A Novel Furan Ring Construction and Syntheses of 4- and 4,5-Substituted 2-(.alpha.-Heterocyclylalkyl)furans

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A Novel Furan Ring Construction and Syntheses of 4- and 4,5-Substituted 2-(α-Heterocycloalkyl)furans

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4-Substituted and 4,5-disubstituted 2-(benzotriazol-1-ylmethyl)furans **3** have been prepared in good yields from 1-propargylbenzotriazole (**1**) and α-bromo ketones *via* one-pot processes. The 2-(benzotriazol-1-ylmethyl) side chain of **3** was alkylated by lithiation followed by quenching with electrophiles to afford 4- and 4,5-substituted 2-(α-benzotriazol-1-ylalkyl)furans **11**. Substitution of the benzotriazolyl groups of **3** and **11** with other heterocycles in the presence of $ZnCl_2$ gave a variety of 4- and 4,5-substituted 2-(α-heterocycloalkyl)furans **10** and **12** in good yields.

Introduction

The synthesis of furans is of importance since the furan ring is present in numerous natural compounds which exhibit interesting biological activities.[1] The ring system is also found in industrially significant substances and in many useful synthetic building blocks.[2,3] A variety of approaches leading to the generation of the furan ring have been documented[2,4-6] and among them, several general methods utilize an intramolecular cycloaddition of alkoxides to double and triple bonds as the key reaction. Recently, many acyclic precursors have been employed for the synthesis of a wide range of substituted furans.[7] For example, alkynyloxiranes, prepared by coupling vinylic halides or triflates with terminal alkynes followed by epoxidation with *m*-CPBA, are isomerized under strongly basic conditions or reduced with samarium diiodide/Pd to afford 2,4-, 2,5-, and 2,3,5-substituted furans,[7-10] in a reaction pathway involving 5-*endo-dig* cyclization of the corresponding cumulenyl alkoxides.

In previous reports, we demonstrated that 1-propargylbenzotriazole (**1**), readily available from the reaction of benzotriazole with propargyl bromide in the presence of sodium hydroxide,[11] is a useful reagent for the synthesis of furans, dihydrofurans,[5] pyrroles,[12] and indoles.[13] Thus, the reactions of 1-(3-lithiopropargyl)benzotriazole (**4**) with aromatic aldehydes give 1-[3-(hydroxyarylmethyl)propargyl]benzotriazoles which undergo base-assisted rearrangement to form α-hydroxyallenes. Subsequent intramolecular cyclization to 2-(benzotriazol-1-yl)-5-aryldihydrofurans and elimination of benzotriazole affords 2-arylfurans.[5]

We now report a novel one-pot procedure for furan ring construction from 1-propargylbenzotriazole (**1**) and α-bromo ketones. The resulting 4- and 4,5-substituted 2-(benzotriazol-1-ylmethyl)furans can undergo, either directly or following alkylation, displacement of the benzotriazole groups by other heterocycles to give the corresponding 4- and 4,5-substituted 2-(α-heterocycloalkyl)furans **10** and **12**. Compounds of types **10** and **12** play important roles in the food industry and as intermediates for the synthesis of other organic compounds and polymers.[14] Few previous methods are reported for the synthesis of **10** and **12**. In particular, such systems with two different simple heterocyclic rings were unknown until our previous work.[14]

Results and Discussion

Furan Ring Construction—Preparation of 4- and 4,5-Substituted 2-(Benzotriazol-1-ylmethyl)furans. As an extension of our investigation concerning the reactivity of lithiated 1-propargylbenzotriazole (**4**) toward ketones for the preparation of dihydrofurans,[5] we found that treatment of 1-propargylbenzotriazole (**1**) with 1 equiv of *n*-BuLi followed by quenching with 1 equiv of α-bromo ketone at −78 °C and subsequent warming to room temperature gave the corresponding alkynyloxirane **2** as the major product with smaller amounts of the substituted furan **3**. The structures of both derivatives **2** and **3** were supported by ^1H and APT NMR spectra. When the reaction was carried out at −78 °C without warming, the alkynyloxirane **2** could be isolated exclusively (as was done for **2d**, see Experimental Section). Assuming that product **3** was formed *via* isomerization of intermediate **2** in the presence of a trace of base, we treated alkynyloxirane **2** with $KOBu^t$ in $HOBu^t$ at 50 °C for several hours. The expected product **3** was afforded in good yield. Similar base-catalyzed transformations of alkynyloxiranes into furans are found in the literature; however, the corresponding alkynyloxiranes are prepared by multistep methods and 18-crown-6 is required for the ring formation.[9]

In practice, it is not necessary to isolate the alkynyloxirane **2**. Thus, a one-pot synthesis of 4- and 4,5-

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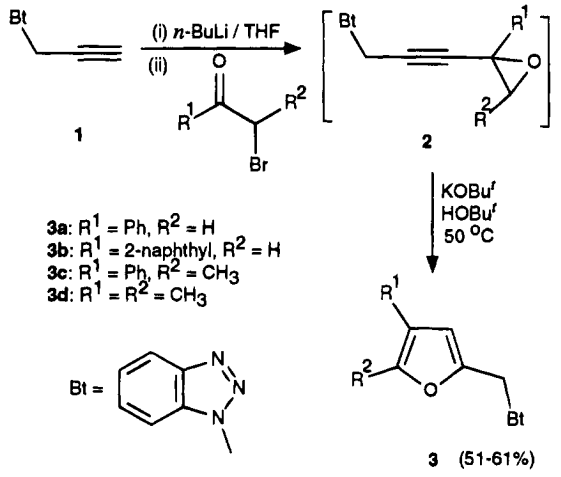
Table 1. Synthesis of 4- and 4,5-Substituted 2-(α-Benzotriazol-1-ylalkyl)furans 3 and 11

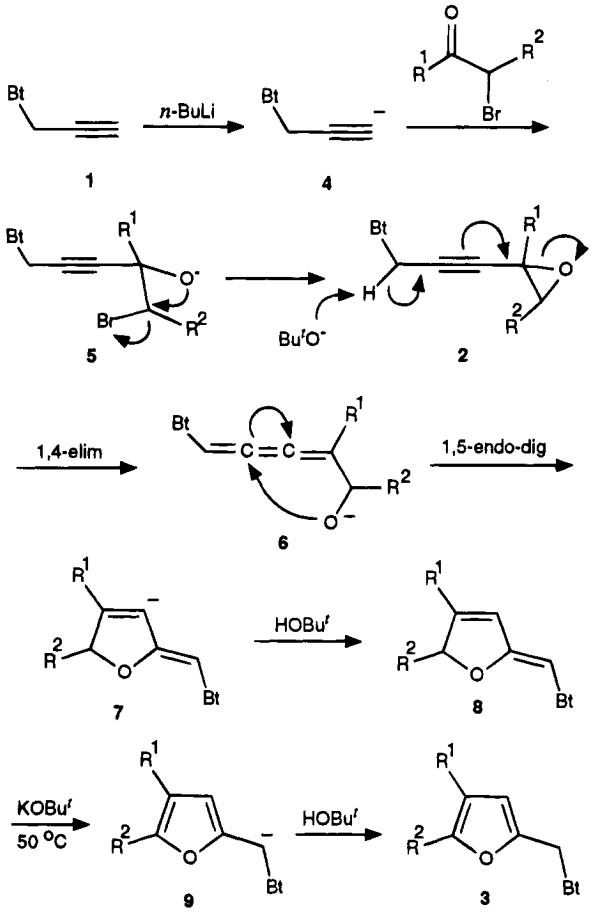
compd	yield (%)	mp (°C)	appearance	molecular formula	found C	found H	found N	calcd C	calcd H	calcd N
3a	61	121–122	powder[a]	$C_{17}H_{13}N_3O$	74.42	4.81	15.18	74.17	4.76	15.26
3b	51	152–153	powder[a]	$C_{21}H_{15}N_3O$	77.85	4.68	12.83	77.52	4.65	12.91
3c	53	98–99	powder[b]	$C_{18}H_{15}N_3O$	75.09	5.29	14.16	74.72	5.23	14.52
3d	55	129–130	needles[c]	$C_{13}H_{13}N_3O$	68.97	5.83	18.64	68.69	5.77	18.50
11a	87	–	oil[b]	$C_{24}H_{19}N_3O$	78.95	5.22	11.25	78.88	5.24	11.50
11b	78	65–67	powder[b]	$C_{24}H_{21}N_3O$	78.76	5.79	11.16	78.45	5.76	11.44
11c	65	–	oil[b]	$C_{22}H_{23}N_3O$	76.49	6.76	12.10	76.48	6.72	12.17
11d	82	–	oil[b]	$C_{14}H_{15}N_3O$	69.64	6.33	17.45	69.67	6.27	17.42

[a] Recrystallized from EtOH. [b] Column chromatography (EtOAc/hexane 1:1). [c] Recrystallized from EtOAc/hexane.

Scheme 1



Scheme 2



substituted 2-(benzotriazol-1-ylmethyl)furans **3** is available (Scheme 1). 1-Propargylbenzotriazole (**1**) was treated with one equiv of *n*-butyllithium at −78 °C for 1 h, followed by treatment with α-bromo ketones for 4 h at the same temperature. A solution of KOBu^t in HOBu^t was added and the reaction mixtures were warmed to 50 °C overnight to give the products **3** in 51−61% yields (Table 1). The products **3** were characterized by ^{1}H and ^{13}C NMR spectra and elemental analyses (Tables 1, 2, and 3).

Mechanism of Furan Ring Construction. The following mechanism is proposed based on experimental and literature evidence (Scheme 2). 1-Propargylbenzotriazole (**1**) was deprotonated on treatment with *n*-BuLi to generate anion **4** which attacks the carbonyl group of the α-bromo ketone to yield adduct **5**. The oxygen anion of **5** intramolecularly displaced bromide to form epoxide **2** which is isolable. Since benzotriazole is electron withdrawing, the propargyl triple bond can readily rearrange to an allene under basic conditions.[5] Therefore, KOBu^t efficiently promoted 1,4-elimination of alkynyloxirane **2** to form cumulenyl alkoxide **6** which underwent 1,5-*endo-dig* cyclization to afford vinyl anion **7** followed by rapid protonation to give compound **8**. Intermediate **8** (which could be isolated at room temperature as demonstrated for **8c**, see Experimental Section) rearranged upon heating with KOBu^t to form **9** which was protonated to give 4- or 4,5-substituted 2-(benzotriazol-1-ylmethyl)furans **3**.

Alkylation of 4- and 4,5-Substituted 2-(Benzotriazol-1-ylmethyl)furans and Formation of 4- and 4,5-Substituted 2-(α-Heterocycloalkyl)furans. Benzotriazole has been extensively used in our laboratory as a synthetic auxiliary due to its electron withdrawing and good leaving group properties.[14,15] Therefore, the benzotriazol-1-ylmethyl side chain of **3** can be elaborated by alkylation and substitution (Scheme 3). Compound **3** was treated with 1 equiv of *n*-BuLi at −78 °C to generate anion **9** which then reacted with electrophiles such as benzyl bromide, *n*-butyl iodide, *i*-propyl iodide, and methyl iodide to give the alkylated products **11** in 65−87% yields.

Compounds **3** and **11**, upon treatment with $ZnCl_2$ in CH_2Cl_2, underwent Friedel−Crafts type reactions with other heterocycles such as 2-methylfuran, 2-methylthiophene, and *N*-methylindole to afford 4- and 4,5-substituted 2-(α-heterocycloalkyl)furans **10** and **12** in good to excellent yields. The function of $ZnCl_2$ is to coordinate the nitrogen lone pair electrons of the benzotriazolyl group and assist benzotriazolyl group removal to generate the carbocation. Since the reaction involved the formation of carbocation **13** (Scheme 4), the R^3 and

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Table 2. ^{1}H NMR Data of 4- and 4,5-Substituted 2-(α-Benzotriazol-1-ylalkyl)furans 3 and 11 ($CDCl_3$), δ (ppm), J (Hz)

	Bt								
compd	H-4	H-5	H-6	H-7	H-3 (furan)	CH or CH_2	R^1	R^2	R^3
3a	8.03 (d, 8.4)	7.22–7.46 (m)[a]	7.22–7.46 (m)[a]	7.57 (d, 8.3)	6.71 (s)	5.69 (2H, s)	7.22–7.46 (5H, m)[a]	7.61 (1H, s)	–
3b	8.06 (d, 8.3)	7.32–7.51 (m)[a]	7.32–7.51 (m)[a]	7.59 (d, 8.3)	6.82 (s)	5.83 (2H, s)	7.76–7.82 (4H, m), 7.32–7.51 (3H, m)[a]	7.73 (1H, s)	–
3c	8.02 (d, 8.3)	7.20–7.35 (m)[a]	7.41 (dd, 8.2 and 7.3)	7.60 (d, 8.2)	6.54 (s)	5.74 (2H, s)	7.20–7.35 (5H, m)[a]	2.32 (3H, s)	–
3d	8.03 (d, 8.3)	7.33 (dd, 8.3 and 7.4)	7.44 (dd, 8.1 and 7.4)	7.57 (d, 8.1)	6.20 (s)	5.70 (2H, s)	2.12 (3H, s)	1.87 (3H, s)	–
11a	7.98 (d, 8.3)	6.98–7.37 (m)[a]	6.98–7.37 (m)[a]	7.44 (d, 8.3)	6.70 (s)	6.22 (1H, t, 7.4)	6.98–7.37 (5H, m)[a]	7.60 (1H, s)	6.98–7.37 (5H, m),[a] 3.83 (2H, d, 7.3)
11b	8.07 (d, 8.3)	7.31–7.54 (m)[a]	7.31–7.54 (m)[a]	7.74–7.85 (m)[a]	6.91 (s)	5.69 (1H, d, 10.6)	7.74–7.85 (4H, m),[a] 7.31–7.54 (3H, m)[a]	7.72 (1H, s)	3.11–3.19 (1H, m), 1.13 (3H, d, 6.6), 0.79 (3H, d, 6.6)
11c	8.07 (d, 8.2)	7.23–7.44 (m)[a]	7.23–7.44 (m)[a]	7.59 (d, 8.3)	6.55 (s)	6.03 (1H, dd, 9.0 and 6.8)	7.23–7.44 (5H, m)[a]	2.36 (3H, s)	2.51–2.50 (2H, m), 1.22–1.40 (4H, m), 0.86 (3H, t, 7.3)
11d	8.03 (d, 8.3)	7.28–7.45 (m)	7.28–7.45 (m)	7.28–7.45 (m)	6.19 (s)	6.17 (1H, q, 7.2)	2.10 (3H, s)	1.90 (3H, s)	2.01 (3H, d, 7.2)

[a] Overlapped with other aromatic signals.

Table 3. ^{13}C NMR of 4- and 4,5-Substituted 2-(α-Benzotriazol-1-ylalkyl)furans 3 and 11 ($CDCl_3$), δ (ppm)

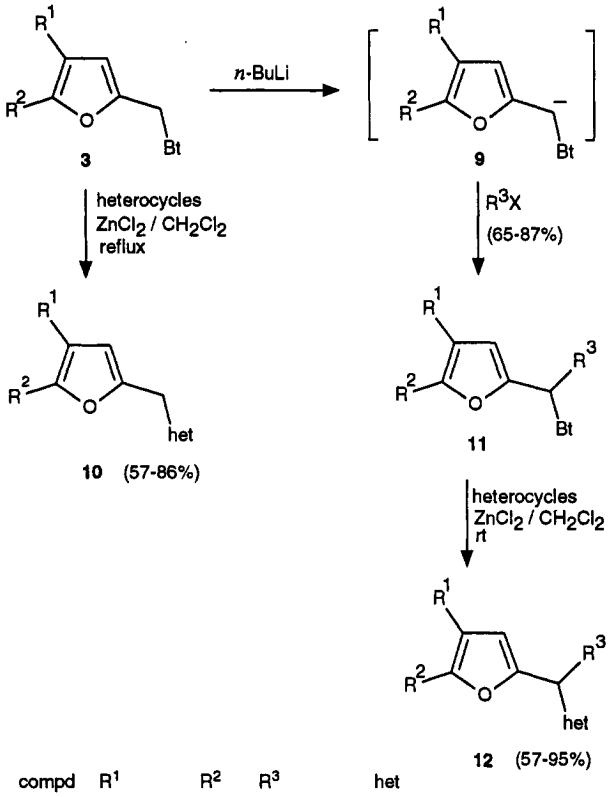
	Bt						furan							
compd	C-4	C-5	C-6	C-7	C_{3a}	C_{7a}	C-2	C-3	C-4	C-5	CH_2 or CH	R^1	R^2	R^3
3a	119.8	127.4	123.9	109.6	146.0	132.6	148.7	108.7	127.3	138.7	44.9	131.4, 128.7, 127.2, 125.6	–	–
3b	119.9	127.6	124.0	109.6	146.1	132.7	149.0	108.8	127.5	139.2	45.1	133.5, 132.5, 128.9, 128.5, 127.7, 127.6, 126.4, 125.8	–	–
3c	119.6	127.2	123.7	109.6	145.9	132.5	148.4	110.9	121.7	145.2	44.8	133.0, 128.3, 127.1, 126.3	12.8	–
3d	119.7	127.2	123.7	109.8	146.1	132.6	148.3	112.9	114.9	144.4	45.2	11.2	9.6	–
11a	119.7	127.1	123.6	109.6	145.8	132.3	151.5	107.8	126.8	138.2	58.7	135.8, 128.5, 128.3, 127.1	–	131.4, 128.4, 127.1, 127.0, 38.4
11b	120.0	127.3	123.8	110.3	146.2	132.4	152.0	108.5	127.2	138.5	64.2	133.5, 132.5, 129.0, 128.4, 127.7, 127.6, 126.3, 125.7	–	31.2, 20.2, 19.5
11c	120.0	127.1	123.7	110.3	146.4	132.1	149.0	109.6	121.6	148.0	57.7	133.4, 128.5, 127.3, 126.5	13.0	31.5, 28.2, 22.0, 13.7
11d	119.7	126.9	123.6	110.3	146.1	131.8	148.3	111.1	114.6	147.7	53.0	11.6	9.6	18.2

Table 4. Preparation of 4- and 4,5-Substituted 2-(α-Heterocycloalkyl)furans 10 and 12

entry[a]	reactant	heterocycle	product[b]	yield (%)	molecular formular	found (calcd) C	H	N
1	**3c**	2-methylfuran	**10a**	57	$C_{17}H_{16}O_2$	80.88 (80.92)	6.49 (6.40)	
2	**3c**	2-methylthiophene	**10b**	86	$C_{17}H_{16}OS$	75.99 (76.09)	6.01 (6.01)	
3	**3d**	2-methylthiophene	**10c**	67	$C_{12}H_{14}OS$	70.09 (69.88)	6.84 (6.85)	
4	**3d**	*N*-methylindole	**10d**	63	$C_{16}H_{17}NO$	80.61 (80.29)	7.52 (7.16)	5.81 (5.86)
5	**11a**	2-methylthiophene	**12a**	61	$C_{23}H_{20}OS$	80.09 (80.20)	5.84 (5.86)	
6	**11a**	*N*-methylindole	**12b**	57	$C_{27}H_{23}NO$	85.99 (85.90)	6.12 (6.15)	3.54 (3.71)
7	**11b**	2-methylfuran	**12c**	68	$C_{23}H_{22}O$	83.34 (83.60)	6.81 (6.72)	
8	**11c**	2-methylfuran	**12d**	95	$C_{21}H_{24}O_2$	81.72 (81.77)	7.97 (7.85)	
9	**11d**	*N*-methylindole	**12e**	79	$C_{17}H_{19}NO$	80.93 (80.59)	7.67 (7.56)	5.45 (5.53)

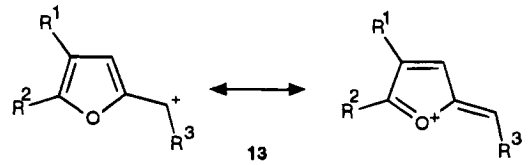
[a] Reactions 1–4 were carried out under reflux in CH_2Cl_2, and reactions 5–9 were carried out at room temperature. [b] All products were oily and separated by column chromatography (CH_2Cl_2/hexane 1:4).

Scheme 3



compd	R^1	R^2	R^3	het
10a	Ph	CH_3	-	5-methylfuran-2-yl
10b	Ph	CH_3	-	5-methylthiophen-2-yl
10c	CH_3	CH_3	-	5-methylthiophen-2-yl
10d	CH_3	CH_3	-	*N*-methylindol-3-yl
11a	Ph	H	$PhCH_2$	-
11b	2-naphthyl	H	*i*-Pr	-
11c	Ph	CH_3	*n*-Bu	-
11d	CH_3	CH_3	CH_3	-
12a	Ph	H	$PhCH_2$	5-methylthiophen-2-yl
12b	Ph	H	$PhCH_2$	*N*-methylindol-3-yl
12c	2-naphthyl	H	*i*-Pr	5-methylfuran-2-yl
12d	Ph	CH_3	*n*-Bu	5-methylfuran-2-yl
12e	CH_3	CH_3	CH_3	*N*-methylindol-3-yl

Scheme 4



R^2 groups are essential for the reactivity of compounds **3** and **11**. Accordingly, the reactions of alkylated products **11** were carried out at room temperature. However, the reactions of compounds **3c,d** must be carried out under reflux in CH_2Cl_2. Compounds **3a,b** ($R^3 = R^2 = H$) did not undergo the reaction under reflux either in CH_2Cl_2 or in $CHCl_3$ and were recovered unchanged after such treatment. The mixture of **3a** and 2-methylthiophene, when heated under reflux in $CHCl_2CHCl_2$ in the presence of $ZnCl_2$, gave a complicated mixture.

As shown in Scheme 3, the reactions took place at the 5-positions of 2-methylfuran and 2-methylthiophene and at the 3-position of *N*-methylindole. The attached proton test (APT) spectra clearly showed quaternary carbon signals (δ = 149.6–153.7) indicating C-2 of the 5-methylfuran-2-yl groups of compounds **10a**, **12c**, and **12d**. Similarly, the C-2 signals of the 5-methylthiophen-2-yl groups of products **10b**, **10c**, and **12a** appeared at δ = 138.5–142.5. The ^1H singlets at δ = 6.65–6.87, which are characteristic resonances of the α-H in 3-substituted indoles, and the quaternary carbon signals at δ = 111.3–117.7 in the ^1H and APT NMR spectra of compounds **10d**, **12b**, and **12e**, are strong evidence for the 3-substituted *N*-methylindole. Interestingly, the ^1H NMR spectra of compounds **12a** and **12b** clearly showed two sets of doublet of doublets between δ = 3.22 and 3.47 ppm with large couplings (J = 13.4–13.5 and 7.1–8.1 Hz) indicating the CH_2 diastereotopic signals are attached to chiral centers. Detailed assignments of the NMR spectra are listed in Tables 5 and 6.

All products are novel and are characterized by ^1H, ^{13}C, and APT NMR spectra and combustion analyses (Tables 4, 5 and 6). Excess 2-methylfuran or 2-methylthiophene was used to minimize polymerization of compounds **3** and **11** and was removed by distillation at the completion of the reactions. $ZnCl_2$ was removed by washing with 2 N HCl solution and benzotriazole was extracted into the aqueous phase with 5% NaOH. The products were readily isolated by short column chromatography. Upon heating in air, products **10** and **12** were polymerized and their ^1H NMR spectra showed broad signals.

Conclusion

We have described a simple one-pot synthesis of 2,4- and 2,4,5-substituted furans **3** from the readily and commercially available starting materials 1-propargylbenzotriazole (**1**) and α-bromo ketones. The benzotriazolyl group assisted the base-catalyzed isomerization of the intermediate alkynyloxiranes **2**, and therefore, 18-crown-6 was not required. In addition, since the benzotriazolyl group acts as either an electron-withdrawing substituent or as a good leaving group, the benzotriazol-1-ylmethyl group of compounds **3** is readily elaborated by alkylation and substitution. A variety of 4- and 4,5-substituted 2-[(α-heterocyclo)alkyl]furans **10** and **12** were prepared in this manner.

Table 5. ^{1}H NMR Data of 4- and 4,5-Substituted 2-(α-Heterocycloalkyl)furans 10 and 12 ($CDCl_3$), δ (ppm), *J* (Hz)

compd	H-3 (furan)	heterocycle	CH or CH_2	R^1	R^2	R^3
10a	6.12 (s)	5.92 (1H, d, 2.7), 5.79–5.81 (1H, m), 2.32 (3H, s)	3.84 (2H, s)	7.25–7.30 (4H, m), 7.12–7.17 (1H, m)	2.18 (3H, s)	–
10b	6.12 (s)	6.60 (1H, d, 3.4), 6.12–6.50 (1H, m), 2.34 (3H, s)	3.97 (2H, s)	7.25–7.29 (4H, m), 7.12–7.16 (1H, m)	2.32 (3H, s)	–
10c	5.83 (s)	6.63 (1H, d, 3.3), 6.54–6.55 (1H, m), 2.41 (3H, s)	3.98 (2H, s)	2.45 (3H, s)	1.88 (3H, s)	–
10d	5.76 (s)	7.57 (1H, d, 7.8), 7.17–7.17 (2H, m), 7.05–7.11 (1H, m), 6.87 (1H, s), 3.69 (3H, s)	4.00 (2H, s)	2.15 (3H, s)	1.85 (3H, s)	–
12a	6.35 (s)	6.57 (1H, d, 4.0), 6.49–6.51 (1H, m), 2.39 (3H, s)	4.43 (1H, t, 7.8)	7.11–7.33 (5H, m)[a]	7.61 (1H, s)	7.40 (2H, d, 7.3), 7.11–7.33 (1H, m),[a] 7.05 (2H, d, 7.0), 3.44 (1H, dd, 13.5 and 7.8), 3.22 (1H, dd, 13.5 and 7.8)
12b	6.32 (s)	7.58 (1H, d, 8.6), 7.03–7.30 (3H, m),[a] 6.82 (1H, s), 3.62 (3H, s)	4.52 (1H, t, 7.6)	7.03–7.30 (5H, m)[a]	7.60 (1H, s)	7.38 (2H, d, 8.3), 7.03–7.30 (3H, m),[a] 3.47 (1H, dd, 13.4 and 8.1), 3.37 (1H, dd, 13.4 and 7.1)
12c	6.56 (s)	7.58 (1H, d, 3.0), 5.88–5.90 (1H, m), 2.27 (3H, s)	3.79 (1H, d, 8.1)	7.87 (1H, s), 7.76–7.79 (3H, m), 7.57 (1H, d, 8.5), 7.36–7.46 (2H, m)	7.72 (1H, s)	2.36–2.43 (1H, m), 0.95 (6H, d, 6.8)
12d	6.18 (s)	5.97 (1H, d, 2.9), 5.86–5.87 (1H, m), 2.40 (3H, s)	3.94 (1H, t, 7.6)	7.31–7.38 (4H, m), 7.17–7.23 (1H, m)	2.25 (3H, s)	1.94–2.02 (2H, m), 1.29–1.33 (4H, m), 0.89 (3H, t, 6.7)
12e	5.65 (s)	7.45 (1H, d, 7.9), 7.01–7.09 (2H, m), 6.89–6.95 (1H, m), 6.65 (1H, s), 3.45 (3H, s)	4.21 (1H, q, 7.2)	2.01 (3H, s)	1.74 (3H, s)	1.53 (3H, d, 7.2)

[a] Overlapped signals.

Table 6. ^{13}C NMR Data of 4- and 4,5-Substituted 2-(α-Heterocycloalkyl)furans 10 and 12 ($CDCl_3$), δ (ppm)

	furan								
compd	C-2	C-3	C-4	C-5	heterocycle	CH or CH_2	R^1	R^2	R^3
10a	151.0	107.7	121.5	149.5	149.6, 146.5, 107.1, 106.1, 13.0	27.4	134.3, 128.4, 127.3, 126.1	13.5	–
10b	151.5	107.6	121.4	146.5	138.5, 138.0, 125.3, 124.7, 15.3	28.9	134.3, 128.4, 127.3, 126.1	13.0	–
10c	150.6	109.2	114.4	146.1	138.6, 138.3, 125.0, 124.7, 15.3	28.9	11.3	9.9	–
10d	151.8	108.7	114.3	145.5	137.0, 127.7, 127.0, 121.5, 119.2, 118.7, 111.3, 109.1, 32.5	24.2	11.3	9.9	–
12a	157.4	105.3	126.9	137.1	142.5, 139.1, 126.2, 124.5, 15.3	42.8	138.3, 128.9, 128.6, 125.6	–	132.5, 128.1, 126.8, 124.6, 42.0
12b	158.4	105.1	126.8	136.8	137.1, 126.8, 126.0, 121.5, 119.3, 118.9, 115.0, 109.3, 38.9	32.6	140.1, 128.9, 128.6, 128.1	–	132.7, 128.2, 126.6, 125.6, 40.7
12c	156.5	107.1	126.8	137.3	152.6, 150.7, 106.0, 105.5, 13.6	46.4	133.7, 132.4, 130.1, 128.3, 127.7, 127.6, 126.2, 125.5, 124.3, 123.7		31.8, 20.7
12d	153.8	106.8	121.2	150.6	153.7, 146.1, 106.2, 105.9, 13.1	38.9	134.4, 128.4, 127.3, 126.0	13.6	32.7, 29.6, 22.5, 14.0
12e	156.3	107.5	114.0	145.3	137.1, 126.9, 125.7, 121.3, 119.5, 118.5, 117.7, 109.1, 30.6	32.3	11.3	9.9	20.3

Experimental Section

Melting points were determined on a bristoline hot-stage microscope and are uncorrected. NMR spectra were taken in $CDCl_3$ with TMS as an internal standard for ^1H (300 MHz) or $CDCl_3$ as an internal standard for ^{13}C (75 MHz). Assignments for ^{13}C NMR spectra in necessary cases were confirmed by APT experiments. Elemental analyses (C, H, N) were carried out within the department. Column chromatography was conducted over silica gel (230–400 mesh). All α-bromo ketones and $ZnCl_2$ were used as purchased. 1-Propargylbenzotriazole (**1**) was prepared by the previously reported method.[11]

6-(Benzotriazol-1-yl)-2,3-epoxy-3-methyl-4-hexyne (2d). To a stirred solution of 1-propargylbenzotriazole (**1**) (1.57 g, 10 mmol) in THF (30 mL) at −78 °C was added a solution of *n*-BuLi (5.5 mL, 2.0 M in cyclohexane, 11 mmol). The mixture was stirred at this temperature for 1 h and 3-bromo-2-butanone (1.66 g, 11 mmol) in THF (5 mL) was added slowly. After stirring at −78 °C for 4 h, ether (100 mL) was added and the reaction mixture was washed with saturated NH_4Cl solution (3 × 100 mL) and dried ($MgSO_4$). Evaporation of the solvent gave a crude product which was purified by column chromatography using EtOAc/hexane (1:4) as the eluent to afford pure **2d** (1.82 g, 80%) as a white solid: mp 83–84 °C; ^1H NMR δ 8.05 (d, J = 8.4 Hz, 1 H, Bt), 7.69 (d, J = 8.3 Hz, 1 H, Bt), 7.50–7.55 (m, 1 H, Bt), 7.36–7.42 (m, 1 H, Bt), 5.48 (s, 2 H, CH_2), 3.21 (q, J = 5.5 Hz, 1 H, CH), 1.45 (s, 3 H, CH_3), 1.27 (d, J = 5.5 Hz, 3 H, CH_3); ^{13}C NMR δ 145.9 (Bt), 132.2 (Bt), 127.4 (Bt), 123.8 (Bt), 119.7 (Bt), 109.5 (Bt), 87.1 (C≡*C*), 73.1 (CH_2*C*≡C), 60.0 (CH), 50.1 (O*C*CH_3), 37.9 (CH_2), 17.5 (CH_3), 13.1 (CH_3). Anal. Calcd for $C_{13}H_{13}N_3O$: C, 68.69; H, 5.77; N, 18.50. Found: C, 68.74; H, 5.77; N, 18.49.

Preparation of 4- and 4,5-Substituted 2-(α-Benzotriazol-1-ylmethyl)furans (3a-d). General Procedure. A solution of *n*-BuLi (10.5 mL, 2.0 M in cyclohexane, 21 mmol) was added dropwise with stirring to a solution of 1-propargylbenzotriazole (**1**) (3.14 g, 20 mmol) in THF (100 mL) at −78 °C. The mixture was stirred at this temperature for 1 h, and α-bromo ketone (21 mmol) in THF (10 mL) was added slowly. The mixture was stirred for 4 h, and $KOBu^t$ (2.24 g, 20 mmol) in $HOBu^t$ (20 mL) was added. The reaction solution was allowed to warm to room temperature and then heated at 50 °C overnight. H_2O (100 mL) and EtOAc (100 mL) were added. The organic phase was washed with saturated NH_4Cl solution (3 × 100 mL) and dried ($MgSO_4$). The solvent was removed under reduced pressure to give an oil which was subjected to either recrystallization or column chromatography to afford the product **3** (Table 1).

2-(Benzotriazol-1-ylmethylene)-4-phenyl-5-methyl-2,5-dihydrofuran (8c). To a stirred solution of 1-propargylbenzotriazole (**1**) in THF (30 mL) at −78 °C was added a solution of *n*-BuLi (5.5 mL, 2.0 M in cyclohexane, 11 mmol). After 1 h, 2-bromopropiophenone (2.60 g, 90%, 11 mmol) in THF (5 mL) was added and the reaction mixture was stirred for 4 h. $KOBu^t$ (1.12 g, 10 mmol) in $HOBu^t$ (10 mL) was added at −78 °C, and the reaction solution was allowed to warm to room temperature overnight. The reaction mixture was quenched with saturated NH_4Cl solution (100 mL), extracted with EtOAc, washed with saturated NH_4Cl solution (3 × 100 mL), and dried ($MgSO_4$). Removal of the solvent under reduced pressure gave an oil which was subjected to column chromatography to afford pure **8c** (1.50 g, 52%) as a yellow oil: ^1H NMR δ 8.05 (d, J = 8.4 Hz, 1 H, Bt), 7.67 (d, J = 8.3 Hz, 1 H, Bt), 7.32–7.50 (m, 7 H, Bt and Ph overlapped), 6.64 (s, 1 H, C=CH), 6.58 (s, 1 H, C=CH), 5.82 (q, J = 6.5 Hz, 1 H, CH), 1.51 (d, J = 6.5 Hz, 3 H, CH_3); ^{13}C NMR δ 156.2 (*C*=CH), 151.5 (*C*=CH), 145.3 (Bt), 132.8 (Bt), 131.0 (Ph), 129.5 (Ph), 128.8 (2C, Ph), 126.8 (Bt), 126.4 (2C, Ph), 123.6 (Bt), 119.5 (Bt), 117.0 (C=*C*H), 111.7 (Bt), 93.9 (C=*C*H), 85.7 (CH), 20.4 (CH_3). Anal. Calcd for $C_{18}H_{15}N_3O$: C, 74.71; H, 5.23; N, 14.53. Found: C, 75.09; H, 5.32; N, 14.40.

Alkylation of 4- and 4,5-Substituted 2-(α-Benzotriazol-1-ylmethyl)furans (3). General Procedure. To a solution of compound **3** (5 mmol) in THF (50 mL) was added a solution of *n*-BuLi (2.75 mL, 2.0 M in cyclohexane, 5.5 mmol) dropwise with stirring at −78 °C. The mixture was stirred for 1 h, and alkyl halide (5.5 mmol) was added. The mixture was stirred at −78 °C for 5 h and was then allowed to warm to room temperature. H_2O (100 mL) and Et_2O (100 mL) were added, and the organic phase was washed with NaCl solution (3 × 100 mL) and dried ($MgSO_4$). Et_2O was evaporated under reduced pressure to give an oil which was purified by column chromatography to yield the product **11** (Table 1).

Formation of 4- and 4,5-Substituted 2-(α-Heterocycloalkyl)furans (10, 12). A mixture of 4- or 4,5-substituted 2-(α-benzotriazol-1-ylalkyl)furan **3** or **11** (2 mmol), $ZnCl_2$ (2 mmol), and heterocycle (20 mmol and for 2-methylfuran and 2-methylthiophene and 2 mmol for *N*-methylindole) in CH_2Cl_2 (50 mL) was stirred at room temperature (for **3c** and **3d** under reflux) under nitrogen overnight. The reaction was washed with HCl solution (2 N, 50 mL) and NaOH solution (5%, 3 × 50 mL) and dried ($MgSO_4$). CH_2Cl_2 was removed under reduced pressure to give a residue. The product **10** or **12** was separated from the residue by column chromatography (Table 4).