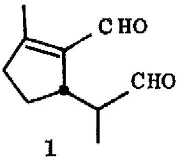
Tetrahedron Letters Vol. 21, pp 1701 - 1704   0040-4039/80/0429-1701$02.00/0
© Pergamon Press Ltd. 1980. Printed in Great Britain

CHRYSOMELIDIAL BY CHROMYL CHLORIDE OXIDATION: A REVISED STRUCTURE FOR GASTROLACTONE

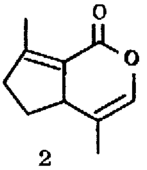
Tappey H. Jones* and Murray S. Blum
Department of Entomology, University of Georgia, Athens, GA 30602
H. M. Fales
Laboratory of Chemistry, National Heart, Lung and Blood Institute
Bethesda, MD 20014

Summary Non-conjugated *gem*-dialkylated alkenes were oxidized to aldehydes in the presence of α,β-unsaturated carbonyl functional groups, providing a new synthesis of 1 and a synthesis of 2 that led to a revised structure for gastrolactone.

The cyclopentenoid monoterpene chrysomelidial (1) has been identified as a major constituent in the larval defensive secretions of the chrysomelid beetles *Gastrophysa cyanea*[1] and *Plagiodera versicolora*[2], and its enantiomer has been isolated from the plant *Actinidia polygama*[3]. In addition, on the basis of its mass spectrum, a major component of the defensive exudate of *G. cyanea* was reported to be 5,6-dihydro-4,7-dimethylcyclopenta[c]pyran-1-(4aH)one (2)[1]. We now wish to report the preparation of these labile compounds in which the key step is oxidation of a *gem*-disubstituted olefin to an aldehyde utilizing chromyl chloride.[4] This synthesis provides a useful route to 1 and demonstrated that 2 is not the $C_{10}H_{12}O_2$ lactone that occurs in *G. cyanea*.

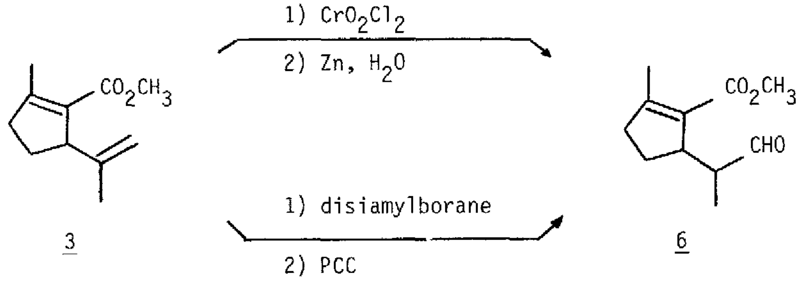


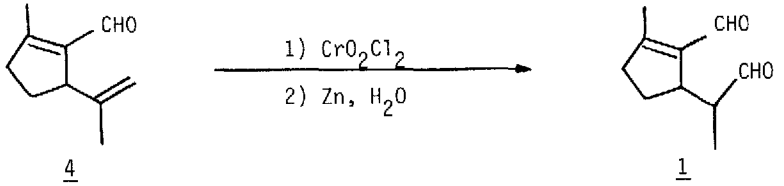
1

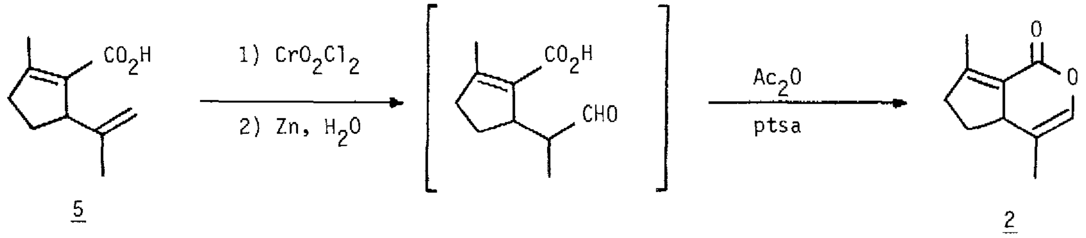


2

Methyl 2-methyl-5-isopropenyl-1-cyclopenten-1-carboxylate (3), the corresponding aldehyde (4), and free carboxylic acid (5) were prepared as described by Wolinsky[5,6] from R-limonene. In a preliminary experiment, a well stirred solution of 3 in methylene chloride was cooled to





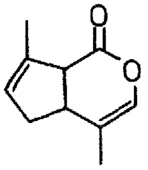


0°C and treated with one equivalent of chromyl chloride. After 15 min., the mixture was worked up with zinc dust and ice water[4], carefully filtered through celite, and extracted with ether. The organic solution was dried, and the solvent removed to give an 80% yield of the aldehyde ester 6; IR 2820, 2710, 1720, 1640, 1430, 1350, 1215, 1110, and 1050 cm^{-1}; NMR (60 MHz) δ 9.62 (1H, d, J=3Hz, C$\underline{H}$O), 3.70 (3H, s, OC$\underline{H}_3$), 3.1-3.3 (4H, complex multiplet), 2.01 (3H, br s, =C-C$\underline{H}_3$) 1.6-1.8 (2H, complex multiplet), 0.95, 0.88 (3H, a pair of doublets, J= 7.5Hz, CH-C$\underline{H}_3$); MS, m/z (rel %) 196(5, M^+), 178(8), 164(35), 149(30), 139(60), 121(12), 111 (10), 109(9), 107(70), 93(20), 91(25), 81(15), 80(10), 79(100), 78(5), 77(20), 67(10), 59(25), 55(11), 53(4), 43(10), 41(14). These spectra are identical with those displayed by the aldehyde ester 6 obtained by hydroboration of 5 with disiamylborane[6] and subsequent pyridinium chlorochromate oxidation[7] of the resulting hydroxy ester.

Oxidation of aldehyde 4 in a similar manner required two equivalents of chromyl chloride for the reaction to go to completion, and gave a 69% yield of chrysomelidial 2 which was identical in all respects to previously synthesized material.[8,9,10]

Oxidation of the carboxylic acid 5 was also carried out with two equivalents of chromyl chloride to give 20% of the crude aldehyde acid which was cyclized with acetic anhydride and a trace of p-toluenesulfonic acid in benzene.[11] The dienelactone 2 was isolated by preparative GLC as an unstable liquid;[12] IR 3080, 1740 (broad), 1680, 1645, 1435, 1377, 1330, 1249, 1202, 1115, 1068, 1045, 1020, 979, 960, 905, and 838 cm; NMR, (100MHz) δ 6.2 (1H, multiplet, C=C$\underline{H}$-O), 3.5 (1H, broad multiplet, C=C-C$\underline{H}$-C=C), 2.5-2.4 (2H, multiplet, -C$\underline{H}_2$-C=C), 2.2 (3H, complex multiplet, C=C-C$\underline{H}_3$), 1.62 (3H, d of d, J=1.5, 1.2 Hz, C$\underline{H}_3$-C=C-O), 1.3 (2H, multiplet, -CH_2-); MS, m/z (rel %) 164 (100, M^+), 151(13), 149(61), 136(13), 135(32), 121(36), 107(29), 105(10), 93(39), 91(42), 81(6), 80(13), 79(39), 77(36), 67(6), 65(10), 55(6), 53(13), 51(13), 43(42), 41(16). The structural relationship of the methyl groups and the double bonds was confirmed by decoupling experiments. Irradiation of the multiplet at 6.2 ppm collapsed the doublet of doublets at 1.62 ppm to a doublet, J=1.2Hz, and did not change the methyl multiplet at 2.2 ppm. Irradiation of the broad multiplet at 3.5 ppm collapsed the doublet of doublets at 1.62 ppm to a doublet, J=1.5 Hz, and simplified the methyl multiplet at 2.2 ppm into a broad doublet of doublets. Finally, irradiation of the methyl signal at 1.62 ppm collapsed the olefinic signal at 6.2 ppm to a sharp doublet, J=2.1 Hz.

The mass spectrum of 2 is quite different from that reported for gastrolactone.[1] Reexamination of an NMR spectrum of partially polymerized[12] gastrolactone showed two olefinic proton multiplets (6.28 and 5.6 ppm) and no aliphatic methyl groups. These data indicate that the structure of gastrolactone may be represented by (7).[13] Synthesis of this diene lactone is now in progress.



7

ACKNOWLEDGEMENTS. We thank Mr. E. A. Sokoloski of the National Institues of Health for performing the decoupling experiments. Support of this work by the Research Corporation is gratefully acknowledged.

REFERENCES

1. M. S. Blum, J. B. Wallace, R. M. Duffield, J. M. Brand, H. M. Fales, and E. A. Sokoloski, J. Chem. Ecol., 4, 47 (1978).
2. J. Meinwald, T. H. Jones, T. Eisner, and K. Hicks, Proc. Natl. Acad. Sci. USA, 74, 2189 (1977).
3. K. Yoshihara, T. Sakai, and T. Sakan, Chem. Lett., 433 (1978).
4. F. Freeman, R. H. DuBois, and T. G. McLaughlin, Org. Syn., 51, 4 (1971).
5. J. Wolinsky, M. R. Slabaugh, and T. Gibson, J. Org. Chem., 29, 3740 (1964).
6. J. Wolinsky, and D. Nelson, Tetrahedron, 25, 3767 (1969).
7. E. J. Corey and J. W. Suggs, Tetrahedron Lett., 2647 (1975).
8. J. Meinwald, and T. H. Jones, J. Am. Chem. Soc., 100, 1883 (1978).
9. Chrysomelidial prepared in this way is a mixture of epimers at the Cα methyl. This mixture occurs in P. versicolora but not in G. cyanea. This method constitutes a formal synthesis of the enantiomer of this compound (ref. 3), which would be formed starting from S-limonene.
10. Since this work was completed, chrysomelidial has been reported in two other species of chrysomelid larvae. See F. Sugawara, K. Matsuda, A. Kobayashi, and K. Yamashita, J. Chem. Ecol., 5, 635 (1979).
11. K. D. Zwahlen, W. J. Horton, and G. I. Fujimoto, J. Am. Chem. Soc., 79, 3131 (1957).
12. Both 1 and 2 decomposed in a few hours upon isolation by preparative GLC, but could be stored for a short time in frozen benzene.
13. Clearly the ultraviolet spectrum of gastrolactone should have revealed the presence of the unsaturated lactone in structure 2. With one sample isolated by preparative GLC, no such absorption was seen; however in view of the very unstable nature of the purified product (see ref. 12) the experiment was not regarded as definitive. In retrospect, the absence of such an ultraviolet absorption is supportive of structure 7.

(Received in USA 19 November 1979)