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CHIRAL SYNTHONS FOR THE MULTISTRIATINS[1]

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Summary. The readily-obtained carbohydrate α-enones 2, 5 and 8 are converted into the four diastereomeric 2,4-di-C-methyl glycopyranosides 4,7,10,11, which are chiral synthons for the four multistriatins 1a-1d.

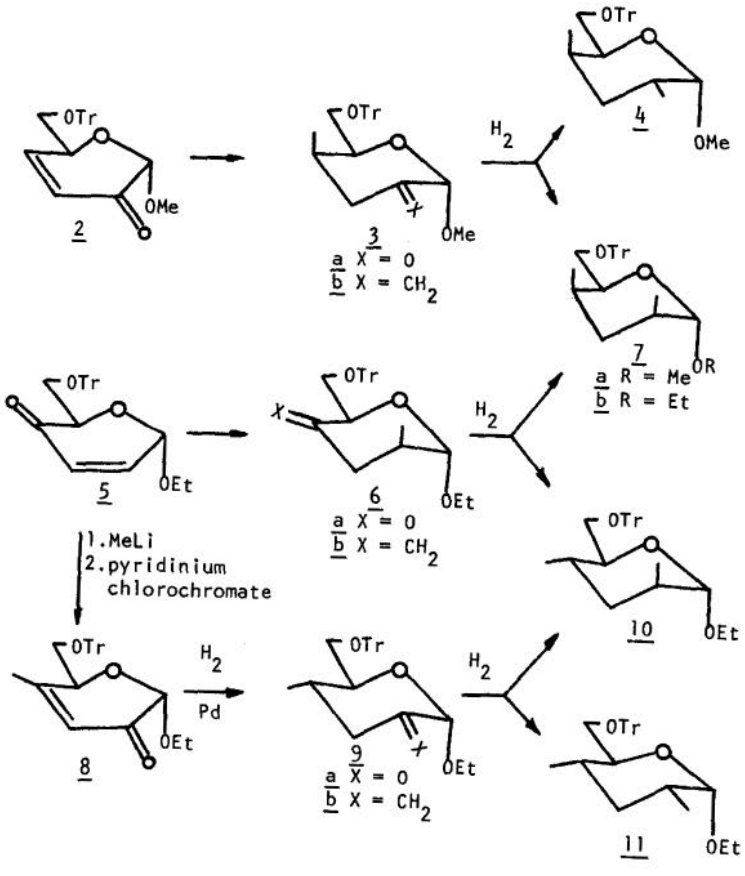
In connection with our studies on the use of carbyhydrates as chiral synthons[2] we have been developing approaches to the dioxabicyclo [3.2.1] octyl pheromones frontalin[3], exo-brevicomin[4], and the multistriatins, 1.[1a] Interest in these substances continues to be high because of the devastation wrought by the beetles in which they occur, and this is particularly true in the case of the multistriatins, 1, since the elm bark beetle continues to spread Dutch-elm disease at an alarming rate. This communication describes some of our work on the multistriatins and is prompted, in part, by the results of Sum and Weiler[5] published while our work was in progress.

The pyranose ring of 1 is locked in the $_4C^1$ conformation[6], and hydrolytic cleavage leads to an hemiacetal which may be represented in the $^4C_1$ conformation, for example 14. This analysis therefore leads to the four di-C-methyl pyranosides 4, 7, 10 and 11 as the synthons for γ, α, δ and β multistriatins, 1a, 1b, 1c and 1d respectively. Apart from the multistriatins, these compounds are also of interest as chiral synthons for the related di-C-methyl-pyrano moieties found, for example, in Prelog-Djerassi lactone[7] and monensin[8].

Hydrogenation of the alkenes 3b, 6b and 9b affords a complete set of the related diastereomers 4, 7, 10 and 11. Unambiguous structural assignments are faciliated by noting, for example, that the same compound, 7, is obtainable from both 3b and 6b; the "other" diastereomers obtained from 3b and 6b must therefore be 4 and 10 respectively. These assignments can be further verified since 4 is also obtainable from 3b, and 10 from 9b.

The three alkenes 3b, 6b and 9b are obtained[9] by Wittig reactions on the corresponding ketones, two of which 3a and 6a have been previously shown by us to be exclusive products of lithium dimethyl cuprate additions to 2 and 5 respectively[10]. Ketone 9a[9], whose structure follows from comparison with the known epimer 3a, was obtained as the exclusive product of hydrogenation

S C H E M E 1



isomer	R_f [a]	NMR DATA (220 MHz) H-1 ppm	J_{12}	C-2	C-4	Catalyst [b] Ni	Pt	$(Ph_3P)_3RhCl$
4	0.27	not determined				-	10	-
7a	0.23	4.30	5.0	0.96	0.71	-	90	-
7b	0.23	4.41	6.0	0.96	0.70	-	50	70
10	0.31	4.62	0	1.11	0.61	50	50	30
						90	50	67
11	0.40	4.71	3.0	0.86	0.59	10	50	33

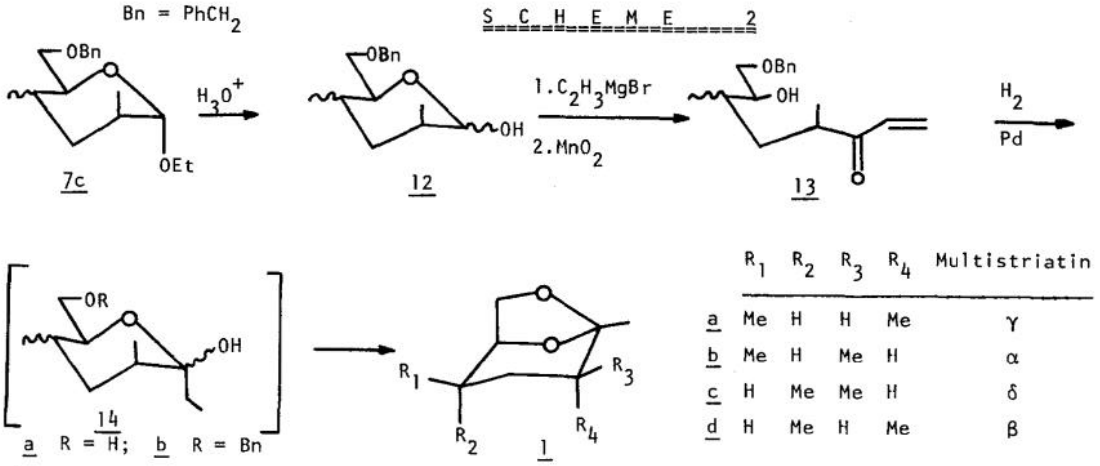
a ethyl acetate ; petroleum ether (95:5)
b relative percent form NMR spectra

of enone 8. The latter was in turn obtained by treating enone 5 with methyl lithium and pyridinium chlorochromate as described by Dauben and Michno[11].

The data in Scheme 1 indicate that the two diastereomers produced by hydrogenating each of the alkenes are well resolved on tlc. Thus each diastereomer was obtained pure and subjected to NMR analysis at 220 MHz. With these parameters in hand, it was then possible to determine accurately the ratio of diastereomers produced under the various hydrogenation conditions shown in Scheme 1, the crude product being used for these analyses, prior to chromatography, crystallization or any such tampering.

With regard to the diaxial diastereomer 7, the synthon for α-multistriatin 1b, our initial assessments suggested that 6b would be a better precursor than 3b, since the axial C-2 methyl group of 6b would be expected to exercise strong stereocontrol favouring production of 7. On the other hand the thorough studies of Miljkovic and Glissin had shown that hydrogenation of 2-C-exo-methylene-α-D-hexopyranosides related to 3b (and 9b) occurs with very low stereoselectivity.[12]

However our data, some of which are summarized in Scheme 1, show that neither 3b nor 6b is hydrogenated stereospecifically, and that the best route to 7 is by hydrogenating 3b over platinum. Reactions of 6b were less stereoselective even with the use of freshly prepared Wilkinson's cata-



lyst†. Furthermore in our hands the latter reaction required several days at room temperature and rarely went to completion.

†Although the title of the paper by Sum and Weiler[5] referred to a stereospecific synthesis of α-multistriatin, the text of the paper, and our results, suggest that stereoselective should have been used.

Our route from the hexopyranoside to the multistriatin skeleton has been developed as shown in Scheme 2 using a 4:1 mixture[12] of the benzylated analogue 7c and its 4-epi isomer. Compound 7c was obtained as in Scheme 1 from the benzylated analogue of 5 which was in turn prepared according to the standard procedures developed in our laboratory for these enones[13]. Gentle acid hydrolysis of 7c afforded a mixture of hemiacetals 12 having the same 4:1 ratio (glc analysis) indicating that epimerisation at C-2 had not occurred (cf. reference 15). Furthermore the enone 13 also proved to be a 4:1 mixture, presumably of 13 and 6-epi-13 (λ_{max}: 213 nm; ε = 10,900). After chromatographic purification, the enone 13 was hydrogenated, the stepwise transformations leading first to 14b, then to 14a and finally to 1b being readily monitored by tlc. GLC comparison with the authentic substances[15] showed that our material consisted of a 4:1 mixture of α- and δ-multi striatin, 1b and 1c.

Work on various aspects of the synthesis is continuing and will be reported in due course.

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References

1. Taken from the University of Waterloo M.Sc. Thesis of (a) B. J.Fitzsimmons, 1979 and (b) D. E. Plaumann, 1977.
2. B. Fraser-Reid and R. C. Anderson, Fortschritte der Chemie Organischer Naturstoffe, in press; B. Fraser-Reid, Accts. Chem. Res. 8, 192 (1975).
3. D. R. Hicks and B. Fraser-Reid, J.C.S. Chem. Comm., 869, (1976).
4. A. E. Sherk, M.Sc. Thesis, University of Waterloo, 1978.
5. P-E. Sum and L. Weiler, Can. J. Chem., 56, 2700 (1978).
6. J. C. P.Schwarz. J.C.S. Chem. Commun. 505 (1973).
7. C. Djerassi and J. A. Zderic, J. Am. Chem. Soc., 78, 6390 (1956); R. Anliker, D. Dvornik, K. Cubler, H. Heusser, and V. Prelog, Helv. Chim. Acta, 39, 1785 (1956).
8. A. Agtarap, J. W. Chamberlin, M. Pinkerton, and L. Steinrauf, J. Am. Chem. Soc. 89, 5737(1967); M. Pinkerton and L. K. Steinrauf, J. Mol. Biol. 49, 533 (1970).
9. All new compounds gave satisfactory 220 MHz nmr spectra as well as the desired elemental analyses or high-resolution mass spectra.
10. M. B. Yunker, D. E. Plaumann, and B. Fraser-Reid, Can. J. Chem. 55, 4002 (1977).
11. W. G. Dauben and D. M. Michno, J. Org. Chem. 42, 682 (1977).
12. (a) M. Miljkovic and D, Glissin, ibid., 40, 3351 (1975).
    (b) Stereoselectivity in these hydrogenations was found to depend on the protecting groups as well as on the catalyst used.
13. As expected from the work of Miljkovic and Glissin[12a], the benzylated alkenes showed different stereoselectivities than the tritylated analogues in Scheme 1.
14. B. Fraser-Reid, A. McLean, E. W. Usherwood and M. B. Yunker, Can. J. Chem., 48, 2877 (1970).
15. W. E. Gore, G. T. Pearce and R. M. Silverstein, J. Org. Chem., 41, 2797 (1976).

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