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A Concise Enantiospecific Synthesis Of Analogues Of Monocerin

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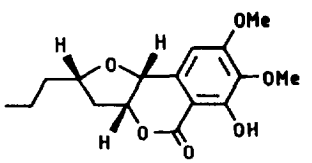
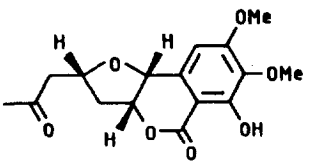
Abstract : Two analogues of the antifungal metabolite, monocerin have been synthesised from D-glucose making use of the facile intramolecular C-glycosidation as the key step.

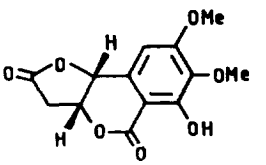
Monocerin **1**, first isolated from the culture filtrates of Helminthosporium monoceras[1] and subsequently from several other fungal species[2] was shown to exhibit antifungal, insecticidal and phytotoxic activities.



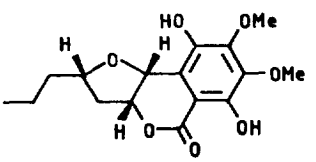
Monocerin 1



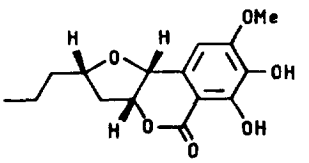
Monocerone 2



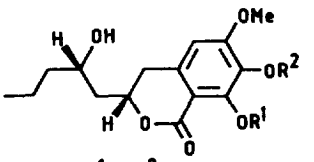
Monocerolide 3



Hydroxymonocerin 4



Demethylmonocerin 5



$R^1 = R^2 = H$
$R^1 = OMe, R^2 = H$
$R^1 = H, R^2 = OMe$

Fusarentin ethers 6

Compounds **2-6**, bearing analogous structures were isolated from one or the other of these sources as minor congeners of monocerin. Fusarentin ethers **6** have been shown to be the biogenetic precurcors[3] to monocerins.

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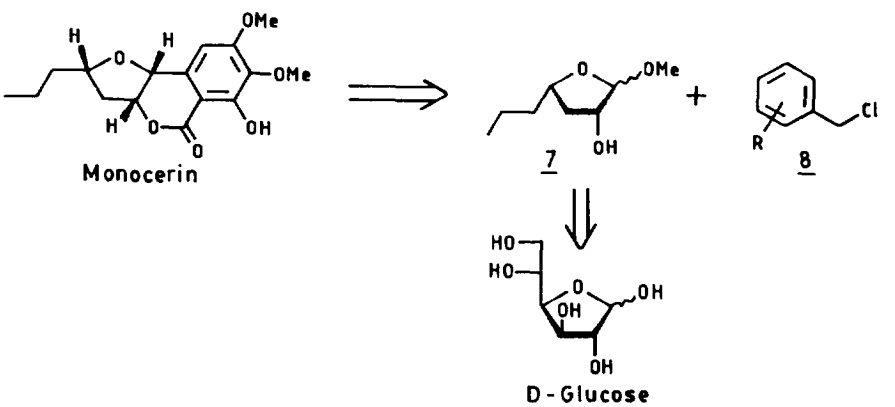
Broad spectrum of activity apart, monocerins have attracted the attention of synthetic chemists because of their unique and hitherto unkown structural feature, namely the *cis*-fused furobenzopyranone skeleton.

The absolute configuration[2a] of monocerin was established as 2S, 3aR and 9bR, which was confirmed by two syntheses from non-carbohydrate precursors. While one synthesis[4] utilised rather lenghty sequence of reactions, the other[5] employed uncommon reagents and reaction conditions to construct certain bonds. For the convenience of synthesis, we have diagnosed monocerin as a C-glycoside, a viewpoint surprisingly missing in all the literature reports on this compound as well as in reviews/reports[6] on C-glycosidic natural products. Carbohydrates as starting materials for synthesis[7] offer distinct advantages especially in forming stereogenic bonds. In the cyclic furanose or pyranose forms, they exhibit remarkable template effects permitting the approach of reagents/reactants predominantly, and in many cases exclusively, from one face. Making use of this aspect and employing the facile Lewis acid-mediated intramolecular C-glycosidation methodology[8] developed by Martin et.al, we have accomplished an easy and short synthesis of two analogues of monocerin, details of which are presented in this article.

Retrosynthesis (**Scheme 1**) revealed two units--a chiral one **7**, derivable from D-glucose and the

Scheme - 1



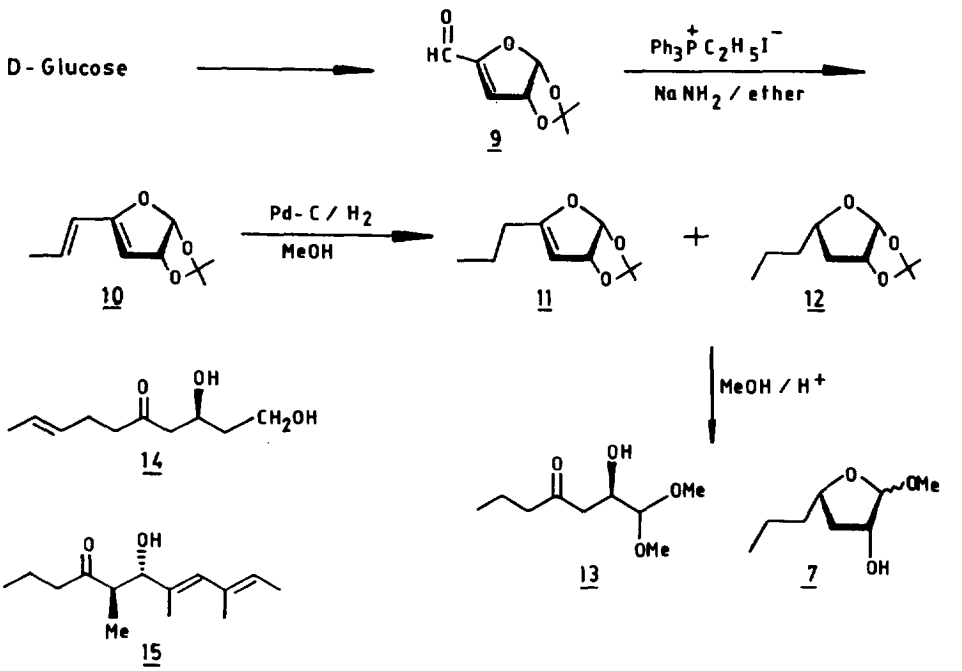
achiral "aglycon" **8**, an arylmethyl halide. The crucial bond to be formed between these two subunits is C-glycosidic in nature.

Synthesis of the chiral unit from D-Glucose:

Diacetone glucose was converted into the known unsaturated dialdose **9** by a standard set of reactions[9]. **9** could be chain-extended to the *threo*-L- heptose **12** by either of two routes- a two step sequence involving first a Wittig followed by the reduction of the diene or a three-step sequence involving reduction, Wittig and

again reduction. The latter option, although longer, proved to be neat and more efficient. The two step sequence is described first. Wittig olefination of **9** (**Scheme 2**) with ethyltriphenylphosphonium iodide

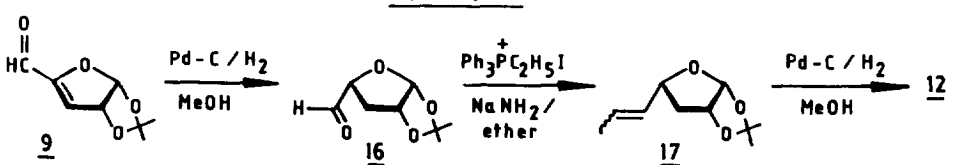
Scheme - 2



and sodamide in ether afforded the diene **10**, with the new C=C having exclusively the E-configuration! Catalytic reduction with 10% Pd-C in methanol yielded the desired aldoheptose **12** contaminated with partially reduced product **11**. The endocyclic double bond in **10**, being electron-rich, offered resistance to hydrogenation and prolonged reaction resulted in the formation of other products as monitored by TLC. Column chromatography yielded most of **12** as pure material while the remainder eluted as a mixture with **11**. However, methanolysis of this mixture of **12** and **11** resulted in the acetals **7** and **13** respectively, which were neatly separable. A literature search for **13** resulted in the identification of two natural products, **14**[10] and **15**[11] which have a striking structural similarity with **13**.

Because of the aforementioned difficulty in efficiently reducing the endocyclic double bond, the three-step alternative depicted in **Scheme 3** was tried. The endocyclic

Scheme - 3

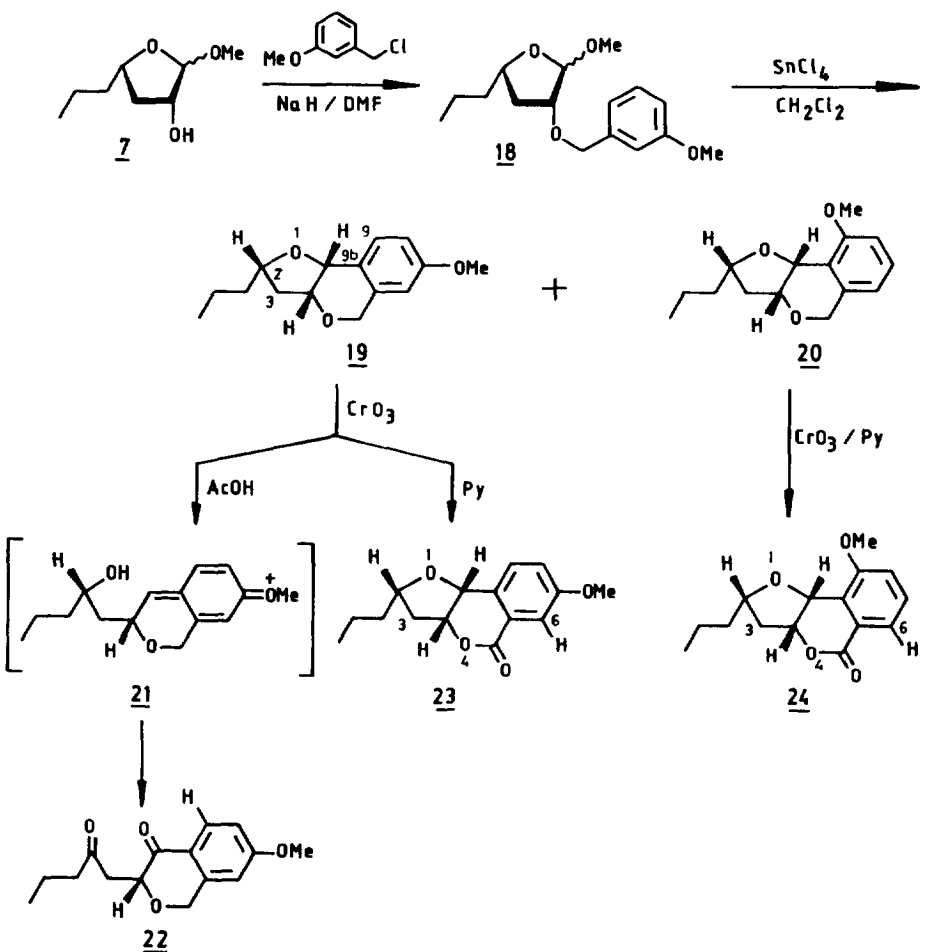


double bond in **9**, being in conjugation with the aldehyde moiety was easily reduced and the resulting L-*threo*-pentodialdose[12] **16** was subjected to two-carbon Wittig olefination as before, which in this case yielded an E/Z mixture **17**, in about 1:2 ratio. Catalytic reduction then neatly afforded **12**. Thus the three step sequence proved uneventful and high yielding. It may be mentioned that the reduction of the endocyclic double bond in **9** and **10** is highly stereospecific with the hydrogen adding exclusively from the β- face of the furanose, the α- side being blocked by the acetonide moiety.

2-O-Arylmethylation of 7 and C-glycosidation:

The hydroxyl at 2-position of 12 was made free by methanolysis to obtain **7** as an anomeric mixture predominating in the β-anomer. This was then derivatised as an arylmethyl ether by treating with *meta*-methoxybenzyl chloride and sodium hydride in DMF to afford **18** (**Scheme 4**). The stage was now set for the crucial intramolecular C-glycosidation reaction.

Scheme - 4



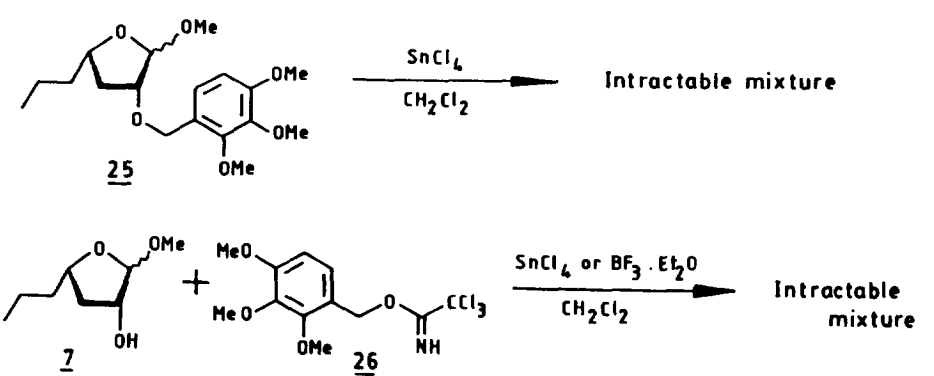
Thus **18** was treated with one eq. of $SnCl_4$ in CH_2Cl_2 for 2 hrs. at room temperature. Cleanly two *regio*-isomeric C-glycosides **19** and **20** were isolated. The *para*- C-glycosidated product, **19** predominated as can be expected. These isomers could easily be identified and distinguished by analysing their ^{1}H-NMR spectra. The resonances due the the "aglycon" moiety were characteristic. In both cases, the benzylic methylene protons were anisochronous appearing as doublet of doublets with the characteristic[13] geminal J value of about 15 Hz unlike in the precursor **18,** where this methylene resonated as a singlet. Additional diagnostic difference was in the multiplicity pattern for the aryl protons, which in **19** have a 1,2,4-relationship unlike those in **20**, which are 1,2,3-related. That C-glycosidation was stereospecific was obvious from the coupling constant of 3.3 Hz between 3a-H and 9b-H which are *cis*-related[1]. Literature precedents[8a,11] are in agreement with 1,2-*cis*-C-glycosidation.

At this point, all that was needed to realise the ring system, present in monocerin was to oxidise the benzylic methylene to carbonyl. To this end[13], **19** was treated with CrO_3 in acetic acid. The reaction proceeded very smoothly resulting in a single product, which however, turned out to be the diketone **22**. The assigned structure was obvious from the chemical shift of the proton *meta* to the methoxyl group at 8.0 ppm, considerably downfield from its counterpart 9-H in **19,** which resonated at 7.36 ppm. This is due to the parallel orientation of the proton with the highly anisotropic carbonyl moiety. In addition, the resonance due to 9b-H and 2-H seen in **19**, were absent and the aliphatic protons displayed the matching muliplicities. The benzylic methylene was surprisingly intact. Formation of this product can be explained as follows: protonation of the furanose ring oxygen might have triggered the ring-opening process, made facile by the *para*-methoxy group, resulting in the quinonoid-like structure **21**, which got oxidised to **22.** This problem was, however, overcome when pyridine was used in place of acetic acid, affording the desired lactone, **23**. Similarly **20** was converted to **24**. Formation of the lactone resulted in a substantial downfield shift of H-6 in both **23** and **24** by about 1.0 ppm with respect to those in the precursors, **19** and **20**. Resonance due to the benzylic methylene was, of course, absent. Thus, our visualisation of monocerin as a C-glycoside was fruitful and resulted in an easy and enantiospecific synthesis of analogues. Also, we have shown for the first time an application of the Lewis acid mediated intramolecular C- glycosidation methodology.

Attempted Synthesis of Monocerin:

To synthesise monocerin itself, we needed to change only the aryl moiety. Accordingly, **25** was prepared from **7** and 2,3,4-trimethoxybenzyl chloride and subjected to C-glycosidation conditions as before (**Scheme 5**). TLC-monitoring of the reaction

Scheme - 5



indicated the formation of several products and the work-up resulted in muck. Several repetitons were to no avail. Alternatively. we sought to O- benzylate **7** with the imidate **26** under acidic conditions[14] ($SnCl_4$ or BF_3-Et_2O) with a faint hope to obtain directly the C-glycoside. Disappointingly, not even the O-benzylated compound **25** could be isolated. From the foregoing, it is obvious that the benzyl ether moiety in **25** does not survive acidic conditions which probably lead to decomposition or formation of multiple products. Nuclear bromination of **19** and the subsequent nucleophilic displacement of the bromines by methoxyls is being explored as an alternative route.

Acknowledgement : We thank Dr.A.V.Rama Rao, ex-director of IICT for evincing keen interest and Miss B.Sulatha of Recon Limited and S.Shravan(son of SPR) for typing the manuscript.

Experimental

General : Melting points were determined on Fischer-Johns apparatus and are uncorrected. NMR spectra were recorded at 200 MHz for proton and 50 MHz for ^{13}C nuclei (Varian Gemini 200 spectrometer) in CDC^{13} solutions using TMS as internal standard for ^1H-spectra and the central line of $CDCl_3$ triplet for ^{13}C-spectra. Chemical shifts in δ values and coupling constants in Hz were obtained from the first order analysis of the spectra. Optical rotations were measured at 25° C with a Jasco DIP-370 digital polarimeter in a 0.1 dm cell from solutions in chloroform. Mass spectra were recorded on Finnigan MAT 1020B or micromass VGT-70-70H spectrometer operating at 70 eV using direct inlet system. Column chromatography was done using Acme silica gel finer than 200 mesh. Analytical TLC was performed on pre-coated glass plates from Merck. Reagents and solvents were purified/dried by standard methods. Elemental analyses were conducted by IDPL laboratories, Hyderabad. The following solvent systems were used for chromatography: (A) 1:4, (B) 1:9, (C) 15:85 ethyl acetate: pet. ether (D) 1:29:70 and (E) 1:45:50 MeOH : EtOAc: pet. ether.

(3Z, 5E)-3,5-Dienyl-1,2-O-methylethylidene-D-*glycero*heptose (10):

To a suspension of ethyltriphenylphosphonium iodide (921 mg, 2.2 mmol) in dry ether (20 ml), sodamide (114 mg, 2.94 mmol) was added and the mixture stirred at room temperature for 7 hrs. and allowed to settle. The supernatant layer was cannulated into the aldehyde **9** (250 mg, 1.47 mmol) dissolved in anh. ether (4 ml) at 0o C. After 15 min., the solvents were removed in vacuo and the residue chromatographed (solvent B) to afford 220 mg (82%) of the oily **10** exclusively as the 5-E isomer, R_f 0.68 (solvent B).

^1H-NMR: 6.2 (dq, 1H, J=15.6 and 8.0, H-6), 6.0 (d, 1H, J=5.3, H-1), 5.84 (d, 1H, J=15.6, H-5), 5.24 (dd, 1H, J=2.4 and 5.3, H-2), 4.94 (d, 1H, J=2.4, H-3), 1.79 (d, 3H, J=8.0, Me-7), 1.38 and 1.37 (2xs, 2x3H, isoprop. Me's).

Analysis: Calcd. for $C_{10}H_{14}O_3$: C, 65.93; H, 7.69. Found: C, 65.92; H, 7.68.

1,2-O-Isopropylidene-D-*threo*-pentodialdose (16):

To a solution of **9** (230 mg, 1.352 mmol) in methanol (20 ml) was added 5% Pd-C (30 mg) and the mixture stirred for 15 min. at room temperature under an atmosphere of hydrogen. The mixture was filtered

through a celite pad and concentrated to give **16** (210 mg, 90.5%) as a syrup, R_f = 0.37 (solvent E).

^{1}H-NMR: 9.0 (s, 1H, H-5), 5.9 (d, 1H, J=3.2, H-1), 4.75 (m, 2H, H-2 and H-4), 2.56 (d, 1H, J=14.2, H-3a), 2.21 (m, 1H, H-3b), 1.28 and 1.45 (2xs, 2x3H, isoprop. Me's).

Methyl 3,5,6,7-tetradeoxy-L-*threo*-heptofuranoside (7) and (2R)-2-hydroxy-4-oxo-heptane dimethyl acetal (13):

To a solution of **11** (900 mg, 4.85 mmol) in methanol (20 ml), 10% Pd-C (100 mg) was added and the mixture stirred vigorously at room temperature for 8 hrs. under a blanket of hydrogen. The catalyst was filtered off through a celite pad and the solvent removed to afford 860 mg (95%) of **12** as a syrup, R_f 0.47 (solvent B).

Methanolysis of **12** (840 mg. 4.85 mmol) in 2% methanolic sulphuric acid (10 ml) for 1 hr at reflux temperature gave after neutralisation with solid $NaHCO_3$ and usual work-up, 650 mg (89%) of **7** as an anomeric mixture predominating in the β-anomer, syrup, $[\alpha]_D$ -102.5 (c 1.0), R_f 0.25 (Solvent C)

^{1}H-NMR (**7**): 4.8 (s, 1H, H-1), 4.18 (br.m, 1H, H-2), 4.06 (m, 1H, H-4), 3.30 (s, 3H, OCH3), 2.42 (m, 2H, H-3a,3b), 1.2-1.8 (m, 4H, H-5a,5b,6a,6b) and 0.92 (t, 3H, J=7.2, Me-7).

^{13}C-NMR (**7**): 109.8 (C-1), 78.0 (C-4), 76.0 (C-2), 54.4 (OCH3), 39.0 and 38.5 (C-3 and C-5), 20.0 (C-6) and 14.0 (C-7).

Analysis: calcd. for $C_8H_{16}O_3$: C, 60.0; H, 10.0. Found C, 60.25; H, 10.1

Hydrogenation of **11** yielded **12** partly contaminated with **13**. Methanolysis of this mixture yielded **7** and **13**.

(5-E/Z)-3,7-Dideoxy-5,6-Dideoxydidehdro-1,2-O-isopropylidene-L-*threo*-heptofuranose (17):

To a suspension of ethyltriphenylphosphonium iodide (3.6 g, 8.70 mmol) in anh. ether (50 ml), sodamide (450 mg, 11.6 mmol) was added and stirred for 8 hrs. at room temperature. The supernatant solution was cannulated into the aldehyde **16** (1.0 g, 8.1 mmol) dissolved im anh. ether (20 ml) and cooled to 0° C. After 1 hr. the ethereal layer was separated and the residue extracted into chloroform (2x15 ml). The combined organic extracts were concentrated and chromatographed (solvent E) to afford 925 mg (87%) of **17** as an inseparable mixture of E/Z isomers in 3:7 ratio as measured by the integration of the ^{1}H-NMR signals due to the olefinic methyls, R_f 0.58 (Solvent E).

^{1}H-NMR (**17** E): 5.75 (m, 2H, H-1 and H-5), 5.5 (dq, 1H, J=14.0 and 6.8, H-6), 4.92 (m, 1H, H-4), 4.75 (m, 1H, H-2), 2.3 (ddd, 1H, J=6.3, 9.0, 13.8, H-3a), 2.0 (dd, 1H, J=13.8 and 3.3, H-3b), 1.65 (dd, 3H, J=6.8 and 2.0, Me-7), 1.55 and 1.3 (2xs, 2x3H, isoprop. Methyls).

Analysis: calcd. for $C_{10}H_{16}O_3$: C, 65.217; H, 8.695. Found: C, 65.53; H, 8.82

Methyl 2 -O-(3-methoxybenzyl)-3,5,6,7-tetradeoxy-L-*threo*-heptofuranoside (18):

To a stirred solution of **7** (600 mg, 3.75 mmol) in anh. DMF (5 ml), hexane-washed NaH (270 mg, 5.7 mmol) was added and after 10 min. 3- methoxybenzyl chloride (700 mg, 4.5 mmol) was added and stirred at room temp. for 3 hrs. Satd. NH_4Cl solution (1 ml) was added and extracted into hexane (5x10 ml). Combined extracts were dried (Na_2SO_4), concentrated and chromatographed (solvent A) to get 1.08g (93%) of **18** as a syrupy mixture of anomers predominating in the β-anomer, $[\alpha]_D$ -43.7° (c 1.08), R_f 0.68 (solvent A).

^{1}H-NMR (β-anomer): 7.25 (t, 1H, J=7.6), 6.92 (m, 2H), 6.8 (dd, 1H)--Aryl H's, 4.96(s, 1H, H-1), 4.5 (s, 2H, benzylic CH_2), 4.0 (m, 2H, H-2 and H-4), 3.81 (s, 3H, Ar-OCH_3), 3.34 (s, 3H, anomeric OCH_3), 2.35 (m, 1H, H-3a), 1.3 to 1.8 (m, 5H, H-3b,5a,5b,6a and 6b), 0.95 (t, 3H, J=7.0, CH_3-7).

^{13}C-NMR(β-anomer): 159.6, 139.5(aryl quaternaty carbons), 129.3, 119.6, 113.1, 112.7 (H- bearing Aryl C's), 107.3 (C-1), 83.9 (C-2), 77.8 (C-4), 71.4 (benzylic carbon), 54.9, 54.3 (OCH3's), 37.9, 36.7 (C-3 and C-5), 19.2 (C-6) and 14.0 (C-7).

Analysis: calcd. for $C_{16}H_{24}O_4$: C, 68.57; H, 8.57. Found: C, 68.92; H, 8.56.

[2S,3aR,9bR] -3,3a,5,9b-Tetrahydro-7-(19) & 9-methoxy-2-n-propyl-2H-furo[3,2-c [2]benzopyran (20):

To a solution of **18** (0.9 g, 3.2 mmol) in anh. CH_2Cl_2 (5 ml), 1M solution of $SnCl_4$ (3 ml) was added at 0° C. After two hrs. at room temperature, saturated aq. $NaHCO_3$ (3 ml) was added and stirred for 30 min., diluted with CH_2Cl_2 (20 ml) and the organic layer separated, washed with water (2x5 ml), dried ($MgSO_4$), concentrated and chromatographed (solvent B) which afforded **19** (700 mg, 88%) and **20** (40 mg, 5%). **19:** m.p. 37-38° C, $[\alpha]_D$ + 10.76 (c 1.0), R_f 0.59 (solvent A). ^{1}H-NMR: 7.36 (d, 1H, J = 8.5, H-9), 6.81 (dd, 1H; J = 8.5 and 2.4, H-8), 6.55 (d, 1H, J = 2.4, H-6), 4.63 (dd, 2H, J=14.7, H-5a, 5b), 4.3 (d, 1H, J=3.3, H-9b), 4.2 (m, 1H, H-3a), 3.93 (m, 1H, H-2), 3.8 (s, 3H, OCH_3), 2.5 (dt, 1H, J=15.8 and 7.3, H-3'), 1.25-1.8 (m, 5H, H-3",5a,5b,6a,6b) and 0.93 (t, 3H, J=7.0, CH_3). ^{13}C-NMR: 159.3, 136.8, 123.6 (C-7, 9a and 5b), 131.5, 113.3, 109.1 (C-6,8 and 9), 78.3, 77.9 (C- 9b and 2), 75 (C-3a), 67.5 (C-5), 55.3 (OCH_3), 39.6, 38.0 (C-3 and 2a), 19.5, 14.1 (C-2b and 2c).

Analysis: calcd. for $C_{15}H_{20}O_3$: C, 72.58; H, 8.064. Found: C, 72.53; H, 8.11.

20: Syrup, R_f 0.55 (solvent A), ^{1}H-NMR: 7.24 (t, 1H, J=7.9, H-7), 6.8 (d, 1H, H-6), 6.67 (d, 1H, H-8), 4.6 (dd, 2H, J = 15.0 and 1.0, H-5a, 5b), 4.54(d, 1H, H-9b), 4.15 (dd, 1H, J = 2.8 and 6.0, H-3a), 4.04 (m, 1H, H-2), 3.88 (s, 3H, OCH_3), 2.47 (ddd, 1H,=14.0,10.0 and 8.2, H-3a), 1.2-1.9 (m, 5H, H-3b,5a,5b,6a and 6b) and 0.91 (t, 3H, J=7.3, Me-7).

Mass: 248 (M+), 205, 177, 176, 150 ,149, 135, 105, 91, 55, 43.

Analysis: calcd. for $C_{15}H_{20}O_3$: C, 72.58; H, 8.064. Found: C, 72.49; H, 8.12.

[2s, 3aR, 9bR]-2, 3, 3a, 9b-Tetrahydro-7-(23) and 9-methoxy-2n-propyl-5H-furo[3, 2 c] [2] benzopyran-5-one (24):

To a solution of **19** (50 mg, 0.2 mmol) in CH_2C_{l2} (5 ml), pyridine (0.09 ml, 1.206 mmol) and CrO_3 (60 mg, 0.603 mmol) were added and stirred for 36 hrs. at room temperature. CH_2C_{l2} was pulled off and ethyl acetate (10 ml) was added and filtered. The filtrate was washed with aq. $CuSO_4$ solution (5x5 ml) followed by water (2x5 ml). The organic phase was dried (Na_2SO_4), concentrated and chromatographed (solvent B) to afford **23** (38 mg, 73%) as a syrup, R_f 0.2 (solvent A), $[\alpha]_D$ + 5.2° (c 0.8). Similarly **20** was converted to **24** in a yield of 62%, R_f 0.15 (solvent A), $[\alpha]_D$ + 27.6° (c 0.7)

^{1}H-NMR (**23**): 7.67 (d, 1H, J=2.7, H-6), 7.42 (d, 1H, J=8.4, H-9), 7.19 (dd, 1H, J=2.7 and 8.4, H-8), 5.06 (m, 1H, H-3a), 4.59 (d, 1H, J=3.1, H-9b), 4.12 (m, 1H , H-2), 3.87 (s, 3H, OCH_3), 2.59 (ddd, 1H, J=14.3, 8.6 and 6.0, H-3'), 2.15 (dd, 1H, J=14.3 and 5.8, H-3"), 1,2-1.8 (m, 4H, H- 2a,2a",2b,2b"), 0.91 (t, 3H, CH_3-2c).

Mass: 262 (M+), 219 (base peak), 163, 149, 135, 120, 105, 91, 77, 63 and 51.

Analysis: calcd. for $C_{15}H_{18}O_4$: C, 68.702; H, 6.87. Found: C, 68.72; H, 6.86.

^{1}H-NMR (**24**): 7.78 (d, 1H, J=7.9, H-6), 7.48 (dd, 1H, J=7.9 and 8.1, H-7), 7.16(d, 1H, J=8.1, H-8), 5.0 (dd, 1H, J=2.9 and 7.9, H-3a), 4.92 (d, 1H, J=2.9, H-9b), 4.2 (m, 1H, H-2), 3.9 (s, 3H, OCH_3), 2.55 (ddd, 1H, J=13.5, 9.0 and 6.5, H-3'), 2.2 (dd, 1H, J=13.5 and 5.6, H-3"), 1.2-1.8 (m, 4H, H- 2a,2a",2b,2b"), 0.9 (t, 3H, J=7.0, CH_3-2c).

Analysis: calcd. for $C_{15}H_{18}O_4$: C, 68.702; H, 6.87. Found: C, 68.71; H, 6.769.

(2S)-7-Methoxy-2-[2-oxopentyl]isochromanone (22):

Compound **19** (50 mg, 0.2 mmol) was dissolved in glacial acetic acid (1 ml) and cooled to 15-20° C. To this a solution of CrO_3 (60 mg, 0.604 mmol) in water (0.1 ml) and glacial acetic acid (0.4 ml) was added dropwise over 10 min.. The reaction mixture was stirred at that temperature for 2 hrs. and then at room temperature for 3 hrs.. Water was added and extracted into chloroform (3x10 ml). Combined organic extracts was washed successively with $NaHCO_3$ solution, brine and water, dried (Na_2SO_4) and concentrated to afford 48 mg (92.3%) of **22** as a solid, M.P. 72-73° C, R_f 0.32 (solvent A), $[\alpha]_D$ -7.6 (c 0.9)

^{1}H-NMR: 8.0 (d, 1H, J=8.7), 6.9 (dd, 1H, J=8.7 and 2.3), 6.65 (d, 1H, J=2.3)--Aryl H's, 4.9 (dd, 2H, J=15.2), 4.65 (dd, 1H, J=2.8 and 8.0), 3.87 (s, 3H, OCH_3), 3.2 (dd, 1H, J=4.8 and 19.2), 2.85 (dd, 1H, J=8.0 and 19.2), 2.5 (t, 2H, J=7.8), 1.7 (m, 2H), 0.96 (t, 3H, J=7.2, CH_3).

Reference and Notes

1. Aldridge, D.C. and Turner W.B., *J.Chem.Soc.* (C), 1970, 2598.

2. a) Grove, J.F. and Pople , M. J. *Chem. Soc. Perkin Trans. I,* 1979, 2048.
   b) Robeston, D.J. and Strobel, G.A. *Agr. Biol. Chem.* 1982, *46,* 2681
   c) Birch, A.J.; Baldas, J.R.; Hlubucek, J.R.; Simpson, T.J. and Westerman, P.W. *J. Chem. Soc. Perkin Trans. I,* 1976, 989.
   d) Hill, J.G.; Nakashima, T.T. and Vederas, J.C. *J. Am. Chem. Soc.* 1982, *104,* 1745.

3. Scott, F.E.; Simpson, T.J.; Trimble, L.A. and Vederas, J.C. *J.Chem. Soc. Chem. Comm.* 1984, 756.

4. Mori, K. and Takaishi, H. *Tetrahedron,* 1989, *45,* 1639.

5. Dillon, M.P.; Simpson, T.J. and Sweeney, J.B. *Tetrahedron Lett.* 1992, *33,* 7569

6. a) Hacksell, V. and Doyle Daves Jr. *Prog. Med. Chem.* 1985, *22,* 1
   b) Postema, M.H.D. *Tetrahedron,* 1992, *48,* 8545
   c) Atta-Ur-Rahman, editor, *Studies in Natural Product Chemistry,* 1992, *10,* 337
   d) Knapp, S. *Synthesis,* 1994, 1.

7. Hanessian, S., *Total synthesis of Natural Products, the Chiron Approach,* Pergmon Press, Oxford, 1983.

8. a) Martin, O.R. *Tetrahedron Lett.* 1985, *26,* 2055.
   b) Martin, O.R.;Prahlada Rao, S.; Kurz, K.G. and El-Shenawy, H.A. *J.Am.Chem. Soc.* 1988, *110,* 6898.

9. a) Kim, K.S.; Kim J.H.; Kim Y.K.; Park Y.S. and Hahn, C.S. *Carbohydrate Res.* 1989, *194,* C1-C3.
   b) Stork, G. and Mook, R.Jr. *J.Am. Chem. Soc.* 1983, *105,* 3720.

10. Keller-Scherlein, W. and Wuthier, D. *Helv. Chim. Acta,* 1983, *66,* 1253.

11. Yoshida, W.Y.; Bryan, P.J.; Baker, B.J. and McClintock, J.B., *J. Org. Chem.,* 1995, *60,* 780.

12. Trost, B.M. and Klun, T.P., *J. Am. Chem. Soc.* 1981, *103,* 1864.

13. For this type of oxidation using RuO_4, which did not work for us, see Martin, O.R.; Hendricks, C.A.V.; Deshpande, P.; Cutler, A.; Mahnken, R.M. and Rao, S.P., *Carbohydrate Research,* 1990, *196,* 41.

14. Eckenberg, P.; Groth, U.; Huhn, T.; Richter, N. and Schemeck, C., *Tetrahedron,* 1993, *49,* 1619.•

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