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LETTERS

A Formal Synthesis of the Syributins and Secosyrins and A Synthetic Approach Towards the Syringolides

Miguel Carda,*[a] E. Castillo,[a] S. Rodríguez,[a] E. Falomir[a] and J. Alberto Marco,*[b]

[a]*Depart. de Q. Inorgánica y Orgánica, Univ. Jaume I, Castellón, E-12080 Castellón, Spain.*
[b]*Depart. de Q. Orgánica, Univ. de Valencia, E-46100 Burjassot, Valencia, Spain.*

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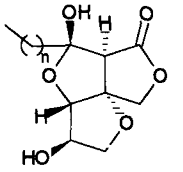
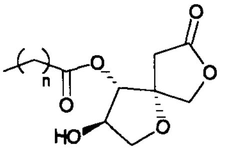
Abstract: The indium-mediated allylation of a protected derivative of D-xylulose in aqueous THF is highly diastereoselective. The obtained product has been converted in four steps into a spiro lactone previously transformed into syributins and secosyrins. This remarkably short reaction sequence constitutes therefore a formal synthesis of these compounds and provides also a promising synthetic approach towards the syringolides.

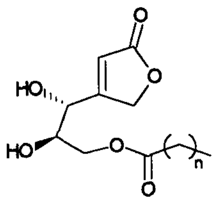
Syringolides 1 and 2 are biologically active metabolites recently isolated by Sims *et al.* from culture fluids of microbial pathogens such as *Pseudomonas syringae* pv. *tomato*, *P. syringae* pv. *glycinea* and others.[1] These highly oxygenated molecules are the first known nonproteinaceous metabolites found to elicit hypersensitive responses on soybean plants carrying the resistance gene *Rpg4*. Two years later, Sims *et al.*[2] reported the isolation from the same source of four structurally related metabolites, the syributins 1 and 2 and secosyrins 1 and 2. Although not active elicitors, these products display biosynthetic interest as they are coproduced with the syringolides and may provide clues to the nature of the genes involved in the hypersensitive response.



Syringolide 1 (n=4)
Syringolide 2 (n=6)



Secosyrin 1 (n=4)
Secosyrin 2 (n=6)



Syributin 1 (n=4)
Syributin 2 (n=6)

The interesting and rather unusual nature of the biological properties of these compounds has motivated several total syntheses.[3] The first synthesis of the syringolides, which also served to establish their absolute configurations, was patterned along the presumed biosynthetic pathway.[3a] Syntheses of the syributins and secosyrins have appeared very recently.[3f,4] We here wish to present a short synthesis of the latter compounds, which is based on our recently described ketone allylation methodology in aqueous media.[5]

The synthesis begins with D-xylulose, a starting material used in one of the previous syntheses of syringolide 2.[3e] Commercial D-xylulose (Aldrich) is very expensive but the sugar can be easily prepared by basic isomerization of the cheap D-xylose.[6] Indium-mediated allylation of D-xylulose was not very stereoselective and gave a ca. 7:3 mixture of stereoisomers. In contrast, allylation of the 1,5-bis-O-silyl derivative **1** gave essentially one diastereoisomer with structure **2**.[7] Benzylation of the secondary alcohol groups in **2**, followed by ozonolysis in basic medium,[8] afforded hydroxy ester **4**. Desilylation of **4** was accompanied by simultaneous lactonization to **5**. Finally, tosylation of the primary hydroxyl group in **5** took place smoothly with spontaneous

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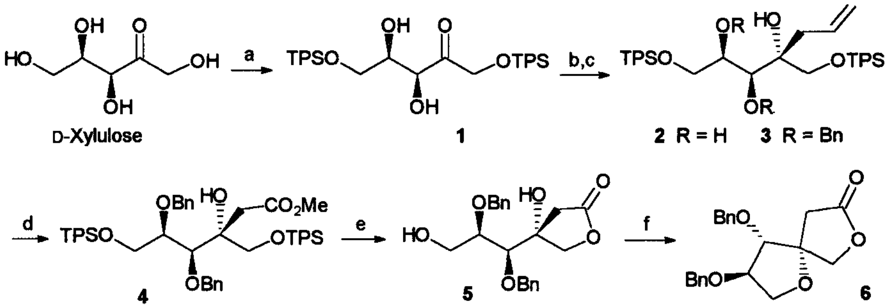
ether ring closure to yield spiro lactone **6**, which displayed physical and spectral data identical with those published.[4b] This compound has previously been converted into the syributins and secosyrins. Our synthesis therefore constitutes a formal, total synthesis of these natural metabolites.



Reaction conditions: a) $Ph_2\textit{t}BuSiCl$, imidazole, DMAP, DMF (75%). b) allyl bromide, In, aq THF, RT. c) BnBr, NaH, THF, RT (50% overall). d) O_3, CH_2Cl_2, NaOH/MeOH. e) TBAF, THF, RT (50% overall). f) TsCl, Et_3N, DMAP, CH_2Cl_2, RT (72%).

Compounds **4**, **5** or **6** should also be suitable intermediates in the synthesis of the syringolides. Efforts in these directions are in progress and will be reported in due course.

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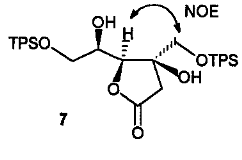
REFERENCES AND NOTES

1. Midland, S.L.; Keen, N.T.; Sims, J.J.; Midland, M.M.; Stayton, M.M.; Burton, V.; Smith, M.J.; Mazzola, E.P.; Graham, K.J.; Clardy, J. *J.Org.Chem.* **1993**, *58*, 2940-2945.
2. Midland, S.L.; Keen, N.T.; Sims, J.J. *J.Org.Chem.* **1995**, *60*, 1118-1119.
3. (a) Wood, J.L.; Jeong, S.; Salcedo, A.; Jenkins, J. *J.Org.Chem.* **1995**, *60*, 286-287. (b) Wood, J.L.; Jeong, S.; Salcedo, A.; Jenkins, J. *J.Org.Chem.* **1995**, *60*, 6641. (c) Kuwahara, S.; Moriguchi, M.; Miyagawa, K.; Konno, M.; Kodama, O. *Tetrahedron* **1995**, *51*, 8809-8814. (d) Ishihara, J.; Sugimoto, T.; Murai, A. *Tetrahedron* **1997**, *53*, 16029-16040. (e) Henschke, J.P.; Rickards, R.W. *Tetrahedron Lett.* **1996**, *37*, 3557-3560. (f) Honda, T.; Mizutani, H.; Kanai, K. *J.Org.Chem.* **1996**, *61*, 9374-9378. (g) Zeng, C.M.; Midland, S.L.; Keen, N.T.; Sims, J.J. *J.Org.Chem.* **1997**, *62*, 4780-4784. (h) Yu, P.; Wang, Q.G.; Mak, T.C.W.; Wong, H.N.C. *Tetrahedron* **1998**, *54*, 1783-1788.
4. (a) Yu, P.; Yang, Y.; Zhang, Z.Y.; Mak, T.C.W.; Wong, H.N.C. *J.Org.Chem.* **1997**, *62*, 6359-6366. (b) Mukai, C.; Moharram, S.M.; Azukizawa, S.; Hanaoka, M. *J.Org.Chem.* **1997**, *62*, 8095-8103.
5. Carda, M.; Castillo, E.; Rodríguez, S.; Murga, J.; Marco, J.A. *Tetrahedron: Asymmetry* **1998**, *9*, 1117-1120.
6. (a) Schmidt, O.T.; Treiber, R. *Ber.Deutsch.Chem.Ges.* **1933**, *66*, 1765-1769. (b) Zinner, H.; Rehpenning, W. *Carbohydr.Res.* **1967**, *5*, 176-183. (c) Tipson, R.S.; Brady, R.F. *Carbohydr.Res.* **1969**, *10*, 549-563.
7. The configurational assignment of the new stereogenic centre in **2** was based both on NOE measurements in lactone **7**, obtained from **2** in two straightforward steps, as well as by conversion into the known compound **6**.[4b]



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8. Marshall, J.A.; Garofalo, A.W. *J.Org.Chem.* **1993**, *58*, 3675-3680.