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AN APPROACH TO STEREOSELECTIVE FORMATION OF GLYCINOECLEPIN A SIDE CHAIN

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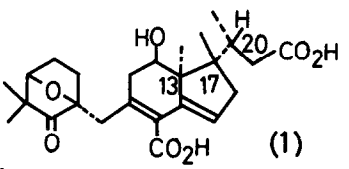
Abstract: Claisen rearrangement was found to be an efficient method for the stereoselective construction of the glycinoeclepin A side chain.

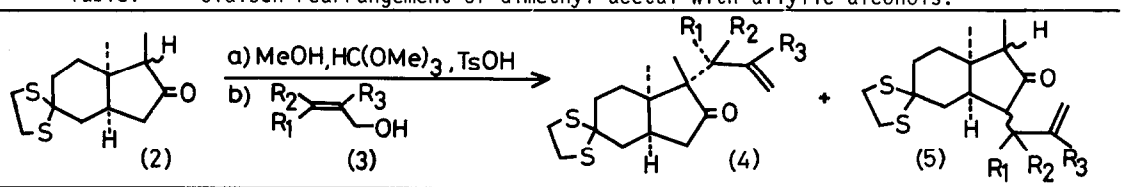
Glycinoeclepin A (1)[1], a natural hatching stimulas for the soybean cyst nematode, possesses three sequential chiral carbons (C_{13}-C_{17}-C_{20}) bearing methyl groups in its structure. Stereoselective construction of the carbon sequence (C_{13}-C_{17}-C_{20}) is one of the problems to be surmounted for the total synthesis of the natural product. Our strategy for it contains Claisen rearrangement.[2] We report here an approach to a stereoselective formation of the glycinoeclepin A side chain.[3]



(1)

An optically active ketone (2)[4] was acetalyzed with $HC(OMe)_3$ and TsOH in MeOH. A crude product obtained was heated with an allylic alcohol (3)[5] in toluene, xylene, or mesitylene without any acidic catalyst[6] to give a desired rearranged product (4) together with an undesired product (5). The results of the rearrangement reaction are summarized in Table. The stereochemical outcome for (4a)[7] and (4b)[8] suggests the reaction proceeds through a chair-form like transition state. The terminal double bond of (4a) may be a good precursor for an acetic acid residue of the glycinoeclepin A side chain.

Table: Claisen rearrangement of dimethyl acetal with allylic alcohols.



run	substrate	alcohol	product and yield (isolated)			
1	(2)	(3a), R_1=Me, R_2=R_3=H,	(4a)+(4b)≒4:1[a],	y=62%[b],	(5a)	y=16%
2	(2)	(3b), R_2=Me, R_1=R_3=H,	(4b)	61,	(5b)	24
3	(2)	(3c), R_3=Me, R_1=R_2=H,	(4c)	74,	(5c)	17
4	(2)	(3d), R_1=R_2=R_3=H,	(4d)	66,	(5d)	7,

a: products' ratio was determined by ^{1}H-NMR spectroscopy.
b: combined isolated yield. see ref. 7.

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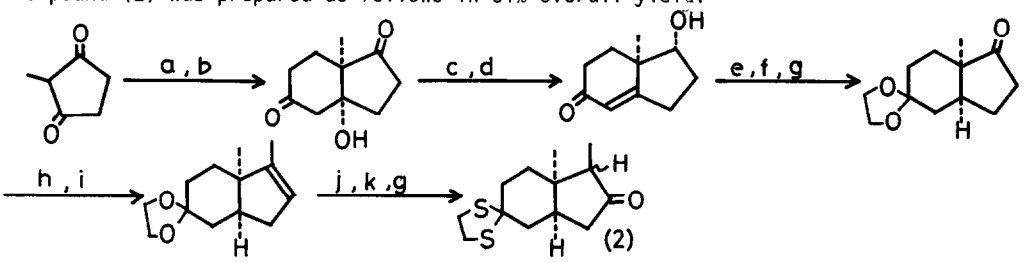
2) L. Claisen, Ber., 45, 3157(1912). L. Claisen and E. Tietze, Ber., 58, 275(1925).
3) A synthetic approach to glycinoeclepin A, involving the stereoselective formation of the three sequential chiral centers in question, has recently been reported. For a chiral approach; A. Murai, N. Tanimoto, N. Sakamoto and T. Masamune, 28th Symposium on the chemistry of natural products, Sendai, October 1986, Abstr. p393.
For a racemic approach; H. Sasai and K. Sakai, 54th Meeting of the Chemical Society of Japan, Tokyo, April 1987, Abstr. p1117.
4) Compound (2) was prepared as follows in 31% overall yield.



a) MVK, b) D-proline[9], c) TsOH, PhH, d) $NaBH_4$, EtOH, e) Pd/C, H_2, EtOH[10], f) ethylen glycol TsOH, PhH, g) PCC, CH_2Cl_2, h) $Ph_3P^+CH_3Br^-$, NaH in DMSO, i) cat. I_2 in toluene[11], j) 1,2-ethanedithiol, BF_3Et_2O, CH_2Cl_2, k) BH_3Me_2S/H_2O_2, NaOH.
5) cis-Crotyl alcohol employed here was prepared by hydrogenation of 2-butyn-1-ol on p-2 nickel boride catalyst. For the catalyst, see the follows; C. A. Brown and V. K. Ahuja, J. Org. Chem., 38, 2226(1973). C. A. Brown and V. K. Ahuja, J. Chem. Soc., Chem. Comm., 553(1973).
6) When an acidic catalyst was employed, the reaction gave a complex mixture.
7) Compound (4a) was separable from (4b) by column chromatography on silica gel in a low yield though, the diastereomeric mixture was completely separated at the next stage in our synthesis. Spectrum data for (4a) are as follows: mp. 113-113.5°C (ether-hexane). $[\alpha]_D^{20}$ +73.0° (c 1.0, $CHCl_3$). ^{1}H-NMR (500MHz, $CDCl_3$); 0.83(3H,s), 0.89(3H, d, J=6.7Hz), 1.13(3H, s), 1.28(2H, m), 1.95(1H, m), 2.1(1H, m), 2.21(1H, m), 2.37(1H, m), 2.44(1H, m), 2.59(2H, br), 2.85(1H, m), 3.3(4H, m), 5.0(2H, m), 5.88(1H, m). IR($CHCl_3$): 1731, 1635, 1218, 1080, 920cm^{-1}. FDMS(m/z), 310(M^+).
8) The stereochemistry of (4b) was determined by the X-ray crystallographic analysis. Crystal data for (4b): $C_{17}H_{26}OS_2$ (MW=310.5), space group $p2_12_12_1$, (Z)=4, lattice const. a=11.453 (6), b=20.409(11), c= 7.292(5)Å, U=1704Å^3, Dcal= 1.210gcm^{-3}, final R factor=0.063.
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