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Four component synthesis of (*Z*)-4-alkoxy-1,3-dimethylalk-2-enyl methyl sulfones: on the intermediacy of sultines (3,6-dihydro-1,2-oxathiin-2-oxides) arising from suprafacial hetero-Diels–Alder additions of sulfur dioxide

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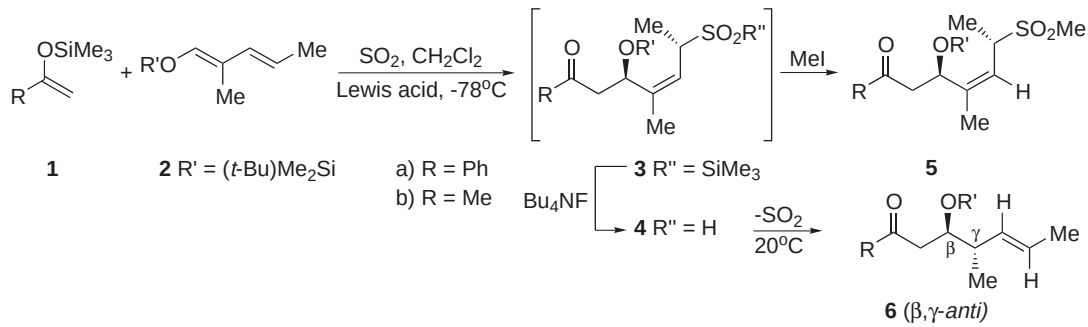
Abstract—The reactions of (*E*,*E*)-1-benzyloxy-2-methylpenta-1,3-diene (**9**) with 3,3-dimethyl-2-(trimethylsilyloxy)butene and (*Z*)-3-(trimethylsilyloxy)pent-2-ene in SO_2 and a Lewis acid give silyl sulfinates that are quenched with MeI to generate the corresponding (*Z*)-4-benzyloxy-1,3-dimethylalk-2-enyl methyl sulfones with unlike relative configuration at C-1 and C-4 (by X-ray diffraction studies), in support of processes involving the intermediacy of a sultine arising from the suprafacial hetero-Diels–Alder addition of SO_2 to diene **9**. © 2001 Elsevier Science Ltd. All rights reserved.

When enoxysilanes **1** and (*E*,*E*)-2-methyl-1-silyloxypenta-1,3-diene **2** are mixed in SO_2/CH_2Cl_2 at −78°C containing a Lewis acid ($Yb(OTf)_3$, (*t*-Bu)Me_2SiOTf), a carbon–carbon bond is formed between the electron-rich alkene and the electron-rich diene with formation of the corresponding unstable sulfinates **3** (Scheme 1). Treatment of **3** with Bu_4NF liberates the corresponding sulfinic acids **4** that can be quenched with MeI to generate the corresponding methyl sulfones **5**, or be allowed to undergo retro-ene eliminations of SO_2 with the exclusive formation of (*anti*,*E*)-3-hydroxy-4-methyl-1-phenylhept-5-en-1-one (**6a**) and (*anti*,*E*)-4-hydroxy-5-methyloct-6-en-2-one (**6b**).[1] The structures of **6a**,**b** were established unambiguously, but not those of **5a**,**b**. We have now carried out further studies with (*E*,*E*)-1-benzyloxy-2-methylpenta-1,3-diene (**9**), SO_2 and the two enoxysilanes **10** (3,3-dimethyl-2-trimethylsilyloxy)butene) and **26** ((*Z*)-3-(trimethylsilyloxy)pent-2-ene). Crystalline sulfones have been isolated and their structures have been established unambiguously by X-ray diffraction studies.[2] The results shed light on the mechanism of reactions shown in Scheme 1.

Boiling of **7** with benzyl alcohol in toluene under acidic conditions[3] generated **8** (77%) that was reduced with $LiAlH_4$ to furnish an allylic alcohol that was esterified



Scheme 1.

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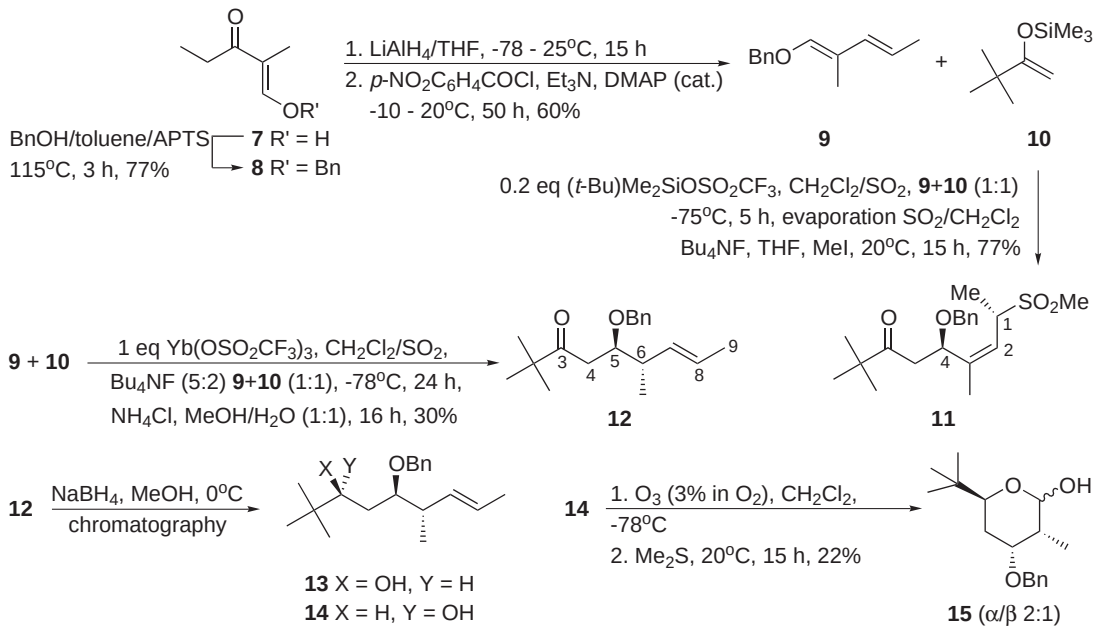
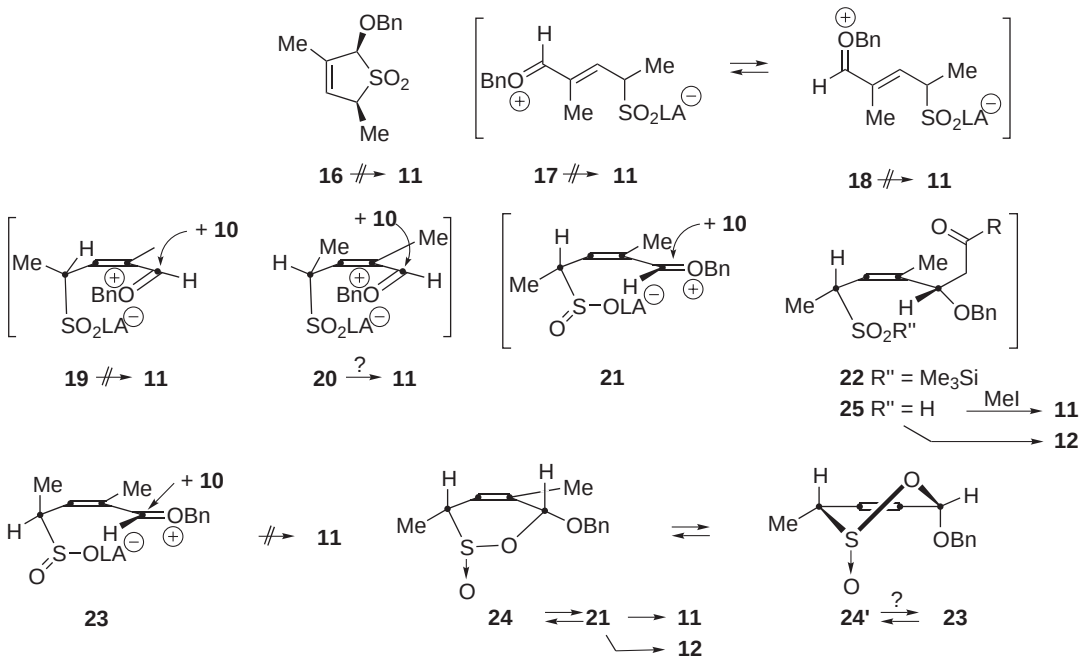
with *p*-nitrobenzoyl chloride (Scheme 2). The corresponding ester eliminated 1 equivalent of *p*-nitrobenzoic acid at 20°C in the presence of Et_3N, providing diene **9** (60%). When a 1:1 mixture of **9** and enoxysilane **10** was added to a stirred solution of 0.2 equivalents of (*t*-Bu)$Me_2SiOSO_2CF_3$ in 2:1 CH_2Cl_2/SO_2, an unstable silyl sulfinate (**22**, see Scheme 3) was formed that was reacted with Bu_4NF in THF, then with an excess of MeI to produce methyl sulfone **11** as single product (77%).[4] X-ray diffraction of a monocrystal of **11** established its structure ((*Z*)-alkene, *unlike* configuration at C-1 and C-4).[2] In the absence of MeI retro-ene elimination of SO_2 occurred with formation of β-benzyloxyketone **12** (30% yield).[5] Its structure was proven by its reduction with $NaBH_4$, which produced a 1:2 mixture of alcohols **13** and **14** that were separated by flash chromatography on silica gel. Ozonolysis of **14** gave a 2:1 mixture of α- and β-pyranose **15**, the ^1H and ^{13}C NMR spectra of which proved (^3J(H,H), NOESY) their relative configurations.

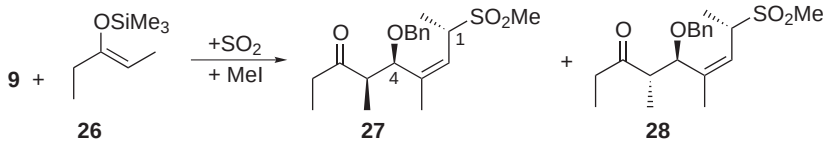
Contrary to (*E*)-1-acetoxybutadiene that adds SO_2 in the presence of CF_3COOH at −75°C giving 6-acetoxy-3,6-dihydro-1,2-oxathiin-2-oxides,[6] in the absence of enoxysilane **10**, SO_2 added to diene **9** (−10 to −50°C) producing the sulfolene **16**. No trace of the expected



Scheme 2.



Scheme 3.



Scheme 4.

sultine was observed. Sulfolene **16** did not react with **10** in the presence of SO_2 and (*t*-Bu)Me_2SiOTf or $Yb(OTf)_3$, but underwent polymerization above −40°C. Similar observations were made with (*E*)-1-methoxybutadiene.[7] Thus, **16** is not an intermediate of the oxyallylation process. Because of the exclusive formation of **11** with a (*Z*) olefinic moiety, zwitterionic intermediates **17** and **18**, resulting from a hypothetical direct addition of SO_2 onto the *s-trans* conformer of **9**, cannot be intermediates of the reactions **9**+**10**+SO_2→**22**→**11**. Direct additions of SO_2 to the *s-cis*-conformer of diene **9** could lead to zwitterions **19**, **20**, **21** and **23**. Intermediates **19** and **23** cannot produce **11**. Zwitterion **20** might lead to **11**, but it is expected to be disfavored for steric reasons. Zwitterion **21** appears to be the most reasonable intermediate that probably arises from the hetero-Diels–Alder addition of SO_2 to **9**, producing sultine **24**=**24′** or its diastereomer with *trans* S=O and BnO groups. The boat conformer **24** of the sultine intermediate is expected to be ionized into **21** that adds to **10**, or alternatively, **24** adds directly to **10** producing **22**, then **11** (Scheme 3). The formation of **12** is explained by invoking a stereoselective retro-ene elimination of SO_2 from the sulfinic acid intermediate **25** as for the other cases already discussed.[1] This hypothesis is now *firmly* confirmed by the establishment of the relative configuration of **11**, and thus of intermediate **25**.

In order to test the generality of the above mechanism we have reacted diene **9** with enoxysilane **26** and SO_2/$Yb(OTf)_3$ (Scheme 4). After the usual work-up with Bu_4NF and MeI, the two diastereomeric methyl sulfones **27**[8] and **28**[9] were isolated in 29 and 33% yield, respectively (the other products are polymers). Their structures were established by X-ray diffraction[2] and showed for both of them 1,4-*anti* (unlike) relative configurations, in agreement with the mechanism proposed in Scheme 3.

This study confirms the hypothesis that our four component[10,11] synthesis of (*Z*)-4-alkoxy-1,3-dimethylalk-2-enyl methyl sulfones involves sultine intermediates arising from the hetero-Diels–Alder addition of 1-oxydienes to SO_2 rather than the corresponding more stable sulfolenes.

Acknowledgements

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References

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2. Complete data have been deposited with the Cambridge Crystallographic Data Centre for **11**: CDCC 140985; **27**: CDCC 140983; **28**: CDCC 140984.
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4. Selected data for **11**: mp 101.5–103°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ_H 7.35–7.27 (5H), 5.37 (dq, 1H, ^3J 11.0 ^4J 1.4, H-7), 4.83 (dd, 1H, ^3J 6.7, 6.2, H-5), 4.47–4.39 (m, 2H), 4.33 (dq, 1H, ^3J 11.0, 6.7, H-8), 3.00 (dd, 1H, ^3J 11.0, 6.7, H-4), 2.81 (s, 3H), 2.72 (dd, 1H, ^3J 11.0, 6.2, H′-4), 1.84 (d, 3H, ^3J 1.4), 1.42 (d, 3H, ^3J 6.7, H-9), 1.12 (s, 9H).
5. Data for **12**: colorless oil, ^{1}H NMR (400 MHz, $CDCl_3$) δ_H 7.34–7.24 (m, 5H), 5.47–5.36 (m, 2H), 4.52 (m, 2H), 3.98 (ddd, 1H, ^3J 7.6, 4.4, 3.8, H-5), 2.80 (dd, 1H, ^2J 17.2, ^3J 7.6, H-4), 2.45 (dd, 1H, ^2J 17.2, ^3J 4.4, H′-4), 2.43 (m, 1H, H-6), 1.67 (d, 3H, ^3J 5.4, H-9), 1.12 (s, 9H), 1.04 (d, 3H, ^3J 6.9, Me-C(6)).
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8. Data for **27**: mp 88–89°C, ^{1}H NMR (400 MHz, $CDCl_3$) δ_H 7.36–7.22 (m, 5H), 5.35 (dq, 1H, ^3J 11.0, ^4J 1.4, H-7), 4.52 and 4.39 (2d, 2H, ^2J 11.7), 4.34 (d, 1H, ^3J 9.8, H-5), 4.13 (dq, 1H, ^3J 11.0, 6.6, H-8), 3.03 (dq, 1H, ^3J 9.8, 6.7, H-4), 2.85 (s, 3H), 2.53 & 2.32 (2dq, ^2J 18.4, ^3J 7.2, H-2), 1.84 (d, 3H, ^4J 1.4, Me-C(6)), 1.40 (d, 3H, ^3J 6.6, H-9), 1.24 (d, 3H, ^3J 6.7, Me-C(4)), 0.99 (t, 3H, ^3J 7.2, H-1).
9. Data for **28**: mp 60–61°C, ^{1}H NMR (400 MHz, $CDCl_3$) δ_H 7.33–7.20 (m, 5H), 5.60 (dq, 1H, ^3J 11.0, ^4J 1.5, H-7), 4.41 and 4.28 (2d, 2H, ^2J 11.3), 4.40 (d, 1H, ^3J 10.1, H-5), 4.12 (dq, 1H, ^3J 11.0, 6.8, H-8), 2.93 (dq, 1H, ^3J 10.1, 7.1, H-4), 2.85 (s, 3H), 2.60 and 2.52 (2dq, 2H, ^2J 18.3, ^3J 7.2, H-2), 1.83 (d, 3H, ^4J 1.5, Me-C(6)), 1.46 (d, 3H, ^3J 6.8, H-9), 1.05 (d, 3H, ^3J 7.2, Me-C(4)), 0.99 (t, ^3J 7.1, H-1).
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