

A NEW INTERMEDIATE FOR METHYL JASMONATE AND PG'S FROM IRIDOID
GLUCOSIDE AUCUBIN¹

Enrico Davini,² Carlo Iavarone, and Corrado Trogolo

Centro C.N.R. per lo Studio della Chimica delle Sostanze Organi-
che Naturali - Dipartimento di Chimica - Università "La Sapienza",
Piazzale Aldo Moro 2 - 00185 Roma, Italy

Abstract - A synthetic approach to biologically active cyclo-
pentanoids or their intermediates starting from natural hetero-
cyclic precursors (iridoid glucosides) has been devised. Aucubin
1 was efficiently converted into chiral cyclopentenone 2, inter-
mediate for synthesis of methyl jasmonate-type compounds and pro-
staglandins.

Iridoid glucosides are a widespread class of natural compounds with heterocyclic
(cyclopenta[c]pyran) skeleton whose most common and abundant representative is au-
cubin 1.

Starting by this natural chiral template we are running³⁻⁶ a program of syntheses
of biologically active cyclopentanoids or their intermediates. In continuation of
our work we put now our attention upon isoeucommiol 3 whose unique utilization for
synthetic purposes was the acid-catalyzed transformation into cis-2-oxa-bicyclo[3.
3.0]-6,7-dihydroxymethyl-oct-7-ene 4, a precursor of modified PG's.^{3,7} The inte-
rest for the cyclopentenetetrol 3 is due also to its easy preparation by NaBH₄ re-
duction of the aglycone of 1 (aucubigenin 2) carried out at first on the isolated
aglycone⁸ and then directly "one-pot" on the enzymatic (β -glucosidase) hydrolyzate
of 1³ ($\gamma_{1 \rightarrow 3} = 92\%$).

In this report we describe the conversion of 3 into bis-O-acetylcyclopentenone 2,
a chiral intermediate useful either for syntheses of PG's or of methyl dehydroja-
smonate 13 and methyl jasmonate 14, the latter identified as an insect sex-attrac-
tant pheromone⁹ or a senescence promoting substance in some plants¹⁰ and both used
in perfume industry.¹¹

Epoxidation of 3 with *m*-chloro perbenzoic acid in EtOH (12 h at r.t.) proceeded in
a stereoselective way affording only the epoxide 5¹² with the oxirane ring in β con-
figuration. This result was in agreement with the well known syn orienting effect¹³
exerted by the allylic hydroxyl function in the epoxidation of 1-hydroxy-2-cyclo-
pentenes. LiAlH₄ reduction of acetylepoxo derivative 6¹⁴ in anhydrous DME afforded
the cyclopentanepentol 7¹⁵ (68% overall yield from 3), whose vic-diol function was

successively oxidized (NaIO_4) to give the β -hydroxy cyclopentanone derivative 8 ($y = 48\%$).

In spite of literature data¹⁶ describing the great tendency of similar cyclic β -ketols to be dehydrated to the corresponding enones by acid or basic catalysis, 8 resulted in rather stable compound under these conditions and the dehydration to the enone system was achieved only under acetylation conditions which transformed 8 into the acetylenone 9¹⁷ ($y = 61\%$).

This readily available cyclopentenone may be considered a useful chiral intermediate for the synthesis of jasmonate-type compounds and PG's.

In fact 9 can be easily converted, by routine methodologies, into diesters 11 and 12, in their turn reported precursors^{18,19} of methyl jasmonate 14 and methyl dehydrojasmonate 13 respectively, through known and well established chemistry (C-alkylation of β -ketoester function with 2-pentynyl bromide followed by *cis*-hydrogenation of triple bond by Lindlar¹⁹ or palladium-on-barium sulfate¹⁸ catalyst and final acid-catalyzed decarboxylation¹⁹ providing the thermodynamically stable *trans* isomer).

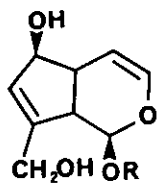
On the other side the Corey lactone analogue 15 should be obtained from γ,δ unsaturated carboxylic acid 10²⁰ by direct lactonization²¹ or through iodolactonization procedure.²²

Various attempts to obtain 7 (or its epimer at C-4) directly from 3 by Markownikoff hydration of double bond through classical oxymercuration-demercuration (OM-DM) procedure²³ (mercuric acetate in H_2O -THF) were unsuccessful.

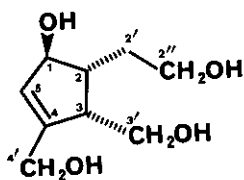
The lack of reactivity of 3 was absolutely unpredictable as OM-DM of trisubstituted cyclopentene double bonds (e.g. 2,4,5-trimethylcyclopentene²⁴ and 3-methyl-*cis*-bicyclo[3.3.0]oct-2-ene²⁵) or of acyclic allylic alcohols²⁶ were described to give the expected hydration products.

This failure however could hide a positive aspect. In fact if the cyclopentene allylic 1,4-diol system of 3 would retain its unreactivity towards OM-DM also in the parent iridoid 1, it could be possible to guess a chemoselective OM-DM reaction of the only enol-ether double bond of aucubin 1, with results of predictable practical interest.

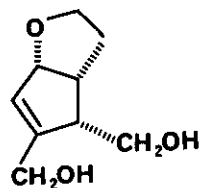
We are investigating at present the OM-DM reaction of 1 and the first results will be next published.



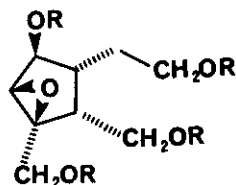
1 R = β -D-Gluc
2 R = H



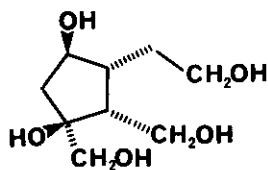
3



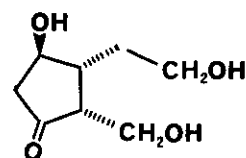
4



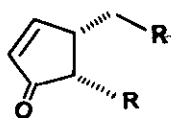
5 R = H
6 R = Ac



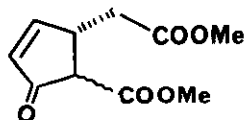
7



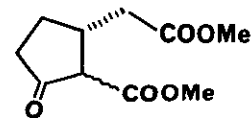
8



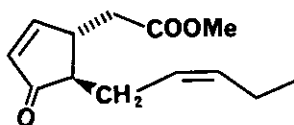
9 R = CH₂OAc
10 R = COOH



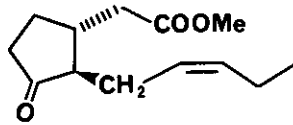
11



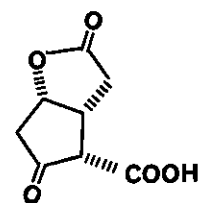
12



13



14



15

REFERENCES AND NOTES

1. Abstracted in part from the "Dottorato di Ricerca" Thesis of E.D., Rome University, 1984-86.
2. Present address : Eni Ricerche Spa., Via Ercole Ramarini 32, 00015 Monterotondo, Italy.
3. C.Bonini, C.Iavarone, C.Trogolo, and R. Di Fabio, *J. Org. Chem.*, 1985, 50, 958.
4. E.Davini, C.Iavarone, C.Trogolo, P.Aureli, and B.Pasolini, *Phytochemistry*, 1986, 25, 2420.
5. R.Bernini, E.Davini, C.Iavarone, and C. Trogolo, *J. Org. Chem.*, 1986, 51, 4600.
6. E.Davini, C.Iavarone, and C.Trogolo, *Phytochemistry*, 1987, 26, 1449.
7. C.Bonini, R.Di Fabio, C.Iavarone, and C.Trogolo, *Ital. Pat. Appl.*, 1981, 49042 A/81.
8. A.Bianco, M.Guiso, C.Iavarone, P.Passacantilli, and C.Trogolo, *Tetrahedron*, 1977, 33, 851.
9. R.Nishida, T.C.Baker, W.L.Roeloffs, and T.E.Acree, "Abstract of Papers", 186th National Meeting of the American Chemical Society, Washington DC, Aug.28-Sept. 2, 1983; American Chemical Society: Washington DC, 1983; AGFD 100.
10. S.O.Satler and K.V.Thimann, *C. R. Acad. Sc. Paris*, t293, 1981, 735.
11. (a) E.Demole, E.Lederer, and D.Mercier, *Helv. Chim. Acta*, 1962, 45, 675.
 (b) J.Ueda and J.Kato, *Plant Physiol.*, 1980, 66, 246.
 (c) T.Yamanishi, M.Kosuge, Y.Tokimoto, and R.Maeda, *Agric. Biol. Chem.*, 1980, 44, 2139.
12. For comparative reasons, the carbon numbering of compounds was the same as for cyclopentenetetrol 3.⁸
13. (a) H.Z.Sable, T.Anderson, B.Tolbert, and T.Posternak, *Helv. Chim. Acta*, 1963, 46, 1157.
 (b) G.Berti, "Topics in Stereochemistry", vol.7, ed. by E.L.Elivel and N.L.Alinger, Wiley-Interscience, New York, 1972, p.135.
14. ¹H-nmr (300 MHz, CDCl₃): δ 4.91 (d, 1H, H-1, J_{1,5} = 9.0 Hz), 4.51 (d, 1H, H_A-4', J_{AB} = 12.0 Hz), 4.21 (octet, 2H, 2H-3', AB part of an ABX), 4.06 (d, 1H, H_B-4', J_{AB} = 12.0 Hz), 4.03 (dt, 2H, 2H-2"), 3.69 (s, 1H, H-5), 2.63 (d, 1H, H-3), 2.20 (m, 1H, H-2), 2.10-2.03 (12H, 4 AcO signals), 1.69 (q, 2H, 2H-2', J = 9.0 Hz); ¹³C-nmr (75 MHz, CDCl₃): δ 78.51 (d, C-1), 70.40 (s, C-4), 62.70 (d, C-5), 62.50 (t, C-4'), 60.20 (t, C-2"), 59.37 (t, C-3'), 39.62 (d, C-3), 36.43 (d, C-2), 26.64 (t, C-2'); AcO signals: 171.20, 170.79, 170.30 (C=O) and 20.97, 20.61 (CH₃).
15. ¹H-nmr (300 MHz, D₂O): δ 3.91 (sextet, 1H, H-1, J = 3.6 Hz), 3.65-3.40 (m, 6H, 2H-2", 2H-3', 2H-4'), 2.26 (p, 1H, H-2, J = 6.9 Hz), 2.16 (dd, 1H, H_B-5, J_{AB} = 15.0 Hz, J_{1,5B} = 8.4 Hz), 2.05 (bq, 1H, H-3), 1.59 (m, 2H, 2H-2'), 1.43 (dd,

- $^1\text{H}, H_A-5, J_{AB} = 15.0 \text{ Hz}, J_{1,5A} = 4.5 \text{ Hz}$); ^{13}C -nmr (75 MHz, D_2O): δ 83.02 (s, C-4), 76.67 (d, C-1), 66.71 (t, C-4'), 61.73 (t, C-2''), 58.53 (t, C-3'), 52.25 (d, C-3), 45.91 (d, C-2), 44.25 (t, C-5), 31.34 (t, C-2').
16. D.P.Strike and H.Smith, Tetrahedron Lett., 1970, 4393; J.E.Pike, F.H. Lincoln, and W.P. Schneider, J. Org. Chem., 1969, 34, 3552.
17. ^1H -nmr (300 MHz, CDCl_3): δ 7.66 (dd, 1H, H-1, $J_{1,5} = 6.3 \text{ Hz}, J_{1,2} = 2.4 \text{ Hz}$), 6.23 (dd, 1H, H-5), 4.2-3.8 (m, 4H, 2H-2'', 2H-3'), 2.91 (t, 1H, H-2), 2.34 (m, 1H, H-3), 2.00-1.75 (m, 2H, 2H-2'), 2.04 and 2.03 (6H, 2 AcO signals); ^{13}C -nmr (75 MHz, CDCl_3): δ 207.13 (s, C-4), 166.41 (d, C-1), 133.57 (d, C-5), 63.04 (t, C-3'), 62.35 (t, C-2''), 50.82 (d, C-3), 42.76 (d, C-2), 32.81 (t, C-2'); AcO signals: 170.88, 170.83 (C=O) and 20.94, 20.75 (CH_3).
18. F. Johnson, K.G.Paul, and D.Favara, J. Org. Chem., 1982, 47, 4254; Germ. Pat., 1975, 2508295.
19. (a) S.Torii, H.Tanaka, and T.Mandai, J. Org. Chem., 1975, 40, 2221.
 (b) S.Torii, H.Tanaka, and Y.Kobayasi, J. Org. Chem., 1977, 42, 3473.
 (c) A.Wisser, J. Org. Chem., 1977, 42, 356.
20. F.Johnson, K.G.Paul, D.Favara, R.Ciabatti, and U.Guzzi, J. Am. Chem. Soc., 1982, 104, 2190.
21. P.A.Grieco, N.Fukamiya, and M.Miyashita, J. Chem. Soc. Chem. Comm., 1976, 573.
22. H.L.Slates, Z.L.Zelawski, D.Taub, and N.L.Wendler, Tetrahedron, 1974, 30, 819.
23. H.C.Brown and P.J.Geoghegan jr., J. Org. Chem., 1970, 35, 1844.
24. H.C.Brown, G.J.Lynch, W.J.Hammar, and L.C.Liu, J. Org. Chem., 1979, 44, 1910.
25. H.C.Brown and W.J.Hammar, Tetrahedron, 1978, 34, 3405.
26. H.C.Brown and G.J.Lynch, J. Org. Chem., 1981, 46, 531.

Received, 31st August, 1987