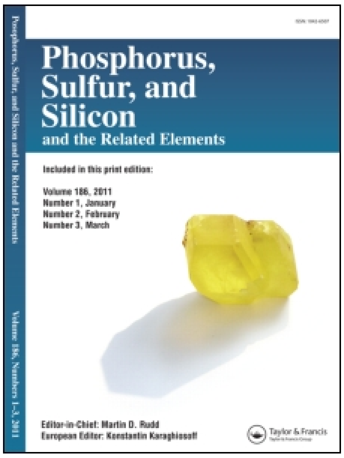


Phosphorus, Sulfur, and Silicon and the Related Elements
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713618290

Construction of the 17-Thiasteroid Ring System by the Diene-Sulfur Dioxide Cycloaddition Reaction

Louis D. Quin[a]; Nandakumar Rao[a]
[a] Paul M. Gross Chemical Laboratory, Duke University, Durham, North Carolina

To cite this Article Quin, Louis D. and Rao, Nandakumar(1979) 'Construction of the 17-Thiasteroid Ring System by the Diene-Sulfur Dioxide Cycloaddition Reaction', Phosphorus, Sulfur, and Silicon and the Related Elements, 5: 3, 371 — 373
To link to this Article: DOI: 10.1080/03086647908077740
URL: http://dx.doi.org/10.1080/03086647908077740

Phosphorus and Sulfur
1979, Vol. 5, pp. 371–373

SHORT COMMUNICATION

Construction of the 17-Thiasteroid Ring System by the Diene-Sulfur Dioxide Cycloaddition Reaction

LOUIS D. QUIN and NANDAKUMAR RAO[1]

Paul M. Gross Chemical Laboratory, Duke University, Durham, North Carolina 27706

(*Received September 15, 1978*)

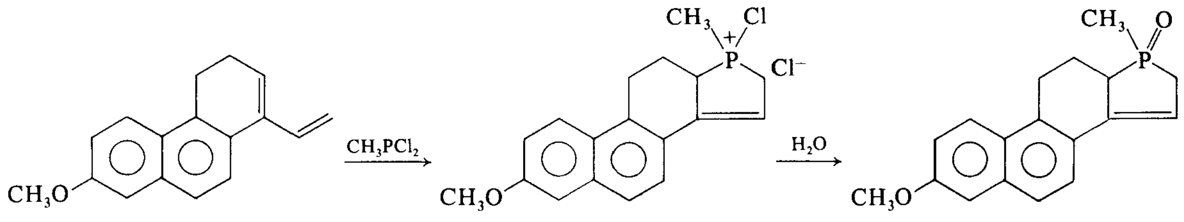
We recently showed[2] that the steroid ring system can be constructed with a phosphorus atom replacing a carbon in the D-ring by the cycloaddition of a phosphorus (III) halide with a diene that is a vinyl dihydrophenanthrene derivative, such as (**1**). The phosphine oxide (**3**) resulting from the hydrolysis of the initial cycloadduct (**2**) has some resemblance to the hormone equilenin, which also has rings A and B in naphthalene form.

The cycloaddition reaction has a counterpart in sulfur chemistry,[3] indeed one that predates the extension to phosphorus chemistry by McCormack in 1953;[4] it involves the use of sulfur dioxide as the one-atom participant in this cheletropic process.[5] We reasoned that this simple reaction could similarly provide the skeleton of the 17-thiasteroid system. 1-Vinylcycloalkenes are included in the numerous dienes useful in the cycloaddition, but we felt it necessary to test the utility of the reaction for multicyclic synthesis by first performing it with a benzocycloalkene, and we have employed a 1-vinyl-3,4-dihydronaphthalene (**4**) for this test. The cycloadduct was obtained as a stable crystalline solid in 38% yield. This product had the normal chemistry of the sulfolene ring; treatment with base rearranged the double bond into conjugation with the sulfuryl group forming (**6**), and catalytic hydrogenation reduced the double bond of (**6**) to give the sulfolane (**7**).

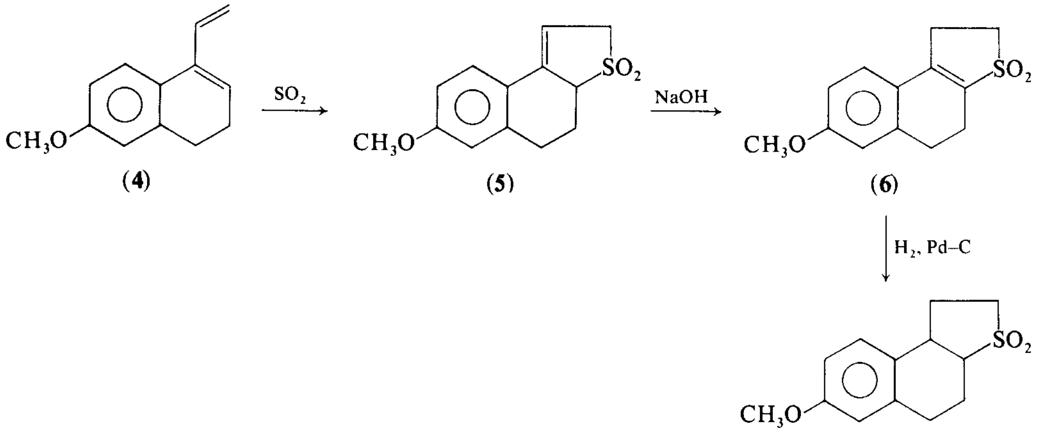
We then performed the SO_2 reaction with diene (**1**), and indeed obtained the cycloadduct (**8**) in 60% yield as a stable, easily crystallized solid. Since diene (**1**) is formed in only two steps[2] (addition of vinylmagnesium bromide to the well-known 1-keto-1,2,3,4-tetrahydrophenanthrene,[6] followed by dehydration by the I_2-quinoline method), the thiasteroid ring system is seen to be established in quite simple fashion. A wide variety of ring-D substituted thiasteroids can be constructed by using other dienes in the cycloaddition, and by modifying the initially formed products to resemble more closely natural steroids of high potency.

SYNTHESES

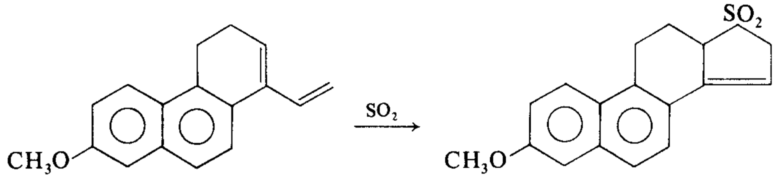
The cycloadditions of dienes (**1**) and (**4**) were carried out in a 2:1 methanol–benzene solvent (150 ml for about 20–30 g of diene) containing a trace of hydroquinone. Liquid SO_2 (about 1.5 equivalents) was added to the cold solution in a pressure bottle, which was then sealed and allowed to stand at room temperature for 12 hours. The mixture was chilled and the precipitated solid adduct was filtered off, washed



(**1**) (**2**) (**3**)



(4) (5) (6) (7)



(1) (8)

with ether, and recrystallized from acetone: (**4**), 30%, mp 124–130°C; (**8**), 60%, mp 173–175°C. Both gave the correct C, H, S analyses.

Rearrangement of cycloadduct (**5**) (1.0 g) to (**6**) was accomplished in a dioxane (20 ml)–water (10 ml) medium containing 0.2 g of KOH at room temperature for 2 days. The solution after neutralization was stripped to dryness and the organic product recovered by ether extraction; yield 98%, mp 125–126°C from methanol. Compound (**6**), which no longer had the olefinic proton nmr signal of (**5**) at δ 6.3, was hydrogenated (50 psi) in absolute ethanol for 12 hours with a Raney nickel catalyst. The recovered product was recrystallized from ethanol, mp 121°C. Both (**6**) and (**7**) gave correct C, H, S analyses.

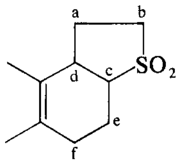
TABLE I

^{13}C nmr data[a] for non-aromatic ring carbons[b]

Compound	C–a	C–b	C–c	C–d	C–e	C–f
(**5**)	109.6 (113.1)	55.3 (55.8)	61.9	135.9 (137.6)	20.6	28.5
(**6**)	23.7	48.8	138.7 (140.1)	138.7 (140.1)	17.1	28.1
(**7**)	30.1	51.6	59.1	38.1	20.3	28.1
(**8**)	107.1 (111.5)	56.3 (55.4)	61.5		20.5	24.6

[a] Taken with a JEOL FX-60 spectrometer by the FT method with proton noise decoupling, TMS = 0. Values in parentheses are alternative assignments.

[b] Designated by the general structure



^{13}C NMR SPECTRA

Structures of the four new compounds were confirmed by their ^{13}C nmr spectra, some features of which are given in Table I. Especially notable were two effects of steric compression. Attachment of a second benzene ring onto (**5**) to form (**8**) introduces compression at γ-related C–f, causing pronounced shielding. Shifting the double bond from the β,γ-position of (**5**) to the α,β-position of (**6**) brings C–e into closer steric interaction with the oxygens of the sulfone group, and a 3.5 ppm upfield shift results. Both effects are seen in the corresponding phosphine oxides,[7] which were useful models for interpreting the spectra. Other assignments of sp^3 carbons were easily made. Olefinic ring carbons were close to, or intermingled with, aromatic carbons; they were not positively identified.

REFERENCES

1. A National Science Foundation Undergraduate Research Participant, Summer, 1978.
2. C. Symmes, Jr., J. Morris and L. D. Quin, *Tetrahedron Letters* 335 (1977).
3. S. D. Turk and R. L. Cobb, in *1,4-Cycloaddition Reactions*, edited by J. Hamer (Academic Press, N.Y., 1967), Chapt. 2.
4. W. B. McCormack, U.S. Patents 2,663,736 and 2,663,737 (1953); reviewed by L. D. Quin in Chapt. 3 of Ref. 3.
5. E. Block, *Reactions of Organosulfur Compounds* (Academic Press, N.Y., 1978), pp. 268–276.
6. G. Stork, *J. Am. Chem. Soc.* **69**, 2936 (1947).
7. W. L. Orton, K. A. Mesch and L. D. Quin, *Phosphorus and Sulfur*, in press.