A Radical Version of the Bromo- and the Iodocyclization of Bis(homoallylic) Alcohols — The Synthesis of Halogenated Tetrahydrofurans by Stereoselective Alkoxyl Radical Ring Closures

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Dedicated to Prof. Dr. Manfred Christl on the occasion of his 62nd birthday

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A new synthesis of bromo- and iodomethyl-substituted tetrahydrofurans has been devised. The sequence starts with the conversion of aryl-functionalized bis(homoallylic) alcohols **1** into *N*-alkenoxythiazole-2(3*H*)-thiones **6** or pyridine-2(1*H*)-thiones **7**. When photolyzed in the presence of appropriate trapping reagents, thiones **6** and **7** efficiently liberated substituted 4-penten-1-oxyl radicals **2**, which underwent synthetically useful 5-*exo*-trig cyclizations. Cyclized radicals **3** were trapped with $BrCCl_3$ or an adequate iodine atom donor (either *n*-C_4F_9I or diethyl 2-iodo-2-methyl malonate) to provide halocyclization products **4** or **5**. This strategy has been applied for the synthesis of 3-, 4-, or 5-phenyl-substituted 2-(1-bromo-1-methylethyl)tetrahydrofurans **4a–c** (75–90%, 36–96% *de*), which were not attainable as major products from polar, for example NBS-mediated, bromocyclizations. Aryl-substituted 2-iodomethyl tetrahydrofurans **5** (46–80%) were prepared in a similar way starting from *N*-alkenoxypyridine-2(1*H*)-thiones **7** and a suitable iodine atom donor. Diastereomerically pure iodides *cis*-**5** and *trans*-**5** served as starting materials for a stereochemical analysis of disubstituted tetrahydrofurans by NMR spectroscopy and X-ray diffraction analysis. The results of this investigation clarified that all new alkoxyl radical cyclizations followed in terms of regio- and diastereoselectivity the general guidelines which had been established for this type of ring-closure reaction.

Introduction

Halogenated tetrahydrofurans,[1] in particular those with an exocyclic chloro, bromo or iodo functionality located in the β-position to the ring oxygen atom, have become attractive targets in organic synthesis.[2,3] Their significance has been emphasized in the last decades due to the discovery that β-brominated tetrahydrofurans occur widely as secondary metabolites in the marine environment.[4] If purified and subjected to screening assays, several of these compounds exhibit marked cytotoxic properties and therefore have the potential to contribute to future developments in pharmacology.[5]

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The most versatile and reliable procedure for the synthesis of β-halogenated tetrahydrofurans generally starts from bis(homoallylic) alcohols **1**, which, upon treatment with compounds such as molecular bromine,[6–8] iodine,[6–8] organic trihalide salts,[9] *N*-bromosuccinimide (NBS),[10] *N*-iodosuccinimide (NIS),[11] or more specialized reagents such as 2,4,4,6-tetrabromocyclohexadienone[12] or 2,2-dibromomalodinitrile,[13] afford halocyclized products in generally useful yields. The role of the halogenating reagent has been associated with an electrophilic activation of the olefinic π-bond. Intramolecular C-O bond formation follows.[6,14] The regioselectivity of this step is governed by a combination of stereoelectronic and polar effects. The observed diastereoselectivity, i.e. the facial selectivity for addition of the oxygen nucleophile to the π-bond, originates in most instances from substrate control, unless the reaction is governed by thermodynamic effects.[6]

Recent developments in this field of research have, however, clarified that the synthesis of bromomethyl-substituted oxolanes starting from bis(homoallylic) alcohols such as **1** is also feasible if the heterocyclic core is constructed by an alkenoxyl cyclization **2** → **3** (Figure 1).[15] Since intermediates **2** exhibit electrophilic properties, this strategy corre-

sponds to an Umpolung of the polar bromocyclization and is therefore expected to provide selectivities (ring size, relative configuration, functional group compatibility), which are, in principle, not attainable in ionic transformations.[16,17] In view of these perspectives, we have performed a mechanistic study on the radical version of the halocyclization by addressing three major issues: (i) *N*-alkoxy-substituted thiazole-2(3*H*)-thiones **6** and pyridine-2(1*H*)-thiones **7**,[18−21] in combination with a larger set of reactive halogen atom donors, were assessed in regard of their utility to serve as reagents for the synthesis of halocyclization products **4** and **5**; (ii) a stereochemical analysis of alkoxyl radical cyclization products was accomplished by combining results from NMR *and* X-ray diffraction experiments; (iii) selectivities from the radical version of the bromocyclization were compared to those from NBS-mediated transformations, in order to characterize fields of application for both methods.

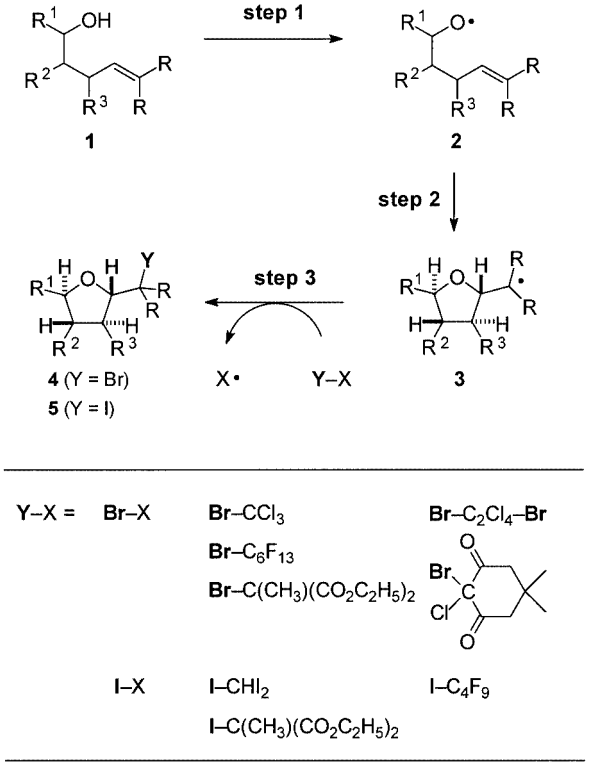


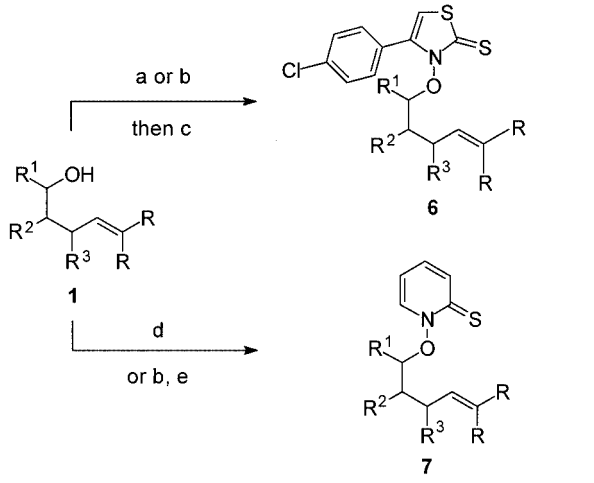
Figure 1. Key steps for the design of a radical version of the halocyclization. Step 1: generation of alkoxyl radicals **2**; step 2: stereo- and regioselective ring-closure reaction; step 3: halogen atom trapping; R^1-R^3 = aryl or H; R = H or CH_3

Results

1. Preparation of Alkoxyl Radical Precursors

N-Alkoxy-4-(*p*-chlorophenyl)thiazole-2(3*H*)-thiones (**6**) were prepared from *N*-hydroxy-4-(*p*-chlorophenyl)thiazole-2(3*H*)-thione tetraethylammonium salt (not shown in Table 1)[22,23] and suitable alkylating reagents. 6-Chloro-2-methyl-6-phenyl-2-hexene was synthesized from 5-methyl-1-phenyl-4-hexen-1-ol (**1a**)[21] and a combination of PPh_3 and CCl_4 (47%).[24] Treatment of this chloride with a 2.6-fold excess of 4-(*p*-chlorophenyl)-*N*-hydroxythiazole-2(3*H*)-thione tetraethylammonium salt provided, upon work up of the reaction mixture, 57% of 4-(*p*-chlorophenyl)-*N*-(5-methyl-1-phenyl-4-hexen-1-oxy)thiazole-2(3*H*)-thione (**6a**, entry 1, Table 1) and 1,2-bis[4-(*p*-chlorophenyl)-2-thiazyl]disulfane (23%, not shown in Table 1).[23] 2-, and 3-Phenyl-substituted bis(homoallylic) alcohols **1b**,[25] **1c**, and **1f**[26] were esterified with *p*-toluenesulfonyl chloride in the presence of 1,4-diazabicyclo[2.2.2]octane (DABCO) to furnish the corresponding tosylates (96% from **1b**, 88% from **1c**, and 83% from **1f**, not shown in Table 1).[20,27] Treatment of these alkylating reagents with 4-(*p*-chlorophenyl)-*N*-hydroxythiazole-2(3*H*)-thione tetraethylammonium salt in anhydrous DMF afforded alkoxyl radical precursors **6b**, **6c**, and **6f**[23] in 45−53% yield (entries 2, 3, 7, Table 1). *N*-Alkoxypyridine-2(1*H*)-thiones **7a**,[21] **7d**, and **7e** were prepared by adding PPh_3 to a solution of 2,2′-dithiopyridine-1,1′-dioxide[28] and a benzylic alkenol (i.e. **1a**, **1d**, or **1e**) in CH_2Cl_2 (entries 4−6, Table 1).[29] Phase-transfer-catalyzed

Table 1. Syntheses of *N*-alkoxythiazole-2(3*H*)-thiones **6** and *N*-alkoxypyridine-2(1*H*)-thiones **7** from bis(homoallylic) alcohols **1**[a]



Entry	6, 7	R^1	R^2	R^3	R	Method[a]	Yield [%]
1	**6a**	C_6H_5	H	H	CH_3	a,c	57[b]
2	**6b**	H	C_6H_5	H	CH_3	b,c	48
3	**6c**	H	H	C_6H_5	CH_3	b,c	53
4	**7a**	C_6H_5	H	H	CH_3	d	55
5	**7d**	*p*-$C_6H_5C_6H_4$	H	H	H	d	44
6	**7e**	2-$C_{10}H_7$	H	H	H	d	52
7	**6f**	H	C_6H_5	H	H	b,c	45
8	**7f**	H	C_6H_5	H	H	b,e	42
9	**7g**	H	2-$C_{10}H_7$	H	H	b,e	40
10	**7h**	H	H	C_6H_5	H	b,e	39

[a] Reagents and conditions: (a) CCl_4, PPh_3; (b) TsCl, DABCO, CH_2Cl_2; (c) 4-(*p*-chlorophenyl)-*N*-hydroxythiazole-2(3*H*)-thione tetraethylammonium salt, DMF; (d) 2,2′-dithiopyridine-1,1′-dioxide, PPh_3, CH_2Cl_2; (e) *N*-hydroxypyridine-2(1*H*)-thione, NBu_4HSO_4, K_2CO_3, CH_3CN. [b] In addition: 23% of 1,2-bis[4-(*p*-chlorophenyl)-2-thiazyl]disulfane.[23]

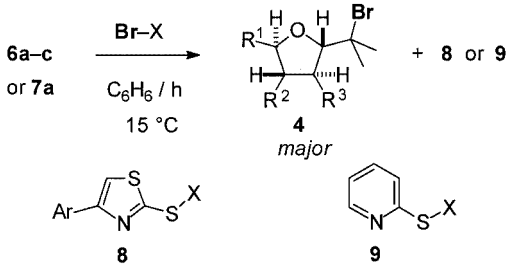
selective *O*-alkylations of *N*-hydroxypyridine-2(1*H*)-thione (not shown in Table 1) with *p*-toluenesulfonic acid esters of bis(homoallylic) alcohols **1f**, **1g**, and **1h** in the presence of K_2CO_3 and NBu_4HSO_4 [20,30] afforded 2-phenyl-, 2-(2-naphthyl)-, or 3-phenyl-substituted *N*-(4-penten-1-oxy)pyridinethiones **7f**, **7g**, and **7h** in 39−42% yield (entries 8−10, Table 1).

2. Formation of Bromo- and Iodocyclization Products from *N*-Alkoxythiazolethiones 6 and Pyridinethiones 7

Optimized conditions for the synthesis of bromocyclization products **4** were established in photochemically initiated reactions between *N*-(5-methyl-1-phenyl-4-hexen-1-oxy)thiazolethione (**6a**) or pyridinethione **7a** and selected bromine atom donors (Table 2). Other parameters, such as the solvent (C_6H_6), the reaction temperature (T = 15 °C), and the method for initiating the alkoxyl radical reaction starting either from **6** (250 W visible light discharge lamp) or from **7** (150 W light bulb) were kept constant, since they had been optimized in previous studies.[23,31] Photolysis of a solution of thiazolethione **6a** (c_o = 0.18 M) and $BrCCl_3$ (c_o = 0.8 M) in C_6H_6 for 20 min provided, upon work up, 87% of 2-(1-bromo-1-methylethyl)-5-phenyltetrahydrofuran (**4a**; *cis*:*trans* = 28:72, for stereochemical analysis see section 3) and 71% of 4-(*p*-chlorophenyl)-2-(trichloromethylsulfanyl)thiazole (**8**, X = CCl_3; Table 2, entry 1). In addition, 8% of 5-methyl-1-phenyl-4-hexen-1-one[33] and alkenol **1a** were formed in a 3:1 ratio (GC). Replacement of $BrCCl_3$ by alternative bromine atom donors led to a gradual decrease in the yield of bromocyclization product **4a** to 32% (1-bromo-1-chlorodimedone[34]), 26% (diethyl 2-bromo-2-methylmalonate[35]), 25% ($Br_2C_2Cl_4$), and 9% (*n*-BrC_6F_{13}, Table 2, entries 2−5). In view of these findings $BrCCl_3$ was applied in photochemically initiated reactions starting from 2- or 3-phenyl-substituted *N*-(5-methyl-4-hexene-1-oxy)thiazolethiones **6b** or **6c**, which provided 75% of 2,4-substituted oxolane **4b** (*cis*:*trans* = 68:32) and 90% of diastereomerically pure tetrahydrofuran *trans*-**4c**[15] (Table 2, entries 6 and 7). Photolysis of *N*-(5-methyl-1-phenyl-4-hexen-1-oxy)pyridinethione (**7a**) in the presence of $BrCCl_3$ afforded 88% (GC) of brominated tetrahydrofuran **4a** (*cis*:*trans* = 28:72, Table 2, entry 8). Application of diethyl 2-bromo-2-methyl malonate (59% of **4a**, GC), or *n*-BrC_6F_{13} (32% of **4a**, GC) as trapping reagents was again associated with a decrease in yield of target product **4a** (Table 2, entries 9 and 10).

Parameters for the synthesis of iodomethyl-substituted tetrahydrofurans **5** were elaborated starting from *N*-(2-phenyl-4-penten-1-oxy)-substituted thiones **6f** and **7f**.[36] Optimized conditions were found by photolyzing a solution of thione **7f** and diethyl 2-iodo-2-methylmalonate (c_0 = 0.1 M) in C_6H_6 for 3 min at 20 °C (visible light, Table 3, entry 1). Purification of this reaction mixture by column chromatography provided 72% of 2-iodomethyl-4-phenyltetrahydrofuran (**5f**; *cis*:*trans* = 87:13, for stereochemical analysis refer to section 3) and 74% of diethyl 2-methyl-2-(pyridine-2-sulfanyl)malonate [**9**, X = $C(CH_3)(CO_2C_2H_5)_2$]. Neither a change in solvent to CH_2Cl_2 (26% of **5f**, GC), nor a modification of the iodine atom donor to *n*-C_4F_9I (reaction in

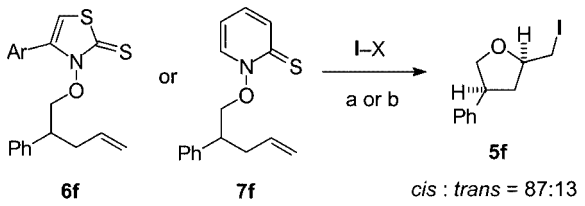
Table 2. Stereoselective synthesis of bromocyclization products **4a**−**c** from alkoxyl radical precursors **6a**−**c** and **7a**[a]



Entry	**6**, **7**	**Br**−X	**4**	R^1	R^2	R^3	**4** [%] (*cis*:*trans*)	**8**, **9** [%]
1	**6a**	**Br**CCl_3	**4a**	C_6H_5	H	H	87[b] (28:72)	71 (**8**)[c]
2	**6a**	**Br**$C_8H_{10}ClO_2$ [d]	**4a**	C_6H_5	H	H	32 (28:72)	−[e]
3	**6a**	**Br**$C_8H_{13}O_4$ [f]	**4a**	C_6H_5	H	H	26[g] (30:70)	−[e]
4	**6a**	**Br**$_2C_2Cl_4$	**4a**	C_6H_5	H	H	25 (28:72)	−[e]
5	**6a**	**Br**C_6F_{13}	**4a**	C_6H_5	H	H	9 (30:70)	−[e]
6	**6b**	**Br**CCl_3	**4b**	H	C_6H_5	H	75 (68:32)	67 (**8**)[c]
7	**6c**	**Br**CCl_3	**4c**	H	H	C_6H_5	90 (<2:>98[h])	70 (**8**)[c]
8	**7a**	**Br**CCl_3	**4a**	C_6H_5	H	H	88 (28:72)	−[e]
9	**7a**	**Br**$C_8H_{13}O_4$ [f]	**4a**	C_6H_5	H	H	59 (29:71)	−[e]
10	**7a**	**Br**C_6F_{13}	**4a**	C_6H_5	H	H	32 (28:72)	−[e]

[a] Ar = *p*-ClC_6H_4. Except for entries 1, 6, and 7, all yields were determined by GC using *n*-$C_{14}H_{30}$ as internal standard. [b] Additional products: 6% of 5-methyl-1-phenyl-4-hexen-1-one,[33] 2% of 5-methyl-1-phenyl-4-hexen-1-ol (**1a**). [c] **8**: X = CCl_3. [d] 2-Bromo-2-chlorodimedone.[34] [e] Not determined. [f] Diethyl 2-bromo-2-methylmalonate.[35] [g] Additional products: 15% of 5-methyl-1-phenyl-4-hexen-1-one,[33] 7% of 5-methyl-1-phenyl-4-hexen-1-ol (**1a**). [h] *cis*-**4c** was not detected (^{1}H NMR spectroscopy).

Table 3. Synthesis of 2-(iodomethyl)-4-phenyltetrahydrofuran (**5f**) from thiones **6f** and **7f**[a]



Entry	6f,7f	I−X	Equiv.[b]	Solvent	Method[a]	Yield of 5f [%]
1	**7f**	$IC_8H_{13}O_4$ [c]	3.7	C_6H_6	a	72[d]
2	**7f**	$IC_8H_{13}O_4$ [c]	1.5	CH_2Cl_2	a	26
3	**7f**	IC_4F_9	2.5	C_6H_6	a	42
4	**7f**	$ICHI_2$	1.2	CH_2Cl_2	a	46
5	**7f**	$ICHI_2$	1.3	C_6H_6	a	55
6	**6f**	IC_4F_9	2.5	C_6H_6	a	38
7	**6f**	$ICHI_2$	1.2	CH_2Cl_2	a	32
8	**6f**	$ICHI_2$	2.5	C_6H_6	a	18
9	**6f**	IC_4F_9	2.5	C_6H_6	b	72

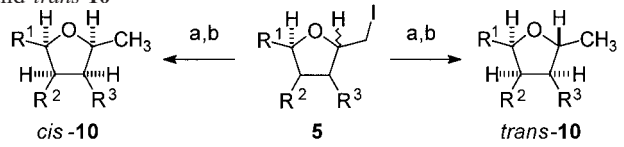
[a] Ar = *p*-ClC_6H_4. For all reactions: *cis*-**5f**:*trans*-**5f** = 87:13; reagents and conditions: (a) hν, 15 °C; (b) BEt_3/O_2, 20 °C; except for entry 1, all yields were determined by GC using *n*-$C_{14}H_{30}$ as internal standard. [b] Equiv. of **I**-X. [c] Diethyl 2-iodo-2-methylmalonate.[35] [d] Preparative scale; in addition, 74% of diethyl 2-methyl-2-(pyridine-2-sulfanyl)malonate (**9**) [X = $C(CH_3)(CO_2C_2H_5)_2$, for structure refer to Table 2] was formed.

C_6H_6: 42% of **5f**) nor to CHI_3 (**5f**: 55% in C_6H_6, 46% in CH_2Cl_2, GC) led to comparable yields of target compound **5f** (Table 3, entries 2−5). If *N*-(2-phenyl-4-penten-1-oxy)thiazolethione (**6f**) [λ_{max} = 320 nm (EtOH)] was used as radical precursor, the synthesis of iodocyclization product **5f** was preferentially conducted in a Rayonet® chamber reactor (350 nm).[36] For example, 38% of iodide **5f** (*cis*:*trans* = 87:13, GC) was obtained by photolyzing a solution thiazolethione **6f** and *n*-C_4F_9I in C_6H_6 (Table 3, entry 6). Replacement of the iodine atom donor by CHI_3 provided 32% of product **5f**, if thione **6f** was irradiated in a solution of CH_2Cl_2, and 18% using C_6H_6 as solvent (Table 3, entries 7, 8). In a final experiment, a solution of thiazolethione **6f** and *n*-C_4F_9I in C_6H_6 was treated at 20 °C with BEt_3/O_2 [37] to afford target compound **5f** in 72% yield (GC, 20 °C, Table 3, entry 9).

According to the results from the optimization study (Table 3), diethyl 2-iodo-2-methylmalonate and *n*-C_4F_9I were applied as trapping reagent for the synthesis of iodomethyl-substituted tetrahydrofurans **5a**, **5d**, **5e**, **5g**, and **5h** on a preparative scale. The most effective of both transformations are reported in Table 4. The stereochemical analysis of iodocyclization products **5** is outlined in section 3.

Photolysis of *N*-(5-methyl-1-phenyl-4-hexen-1-oxy)pyridinethione **7a** in the presence of *n*-C_4F_9I afforded 80% of 2-(1-iodo-1-methylethyl)-5-phenyl tetrahydrofuran (**5a**; *cis*:*trans* = 29:71) as well as 84% of 2-perfluorobutylsulfanyl

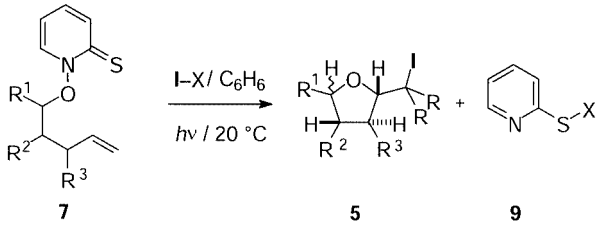
Table 5. Preparation of methyl-substituted tetrahydrofurans *cis*-**10** and *trans* **10**[a]



Entry	5, 10	R^1	R^2	R^3	*cis*-**10** [%]	*trans*-**10** [%]
1	**d**	*p*-$(C_6H_5)C_6H_4$	H	H	90	89
2	**e**	2-$C_{10}H_7$	H	H	63	91
3	**f**	H	C_6H_5	H	75	44
4	**g**	H	2-$C_{10}H_7$	H	86	77
5	**h**	H	H	C_6H_5	56	74

[a] Reagents and conditions: (a) column chromatography; diastereomeric purity of iodomethyl tetrahydrofurans **5** (*cis*:*trans*, GC): 99:1 for *cis*-**5d**, <0.5:>99.5 for *trans*-**5d**, >99.5:<0.5 for *cis*-**5e**, 2:98 for *trans*-**5e**, 97:3 for *cis*-**5f**, 3:97 for *trans*-**5f**, 99.5:0.5 for *cis*-**5g**, 0.5:99.5 for *trans*-**5g**, 96:4 for *cis*-**5h**, 2:98 for *trans*-**5h**; (b) LiH, $LiAlH_4$, THF, Δ.

Table 4. Preparation of iodomethyl-substituted tetrahydrofurans **5** from *N*-alkoxypyridinethiones **7**[a]



Entry	7	I−X	R^1	R^2	R^3	R	**5** [%] (*cis*:*trans*)	5	**9** [%]
1	**7a**	IC_4F_9	C_6H_5	H	H	CH_3	80 (29:71)	**5a**	84
2	**7d**	IC_4F_9	*p*-$C_6H_5C_6H_4$	H	H	H	40 (53:47)	**5d**	−[b]
3	**7e**	$IC_8H_{13}O_4$ [c]	2-$C_{10}H_7$	H	H	H	72 (50:50)	**5e**	73
4	**7g**	$IC_8H_{13}O_4$ [c]	H	2-$C_{10}H_7$	H	H	46 (87:13)	**5g**	−[b]
5	**7h**	$IC_8H_{13}O_4$ [c]	H	H	C_6H_5	H	72 (3:97)	**5h**	−[b]

[a] Isolated yields. [b] Not determined. [c] Diethyl 2-iodo-2-methylmalonate.[35]

pyridine (**9**, X = C_4F_9, Table 3, entry 1). 5-(*p*-Biphenylyl)-2-(iodomethyl)tetrahydrofuran (**5d**) was prepared from pyridinethione **7d** and *n*-C_4F_9I in 40% yield (*cis*:*trans* = 53:47, Table 4, entry 2). Photolysis of *N*-[1-(2-naphthyl)-4-pentenoxy]pyridinethione **7e** in the presence of diethyl 2-iodo-2-methylmalonate afforded 72% of 2-(iodomethyl)-5-(2-naphthyl)tetrahydrofuran (**5e**, *cis*:*trans* = 50:50) and 73% of diethyl 2-methyl-2-(pyridine-2-sulfanyl)malonate [**9**, X = $C(CH_3)(CO_2C_2H_5)_2$, Table 4, entry 3]. In the same manner, 2-(iodomethyl)-4-(2-naphthyl) tetrahydrofuran (**5g**; 46%, *cis*:*trans* = 87:13, Table 4, entry 4), and 2-(iodomethyl)-3-phenyltetrahydrofuran (**5h**; 72%, *cis*:*trans* = 3:97, Table 4, entry 5) were obtained from pyridinethiones **7g** and **7h** (Table 4).

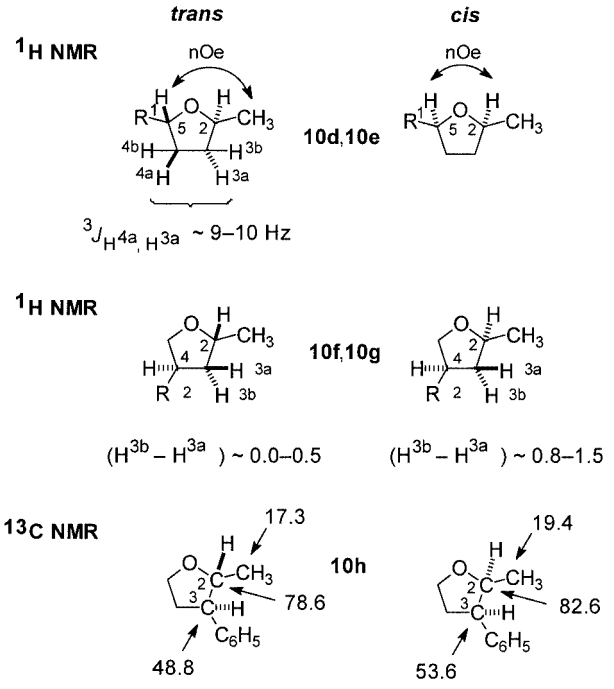
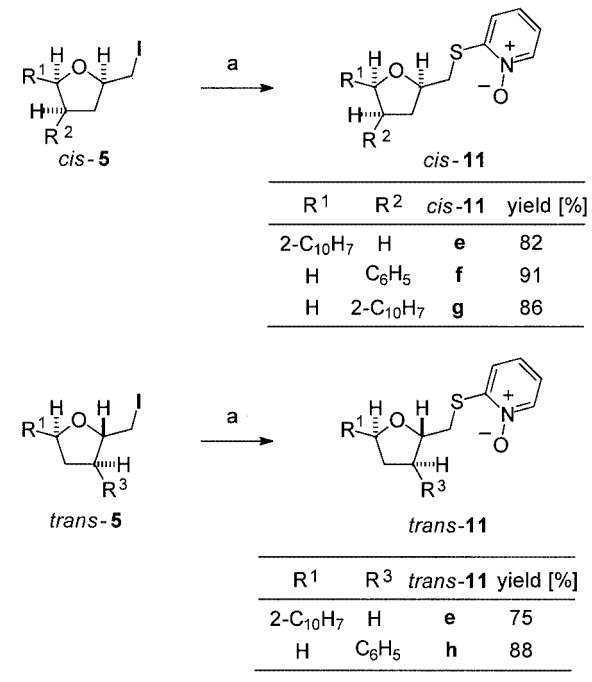


Figure 2. Characteristic spectroscopic information for a stereochemical analysis of disubstituted tetrahydrofurans **10** by NMR spectroscopy; R^1 = *p*-$(C_6H_5)C_6H_4$, 2-$C_{10}H_7$; R^2 = C_6H_5, 2-$C_{10}H_7$



R^1	R^2	*cis*-**11**	yield [%]
2-$C_{10}H_7$	H	**e**	82
H	C_6H_5	**f**	91
H	2-$C_{10}H_7$	**g**	86

R^1	R^3	*trans*-**11**	yield [%]
2-$C_{10}H_7$	H	**e**	75
H	C_6H_5	**h**	88

Scheme 1. Synthesis of 2-(alkylsulfanyl)pyridine *N*-oxides **11**; reagents and conditions: (a) *N*-hydroxypyridine-2(1*H*)-thione potassium salt, DMF, 20 °C

3. Stereochemical Analysis of Disubstituted Tetrahydrofurans

The relative configuration of the major bromocyclization products (Table 2) was determined by NMR spectroscopy

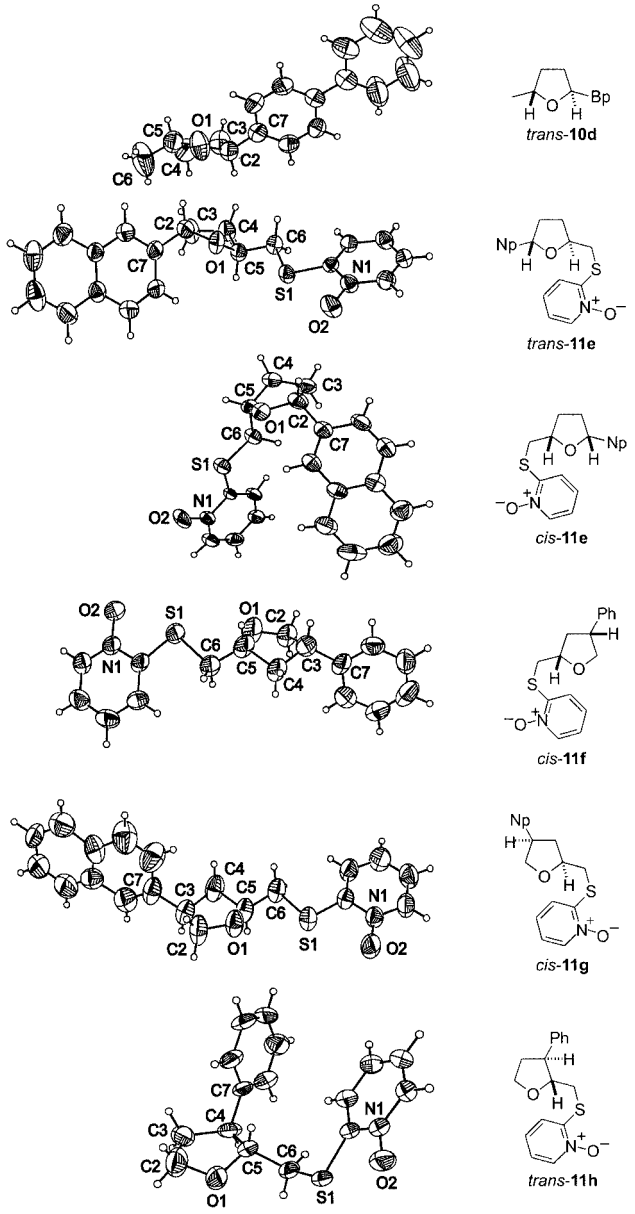


Figure 3. Structures of disubstituted tetrahydrofurans *trans*-**10d**, *trans*-**11e**, *cis*-**11e**, *cis*-**11f**, *cis*-**11g**, *trans*-**11h** in the solid state (anisotropic displacement parameters are drawn at the 50% level) showing labeling of selected non-H atoms; hydrogen atoms are depicted as small circles of an arbitrary radius; Bp = *p*-biphenylyl, Np = 2-naphthyl; see also ref. 1

(chemical shift values, NOE experiments). This information was compared to results from a concise stereochemical analysis on diastereomerically pure iodocyclization products *cis*-**5a**, *cis*-**5d**−**5h** and *trans*-**5a**, *trans*-**5d**−**h** (diastereomeric ratio: 99.5:0.5 to 96:4, GC, Table 5). The diastereomeric purity of tertiary iodides *cis*-**5a** and *trans*-**5a** was determined by ^{1}H NMR spectroscopy (> 96% *de* in both cases) since both compounds decompose at elevated temperatures. In view of this observation, only iodides *cis*-**5d**−**5h** and *trans*-**5d**−**5h** were converted into methyl-substituted tetrahydrofurans *cis*-**10d**−**h** (56−90%) and *trans*-**10d**−**h** (44−91%) using a mixture of LiH and $LiAlH_4$ in hot THF.

Disubstituted tetrahydrofurans **10** were investigated by one- and two-dimensional NMR spectroscopy (HMBC, HMQC, NOE, Figure 2). Significant NOEs were observed for protons which were located in relative 1,3-*cis*-arrangement at the tetrahydrofuran nucleus. This finding allowed a clear cut differentiation between 2,5-*cis*-configured tetrahydrofurans *cis*-**10d** and *cis*-**10e** from diastereomers *trans*-**10d** and *trans*-**10e**. 2,5-*trans*-Disubstituted heterocycles *trans*-**10d** and *trans*-**10e** were characterized by large vicinal coupling constants between one of the protons at C3 and one of those at C4 ($^3J_{H,H} \approx 9-10$ Hz, compare to $^2J_{H,H} \approx$ 12 Hz for 3-H and 4-H). The second pair of protons bound to C3 and C4 in *trans*-**10d** exhibited a significantly smaller $^3J_{H,H}$ value of 3.3 Hz.[38] No comparable values were located in the spectra of *cis*-**10d** and *cis*-**11e**. NOEs from the methyl substituents at C5 to the *cis*-arranged protons at C2 were typical for 2,5-*trans*-disubstituted tetrahydrofurans *trans*-**10d** and *trans*-**10e**. Similar NOEs were absent in 2,4-*trans*-disubstituted heterocycles *trans*-**10f** and *trans*-**10g**. In the latter case, however, comparatively large chemical shift differences between the two protons at C3 were indicative of a *cis* isomer ($\Delta\delta = \approx 0.8-1.5$ ppm). Smaller differences of between 0.5 and 0.0 ppm pointed to 2,4-*trans*-configured heterocycles *trans*-**10f**, and *trans*-**10g**. Assignment of relative configurations for 2,3-disubstituted tetrahydrofurans was possible by ^{13}C NMR spectroscopy, since the γ-effect of vicinal *cis*-arranged substituents in, for example, *cis*-**10h** led to a marked high-field shift of C2 (approx. 4 ppm) and C3 (approx. 5 ppm).[39]

The stereochemical information obtained from experiments in solution (NMR) was supplemented by results from X-ray diffraction analysis. *trans*-2-(*p*-Biphenylyl)-5-methyltetrahydrofuran (*trans*-**10d**) crystallized from EtOH as colorless needles which were suitable for this purpose. Attempts to grow appropriate crystals from selected iodides **5** were not successful. Therefore, the major diastereomers from each iodocyclization reaction, i.e. heterocycles *cis*-**5e**−**g**, *trans*-**5e**, and *trans*-**5h** (for **5a** vide supra), were treated with *N*-hydroxypyridine-2(1*H*)-thione potassium salt in anhydrous DMF to provide 2-(alkylsulfanyl)pyridine *N*-oxides **11** in 75−91% yield (Scheme 1).

Products **11** were recrystallized from appropriate solvent mixtures and analyzed by X-ray diffraction. The results of this study are shown in Figure 3 and Table 6. For the sake of clarity, the numbering of the ring carbon atoms in tetrahydrofurans **11** has been adapted to that of *trans*-**10d**.[1,40] The assignment of conformers (Table 6) follows the twist (T) and envelope (E) convention for saturated five-membered compounds.[41−44]

trans-2-(*p*-Biphenylyl)-5-methyltetrahydrofuran (*trans*-**10d**) crystallizes in the space group *C*2. The unit cell con-

Table 6. Selected distances [Å] and angles [°] of tetrahydrofurans *trans*-**10d** and **11** (X-ray crystallographic data)

Entry	Parameter[a]	*trans*-**10d**	*trans*-**11e**	*cis*-**11e**	*cis*-**11f**	*cis*-**11g**	*trans*-**11h**
1	conformer[a]	$_3T^4$	E_3	$_2T^3$	$^3T_4$	$^2T_3$	$^1T_2$
2	O1−C5	1.399(7)	1.420(8)	1.427(6)	1.43(1)	1.425(8)	1.424(4)
3	C5−C4	1.50(1)	1.515(9)	1.522(7)	1.52(1)	1.533(8)	1.522(5)
4	C4−C3	1.487(8)	1.52(1)	1.504(8)	1.53(1)	1.55(1)	1.539(6)
5	C3−C2	1.518(8)	1.52(1)	1.535(7)	1.52(1)	1.528(9)	1.448(7)
6	C2−O1	1.421(7)	1.438(8)	1.436(6)	1.40(1)	1.407(7)	1.389(5)
7	C2−O1−C5	110.9(5)	109.7(5)	109.4(4)	109.0(6)	108.8(4)	107.0(3)
8	O1−C5−C4	106.0(6)	104.9(6)	105.1(4)	105.4(7)	103.6(5)	104.9(3)
9	C5−C4−C3	102.9(5)	101.4(6)	102.5(4)	101.6(6)	100.9(5)	102.6(3)
10	C4−C3−C2	101.8(5)	102.6(6)	103.4(5)	98.1(7)	102.0(5)	105.1(6)
11	C3−C2−O1	104.8(4)	106.3(6)	106.8(4)	107.6(7)	108.5(5)	109.6(4)
12	O1−C5−C4−C3	−29.0(7)	−37.3(8)	35.8(5)	35.1(9)	−40.2(7)	25.6(7)
13	C5−C4−C3−C2	36.2(7)	36.1(8)	−31.9(5)	−41.0(9)	31.4(7)	−9.4(5)
14	C4−C3−C2−O1	−31.4(6)	−23.0(8)	17.9(5)	35.1(9)	−12.8(8)	−10.9(7)
15	C2−O1−C5−C4	9.2(7)	23.9(7)	−25.4(5)	−13(1)	33.9(7)	−33.9(5)
16	C3−C2−O1−C5	14.0(6)	−0.4(8)	4.7(5)	−15(1)	−13.1(8)	28.6(5)
17	C6−C5−O1−C2	136(1)	146.0(6)	96.1(4)	−139.3(8)	158.6(6)	−156.9(4)
18	C5−O1−C2−C7	138.5(5)	124.6(6)	−119.4(4)	−	−	−
19	O1−C2−C3−C7	−	−	−	161.1(8)	−135.4(7)	−
20	O1−C5−C4−C7	−	−	−	−	−	149.3(3)

[a] The atom count within the tetrahydrofuran nucleus follows the Hantzsch−Widman convention for conformational analysis (i.e. oxygen has a higher priority than carbon).[40] For illustration purposes of results from X-ray crystallographic studies, the notation which is outlined in Figure 3 has been applied consistently.[1] The graphics in Figure 3 and the parameters in Table 6 refer to the same enantiomer, which was arbitrarily selected from the racemate that was present in the unit cell of *trans*-**10d** and **11**.

tains both enantiomers, which adopt twist conformers of opposite chirality [i.e. $_3T^4$ for (2*R**,5*S**) and $^3T_4$ (2*S**,5*R**)]. In each enantiomer, the methyl and the *p*-biphenylyl group are located in *pseudo*-equatorial positions.[45] The structure of *trans*-2-[5-(2-naphthyl)-2-tetrahydrofurylmethylsulfanyl]pyridine *N*-oxide (*trans*-**11e**) was solved and refined in space group $P2_1/n$. The heterocyclic core for the (2*S**,5*S**)-enantiomer adopts an E_3 conformation with the methylsulfanyl group positioned in an equatorial and the naphthyl entity in a bisectional arrangement. The enantiomer exhibits E^3 geometry. The unit cell of *cis*-**11e** (space group $P2_1/n$) contains $_2T^3$- [(2*S**,5*R**)-enantiomer] and $^2T_3$-configured tetrahydrofurans in a 1:1 ratio [(2*R**,5*S**)-enantiomer]. The naphthyl substituent is positioned bisectionally and the methylsulfanyl group axially. Structure solution and refinement from data which were collected for *cis*-2-(4-phenyl-2-tetrahydrofurylmethylsulfanyl)pyridine *N*-oxide (*cis*-**11f**) was successful in the triclinic space group $P\bar{1}$. The heterocyclic core adopts a $^3T_4$ conformer for the (2*R**,4*S**)-configured compound and a $_3T^4$ arrangement for the enantiomer. The phenyl group in *cis*-**11f** is situated in an equatorial and the methylsulfanyl entity in a pseudo-equatorial location. *cis*-2[4-(2-Naphthyl)-2-tetrahydrofurylmethylsulfanyl]pyridine *N*-oxide (*cis*-**11g**) crystallizes in the orthorhombic space group *Pbca*. In (2*S**,4*R**)-**11g**, the β-naphthyl group is found in a pseudo-equatorial and the methylsulfanyl side chain in an equatorial position. The tetrahydrofuran nucleus adopts a $^2T_3$ geometry. The unit cell contains four pairs of enantiomers of *cis*-**11g**. The structure of *trans*-**11h** is characterized by a $_1T^2$ conformation of the heterocyclic core for the (2*S**,3*R**)-configured isomer; the substituents are positioned in a pseudo-equatorial (C_6H_5) and equatorial ($CH_2SC_5H_4NO$) arrangement. This structure and its enantiomer are present in a 1:1 ratio in the unit cell of *trans*-**11h**. The torsion angles O1−C5−C6−S1 are 50.6(6)° (*cis*-**11g**), −61.4(10)° (*cis*-**11f**), 62.1(6)° (*cis*-**11e**), 68.7(5)° (*trans*-**11e**), and 83.0(4)° (*trans*-**11h**). This observation is in agreement with the an approximate gauche arrangement, which is energetically favored in 1,2-diacceptor-substituted ethane entities.[46]

Discussion

The results from the present investigation show that the radical version of the bromo- and the iodocyclization is a feasible and synthetically very useful transformation. Its significant contribution for diastereoselective synthesis arises from the fact that it is so far the only known method for selectively converting 5,5-dimethyl-substituted bis(homoallylic) alcohols — a widespread structural motif among naturally occurring terpenols[47] — into 5-*exo*-halocyclized products without a notable interference from tetrahydropyran formation. With the advent of thiohydroxamate-derived alkoxyl radical precursors,[18,19] the long-standing problem of generating primary and secondary alkoxyl radicals under neutral conditions, i.e. in the absence of oxidants, has been solved. This knowledge has been applied in the present study in order to develop a halocyclization of alkenols, which profits from mild reaction conditions and synthetically useful radical selectivities.[16] The choice of aryl-substituted bis(homoallylic) alcohols **1** for this purpose has been governed by their UV activity, which also facilitated spotting of bromo- or iodocyclization products **4** or **5** even in minor concentrations on TLC plates in the course of the purification step (column chromatography). The major task of the present contribution has been associated with finding matching combinations of: (i) a suitable method for initiating bromo- or iodocyclizations in a radical chain reaction, (ii) an adequate trapping reagent for halogen atom delivery onto a cyclized radical **3**, and (iii) an appropriate chain-carrying radical X· that preferentially regenerates alkoxyl radical **2** in a succeeding step before competing side reactions consume either the alkoxyl radical precursor, for example **6a**, or any essential intermediate of the cycle that is outlined in Figure 4.[19]

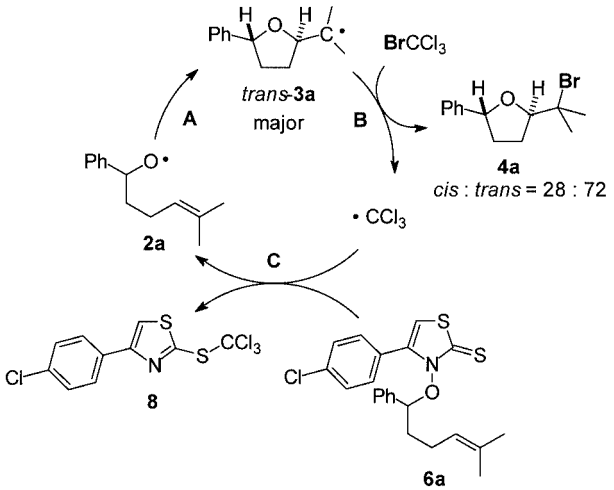


Figure 4. Elementary reactions for the formation of bromocyclization product **4a** in a radical chain reaction starting from thiazolethione **6a**. Step A: 5-*exo*-trig cyclization of alkoxyl radical **2a**; step B: bromine atom transfer onto cyclized radical **3a**; step C: addition of chain carrying ·CCl_3 radical to starting thione **6a** − regeneration of alkoxyl radical **2a**

1. Properties and Preparation of Alkoxyl Radical Precursors

N-Alkoxythiazole-2(3*H*)-thiones **6** and *N*-alkoxypyridine-2(1*H*)-thiones **7** are similarly efficient sources of oxygen centered radicals.[23] Both types of compounds, however, differ in regard of their thermal stability and absorption spectra.[23,48] Since light bulbs, which are commercially available in any hardware store, are suited for initiating transformations starting from pyridinethiones **7**, no specialized photochemical equipment was necessary in this case. This set up also facilitated formation of photolabile alkyl iodides **5** in synthetically useful yields since reaction times never exceeded 3 min.

The synthesis of pyridinethiones **7** is reasonably well-established. All compounds were purified by column chromatography. The inherent lability of pyridinethiones **7**, how-

ever, precluded their extended storage. In particular the rearrangement of secondary *N*-benzyloxy-substituted thiones (e.g. **7a**, **7d**, and **7e**, see Table 1) into corresponding 2-alkylsulfanylpyridine N-oxides (i.e. the non-cyclized derivatives of **11**), was disturbing, since it often led to a complete waste of alkoxyl radical precursors within 12 h.[21] Therefore, thiones **7** were immediately applied once they had been prepared and purified. If product stability tolerated extended photochemical reaction times (approx. 20 min), or the use of near UV/A-light (e.g. from a Rayonet® photoreactor equipped with 350 nm lamps), *N*-alkoxy-4-(*p*-chlorophenyl)thiazole-2(3*H*)-thiones **6** were used as *O*-radical sources instead. Rearrangements of *N*-alkoxy compounds, such as **6a**, into isomeric *N*-oxides have not been observed in this study. Storage of heterocycles **6b** and **6c** in standard glassware for months was feasible without decomposition of the material, although it was noted that thione **6a** tended to fragment into 5-methyl-1-phenyl-4-hexen-1-one,[33] and 4-(*p*-chlorophenyl)thiazole-2(3*H*)-thione if the sample was kept in a refrigerator for more than a month.

The synthesis of *N*-alkoxythiazolethiones **6** has been performed in extension to established methods.[23,30] Isolation of 1,2-bis[4-(*p*-chlorophenyl)-2-thiazyl]disulfane[23] as a side product in significant amounts from one of these reactions was unexpected. This finding may contribute to uncover, in upcoming studies, the fate of the major fraction of 4-(*p*-chlorophenyl)-*N*-hydroxythiazole-2(3*H*)-thione tetraethylammonium salt, which does not get converted into *N*-alkoxy derivatives **6** in *O*-alkylation reactions.

2. Formation of Bromo- and Iodo-Functionalized Disubstituted Tetrahydrofurans

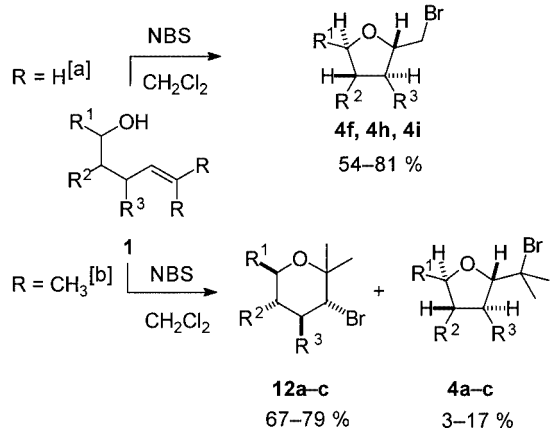
Alkoxyl radical precursors **6** and **7** have been applied for the synthesis of halocyclization products **4** and **5** (Table 2−4). The discussion of heterocycle syntheses will succeed that of a stereochemical analysis for disubstituted tetrahydrofurans **4** and **5**, since the diastereoselectivity of an alkoxyl radical cyclization is independent of the terminal halogen atom trapping step.

(i) Stereochemical Analysis: Emphasis has been placed on an investigation of diastereomerically pure iodides *cis*-**5** and *trans*-**5**. Replacement of the iodine functionality in **5** by hydrogen furnishes aryl-substituted 2-methyltetrahydrofurans **10**. Heterocycles **10** exhibit considerably simplified ^{1}H NMR spectra in terms of multiplicity and overlap of signals and therefore provided significant information in order to assign the relative configuration of each product (Figure 2). The feasibility of this approach for conformationally flexible saturated five-membered cyclic compounds has been questioned in the literature.[49] The results from the present study, however, show that guidelines exist which are suited to assign relative configurations in disubstituted oxolanes from NMR spectroscopic information alone. The potential of this approach has been emphasized by results of X-ray diffraction analyses. The task of converting the major diastereomer of each iodocyclization product into an appropriate crystalline derivative was accomplished by preparing the corresponding 2-alkylsulfanyl pyridine N-oxides **11**. This choice was straightforward as in earlier mechanistic studies the propensity of alkyl iodides to attack preferentially the sulfur instead of the oxygen nucleophile in *N*-hydroxypyridine-2(1*H*)-thione-derived salts had been observed.[50−53] This reaction provided extremely well crystallizing 2-alkylsulfanyl pyridine N-oxides **11**, which were in all instances suitable for X-ray diffraction experiments (Figure 3). The results of this study were in agreement with the configurations that had been derived from NMR spectroscopic investigations (Figure 2).

(ii) Bromocyclizations: Photochemically induced reactions between *N*-alkoxy-4-(*p*-chlorophenyl)thiazolethione **6a** and $BrCCl_3$ provided 2-(1-bromo-1-methylethyl)-5-phenyltetrahydrofuran (**4a**) in synthetically useful yields. This reaction proceeds via a chain mechanism (Figure 4). It is known from laser flash photolysis studies that UV/A- excitation of *N*-alkoxy-4-(*p*-chlorophenyl)thiazole-2(3*H*)-thiones [$\lambda_{max} \approx$ 320 nm (EtOH)] is followed by the generation of alkoxyl radicals.[54] Therefore, it was straightforward to assume in this work that photoexcitation of thiazolethione **6a** initiated N-O homolysis and thus formation of the 5-methyl-1-phenyl-4-hexen-1-oxyl radical (**2a**). Intermediate **2a** preferentially undergoes a 5-*exo*-trig-selective cyclization with a rate constant k of more than 10^9 s^{-1} (30 °C) to afford carbon radical **3a** in a kinetically controlled reaction (step A, Figure 4).[21] Trapping of cyclized radical **3a** with a bromine atom donor provided target compound **4a** and radical X$^{\cdot}$ (step B, Figure 4). Favorable kinetics for the latter step are in most instances, although not necessarily, associated with low C-Br bond dissociation energies.[55] Since structurally related bromine atom donors such as $BrCCl_3$ (87% of **4a**) and $Br_2C_2Cl_4$ (25% of **4a**) provided strongly deviating results, step C was considered to significantly contribute to the effectiveness of the chain reaction. This interpretation originated from the fact that the chemical nature of chain carrying radical X$^{\cdot}$ differs considerably in all instances. Support for this argument was taken from a control experiment that was performed by photolyzing alkoxyl radical precursor **6a** in the absence of an additional trapping reagent for about 30 min (typical reaction time for the synthesis of **4**). 4-(*p*-chlorophenyl)-2-[5-phenyltetrahydrofuryl-2-(1-methylethyl-1-sulfanyl)]thiazole, the expected addition product of cyclized radical **3a** and the thiocarbonyl group in starting thione **6a**, was not identified in such an experiment.[56] This observation implies that a suitable bromine atom donor in this sequence has to a combine a favorable C-Br bond dissociation energy (231 ± 4 kJ·mol^{-1} for $BrCCl_3$) with an adequate affinity of the newly formed radical X$^{\cdot}$ (e.g. $^{\cdot}CCl_3$) for addition to the thiocarbonyl group in thiones **6**. The same principles should apply for bromocyclizations starting from the corresponding *N*-alkenoxypyridine-2(1*H*)-thione, for example **7a**. In view of their favorable characteristics, however, we restricted ourselves to the use of thiazolthiones **6b** and **6c** for conducting syntheses of tetrahydrofurans **4b** and **4c**. It was noteworthy that 5-*exo*-trig cyclizations of 5,5-dimethyl-1- or -3-phenyl-4-penten-1-oxyl radicals **2a** or **2c** proceeded with an increased stereochemical preference for the formation of products *trans*-**4a** or *trans*-**4c** in com-

parison to those intermediates lacking the two methyl substituents at the terminal position of the olefinic π-bond.[15,20] The opposite, however, was the case in cyclizations of the 5,5-dimethyl-2-phenyl-4-penten-1-oxyl radical **2b**. This transformation proceeded with a decreased 2,4-*cis*-selectivity (**4b**: *cis*:*trans* 68:32) in comparison to its derivative **2f** (e.g. see below for **5f**: *cis*:*trans* = 87:13).

The synthetic utility of the new bromocyclization became obvious once the radical selectivities were compared to those from polar reactions (see Exp. Sect.). In contrast to a persistent selectivity for tetrahydrofuran formation as seen in the ring-closure reaction of radicals **2a**−**h**, regioselectivities in polar bromocyclizations of bis(homoallylic) alcohols **1** were strongly dependent on the substitution pattern at the terminal position of the olefinic π-bond.[2,57] For example, treatment of 1-, 2-, or 3-substituted 4-penten-1-ols **1f**, **1h**, and **1i** with NBS furnished tetrahydrofurans **4f**, **4h**, **4i**, whereas bromocyclizations of 5,5-dimethyl-substituted bis(homoallylic) alcohols **1a**−**c** under these conditions proceeded 6-*endo*-selectively (Scheme 2).



Scheme 2. Regioselectivities in polar bromocyclizations of selected bis(homoallylic) alcohols **1**; for details see Exp. Sect. [a] **4f**: R^1, R^3 = H, R^2 = C_6H_5, 60% (*cis*:*trans* = 78:22); **4h**: R^1, R^2 = H, R^3 = C_6H_5, 54% (*cis*:*trans* = 33:67); **4i**: R^1 = C_6H_5, R^2, R^3 = H, 81% (*cis*:*trans* = 33:67). [b] from **1a** (R^1 = C_6H_5, R^2, R^3 = H): 79% of **12a** (*cis*:*trans* = 6:94), 7% of **4a** (*cis*:*trans* = 33:67); from **1b** (R^1, R^3 = H, R^2 = C_6H_5): 67% of **12b** (*cis*:*trans* = >98:<2), 17% of **4b** (*cis*:*trans* = 67:33); from **1c** (R^1, R^2 = H, R^3 = C_6H_5): 76% of **12c** (*cis*:*trans* = <2:>98), 3% of **4c** (*cis*:*trans* = <2:>98)

(iii) Iodocyclizations: Iodomethyl-substituted tetrahydrofurans **5** were preferentially obtained in photochemically induced radical reactions starting from *N*-alkoxypyridine-2(1*H*)-thiones **7**. Compounds with low C-I bond dissociation energies [(BDE): 205 ± 4 kJ·mol^{-1} in *n*-C_4F_9I; 193.1 kJ·mol^{-1} in CHI_3)[55b]] and high rate constants for iodine atom transfer onto alkyl radicals (k = 2.2−5.6 × 10^8 M^{-1} s^{-1}, T = 50 °C, C_6H_6 for diethyl 2-iodo-2-methylmalonate)[35] have been applied for this purpose. The fact that 2-perfluorobutylsulfanyl pyridine (**9**, X = C_4F_9) and diethyl 2-methyl-2-(2-pyridylsulfanyl)malonate [**9**, X = $C(CH_3)(CO_2C_2H_5)_2$] have been isolated in yields that corresponded to those of heterocycles **5** is in agreement with the mechanism that is outlined in Figure 4. 2-(Diiodomethylsulfanyl)pyridine, the assumed $^{\cdot}CHI_2$-radical trapping product of pyridinethione **7f**, was not identified. Optimized conditions were applied for the synthesis of 2-(1-iodo-1-methylethyl)-5-phenyltetrahydrofuran (**5a**). This compound is not accessible from alkenol **1a** and molecular iodine because the polar iodocyclization affords *trans*-3-iodo-2,2-dimethyl-6-phenyltetrahydropyran as the sole product (Exp. Sect.).

In terms of efficiency of the reagents *n*-C_4F_9I and diethyl 2-iodo-2-methylmalonate, it was not possible to predict in advance which iodine atom donor would serve for what synthetic purpose. On an experimental level, a complete decolorization of a previously yellow reaction mixture (color of thione **7**) pointed to an efficient tetrahydrofuran synthesis, whereas faint yellow to brown solutions were frequently indicative of low yields of iodides **5**.

The observed diastereoselectivities for the synthesis of aryl-substituted 2-iodomethyl tetrahydrofurans **5** are in agreement with the alkoxyl radical mechanism that is outlined in Figures 1 and 4. For example, a lack of stereochemical preference for the formation of either diastereomer of **5d** and **5e** is indicative of alkoxyl radicals **2d** and **2e** as reactive intermediates.[20] Polar iodocyclizations of alkenols **1d** and **1e** would have been in favor of the corresponding *trans*-diastereomer (**5d** from **1d**: *cis*:*trans* = 23:77, **5e** from **1e**: *cis*:*trans* = 27:73). Cyclizations of 2-substituted 4-penten-1-oxyl radicals **2f** and **2g** proceeded *cis*-selectively and furnished, after iodine atom trapping, heterocycles **5f** and **5g** (both: *cis*:*trans* = 87:13). The latter two transformations were qualitatively and quantitatively similar to results from polar iodocyclizations (**5f** from **1f**: *cis*:*trans* = 84:16; **5g** from **1g**: *cis*:*trans* = 82:18). The observed diastereoselectivity in the synthesis of 2,3-disubstituted tetrahydrofuran *trans*-**5h** from the alkoxyl radical pathway (*cis*:*trans* = 3:97) exceeded that from the polar iodocyclization (*cis*:*trans* = 20:80) significantly.[51]

Finally, the formation of 2-(iodomethyl)-4-phenyltetrahydrofuran (**5f**) from thiazolethione **6f** and *n*-C_4F_9I in a BEt_3/O_2-initiated reaction deserves a comment. We refrained from pursuing this chemistry further in the present work because its efficiency on an analytical level was not superior to the yield of iodide **5f** on a preparative scale using a photochemically initiated transformation. Still, the approach to initiate halocyclizations with the BEt_3/O_2 system has the potential to further contribute to the development of this chemistry and is therefore under current investigation.

Conclusion

The radical version of the halocyclization is a feasible and synthetically very useful transformation. Its potential for stereoselective synthesis arises from the fact that it is the only known method so far for preparing 5-*exo*-halocyclized products from 5,5-dimethyl-substituted bis(homoallylic) alcohols **1** without a notable interference from tetrahydropyran formation. The general sequence starts with the conversion of alkenols **1** into *N*-(alkenoxy)-4-(*p*-chlorophenyl)thia-

zole-2(3*H*)-thiones **6**, or the corresponding pyridine-2(1*H*)-thiones **7**. Photolysis of thiazolethiones **6** in the presence of $BrCCl_3$ furnished bromocyclization products **4** in synthetically useful yields (75−90%) and diastereoselectivities (36−96% *de*). Other bromine atom donors such as *n*-BrC_6F_{13}, $Br_2C_2Cl_4$, 2-bromo-2-chlorodimedone, or diethyl 2-bromo-2-methylmalonate were less efficient for this purpose. Iodocyclized tetrahydrofurans **5** were preferentially obtained in photochemically initiated reactions between *N*-alkenoxypyridine-2(1*H*)-thiones **7** and either *n*-C_4F_9I or diethyl 2-iodo-2-methyl malonate.

Experimental Section

General Remarks: NMR: Unless otherwise noted in $CDCl_3$ with Bruker AC 200, AC 250, WM 400, or DMX 600 instruments at 20 °C. Residual protons of deuterated solvent [δ_H ($CDCl_3$) = 7.26 ppm; δ_H (CD_3OD) = 3.38 ppm] or their respective resonances in ^{13}C NMR spectra [δ_C ($CDCl_3$) = 77.0 ppm; δ_C (CD_3OD) = 49.3 ppm] were used as internal standards. ^{19}F NMR spectra were referenced against $CFCl_3$ as internal standard. NOE experiments: Samples were dissolved in $CDCl_3$, deaerated by three consecutive freeze-pump-thaw cycles and sealed, irradiation time D2 = 3.0 s (derived from inversion recovery experiments). Spectra were recorded with a Bruker WM 400 spectrometer. IR: in CCl_4 in NaCl cuvettes (0.5 mm) with Perkin−Elmer 1600 FTIR. UV: in EtOH in 1-cm quartz cuvettes with Perkin−Elmer spectrophotometer 330. MS: Varian MATCH 7 spectrometer (electroimpact, El, 70 eV). DTA: DuPont thermal analyzer 9000; scanning rate 10 °C min^{-1}; samples were enclosed in metal containers under nitrogen atmosphere. C,H,N,S analyses: Microanalytisches Labor, Universität Würzburg, Carlo Erba 1106 or LECO CHNS-932. GC: Carlo Erba GC 6000 (Vega Series), FID, connected to Spectra Physics integrator 4290. Helium was used as carrier gas, injector and detector temperature 240 °C, DB-5 (for bromides **4** and iodides **5**) and DB-225 (for aryl-substituted methyltetrahydrofurans **10**) from J & W Scientific. Photochemical equipment: Osram Power Star HQI/D, 250 W or Southern New England Rayonet® chamber reactor equipped with 350 nm light bulbs (for thiazolethiones **6**); Philips 150 W Spotline® R 80 (for pyridinethiones **7**). 5-Methyl-1-phenyl-4-hexen-1-ol (**1a**),[21] 5-methyl-2-phenyl-4-hexen-1-ol (**1b**),[25] 2-phenyl-4-hexen-1-ol (**1f**),[20] 3-phenyl-4-penten-1-ol (**1h**),[20] 2-bromo-2-chlorodimedone,[34] diethyl 2-bromo-2-methylmalonate,[35] diethyl 2-iodo-2-methylmalonate,[35] 2,2′-dithiopyridine-1,1′-dioxide,[28] *N*-hydroxypyridine-2(1*H*)-thione,[28] (*E*)-4-phenyl-3-buten-1-ol,[58] and 1-chloro-5-methyl-1-phenyl-4-hexene[21] were prepared according to published procedures. Trapping reagents $BrCCl_3$, *n*-BrC_6F_{13}, $Br_2C_2Cl_4$, CHI_3, *n*-C_4F_9I were obtained from commercial suppliers and were used as received. All solvents were distilled prior to use and purified according to standard procedures.[59] Petroleum ether refers to the fraction boiling between 55−60 °C. Silica gel for column chromatography (0.063−0.200 mm) was obtained from Woelm.

1. Preparation of Substituted Bis(homoallylic) Alcohols 1

5-Methyl-3-phenyl-4-hexen-1-ol (1c): $Hg(OAc)_2$ (0.505 g, 1.58 mmol) was added to a solution of (*E*)-4-phenyl-3-buten-1-ol[58] (4.00 g, 31.7 mmol) in ethyl vinyl ether (20 mL). The reaction mixture was stirred for 24 h at 50 °C.[60] Afterwards, K_2CO_3 (0.5 g) was added and the volatiles were removed under reduced pressure (600 mbar/ 40 °C). The remaining oil was purified by column chromatography [SiO_2, petroleum ether/acetone = 9:1 (v/v)] to afford 2.56 g (43%) of 5-methyl-3-phenyl-4-hexenal as a colorless oil. ^1H NMR (250 MHz): δ = 1.72 (s, 6 H, 6-H, 7-H), 2.76 (m_c, 2 H, 2-H), 4.13 (dt, J_d = 6.7, J_t = 9.3 Hz 1 H, 3-H), 5.29 (dquint, J_d = 9.3, J_{quint} = 1.5 Hz, 1 H, 4-H), 7.15−7.36 (m, 5 H, Ar-H), 9.70 (t, J_t = 2.2 Hz 1 H, 1-H) ppm. ^{13}C NMR (63 MHz): δ = 18.7 (C-6), 26.5 (C-7), 39.4 (C-3), 42.0 (C-2), 126.7 (C-Ar), 127.2 (C-Ar), 128.4 (C-4, C-Ar), 133.6 (C-5), 139.8(C-Ar), 200.2 (C-1) ppm. MS (70 eV, EI): *m*/*z* (%) = 188 (21) [M^+], 173 (45) [$M^+ - CH_3$], 145 (100) [$C_{11}H_{13}^+$], 117 (62) [$C_9H_9^+$]. $C_{13}H_{16}O$ (188.3): calcd. C 82.94, H 8.57; found C 83.16, H 8.51. 5-Methyl-3-phenyl-4-hexenal (2.48 g, 13.17 mmol) was added to a slurry of $LiAlH_4$ (0.25 g, 6.6 mmol) and anhydrous Et_2O (35 mL) according to a general method for reducing carbonyl compounds into alcohols.[61] Standard work up of the reaction mixture provided a residue, which was purified by distillation (150 °C/0.05 mbar) to afford 2.00 g (80%) of bis(homoallylic) alcohol **1c** as a colorless oil. ^1H NMR (250 MHz): δ = 1.69 (d, *J* = 1.4 Hz, 3 H, 6-H), 1.71 (d, *J* = 1.4 Hz, 3 H, 7-H), 1.81−2.03 (m, 2 H, 2-H), 3.62 (t, *J* = 6.4 Hz, 2 H, 1-H), 3.67 (dt, J_d = 6.4, J_t = 9.3 Hz, 1 H, 3-H), 5.30 (dquint, J_d = 9.3, J_{quint} = 1.4 Hz, 1 H, 4-H), 7.16−7.33 (m, 5 H, Ar-H) ppm. ^{13}C NMR (63 MHz): δ = 18.6 (C-6), 26.4 (C-7), 35.8 (C-3), 43.6 (C-2), 65.8 (C-1), 126.4 (C-Ar), 127.8 (C-Ar), 128.6 (C-4, C-Ar), 134.1 (C-5), 143.5 (C-Ar) ppm. MS (70 eV, EI): *m*/*z* (%) = 190 (10) [M^+], 145 (100) [$C_{11}H_{13}^+$], 117 (32) [$C_9H_9^+$]. $C_{13}H_{18}O$ (190.3): calcd. C 82.06, H 9.53; found C 81.73, H 9.21.

1-(*p*-Biphenylyl)-4-penten-1-ol (1d) and 1-(2-Naphthyl)-4-penten-1-ol (1e): Bis(homoallylic) alcohols **1d** or **1e** were prepared from a solution of 3-butenylmagnesium bromide (0.06 mol) in anhydrous THF (25 mL), which was treated in a dropwise manner with either 4-(*p*-biphenylyl)carbaldehyde (preparation of **1d**: 9.91 g, 0.06 mol dissolved in 20 mL of dry THF) or naphthalene-2-carbaldehyde (preparation of **1e**: 8.76 g, 0.06 mol dissolved in 20 mL of anhydrous THF).[62] Crude products were purified by column chromatography [SiO_2, gradient: petroleum ether/ EtOAc = 9:1 (v/v) → petroleum ether/EtOAc = 8:2 (v/v)] or by recrystallization from petroleum ether (ca. 50 mL).

1-(*p*-Biphenylyl)-4-penten-1-ol (1d): Yield: 9.50 g (72%), colorless needles, m.p. 69−70 °C. ^1H NMR (250 MHz): δ = 1.78 (m, 2 H, 2-H), 2.03 (br. s, 1 H, OH), 2.19 (m_c, 2 H, 3-H), 4.85 (dd, *J* = 5.5, 7.3 Hz, 1 H, 1-H), 5.00−5.13 (m, 2 H, 5-H), 5.88 (ddt, J_d = 10.1, 17.1, J_t = 6.7 Hz, 1 H, 4-H), 7.34−7.49 (m, 5 H, Ar-H), 7.57−7.64 (m, 4 H, Ar-H) ppm. ^{13}C NMR (63 MHz): δ = 30.5, 38.5, 74.2, 115.5, 126.8, 127.5, 127.6, 127.7, 129.2, 138.6, 140.9, 141.3, 144.1 ppm. MS (70 eV, EI): *m*/*z* (%) = 238 (12) [M^+], 183 (100) [$M^+ - C_4H_7$], 77 (34) [$C_6H_5^+$]. $C_{17}H_{18}O$ (238.3): calcd. C 85.67, H 7.61; found C 85.33, H 7.53.

1-(2-Naphthyl)-4-penten-1-ol (1e): Yield: 7.11 g (61%), colorless needles, m.p. 38−39 °C. ^1H NMR (250 MHz): δ = 1.83−2.07 (m, 2 H, 2-H), 2.09−2.24 (m, 2 H, 3-H), 2.37 (br. s, 1 H, OH), 4.84 (t, *J* = 6.1 Hz, 1 H, 1-H), 5.01−5.13 (m, 2 H, 5-H), 5.88 (ddt, J_d = 10.1, 17.1, J_t = 6.7 Hz, 1 H, 4-H), 7.46−7.55 (m, 3 H, Ar-H), 7.77−7.89 (m, 4 H, Ar-H) ppm. ^{13}C NMR (63 MHz): δ = 30.5, 38.8, 74.5, 115.5, 124.5, 125.1, 126.3, 126.6, 128.2, 128.4, 128.8, 133.4, 133.7, 138.6, 142.4 ppm. MS (70 eV, EI): *m*/*z* (%) = 212 (32) [M^+], 194 (9) [$M^+ - H_2O$], 157 (100) [$M^+ - C_7H_4$], 129 (88) [$C_{10}H_9^+$]. $C_{15}H_{16}O$ (212.3): calcd. C 84.87, H 7.60; found C 84.52, H 7.47.

2-(2-Naphthyl)-4-penten-1-ol (1g): A solution of allyl bromide (12.10 g, 0.10 mol) in anhydrous Et_2O (20 mL) was added to a slurry of magnesium turnings (2.21 g, 0.09 mol)] and dry Et_2O at 0 °C (80 mL). The reaction mixture was stirred at room tempera-

ture to allow completion of formation of the Grignard reagent and was then treated at 0 °C with a solution of 2-naphthyloxirane[63] (5.45 g, 0.03 mol) in anhydrous THF (50 mL) as described for the synthesis of 2-phenyl-4-penten-1-ol (**1f**) from styrene oxide.[26] The crude product was purified by column chromatography [SiO_2, petroleum ether/ EtOAc = 8:2 (v/v)] to provide 2.99 g (44%) of alkenol **1g** as a colorless oil (R_f = 0.15). ^{1}H NMR (250 MHz): δ = 2.53 (m_c, 2 H, 3-H), 3.05 (quint, J = 7.0 Hz, 2-H), 3.82 (dd, J = 7.3, 11.0 Hz, 1 H, 1-H), 3.88 (dd, J = 6.1, 11.0 Hz, 1 H, 1-H), 4.94−5.10 (m, 2 H, 5-H), 5.75 (ddt, J_d = 10.7, 17.7, J_t = 6.4 Hz, 1 H, 4-H), 7.36 (dd, J = 1.8, 8.5 Hz, 1 H, Ar-H), 7.48 (m_c, 2 H, Ar-H), 7.68 (d, J = 1.5 Hz, 1 H, Ar-H), 7.78−7.48 (m, 3 H, Ar-H) ppm. ^{13}C NMR (63 MHz): δ = 36.5, 48.3, 66.7, 116.4, 125.5, 126.0, 126.1, 126.9, 127.5, 127.6, 128.3, 132.5, 133.4, 136.2, 139.3 ppm. MS (70 eV, EI): *m/z* (%) = 212 (40) [M^+], 181 (51) [$M^+ - CH_2OH$], 153 (100) [$C_{10}H_7C_2H_2^+$], 129 (41) [$C_{10}H_8^+$]. $C_{15}H_{16}O$ (212.8): calcd. C 84.87, H 7.60; found C 84.98, H 7.73.

2. Preparation of Alkoxyl Radical Precursors

2.1 *N*-Alkoxythiazolethiones 6:

Substituted 4-Penten-1-yl *p*-Toluenesulfonates: A solution of bis(homoallylic) alcohol **1b** or **1c** (500 mg, 2.63 mmol) and DABCO (590 mg, 5.26 mmol) in CH_2Cl_2 (2.5 mL) was treated with *p*-toluenesulfonyl chloride (751 mg, 3.94 mmol) at 0 °C. The slurry was stirred for 1 h at 0 °C, diluted with Et_2O (10 mL), and then treated with aqueous 2 N HCl (10 mL) in order to dissolve the colorless precipitate. The organic layer was separated and the aqueous phase was washed with Et_2O (2 × 10 mL). The combined organic phases were extracted with 2 N aqueous HCl, satd. aqueous $NaHCO_3$, and brine (10 mL each), and dried ($MgSO_4$). The solvent was removed under reduced pressure (40 °C/ 900 mbar) to afford analytically pure alkyl *p*-toluenesulfonate.

5-Methyl-2-phenyl-4-hexen-1-yl *p*-Toluenesulfonate: Yield 2.52 g (96%), colorless oil. ^{1}H NMR (250 MHz): δ = 1.50 (s, 3 H, 6-H), 1.60 (s, 3 H, 7-H), 2.21−2.30 (m, 1 H, 3 H), 2.35−2.50 (m, 1 H, 3 H), 2.43 (s, 3 H, CH_3), 2.91 (quint, J_{quint} = 6.4 Hz, 1 H, 2-H), 4.13 (ddd, J = 6.4, 6.7, 9.6 Hz, 2 H, 1-H), 4.92 (m_c, 1 H, 4-H), 7.06 (m, 2 H, Ar-H), 7.21−7.38 (m, 5 H, Ph-H), 7.62 (d, J_d = 8.2 Hz, 2 H, Ar-H) ppm. ^{13}C NMR (63 MHz): δ = 17.8 (C-6), 21.6 (CH_3), 25.7 (C-7), 30.5 (C-3), 45.2 (C-2), 73.2 (C-1), 120.6 (C-4), 126.9, 127.8, 127.8 (C-Ar), 128.4 (C-5), 128.5, 129.7, 134.0, 140.5, 144.5 (C-Ar) ppm. MS (70 eV, EI): *m/z* (%) = 190 (6) [$M^+ - C_7H_7SO_3$], 155 (20) [$C_7H_7SO_3^+$], 104 (41) [$C_8H_8^+$], 91 (100) [$C_7H_7^+$]. $C_{20}H_{24}O_3S$ (344.5): calcd. C 69.74, H 7.02, S 9.31; found C 70.02, H 6.92, S 8.96.

5-Methyl-3-phenyl-4-hexen-1-yl *p*-Toluenesulfonate: Yield 2.32 g (88%), colorless oil. ^{1}H NMR (250 MHz): δ = 1.60 (d, J = 1.4 Hz, 3 H, 6-H), 1.66 (d, J = 1.4 Hz, 3 H, 7-H), 1.83−2.08 (m, 1 H, 2-H), 2.45 (s, 3 H, CH_3), 3.59 (dt, J_d = 6.9, J_t = 9.3 Hz, 1 H, 3-H), 3.91− 4.06 (m, 2 H, 1-H), 5.16 (dquint, J_d = 9.3, J_{quint} = 1.4 Hz, 1 H, 4-H), 7.08−7.35 (m, 7 H, Ar-H), 7.76 (d, J = 8.2 Hz, 2 H, Ar-H) ppm. ^{13}C NMR (63 MHz): δ = 18.1 (C-6), 25.9 (C-7), 29.9 (CH_3), 34.6 (C-3), 40.9 (C-2), 71.1 (C-1), 126.0 (C-4). 126.4, 127.2, 127.4, 127.9 (C-Ar), 128.3 (C-5), 128.5, 136.9, 137.5, 144.5 (C-Ar) ppm. MS (70 eV, EI): *m/z* (%) = 190 (10) [$M^+ - C_7H_7SO_3$], 155 (30) [$C_7H_7SO_3^+$], 91 (100) [$C_7H_7^+$]. $C_{20}H_{24}O_3S$ (344.5): calcd. C 69.74, H 7.02, S 9.31; found C 68.96, H 6.78, S 9.58.

***N*-Alkoxythiazolethiones 6:** A flame-dried, round-bottomed flask was charged with 4-(*p*-chlorophenyl)-*N*-hydroxythiazole-2(3*H*)-thione tetraethylammonium salt (1.28 g, 5.27 mmol) and a solution of 6-chloro-2-methyl-6-phenyl-2-hexene (417 mg, 2.00 mmol, for **6a**) or an appropriate alkenyl tosylate (689 mg, 2.00 mmol, for **6b** and **6c**) in anhydrous DMF (11 mL) under argon. The reaction mixture was stirred for 4−7 days in the dark and was afterwards poured into H_2O (40 mL). The mixture was extracted with Et_2O (2 × 40 mL). The combined organic phases were washed with 2 N aqueous sodium hydroxide (30 mL) and dried ($MgSO_4$). The solvent was removed (40 °C/900 mbar) to afford a brown oil, which was purified by column chromatography [SiO_2, petroleum ether/ Et_2O = 1:1 (v/v) or petroleum ether/Et_2O/CH_2Cl_2 = 5:1:1 (v/v/v)].

4-(*p*-Chlorophenyl)-*N*-[5-Methyl-1-phenyl-4-hexen-1-oxy]thiazole-2(3*H*)-thione (6a): Yield: 476 mg (1.14 mmol, 57%), colorless crystals, R_f = 0.35 [petroleum ether/Et_2O = 1:1 (v/v)], m.p. 102 ± 2 °C (DTA). ^{1}H NMR ($CDCl_3$, 250 MHz): δ = 1.44 (s, 3 H, 6-H), 1.64 (s, 3 H, 7-H), 1.75−2.10 (m, 4 H, 2-H, 3-H), 5.07 (t, J = 6.8 Hz, 1 H, 1-H), 5.99 (dd, J = 8.2, 6.4 Hz, 1 H, 4-H), 6.18 (s, 1 H, 5′-H), 6.81 (d, J = 7.5 Hz, 2 H, Ar-H), 6.98 (d, J = 8.4 Hz, 2 H, Ar-H), 7.17−7.35 (m, 5 H, Ph-H) ppm. ^{13}C NMR ($CDCl_3$, 63 MHz): δ = 17.7, 24.1, 25.6, 32.3, 86.3, 104.3, 123.0, 127.3, 128.0, 128.4, 128.9, 129.1, 129.6, 132.6, 135.7, 141.7, 172.3 (C=S) ppm. MS (70 eV, EI): *m/z* (%) = 416 (0.1) [$M^+ - H$], 227 (100) [$Cl(C_6H_4)C_3H_2NS_2^+$], 192 (17) [$(C_6H_4)C_3H_2NS_2^+$], 168 (46) [$Cl(C_6H_4)C_2H_3NO^+$], 134 (22) [$C_9H_{10}O^+$]. $C_{22}H_{22}ClNOS_2$ (416.0) calcd. C 63.52, H 5.33, N 3.37, S 15.42; found C 63.29, H 5.61, N 3.18, S 14.29.

1,2-Bis[4-(*p*-chlorophenyl)-2-thiazyl]disulfane:[23] Yield: 208 mg (23%), colorless crystals, R_f = 0.45 [petroleum ether/Et_2O = 1:1 (v/v)], m.p. 156 °C (ref.[30] 156−158 °C). ^{1}H NMR spectroscopic data are in agreement with reported values.[30]

4-(*p*-Chlorophenyl)-*N*-[5-Methyl-2-phenyl-4-hexen-1-oxy]-thiazole-2(3*H*)-thione (6b): Yield: 398 mg (0.96 mmol, 48%), colorless crystals, R_f = 0.40 [petroleum ether/Et_2O/CH_2Cl_2 = 5:1:1 (v/v/v)], m.p. 98 ± 2 °C (DTA). ^{1}H NMR ($CDCl_3$, 250 MHz): δ = 1.64 (s, 3 H, 6-H), 1.76 (s, 3 H, 7-H), 2.29−2.40 (m, 1 H, 3-H), 2.49−2.61 (m, 1 H, 3-H), 3.17 (quint, J = 6.4 Hz, 1 H, 2-H), 4.26 (t, J = 7.6 Hz, 1 H, 1-H), 4.56 (dd, J = 5.7, 7.6 Hz, 1 H, 1-H), 5.10 (m_c, 1 H, 4-H), 6.61 (s, 1 H, 5′-H), 7.15−7.21 (m, 2 H, Ph-H), 7.35−7.55 (m, 7 H, Ar-H) ppm. ^{13}C NMR ($CDCl_3$, 63 MHz): δ = 17.8, 25.6, 31.1, 44.6, 79.2, 105.2, 120.9, 126.0, 126.7, 127.7, 128.3, 128.9, 129.3, 133.6, 135.9, 139.8, 140.9, 176.6 (C=S) ppm. MS (70 eV, EI): *m/z* (%) = 188 (12) [$C_{13}H_{16}O^+$], 120 (100) [$C_8H_8O^+$], 104 (39) [$C_8H_8^+$], 91 (46) [$C_7H_7^+$]. $C_{22}H_{22}ClNOS_2$ (416.0) calcd. C 63.52, H 5.33, N 3.37, S 15.42; found C 63.23, H 5.24, N 3.39, S 15.43.

4-(*p*-Chlorophenyl)-*N*-[5-methyl-3-phenyl-4-hexen-1-oxy]-thiazole-2(3*H*)-thione (6c): Yield: 443 mg (1.07 mmol, 53%), colorless crystals, R_f = 0.40 [petroleum ether/Et_2O/CH_2Cl_2 = 5:1:1 (v/v/v)], m.p. 100 ± 2 °C (DTA). ^{1}H NMR ($CDCl_3$, 250 MHz): δ = 1.69 (s, 3 H, 6-H), 1.74 (s, 3 H, 7-H), 2.02 (m_c, 2 H, 2-H), 3.56 (dt, J_d = 6.3, J_t = 7.5 Hz, 1 H, 3-H), 4.12 (t, J = 6.7 Hz, 2 H, 1-H), 5.20 (dquint, J_d = 9.3, J = 1.2 Hz, 1 H, 4-H), 6.57 (s, 1 H, 5′-H), 7.09 (m_c, 2 H, Ar-H), 7.23−7.36 (m, 3 H, Ph-H), 7.52−7.59 (m, 4 H, Ph-H, Ar-H) ppm. ^{13}C NMR ($CDCl_3$, 63 MHz): δ = 18.6, 26.2, 35.0, 40.8, 75.4, 105.8, 126.5, 127.1, 127.8, 128.4, 129.6, 130.0, 133.1, 136.7, 140.3, 144.8, 181.1 (C=S) ppm. MS (70 eV, EI): *m/z* (%) = 226 (5) [$C_9H_5NClS_2^+$], 188 (31) [$C_{13}H_{16}O^+$], 117 (47) [$C_9H_9^+$], 91 (42) [$C_7H_7^+$]. $C_{22}H_{22}ClNOS_2$ (416.0) calcd. C 63.52, H 5.33, N 3.37, S 15.42; found C 63.16, H 5.28, N 3.37, S 15.19.

2.2 Preparation of *N*-(Alkoxyl)pyridine-2(1*H*)-thiones 7d and 7e from 2,2′-Dithiopyridine-1,1′-dioxide

A solution of bis(homoallylic) alcohols **1d** or **1e** (3.60 mmol) in anhydrous CH_2Cl_2 was treated with 2,2′-dithiopyridine-1,1′-dioxide[28] (1.00 g, 4.00 mmol) and triphenylphosphane (1.05 g, 4.00 mmol), in an extension of the method outlined in ref.[29]

***N*-[1-(*p*-Biphenylyl)-4-penten-1-oxy]pyridine-2(1*H*)-thione (7d):** Yield: 1.28 g (37%), yellow oil. ^{1}H NMR (250 MHz): δ =

2.06−2.20 (m, 3 H, 2-H, 3-H), 2.51−2.59 (m, 1 H, 2-H), 4.16−5.05 (m, 2 H, CH_2), 5.86 (ddt, J_d = 10.3, 16.2, J_t = 5.9 Hz, 1 H, 4-H), 5.95 (dd, J = 6.3, 8.5 Hz, 1 H, 1-H), 6.18 (dt, J_d = 1.8, J_t = 7.0 Hz, 1 H, 5′-H), 7.00 (ddd, J = 1.8, 7.0, 8.8 Hz, 1 H, 4′-H), 7.02 (m_c, 1 H, Ar-H), 7.31−7.40 (m, 3 H, Ar-H), 7.44 (m_c, 2 H, Ar-H), 7.59 (m_c, 4 H, Ar-H), 7.64 (dd, J = 1.5, 7.9 Hz, 1 H, 6′-H) ppm. ^{13}C NMR (63 MHz): δ = 29.4, 32.3, 85.8, 111.6, 115.2, 127.0, 127.4, 127.7, 128.8, 129.2, 132.5, 135.7, 137.4, 137.7, 139.4, 140.1, 142.3, 175.9 (C=S) ppm. IR (CCl_4): ṽ = 1087, 1131, 1176, 1276, 1408, 1447, 1525, 1609, 1639, 2975, 3087 cm^{-1}. MS (70 eV, EI): *m*/*z* (%) = 238 (3) [$C_{17}H_{18}O^+$], 181 (100) [$C_{12}H_9CO^+$], 152 (41) [$C_{12}H_8^+$], 127 (4) [$C_5H_5NOS^+$]. $C_{22}H_{21}NOS$ (347.5): calcd. C 76.05, H 6.09, N 4.03, S 9.27; found C 75.99, H 6.49, N 3.97, S 8.79.

***N*-[1-(2-Naphthyl)-4-penten-1-oxy]pyridine-2(1*H*)-thione (7e):** Yield: 1.08 g (46%), tan solid, m.p. 104−105 °C. ^{1}H NMR (250 MHz): δ = 2.07−2.21 (m, 3 H, 2-H, 3-H, 3-H), 2.58−2.69 (m, 1 H, 2-H), 4.96−5.03 (m, 2 H, 5-H), 5.86 (ddt, J_d = 16.9, 10.3, J_t = 6.2 Hz 1 H, 4-H), 6.02−6.08 (m, 2 H, 1-H, 5′-H), 6.92−6.96 (m, 2 H, Ar-H), 7.49−7.55 (m, 2 H, Ar-H, 4′-H), 7.59 (dd, J = 1.8, 8.4 Hz, 1 H, 3′-H), 7.62−7.66 (m, 2 H, Ar-H), 7.76 (m_c, 1 H, Ar-H), 7.86 (m_c, 1 H, 6′-H), 7.91 (d, J = 8.4 Hz, 1 H, Ar-H) ppm. ^{13}C NMR (63 MHz): δ = 29.4, 32.4, 86.4, 111.6, 115.2, 124.8, 126.6, 127.7, 128.2, 129.1, 129.3, 132.5, 133.1, 133.8, 134.1, 137.4, 137.8, 139.3, 176.0 (C=S) ppm. IR (CCl_4): ṽ = 1132, 1176, 1224, 1276, 1408, 1448, 1525, 1609, 1639, 2905, 3048 cm^{-1}. MS (70 eV, EI): *m*/*z* (%) = 321 (2) [M^+], 194 (28) [$C_{15}H_{14}^+$], 141 (41) [$C_{11}H_9^+$], 127 (25) [$C_5H_5NOS^+$]. $C_{20}H_{19}NOS$ (321.4): calcd. C 74.73, H 5.96, N 4.63, S 9.97; found C 74.53, H 6.08, N 4.57, S 9.97.

2.3 *N*-[2-(2-Naphthyl)-4-penten-1-oxy]pyridine-2(1*H*)-thione (7g): 2-(2-Naphthyl)-4-penten-1-ol (**1g**) (580 mg, 2.73 mmol) and *p*-toluenesulfonyl chloride (781 mg, 4.10 mmol) were dissolved in CH_2Cl_2 (3 mL) and treated with DABCO (613 mg, 5.46 mmol) according to the method reported in ref.[27] Work up of the reaction mixture provided 981 mg (98%) of 2-(2-naphthyl)-4-penten-1-yl *p*-toluenesulfonate as a colorless liquid. R_f = 0.76 [SiO_2, petroleum ether/CH_2Cl_2/ CH_3OH = 10:4:1 (v/v/v)]. ^{1}H NMR (250 MHz): δ = 2.34 (s, 3 H, CH_3), 2.52 (m_c, 2 H, 3-H), 3.17 (m_c, 1 H, 2-H), 4.18 (dd, J = 6.4, 9.5 Hz, 1 H, 1-H), 4.26 (dd, J = 7.0, 9.8 Hz, 1 H, 1-H), 4.95 (d, J = 10.1 Hz, 1 H, 5-H), 5.00 (d, J = 17.1 Hz, 1 H, 5-H), 5.63 (ddt, J_d = 10.1, 17.1, J_t = 7.0 Hz, 1 H, 4-H), 7.08 (d, J = 8.9 Hz, 2 H, Ar-H), 7.19 (dd, J = 1.8, 8.6 Hz, 1 H, Ar-H), 7.44−7.48 (m, 3 H, Ar-H), 7.54 (d, J = 8.2 Hz, 2 H, Ar-H), 7.69−7.73 (m, 2 H, Ar-H), 7.79 (m_c, 1 H, Ar-H) ppm. ^{13}C NMR (63 MHz): δ = 21.5, 36.0, 44.8, 73.1, 117.4, 125.7, 125.8, 126.1, 126.6, 127.5, 127.6, 127.7, 128.2, 129.5, 132.6, 132.6, 134.9, 137.3, 144.5 ppm. MS (70 eV, EI): *m*/*z* (%) = 366 (5) [M^+], 325 (3) [$C_{19}H_{17}O_3S^+$], 194 (59) [$C_{15}H_{14}^+$], 179 (32) [$C_{14}H_{11}^+$], 155 (79) [$C_7H_7O_2S^+$], 91 (100) [$C_7H_7^+$]. $C_{22}H_{22}O_3S$ (366.5): calcd. C 72.10, H 6.05, S 8.75; found C 71.86, H 6.10, S 8.47. A flame-dried, round-bottomed flask was charged with *N*-hydroxypyridine-2(1*H*)-thione tetraethylammonium salt (169 mg, 0.657 mmol), 2-(2-naphthyl)-4-penten-1-yl *p*-toluenesulfonate (219 mg, 0.598 mmol) and anhydrous DMF (1 mL). The reaction mixture was stirred for 48 h in the dark at 20 °C and was then poured into H_2O (10 mL). The organic layer was separated and the aqueous phase extracted with Et_2O (3 × 10 mL). The combined organic phases were washed with 2 N aqueous NaOH (10 mL) and dried ($MgSO_4$). Removal of the solvent under reduced pressure afforded a dark yellow oil which was purified by column chromatography [SiO_2, MTB/petroleum ether = 2:1 (v/v)] to afford analytically pure *N*-[2-(2-naphthyl)-4-penten-1-oxy]pyridine-2(1*H*)-thione (**7g**) (76.6 mg, 40%). Yellow oil, R_f = 0.50 [MTB/petroleum ether = 2:1 (v/v)]. ^{1}H NMR (400 MHz): δ = 2.60 (m_c, 1 H, 3-H), 2.74 (m_c, 1-H, 3-H), 3.44 (m_c, 1 H, 2-H), 4.54 (t, J = 8.1 Hz, 1 H, 1-H), 4.88 (dd, J = 5.9, 8.5 Hz, 1 H, 1-H), 4.99 (d, J = 9.9 Hz, 1 H, 5-H), 5.07 (d, J = 16.9 Hz, 1 H, 5-H), 5.74 (ddt, J_d = 9.9, 16.9, J_t = 7.0 Hz, 1 H, 4-H), 6.43 (dt, J_d = 1.8, J_t = 7.0 Hz, 1 H, CH), 7.07 (m_c, 1 H, CH), 7.33 (m_c, 1 H, Ar-H), 7.42 (dd, J = 1.8, 8.5 Hz, 1 H, CH), 7.48 (m_c, 2 H, Ar-H), 7.62 (dd, J = 1.8, 8.8 Hz, 1 H, CH), 7.74 (br. s, 1 H, Ar-H), 7.80−7.85 (m, 3 H, Ar-H) ppm. ^{13}C NMR (100 MHz): δ = 36.9, 44.4, 79.6, 112.9, 117.2, 125.8, 125.9, 126.2, 126.9, 127.7, 127.8, 128.4, 132.6, 132.7, 135.3, 137.7, 138.1, 138.1, 176.0 (C=S) ppm. MS (70 eV, EI): *m*/*z* (%) = 321 (13) [M^+], 211 (35) [$C_{15}H_{15}O^+$], 194 (61) [$C_{15}H_{14}^+$], 179 (64) [$C_{14}H_{11}^+$], 141 (90) [$C_{11}H_9^+$], 111 (100) [$C_5H_5NS^+$]. $C_{20}H_{19}NOS$ (321.4): calcd. C 74.73, H 5.96, N 4.36, S 9.98; found C 74.09, H 5.72, N 4.19, S 9.68.

3. Bromocyclizations

3.1 Preparation of Bromocyclized Products 4 from *N*-Alkoxythiazolethiones 6: A solution of an *N*-alkenoxy-4-(*p*-chlorophenyl)thiazole-2(3*H*)-thione **6** (34.5 mg, 0.100 mmol) and $BrCCl_3$ (159 mg, 0.800 mmol) in deaerated (Ar) C_6H_6 (1 mL) was photolyzed for 15 min in a Rayonet® chamber reactor. Afterwards, solvent and residual $BrCCl_3$ were removed under reduced pressure (40 °C/ 200 mbar) to provide an oily residue which was distilled (150 °C/ 0.05 mbar) and purified by column chromatography (SiO_2).

2-(1-Bromo-1-methylethyl)-5-phenyltetrahydrofuran (4a): Yield: 23.5 mg (87%), colorless oil, b.p. 130 °C/ 10^{-2} mbar (Kugelrohr), *cis*:*trans* = 28:72, R_f = 0.60 [petroleum ether/EtOAc = 9:1(v/v)] ppm. MS (70 eV, EI): *m*/*z* (%) = 270/268 (2) [M^+], 147 (100) [$C_{10}H_{11}O^+$], 129 (29) [$C_{10}H_{11}O^+ - H_2O$], 104 (100) [$C_8H_8^+$], 91 (39) [$C_7H_7^+$], 77 (12) [$C_6H_5^+$], 43 (18) [$C_2H_3O^+$], 41 (19) [$C_3H_5^+$]. $C_{13}H_{17}BrO$ (269.2) calcd. C 58.00, H 6.37; found C 57.90, H 6.30.

***cis*-4a:** ^{1}H NMR ($CDCl_3$, 250 MHz): δ = 1.82 (s, 3 H, 2′-H), 1.84 (s, 3 H, 3′-H), 2.04−2.19 (m, 2 H, 3-H), 2.20−2.34 (m, 2 H, 4-H), 3.96 (dd, J = 6.1, 7.6 Hz, 1 H, 2-H), 4.90 (dd, J = 5.8, 9.5 Hz, 1 H, 5-H), 7.24−7.38 (m, 5 H, Ph-H) ppm. ^{13}C NMR ($CDCl_3$, 63 MHz): δ = 29.2 (C-2′), 29.7 (C-3′), 31.4 (C-4), 34.7 (C-3), 69.3 (C-1′), 82.0 (C-2), 86.4 (C-5), 126.0, 127.3, 128.5, 142.0 (C-Ph).

***trans*-4a:** ^{1}H NMR ($CDCl_3$, 250 MHz): δ = 1.78 (s, 3 H, 2′-H), 1.84 (s, 3 H, 3′-H), 1.81−1.98 (m, 1 H, 3-H), 2.03−2.19 (m, 1 H, 4-H), 2.14−2.36 (m, 1 H, 3-H), 2.38−2.47 (m, 1 H, 4-H), 4.11 (dd, J = 6.7, 8.2 Hz, 1 H, 2-H), 5.12 (dd, J = 5.7, 9.0 Hz, 1 H, 5-H), 7.24−7.38 (m, 5 H, Ph-H) ppm. ^{13}C NMR ($CDCl_3$, 63 MHz): δ = 29.8 (C-2′), 29.9 (C-3′), 31.1 (C-4), 35.7 (C-3), 68.4 (C-1′), 82.0 (C-2), 87.1 (C-5), 125.7, 127.4, 128.3, 142.9 (C-Ph) ppm.

4-[(*p*-Chlorophenyl)-2-trichloromethylsulfanyl]thiazole (8) (X = CCl_3): Distillation of the reaction mixture from the photoreaction of thione **6a** and $BrCCl_3$ provided tetrahydrofuran **4a** and a residue. This residue was recrystallized from petroleum ether/CH_2Cl_2 to provide 24.5 mg (71%) of thiazole **8** as colorless crystals: m.p. 102 °C, R_f = 0.85 [petroleum ether/Et_2O/CH_2Cl_2 = 10:1:1 (v/v/v)]. ^{1}H NMR (250 MHz): δ = 7.42 (m_c, 2 H, 2′-H), 7.84 (s, 1 H, 5-H), 7.89 (m_c, 2 H, 3′-H) ppm. ^{13}C NMR ($CDCl_3$, 63 MHz): δ = 96.7, 120.8, 127.8, 129.1, 131.8, 134.8, 154.8, 156.7 ppm. MS (70 eV, EI): *m*/*z* (%) = 345 (28) [M^+], 310 (8) [$M^+ - Cl$], 226 (63) [$M^+ - CCl_3$], 191 (26) [$C_9H_5NS_2^+$], 168 (100) [$C_8H_5ClS^+$]. $C_{10}H_5Cl_4NS_2$ (345.1): calcd. C 34.81, H 1.46, N 4.06, S 18.58; found C 35.78, H 2.06, N 3.94, S 17.88.

2-(1-Bromo-1-methylethyl)-4-phenyltetrahydrofuran (4b): Yield: 20.2 mg (75%), colorless oil, b.p. 130 °C/ 10^{-2} mbar (Kugelrohr), *cis*:*trans* = 68:32. MS (70 eV, EI): *m*/*z* (%) = 270/268 (7) [M^+], 147 (59) [$C_{10}H_{11}O^+$], 131 (90) [$C_{10}H_{11}^+$], 117 (35) [$C_9H_9^+$], 104 (100) [$C_8H_8^+$], 91 (92) [$C_7H_7^+$], 77 (16) [$C_6H_5^+$], 71 (21) [$C_4H_7O^+$], 51 (15) [$C_4H_3^+$], 43 (30) [$C_2H_3O^+$], 41 (23) [$C_3H_5^+$], 39 (14) [$C_3H_3^+$].

$C_{13}H_{17}BrO$ (269.2) calcd. C 58.00, H 6.37; found C 57.71, H 6.10. ***cis*-4b:** R_f = 0.70 [petroleum ether/Et_2O/CH_2Cl_2 = 10:1:1 (v/v/v)]. ^1H NMR ($CDCl_3$, 250 MHz): δ = 1.75 (s, 3 H, 2′-H), 1.84 (s, 3 H, 3′-H), 2.06−2.20 (m, 1 H, 3-H), 2.43−2.53 (m, 1 H, 3-H), 3.45−3.60 (m, 1 H, 4-H), 3.90 (dd, *J* = 8.1, 10.1 Hz, 1 H, 5-H), 3.98 (dd, *J* = 6.1, 9.3 Hz, 1 H, 2-H), 4.26 (t, *J* = 8.1 Hz, 1 H, 5-H), 7.21−7.36 (m, 5 H, Ph-H) ppm. ^{13}C NMR ($CDCl_3$, 63 MHz): δ = 30.3 (C-2′), 30.7 (C-3′), 37.7 (C-3), 45.6 (C-4), 68.9 (C-1′), 75.2 (C-5), 87.3 (C-2), 126.3, 127.2, 128.7, 140.0 (C-Ph) ppm.

***trans*-4b:** R_f = 0.80 [petroleum ether/Et_2O/CH_2Cl_2 = 10:1:1 (v/v/v)]. ^1H NMR ($CDCl_3$, 250 MHz): δ = 1.74 (s, 3 H, 2′-H), 1.81 (s, 3 H, 3′-H), 2.09−2.19 (m, 1 H, 3-H), 2.37−2.49 (m, 1 H, 3-H), 3.51 (dq, J_d = 8.8, J_q = 6.9 Hz, 1 H, 4-H), 3.88 (dd, *J* = 6.9, 8.6 Hz, 1 H, 5-H), 4.03 (dd, *J* = 6.7, 7.9 Hz, 1 H, 2-H), 4.33 (dd, *J* = 6.9, 8.6 Hz, 1 H, 5-H), 7.20−7.37 (m, 5 H, Ph-H) ppm. ^{13}C NMR ($CDCl_3$, 63 MHz): δ = 29.8 (C-2′), 30.9 (C-3′), 37.3 (C-3), 44.9 (C-4), 68.7 (C-1′), 75.3 (C-5), 88.2 (C-2), 126.6, 127.1, 128.6, 140.0 (C-Ph) ppm.

2-(1-Bromo-1-methylethyl)-3-phenyl tetrahydrofuran (4c): Yield: 24.1 mg (90%), colorless oil, b.p. 130 °C/ 10^{-2} mbar (Kugelrohr), *cis*:*trans* = <2:>98. ***trans*-4c**: R_f = 0.75 [petroleum ether/Et_2O/CH_2Cl_2 = 10:1:1 (v/v/v)]. ^1H NMR ($CDCl_3$, 250 MHz): δ = 1.57 (s, 3 H, 2′-H), 1.76 (s, 3 H, 3′-H), 2.00−2.15 (m, 1 H, 4-H), 2.41−2.54 (m, 1 H, 4-H), 3.45 (dt, J_d = 6.9, J_t = 8.4 Hz, 1 H, 3-H), 3.89 (d, *J* = 6.9 Hz, 1 H, 2-H), 4.13 (dd, *J* = 5.7, 7.9 Hz, 2 H, 5-H), 7.18−7.34 (m, 5 H, Ph-H) ppm. ^{13}C NMR ($CDCl_3$, 63 MHz): δ = 31.5 (C-2′), 31.9 (C-3′), 38.2 (C-4), 49.0 (C-3), 69.3 (C-1′), 75.4 (C-5), 93.1 (C-2), 127.7, 128.6, 128.8, 137.3 (C-Ph) ppm. MS (70 eV, EI): *m*/*z* (%) = 270/268 (2) [M^+], 188 (5) [M^+ − HBr], 147 (99) [$C_{10}H_{11}O^+$], 117 (100) [$C_9H_9^+$], 91 (76) [$C_7H_7^+$]. $C_{13}H_{17}BrO$ (269.2) calcd. C 58.00, H 6.37; found C 57.67, H 6.21.

3.2 NBS-Mediated Bromocylizations of Bis(homoallylic) Alcohols 1

Alkenol **1** (190 mg, 1.00 mmol) and NBS (267 mg, 1.50 mmol) were dissolved in CH_2Cl_2 (2 mL). The reaction mixture was stirred for 72 h at 25 °C. Afterwards, petroleum ether was added (2 mL) and the precipitate was filtered off. The solids were washed with petroleum ether (2 × 2 mL) and the combined organic phases were treated with NaOAc (15 mg). Subsequently, the solvent was removed under reduced pressure (40 °C/450 mbar) to afford a crude product, which was distilled (Kugelrohr, 150 °C/0.05 mbar). The distillate was purified by column chromatography (SiO_2).

Bromocyclization of 5-Methyl-1-phenyl-4-hexen-1-ol (1a)

2-(1-Bromo-2-methylethyl)-5-phenyl tetrahydrofuran (4a): Yield: 19.4 mg (7%), *cis*:*trans* = 33:67, colorless oil, R_f = 0.60 [petroleum ether/EtOAc = 9:1 (v/v)].

3-Bromo-2,2-dimethyl-6-phenyltetrahydropyran (12a): Yield: 212 mg (0.79 mmol, 79%), colorless crystals, m.p. 39 °C, b.p. 130 °C/ 10^{-2} mbar (Kugelrohr), *cis*:*trans* = 6:94. MS (70 eV, EI): *m*/*z* (%) = 270/268 (1) [M^+], 212/210 (3) [M^+ − $2CH_3$−$2CH_2$], 172 (24) [M^+ − Br − HO], 147 (30) [$C_{10}H_{11}O^+$], 129 (21) [$C_{10}H_{11}O^+$ − H_2O], 121 (47) [$C_8H_9O^+$], 104 (100) [$C_8H_8^+$], 91 (33) [$C_7H_7^+$], 77 (21) [$C_6H_5^+$]. $C_{13}H_{17}BrO$ (269.2) calcd. C 58.00, H 6.37; found C 57.58, H 6.06.

***cis*-12a:** R_f = 0.30 [petroleum ether/EtOAc = 9:1 (v/v)]. ^1H NMR ($CDCl_3$, 250 MHz): δ = 1.44 (s, 3 H, 1′-H), 1.51 (s, 3 H, 2′-H), 1.61−1.71 (m, 2 H, 4-H), 2.12−2.22 (m, 2 H, 5-H), 4.28 (dd, *J* = 2.5, 3.7 Hz, 1 H, 3-H), 4.70 (dd, *J* = 3.0, 11.6 Hz, 1 H, 5-H), 7.29−7.44 (m, 5 H, Ph-H) ppm. ^{13}C NMR ($CDCl_3$, 63 MHz): δ = 22.5 (C-2′), 28.3 (C-3′), 30.0 (C-4), 32.1 (C-5), 59.3 (C-3), 72.8 (C-6), 74.1 (C-2), 126.2, 127.5, 128.4, 142.1 (C-Ph) ppm.

***trans*-12a:** R_f = 0.60 [petroleum ether/EtOAc = 9:1 (v/v)]. ^1H NMR ($CDCl_3$, 250 MHz): δ = 1.39 (s, 3 H, 1′-H), 1.44 (s, 3 H, 2′-H), 1.61−1.71 (m, 1 H, 5-H), 1.73−1.88 (m, 1 H, 5-H), 2.19−2.29 (m, 2 H, 4-H), 3.99 (dd, *J* = 8.2, 8.5 Hz, 1 H, 3-H), 4.62 (dd, *J* = 2.7, 11.6 Hz, 1 H, 5-H), 7.19−7.28 (m, 5 H, Ph-H) ppm. ^{13}C NMR ($CDCl_3$, 63 MHz): δ = 18.0 (C-2′), 29.6 (C-3′), 32.1 (C-4), 36.5 (C-5), 57.3 (C-3), 72.2 (C-6), 76.1 (C-2), 125.9, 127.5, 128.4, 142.4 (C-Ph) ppm.

Bromocyclization of 5-Methyl-2-phenyl-4-hexen-1-ol (1b)

2-(1-Bromo-1-methylethyl)-4-phenyltetrahydrofuran (4b): Yield: 46.4 mg (17%), colorless oil, b.p. 130 °C/10^{-2} mbar (Kugelrohr), *cis*:*trans* = 67:33.

***cis*-3-Bromo-2,2-dimethyl-5-phenyltetrahydropyran *cis*-(12b):** Yield: 181 mg (67%); colorless crystals, m.p. 64 °C, b.p. 145 °C/10^{-2} mbar (Kugelrohr), *cis*:*trans* = <2:>98, R_f = 0.40 [petroleum ether/acetone/CH_2Cl_2 = 8:1:1 (v/v/v)]. ^1H NMR ($CDCl_3$, 250 MHz): δ = 1.43 (s, 3 H, 1′-H), 1.48 (s, 3 H, 2′-H), 2.31−2.44 (m, 2 H, 4-H), 3.03 (sept, *J* = 5.5 Hz, 1 H, 5-H), 3.64−3.82 (m, 2 H, 6-H), 4.10 (ddd, *J* = 7.3, 9.5, 11.3 Hz, 1 H, 3-H), 7.20−7.33 (m, 5 H, Ph-H) ppm. ^{13}C NMR ($CDCl_3$, 63 MHz): δ = 17.4 (C-2′), 29.2 (C-1′), 38.0 (C-4), 45.5 (C-5), 56.4 (C-3), 66.5 (C-6), 75.0 (C-2), 127.1, 127.2, 128.7, 140.0 (C-Ph) ppm. MS (70 eV, EI): *m*/*z* (%) = 270/268 (6) [M^+], 212/210 (21) [M^+ −$2CH_3$−$2CH_2$], 131 (100) [$C_{10}H_{11}^+$], 117 (24) [$C_9H_9^+$], 104 (87) [$C_8H_8^+$], 91 (70) [$C_7H_7^+$], 77 (12) [$C_6H_5^+$]. $C_{13}H_{17}BrO$ (269.2) calcd. C 58.00, H 6.37; found C 58.17, H 6.16.

Bromocyclization of 5-Methyl-3-phenyl-4-hexen-1-ol (1c)

2-(1-Bromo-1-methylethyl)-3-phenyltetrahydrofuran (4c): Yield: 9.1 mg (3%), colorless oil, b.p. 130 °C/10^{-2} mbar (Kugelrohr), *cis*:*trans* = <2:>98.

***trans*-3-Bromo-2,2-dimethyl-4-phenyltetrahydropyran *trans*-(12c):** Yield: 204 mg (76%), colorless crystals, m.p. 81 °C, b.p. 145 °C/ 10^{-2} mbar (Kugelrohr), *cis*:*trans* = <2:>98, R_f = 0.40 [petroleum ether/acetone/CH_2Cl_2 = 8:1:1 (v/v/v)]. ^1H NMR ($CDCl_3$, 250 MHz): δ = 1.48 (s, 3 H, 1′-H), 1.53 (s, 3 H, 2′-H), 1.85 (dddd, *J* = 1.8, 2.8, 4.6, 13.7 Hz, 1 H, 5-H), 1.97 (dddd, *J* = 1.8, 5.8, 12.0, 13.7 Hz, 1 H, 5-H), 3.17 (ddd, *J* = 4.6, 11.8, 12.0 Hz, 1 H, 4-H), 3.76 (ddd, *J* = 1.8, 5.8, 12.0 Hz, 1 H, 6-H), 3.84 (dt, J_d = 2.8, J_t = 12.0 Hz, 1 H, 6-H), 4.09 (d, *J* = 11.8 Hz, 1 H, 3-H), 7.19−7.39 (m, 5 H, Ph-H) ppm. ^{13}C NMR ($CDCl_3$, 63 MHz): δ = 18.2 (C-2′), 30.0 (C-1′), 37.0 (C-5), 47.0 (C-4), 60.9 (C-3), 63.3 (C-6), 76.0 (C-2), 127.0, 127.3, 128.5, 143.5 (C-Ph) ppm. MS (70 eV, EI): *m*/*z* (%) = 270/268 (7) [M^+], 189 (51) [M^+ − Br], 147 (36) [$C_{10}H_{11}O^+$], 131 (100) [$C_{10}H_{11}^+$], 91 (65) [$C_7H_7^+$]. $C_{13}H_{17}BrO$ (269.2) calcd. C 58.00, H 6.37; found C 58.36, H 6.25.

Bromocyclization of 2-Phenyl-4-penten-1-ol (1f)

2-Bromomethyl-4-phenyltetrahydrofuran (4f): Yield: 144 mg (60%) from **1f** (162 mg, 1.00 mmol) and NBS (267 mg, 1.50 mmol) in CH_2Cl_2 (10 mL), colorless oil, b.p. 125 °C/10^{-2} mbar (Kugelrohr); *cis*:*trans* = 78:22. MS (70 eV, EI): *m*/*z* (%) = 242/240 (6) [M^+], 160 (15) [M^+ − HBr], 147 (100) [M^+ − CH_2Br], 91 (66) [$C_7H_7^+$]. $C_{11}H_{13}BrO$ (241.1) calcd. C 54.80, H 5.85; found C 54.51, H 5.31.

***cis*-4f:** R_f = 0.55 [petroleum ether/acetone/CH_2Cl_2 = 5:1:1 (v/v/v)]. ^1H NMR (250 MHz): δ = 1.87−2.00 (m, 1 H, 3-H), 2.51−2.61 (m, 1 H, 3-H), 3.48 (dd, *J* = 5.4, 1.4 Hz, 2 H, 1′-H), 3.45−3.61 (m, 1 H, 4-H), 3.89 (dd, *J* = 8.2, 9.2 Hz, 1 H, 5-H), 4.25 (t, *J* = 8.2 Hz, 1 H, 5-H), 4.30−4.42 (m_c, 1 H, 2-H), 7.21−7.37 (m, 5 H, Ph-H) ppm. ^{13}C NMR (63 MHz): δ = 35.8 (C-3), 39.4 (C-1′), 45.6 (C-4), 74.8 (C-5), 78.9 (C-2), 126.8, 127.2, 128.6, 140.7 ppm.

***trans*-4f:** R_f = 0.57 [petroleum ether/acetone/CH_2Cl_2 = 5:1:1 (v/v/v)]. ^1H NMR (250 MHz): δ = 2.15−2.36 (m, 2 H, 3-H), 3.48 (dd,

J = 2.0, 5.7 Hz, 2 H, 1′-H), 3.45−3.61 (m, 1 H, 4-H), 3.83 (dd, J = 7.6, 8.5 Hz, 1 H, 5-H), 4.31 (dd, J = 7.0, 8.5 Hz, 1 H, 5-H), 4.41−4.50 (m, 1 H, 2-H), 7.21−7.37 (m, 5 H, Ph-H) ppm. ^{13}C NMR (63 MHz): δ = 29.5 (C-3), 38.3 (C-1′), 44.4 (C-4), 75.1 (C-5), 78.3 (C-2), 126.7, 127.2, 128.6, 141.4 ppm.

Bromocyclization of 3-Phenyl-4-penten-1-ol (1h)

2-Bromomethyl-3-phenyltetrahydrofuran (4h): Yield: 131 mg (54%) from **1h** (162 mg, 1.00 mmol) and NBS (267 mg, 1.50 mmol) in CH_2Cl_2 (10 mL), colorless oil, b.p. 120 °C/ 10^{-2} mbar (Kugelrohr), *cis*:*trans* = 33:67. MS (70 eV, EI): *m*/*z* (%) = 242/240 (6) [M^+], 147 (29) [$M^+ - CH_2Br$], 118 (100) [$C_9H_{10}^+$], 91 (44) [$C_7H_7^+$]. $C_{11}H_{13}BrO$ (241.1) calcd. C 54.80, H 5.85; found C 53.28, H 5.19.
***cis*-4h:** R_f = 0.42 [petroleum ether/acetone/CH_2Cl_2 = 5:1:1 (v/v/v)]. ^{1}H NMR (250 MHz): δ = 2.12−2.27 (m, 1 H, 4-H), 2.37−2.51 (m, 1 H, 4-H), 2.89 (dd, J = 5.2 10.4 Hz, 1 H, 1′-H), 3.04 (dd, J = 7.9, 10.4 Hz, 1 H, 1′-H), 3.50 (dt, J_d = 8.2, J_t = 5.8 Hz, 1 H, 3-H), 3.95 (td, J_t = 8.9, J_d = 7.3 Hz, 1 H, 5-H), 4.20−4.28 (m, 2 H, 5-H, 2-H), 7.15−7.35 (m, 5 H, Ph-H) ppm. ^{13}C NMR (63 MHz): δ = 34.8 (C-1′), 35.3 (C-4), 49.3 (C-3), 68.5 (C-5), 84.7 (C-2), 127.1, 127.5, 128.9, 140.5 ppm.
***trans*-4h:** R_f = 0.46 [petroleum ether/acetone/CH_2Cl_2 = 5:1:1 (v/v/v)]. ^{1}H NMR (250 MHz): δ = 2.14−2.25 (m, 1 H, 4-H), 2.35−2.48 (m, 1 H, 4-H), 3.21 (td, J_t = 9.5, J_d = 7.9 Hz, 1 H, 3-H), 3.39 (dd, J = 5.3, 10.7 Hz, 1 H, 1′-H), 3.54 (dd, J = 3.7, 10.7 Hz, 1 H, 1′-H), 4.01−4.08 (m, 1 H, 2-H), 4.04−4.16 (m, 2 H, 5-H), 7.16−7.35 (m, 5 H, Ph-H) ppm. ^{13}C NMR (63 MHz): δ = 32.8 (C-1′), 33.1 (C-4), 47.6 (C-3), 67.6 (C-5), 82.1 (C-2), 126.9, 127.7, 128.5, 140.0 ppm.

Bromocyclization of 1-Phenyl-4-penten-1-ol (1i)

2-Bromomethyl-5-phenyltetrahydrofuran (4i):[20] Yield: 196 mg (81%) from **1i** (162 mg, 1.00 mmol) and NBS (267 mg, 1.50 mmol) in CH_2Cl_2 (10 mL), colorless oil, b.p. 120 °C/ 10^{-2} mbar (Kugelrohr), *cis*:*trans* = 33:67.
***cis*-4i:** R_f = 0.42 [petroleum ether/acetone/CH_2Cl_2 = 5:1:1 (v/v/v)]. ^{1}H NMR (250 MHz): δ = 1.86−2.01 (m, 2 H, 3-H, 4-H), 2.17−2.35 (m, 2 H, 3-H, 4-H), 3.50 (dd, J = 6.3, 10.1 Hz, 1 H, 1′-H), 3.58 (dd, J = 5.4, 10.1 Hz, 1 H, 1′-H), 4.31−4.39 (m, 1 H, 2-H), 4.96 (dd, J = 5.9, 8.1 Hz, 1 H, 5-H), 7.24−7.41 (m, 5 H, Ph-H) ppm.
***trans*-4i:** R_f = 0.60 [petroleum ether/EtOAc = 5:1 (v/v)]. ^{1}H NMR (250 MHz): δ = 1.86−2.01 (m, 2 H, 3-H, 4-H), 2.17−2.35 (m, 1 H, 4-H), 2.38−2.56 (m, 1 H, 3-H), 3.46 (dd, J = 7.2, 10.1 Hz, 1 H, 1′-H), 3.55 (dd, J = 3.8, 10.1 Hz, 1 H, 1′-H), 4.43−4.52 (m, 1 H, 2-H), 5.10 (dd, J = 6.1, 8.3 Hz, 1 H, 5-H), 7.24−7.41 (m, 5 H, Ph-H) ppm.

4. Iodocyclizations

4.1 Photolysis of Thiazolethiones 6 and Pyridinethiones 7 in the Presence of Iodine Atom Donors

General procedure 1: A Schlenk flask equipped with an argon inlet was charged with radical precursor **6** or **7** (0.3 mmol) and anhydrous solvent (C_6H_6 or CH_2Cl_2, 5 mL) in the dark. After addition of an iodine atom donor (CHI_3, diethyl 2-iodo-2-methylmalonate, or *n*-C_4F_9I; for exact combinations refer to Table 3 and 4). The air was removed from this mixture by three consecutive freeze-pump-thaw cycles using Ar as inert gas. The reaction mixture was photolyzed at 20 °C (20 min in a Rayonet® for thiazolethiones **6** or 3 min with an 150 W light bulb for pyridinethiones **7**). Upon complete consumption of the alkoxyl radical precursor, the solvent was removed under reduced pressure to provide an oily residue that was purified by column chromatography (SiO_2, petroleum ether/Et_2O).

General Procedure 2: A Schlenk flask equipped with an argon inlet was charged with thiazolethione **6f** (34.3 mg, 88.4 μmol), *n*-$C_{14}H_{30}$ as internal standard (GC), anhydrous C_6H_6 (1.2 mL) and *n*-C_4F_9I (76.5 mg, 0221 mmol) in the dark. Air was removed by freeze-pump-thaw cycles using argon as inert gas. After addition of a solution of BEt_3 (22 μL, 1.0 M in C_6H_{14}), air was introduced into the solution via a syringe pump (25 μL/min) over a period of 20 min. Product formation and yields of 2-iodomethyl-4-phenyl-tetrahydrofuran (**5f**) were determined by GC analysis.

2-(1-Iodo-1-methylethyl)-5-phenyltetrahydrofuran (5a): Application of general procedure 1 [**7a**: 164 mg (0.548 mmol), *n*-C_4F_9I: (474 mg, 1.37 mmol), C_6H_6: 8 mL] afforded 139.1 mg of **5a** (80%): colorless oil, *cis*:*trans* = 29:71. MS (70 eV, EI): *m*/*z* (%) = 316 (1) [M^+], 189 (88) [$M^+ - I$], 147 (18) [$C_{10}H_{11}O^+$], 105 (100) [$C_7H_5O^+$]. $C_{13}H_{17}IO$ (316.2): calcd. C 49.38, H 5.42; found C 49.29, H 5.17.
***cis*-5a:** Yield 40.1 mg (23%), colorless oil, R_f = 0.61 [SiO_2, petroleum ether/ Et_2O = 9:1 (v/v)]. ^{1}H NMR (250 MHz): δ = 1.82−2.10 (m, 2 H, CH_2), 1.97 (s, 3 H, CH_3), 2.01 (s, 3 H, CH_3), 2.13−2.32 (m, 2 H, CH_2), 3.33 (dd, J = 5.8, 7.9 Hz, 1 H, 2-H), 4.90 (dd, J = 5.8, 9.5 Hz, 1 H, 5-H), 7.24−7.37 (m, 3 H, Ar-H), 7.45−7.49 (m, 2 H, Ar-H) ppm. ^{13}C NMR (100 MHz): δ = 31.2, 33.6, 34.5, 82.0 (C-2), 88.1 (C-5), 125.6, 126.1, 127.4, 128.3 ppm.
***trans*-5a:** Yield: 99 mg (57%), colorless oil, R_f = 0.69 [SiO_2, petroleum ether/ Et_2O = 9:1 (v/v)]. ^{1}H NMR (250 MHz): δ = 1.86−2.08 (m, 1 H, CH_2), 1.93 (s, 3 H, CH_3), 2.02 (s, 3 H, CH_3), 2.19−2.58 (m, 3 H, CH_2), 3.53 (dd, J = 6.4, 8.2 Hz, 1 H, 2-H), 5.17 (dd, J = 5.8, 8.9 Hz, 1 H, 5-H), 7.23−7.37 (m, 5 H, Ar-H) ppm. ^{13}C NMR (100 MHz): δ = 18.2, 32.2, 33.6, 34.3, 35.7, 81.9 (C-2), 88.8 (C-5), 125.6, 127.2, 128.3, 128.8 ppm.

2-(Nonafluorobutylsulfanyl)pyridine (9, X = C_4F_9): Yield: 152 mg (84%), colorless liquid. ^{1}H NMR (250 MHz): δ = 7.36 (ddd, J = 1.1, 4.8, 7.5 Hz, 1 H, Ar-H), 7.68 (d, J = 7.8 Hz, 1 H, Ar-H), 7.74 (td, J_t = 7.7, J_d = 2.0 Hz, 1 H, Ar-H), 8.66 (dd, J = 1.9, 4.8 Hz, 1 H, Ar-H) ppm. ^{13}C NMR (63 MHz): δ = 124.6, 131.1, 137.6, 147.5, 150.9. ^{13}C NMR (75 MHz, ^{19}F-decoupled): δ = 108.6, 110.2, 117.3, 123.4, 124.6, 131.1, 137.7, 147.3, 150.9 ppm. ^{19}F NMR (565 MHz): δ = −82.4, −87.2, −121.5, −126.9 ppm. MS (70 eV, EI): *m*/*z* (%) = 329 (28) [M^+], 160 (27) [$C_6H_4F_2NS^+$], 78 (100) [$C_5H_4N^+$]. $C_9H_4F_9NS$ (329.2): calcd. C 32.84, H 1.22, N 4.25, S 9.74; found C 33.10, H 1.40, N 4.54, S 9.77.

2-(Iodomethyl)-5-(*p*-biphenylyl)tetrahydrofuran (5d): Application of general procedure 1 [**7d**: 13.8 mg (0.039 mmol), *n*-C_4F_9I: 43.2 mg (0.125 mmol), C_6H_6: 1 mL] provided 5.68 mg of **5d** (40%), *cis*:*trans* = 53:47.

2-(Iodomethyl)-5-(2-naphthyl)tetrahydrofuran (5e): Application of general procedure 1 [**7e**: 15.9 mg (0.049 mmol), $IC_8H_{13}O_4$: 37.0 mg (0.124 mmol), C_6H_6: 1 mL] furnished 11.9 mg of **5e** (72%), *cis*:*trans* = 50:50.

2-(Iodomethyl)-4-phenyltetrahydrofuran (5f): Application of general procedure 1 [**7f**: 228.0 mg (0.840 mmol), $IC_8H_{13}O_4$: 630.0 mg (2.1 mmol), C_6H_6: 12 mL] yielded 174 mg of **5f** (72%), *cis*:*trans* = 13:87.

Diethyl 2-Methyl-2-(2-pyridylsulfany)malonate [9, X = $C(CH_3)(CO_2C_2H_5)_2$]:[35] Yield: 175 mg (73%): colorless liquid. ^{1}H NMR (250 MHz): δ = 1.21 (t, J = 7.0 Hz, 6 H, CH_3), 1.96 (s, 3 H, CH_3), 4.22 (q, J = 7.0 Hz, 4 H, CH_2), 7.02 (m_c, 1 H, CH), 7.26 (m_c, 1 H, CH), 7.50 (m_c, 1 H, CH), 8.35 (m_c, 1 H, CH) ppm. ^{13}C NMR (63 MHz): δ = 13.9, 23.2, 59.9 (C−S), 62.3, 120.6, 124.0, 136.1, 149.1, 156.1, 169.0 (C=O) ppm.

2-(Iodomethyl)-4-(2-naphthyl)tetrahydrofuran (5g): Application of general procedure 1 [**7g**: 21.8 mg (0.068 mmol), $IC_8H_{13}O_4$: 71.2 mg (0.24 mmol), C_6H_6: 1 mL] provided 9.20 mg of **5g** (40%), *cis*:*trans* = 13:87.

2-(Iodomethyl)-3-phenyl tetrahydrofuran (5h): Application of general procedure 1 [**7** ***h*****:** (193 mg, 0.71 mmol), $IC_8H_{13}O_4$: (521 mg, 1.74 mmol), C_6H_6: 10 mL] furnished 148 mg of **5h** (72%), *cis*:*trans* = 3:97.

4.2 Reaction between Bis(homoallylic) Alcohols 1 and Iodine

General Procedure: Iodine (2.25 g, 8.90 mmol) was dissolved in reagent grade CH_3CN. The flask was immersed in an ice bath and a saturated aqueous solution of $NaHCO_3$ (5 mL) was added. Bis(homoallylic) alcohol **1** (5.00 mmol) was added in a dropwise manner. Solid substrates **1** were added in small portions over a period of 10 min. A likewise prepared reaction mixture was stirred for 1 h at 0 °C and for 4 h at 20 °C. Afterwards, the brown reaction mixture was concentrated under reduced pressure to provide a brown oil that was taken up in MTB (40 mL). The organic phase was washed with an aqueous solution of $Na_2S_2O_3$ [10% (w/w), 2 × 10 mL)], H_2O, brine (20 mL each). It was dried ($MgSO_4$) and concentrated under reduced pressure to afford the product, in all instances, as an orange viscous oil, which was purified by column chromatography [SiO_2 petroleum ether/ MTB = 9:1 (v/v)].

***trans*-3-Iodo-2,2-dimethyl-6-phenyltetrahydropyran:** (not shown in the graphics, refer to discussion, section 2). Yield: 0.96 g (62%), colorless crystals, m.p. 52−53 °C, R_f = 0.82 [petroleum ether/ Et_2O = 5:1 (v/v)]. ^1H NMR (250 MHz): δ = 1.49 (s, 3 H, CH_3), 1.61 (s, 3 H, CH_3), 1.66−1.76 (m, 2 H, CH_2), 2.36−2.60 (m, 2 H, CH_2), 4.25 (dd, *J* = 4.9, 12.2 Hz, 1 H, 3-H), 4.73 (m_c, 1 H, 6-H), 7.25−7.34 (m, 5 H, Ar-H) ppm. ^{13}C NMR (63 MHz): δ = 19.5, 31.1, 34.7, 37.7, 37.8, 72.4 (C-6), 75.8 (C-2), 125.8, 127.2, 128.4, 142.6 ppm. MS (70 eV, EI): *m*/*z* (%) = 316 (1) [M^+], 258 (6) [$M^+ - C_3H_6O$], 189 (12) [$M^+ - I$], 131 (31) [$C_{10}H_{11}^+$], 104 (100) [C_8H_8]. $C_{13}H_{17}IO$ (316.2): calcd. C 49.38, H 5.42; found C 49.09, H 5.27.

5-(*p*-Biphenylyl)-2-iodomethyltetrahydrofuran (5d): Yield 1.69 g (93%), tan oil, *cis*:*trans* = 23:77.
***cis*-5d:** R_f = 0.45 (petroleum ether/EtOAc = 9:1 (v/v)], 0.24 g (13%), tan oil. ^1H NMR (250 MHz): δ = 1.86−2.01 (m, 2 H, 4-H, 3-H), 2.18−2.29 (m, 1 H, 3-H), 2.29−2.44 (m, 1 H, 4-H), 3.37 (dd, *J* = 6.4, 9.8 Hz, 1 H, CH_2I), 3.43 (dd, *J* = 4.6, 9.8 Hz, 1 H, CH_2I), 4.20 (m_c, 1 H, 2-H), 5.02 (t, *J* = 6.3 Hz, 1 H, 2-H), 7.21−7.38 (m, 5 H, Ar-H), 7.46−7.52 (m, 4 H, Ar-H) ppm. ^{13}C NMR (63 MHz): δ = 11.1, 32.4 (C-3), 34.8 (C-4), 79.1 (C-2), 82.4 (C-5),126.8, 127.5, 127.6, 127.7, 129.1, 140.9, 141.4, 141.8 ppm. MS (70 eV, EI): *m*/*z* (%) = 364 (14) [M^+], 237 (4) [$M^+ - I$], 181 (100) [$C_6H_5C_6H_4CO^+$]. $C_{17}H_{17}IO$ (364.2): calcd. C 56.06, H 4.70; found C 55.84, H 4.58.
***trans*-5d:** R_f = 0.50 [petroleum ether/EtOAc = 9:1 (v/v)]; 0.73 g (46%); tan oil. ^1H NMR (250 MHz): δ = 1.69−1.83 (m, 1 H, 3-H), 1.83−1.96 (m, 1 H, 4 H), 2.23 (m_c, 1 H, 3 H), 2.36 (m_c, 1 H, 4 H), 3.21 (dd, *J* = 7.3, 9.8 Hz, 1 H, CH_2I), 3.30 (dd, *J* = 4.6, 9.8 Hz, 1 H, CH_2I), 4.26 (ddt, J_d = 4.6, 13.4, J_t = 7.3 Hz, 1 H, 2-H), 5.07 (dd, *J* = 5.8, 8.2 Hz, 1 H, 5-H), 7.21−7.38 (m, 5 H, Ar-H), 7.46−7.52 (m, 4 H, Ar-H) ppm. ^{13}C NMR (63 MHz): δ = 11.4, 33.4 (C-3), 35.8 (C-4), 79.4 (C-2), 81.8 (C-5), 126.5. 127.5, 127.6, 127.7, 129.2, 140.8, 141.3, 142.2 ppm. MS (70 eV, EI): *m*/*z* (%) = 364 (57) [M^+], 55 (100) [$C_4H_7^+$]. $C_{17}H_{17}IO$ (364.2): calcd. C 56.06, H 4.70; found C 55.95, H 4.78.

2-(Iodomethyl)-5-(2-naphthyl)tetrahydrofuran (5e): Yield: 1.45 g (86%), *cis*:*trans* = 27:73, tan oil.
***cis*-5e:** R_f = 0.45 [petroleum ether/EtOAc = 9:1 (v/v)], 0.30 g (18%), tan oil. ^1H NMR (250 MHz): δ = 1.87−2.08 (m, 2 H, 3-H, 4-H), 2.18−2.32 (m, 1 H, 3-H), 2.34−2.45 (m, 1 H, 4-H), 3.39 (dd, *J* = 6.7, 10.1 Hz, 1 H, CH_2I), 3.47 (dd, *J* = 4.6, 10.1 Hz, 1 H, CH_2I), 4.24 (tt, *J* = 4.9, 7.3 Hz, 1 H, 2-H), 5.14 (dd, *J* = 6.4, 7.6 Hz, 1 H, 5-H), 7.44−7.54 (m, 3 H, Ar-H), 7.80−7.87 (m, 4 H, Ar-H) ppm. ^{13}C NMR (63 MHz): δ = 11.1, 32.4 (C-3), 34.8 (C-4), 79.3 (C-2), 82.8 (C-5), 124.5, 124.9, 126.2, 126.5, 128.1, 128.4, 128.6, 133.4, 133.7, 140.2 ppm. MS (70 eV, EI): *m*/*z* (%) = 338 (13) [M^+], 156 (100) [$C_{10}H_7CHO^+$]. $C_{15}H_{15}IO$ (338.2): calcd. C 53.27, H 4.47; found C 53.23, H 4.31.
***trans*-5e:** R_f = 0.50 [petroleum ether/EtOAc = 9:1 (v/v)], 0.79 g (46%), tan oil. ^1H NMR (250 MHz): δ = 1.69−1.82 (m, 1 H, 3-H), 1.82−1.95 (m, 1 H, 4-H), 2.12−2.27 (m, 1 H, 3-H), 2.28−2.42 (m, 1 H, 4-H), 3.20 (dd, *J* = 7.3, 10.1 Hz, 1 H, CH_2I), 3.29 (dd, *J* = 4.6, 10.1 Hz, 1 H, CH_2I), 4.28 (tdd, J_t = 7.3, J_d = 4.6, 6.1 Hz, 1 H, 2-H), 5.16 (dd, *J* = 6.4, 8.2 Hz, 1 H, 5-H), 7.27−7.39 (m, 3 H, Ar-H), 7.66−7.71 (m, 4 H, Ar-H) ppm. ^{13}C NMR (63 MHz): δ = 11.4, 33.3 (C-3), 35.8 (C-4), 79.6 (C-2), 82.1 (C-5), 124.2, 124.5, 126.1, 126.5, 128.1, 128.3, 128.7, 133.3, 133.7, 140.6 ppm. MS (70 eV, EI): *m*/*z* (%) = 338 (51) [M^+], 211 (12) [$M^+ - I$], 155 (45) [$C_{10}H_7CO^+$], 83 (100). $C_{15}H_{15}IO$ (338.2): calcd. C 53.27, H 4.47; found C 53.02, H 4.20.

2-(Iodomethyl)-4-(2-naphthyl)tetrahydrofuran (5g): Yield: 1.62 g (96%), *cis*:*trans* = 82:18, tan oil.
***cis*-5g:** R_f = 0.40 [petroleum ether/EtOAc = 9:1 (v/v)], 1.25 g (74%), tan oil. ^1H NMR (250 MHz): δ = 1.94 (ddd, *J* = 9.2, 10.7, 12.5 Hz, 1 H, 3-H), 2.65 (ddd, *J* = 5.8, 7.3, 12.8 Hz, 1 H, 3-H), 3.40 (dd, *J* = 6.0, 10.1 Hz, 1 H, CH_2I), 3.43 (dd, *J* = 5.2, 10.1 Hz, 1 H, CH_2I), 4.04 (t, *J* = 8.6 Hz, 1 H, 5-H), 4.22 (dq, J_d = 9.5, J_q = 6.1 Hz, 1 H, 2-H), 4.34 (t, *J* = 8.5 Hz, 1 H, 5-H), 7.42 (dd, *J* = 1.8, 8.6 Hz, 1 H, Ar-H), 7.47−7.54 (m, 2 H, Ar-H), 7.70 (m_c, 1 H, Ar-H), 7.79−7.87 (m, 3 H, Ar-H) ppm. ^{13}C NMR (63 MHz): δ = 10.2, 41.1, 45.9, 74.7, 79.2, 125.4, 125.6, 126.1, 127.5, 127.6, 128.3, 132.3, 133.4, 138.3 ppm. MS (70 eV, EI): *m*/*z* (%) = 338 (28) [M^+], 211 (19) [$M^+ - I$], 155 (100) [$C_{10}H_7CO^+$]. $C_{15}H_{15}IO$ (338.2): calcd. C 53.27, H 4.47; found C 53.24, H 4.40.
***trans*-5g:** R_f = 0.43 [petroleum ether/EtOAc = 9:1 (v/v)], 0.29 g (17%), colorless needles, m.p. 85−86 °C. ^1H NMR (250 MHz): δ = 2.31 (m_c, 2 H, 3-H), 3.33−3.36 (m, 2 H, CH_2I), 3.70 (m_c, 1 H, 4-H), 3.97 (dd, *J* = 7.3, 8.5 Hz, 1 H, 5-H), 4.35 (quint, *J* = 6.4 Hz, 1 H, 6-H), 4.41 (dd, *J* = 7.0, 8.6 Hz, 1 H, 5-H), 7.38 (dd, *J* = 1.8, 8.5 Hz, 1 H, Ar-H), 7.44−7.53 (m, 2 H, Ar-H), 7.69 (br. s, 1 H, Ar-H), 7.79−7.86 (m, 3 H, Ar-H) ppm. ^{13}C NMR (63 MHz): δ = 10.6, 39.8, 44.7, 75.0, 78.5, 125.4, 125.5, 125.6, 126.2, 127.5 (2 C), 128.3, 132.2, 133.4, 139.0 ppm. MS (70 eV, EI): *m*/*z* (%) = 338 (64) [M^+], 211 (26) [$M^+ - I$], 155 (100) [$C_{10}H_7CO^+$]. $C_{15}H_{15}IO$ (338.2): calcd. C 53.27, H 4.47; found C 53.15, H 4.43.

2-(Iodomethyl)-4-phenyltetrahydrofuran (5f) [*trans*-**5f**: R_f = 0.65, *cis*-**5f**: R_f = 0.60, petroleum ether/EtOAc = 9:1 (v/v)], and **2-iodomethyl-3-phenyl tetrahydrofuran (5h)** [*cis*-**5h**: R_f = 0.55, *trans*-**5h**: R_f = 0.50, petroleum ether/ EtOAc = 9:1 (v/v)] have been prepared previously.[20,26]

5. Synthesis of Aryl-Substituted Methyltetrahydrofurans 10

General Procedure: LiH (0.10 g, 12.6 mmol) and $LiAlH_4$ (0.25 g, 6.60 mmol) were placed into a three-necked round-bottomed flask containing nitrogen. Anhydrous THF (30 mL) was added followed by a solution of (iodomethyl)tetrahydrofuran **5** (3.00 mmol) in anhydrous THF (5 mL). The reaction mixture was refluxed for 2 h and stirred for 14 h at 20 °C. H_2O was added at 0 °C until no further hydrogen evolved. Precipitated salts were dissolved by ad-

dition of dilute sulfuric acid [10% (v/v)]. The organic phase was separated and the aqueous phase was extracted with MTB (3 × 20 mL). Combined organic phases were washed with an aqueous solution of $Na_2S_2O_3$ [2 × 30 mL, 10% (w/w)], and brine (30 mL). After drying ($MgSO_4$), the organic solvent was removed under reduced pressure to afford in all instances colorless oils which were purified by column chromatography [petroleum ether/MTB 9:1 (v/v)].

***cis*-2-(*p*-Biphenyl-4-yl)-5-methyltetrahydrofuran (*cis*-10d):** Yield: 0.21 g (91%) from 0.36 g of *cis*-**5d** (1.00 mmol), colorless oil. ^{1}H NMR (600 MHz): δ = 1.43 (d, J = 6.1 Hz, 3 H, CH_3), 1.63 (dddd, J = 6.8, 7.3, 9.0, 12.2 Hz, 1 H, 3-H), 1.89 (dddd, J = 6.4, 7.3, 9.2, 12.7 Hz, 1 H, 4-H), 2.11 (ddt, J_d = 8.3, 12.6, J_t = 6.4 Hz, 1 H, 3-H), 2.33 (ddt, J_d = 8.1, 12.6, J_t = 7.1 Hz, 1 H, 4-H), 4.18 (sext, J = 6.2 Hz, 1 H, 2-H), 4.93 (t, J = 7.3 Hz, 1 H, 5-H), 7.32 (m_c, 1 H, Ar-H), 7.41−7.44 (m, 4 H, Ar-H), 7.76 (m_c, 2 H, Ar-H), 7.78 (m_c, 2 H, Ar-H) ppm. ^{13}C NMR (63 MHz): δ = 21.8, 33.6 (C-3), 35.0 (C-4), 76.4 (C-2), 81.2 (C-5), 126.5, 126.8, 127.5, 127.6, 129.2, 140.5, 141.5, 143.1 ppm. MS (70 eV, EI): *m*/*z* (%) = 283 (100) [M^+], 181 (96) [$C_6H_5C_6H_4CO^+$]. $C_{17}H_{18}O$ (238.3): calcd. 85.67, H 7.61; found C 85.44, H 7.56.

***trans*-2-(*p*-Biphenyl-4-yl)-5-methyltetrahydrofuran (*trans*-10d):** Yield: 0.64 g (89%) from 1.10 g of *trans*-**5d** (3.02 mmol), colorless needles (EtOH), m.p. 34−35 °C. ^{1}H NMR (600 MHz): δ = 1.35 (d, J = 6.2 Hz, 3 H, CH_3), 1.55 (dddd, J = 7.6, 8.0, 9.9, 12.4 Hz, 1 H, 3-H), 1.93 (dddd, J = 7.6, 8.2, 9.9, 12.4 Hz, 1 H, 4-H), 2.19 (dddd, J = 3.3, 7.5, 6.0, 12.4 Hz, 1 H, 3-H), 2.43 (dddd, J = 3.3, 6.9, 7.2, 12.4 Hz, 1 H, 4-H), 4.93 (dquint, J_d = 8.1, J_{quint} = 6.0 Hz, 1 H, 2-H), 5.11 (dd, J = 6.8, 7.9 Hz, 1 H, 5-H), 7.32 (m_c, 1 H, Ar-H), 7.43−7.49 (m, 4 H, Ar-H), 7.57−7.69 (m, 4 H, Ar-H) ppm. ^{13}C NMR (63 MHz): δ = 22.0, 34.7 (C-3), 36.0 (C-4), 76.4 (C-2), 80.5 (C-5), 126.5, 127.5, 127.6, 129.2, 140.4, 141.5, 143.5. MS (70 eV, EI): *m*/*z* (%) = 238 (95) [M^+], 181 (100) [$C_6H_5C_6H_4CO^+$]. HRMS $C_{17}H_{18}O$ (238.3): calcd. 238.1358; found 238.1359.

***cis*-2-Methyl-5-(2-naphthyl)tetrahydrofuran (*cis*-10e):** Yield: 0.19 g (90%) from 0.34 g of *cis*-**5e** (1.00 mmol), colorless oil. ^{1}H NMR (600 MHz): δ = 1.44 (d, J = 6.1 Hz, 3 H, CH_3), 1.59−1.75 (m, 1 H, 4-H), 1.87−2.03 (m, 1 H, 3-H), 2.05−2.26 (m, 1 H, 4-H), 2.32−2.52 (m, 1 H, 3-H), 4.24 (dquint, J_d = 7.3, J_{quint} = 6.1 Hz, 1 H, 5-H), 5.07 (t, J = 7.3 Hz, 1 H, 2-H), 7.42−7.52 (m, 3 H, Ar-H), 7.80−7.88 (m, 4 H, Ar-H) ppm. ^{13}C NMR (63 MHz, $CDCl_3$): δ = 21.8, 33.6 (C-3), 35.0 (C-4), 76.6 (C-2), 81.5 (C-5), 124.4, 124.7, 126.0, 126.4, 128.1, 128.3, 128.5, 133.2, 133.7, 141.4 ppm. MS (70 eV, EI): *m*/*z* (%) = 212 (77) [M^+], 155 (100) [$C_{10}H_8CO^+$], 128 (78) [$C_{10}H_8^+$]. $C_{15}H_{16}O$ (212.3): calcd. C 84.87, H, 7.60; found C 84.58, H 7.35.

***trans*-2-Methyl-5-(2-naphthyl)tetrahydrofuran (*trans*-10e):** Yield: 0.56 g (84%) from 1.06 g of *trans*-**5e** (3.14 mmol), colorless oil. ^{1}H NMR (600 MHz): δ = 1.38 (d, J = 6.1 Hz, 3 H, CH_3), 1.68 (ddt, J_d = 10.2, 12.1, J_t = 7.6 Hz, 1 H, 3-H), 1.96 (dddd, J = 7.6, 8.2, 10.0, 12.4 Hz, 1 H, 4-H), 2.20 (dddd, J = 3.4, 6.0, 7.5, 12.1 Hz, 1 H, 3-H), 2.46 (dddd, J = 3.2, 6.8, 7.3, 12.5 Hz, 1 H, 4-H), 4.45 (dquint, J_d = 8.0, J_{quint} = 6.0 Hz, 1 H, 2-H), 5.22 (t, J = 7.5 Hz, 1 H, 5-H), 7.43−7.48 (m, 3 H, Ar-H), 7.81−7.83 (m, 4 H, Ar-H) ppm. ^{13}C NMR (63 MHz): δ = 22.1, 34.7 (C-3), 36.0 (C-4), 76.5 (C-2), 80.8 (C-5), 124.3, 124.5, 126.0, 126.4, 128.1, 128.3, 128.6, 133.2, 133.8, 141.9 ppm. MS (70 eV, EI): *m*/*z* (%) = 212 (100) [M^+], 155 (72) [$C_{10}H_8CO^+$]. $C_{15}H_{16}O$ (212.3): calcd. C 84.87, H 7.60; found C 84.77, H 7.62.

***cis*-2-Methyl-4-phenyltetrahydrofuran (*cis*-10f):**[20] Yield: 0.37 g (75%) from 0.86 g of *cis*-**5f** (2.00 mmol), colorless liquid. ^{1}H NMR (600 MHz): δ = 1.36 (d, J = 6.1 Hz, 3 H, CH_3), 1.63 (dt, J_t = 9.9, J_d = 12.3 Hz, 1 H, 3-H), 2.46 (ddd, J = 5.4, 7.7, 12.6 Hz, 1 H, 3-H), 3.47 (dq, J_d = 10.1, J_q = 7.9 Hz, 1 H, 4-H), 3.84 (t, J = 8.0 Hz, 1 H, 5-H), 4.13 (t, J = 8.0 Hz, 1 H, 5-H), 4.14 (dquint, J_d = 9.7, J_{quint} = 6.0 Hz, 1 H, 2-H), 7.19−7.37 (m, 5 H, Ph-H) ppm. ^{13}C NMR (63 MHz): δ = 21.3, 43.3 (C-3), 46.4 (C-4), 74.8 (C-5), 77.0 (C-2), 126.9, 127.6, 129.0, 143.3.

***trans*-2-Methyl-4-phenyltetrahydrofuran (*trans*-10f):**[20] Yield: 71.9 mg (44%) from 288 mg of *trans*-**5f** (1.00 mmol), colorless liquid. ^{1}H NMR (600 MHz): δ = 1.30 (d, J = 6.2 Hz, 3 H, CH_3), 1.97 (ddd, J = 6.3, 9.0, 12.5 Hz, 1 H, 3-H), 2.14 (dt, J_d = 12.5, J_t = 7.1 Hz, 1 H, 3-H), 3.47 (quint, J = 7.5 Hz, 1 H, 4-H), 3.70 (t, J = 7.3 Hz, 1 H, 5-H), 4.26 (dd, J = 7.6, 8.0 Hz, 1 H, 5-H), 4.30 (sext, J = 6.3 Hz, 1 H, 2-H), 7.21 (m_c, 1 H, Ph-H), 7.24−7.26 (m, 2 H, Ph-H), 7.31 (m_c, 1 H, Ph-H) ppm. ^{13}C NMR (63 MHz): δ = 22.1, 41.8 (C-3), 45.2 (C-4), 74.8 (C-5), 75.5 (C-2), 126.8, 127.7, 129.0, 143.1 ppm.

***cis*-2-Methyl-4-(2-naphthyl)tetrahydrofuran (*cis*-10g):** Yield: 0.55 g (86%) from 1.01 g of *cis*-**5g** (3.00 mmol), colorless liquid. ^{1}H NMR (600 MHz): δ = 1.44 (d, J = 6.1 Hz, 3 H, CH_3), 1.75 (dt, J_d = 12.2, J_t = 9.8 Hz, 1 H, 3-H), 2.54 (ddd, J = 5.5, 7.6, 12.5 Hz 1 H, 3-H), 3.66 (dq, J_d = 9.5, J_q = 7.9 Hz, 1 H, 4-H), 4.00 (t, J = 8.6 Hz, 1 H, 5-H), 4.21 (dquint, J_d = 9.5, J_{quint} = 5.8 Hz, 1 H, 2-H), 4.24 (t, J = 7.9 Hz, 1 H, 5-H), 7.42−7.54 (m, 3 H, Ar-H), 7.71 (br. s, 1 H, Ar-H), 7.81−7.87 (m, 3 H, Ar-H) ppm. ^{13}C NMR (63 MHz): δ = 20.8, 42.8 (C-3), 45.9 (C-4), 74.2 (C-5), 75.4 (C-2), 125.4, 125.5, 126.0, 127.5, 127.6, 128.3, 132.2, 133.4, 140.4 ppm. MS (70 eV, EI): *m*/*z* (%) = 212 (52) [M^+], 167 (100) [$C_{10}H_7C_3H_4^+$], 128 (17) [$C_{10}H_8^+$]. $C_{15}H_{16}O$ (212.3): calcd. C 84.87, H, 7.60; found C 85.08, H 7.86.

***trans*-2-Methyl-4-(2-naphthyl)tetrahydrofuran (*trans*-10g):** Yield: 0.15 g (77%) from 0.31 g of *trans*-**5g** (0.92 mmol), colorless liquid. ^{1}H NMR (600 MHz): δ = 1.38 (d, J = 6.1 Hz, 3 H, CH_3), 2.06 (ddd, J = 6.4, 8.1, 12.5 Hz, 1 H, 4-H), 2.27 (dt, J_d = 12.5, J_t = 7.0 Hz, 1 H, 4-H), 3.67 (quint, J = 7.3 Hz, 1 H, 3-H), 3.87 (t, J = 8.5 Hz, 1 H, 2-H), 4.37 (dd, J = 7.3, 8.6 Hz, 1 H, 2-H), 4.44 (sext, J = 6.4 Hz, 1 H, 5-H), 7.42 (dd, J = 1.8, 8.6 Hz, 1 H, Ar-H), 7.45−7.54 (m, 2 H, Ar-H), 7.71 (d, J = 0.9 Hz, 1 H, Ar-H), 7.80−7.88 (m, 3 H, Ar-H) ppm. ^{13}C NMR (63 MHz): δ = 21.6, 41.3 (C-3), 44.8 (C-4), 74.5 (C-5), 75.4 (C-2), 125.4, 125.5, 125.7, 126.0, 127.4, 127.5, 128.2, 132.2, 133.4, 140.1 ppm. MS (70 eV, EI): *m*/*z* (%) = 212 (26) [M^+], 167 (66) [$C_{10}H_7C_3H_4^+$], 154 (100) [$C_{10}H_7C_2H_3^+$],128 (24) [$C_{10}H_8^+$]. $C_{15}H_{16}O$ (212.3): calcd. C 84.87, H, 7.60; found C 84.33, H 7.28.

***cis*-2-Methyl-3-phenyltetrahydrofuran (*cis*-10h):**[39b] Yield: 90.8 mg (56%) from 288 mg of *cis*-**5h** (1.00 mmol), colorless liquid. ^{1}H NMR (600 MHz): δ = 0.84 (d, J = 6.4 Hz, 3 H, CH_3), 2.18 (dddd, J = 5.7, 7.8, 8.8, 13.1 Hz, 1 H, 4-H), 2.38 (ddt, J_d = 4.4, 12.8, J_t = 8.4 Hz, 1 H, 4-H), 3.33 (dt, J_d = 8.3, J_t = 6.2 Hz, 1 H, 3-H), 3.86 (dt, J_d = 8.5, J_t = 7.9 Hz, 1 H, 5-H), 4.15 (quint, J = 6.4 Hz, 1 H, 2-H), 4.16 (td, J_t = 8.7, J_d = 4.4 Hz, 1 H, 5-H), 7.21−7.25 (m, 5 H, Ph-H) ppm. ^{13}C NMR (63 MHz): δ = 17.3, 33.2 (C-4), 48.8 (C-3), 67.4 (C-5), 78.6 (C-2), 126.7, 128.6, 128.8. 142.2 ppm.

***trans*-2-Methyl-3-phenyltetrahydrofuran (*trans*-10h):**[39b] Yield: 0.44 g (91%) from 0.86 (3.00 mmol) *trans*-**5h**; colorless liquid. ^{1}H NMR (600 MHz): δ = 1.22 (d, J = 6.0 Hz, 3 H, CH_3), 2.13 (dddd, J = 7.9, 8.1, 9.5, 12.5 Hz, 1 H, 4-H), 2.39 (dddd, J = 5.6, 6.7, 8.5, 12.5 Hz, 1 H, 4-H), 2.80 (q, J = 8.7 Hz, 1 H, 3-H), 3.87 (dq, J_d = 8.7, J_q = 6.1 Hz, 1 H, 2-H), 4.02 (dd, J = 5.4, 8.0 Hz, 1 H, 5-H), 4.03 (dd, J = 6.7, 7.1 Hz, 1 H, 5-H), 7.21−7.25 (m, 5 H, Ph-H)

ppm. ^{13}C NMR (63 MHz): δ = 19.4, 35.9 (C-4), 53.4 (C-3), 67.8 (C-5), 82.6 (C-2), 127.1, 128.0, 129.0, 142.0 ppm.

6. Preparation of 2-Alkylsulfanylpyridine N-oxides 11

6.1 *N*-Hydroxypyridine-2(1*H*)-thione Potassium Salt[64]

A round-bottomed flask was charged with *N*-hydroxypyridine-2(1*H*)-thione[28b] (10.74 g, 0.084 mol) and 95% aqueous EtOH (50 mL). A solution of KOH (4.74 g, 0.084 mol) in EtOH (50 mL) was added at 20 °C and stirring was continued for 15 min. All volatiles were removed under reduced pressure to afford a colorless oil which was freeze dried. The colorless powder was dissolved in a minimum volume of anhydrous EtOH (20 °C). Anhydrous diethyl ether was added at 20 °C until the faint cloudiness no longer disappeared. The flask was stoppered and kept at 5 °C for 14 h whereupon *N*-hydroxypyridine-2(1*H*)-thione potassium salt precipitated. Yield: 12.19 g (88%), colorless needles, ^1H NMR (200 MHz, CD_3OD): δ = 6.76 (ddd, *J* = 2.0, 7.1, 8.7 Hz, 1 H, 5-H), 7.02 (td, J_t = 8.3, J_d = 1.4 Hz, 1 H, 4-H), 7.56 (dd, *J* = 1.8, 8.3 Hz, 1 H, 3-H), 8.05 (d, *J* = 6.6 Hz, 1 H, 6-H) ppm. ^{13}C NMR (50 MHz, CD_3OD): δ = 116.9, 128.4, 134.0, 139.6, 168.0 ppm. C_5H_4KNOS (165.6): calcd. C 36.34, H 2.44, N 8.48, S 19.40; found C 36.18, H 2.24, N 8.43, S 19.24.

6.2 2-Alkylsulfanylpyridine *N*-oxides 11

N-Hydroxypyridine-2(1*H*)-thione potassium salt (0.58 g, 3.50 mmol) and alkyl iodide **5** (3.50 mmol) were dissolved in anhydrous DMF (20 mL) at 20 °C. The reaction mixture was stirred for 24 h at room temperature (20 °C) and was then poured into 2 N aqueous NaOH (20 mL). This mixture was extracted with CH_2Cl_2 (3 × 20 mL) and the combined organic phases were washed with H_2O (2 × 20 mL), saturated aqueous $NaHCO_3$ (20 mL) and brine (20 mL). A clear yellowish solution was obtained, which was dried ($MgSO_4$) and concentrated under reduced pressure. The remaining oil was purified by adsorptive filtration through a short pad of silica gel. MTB was used as eluent to wash off a minor yellowish impurity. Subsequently, pyridine *N*-oxides **11** were eluted from this column using acetone (R_f = 0.35−0.40). Heterocycles **11** were recrystallized from CH_2Cl_2/MTB.

***cis*-2-({[5-(2-Naphthyl)tetrahydrofuran-2-yl]methyl}sulfanyl]pyridine *N*-Oxide (*cis*-11e):** Yield: 0.97 g (82%), colorless block-shaped crystals, m.p. 106−107 °C. ^1H NMR (250 MHz): δ = 1.88−2.07 (m, 2 H, 3-H, 4-H), 2.13−2.30 (m, 1 H, 3-H), 2.30−2.45 (m, 1 H, 4-H), 3.15 (dd, *J* = 7.0, 13.1 Hz, 1 H, 6-H), 3.29 (dd, *J* = 4.6, 13.1 Hz, 6-H), 4.40 (m_c, 1 H, 2-H), 5.04 (t, *J* = 7.0 Hz, 1 H, 5-H), 6.99 (ddd, *J* = 1.8, 6.4, 8.2 Hz, 1 H, 5′-H), 7.16 (dt, J_d = 1.2, J_t = 8.2 Hz, 1 H, 4′-H), 7.31 (dd, *J* = 1.5, 8.2 Hz, 1 H, 3′-H), 7.38−7.47 (m, 3 H, Ar-H), 7.75−7.81 (m, 4 H, Ar-H), 8.24 (dt, J_d = 6.4, J_t = 0.6 Hz, 1 H, 6′-H) ppm. ^{13}C NMR (63 MHz): δ = 31.5 (C-3), 34.4 (C-4), 36.0, 77.9 (C-2), 82.3 (C-5), 120.9, 122.3, 124.4, 124.8, 126.0, 126.2, 126.5, 128.1, 128.3, 128.6, 133.3, 133.6, 139.1, 139.9, 152.5 (C-5) ppm. MS (70 eV, EI): *m*/*z* (%) = 337 (1) [M^+], 320 (8) [M^+ − OH], 211 (89) [M^+ − C_5H_4NOS], 210 (100) [M^+ − C_5H_5NOS]. $C_{20}H_{19}NO_2S$ (337.4): calcd. C 71.19, H 5.68, N 4.15, S 9.50; found C 70.86, H 5.79, N 4.05, S 9.40.

***trans*-2-({[5-(2-Naphthyl)tetrahydrofuran-2-yl]methyl}sulfanyl]-pyridine *N*-Oxide (*trans*-11e):** Yield: 0.89 g (75%), colorless block-shaped crystals, m.p. 155−156 °C. ^1H NMR (250 MHz): δ = 1.89−2.13 (m, 2 H, 3-H, 4-H), 2.22−2.36 (m, 1 H, 3-H), 2.41−2.54 (m, 1 H, 4-H), 3.14 (dd, *J* = 6.7, 12.8 Hz, 1 H, 6-H), 3.25 (dd, *J* = 4.9, 12.8 Hz, 1 H, 6-H), 4.61 (qd, J_q = 6.7, J_d = 4.9 Hz, 1 H, 2-H), 5.21 (t, *J* = 7.3 Hz, 1 H, 5-H), 7.00 (ddd, *J* = 1.8, 6.7, 8.2 Hz, 1 H, 5′-H), 7.19 (dt, J_t = 8.2, J_d = 1.0 Hz, 1 H, 4′-H), 7.32 (dd, *J* = 1.8, 8.5 Hz, 1 H, 3′-H), 7.36−7.49 (m, 3 H, Ar-H), 7.74−7.81 (m, 4 H, Ar-H), 8.23 (dd, *J* = 0.9, 6.5 Hz, 1 H, 6′-H) ppm. ^{13}C NMR (63 MHz): δ = 32.3 (C-3), 35.5 (C-4), 36.3, 78.1 (C-2), 81.8 (C-5), 120.9, 122.2, 124.2, 124.5, 126.1, 126.2, 126.5, 128.1, 128.3, 128.6, 133.2, 133.6, 139.1, 140.6, 152.5 (C-5) ppm. MS (70 eV, EI): *m*/*z* (%) = 320 (100) [M^+ − OH], 210 (17) [M^+ − C_5H_5NOS]. $C_{20}H_{19}NO_2S$ (337.4): calcd. C 71.19, H 5.68, N 4.15, S 9.41; found C 70.93, H 5.75, N 4.12, S. 9.41.

***cis*-2-{[(4-Phenyltetrahydrofuran-2-yl)methyl]sulfanyl}pyridine *N*-Oxide (*cis*-11f):** 0.92 g (91%), colorless needles, m.p. 88−89 °C. ^1H NMR (250 MHz): δ = 1.95 (ddd, *J* = 9.5, 10.4, 12.5 Hz, 1 H, 3-H), 2.56 (ddd, *J* = 5.5, 7.3, 12.8 Hz, 1 H, 3-H), 3.15 (dd, *J* = 6.4, 12.8 Hz, 1 H, 6-H), 3.25 (dd, *J* = 4.9, 12.8 Hz, 1 H, 6-H), 3.49 (tt, *J* = 7.6, 10.7 Hz, 1 H, 4-H), 3.83 (t, *J* = 8.5 Hz, 1 H, 5-H), 4.17 (t, *J* = 7.9 Hz, 1 H, 5-H), 4.37 (dq, J_d = 9.5, J_q = 5.5 Hz, 1 H, 2-H), 7.03 (dt, J_d = 2.1, J_t = 7.3 Hz, 1 H, 5′-H), 7.17−7.33 (m, 7 H, Ar-H), 8.22 (d, *J* = 6.1 Hz, 1 H, 6′-H) ppm. ^{13}C NMR (63 MHz): δ = 36.0, 40.5 (C-3), 45.9 (C-4), 75.1 (C-5), 78.4 (C-2), 120.9, 122.7, 126.0, 127.2, 127.6, 129.1, 139.1, 141.1, 152.4 (C-5) ppm. MS (70 eV, EI): *m*/*z* (%) = 287 (4) [M^+], 270 (20) [M^+ − OH], 161 (79) [M^+ − C_5H_5NOS], 127 (100) [$C_5H_5NOS^+$]. $C_{16}H_{17}NO_2S$ (287.4): calcd. C 66.87, H 5.96, N 4.87, S 11.16; found C 66.77, H 5.92, N 4.82, S 10.96.

***cis*-2-({[5-(2-Naphthyl)tetrahydrofuran-2-yl]methyl}sulfanyl)pyridine *N*-Oxide (*cis*-11g):** 1.02 g (86%), colorless needles, m.p. 105−106 °C. ^1H NMR (250 MHz): δ = 1.99 (ddd, *J* = 9.5, 10.4, 12.5 Hz, 1 H, 3-H), 2.58 (ddd, *J* = 5.8, 7.6, 12.8 Hz, 1 H, 3-H), 3.11 (dd, *J* = 6.4, 12.8 Hz, 1 H, 6-H), 3.21 (dd, *J* = 5.2, 12.8 Hz, 1 H, 6′-H), 3.60 (dq, J_q = 7.9, J_d = 10.1 Hz, 1 H, 4-H), 3.89 (t, *J* = 8.6 Hz, 1 H, 5-H), 4.18 (t, *J* = 8.2 Hz, 1 H, 5-H), 4.35 (dq, J_d = 9.5, J_q = 5.8 Hz, 1 H, 2-H), 6.96 (ddd, *J* = 1.8, 6.4, 8.2 Hz, 1 H, 5′-H), 7.14 (dt, J_t = 8.6, J_d = 1.2 Hz, 1 H, 4′-H), 7.31 (dd, *J* = 1.8, 8.2 Hz, 1 H, 3′-H), 7.32−7.42 (m, 3 H, Ar-H), 7.60 (br. s, 1 H, Ar-H), 7.65−7.70 (m, 3 H, Ar-H), 8.24 (d, *J* = 6.1 Hz, 1 H, 6′-H) ppm. ^{13}C NMR (63 MHz): δ = 35.9, 40.1 (C-3), 45.5 (C-4), 74.5 (C-5), 77.9 (C-2), 120.5, 121.8, 125.3, 125.5 (2 C), 125.6, 126.2, 127.4, 127.5, 128.4, 132.3, 133.3, 138.4, 138.7 (C-6′), 151.9 (C-2′) ppm. MS (70 eV, EI): *m*/*z* (%) = 337 (8) [M^+], 320 (25) [M^+ − OH], 211 (100) [M^+ − C_5H_5NOS], 127 (88) [$C_5H_5NOS^+$]. $C_{20}H_{19}NO_2S$ (337.44): calcd. C 71.19, H 5.68, N 4.15, S 9.50; found C 70.98, H 5.86, N 4.10, S 9.32.

***trans*-2-{[(3-Phenyltetrahydrofuran-2-yl)methyl]sulfanyl}pyridine *N*-Oxide (*trans*-11h):** Yield: 0.82 g (82%), colorless needles, m.p. 115−116 °C. ^1H NMR (250 MHz): δ = 2.15 (dq, J_d = 12.5, J_q = 8.2 Hz, 1 H, 4-H), 2.39 (dddd, *J* = 4.9, 7.0, 8.2, 12.8 Hz, 1 H, 4-H), 2.96 (dd, *J* = 5.8, 13.4 Hz, 1 H, 6-H), 3.16 (dd, *J* = 3.7, 13.4 Hz, 1 H, 6-H), 3.27 (q, *J* = 9.2 Hz, 1 H, 3-H), 3.94−4.08 (m, 2 H, 5-H), 4.13 (ddd, *J* = 3.7, 5.5, 8.9 Hz, 1 H, 2-H), 6.93−7.02 (m, 1 H, Ar-H), 7.07−7.14 (m, 2 H, Ar-H), 7.18−7.35 (m, 5 H, Ar-H), 8.17 (d, *J* = 6.1 Hz, 1 H, 6′-H) ppm. ^{13}C NMR (63 MHz): δ = 34.1, 35.5 (C-4), 50.3 (C-3), 68.7 (C-5), 84.6 (C-2), 120.7, 122.3, 125.9, 127.5, 128.1, 129.3, 139.0, 140.8, 152.7 (C-5′) ppm. MS (70 eV, EI): *m*/*z* (%) = 287 (4) [M^+], 270 (7) [M^+ − OH], 161 (100) [M^+ − C_5H_5NOS]. $C_{16}H_{17}NO_2S$ (287.4): calcd. C 66.87, H 5.96, N 4.87, S 11.16; found C 66.57, H 5.97, N 4.79, S 10.95.

7. X-ray Crystallographic Study

Suitable crystals were obtained by slowly cooling a concentrated solution of *trans*-**10d** in EtOH, *cis*-**11g** in methanol or by slowly condensing MTB into acetone/CH_2Cl_2 solutions of *trans*-**11e** or *cis*-

Table 7. Crystallographic data for tetrahydrofurans *trans*-**10d**, *cis*-**11e**, *trans*-**11e**, *cis*-**11f**, *cis*-**11g**, *trans*-**11h**[a]

	trans-**10d**	*trans*-**11e**	*cis*-**11e**	*cis*-**11f**	*cis*-**11g**	*trans*-**11h**
Empirical formula	$C_{17}H_{18}O$	$C_{20}H_{19}NO_2S$	$C_{20}H_{19}NO_2S$	$C_{16}H_{17}NO_2S$	$C_{20}H_{19}NO_2S$	$C_{16}H_{17}NO_2S$
Molecular mass	238.35	337.46	337.46	287.40	337.46	287.40
Temperature [K]	293(2)	299(2)	299(2)	303(2)	304(2)	300(2)
Wavelength [Å]	0.71093	0.71093	0.71093	0.71093	0.71093	0.71093
Crystal system	monoclinic	monoclinic	monoclinic	triclinic	orthorhombic	monoclinic
Space group	*C*2	$P2_1/n$	$P2_1/n$	$P-1$	*P*bca	$P2_1/c$
a (Å)	16.731(4)	6.510(3)	9.401(3)	5.869(3)	8.772(4)	5.816(2)
b (Å)	5.800(2)	8.507(2)	6.515(3)	9.032(2)	17.828(8)	8.930(2)
c (Å)	14.801(4)	30.452(8)	27.791(3)	14.128(2)	22.041(6)	27.524(5)
α (°)	90	90	90	100.88(1)	90	90
β (°)	108.49(2)	92.10(2)	99.25(2)	97.02(2)	90	91.81(2)
γ (°)	90	90	90	98.57(3)	90	90
Volume (Å^3)	1362.1(7)	1685(1)	1680.0(6)	718.5(4)	3447(2)	1428.8(6)
Z	4	4	4	2	8	4
Absorption coeff. (mm^{-1})	0.066	0.196	0.196	0.215	0.157	0.215
ρ calcd. (g cm^{-1})	1.162	1.330	1.334	1.328	1.301	1.336
F (000)	512	712	712	304	1424	608
Crystal size (mm)	0.75 × 0.10 × 0.05	0.55 × 0.20 × 0.10	0.5 × 0.2 × 0.1	0.80 × 0.13 × 0.05	0.70 × 0.33 × 0.14	0.80 × 0.22 × 0.22
Θ range (°)	1.45−22.99	1.34−22.99	1.49−22.98	1.49−25.97	1.85−25.97	1.48−22.98
Index ranges	$-18 \le h \le 18$	$-7 \le h \le 3$	$-10 \le h \le 3$	$-7 \le h \le 3$	$-10 \le h \le 1$	$-6 \le h \le 6$
	$0 \le k \le 6$	$-9 \le k \le 0$	$-7 \le k \le 0$	$-11 \le k \le 11$	$-21 \le k \le 0$	$-9 \le k \le 0$
	$-16 \le l \le 16$	$-33 \le l \le 33$	$-30 \le l \le 30$	$-17 \le l \le 17$	$-27 \le l \le 10$	$-30 \le l \le 30$
Reflections collected	2133	3582	3312	4420	3528	3984
Independent reflections	1069	2330	2335	2821	3373	1995
Data/restraints/param.	1069/1/176	2318/0/218	2333/0/275	2821/0/182	2132/0/217	1995/0/182
Goodness-of-fit on F^2	1.094	1.217	1.036	1.072	1.045	1.082

[a] All data were collected on an Enraf Nonius CAD4 four circle diffractometer using Mo-K_α radiation. No absorption corrections were applied. The structures were solved with either SHELXS-86[65] (all but *cis*-**11f**) or SHELXS-97 (*cis*-**11f**)[66] and refined with SHELXL-93[67] (all but *cis*-**11f**) or SHELXL-97[68] (*cis*-**11f**). All hydrogen atoms were positioned geometrically. Thermal ellipsoids graphics were obtained from ORTEP-III.[69]

11g, or by condensing cyclohexane in an EtOAc solution of *trans*-**11h** at 20 °C. Further details can be found in Table 7.

CCDC-203365 (*trans*-**10d**), -203367 (*cis*-**11e**), -203366 (*trans*-**11e**), -203368 (*cis*-**11f**), -203370 (*cis*-**11g**) and -203369 (*trans*-**11h**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge at www.ccdc.cam.ac.uk/conts/retrieving.html [or from the Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge CB2 1EZ, UK; Fax: (internat.) +44-1223/336-033; E-mail: deposit@ccdc.cam.ac.uk].

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[1] The configuration of all compounds, which are depicted in the Tables, Schemes, and Figures refer to their relative configuration, since the present investigation had been conducted with racemic compounds. The indexing of compounds **1**−**12** refers to the substituent pattern that is defined in Table 1. The atom numbering of substituted tetrahydrofurans follows, unless otherwise noted, IUPAC convention. However, documentation of data from X-ray diffraction studies are consistent with the labeling that is outlined in Figure 2. For sake of clarity, the numbering of compounds **11** has been adapted in this case to that of *trans*-**10d**. The following abbreviations have been used: Bp = *p*-biphenylyl; DABCO = 1,4-diazabicyclo[2.2.2]octane; DTA = differential thermal analysis; NBS = *N*-bromosuccinimide; MTB = *tert*-butyl methyl ether; Np = 2-naphthyl.

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