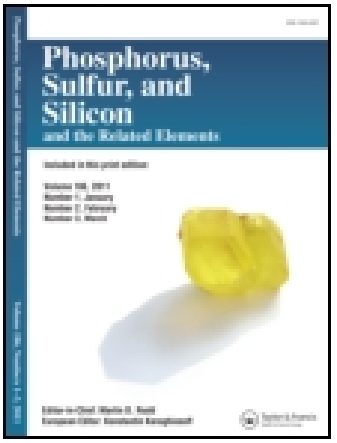


Phosphorus, Sulfur, and Silicon and the Related Elements
Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/gpss20

Efficient Synthesis of Indolizidine Alkaloids from γ-Hydroxy-α,β-unsaturated Sulfones

Juan C. Carretero , Ramon Gomez Arrayas , Isabel Storch De Gracia & Javier Adrio

[a] Departamento de Química Orgánica. , Universidad Autónoma de Madrid , Madrid 28049, Spain

[b] Departamento de Química Orgánica. , Universidad Autónoma de Madrid , Madrid 28049, Spain

[c] Departamento de Química Orgánica. , Universidad Autónoma de Madrid , Madrid 28049, Spain

[d] Departamento de Química Orgánica. , Universidad Autónoma de Madrid , Madrid 28049, Spain

Published online: 17 Mar 2008.

To cite this article: Juan C. Carretero , Ramon Gomez Arrayas , Isabel Storch De Gracia & Javier Adrio (1997) Efficient Synthesis of Indolizidine Alkaloids from γ-Hydroxy-α,β-unsaturated Sulfones, Phosphorus, Sulfur, and Silicon and the Related Elements, 120:1, 347-348, DOI: 10.1080/10426509708545542

To link to this article: http://dx.doi.org/10.1080/10426509708545542

Phosphorus, Sulfur, and Silicon, 1997, Vol. 120 & 121, pp. 347–348
Reprints available directly from the publisher
Photocopying permitted by license only

Efficient Synthesis of Indolizidine Alkaloids from γ-Hydroxy-α,β-unsaturated Sulfones

JUAN C. CARRETERO, RAMON GOMEZ ARRAYAS,
ISABEL STORCH DE GRACIA, JAVIER ADRIO.

Departamento de Química Orgánica. Universidad Autónoma de Madrid. Madrid 28049. Spain

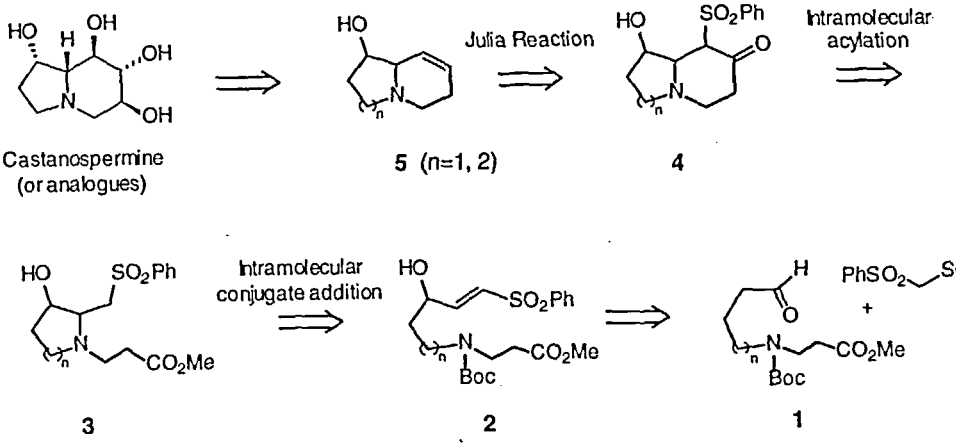
An efficient and stereoselective synthesis of polyhydroxylated indolizidine alkaloids from readily available N-substituted γ-hydroxyvinyl sulfones is described.

Naturally occurring polyhydroxylated indolizidine alkaloids, such as castanospermine or swainsonine, have been shown to be powerful inhibitors of many glycosidases. However, most of the reported syntheses of this kind of natural products utilize monosaccharides as starting materials which limits the flexibility for structural modifications.[1]

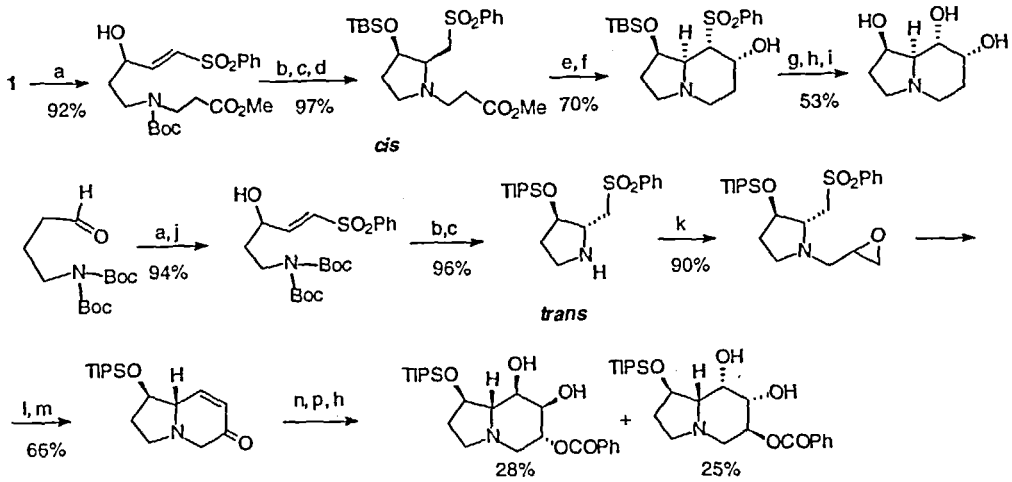
As a part of our current interest concerning the use of γ-oxygenated-α,β-unsaturated sulfones as versatile intermediates in enantioselective and stereoselective synthesis, we have developed a new approach to the synthesis of polyhydroxylated indolizidine alkaloids.[2] As it is shown in the retrosynthetic scheme, all the key steps are based on the reactivity of the sulfonyl group: a) condensation of sulfonyl sulfinyl methanes with the N-substituted aldehydes **1** gives the required N-substituted γ-hydroxy-α,β-unsaturated sulfones **2**; b) intramolecular conjugate addition to the vinylsulfone moiety of **2** yields quantitatively the pyrrolidine (n=1) or piperidine (n=2) intermediates **3**; c) intramolecular Claisen-like condensation of **3** yields quantitatively the ketosulfones **4**, having indolizidine structure; d) finally, removal of the sulfonyl group by Julia reaction lead to a C=C bond (olefins **5**) suitable for stereoselective dihydroxylation reactions.

Interestingly, the stereoselectivity of the intramolecular conjugate addition is highly dependent on the steric size of the γ-oxygenated moiety. Thus, whereas *cis*-pyrrolidines are formed majoritarily from the γ-hydroxyvinyl sulfone, *trans*-

pyrrolidines and *trans*-piperidines are obtained stereoselectively from the γ-OTIPS derivatives.[3]



As two representative examples, in the following schemes are summarized the stereoselective synthesis of a trihydroxylated and a tetrahydroxylated indolizidine alkaloid.



(a) $PhSO_2CH_2SOTol$, piperidine, 0°C; (b) CF_3COOH; (c) Et_3N, THF, -78°C; (d) CITBS, imidazole; (e) LHMDS, THF, 0°C; (f) $LiEt_3BH$, -78°C;(g) Na(Hg); (h) OsO_4, Et_3NO; (i) HCl 5N; (j) TPSTf, 2,6-Lutidine; (k) , K_2CO_3, CH_3CN; (l) MeMgI, THF, 0°C; (m) $(COCl)_2$, DMSO, Et_3N; (n) DIBAL,THF, -78°C; (p) PhCOCl, Py.

REFERENCES

1. K. Burgess, *Tetrahedron*, **48**, 4045 (1992).
2. J. C. Carretero and R. Gómez Arrayás, *J. Org. Chem.*, **60**, 6000 (1995).
3. J. C. Carretero, R. Gómez Arrayás and I. Storch de Gracia, *Tetrahedron Lett.* **37**, 3379 (1996).