3.28 (br s, 4 H, methine and methoxy); ^{2}H NMR (46 MHz, $CDCl_3$) δ 0.56, 1.24, 3.28, ratio 1:5:2.2; GC-MS (70 eV) m/z (relative intensity) no parent, 146 (0.5), 145 (3), 144 (7), 128 (3), 117 (18), 116 (29), 115 (20), 100 (10), 99 (8), 90 (10), 89 (100), 75 (24), 73 (11), 72 (60), 59 (63), 58 (12), 45 (21), 44 (13), 43 (34).

Acknowledgment. Partial support of this research by the Office of Research Support, Marquette University, and the donors of the Petroleum Research Fund, administered by the American Chemical Society, are gratefully acknowledged. We also thank the National Science Foundation (Grant CHE-8905465) for financial support for the purchase of a 300-MHz NMR spectrometer.

Supplementary Material Available: Syntheses of chlorosilane reactants, dimethyl(2,2,2-trifluoroethoxy)(2-propenyl)silane, and 1,1-dimethyl-1-silacyclohexan-3-ol (28), oxymercuration of silacyclopentene 9 and silacyclohexene 10 in 2,2,2-trifluoroethanol, details of photolyses and spectral data for deuterated solvents, sensitized photolyses in 2,2,2-trifluoroethanol, and tables of ratios of product yields, $\%P_i$, to total yields, $\Sigma\%P_i$, for 214-nm photolyses of 1,1-dimethylsilacyclopent-2-ene (9) and 1,1-dimethylsilacyclohex-2-ene (10) in methanol, 2,2,2-trifluoroethanol, and *tert*-butyl alcohol (17 pages). Ordering information is given on any current masthead page.

Electronic Control of Face Selection in the [3,3] Sigmatropic Rearrangement of Allyl Vinyl Sulfoxides

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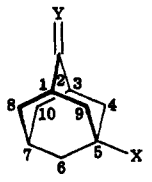
A study has been made of the thermal rearrangement of adamantylidenemethyl allyl sulfoxide 4 as well as of the racemic *RR,SS* and *RS,SR* 5-fluoro diastereomers 8 at 80 °C. The parent compound 4 initially gives a mixture of the (*E*)- and (*Z*)-sulfines 5; the *E* product subsequently isomerizes, more slowly but completely, to the *Z* compound. Under the same conditions, mixtures of the diastereomers 8 produce mixtures of four mesoforms, two of which ((*EE*)- and (*ZE*)-9) subsequently rearrange further to the other two ((*EZ*)- and (*ZZ*)-9). The configurations of the starting materials and products were determined by NMR methods. A study of the rates of these various processes made it possible to define the compositions of the sulfine mixtures that form initially from sulfoxides 8. The conclusion is that both a steric and an electronic effect are operating simultaneously to influence the stereochemistry. The steric effect is a response to the need to avoid axial oxygen in the pseudo-chair transition state; the electronic effect favors the formation of a CC bond antiperiplanar to the more electron-rich vicinal bonds. As was the case in the oxy-Cope reaction studied earlier, the steric effect is the larger of the two by a small margin.

Introduction

Recent studies of face selection in pericyclic reactions have strongly suggested that carbon–carbon bond formation in these processes is characterized by the same preference observed in nucleophilic addition to cations and carbonyl groups, in electrophilic attack on olefins, and in atom abstraction by radicals: approach antiperiplanar to the more electron-rich vicinal bond(s) is favored.[1] Our own contributions in this area have depended primarily on the use of 2,5-disubstituted adamantanes 1 as probes; steric equivalence of the two faces and conformational rigidity are among the advantages possessed by these molecules.



1

The oxy-Cope rearrangement was the first example of a sigmatropic shift to be examined in this fashion.[2] Both the (racemic) diastereomers (*RR*)- and (*RS*)-2 were studied. Each gives a mixture of (*E*)- and (*Z*)-3, the former in the ratio of 36:64 and the latter in the ratio of 81:19, respectively. The reason for the difference in ratio is that in the former the electronically favored face (syn to the fluorine) can only be achieved in a chair transition state with a pseudoaxial phenyl group, whereas in the latter this state has the phenyl group in the pseudoequatorial position. Thus, the steric and electronic factors are opposed in the rearrangement of (*RR*)-2, while in (*RS*)-2 they operate in unison. The steric factor is somewhat stronger than the electronic one in this instance.

Another sigmatropic rearrangement that drew our attention was Corey's thia-Claisen rearrangement, which appears to hold considerable promise as a way to replace a carbonyl oxygen by two carbon appendages.[3] Furthermore, a modification introduced by Block (use of sulfoxides) allows the rearrangement to be carried out under exceptionally mild conditions.[4] We therefore decided to extend our stereochemical investigations to include this reaction.

Results and Discussion

As in the oxy-Cope reactions, the racemic parent compound 4 has two pathways available for rearrangement:

[†] Stony Brook.
[‡] Buffalo.

(1) For references to our earlier work, see: Bodepudi, V. R.; le Noble, W. J. *J. Org. Chem.* **1991**, *56*, 2001.
(2) Lin, M.-h.; le Noble, W. J. *J. Org. Chem.* **1989**, *54*, 997; *Ibid.* **1990**, *55*, 3597.
(3) Corey, E. J.; Shulman, J. I. *J. Am. Chem. Soc.* **1970**, *92*, 5522.
(4) Block, E.; Ahmed, S. *J. Am. Chem. Soc.* **1985**, *107*, 6731.

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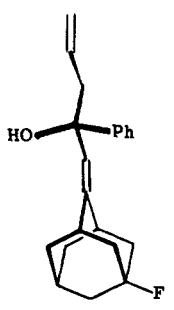
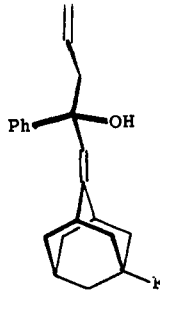
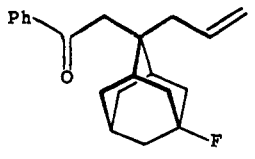


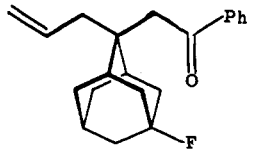
RR-2



RS-2



E-3



Z-3

the pseudo-chair transition state has either an axial or an equatorial oxygen atom linked to the sulfur (see Scheme I; 4 is arbitrarily shown as the *R*-enantiomer). However, there is also an important difference: in the present case, the two transition states give products which are not merely conformationally different but which are geometric isomers 5. Under the conditions of their formation, one of these isomers (*E*) further rearranges into the other (*Z*), as had already been described by Block.[4]

The published approach to 4[4] and its sulfide precursor[3] proved less convenient[5] in our hands than the application of Harpp's synthesis of vinyl sulfides.[6] The products (*E*)- and (*Z*)-5 are readily separated by means of column chromatography. The assignment of their ^{13}C NMR signals (necessary to determine configurations of the 5-F-substituted products, see below) rested in part on chemical shifts and APT experiments. The important distinctions between $C_{4,9}$ and $C_{8,10}$ as well as C_5 and C_7 were evident from the response of these signals to the addition of controlled amounts of the shift reagent Eu(fod)$_3$: the carbon atoms proximal to the oxygen atoms had substantially larger induced shifts than the distal ones.

The first-order rate constants ($k_1 + k_2$) and k_3 were readily evaluated by following the rate of disappearance of 4 in the sigmatropic shift and that of (*E*)-5 in the sulfur inversion reaction. These reactions were done at 80.0 °C in CD_3CN solvent; the ^1H NMR peaks of 4 at δ 5.816, of (*E*)-5 at δ 8.810, and of (*Z*)-5 at δ 7.326 were used, with DMF as the standard (Figure 1). The individual constants k_1 and k_2 can be obtained by means of simplex regression analysis of eq 1. The results are given in Table I; the

$$\frac{[(E)\text{-}5]}{[4]_0} = \frac{k_1}{k_1 + k_2 - k_3}[e^{-k_3 t} - e^{-(k_1+k_2)t}] \qquad (1)$$

degree to which these constants fit the observations may

Scheme I

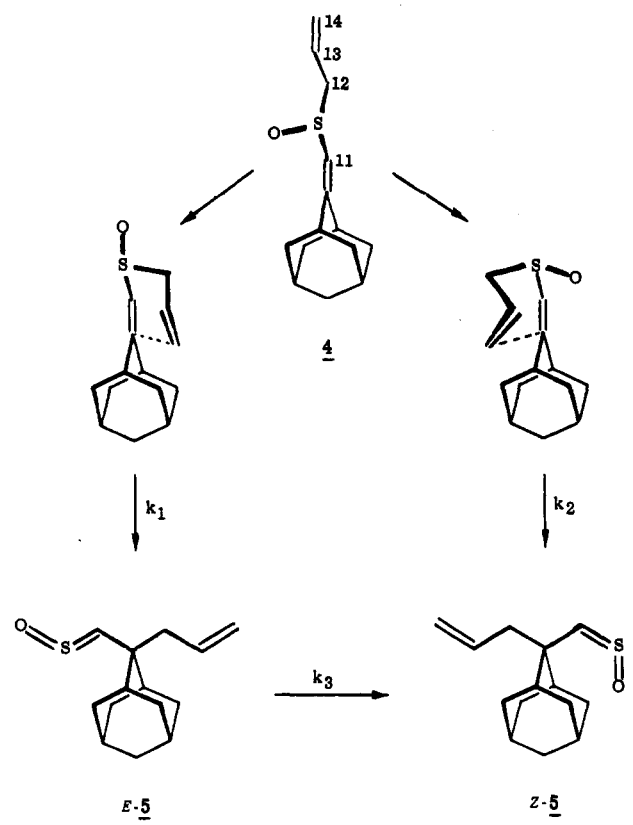


Table I. Rate Constants in CD_3CN at 80 °C

rate constant	scheme	value (s^{-1})
k_1	I	8.0×10^{-5}
k_2	I	5.4×10^{-5}
k_3	I	3.9×10^{-5}
k_4	II	1.08×10^{-4}
k_5	II	3.4×10^{-5}
k_6	II	6.6×10^{-5}
k_7	II	4.6×10^{-5}
k_8	II	1.62×10^{-5}
k_9	II	1.97×10^{-5}

be gauged from Figure 2. Our data agree with Block's in that the (*E*)-sulfine is the kinetically favored product, although our initial ratio (60:40) is slightly smaller than his (65:35).[4]

Application of Harpp's route to the 5-fluoro-substituted sulfides required the availability of the 2-(5-fluoroadamantane) aldehydes 6. To obtain them, we converted 5-fluoroadamantan-2-one into the oxiranes 7 with trimethylsulfoxonium iodide (Scheme II). The *E*/*Z* ratio of the known[7] oxiranes was 35:65 (by GC) and 32:68 (by ^1H NMR). As with the analogous reaction and results with 5-phenyladamantan-2-one, the explanation for this unusual stereochemistry is attributed to thermodynamic control.[1] The oxiranes were converted into the aldehydes with boron trifluoride etherate; the ratio of the aldehydes could not be measured[8] because of their instability, which required their immediate further conversion into the single (racemic) vinyl sulfide[6] precursor to the diastereomeric pair of sulfoxides 8.

The introduction of a 5-fluoro substituent led to the much more complex chemistry shown in Scheme III. Hopes that our study of it would be a simple extension of that of the parent compound vanished when we found that

(5) We found the required intermediate sodium benzenethiosulfonate difficult to characterize, although several others have successfully prepared and used it. See (a) Hayashi, S.; Furukawa, M.; Yamamota, J.; Niigata, K. *Chem. Pharm. Bull.* **1967**, *15*, 1188. (b) Kozikowski, A. P.; Ames, A.; Wetter, H. *J. Organomet. Chem.* **1979**, *164*, C33. (c) Smith, J. G.; Finck, M. S.; Kontoleon, B. D.; Trecoske, M. A.; Giordano, L. A.; Renzulli, L. A. *J. Org. Chem.* **1983**, *48*, 1110.

(6) Harpp, D. N.; Aida, T.; Chan, T. H. *Tetrahedron Lett.* **1985**, *26*, 1795.

(7) Srivastava, S.; le Noble, W. J. *J. Am. Chem. Soc.* **1987**, *109*, 5874.

(8) In the 5-phenyloxiranes, the *E*/*Z* ratio of aldehydes was about 3:2.[1]

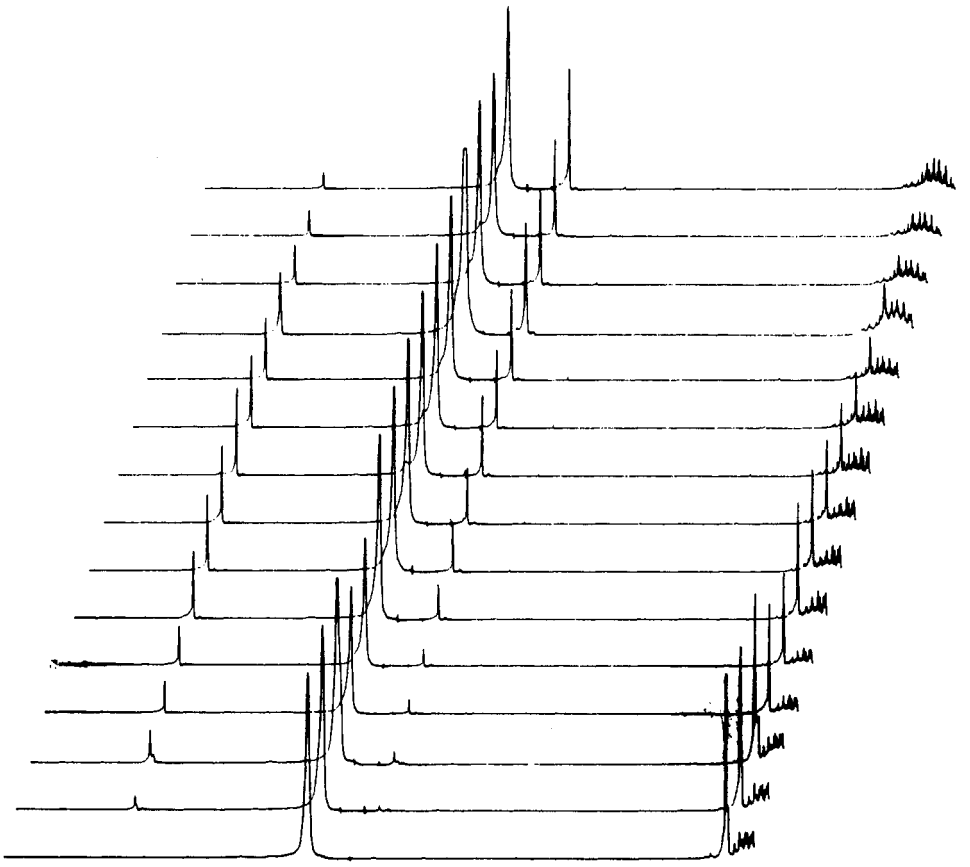


Figure 1. Stack plot showing the evolution of a portion of the ^1H NMR spectrum of a CD_3CN solution of **4** at 80.0 °C. From left to right, the four singlets represent (*E*)-**5** (H_{11}), DMF (reference), (*Z*)-**5** (H_{11}), and **4** (H_{11}). The transient nature of (*E*)-**5** under these conditions is clearly visible.

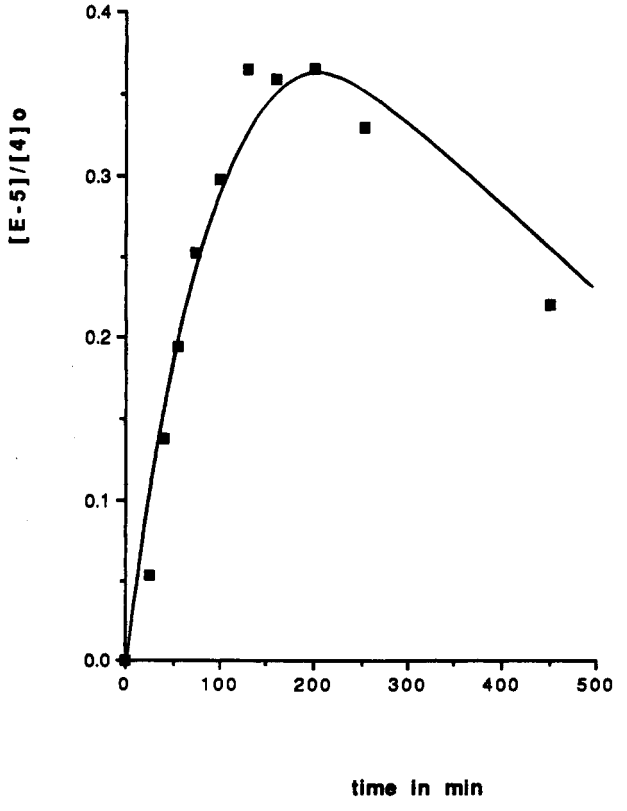


Figure 2. Plot showing the fit of experimental data (squares) with eq 1 if rate constants of Table I are used.

the diastereomers of **8** could not be separated. Fortunately, it was possible to analyze the crude mixture of **8** by means of ^{19}F NMR, which showed two virtually identical peaks; thus, where was no selectivity in the oxidation of the sulfides. Some enrichment occurred during purification, and the mixture used for rearrangement had a 60:40 composition with (*RR*)-**8** in excess. This eventually became clear from the thermal behavior of the mixture, as is explained further below. Scouting experiments showed that **8** behaves in a way similar to that of **4**: each isomer gives rise to its own pair of sulfines and each of the (*E*)-sulfines rearranges further to the corresponding (*Z*)-sulfine. All four of the sulfines have different ^1H NMR signals for H_{11}; hence there was an experimental handle on the problem. The raw data are shown in Figure 3.

Since the (*E*)-sulfines could be chromatographically separated from the (*Z*)-sulfines and since each of the former two isomerizes cleanly by first-order kinetics to the corresponding *Z*-isomer, k_8 and k_9 were accessible by means of ^1H NMR scrutiny of a mixture of the *E*-compounds as a function of time (Figure 4).

The assignment of the four H_{11} NMR singlets was carried out as follows. We succeeded initially, by means of repeated chromatography of sulfine samples that had completely isomerized, to isolate small amounts of a single (*Z*)-sulfine isomer (the major isomer). In fact, some single crystals of this material were grown; unfortunately, however, the compound was unstable to X-irradiation, and no useful diffraction data could be obtained.[9] The mixture of (*E*)-sulfines were then studied by means of the effect of controlled small additions of $Eu(fod)_3$. The results allowed us to distinguish clearly between the signals of (*EE*)-**9** and (*ZE*)-**9**. Thus, carbons $C_{8,10}$ and C_7 in (*EZ*)-**9**

(9) Professor, W. H. Watson (Texas Christian University) made the attempt.

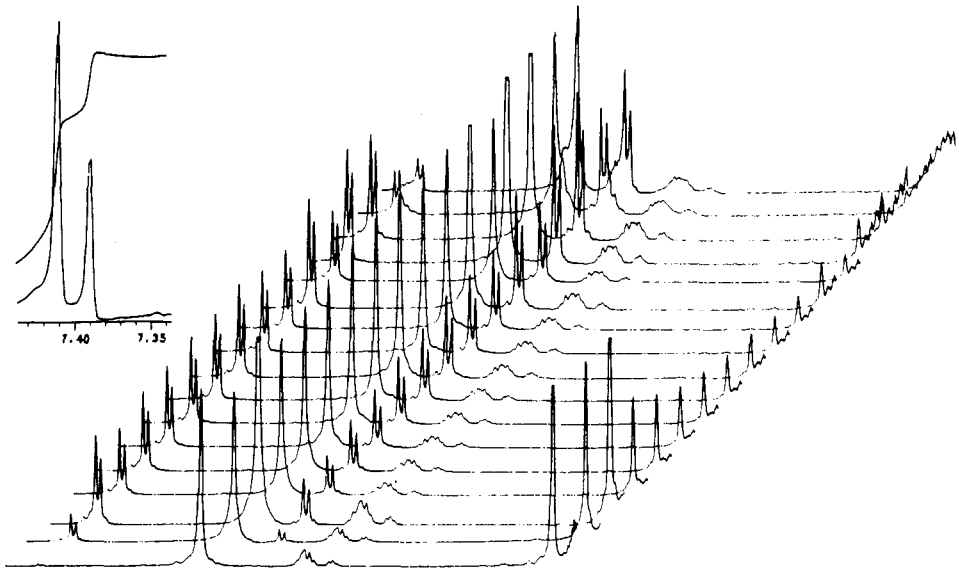
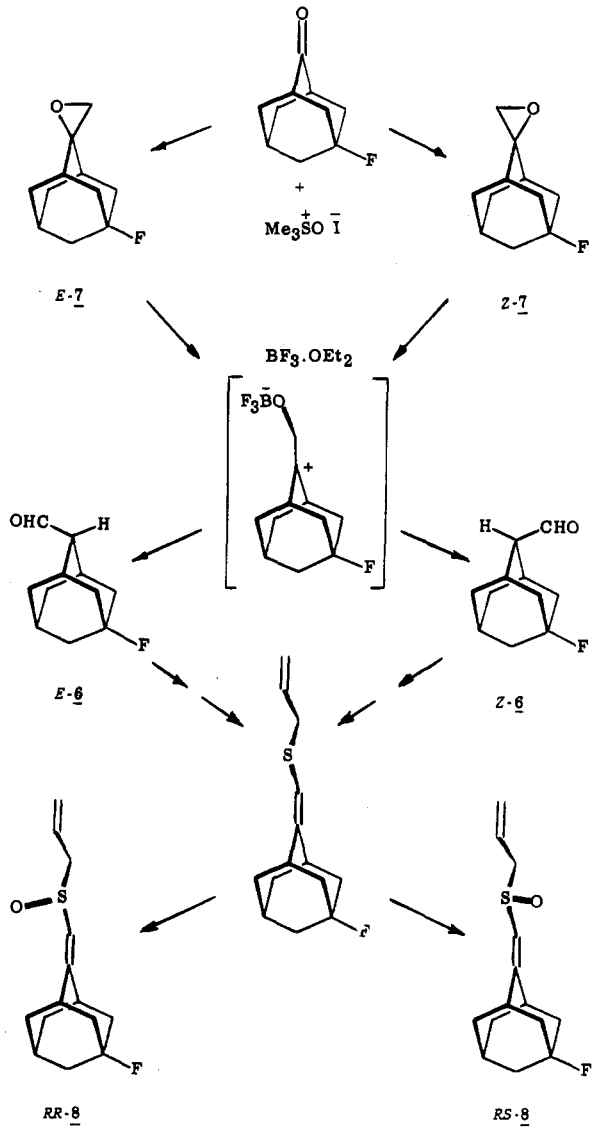
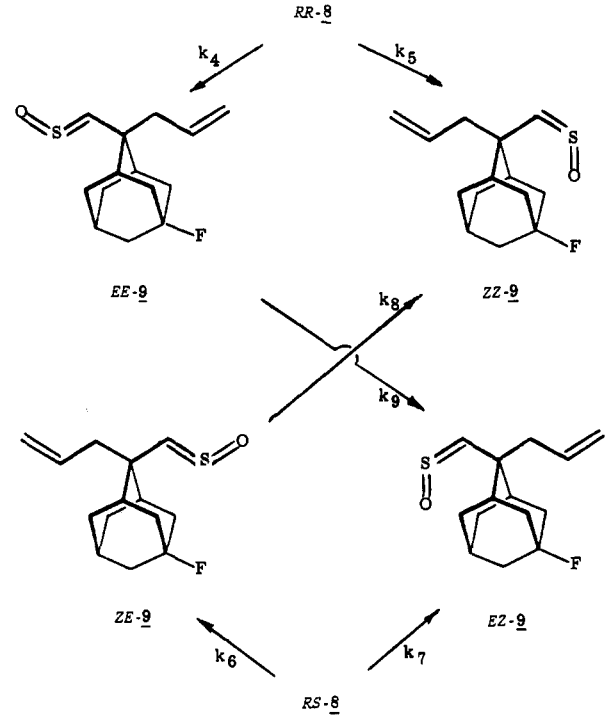


Figure 3. Stack plot showing the chemistry of a CD_3CN solution of **8** at 80 °C by means of a portion of the ^1H NMR spectrum; see Scheme III. From left to right, the six singlets portray (*EE*)-**9**, (*ZE*)-**9**, DMF, (*EZ*)-**9**, (*ZZ*)-**9**, and **8** (compare with Figure 1). (*EZ*)-**9** is clearly the dominant final product (see inset).

Scheme II



Scheme III



were all shifted considerably more strongly by this reagent than $C_{4,9}$ and C_5, respectively, whereas the opposite is true for the corresponding carbons in the *ZZ*-isomer. The results were similar to those obtained earlier with (*E*)- and (*Z*)-**5**. In (*EE*)- and (*ZE*)-**9**, the ^{13}C NMR signals of these six atoms in both compounds are of course readily recognized by the magnitude of the ^{19}F couplings. Integration of the signals was carried out by means of 4020 acquisitions with 30-s delay times and a decoupling program designed to avoid NOE effects; this clearly showed that (*EE*)-**9** was in excess. Inspection of the two pairs of closely spaced H_{11} signals also showed both mixtures of sulphines to have a major and a minor isomer, and the identity of these four peaks was thereby established since during isomerization the major (*E*)-sulfine can only give the major (*Z*)-sulfine (it will be noted that C_2 does not epimerize during that reaction). As a final check, we were able to calculate the ^{13}C signals of the adamantane skeletons of all four sulfines from those of (*E*)- and (*Z*)-**5**, 1-fluoroadamantane, and

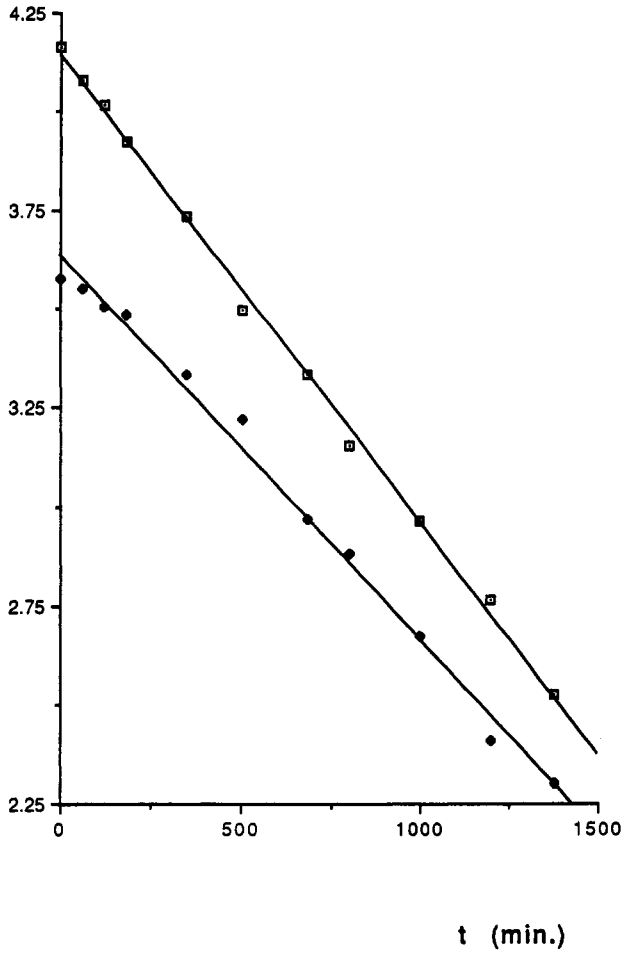


Figure 4. Isomerizations of (*EE*)-**9** to (*EZ*)-**9** (open squares) and of (*ZE*)-**9** to (*ZZ*)-**9** (filled diamonds); ordinate axis, ln [(*EZ*)-**9**]/[(*EE*)-**9**]$_0$ and ln [(*ZE*)-**9**]/[(*ZZ*)-**9**]$_0$, respectively. The first-order rate constants were calculated to have $r = 0.998$ and 0.992, respectively (see Table I).

Table II. Observed and Calculated ^{13}C Resonances of Sulfines 9[a]

	EE		*EZ*		*ZE*		*ZZ*	
C no.	calcd	obsd	calcd	obsd	calcd	obsd	calcd	obsd
1, 3	37.56	37.52 (11.9)	36.51	36.70 (10.1)	37.56	37.68 (11.6)	36.51	36.53 (9.6)
2	47.47	48.21	52.53	52.53	47.47	48.10	51.98	52.53
4, 9	36.99	37.27 (19.6)	36.80	37.09 (18.4)	38.39	38.98 (18.6)	40.34	40.25 (17.9)
5	91.17	92.38 (184.7)	91.12	90.98 (184.5)	92.14	91.56 (184.7)	91.31	90.98 (184.5)
6	43.62	43.72 (17.7)	43.28	43.36 (17.8)	43.62	43.64 (17.6)	43.28	43.36 (17.8)
7	31.02	29.79 (9.0)	30.18	30.09 (10.1)	30.05	30.79 (10.0)	30.00	29.93 (12.0)
8, 10	32.05	32.41	33.41	33.70	30.11	30.55	29.91	30.34
11		190.87		179.78		190.46		180.47
12		42.30		40.13		41.55		39.37
13		131.32		132.54		130.91		132.92
14		120.51		118.60		120.39		118.76

[a] J_{CF} in Hz given in parentheses.

adamantane itself[10] (see Table II).

The major thrust of our work was to learn whether the *en* or *zu* face of the C_2 terminus would be preferred in the [3,3] rearrangement, and the answer to that question is suggested even by a cursory inspection of Figure 3: since

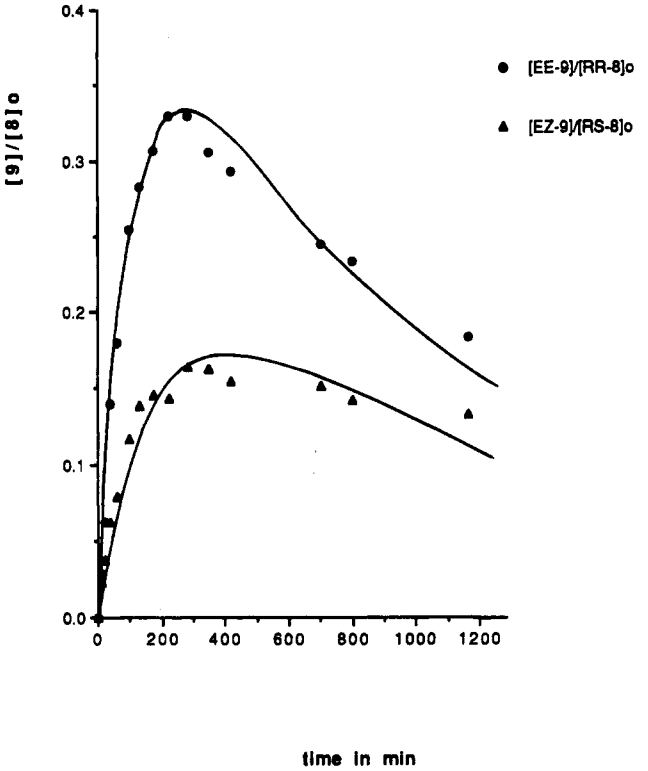


Figure 5. Plot showing the fit of experimental data with eqs 2 and 3 using the data for $k_4 - k_9$ in Table I.

(*EZ*)-**9** is dominant over (*ZZ*)-**9** in the final product, it is apparent that the allyl group attacks the face syn to the fluorine, hence anti to the more electron-rich vicinal CC bonds. This tentative conclusion, of course, ignores the fact that two diastereomers of **8** are present, and our final goal was to find out what the *en*/*zu* preferences would be for each of the two sulfoxides separately. In principle, this can be done by evaluating each of the four rate constants k_4–k_7; as noted, k_8 and k_9 had already been measured.

The rate laws describing the concentration of (*EE*)- and (*ZE*)-**9** and of (*EZ*)- and (*ZZ*)-**9** are:

$$\frac{[(EE)\text{-}9]}{[(RR)\text{-}8]_0} = \frac{k_4}{k_4 + k_5 - k_9}[e^{-k_9 t} - e^{-(k_4+k_5)t}] \quad (2)$$

$$\frac{[(ZE)\text{-}9]}{[(RS)\text{-}8]_0} = \frac{k_6}{k_6 + k_7 - k_8}[e^{-k_8 t} - e^{-(k_6+k_7)t}] \quad (3)$$

The first task was to determine the diastereomeric composition of **8**. In our initial experiments, crude mixtures of **8** were employed in which the two diastereomers were present in exactly equal concentration, as judged by ^{19}F NMR; hence, the fact that the two H_{11} signals coincide did not hinder the analysis. In subsequent experiments, purified mixtures were employed in which some enrichment had evidently occurred. While we could measure the ratio (60:40), we could not at once tell which of the diastereomers was the principal one since the ^{19}F signals could not at first be assigned. This problem was solved as follows. (*EE*)-**9**, which can be formed only from (*RR*)-**8**, dominates over (*ZE*)-**9**, which derives solely from (*RS*)-**8**, *throughout* the reaction (Figure 3 and Scheme III). This means that either (*RR*)-**8** is initially in excess over (*RS*)-**8** or that (*ZE*)-**9** isomerizes to (*ZZ*)-**9** more rapidly than (*EE*)-**9** does to (*EZ*)-**9**. But as already noted, the latter possibility is ruled out by direct measurement: $k_9 > k_8$. Thus, (*RR*)-**8** was initially the dominant stereoisomer, and the ^{19}F NMR signals were thus assigned. Rate constants k_4–k_7 were then obtained by the application of simplex

(10) Srivastava, S.; Cheung, C. K.; le Noble, W. J. *Magn. Reson. Chem.* **1985**, *23*, 232.
(11) Noggle, J. H. *Physical Chemistry on a Microcomputer*, Little, Brown & Co.: Boston, 1985; p 145–165.

nonlinear regression analysis[10] to eqs 2 and 3 and use of the fixed, independently measured values of k_8 and k_9 (Table I). The fit of the curves portraying the concentrations of these intermediates to eqs 2 and 3 using these rate constants is shown in Figure 5.

We estimate the accuracy of the rate constants at 3–5%, based as they are on ^{1}H NMR integrations at 16 time intervals, 32 acquisitions each. To support this appraisal, we compare the ratio of (*RR*)- and (*RS*)-8 as measured by their intensities in the ^{19}F NMR spectrum with that calculated from the data in Table I, as follows. The pure *RR* isomer alone would eventually produce a ratio of (*ZZ*)-**9**/(*EZ*)-**9** equal to k_5/k_4, hence 0.315. The diastereomer would lead to a ratio of these products equal to k_6/k_7, hence 1.43. The observed final product ratio is 0.67; this indicates that the initial diastereomeric composition was 68% *RR* (100(1.43–0.67)/(1.43–0.32)). This result, based on the ^{1}H NMR spectrum of (*ZZ*)- and (*EZ*)-**9** (see inset, Figure 3) agrees with the 60% derived from the ^{19}F NMR spectrum to about the precision claimed.

Finally, we can calculate the relative importance of the steric and electronic influences in the same way as before;[2] we arrive at a ratio of 60:40 for the electronic factor (i.e., the ratio of *zu*/*en* attack in the absence of a steric factor) and of 68:32 for the steric factor (i.e., the ratio by which equatorial oxygen is preferred over axial in the absence of the fluorine electronic effect). These values are similar to the ones observed[2] in the oxy-Cope reactions of **2**.

Experimental Section

All ^{1}H and ^{13}C NMR spectra were measured in $CDCl_3$ at 300 and 80 MHz, respectively. Adamantanespirooxirane was prepared as described previously.[1] It was converted by means of boron trifluoride etherate[1] into 2-adamantanecarboxaldehyde[12] which was not purified because of its instability: ^{1}H NMR δ 1.5–2.4 (m, 15 H), 9.708 (s, 1 H); ^{13}C NMR δ 27.40, 27.81, 28.05, 33.42, 36.90, 37.70, 56.48, 205.83. The aldehyde was converted into trimethyl[adamantyl(methylthio)methoxy]silane via the procedure of Harpp:[13] ^{1}H NMR δ 0.19 (s, 9 H), 1.5–2.2 (m, 16 H), 5.21 (dd, 1 H); ^{13}C NMR δ 0.28, 27.56, 27.75, 28.61, 29.99, 31.66, 31.86, 37.98, 38.58, 38.90, 54.73, 76.50. This product was used without purification to prepare[6] allyl adamantylidenemethyl sulfide as a pale yellow oil: ^{1}H NMR δ 1.5–2.10 (m, 12 H), 2.45 (s, 1 H), 2.97 (s, 1 H), 3.22 (d, 2 H), 5.0–5.15 (m, 2 H), 5.50 (s, 1 H), 5.7–5.9 (m, 1 H); ^{13}C NMR δ 28.35, 34.01, 37.03 (d), 38.40, 39.61, 40.15, 107.84, 116.65, 134.60, 152.01. The sulfide was converted by means of oxazone into the sulfoxide **4**:[4] ^{1}H NMR δ 1.5–2.0 (m, 12 H), 3.19 (d, 2 H), 3.3–3.6 (dd, 2 H), 5.2–5.4 (m, 2 H), 5.6–5.8 (m, 1 H), 5.82 (s, 1 H); ^{13}C NMR δ 27.56 ($C_{5,7}$), 34.36 (C_1), 36.36, 38.48, 38.77, 39.00, 39.69 ($C_{4,6,8-10}$), 40.37 (C_3), 58.14 (C_{12}), 120.88 (C_{11}), 122.93 (C_{14}), 125.80 (C_{13}), 165.13 (C_2) (assignments by means of CSCM and ATP studies).

Rearrangement of Sulfoxide 4 into (*E*)- and (*Z*)-5. Neat parent sulfoxide **4** (50 mg, 0.21 mM) was heated to 90 °C under nitrogen for 2 h. The yellow product was dissolved in $CDCl_3$; the ^{1}H NMR revealed the presence of the two isomers, (*E*)- and (*Z*)-**5**, which could be separated by column chromatography (ethyl acetate–hexane). If the heating process was carried out for a period of 48 h, only (*Z*)-**5** was obtained. (*E*)-**5**: ^{1}H NMR δ 1.5–2.2 (m, 14 H), 2.49 (d, 2 H), 5.1–5.3 (dd, 2 H), 5.75–5.60 (m, 1 H), 8.81 (s, 1 H). The ^{13}C NMR signals were identified in part by means of ATP studies and of the sensitivity of five to seven small and controlled additions of a Eu(fod)$_3$ solution (slopes given in parentheses are in arbitrary units different for each compound): δ 27.01 (C_7, 1.29), 27.97 (C_5, 1.78), 32.07 ($C_{8,10}$, 1.60), 34.02 ($C_{4,9}$, 2.57), 34.51 ($C_{1,3}$, 3.88), 38.70 (C_6, 0.97), 42.26 (C_{12}, 5.94), 49.44 (C_2, 4.53), 119.82 (C_{14}, 2.96), 131.78 (C_{13}, 2.20), 192.62 (C_{11}). The correlations all exceeded 0.994, and most were better than 0.999. (*Z*)-**5**: ^{1}H NMR δ 1.2–2.0 (m, 12 H), 2.18 (bs, 2 H), 2.63 (d, 2 H), 5.00–5.20 (dd, 2 H), 5.6–5.8 (m, 1 H), 7.326 (s, 1 H); ^{13}C NMR δ 26.95 (C_7, 2.80), 27.13 (C_5, 4.09), 31.88 ($C_{8,10}$, 3.81), 33.46 ($C_{1,3}$, 8.85), 35.37 ($C_{4,9}$, 6.64), 38.37 (C_6, 2.36), 40.12 (C_{11}, 11.36), 53.95 (C_2, 13.22), 118.08 (C_{14}, 5.31), 133.40 (C_{13}, 6.09), 182.06 (C_{11}, 8.95). The rate of the rearrangement was studied in CD_3CN solutions containing a trace of DMF as reference; they were warmed in NMR tubes in a bath of refluxing benzene (80.1 °C). The fate of the proton H_{11} signal was followed in order to measure the rate constants. A similar study gave the constant k_3.

5-Fluoroadamantanone[14] was converted into a mixture of (*E*)- and (*Z*)-**7** in an experiment similar to that used for the parent ketone; analysis was carried out by means of both GC and CH_2O integration. The NMR data confirm those obtained earlier by Srivastava[7] but not reported hitherto. (*E*)-**7**: ^{1}H NMR δ 1.55–2.35 (m, 15 H), 2.605 (s, 2 H); ^{19}F NMR (CF_3COOH external standard) δ −60.05; ^{13}C NMR (J_{CF} in Hz, calculated shifts and Eu(fod)$_3$ slopes in arbitrary units given in parentheses) δ 29.94 (C_7, 9.87, 29.90, 2.57), 33.45 ($C_{8,10}$, 32.95, 3.34), 37.73 ($C_{1,3}$, 10.29, 38.79, 6.89), 41.23 ($C_{4,9}$, 18.86 Hz, 41.55, 2.06), 42.34 (C_6, 17.07, 41.84, 1.83), 54.95 (C_{11}, 27.17), 62.97 (C_2, 62.42, 12.01), 91.43 (C_5, 184.8, 91.18, 2.28). (*Z*)-**7**: ^{1}H NMR δ 1.89–1.95 (m, 10 H), 2.23 (m, 1 H), 2.31 (m, 2 H), 2.714 (s, 2 H); ^{19}F NMR δ −57.34; ^{13}C NMR δ 30.12 (C_7, 10.71, 30.04, 2.08), 35.15 ($C_{8,10}$, 34.67, 1.87), 38.53 ($C_{1,3}$, 9.96, 38.79, 6.01), 39.92 ($C_{4,9}$, 17.8, 39.83, 2.94), 42.23 (C_6, 17.4, 41.84, 1.56), 54.20 (C_{11}, 25.12), 62.51 (C_2, 62.42, 8.70), 91.15 (C_5, 185, 91.04, 2.11).

Allyl (5-Fluoroadamantylidene)methyl Sulfide. The mixture of oxiranes **7** was converted into a mixture of (*E*)- and (*Z*)-**6** with boron trifluoride etherate in benzene as described above for the parent compound: ^{1}H NMR δ 1.5–2.01 (m), 2.32 (bs), 2.62 (bs), 9.65 (s), 9.67 (s); ^{13}C NMR δ 29.74–32.09 (m), 36.17, 37.30, 38.74, 41.04, 42.96, 44.51, 44.86, 54.95, 55.16, 203.51, 203.72. The instability of these aldehydes required their immediate conversion into the corresponding *syn*- and *anti*-trimethyl[(5-fluoroadamantyl)(methylthio)methoxy]silane as described above: ^{1}H NMR δ 0.87 (s), 1.25–2.0 (m), 5.11–5.15 (t); ^{13}C NMR δ 0.36, 30.24 (b), 30.46 (b), 30.94 (b), 31.57 (b), 34.75, 37.35, 43.05, 43.23, 53.66, 53.88, 75.93, 76.03. This mixture was also not purified or analyzed but treated with sodium hydride and allyl bromide like the parent compound to give a single (racemic) sulfide: ^{1}H NMR δ 1.51–2.0 (m, 11 H), 2.31 (s, 1 H), 2.70 (s, 1 H), 3.22–3.25 (d, 2 H), 5.10–5.20 (m, 2 H), 5.58 (s, 1 H), 5.78–5.85 (m, 1 H); ^{13}C NMR, (J_{CF} in Hz in parentheses) δ 31.41 (C_7, 9.6), 35.60 ($C_{1 \text{ or } 3}$, 10.3), 36.84 ($C_{8,10}$), 38.06 (C_{12}), 41.70 ($C_{1 \text{ or } 3}$, 10.0), 42.17 ($C_{4 \text{ or } 9}$, 20.0), 42.40 ($C_{4 \text{ or } 9}$, 18.5), 43.58 (C_6, 17.0), 93.17 (C_5, 185), 111.06, 116.96, 134.41, 147.08.

Allyl (5-Fluoroadamantylidene)methyl Sulfoxide (8). The sulfide obtained above was oxidized with oxazone as described for the parent compound. Various NMR data show it to be a mixture of two diastereomers which could be analyzed (^{19}F NMR, 50/50) but not separated: ^{1}H NMR δ 1.66–2.0 (m, 22 H), 2.27 (b, 2 H), 2.72 (b, 2 H), 3.3–3.45 (m, 4 H), 5.2–5.4 (m, 4 H), 5.6–5.8 (m, 2 H), 5.88 (s, 2 H); ^{13}C NMR (F couplings in Hz in parentheses) δ 30.40 (9.28), 35.40 (10.0), 35.72 (10.1), 36.78, 37.10 (6.7), 37.86, 41.19, 41.35 (10.1), 42.07 (21.0), 42.34 (19.2), 43.06 (17.0), 57.66, 90.04 (185), 90.41 (183), 122.82, 123.01, 125.20, 125.23, 159.87, 160.05; ^{19}F NMR (*RR*)-**8** δ −140.28, (*RS*)-**8** −140.65 (see text for assignment). Purification by means of column chromatography led to small changes in the ratio of the two ^{19}F signals, but not to separation of the isomers.

Rearrangement of 8. The rearrangement was studied with the neat diastereomeric mixture of **8** at 90 °C, which produced four stereoisomers of **9**. The two (*E*)-sulfines could be separated from their (*Z*)-isomers; heating the mixture of **8** for longer times resulted in mixtures of the (*Z*)-sulfines alone. It was possible by repeated crystallization from hexane to isolate a very small quantity of pure (*EZ*)-**9**, but the single crystals grown of this compound were unstable under X-irradiation. The ^{1}H NMR spectra showed signals for H_{11} at δ 8.75 and 8.79 for the (*E*)-sulfine mixture and at δ 7.39 and 7.41 for the (*Z*)-sulfine pair; the remainders of these spectra were not analyzed. The carbon spectra were analyzed with help of Eu(fod)$_3$ additions and chemical shift

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calculations; the results are given in Table II. The rates of the isomerizations were measured in CD_3CN solution at 80.1 °C, with DMF as a reference as before.

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Supplementary Material Available: ^1H and ^{13}C NMR spectra of allyl (5-fluoroadamantylidene)methyl sulfide and of mixtures of (*RR*)- and (*RS*)-8, of (*EE*)- and (*ZE*)-9, and of (*EZ*)- and (*ZZ*)-9 (4 pages). Ordering information is given on any current masthead page.

A General Approach to 5-Substitution of 3-Furaldehydes[1]

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Herein we report the details of the conversion of 3-furaldehyde into 2-substituted 4-furaldehydes and the transformations of 2-substituted 4-furaldehydes and 4-substituted 3-furaldehydes into tri- and tetrasubstituted furans. We have developed a new disubstituted furan synthesis by applying metalation to the direct conversion of 3-substituted furans into 2,4-disubstituted furans. In situ protection of 3-furaldehyde with lithium morpholide followed by metalation at the C-5 position and quenching with several electrophiles affords 2-substituted 4-furaldehydes in 30–70% yield. The electrophiles include chlorosilanes, chlorostannanes, aldehydes, ketones, and primary iodides. This work provides a general route to a previously relatively inaccessible furan substitution pattern and is the first example of selective metalation at the C-5 position of 3-substituted furans. Other bulky α-alkoxy substituents at C-3 direct remote metalation to C-5 of furan. We examined other 3-furaldehyde metalations. The amino alkoxide intermediate derived from lithio *N,N,N'*-trimethylethylenediamine and 3-furaldehyde, when treated with BuLi and electrophiles, provided a product mixture which included metalation at the C-4 position of 3-furaldehyde. Several approaches to enhance this unusual C-4 metalation were unsuccessful. Using this amino alkoxide-metalation chemistry, 4-alkyl- or 4-phenyl-3-furaldehyde could be substituted at C-2 or C-5 selectively. Finally we converted trisubstituted furans into tetrasubstituted furans with metalation/electrophilic trapping.

Introduction

Substituted furans play an important role in the field of heterocyclic chemistry, occur widely in nature,[2] and enjoy wide application in a variety of commercially important products such as pharmaceuticals, heterocyclic polymers,[2] and flavor and fragrance compounds.[3] Moreover, furan derivatives are versatile synthetic intermediates for the preparation of a wide range of cyclic and acyclic organic compounds.[4] Although numerous synthetic routes to furans have been developed,[5] *direct* conversion of monosubstituted into 2,4-disubstituted furans has not been generally successful.

The substitution behavior of 2- and 3-substituted furans has been known for many years.[6] Electrophilic substitution of 2-substituted furans gives the product of attack at the 5-position as the major product. Likewise, metalation followed by electrophilic trapping often results in C-5 substitution[7] affording 2,5-disubstituted furans **1** although certain ortho-directing C-2 substituents yield a mixture of 2,3-disubstituted furans **2** and **1**.[7]

Only a handful of methods have been reported for the synthesis of 2,4-disubstituted furans.[5] None of these involves a direct and regiospecific conversion of a 2-substituted into a 2,4-disubstituted furan **3**. Instead, the strategies involve manipulation of acyclic precursors[8] (especially for the synthesis of 2,4-dialkylfurans), of lactones,[9] of 2-substituted furans,[10] of 3-substituted furans,[11,12a] or **1**.[13] All of these synthetic routes require many steps,

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