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Total Synthesis of (±) Stoechospermol.

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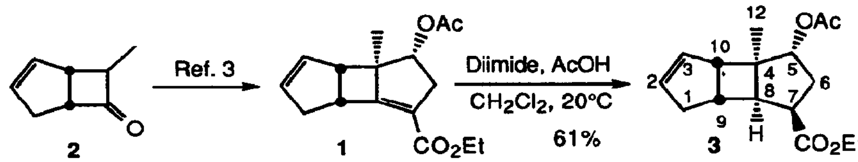
Abstract : The total synthesis of (±) stoechospermol starting from 7-methylbicyclo [3.2.0] hept-2-en-6-one 2 is described.

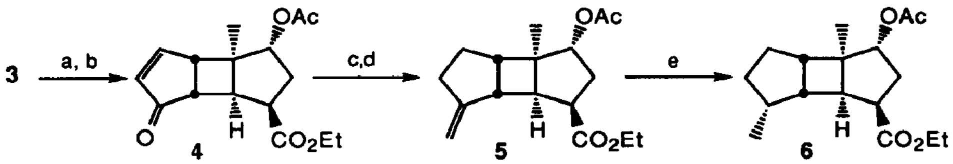
Stoechospermol belongs to the spatane diterpenes isolated from marine algae of the *Dictyotaceae* family[1]. These compounds are characterized by the *cis-anti-cis* tricyclo [5.3.0.0^{2,6}] decane skeleton. To our knowledge, only two syntheses of stoechospermol were reported in the literature, both using as key step a [2+2] photochemical cycloaddition[2].

We disclose here a total non photochemical synthesis of stoechospermol via the tricyclic derivative **1**. The cyclobutanic compound **1** was recently obtained from the bicyclic ketene adduct **2**[3] and seemed therefore to be a convenient intermediate for this synthesis. The problem was now to introduce with the correct configurations the acyclic side chain at C-7 and the methyl group at C-1, the tricyclic compound **1** possessing already the protected hydroxyl group at C-5 with the good configuration.

With diimide,[4] the electrophilic double bond was hydrogenated first to afford stereospecifically the compound **3**[5].

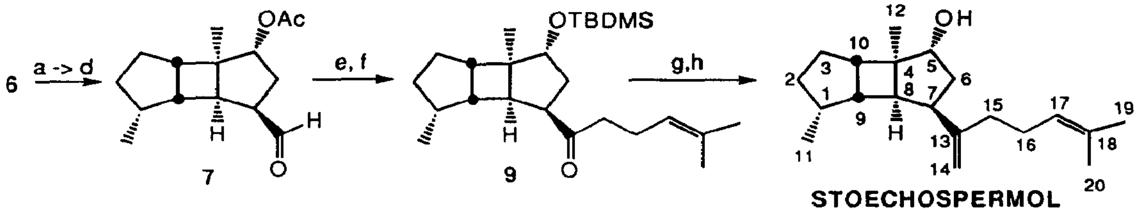


In order to introduce the methyl group at C-1, it was necessary to functionalize adequately that position. This was achieved by allylic hydroxylation[6] with SeO_2 followed by oxydation of the resulting alcohols with PCC[7] to give the α,β-unsaturated ketone **4**. After reduction of the Δ^2 double bond, a Wittig olefination[8] led to the olefin **5**. Catalytic hydrogenation under pressure with palladium on charcoal gave stereoselectively from the less hindered face the tricyclic derivative **6**, with the methyl group at C-1 in the desired configuration.



a : SeO_2, dioxane, 100° C (84%); b : PCC, CH_2Cl_2, 20 °C (quant.); c : H_2, Pd/C 5 %, AcOEt 20° C (quant.);
d : CH_2=$P(C_6H_5)_3$, nBuLi, $C_6H_5CH_3$, -20° C (61%); e : H_2, Pd/C 10 %, AcOEt, 10 bar, (quant.).

The introduction of the C-7 side chain was carried as follows. After saponification of the acetate and protection of the formed alcohol[9] as a silyl ether, the ethoxycarbonyl group was transformed into a formyl group (reduction with DIBAL, oxidation with PCC : aldehyde **7**). Reaction with the Grignard reagent **8**[10], followed by oxydation of the resulting alcohol. Finally, a Wittig olefination followed by deprotection of the silyl ether afforded stoechospermol[11] gave the tricyclic ketone **9**.

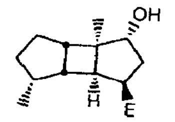


a : KOH, EtOH, 20°C (83%); b : TBDMSOTf, NEt_3, CH_2Cl_2, 20°C (87%); c : DIBAL (2.5 cq.), $C_6H_5CH_3$, -78°C (93%) ; d : PCC, CH_2Cl_2, 20° C (quant.);. c : 8 : $(CH_3)_2CH{=}CH(CH_2)_2MgBr$, THF, -30° C (79%) ; f : PCC, CH_2Cl_2, 20° C (quant.) ; g : $CH_2{=}P(C_6H_5)_3$,60°C (79%) h : TBAF/THF 60°C (84%).

The total synthesis of stoechospermol was thus achieved in 18 steps from the ketene adduct **2**, with an overall yield of 6 %.

References and notes:

1. a) Gerwick, W.H.; Fenical, W.; van Engen, D.; Clardy, J. *J. Am. Chem. Soc.* **1980**, *102*, 7991-7993.
   b) Gerwick, W.H.; Fenical, W.; Sultanbama, M.U.S. *J. Org. Chem.*, **1981**, *46*, 2233-2241.
   c) Gerwick, W.H.; Fenical, W. *J. Org. Chem.*, **1983**, *48*, 3325-3329.
2. Tanaka, M.; Tomioka, K.; Koga, K. *Tetrahedron Lett.*, **1985**, *26*, 3035-3038.
   Salomon, R.G.; Sachinvala, N.D.; Raychaudhuri, S.R.; Miller, D.B. *J.Am.Chem.Soc.*, **1984**, *106*, 2211-2213
   Salomon, G.R.; Basu, B.; Roy, S.; Sachinvala, N.D. *J. Am. Chem. Soc.*, **1991**, *113*, 3096-3106.
3. Miesch, M.; Cotté, A.; Franck-Neumann, M. *Tetrahedron Lett.*, **1993**, *34*, 8085-8086.
4. Pasto, D.J.; Taylor, R.T. *Organic Reactions*, **1991**, *40*, 92-151.
5. Usually the hydrogenation with diimide is known to work better with non polarized double bonds, but, in our case, the more strained electrophilic double bond was hydrogenated first. A similar result was obtained when a vinylcyclopropenic derivative was reduced with diimide: the reduction occurred regio- and stereospecifically on the sole cycloprenic double bond, leading in this case to *cis*-chrysanthemic methyl-ester. Franck-Neumann, M.; Dietrich-Buchecker, C *Tetrahedron Lett.*, **1980**, *21*, 671-674.
6. Rabjohn, N. *Organic Reactions*, **1976**, *24*, 261-415.
7. Corey, E.J.; Suggs, W. *Tetrahedron Lett.*, **1975**, *31*, 2647-2650.
8. Greenwald, R.; Chaykovsky, M.; Corey, E.J. *J. Org. Chem.*, **1963**, *28*, 1128-1129.
9. A



   The NMR data of compound A (6 $\xrightarrow{a}$ A, E = CO_2Et) are in good agreement with those reported by Fenical *et al.* (E = CO_2Me ; ref. 1b) , the sole differences being the signals of the ester groups. a
10. Julia, M.; Julia, S.; Guegan, R. *Bull. Soc. Chim. France*, **1960**, 1072-1079.
11. The ^1H NMR and ^{13}C NMR spectra are in good agreement with those described by Fenical *et al.* (see ref. 1b).

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