table 3



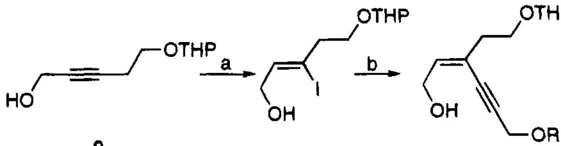
13a R = MOM
13b R = DMB

14E/14Z

entry	R	conditions[a]	time, h	yield, %
1	MOM	A	0.2	85[b,c]
2	MOM	B	3.75	84[d]
3	DMB[a]	B	0.2	81[d]
4	DMB[a]	D	1.75	78[e]
5	DMB[a]	E	21.0	27[f,g]

[a] See Table 1. [b] 67:33 mixture of **14E** and **14Z**. [c] Reference 1. [d] 55:45 mixture of **14E** and **14Z**. [e] 60:40 mixture of **14E** and **14Z**. [f] 78:22 mixture of **14E** and **14Z**. [g] A small amount (*ca.* 2%) of furan alcohol (see **7**) was isolated.

and the alcohol precursor of **13b** were employed in our earlier study.[1]



(4)

9 **10** **11a** R = MOM
11b R = DMB

a) Red-Al; I_2, b) $HCCCH_2OR$, $(Ph_3P)_2PdCl_2$, CuI, Et_2NH

Both the MOM and DMB derivatives **11a** and **11b** were readily converted to the vinylfuran **12** upon treatment with KO-*t*-Bu in DMPU/*t*-BuOH/THF at room temperature (Table 2, entries 1 and 2). As expected, the reaction was faster with the DMB leaving group. The phase-transfer conditions were also effective with the DMB system **11b**, producing the vinylfuran **12** in 76% yield (entry 3). The basic resin IRA-400 proved disappointing, affording the vinylfuran **12** in only 35% yield after prolonged heating (entry 4).

We next turned our attention to the known MOM enynol **13a**[1] and the DMB analogue **13b** as representative vinylfuran precursors with tertiary leaving groups (Table 3). The former afforded furan **14** as a mixture of *E* and *Z* isomers in comparable yield with 18-C-6 or DMPU as cosolvent (entries 1 and 2). We assume the major isomer has the more stable *E* double bond configuration. The DMB system again proved highly reactive under both KO-*t*-Bu/DMPU and phase-transfer conditions affording furans **14** in high yield (entries 3 and 4). The IRA-400 OH resin was less effective. Furan **14** was isolated in modest yield even after prolonged heating (entry 5). However, these conditions led to the highest *E*:*Z* product ratio, possibly a consequence of the longer reaction time allowing for equilibration of the double bond isomers.

The foregoing studies show that DMPU can be substituted for 18-crown-6 in the novel base-promoted conversion of enynol MOM ethers to vinyl furans. Presumably, other analogous ethers would serve equally well as leaving groups. If milder conditions are required, the use of KOH/Aliquot 336 on the 2,6-dimethoxybenzoates is the method of choice. Reactions are clean and efficient. Furthermore, in the case of ester **5c**, the reaction strongly favors the (*E*)-product.

Experimental Section[6]

(*Z*)-1-Hexyl-6-[(*tert*-butyldimethylsilyl)oxy]-4-methyl-4-hexen-2-ynyl Benzoate (4b). To a solution of 1.94 g (5.98 mmol) of TBS ether **3**[1] and a catalytic amount of DMAP in 60 mL of CH_2Cl_2 was added 1.9 mL (23.9 mmol) of pyridine and 2.1 mL (17.9 mmol) of benzoyl chloride at 0 °C. The reaction mixture was allowed to reach room temperature. After 19.5 h, water was added and the mixture was extracted with ether. The extracts were washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure, affording an orange oil, purified by flash chromatography on silica gel (25% EtOAc–hexane) to yield 2.02 g (79%) of TBS ether **4b** as a pale yellow oil: ^1H NMR ($CDCl_3$, 300 MHz) δ 8.04 (dd, $J = 1.4$, 7.1 Hz), 7.55 (t, $J = 7.4$ Hz), 7.43 (dd, $J = 7.3$, 7.7 Hz), 5.77 (t), 5.75 (t), 4.32 (d, $J = 6.4$ Hz), 1.88 (m), 1.83 (d, $J = 1.4$ Hz), 1.30 (m), 0.86 (m), 0.03 (s).

(*Z*)-1-Hexyl-6-[(*tert*-butyldimethylsilyl)oxy]-4-methyl-4-hexen-2-ynyl 2,6-Dimethoxybenzoate (4c). The procedure described for benzoate **4b** was employed with 5.01 g (15.4 mmol) of TBS ether **3** and 9.27 g (46.2 mmol) of 2,6-dimethoxybenzoyl chloride for 17.5 h. The product was purified by flash chromatography (25% EtOAc–hexane) to yield 6.70 g (89%) of TBS ether **4c** as a yellow oil: ^1H NMR ($CDCl_3$, 300 MHz) δ 7.26 (t, $J = 6.4$ Hz), 6.52 (d, $J = 8.4$ Hz), 5.79 (t, $J = 6.6$ Hz), 5.76 (t, $J = 4.9$ Hz), 4.34 (dd, $J = 1.3$, 5.1 Hz), 3.79 (s), 1.89–1.84 (m), 1.55–1.24 (m), 0.87 (m), 0.05 (t, $J = 3.1$ Hz). Anal. Calcd for $C_{28}H_{44}O_5Si$: C, 68.81; H, 9.07. Found: C, 68.56; H, 8.95.

(*Z*)-1-Hexyl-6-hydroxy-4-methyl-4-hexen-2-ynyl Benzoate (5b). To a solution of 2.02 g (4.71 mmol) of TBS ether **4b** in 19 mL of THF was added 0.40 mL (7.07 mmol) of HOAc and 7.1 mL of 1.0 M TBAF at 0 °C. The solution was allowed to reach rt and, after 14 h, water was added and the mixture was extracted with ether. The extracts were washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure to yield 1.98 g of a yellow-orange oil, purified by flash chromatography on silica gel (25% EtOAc–hexane) to yield 1.46 g (99%) of benzoate **5b** as a yellow oil: ^1H NMR ($CDCl_3$, 300 MHz) δ 8.05 (dd, $J = 1.2$, 7.0 Hz), 7.55 (dd, $J = 1.4$, 6.0 Hz), 7.44 (dd, $J = 7.3$, 7.7 Hz), 5.88 (dt, $J = 1.5$, 5.2 Hz), 5.72 (t, $J = 6.5$ Hz), 4.28 (dd, $J = 1.0$, 5.7 Hz), 1.96–1.87 (m), 1.86 (dd, $J = 1.1$, 1.3 Hz), 1.51–1.24 (m), 0.87 (m). Anal. Calcd for $C_{20}H_{26}O_3$: C, 76.40; H, 8.33. Found: C, 76.34; H, 8.34.

(*Z*)-1-Hexyl-6-hydroxy-4-methyl-4-hexen-2-ynyl 2,6-Dimethoxybenzoate (5c). The procedure described for alcohol **5b** was employed with 6.70 g (13.7 mmol) of TBS ether **4c** for 19.5 h. The product was purified by flash chromatography (50% EtOAc–hexane) to yield 4.51 g (88%) of benzoate **5c** as a yellow oil: ^1H NMR ($CDCl_3$, 300 MHz) δ 7.26 (t, $J = 8.4$ Hz), 6.53 (d, $J = 10.4$ Hz), 5.89 (t, $J = 5.8$ Hz), 5.76 (t, $J = 6.6$ Hz), 4.30 (d, $J = 5.8$ Hz), 3.80 (s), 1.87 (m), 1.55–1.22 (m), 0.87 (t, $J = 6.8$ Hz). Anal. Calcd for $C_{22}H_{30}O_5$: C, 70.56; H, 8.07. Found: C, 70.37; H, 8.02.

(*Z*)-3-Methyl-2-dodecen-4-yne-1,6-diol (5d). To a solution of 8.51 g (0.101 mol) of alcohol **1** in 162 mL of THF was added 85 mL of 2.5 M n-BuLi in hexanes at −78 °C, causing the

---

(6) For typical experimental protocols, see Marshall, J. A.; Wang, X.-J. *J. Org. Chem.* **1991**, *56*, 960.

solution to turn a deep red. After 10 min, 31.1 mL (0.223 mol) of heptaldehyde was added at −78 °C. The reaction mixture was allowed to warm to room temperature, a saturated aqueous solution of NH_4Cl was added, and the mixture was stirred until the Li salts had dissolved. The mixture was extracted with ether, and the extracts were washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure to yield 41.52 g of a cloudy orange oil. Bulb to bulb distillation (0.5 torr, 90−130 °C) removed volatile impurities, leaving 19.41 g (97%) of diol **5d** as a yellow-brown oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.86 (dt, J = 1.5, 6.8 Hz), 4.49 (t, J = 6.6 Hz), 4.29 (dd, J = 1.0, 6.8 Hz), 1.87 (s), 1.73−1.67 (m), 1.58−1.28 (m), 0.87 (t, J = 6.9 Hz).

(*E*)-2-(1-Octenyl)-3-methylfuran (6): A. Cyclization of MOM Ether 5a with KO-t-Bu in THF. To a solution of 0.255 g (1.00 mmol) of MOM ether **5a** and 0.30 mL (2.45 mmol) of DMPU in 0.47 mL (5.00 mmol) of t-BuOH and 4.9 mL of THF was added 0.10 g (2.45 mmol) of KH. After 0.7 h, water was added and the mixture was extracted with ether. The extracts were washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure to yield 0.244 g of a yellow oil, which was purified by flash chromatography on silica gel (2.5% EtOAc−hexane) to yield 0.156 g (81%) of furan **6** as a clear, colorless oil (*E:Z*, 70:30) and 0.013 g (5%) of furan **7**. When the reaction time was extended to 72 h, furan **6** was obtained in 93% yield as a 95:5 mixture of **6E** and **6Z**. Furan **6E**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.20 (d, J = 1.7 Hz), 6.19 (d, J = 15.8 Hz), 6.18 (d, J = 1.8 Hz), 6.05 (dt, J = 6.7, 15.7 Hz), 2.17 (q, J = 6.9 Hz), 2.00 (s), 1.42−1.28 (m), 0.87 (dd, J = 6.7, 6.9 Hz). Furan **6Z** (diagnostic peaks): δ 7.30 (d, J = 1.7 Hz), 6.21 (d, J = 1.8 Hz), 5.46 (dt, J = 11.8, 6.8 Hz), 2.50 (q, J = 7.3 Hz). Furan **7**: δ 7.21 (d, J = 1.8 Hz), 6.14 (d, J = 1.8 Hz), 4.56, 4.53 (ABq, J = 6.9 Hz), 3.80 (m), 3.27 (s), 2.81−2.65 (m), 1.95 (s), 1.44−1.18 (m), 0.86 (t, J = 6.5, 7.0 Hz).

B. Cyclization of MOM Ether 5a with KH in THF. To a solution of 0.256 g (1.01 mmol) of MOM ether **5a** and 0.30 mL (2.45 mmol) of DMPU in 5.4 mL of THF was added 0.10 g (2.45 mmol) of KH. After 2.25 h, water was added and the mixture was extracted with ether. The extracts were washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure, affording 0.215 g of a yellow oil, purified by flash chromatography on silica gel (2.5% EtOAc−hexane) to yield 0.101 g (52%) of furan **6** as a clear, colorless oil (*E:Z*, 75:25), 0.004 g (2%) of furan **7**, and 0.030 g (15%) of dihydrofuran **8**. Dihydrofuran **8**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.70 (t, J = 7.6 Hz), 5.52 (q, J = 1.6 Hz), 4.54 (dd, J = 1.6, 2.1 Hz), 2.06−1.86 (m), 1.80 (dd, J = 1.6, 2.0 Hz), 1.35−1.16 (m), 0.85 (dt, J = 2.4, 6.9 Hz).

C. Cyclization of 2,6-Dimethoxybenzoate 5c with KO-t-Bu in THF. To a solution of 0.202 g (0.539 mmol) of 2,6-dimethoxybenzoate **5c** and 0.07 mL (0.58 mmol) of DMPU in 0.06 mL (0.64 mmol) of t-BuOH and 1.35 mL of THF was added 1.35 mL of 1.0 M KO-t-Bu in THF. The addition of the KO-t-Bu solution caused the formation of a yellow solid, so an additional 2.0 mL of THF was added to facilitate stirring. After 0.2 h, water was added and the mixture was extracted with ether. The extracts were washed with aqueous $NaHCO_3$, dried over $MgSO_4$, and concentrated under reduced pressure. Purification by flash chromatography on silica gel (hexane) afforded 0.083 g (80%) of furan **6** as a clear, colorless oil (*E:Z*, 67:33).

D. Cyclization of 2,6-Dimethoxybenzoate 5c with KOH−Aliquot 336. To a mixture of 0.203 g (0.542 mmol) of 2,6-dimethoxybenzoate **5c** and 1.10 g (2.71 mmol) of Aliquot 336 in 1.1 mL of CH_2Cl_2 and 1.1 mL of H_2O was added 0.760 g (13.6 mmol) of KOH pellets. After 3.25 h, water was added and the mixture was extracted with CH_2Cl_2. The extracts were washed with 10% aqueous HCl, dried over $MgSO_4$, and concentrated under reduced pressure to yield an orange-yellow oil. Purification by flash chromatography on silica gel (2.5% EtOAc−hexane, followed by 25% EtOAc−hexane and 50% EtOAc−hexane) afforded 0.080 g (77%) of furan **6** as a clear, colorless oil (*E:Z* ratio of 91:9).

E. Cyclization of 2,6-Dimethoxybenzoate 5c with IRA-400 (OH) Resin. To 1.20 g (3.20 mmol) of benzoate **5c** and 20.46 g of IRA-400(OH) resin was added 9 mL of EtOH and 29 mL of H_2O. The mixture was refluxed with stirring for 24 h, whereupon the condenser was rinsed with CH_2Cl_2 and the mixture was filtered through a plug of Celite with ethanol and CH_2Cl_2. The filtrate was extracted with CH_2Cl_2, and the extracts were washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure to yield 0.524 g (85%) of furan **6** as a 95:5 *E:Z* mixture.

(*Z*)-5-[(Tetrahydropyranyl)oxy]-3-iodo-2-penten-1-ol (10). To a solution of 9.00 g (48.8 mmol) of alcohol **9**[7] in 98 mL of THF was added 39.1 mL of 2.0 M Red-Al in toluene at 0 °C. After stirring for 19 h at room temperature, the solution was cooled to −78 °C and 23.6 g (92.8 mmol) of I_2 dissolved in THF was added dropwise. The solution was warmed to room temperature and stirred for 1 h. An aqueous solution of $Na_2S_2O_3$ was added until the color of the solution changed from deep red to yellow and a precipitate of Al salts formed. The mixture was extracted with ether. The extracts were washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure to yield a yellow-orange oil. Purification by flash chromatography on silica gel (50% EtOAc−hexanes, followed by 80% EtOAc-hexanes) afforded 6.82 g (45%) of vinyl iodide **10**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.94 (t, J = 5.8 Hz), 4.59 (t, J = 3.0 Hz), 4.18 (d, J = 5.8 Hz), 3.83 (m), 3.56 (m), 2.79 (t, J = 6.0 Hz), 1.95−1.51 (m).

(*Z*)-3-[2-(Tetrahydropyranyloxy)ethyl]-6-(methoxymethoxy)-2-hexen-4-yn-1-ol (11a). To a solution of 5.31 g (17.0 mmol) of vinyl iodide **10** in 113 mL of $HNEt_2$, degassed with argon, was added 0.60 g (0.85 mmol) of $(Ph_3P)_2PdCl_2$ and 0.32 g (1.70 mmol) of CuI followed by 2.55 g (25.5 mmol) of 3-(methoxymethoxy)-1-propyne. After 5.0 h, aqueous NH_4Cl was added slowly to quench the reaction. The mixture was extracted with ether, and the extracts were washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure affording a brownish red oil which was purified by flash chromatography on silica gel (80% EtOAc−hexane) to yield 2.80 g (58%) of alcohol **11a**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.97 (t, J = 6.6 Hz), 4.70 (s), 4.58 (t, J = 4.1 Hz), 4.35 (s), 4.32 (t, J = 6.3 Hz), 3.90−3.50 (m), 3.37 (s), 2.43 (t, J = 6.9 Hz), 1.77−1.24 (m).

(*Z*)-6-Hydroxy-4-[2-(tetrahydropyranyloxy)ethyl]-4-hexen-2-ynyl 2,6-Dimethoxybenzoate (11b). To a solution of 1.00 g (17.2 mmol) of propargyl alcohol and a catalytic amount of DMAP in 50 mL of pyridine was added 10.34 g (51.5 mmol) of 2,6-dimethoxybenzoyl chloride at 0 °C. After 43.5 h, 1:1 EtOAc−hexanes, H_2O, and 10% aqueous HCl were added, and the mixture was extracted with 1:1 EtOAc−hexanes. The extracts were washed with brine, dried over $MgSO_4$, filtered through silica gel on Celite with 1:1 EtOAc−hexanes followed by 4:1 EtOAc−hexanes, and concentrated under reduced pressure to yield 2.31 g (61%) of 2-propynyl 2,6-dimethoxybenzoate: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.28 (t, J = 8.5 Hz), 6.53 (d, J = 8.4 Hz), 4.90 (d, J = 2.5 Hz), 3.80 (s), 2.49 (t, J = 2.5 Hz). Anal. Calcd for $C_{12}H_{12}O_4$: C, 65.45; H, 5.49. Found: C, 65.34; H, 5.46.

To a solution of 0.223 g (0.714 mmol) of vinyl iodide **10** in 1.4 mL of CH_2Cl_2 was added 0.19 mL (0.90 mmol) of $((CH_3)_3Si)_2NH$. After stirring at room temperature for 1.5 h, the reaction solution was concentrated under reduced pressure. The procedure described for MOM ether **11a** was followed with the concentrated reaction solution and 0.025 g (0.036 mmol) of $(Ph_3P)_2PdCl_2$, 0.014 g (0.074 mmol) of CuI, 0.314 g (1.43 mmol) of 2-propynyl 2,6-dimethoxybenzoate, 0.50 mL (2.87 mmol) of Hunig's base, and 4.8 mL of THF. The product was purified by flash chromatography on silica gel (1:1 EtOAc−hexanes, followed by 4:1 EtOAc−hexanes) to yield 0.075 g (30% based on 0.032 g of recovered vinyl iodide **10**) of benzoate **11b**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.28 (t, J = 8.4 Hz), 6.54 (d, J = 8.4 Hz), 6.00 (t, J = 6.6 Hz), 5.03 (s), 4.58 (t, J = 3.6 Hz), 4.33 (d, J = 6.6 Hz), 3.85 (m), 3.81 (s), 3.56 (m), 2.44 (t, J = 6.5 Hz), 1.80−1.40 (m). Anal. Calcd for $C_{22}H_{28}O_7$: C, 65.33; H, 6.98. Found: C, 65.11; H, 6.96.

3-[2-(Tetrahydropyranyloxy)ethyl]-2-vinylfuran (12): A. Cyclization of MOM Ether 11a with KO-t-Bu in THF. Procedure A described for furan **6** was followed with 0.204 g (0.717 mmol) of MOM ether **11a** for 1.1 h. The product, a yellow oil, was purified by flash chromatography on silica gel (5% EtOAc−hexane) to yield 0.125 g (78%) of furan **12** as a clear, colorless oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.26 (d, J = 1.9 Hz), 6.54 (dd, J = 6.1, 11.3 Hz), 6.30 (d, J = 1.8 Hz), 5.59 (dd, J = 1.5, 15.9 Hz), 5.11 (dd, J = 1.5, 9.8 Hz), 4.58 (t, J = 3.8 Hz), 3.88−3.46 (m), 2.72 (t, J = 7.0 Hz), 1.67−1.50 (m).

B. Cyclization of 2,6-Dimethoxybenzoate 11b with KOH−Aliquot 336. A solution of 1.0 mL of 0.30 M benzoate

---

(7) Hart, D. J.; Tsai, Y-M. *J. Am.. Chem. Soc.* **1984** *106*, 8209.

11b in THF was concentrated under reduced pressure. To this oil was added 0.61 g (1.5 mmol) of Aliquot 336, 0.6 mL of CH_2Cl_2, and 0.6 mL of H_2O, followed by 0.42 g (7.5 mmol) of KOH. After stirring for 1.0 h at room temperature, the mixture was diluted with water and extracted with ether. The extracts were washed with brine, dried over $MgSO_4$, filtered through a plug of silica gel on Celite with ether, and concentrated under reduced pressure, affording a yellow oil. Purification by flash chromatography on silica gel (15% EtOAc−hexane, followed by 25% EtOAc−hexane) yielded 0.051 g (76%) of furan **12** as a light yellow oil.

(*Z*)-6-[(*tert*-Butyldimethylsilyl)oxy]-1-hexyl-1,4-dimethyl-4-hexen-2-ynyl 2,6-Dimethoxybenzoate (13b). The procedure described for benzoate **4b** was followed with 2.00 g (5.91 mmol) of (*Z*)-1-[(*tert*-butyldimethylsilyl)oxy]-3,6-dimethyl-2-dodecen-4-yn-6-ol[1] and 3.56 g (17.7 mmol) of 2,6-dimethoxybenzoyl chloride for 47 h. The product was purified by flash chromatography on silica gel (10% EtOAc−hexane, followed by 25% EtOAc−hexane) to yield 2.64 g (89%) of benzoate **13b** as a yellow oil: ^1H NMR (300 MHz, $CDCl_3$) δ 7.23 (t, J = 8.4 Hz), 6.51 (d, J = 8.4 Hz), 5.73 (dt, J = 1.5, 4.9 Hz), 4.38 (dt, J = 1.3, 5.1 Hz), 3.78 (s), 1.85 (q, J = 1.3, 1.4 Hz), 1.79 (s), 1.52−1.28 (m), 0.87 (m), 0.05 (m).

(*Z*)-6-Hydroxy-1-hexyl-1,4-dimethyl-4-hexen-2-ynyl 2,6-Dimethoxybenzoate (14b). The procedure described for alcohol **5b** was followed with 2.64 g (5.25 mmol) of benzoate **13b** for 45 h. The product was purified by flash chromatography on silica gel (25% EtOAc−hexane, followed by 50% EtOAc−hexane) to yield 0.541 g (27%) of a pure benzoate **14b** and 1.190 g (58%) of slightly impure benzoate **14b**: ^1H NMR (300 MHz, $CDCl_3$) δ 7.24 (t, J = 8.4 Hz), 6.52 (d, J = 8.4 Hz), 5.91 (dt, J = 1.5, 5.3 Hz), 4.29 (d, J = 6.9 Hz), 3.79 (s), 2.01−1.92 (m), 1.88 (d, J = 1.5 Hz), 1.77 (s), 1.70 (s), 1.53−1.28 (m), 0.87 (t, J = 6.7 Hz). Anal. Calcd for $C_{23}H_{32}O_5$: C, 71.11; H, 8.30. Found: C, 70.86; H, 8.32.

(*E*)-2-(2-Methyl-1-octenyl)-3-methylfuran (15): A. Cyclization of MOM Ether 14a with KO-t-Bu in THF. Procedure A described for furan **6** was followed with 0.255 g (0.950 mmol) of MOM ether **14a** for 3.75 h. The product was purified by flash chromatography on silica gel (2.5% EtOAc−hexane) to yield 0.164 g (84%) of furan **15** as a 1:1 mixture of *E* and *Z* isomers: ^1H NMR (300 MHz, $CDCl_3$) δ 7.27 (d, J = 1.8 Hz), 7.25 (s), 6.19 (d, J = 2.6 Hz), 6.18 (d, J = 2.0 Hz), 5.92 (s), 5.90 (s), 2.43 (t, J = 7.5 Hz), 2.12 (t, J = 7.5 Hz), 1.99 (s), 1.86 (d, J = 1.3 Hz), 1.46−1.28 (m), 0.86 (m).

B. Cyclization of 2,6-Dimethoxybenzoate 14b with KOH−Aliquot 336. Procedure D described for furan **6** was followed with 0.196 g (0.504 mmol) of benzoate **14b** at 55−65 °C for 1.75 h. The product was purified by flash chromatography on silica gel (2.5% EtOAc−hexane) to yield 0.081 g (78%) of furan **15**, a light yellow oil, as a 60:40 mixture of *E* and *Z* isomers.

Acknowledgment. This work was supported by research grant GM 29475 from the National Institutes of Health (NIAID), for which we are grateful.

Supplementary Material Available: ^1H NMR spectra of all new compounds (16 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.