ORGANIC LETTERS

2005
Vol. 7, No. 8
1565−1568

2-Alkylidenesulfol-3-enes by (Regio- and) Stereoselective Cheletropic Addition of SO_2 to (Di)vinylallenes

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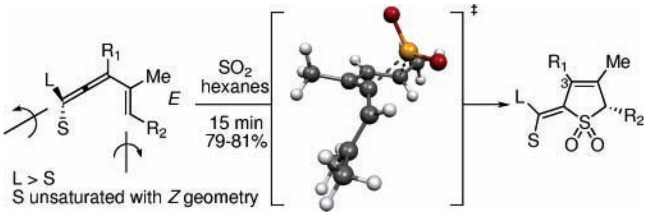
Received February 4, 2005

ABSTRACT



The cheletropic addition of SO_2 to divinylallenes is regioselective, taking place at the most substituted vinylallene and at the *E* unit if vinyl groups of opposite geometry are competing. Diastereofacial differentiation results from the approach of the reagent from the less-substituted direction of the allene and from the concomitant disrotatory movement of the termini of the vinylallene to afford the sterically more congested 2-alkylidenesulfol-3-ene isomer. DFT computations confirm the regio- and the stereoselectivity of these cheletropic additions.

Thermal additions of SO_2 to conjugated dienes and the extrusions from sulfol-3-enes[1] are concerted cheletropic reactions. Woodward and Hoffmann established the preferred approach of SO_2 along a linear trajectory in a suprafacial manner with respect to the diene part[2] and the disrotatory nature of the movement of the diene termini to afford the cyclic sulfones[3] (sulfol-3-enes). These species are useful in organic synthesis as masked dienes,[4,5] and tactics of thermal extrusion of SO_2 from a sulfol-3-ene and subsequent intramolecular Diels−Alder reactions as pericyclic cascade processes have been used in complex natural product synthesis.[6]

cis-2,5-Dimethylsulfol-3-ene **1** undergoes thermal desulfonylation more readily than the trans isomer **3** and yields (*E*,*E*)-hexa-2,4-diene by *out*,*out* disrotation, a rotational selectivity likely due to steric reasons[7] (Scheme 1).

As a continuation of our studies on the regio- and torquoselective thermal electrocyclic reactions of (di)vinylallenes,[8] we recently focused on the cheletropic addition of SO_2 to these compounds. Although the addition of SO_2 to

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(1) (a) Mock, W. L. *J. Am. Chem. Soc.* **1966**, *88*, 2857. (b) McGregor, S. D.; Lemal, D. M. *J. Am. Chem. Soc.* **1966**, *88*, 2858.

(2) Woodward, R. B.; Hoffmann, R. *Angew. Chem., Int. Ed. Engl.* **1969**, *8*, 781.

(3) (a) Schank, K. In *The Chemistry of Sulphones and Sulfoxides*; Patai, S., Rappoport, Z., Stirling, C., Eds.; John Wiley & Sons: New York, 1988. (b) Simpkins, N. S. *Sulphones in Organic Synthesis*; Pergamon: Oxford, 1993.

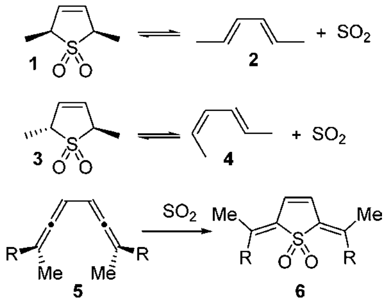
(4) (a) Dendralenes have been obtained by thermal extrusion of SO_2 (450 °C) starting from 2-vinylsulfolenes: Fielder, S.; Rowman, D. D.; Sherburn, M. S. *Angew. Chem., Int. Ed.* **2000**, *39*, 4331. (b) The methodology has been adapted to solid phase: Cheng, W.; Olmstead, M. M.; Kurth, M. *J. Org. Chem.* **2001**, *66*, 5528.

(5) Aromatic derivatives, in turn, are considered precursors of highly reactive *o*-quinodimethane systems, but the temperatures required to generate the *o*-xylylene are usually much higher (240 °C or greater). (a) Cava, M. P.; Deana, A. A. *J. Am. Chem. Soc.* **1959**, *81*, 4266. (b) Cava, M. P.; McGrady, J. *J. Org. Chem.* **1975**, *40*, 72. (c) Nicolaou, K. C.; Barnette, W. E.; Ma, P. *J. Org. Chem.* **1980**, *45*, 1463. (d) Oppolzer, W.; Roberts, D. A. *Helv. Chim. Acta* **1980**, *63*, 1703. (e) Durst, T.; Lancaster, M.; Smith, D. J. H. *J. Chem. Soc., Perkin Trans. 1* **1981**, 1846. (f) Levy, L. A.; Sashikumar, V. P. *J. Org. Chem.* **1985**, *50*, 1760.

(6) Leonard, J.; Hague, A. B.; Knight, J. A. In *Organosulfur Chemistry*; Page, P., Ed.; Academic Press: San Diego, 1998; Vol. 2, Chapter 6. For recent examples, see: (a) Nicolaou, K. C.; Vassilikogiannakis, G.; Mägerlein, W.; Kranich, R. *Angew. Chem., Int. Ed.* **2001**, *40*, 2482. (b) Nicolaou, K. C.; Vassilikogiannakis, G.; Mägerlein, W.; Kranich, R. *Chem.−Eur. J.* **2001**, *7*, 5359.

10.1021/ol050240p CCC: $30.25

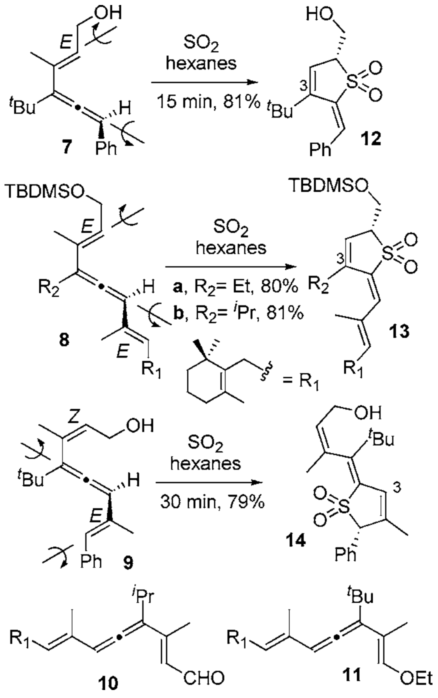
Scheme 1. Model Cheletropic Reactions of SO$_2$ and Dienes



bis-allenes was reported by Skattebøl in 1973 (Scheme 1),[9] the corresponding reaction with vinylallenes is unprecedented to the best of our knowledge.

A series of (di)vinylallenes was designed (Scheme 2) to analyze the regio- and stereoselectivity of the cheletropic addition in order to gauge both steric and electronic effects on reactivity. Their preparation followed the general procedure previously reported,[8] in which the allene is generated by the S$_N$2′ anti displacement of propargylic benzoates with cuprates (see Supporting Information for details).

Scheme 2. Cheletropic SO$_2$ Addition to (Di)vinylallenes



Simply bubbling SO$_2$ into a solution of the (di)vinylallenes in hexane at ambient temperature effected the consumption of starting materials in short reaction times (less than 15 min). (Di)vinylallenes **7**−**9** provided a single cheletropic SO$_2$ adduct (Scheme 2). Signals for the diastereotopic (protected) hydroxyalkyl methylene protons (δ 4.2−4.1 ppm for **12**; δ 4.1−4.0 ppm for **13a**; δ 4.0−3.9 ppm for **13b**) and sulfolene H$_5$ atom (δ 3.80 ppm for **12**; δ 3.57 ppm for **13a**; δ 3.45 ppm for **13b**) in the ^{1}H NMR spectra of **12** and **13a**,**b** were considered diagnostic of the incorporation of SO$_2$ at the terminal polar diene unit.[10] Compound **9**, in contrast, provided an adduct that exhibited a singlet resonating at δ 4.72 ppm, tentatively assigned to sulfolene H$_5$, which suggested that isomer **14** had formed instead. The alkylidene geometry (*E* for **12** and **13**; *Z* for **14**, as result of the CIP rules) was inferred from the observation of cross-correlation signals in the NOE spectra between the C$_3$-alkyl substituent of the sulfolene ring and the exocyclic methyl (phenyl) group at C$_{2'}$ of **13a**,**b** (C$_{1'}$ of **12**) and the corresponding cross-correlation signals between the C$_{1'}$-^{t}Bu group and H$_3$ of **14**. In addition, the structure of the latter was secured by X-ray analysis (Figure 1).

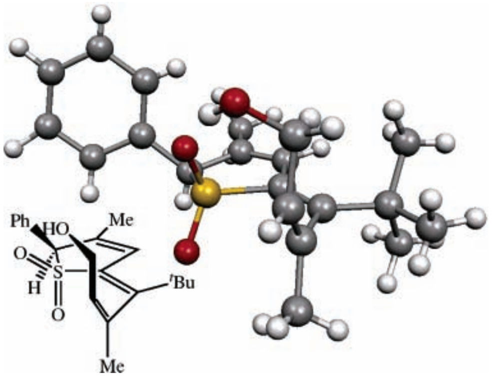


Figure 1. X-ray structure of compound **14**.

Although limited in number, the results illustrated in Scheme 2 reveal some interesting trends:

(a) SO$_2$ adds regioselectively to the more substituted diene unit of divinylallenes **8a**,**b** to afford **13a**,**b**. Although electronically richer due to the greater number of alkyl substituents, other structural factors such as dominant s-cis conformations and shorter distances between the diene termini due to the presence of bulky groups located at the

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(7) (a) Mock, W. L. *J. Am. Chem. Soc.* **1966**, *88*, 2857. (b) McGregor, S. D.; Lemal, D. M. *J. Am. Chem. Soc.* **1966**, *88*, 2858. (c) Mock, W. L. *J. Am. Chem. Soc.* **1975**, *97*, 3666.

(8) (a) López, S.; Rodríguez, J.; García, J.; de Lera, A. R. *J. Am. Chem. Soc.* **1996**, *118*, 1881. (b) de Lera, A. R.; Iglesias, B.; López, S.; Rodríguez, J. *Chem.*—*Eur. J.* **2000**, *6*, 4021. (c) de Lera, A. R.; Alvarez, R.; Lecea, B.; Torrado, A.; Cossío, F. P. *Angew. Chem., Int. Ed.* **2001**, *40*, 557.

(9) Skattebøl, L. *J. Chem. Soc., Chem. Commun.* **1973**, 432.

(10) Addition of SO$_2$ to dienes has been shown to result in a complex competition between a hetero Diels−Alder reaction to provide sultines (kinetic control, occurring at −75 °C) and a cheletropic addition to afford sulfolenes (thermodynamic control), and the competing pathways are further tuned by the nature of the substituents on the diene. For the case at hand, the alternative alkylidenesultines, corresponding to a formal hetero Diels−Alder addition of SO$_2$ to vinylallenes, were discarded on the basis of these kinetic precedents and the X-ray structure of **14**. (a) Roversi, E.; Monnat, F.; Schenk, K.; Vogel, P.; Braña, P.; Sordo, J. A. *Chem.*—*Eur. J.* **2000**, *6*, 1858. (b) Deguin, B.; Vogel, P. *J. Am. Chem. Soc.* **1992**, *114*, 9210. (c) Fernández, T.; Suárez, D.; Sordo, J. A.; Monnat, F.; Roversi, E.; Estrella, A.; Schenk. K.; Vogel, P. *J. Org. Chem.* **1998**, *63*, 9490.

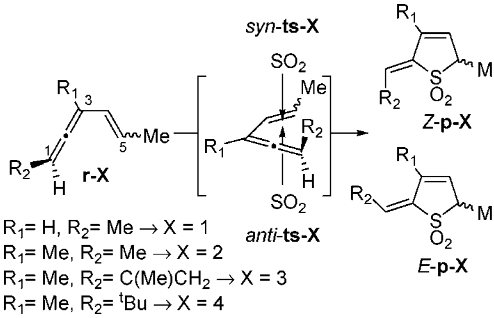
internal position of the vinylallenes may play a role in the regioselectivity.[8]

(b) Electron-withdrawing groups at the vinylallene termini (CHO), on the other hand, inhibited the addition of SO_2, and vinylallenal **10** was recovered unchanged after 1 h at 25 °C (at 80 °C, decomposition was observed). Electron-rich divinylallene **11** suffered extensive decomposition under the reaction conditions.

(c) (*Z*)-Vinylallenes are less reactive than the corresponding *E* isomers. The structure of **14** confirms that the cheletropic reaction occurred at the diene subunit of *E* geometry despite being less substituted.

(d) Diastereoselectivity (or rotational selectivity on the vinylallene) appears to be governed by steric factors. The approach of the reagent from the less-hindered side of the vinylallene dictates the disrotatory movement of the termini (*out,out* in the enantiomers shown in Scheme 2), due to the requirement of orbital overlap between the two reactants. The allene axis configuration is thus transferred to the exocyclic double-bond geometry (Scheme 3), and therefore if enantiopure reactants were used, the absolute configuration of the sulfolene stereocenter would also be under the control of the allene axial chirality.

Scheme 3. Models of Computed Cheletropic Additions of SO_2 to Vinylallenes[a]



[a] Note that the *Z/E* geometry of the olefin remains undefined in the proposed nomenclature and will be specified along the discussion.

To theoretically support the above findings and to get further insight into the factors responsible for the regio- and the stereoselectivity, computations were carried out on reactions of SO_2[11,12] with model (*E*)- and (*Z*)-vinylallenes substituted at C1 and C5 (and C3). DFT was chosen due to the satisfactory results reported in precedent studies with dienes.[13] The multilevel B3LYP/6-311++(3df,2p)//B3LYP/6-31+(d,p) methodology was selected in order to obtain accurate energies. The nature of all the stationary points was resolved through harmonic analysis. Solvent effects were taken into account with sequential single-point calculations at the gas-phase optimized geometries. A variation of the conductor-like screening model (COSMO)[14] method was chosen (heptane) using the parameters proposed by Klamt.[15] All the calculations were performed with the Gaussian 03[16] suite of programs.

Transition structure geometries are highly asymmetric, with sulfur−cumulene carbon bond lengths shorter (2.10−2.27 Å) than the sulfur−olefin carbon counterparts (2.55−2.69 Å). Small variations of these bond distances are observed upon changes in the olefin geometry and the face approach (*syn*/*anti*, see Scheme 3). Interestingly, the greatest difference in forming bond lengths is observed with C_3-methyl-substituted vinylallenes. This effect, likely due to back-strain, has also direct energetical implications, since these substrates proceed through transition states that are from 1 to 5 kcal/mol lower in energy than their unsubstituted counterparts (see Table 1).

Table 1. Gas Phase and Solution (COSMO, Heptane) Relative Free Energies of Activation (kcal/mol, 298 K) of Models **1**−**4**

	gas phase		COSMO	
	syn	anti	syn	anti
(*E*)-**r-1**	27.37	26.63	26.38	24.99
(*Z*)-**r-1**	34.15	33.59	33.04	31.99
(*E*)-**r-2**	26.33	25.10	24.42	22.79
(*Z*)-**r-2**	29.06	28.40	27.28	26.05
(*E*)-**r-3**	27.54	25.47	25.63	23.63
(*Z*)-**r-3**	30.37	28.78	28.33	26.89
(*E*)-**r-4**	31.03	26.55	29.25	24.18
(*Z*)-**r-4**	33.97	30.61	32.82	28.88

Further inspection of Table 1 reveals the sources of selectivity in the cheletropic additions. First, the *Z* geometry of the vinyl moiety is a major contributor to the reaction energetics. Transition structures of these isomers present even more destabilization (2.83−6.96 kcal/mol) than that due to allene substitution (1.45−4.91 kcal/mol). The trend of greater

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[11] Kinetic studies revealed that the reaction of dienes is second order in SO_2, and in fact theoretical computations suggested a role for SO_2 as a Lewis acid.[12] However regio- and diastereoselectivity are considered not to be affected by the SO_2 molecularity since the second SO_2 molecule does not modify the disrotatory nature of the reaction and merely acts as an activating species for the reacting SO_2 molecule.

[12] Fernández, T.; Sordo, J. A.; Monnat, F.; Deguin, B.; Vogel, P. *J. Am. Chem. Soc.* **1998**, *120*, 13276.

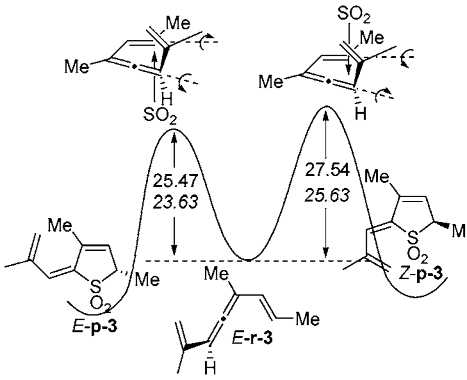
[13] Monnat, F.; Vogel, P.; Rayón, V. M.; Sordo, J. A. *J. Org. Chem.* **2002**, *67*, 1882.

[14] Klamt, A.; Schüürmann, G. *J. Chem. Soc., Perkin Trans. 2* **1993**, *2*, 799.

[15] Klamt, A.; Jonas, V.; Bürger, T.; Lohrenz, J. C. W. *J. Phys. Chem. A* **1998**, *102*, 5074.

[16] Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Montgomery, J. A., Jr.; Vreven, T.; Kudin, K. N.; Burant, J. C.; Millam, J. M.; Iyengar, S. S.; Tomasi, J.; Barone, V.; Mennucci, B.; Cossi, M.; Scalmani, G.; Rega, N.; Petersson, G. A.; Nakatsuji, H.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Klene, M.; Li, X.; Knox, J. E.; Hratchian, H. P.; Cross, J. B.; Adamo, C.; Jaramillo, J.; Gomperts, R.; Stratmann, R. E.; Yazyev, O.; Austin, A. J.; Cammi, R.; Pomelli, C.; Ochterski, J. W.; Ayala, P. Y.; Morokuma, K.; Voth, G. A.; Salvador, P.; Dannenberg, J. J.; Zakrzewski, V. G.; Dapprich, S.; Daniels, A. D.; Strain, M. C.; Farkas, O.; Malick, D. K.; Rabuck, A. D.; Raghavachari, K.; Foresman, J. B.; Ortiz, J. V.; Cui, Q.; Baboul, A. G.; Clifford, S.; Cioslowski, J.; Stefanov, B. B.; Liu, G.; Liashenko, A.; Piskorz, P.; Komaromi, I.; Martin, R. L.; Fox, D. J.; Keith, T.; Al-Laham, M. A.; Peng, C. Y.; Nanayakkara, A.; Challacombe, M.; Gill, P. M. W.; Johnson, B.; Chen, W.; Wong, M. W.; Gonzalez, C.; Pople, J. A. *Gaussian 03*, revision B.02; Gaussian, Inc.: Pittsburgh, PA, 2003.

Scheme 4. Activation Barriers (kcal/mol) of the Two Alternate Approaches in the Cheletropic Addition of SO_2 to Model Divinylallene (*E*)-**r-3** and Their Corresponding Products (Gas Phase, COSMO Values in Italics)



destabilization of the *Z*-anti relative to the *E*-syn approach along the R_2 series (Me, $C(Me)CH_2$, ^{t}Bu) shows reversal only for the bulkier ^{t}Bu substituent. Thus, in divinylallenes with *E* and *Z* vinyl geometries, the addition of sulfur dioxide will occur preferentially at the *E* unit, in keeping with the experimental findings (see Scheme 2). Moreover, the difference in activation barriers between the anti and syn approaches is enhanced by solvation (modeled through a dielectric continuum). The differences computed with the COSMO method confirm that facial selectivity in vinylallenes can be achieved with substituents of moderate size (1.63 kcal/mol with methyl in (*E*)-**r-2** already accounts for 94:6 facial selectivity at 25 °C, whereas more than 5 kcal/mol ensures a 99.9:0.01 ratio even at 250 °C in (*E*)-**r-4**).

Once the facial selectivity is attained, the Woodward–Hoffmann rules ensure the stereoselectivity of the reaction, due to the sulfur dioxide addition proceeding with disrotation of the diene termini in the direction that maximizes the orbital overlap with the sulfur center. As a consequence, the *E* substituent of the alkene rotates toward the approaching SO_2 (see Scheme 4).

In summary, adducts of SO_2 and vinylallenes have been isolated and characterized. Structural studies and computational analysis confirm that the cheletropic reactions are stereoselective and favor the approach that avoids steric interactions with the substituents on the allene acccompanied by the *out*,*out* disrotation of the termini carbons. Moreover, cheletropic additions of SO_2 to (*E*,*E*)-divinylallenes select the more substituted diene unit, whereas with (*Z*,*E*)-divinylallenes, the addition proceeds on the *E* terminus, a regioselectivity trend that is confirmed by DFT computations on model systems.

Acknowledgment. We are grateful to the European Commission ("Anticancer Retinoids", QLK3-2002-02029), the Spanish Ministerio de Ciencia y Tecnología (Grant SAF2004-07131, Ramón y Cajal Research Contract to R.A. and FPU fellowship to C.S. and O.N.), FEDER and the Xunta de Galicia (Grant PGIDIT02PXIC30108PN) for financial support. We also thank Dr. José García Rey for the synthesis of **11**.

Supporting Information Available: Typical experimental procedures for the synthesis of all compounds and their physical and spectroscopic data; X-ray structural data of compound **14** (CIF); and final SCF energies, geometries, and number of imaginary frequencies. This material is available free of charge via the Internet at http://pubs.acs.org.

OL050240P