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AN AROMATIC VERSION OF CLAISEN REARRANGEMENT OF LACTONIC SILYL ENOLATES - A NEW ACCESS TO POTENTIAL INTERMEDIATES FOR EUDESMANE TYPE OF SESQUITERPENES†

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Abstract —— A new stereoselective synthesis of suitably substituted furanodecalins **(9)** ∿ **(12)** via the Claisen rearrangement of furfuryl lactonic silyl enolate **(6)** derived from the furfuryl lactone **(4)** is described.

In the preceeding reports[1], we demonstrated that the [3,3]sigmatropic rearrangement in systems where the allylic double bonds of the allyl vinyl ethers were formally incorporated in furan rings, could be induced under rather mild conditions by the application of Ireland's allylic ester silyl enolate rearrangement to this systems. Now, we wish to report a new access to a potential intermediate for the synthesis of eudesmane type of sesquiterpenes via the aromatic version of an Ireland's allylic ester silyl enolate rearrangement.

Thus, firstly the keto acid **(2)**, mp 96 ∿ 97°C, [m/z 198(M^+)], prepared in 66 % yield by the hydrolysis (KOH, H_2O-EtOH, reflux, 4 h) of the keto nitrile **(1)** [m/z 179(M^+)] which was derived in 41 % yield by the Michael reaction (NaOEt, EtOH, 60°C, 2 h)[2] between 2,6-dimethylcyclohexanone and acrylonitrile, was reacted with 2-lithiofuran[3] (THF, -78°C, 1 h) to give the furfuryl acid **(3)** which was then directly lactonized (Silica gel, CH_2Cl_2, room temperature, 12 h) affording the furfuryl lactone **(4)**, mp 152 ∿ 153°C, [m/z 248(M^+); $\nu_{max.}$($CHCl_3$) 1720 cm^{1}; δ(CCl_4) 0.70(3H, d, J=6 Hz, Me), 0.74(3H, s, Me), 6.20 ∿ 6.55(2H, m, ArH) and 7.25 7.40(1H, m, ArH)] and its isomer **(5)**[m/z 248(M^+); $\nu_{max.}$($CHCl_3$) 1720 cm^{-1}; δ(CCl_4) 0.70(3H, d, J=6 Hz, Me), 1.15(3H, s, Me), 6.03 ∿ 6.40(2H, m, ArH) and 7.25 7.40(1H, m, ArH)] in 58 % and 5 % overall yields, respectively. On the basis of nmr spectra, the angular methyl groups of **4** and **5** were shown to be cis and trans with respect to the furan rings, respectively and the methyl groups of **4** and **5** corresponding to C_4-methyl group of eudesmane types of sesquiterpenes were strongly suggested to be α-configuration i.e. equatorial because of the same chemical shifts (0.70 ppm). These assignments were also supported by the analysis of the rearrangement product **(9)**. Thus, the furfuryl lactonic silyl enolate **(6)** resulted from the silylation (TBSCl, lithium hexamethyldisilazide, THF, -30°C,

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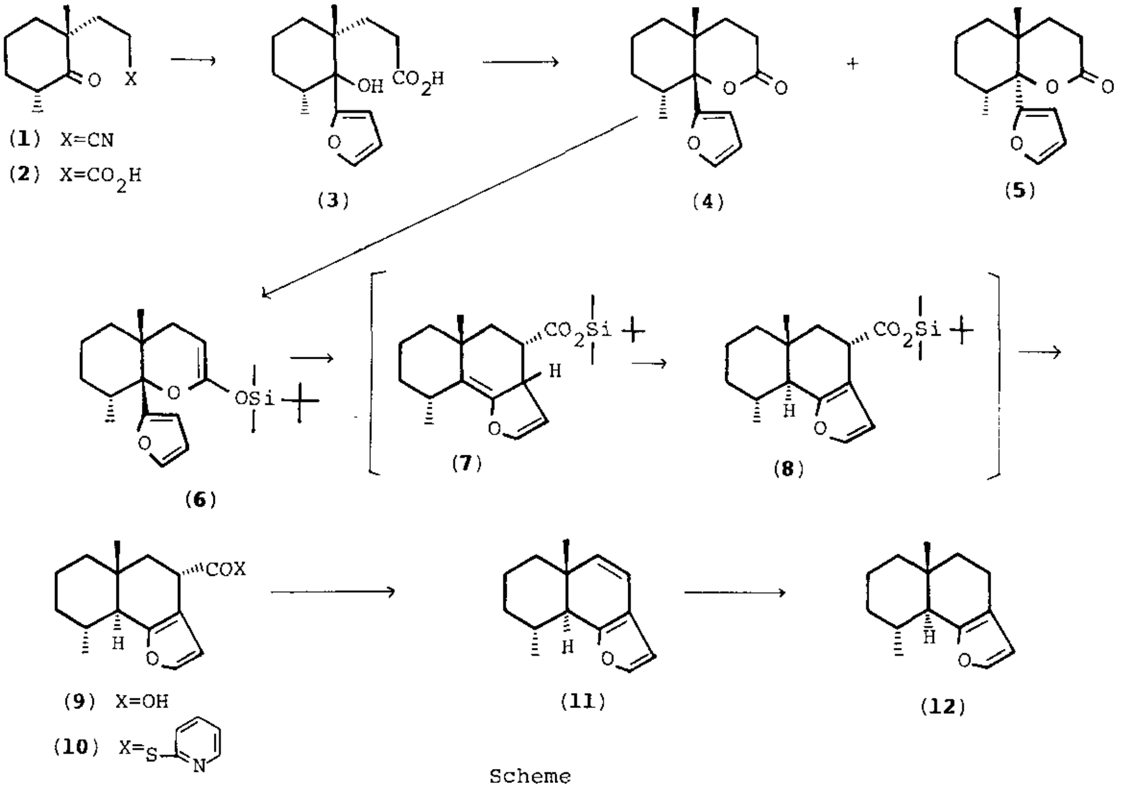
† Dedicated to professor Gilbert Stork on the occasion of his 65th birthday.

1 h) of **4** was subjected subsequently to the rearrangement (toluene, reflux, 12 h) and then the hydrolysis (10 % HCl, THF, room temperature, 5 min) of the resulting silyl ester (**8**), affording the carboxylic acid (**9**), mp 147 ∿ 148°C, [m/z 248(M$^+$); $\nu_{max.}$(CHCl$_3$) 1710 cm^{-1}; δ(CCl$_4$) 0.96(3H, d, J=6 Hz, Me), 0.99(3H, s, Me), 3.60(1H, dd, J=6 and 10 Hz, C$_8$-H), 6.33(1H, d, J=2 Hz, ArH), 7.20(1H, d, J=2 Hz, ArH), and 11.23(1H, br s, CO$_2$H)] in 45 % overall yield based on **4**. The nmr spectrum of **9** showed the C$_8$-hydrogen to be quasi-axial, rationalizing the right stereochemistry of **4**. Although the stereochemistry around the ring juncture could not be determined unambiguously at this stage, the aromatizing step, i.e. **7**⟶**8** should give the most stable isomer as shown. This was supported by the transformation of **9** into **11**. Thus, the acid (**9**) was subjected to Mukaiyama's conditions[5] [2-dipyridyl disulfide, Ph$_3$P, CH$_3$CN, room temperature, 0.5 h; Zn, NiCl$_2$, DMF, 100°C, 1 h] to afford the olefinic compound (**11**) [m/z 202(M$^+$); δ(CCl$_4$) 0.97(3H, s, Me), 1.20(3H, d, J=8 Hz, Me), 2.97(1H, d, J=8 Hz, C$_5$-H), 5.37(1H, d, J=10 Hz, olefinic), 5.83 ∿ 6.30(2H, m, olefinic and aromatic), and 7.20(1H, br s, ArH)] _via_ the thioester (**10**) in 36 % overall yield. In the nmr spectrum of **11**, the signal corresponding to C$_5$-hydrogen was observed at 2.97 ppm as doublet having J=8 Hz and any long range coupling was not detected, showing the ring juncture to be _trans_ and C$_5$-hydrogen to be axially oriented. Finally the olefinic compound (**11**) was converted (H$_2$, Pd-C, MeOH, room temperature, 3 h) into the initial target compound (**12**), mp 97 ∿ 98°C, [m/z 204(M$^+$); δ(CCl$_4$) 0.97(3H, d, J=8 Hz, Me), 1.00(3H, s, Me), 6.05(1H, d, J=2 Hz, ArH), and 7.13(1H, d, J=2 Hz, ArH)] in 80 % yield.



Scheme

Thus, we could develope a new stereoselective methodology for the synthesis of eudesmane type of sesquiterpenes.

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