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New Carbon-Carbon Bond Formation through Oxyallylation of Enoxysilanes with Sulfur Dioxide Adduct of 1-Methoxybutadiene. Stereoselective Synthesis of (*Z*)-4-Methoxy-6-oxoalk-2-enyl Methyl Sulfones.

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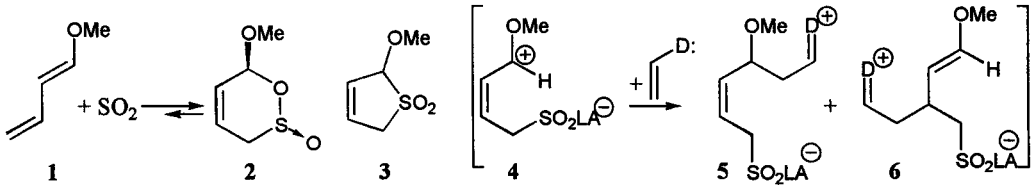
Abstract: Mixtures of 1-methoxybutadiene, trimethylsilyl enol ethers, SO_2 and a Lewis acid catalyst generate trimethylsilyl (*Z*)-4-methoxy-6-oxoalk-2-enesulfinates that can be converted into 4-methoxy-6-oxoalk-2-enyl methyl sulfones and 5-alkyl-4-methoxy-6-oxoalk-2-enyl methyl sulfones with 100% (*Z*) selectivity and good *syn* diastereoselectivity for the 5-alkyl and 4-methoxy substituents. © 1997 Elsevier Science Ltd.

At low temperature and in the presence of a suitable protic or Lewis acid catalyst, simple 1,3-dienes add reversibly to sulfur dioxide via a hetero-Diels-Alder process giving the corresponding 3,6-dihydro-1,2-oxathiin-2-oxides (= sultines).[3,4] For isoprene, (*E*)-piperilene[3] and (*E*)-hexa-1,3-diene,[5] equilibrium constants K = [sultine]/[SO_2]·[1,3-diene] lie between 10^{-4} to 10^{-2} $mol^{-1}dm^3$ at -60°C. The sultines are unstable above -50°C and undergo fast cycloreversion liberating the starting diene and SO_2 that undergo cheletropic additions[5] above -40°C giving the corresponding 2,5-dihydrothiophene-1,1-dioxides (sulfolenes).[6] Electron-rich 1,3-dienes such as 1-methoxybutadiene (**1**), react with SO_2 at -60°C without acid catalysis providing quantitative formation of a single adduct (K = [adduct]/[**1**][SO_2] > 3 $mol^{-1}dm^3$) the structure of which was assigned as sultine **2** on the basis of its ^{1}H- and ^{13}C-NMR data.[7] Although the alternative sulfolene structure **3** could not be ruled out, this result suggested to us that this adduct, contrary to the sultine derived from alkyl-substituted 1,3-dienes, could be used as a synthetic intermediate as it was shown to be stable up to -30°C in the presence of an excess of SO_2. Similar results were obtained with 1-methoxy-3-[(trimethylsilyl)oxy]buta-1,3-diene (Danishefsky's diene).[7] Above -20°C **2** (or **3**) decomposes quickly into polymeric material. In the presence of a Lewis acid (LA) adduct **2** (or **3**) was expected to undergo ring opening with the formation of a zwitterionic intermediate of type **4** which should react with electron-rich alkenes either as an oxy-allylating agent, giving cationic intermediates of type **5**, or as an allylating agent leading to intermediates of type **6**.



We report herein our preliminary results which demonstrate that only mode **4** → **5** is followed with enoxysilanes, realizing a new oxyallylating process and a new method to create carbon-carbon bonds with the

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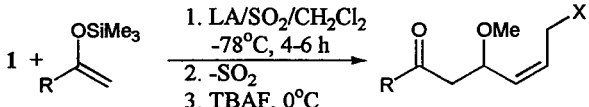
generation of polyfunctional (*Z*)-alkenes. Good *syn*-diastereoselectivity has been observed for the oxyallylation of (*Z*)- and (*E*)-enoxysilanes derived from diethyl ketone and cyclohexanone, respectively. The method is illustrated with the stereoselective synthesis of (*Z*)-4-methoxy-6-oxoalk-2-enyl methyl sulfones.

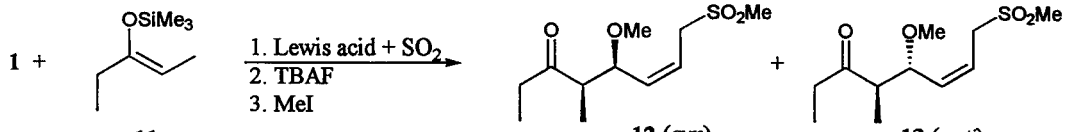


7 a: R = Ph
b: R = *t*-Bu

8 X = S(O)O-SiMe$_3$
9 X = SO$_2^-$NBu$_4^+$
10 X = S(O)$_2$Me

In a typical experiment, a 1:2 mixture of diene **1** and enoxysilane **7a**, derived from acetophenone, were dissolved in CH_2Cl_2 containing 0.01 molar-equivalents of Yb(OTf)$_3$.[8] After degassing (freeze/ thaw cycles), SO_2 was condensed and the reaction mixture allowed to stand at -78°C for 4-6 h. Under these conditions the Lewis acid catalyses the addition of SO_2 to **1** generating **2** (or **3**) faster than the sila-ene reaction of **7a** with SO_2. The Lewis acid induces the oxyallylation of **7a** leading to the unstable trimethylsilyl sulfinates **8a**. After disappearance of **1**, the excess SO_2 was distilled off at -78°C. Acetone (solvent) and a THF solution of $Bu_4N^+F^-$ (TBAF) were added and the mixture allowed to warm up to 0°C. This generated the tetrabutylammonium sulfinates **9a** that were reacted with an excess of MeI (0°C, 90 min)[9] to provide the (*Z*)-alkenyl methyl sulfone **10a** (71%).[10,11] The same procedure, when applied to the trimethylsilyl enol ether of 3,3-dimethylbutan-2-one (**7b**), led to **10b** in 60-75% yield.

With the (*Z*)-enoxysilane **11** derived from diethyl ketone,[12] the oxyallylation with **2** (or **3**) engendered diastereomeric adducts that were converted, as above, to the *syn* and *anti* β-methoxy-α-methyl ketones **12** and **13**,[13] respectively. These compounds were separated and purified by flash column chromatography on silica gel (yield up to 89%, based on **1**). The diastereoselectivity (**12/13** product ratio) depended somewhat on the nature of the Lewis acid catalyst (see Table) and was highest (81:19) with (*t*-Bu)Me$_2$SiOTf.



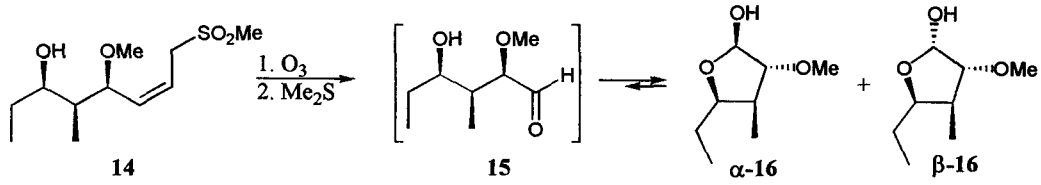
11 **12** (*syn*) **13** (*anti*)

Table. Diastereoselectivity of the oxyallylation of **11** with **1** + SO_2 as a function of the Lewis acid catalyst.

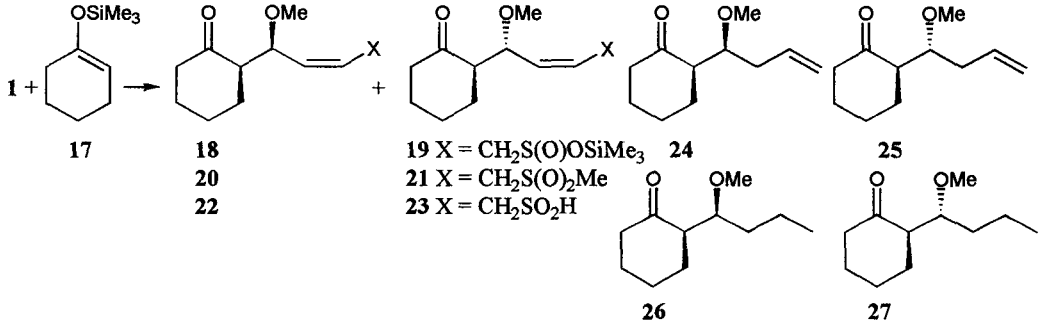
Lewis acid	mol. equiv.	12/13[a)]	yield[b)]
Yb(OTf)$_3$	0.02	70:30	89%
Sc(OTf)$_3$	0.03	70:30	81%
Sn(OTf)$_2$	0.04	70:30	76%
Me$_3$SiOTf	0.37	75:25	78%
(*t*-Bu)Me$_2$SiOTf	0.43	81:19	63%

a) measured by ^{1}H-NMR of the crude reaction mixture
b) non-optimized yields, after chromatographic purification

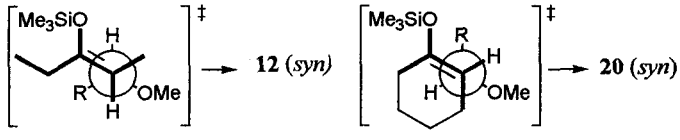
The relative configurations of **12** and **13** were established in the following way: reduction of the *syn* product **12** with L-Selectride (Li(*s*-Bu)$_3$BH)[14] (THF, -78°C), followed by treatment with H_2O_2/NaOH, generated the *syn* alcohol **14** (47%, 40% of recovered **12**), the ozonolysis of which (O_3, CH_2Cl_2, -78°C, then Me_2S, 20°C) produced aldehyde **15** that equilibrated with a 5:3 mixture of the α- and β-furanose α-**16** and β-**16** (69%). The 2D-NOESY ^{1}H-NMR (400 MHz) spectrum of these two compounds proved the *trans* relationship between the methoxy and methyl substituents, and thus the *syn* relative configuration of **12**.



The oxyallylation of the trimethylsilyl enol ether of cyclohexanone (**17**) with **2** (or **3**) generated a mixture of adducts **18** and **19** which was converted, as above, into the corresponding sulfones **20** and **21**.[15] With various Lewis acids the *syn* diastereomer **20** was always favoured. The best diastereoselectivity was observed with (*i*-Pr)$_3$SiOTf (0.37 mol equiv.) which led to a 83:17 mixture of **20/21** (74%). With (*t*-Bu)Me$_2$SiOTf, it was 81:19 (88% yield). The relative configurations of **20** and **21** were established by chemical correlation with the known derivatives **26** and **27**[16] that were obtained in the following way: instead of reacting the intermediate sulfinates **18** and **19** with TBAF, they were hydrolyzed with an aqueous methanolic solution of NH_4Cl. The corresponding sulfinic acids **22** and **23** underwent retro-ene eliminations[17] of SO_2 at 20°C giving the terminal alkenes **24** and **25** that were hydrogenated to provide **26** and **27**, respectively.[10]



As for the Mukaiyama reaction,[18] our oxyallylations with **11** and **17** show preference for the *syn* diastereomers irrespective of the enoxysilane (*Z*) or (*E*)-geometry.[19] Although more data must be collected before reasonable transition state models can be discussed for our reactions, the available results are consistent with the Noyori open chain models[16,19,20] shown here-below (minimal steric and electrostatic repulsions).



Our work demonstrates for the first time that SO_2 can be used to promote carbon-carbon bond formation between an electron-rich 1,3-diene and an electron-rich alkene without polymerization. A new oxyallylation process is disclosed that can be applied to the synthesis of 6-oxo-4-methoxy-5-alkylalk-2-enyl methyl sulfones with 100% (*Z*) selectivity for the olefinic moiety and good *syn* diastereoselectivity for the 4-methoxy- and 5-alkyl-substituted centers. Work is underway in our laboratory to extend the new chemistry disclosed here.

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References and Notes

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11. Data for **10a**: IR (film) ν: 3010, 2930, 2895, 2820, 1680, 1595, 1580 cm^{-1}; ^{1}H-NMR (250 MHz, $CDCl_3$) δ_H: 7.92, 7.56, 7.44 (5 Harom.), 5.80 (m), 4.62 (m, HC(3)), 4.02 (m, $H_2C(6)$), 3.40 (dd, ^2J=17.0, ^3J=5.8, H-C(2)), 3.28 (s, OMe), 3.16 (dd, ^2J=17.0, ^3J=6.5, H-C(2)), 2.92 (s, SO_2Me); ^{13}C-NMR (100.61 MHz, $CDCl_3$) δ_C: 197.3 (s), 138.3 (d, ^1J(C,H)=158 C(4)), 136.7 (s), 133.4, 128.7, 128.1 (d, 161), 119.5 (d, 164, C(5)), 73.1 (d, 145, C(3)), 56.6 (q, MeO), 54.0 (t, 136, C(6)), 43.0 (t, 128, C(2), 40.1 (q, 138, Me).
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13. Data for **12**: ; ^{1}H-NMR (400 MHz, $CDCl_3$) δ_H: 5.77 (dddd, ^3J= 11.2, 7.8, 7.2, ^4J=0.8, H-C(7)), 5.65 (ddt, ^3J=11.2, 9.0, ^4J=1.4, H-C(6)), 4.02 (ddd, ^3J=9.0, 7.8, ^4J=0.8, H-C(5)), 3.91 (ddd, ^2J=14.6, ^3J=7.8, ^4J=1.4, H-C(8)), 3.82 (dd, ^2J=14.6, ^3J=7.2, ^4J=1.4, H-C(8)), 3.28 (s, MeO), 2.90 (s, $MeSO_2$), 2.75 (dq, ^3J=7.8, 7.0, H-C(4)), 2.51 & 2.37 (2dq, ^2J=18.2, ^3J=7.2, $H_2C(2)$), 1.14 (d, ^3J=7.0, MeC(4)), 0.95 (t, ^3J=7.2, $CH_3(1)$); data for **13**: ^{1}H-NMR (400 MHz, $CDCl_3$) δ_H: 5.92 (dddd, ^3J=11.2, 8.3, 7.2, ^4J=0.7), 5.69 (ddt, ^3J=11.2, 9.3, ^4J=1.4), 4.09 (ddd, ^3J=9.3, 8.9, ^4J=0.7), 3.98 (ddd, ^2J=14.5, ^3J=8.3, ^4J=1.4), 3.87 (ddd, ^2J=14.5, ^3J=7.2, ^4J=1.4), 3.18 (s), 2.92 (s), 2.74 (dq, ^3J=8.9, 7.2), 2.52 (q, ^3J=7.2), 1.04 (t, ^3J=7.2), 0.95 (d, ^3J=7.2).
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15. Data for **20**: UV (MeCN): 280 (ε=200), 207 (1500). ^{1}H-NMR (400 MHz, $CDCl_3$) δ_H: 5.78 (dtd, ^3J=11.2, 7.5, ^4J=0.5, 1H), 5.71 (ddt, ^3J=11.2, 8.6, ^4J=1.3, 1H), 4.24 (ddd, ^3J=8.6, 6.5, ^4J=0.5, 1H), 4.04 (ddm, ^2J=14.5, ^3J=7.5, ^4J=1.3, 1H), 3.99 (ddm, ^2J=14.5, ^3J=7.5, 1H), 3.27 (s, MeO), 2.94 (s, $MeSO_2$), 2.49 (dm, ^3J=6.5), 2.40-1.50 (m, 8H); ^{13}C-NMR (100.61 MHz, $CDCl_3$) δ_C: 210.9 (s), 137.8, 119.2, 74.6 (3d), 56.8 (q), 55.5 (d), 54.1, 42.5 (2t), 40.2 (q), 29.1, 27.8, 24.9 (3t); data for **21**: ^{1}H-NMR (400 MHz, $CDCl_3$) δ_H: 5.85 (ddd, ^3J=11.3, 7.8, 6.8, 1H), 5.72 (dd, ^3J=11.3, 9.0, 1H), 4.40 (dd, ^3J=9.0, 4.8, 1H), 4.07 (dd, ^2J=14.7, ^3J=7.8, 1H), 4.02 (dd, ^2J=14.7, ^3J=6.8), 3.27, 2.92 (2Me), 2.70 (ddd, ^3J=12.7, 5.4, 4.8, 1H), 2.40-1.50 (m, 8H).
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