Unusual expressions of Michael reactivity of 1,3-bis(phenylsulfonyl)allene

James R. Bull, Nicholas S. Desmond-Smith, Steven J. Heggie, Roger Hunter,* and Sophie C. M. Rees-Jones

Department of Chemistry, University of Cape Town, Rondebosch 7701, South Africa
E-mail: roger@science.uct.ac.za

Dedicated to Professor James Ronald Bull on occasion of his retirement as Mally Professor of Organic Chemistry at the University of Cape Town

Abstract: An improved procedure for producing the potent cycloaddition dienophile 1,3-bis(phenylsulfonyl)allene **1** is described based on ensuring removal of excess triethylamine in the work-up of the final dehydroiodination step. Triethylamine, as well as other tertiary amines, promote trimerisation of **1** to **3** (X-ray shown), and a possible mechanism involving potentiation via a Michael addition to **1** is proposed. A further expression of the potent Michael acceptor character of **1** is provided by insertion into the α-position of THF to form **5**. Mechanistically, this is suggested as proceeding via an oxonium-ion ylide, also generated via initial Michael addition of THF to **1**.

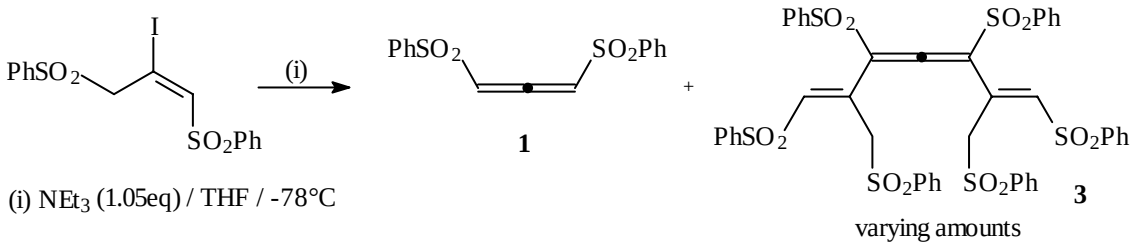
Keywords: Michael addition, electrophilic allene, oxonium-ion ylide, α-insertion

Introduction

We have recently reported the synthesis of 1,3-bis(phenylsulfonyl)allene **1** and its application as a useful dienophile in Diels-Alder reactions.[1] During development of its chemistry, several unusual facets of reactivity were noted based on its ability to act as a potent Michael acceptor. This paper reports on two unusual expressions of Michael-based reactivity of **1**, as well as an improved procedure for preparing it.

Results and Discussion

The first observation was that the final key dehydroiodination step of the synthesis (details in experimental) invariably gave quantities of a by-product **3**, the amount depending on work-up and isolation procedure, Scheme 1.



Scheme 1

Eventually it became clear that formation of **3** was promoted by traces of unremoved triethylamine in the work-up, and that complete conversion could be effected in about 60% isolated yield after chromatography by exposing pure allene to triethylamine in dichloromethane at 0°C. Other tertiary amines (*N*-methylmorpholine, *N*-methylpyrrolidine, *N*-methylpiperidine; 2eq at 0°C in CH_2Cl_2) similarly promoted conversion of **1** to trimer in around 60% isolated yield following chromatography. Compound **3** could be crystallised from ethyl acetate / pet ether, and the presence of three sets of signals for the phenylsulfonyl groups in the ^1H and ^{13}C NMR spectra suggested a trimer containing an allene motif (δ_C = 206.4 ppm for the central allenic carbon), which was confirmed by mass spectrometry (M^+ = 960). Several structures were considered, but eventually single X-ray analysis established the product to be the terminally tetrasubstituted allene **3**, Figure 1.

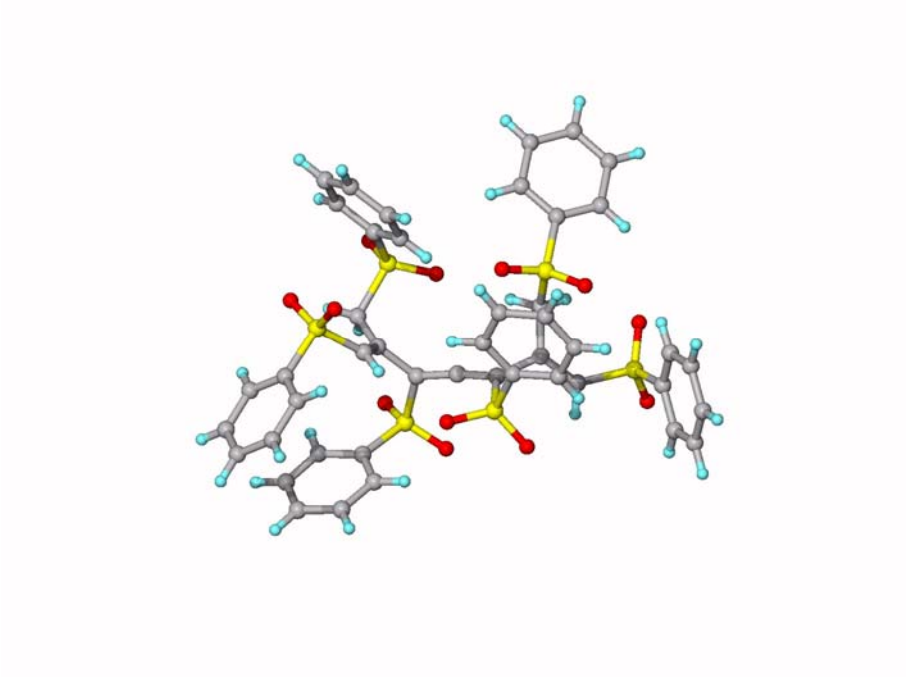
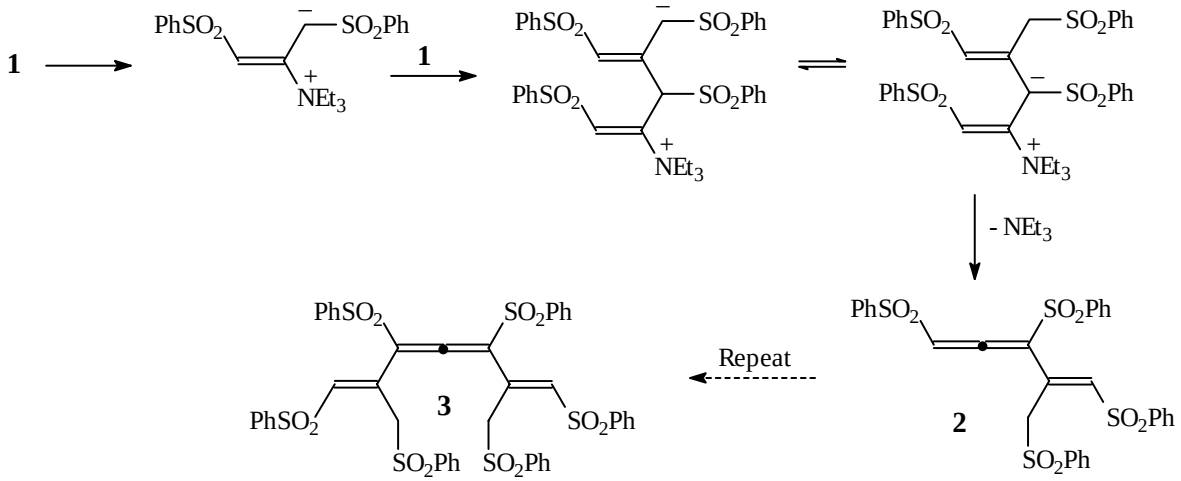


Figure 1. X-Ray Structure of 3.

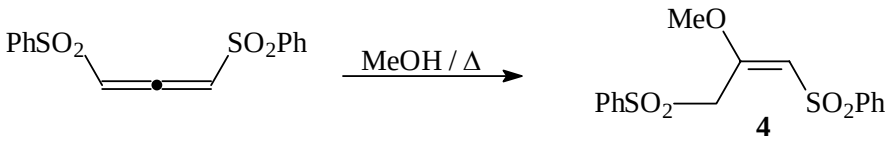
Mechanistically, it seems plausible to suggest that **3** forms from **1** via initial nucleophilic activation as a result of Michael addition to the allene central carbon. Triethylamine as

nucleophile[2,5] is the most logical candidate for such a process, although a SET process cannot be ruled out.[3] The resultant carbanion may then add (anti) to a second molecule of **1** and the new carbanion may then restore the original allenic character of **1** via a proton transfer-elimination (of triethylamine or an electron in the case of SET) combination to afford **2**. The process may then be repeated at the other terminus to generate tetrasubstituted allene **3**. Scheme 2 summarises the mechanism.



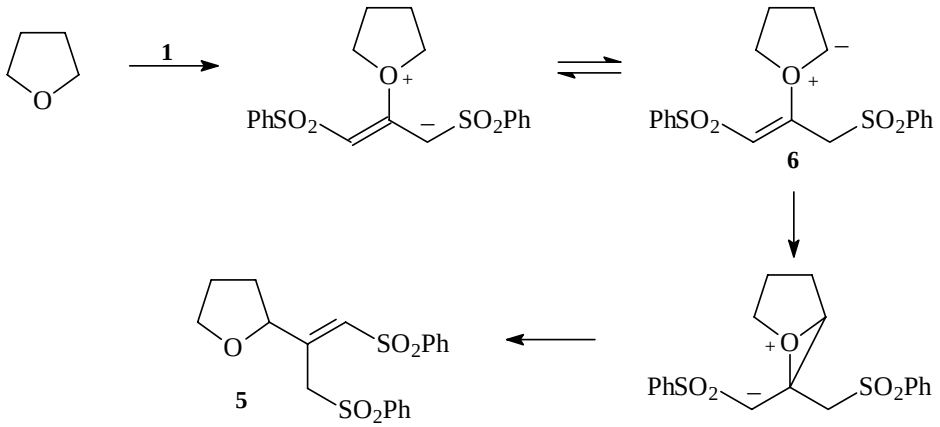
Scheme 2

Identification of **1** as a potent Michael acceptor promoted an interest in trying to exploit it for other expressions of C-C bond formation. The addition of nucleophiles at the central allenic carbon to allenes bearing electron-withdrawing groups at the terminus is well documented in the literature. Stirling[4] demonstrated that thiolate, methoxide and phenylsulfinate all attack phenylsulfonylpropadiene, while other workers have demonstrated other nucleophiles such as tertiary amines[5], allyl alcohols[6] (with catalytic allyl alkoxide) as well as enamines[7] can be used to produce 3-phenylsulfonyl-2-substituted propenes as 2-substituted allyl sulfones. The superior Michael acceptor ability of **1** compared with phenylsulfonylpropadiene allows even neutral methanol[4] to be added (Δ, 24hr) to afford (*E*)-2-methoxy-1,3-bis(phenylsulfonyl)prop-1-ene **4** exclusively, Scheme 3. Addition in this case was assumed on steric grounds to be anti to the C-S bond that is coplanar with the π-system undergoing addition, consistent with recent findings on related systems.[8]



Scheme 3

Further work on the solvent compatibility study revealed that refluxing **1** in dry THF over a number of days resulted in conversion to the 2-insertion product **5**. Structure **5** was elucidated from a full characterisation, with the α-tetrahydrofuranyl proton (H-2') resonating at 4.92 ppm and 79.4 ppm in the ^{1}H and ^{13}C NMR spectra respectively. A possible mechanism for the conversion is shown in Scheme 4 invoking the intermediacy of an oxonium-ion ylide. The initial step involves Michael addition of THF to the allene central carbon followed by tautomeric equilibration to the oxonium ion ylide **6**. A second Michael addition (Stevens-type[9]) followed by elimination produces insertion product **5**.



Scheme 4

Oxonium-ion ylides have been elegantly exploited in organic synthesis[10] in recent years and without question the most popular way of generating them is via trapping carbenoid intermediates, particularly ketocarbenoids, generated by metal-catalysed decomposition of diazo compounds.[11] To the best of our knowledge this is a unique case of one being generated via nucleophilic addition to an allene. Furthermore, this insertion reaction constitutes an interesting alternative to transition-metal mediated[12] or radical processes.[13] Investigation of the scope of the reaction by varying the ring size gave disappointing results. Neither styrene oxide, as a representative epoxide, nor tetrahydropyran under a wide range of reaction conditions of temperature, time and solvent gave any discernible product. Either unreacted **1** was recovered or, at the higher temperatures, decomposition products. Presumably the greater Lewis basicity of tetrahydrofuran is responsible for its exclusive reactivity profile. The lack of reactivity of tetrahydropyran suggests that addition of α-tetrahydrofuranyl radical to the allene is not operating. Moreover, the latter type of reaction is normally carried out using reagents that promote radical formation such as benzoyl peroxide / Δ[13a] or triethylborane / O_2[13b] (the reaction in this paper was conducted under a nitrogen atmosphere but the long reaction times may have allowed introduction of traces of O_2). The difference in reactivity between triethylamine and tetrahydrofuran as nucleophilic activators is also striking. The preferred intramolecular pathway followed by the tetrahydrofuran reaction suggests that tautomerism to the oxonium-ion ylide **6** is

faster than intermolecular addition to a second allene, owing to the greater acidity of the tetrahydrofuran C-2 hydrogens of the oxonium ion compared to those in the case of triethylamine.

In conclusion, some interesting expressions of Michael reactivity of allene **1** have been uncovered suggesting the possibility for other Michael-based methodologies involving **1** for C-C bond formation to be developed.

Acknowledgements

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Experimental Section

General Procedures. Melting points were measured on a Reichert-Jung Thermovar hot stage microscope and are uncorrected. Microanalyses were determined using a Fisons EA 1108 CHNS-O instrument. Mass spectra were recorded on a VG micromass 16F spectrometer operating at 70eV. Infrared spectra were recorded in chloroform solutions using a Perkin-Elmer Paragon 1000 FT-IR spectrometer, over the range 800 – 4000 cm^{-1}. ^{1}H NMR and ^{13}C spectra were recorded in $CDCl_3$ on either a Varian VXR-200 (200 MHz) or Varian Unity (400 MHz) spectrometer. Thin layer chromatography was performed on aluminium-backed silica gel 60 F_{254} plates in ethyl acetate/petrol or ethyl acetate/toluene solvent systems, that were visualised by illumination under UV or sprayed with anisaldehyde / H_2SO_4 and heated. Column chromatography was carried out using Merck Kieselgel 60, 70-230 mesh, eluting with ethyl acetate / petrol or ethyl acetate/toluene mixtures.

Optimised procedure for 1,3-bis(phenylsulfonyl)allene. 3-Phenylsulfonylprop-1-yne (4.65g, 25.8 mmol) and AIBN (5 mg) were added to degassed toluene (20 ml) and the solution heated to 90°C. Freshly prepared benzenesulfonyl iodide[14] (6.92g, 25.8 mmol) in toluene (10 ml) was added dropwise over 1 h and the mixture stirred for a further 20 h at rt. The solution was cooled to 0°C and the crystals collected by filtration. These were washed (40% $Na_2S_2O_3$; cold H_2O), and dried *in vacuo* to yield (*E*)-2-iodo-1,3-bis(phenylsulfonyl)propene (11.22g, 97%) as a brown crystalline product, m.p. 118-120°C (from CCl_4); (Found: C, 40.5; H, 2.9; S, 14.4%. $C_{15}H_{13}IO_4S_2$ requires C, 40.2; H, 2.9; S, 14.3%); ν_{max} ($CHCl_3$) / cm^{-1} 1326, 1154; δ_H (200 MHz, $CDCl_3$) 5.21 (2H, s), 7.20 (1H, s), 7.51-7.79 (6H, m, Ar-H), 7.91-8.08 (4H, m, Ar-H); δ_C (50 MHz, $CDCl_3$) 62.9, 98.7, 128.1, 128.8, 129.4, 129.6, 134.4, 138.9, 139.1, 143.8; m/z M^+ 448.

Triethylamine (0.44 ml, 3.15 mmol) in THF (2 ml) was added slowly to a stirred solution of 2-iodo-1,3-bis(phenylsulfonyl)propene (1.34g, 3.0 mmol) in THF (5 ml) at -78°C. After 30 min

the reaction was quenched with cold HCl (1M, 5 ml) and the product extracted into ethyl acetate. The combined organic extracts were washed with aq. sodium bicarbonate, dried ($MgSO_4$) and the solvent removed to give a residue, which was subjected to flash chromatography (eluent = EtOAc / petrol) to yield **1** (0.91g, 95%), m.p.105-106°C (from CCl_4 or EtOAc/petrol); (Found: C, 56.3; H, 3.8; S, 20.05%. $C_{15}H_{12}O_4S_2$ requires C, 56.2; H, 3.8; S, 20.0%); ν_{max} ($CHCl_3$)/cm^{-1} 1965, 1331, 1158; δ_H (200 MHz, $CDCl_3$) 6.73 (2H, s), 7.55 – 7.76 (6H, m, Ar-H), 7.93-8.01 (4H, m, Ar-H); δ_C (50 MHz, $CDCl_3$) 108.0, 128.1, 129.5, 134.5, 139.9, 206.4.

(1*E*, 6*E*)- 2,6-Bis(methylphenylsulfonyl)-1,3,5,7-tetrakis(phenylsulfonyl)-1,3,4,6-heptatetraene (3). Triethylamine (0.17ml, 1.25 mmol) was added slowly via syringe to a solution of 1,3-bis(phenylsulfonyl)allene **1** (200mg, 0.63 mmol) in dry dichloromethane (4 ml) at 0ºC. After 2h the solvent was removed *in vacuo* and the residue purified directly by column chromatography-(eluent EtOAc / light petrol) to afford trimer **3** (120mg, 60%), m.p. 141º - 142ºC (from EtOAc / hexane); (Found: C, 56.1; H, 3.8; S, 20.1%. $C_{45}H_{36}O_{12}S_6$ requires C, 56.2; H, 3.8; S, 20.0%); ν_{max} ($CHCl_3$) cm^{-1} 1318, 1307, 1151; δ_H (400 MHz), $CDCl_3$) 4.86 (2H, d, J_{AB} 13.4 Hz, CH_2), 5.13 (2H, d, J_{AB} 13.4 Hz, CH_2), 6.92 (2H, s, CH), 7.40 (4H, t, Ar), 7.50-7.60 (10H, m, Ar), 7.62-7.69 (4H, Ar), 7.76 (4H, dd, *J* 1.2, 7.4 Hz, o-Ar), 7.89 (4H, dd, *J* 2.1, 7.4 Hz, o-Ar), 8.00 (4H, dd, *J* 1.2, 7.4 Hz, o-Ar); δ_C (100.6 MHz) 54.7 (CH_2), 123.3(vinyl), 127.8(vinyl), 128.1 (*o*-C), 128.8 (*o*-C), 129.0 (*o*-C), 129.1 (*m*-C), 129.4 (*m*-C), 129.5 (*m*-C), 134.2 (*p*-C), 135.1 (*p*-C), 136.9 (*q*-C), 137.2(vinyl), 138.5 (*q*-C), 139.2 (*q*-C), 207.0 (C-4); M^+ 960.

(*E*)-2-Methoxy-1,3-bis(phenylsulfonyl)propene (4). A solution of **1** (180mg, 0.56mmol) in dry methanol (5 ml) was refluxed under nitrogen for 24hr. Following removal of solvent, the residue was subjected to column chromatography directly (eluent = EtOAc / toluene) to afford **4** (163 mg, 82%), m.p.148-149°C (from EtOAc / toluene); (Found: C, 54.45%; H, 4.6; S, 18.2%. $C_{16}H_{16}O_5S_2$ requires C, 54.5; H, 4.6; S, 18.2%); ν_{max} ($CHCl_3$)/cm^{-1} 1310, 1276 (OMe), 1149; δ_H (200 MHz, $CDCl_3$) 3.54 (3H, s, OMe), 4.79 (2H, s, 3-H_2), 5.59 (1H, s, 1-H), 7.44-7.71 (6H, m, Ar-H), 7.88-8.00 (4H, m, Ar-H); δ_C (50 MHz) 56.5, 56.8, 107.4, 127.1, 128.2, 129.1, 133.2, 133.9, 139.5, 142.1, 158.7. m/z 211 (M^+-$PhSO_2$).

(*E*)-2-(2-Tetrahydrofuranyl)-1,3-bis(phenylsulfonyl)propene (5). A solution of 1,3-bis(phenylsulfonyl)allene **1** (180mg, 0.56mmol) in dry THF was refluxed for 5 days, after which the solvent was removed *in vacuo* and the residue subjected to column chromatography (eluent ethyl acetate / toluene) to afford **5** (157mg, 71%) as a colourless solid, m.p.133 - 135ºC (from ethyl acetate / toluene); (Found: C, 58.1; H, 5.3; S, 16.2%. $C_{19}H_{20}O_5S_2$ requires C, 58.1; H, 5.1; S, 16.3%); ν_{max} ($CHCl_3$)/cm^{-1} 1149, 1308; δ_H (400 MHz), $CDCl_3$) 1.64 (1H, dq, *J* 3 x 7.9, 12.2 Hz, 3'- H), 1.88 -1.99 (2H, m, 4'- H_2), 2.39 (1H, dtd, *J* 5.3, 2 x 7.3, 12.2 Hz, 3'- H), 3.84 - 3.88 (2H, m, 5'- H_2), 3.91 (1H, d, *J* 13.2 Hz, 3 - H), 4.92 (1H, dt, *J* 2 x 1.6, 7.3 Hz, 2'- H), 5.65 (1H, d, *J* 13.2 Hz, 3 - H), 6.66 (1H, d, *J* 1.6 Hz, 1-H), 7.50 – 7.72 (6H, m, Ar), 7.87 – 7.89 (2H, m, o-Ar), 8.01 – 8.04 (2H, m, *o*-Ar); δ_C (100.6 MHz) 25.6 (C-4'), 31.5 (C-3'), 54.3 (C-3), 68.8 (C-5'), 79.4 (C-2'), 127.7 (*o*-C), 128.5 (*o*-C), 129.0 (C-1), 129.2 (*m*-C), 129.3 (*m*-C), 133.7 (*p*-C), 134.1 (*p*-C), 139.2 (*q*-C), 140.5 (*q*-C), 144.3 (C-2); m/z 251 (100%, M^+- $PhSO_2$).

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