## A NOVEL ONE-STEP OXIDATION OF TERMINAL EPOXIDES TO ALLYLIC ALDEHYDES

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<u>Summary</u> – Various gibberellin epoxides have been oxidised with sulphuryl chloride to  $\alpha,\beta$ -unsaturated aldehydes in >70% isolated yield. This novel one-step oxidation occurs in the presence of hydroxy (except at C-13), ester, lactone and olefinic functions.

Epoxides are versatile intermediates in organic synthesis, undergoing ring opening reactions with a range of nucleophiles and rearrangement to allylic alcohols and carbonyl compounds<sup>1</sup>. In studies with the gibberellin (GA) plant hormones the 16,17-epoxide has been used to protect the exocyclic double bond<sup>2</sup>; however no one-pot transformation of the epoxide to introduce functionality into ring D of the gibberellins has been reported.<sup>3</sup> In the course of investigations on the functionalisation of ring D of the gibberellins a novel oxidation<sup>4</sup> of gibberellin 16,17-epoxides to 15-en-17-als was discovered.

Treatment of GA<sub>9</sub> methyl ester 16,17-epoxide (1) with sulphuryl chloride in dry dichloromethane gave the allylic aldehyde (2) in 90% overall yield. The structure of the product (2) was established by <sup>1</sup>H-nmr ( $\delta$  6.89, s, 15-H; 9.65, s, 17-H) and <sup>13</sup>C-nmr ( $\delta$  154.33, C-15; 134.69, C-16; 188.61, C-17).



To explore the generality of this reaction a series of gibberellin 16,17-epoxides, cyclohexene oxide and the epoxide of a 3-methylene steroid were treated with sulphuryl chloride<sup>5</sup> (Table). Although sulphuryl chloride is a powerful chlorinating agent<sup>6</sup> reacting with alcohols, olefins and enones as well as epoxides, the results show that attack occurs preferentially on the epoxide and not on the  $3\beta$ -hydroxyl (entries (ii) and (iii)) or 1,2-double bond (entry (iv)). In the presence of a 13-hydroxyl or 13-acetoxyl moiety (entries (v) and (vi)) a Wagner-Meerwein type rearrangment of rings C/D leads to the ketones (4) and (5)<sup>7</sup>. Reaction (viii) with the terminal epoxide of a steroid (8) gave several chlorinated by-products as well as a mixture of the allylic aldehydes (9) and (10). Reaction (vii) with the 1,2-disubstituted epoxide (6) gave mainly the <u>cis</u> dichloride (7) for which there are precedents.<sup>8</sup>

Entry	Substrate	Product	Yield 9
(i)	Aco H CO Me	Action CO H	90%
(ii)	HO I H CO <sub>2</sub> Me	H0 H CO <sub>2</sub> Me (3)	85%
(iii)	HO CO2Me	HO CO2Me CO2Me	80%
(iv)	HO H CO2Me	HO HO CO2Me	80%
(v)	HO HO CO2Me	HO $HO$ $HO$ $HO$ $HO$ $HO$ $HO$ $HO$ $H$	70%
(vi)	HO H CO <sub>2</sub> Me	$H_{0} \xrightarrow{\begin{array}{c} 0 \\ C 0 \\ H \end{array}} \xrightarrow{\begin{array}{c} 0 \\ C 0 \\ H \end{array}} \xrightarrow{\begin{array}{c} C H_{2} GAc}{\begin{array}{c} 0 \\ C \\ C$	65%
(vii)	(6)	Cl (7)	55%
(viii)		ОНС <u>Н</u> (9) (10)	35%

The formation of the allylic aldehydes may occur by nucleophilic attack of the oxirane oxygen on sulphuryl chloride to give (11) possessing a stabilised carbocation. Proton abstraction from C-15, possibly by an intramolecular process, would then give the allylic aldehyde. Work is currently underway to determine the mechanism of this reaction.



(11)

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## References and Notes

- Reviews: J.R. Crandall, M. Apparu, <u>Organic Reactions</u>, 1983, <u>29</u>, 345; A.S. Rao, S.K. Paknikar, J.G. Kirtane <u>Tetrahedron</u>, 1983, 2323; J.G. Smith <u>Synthesis</u>, 1984, 629.
- For example: N. Murofushi, R.C. Durley, R.P. Pharis, <u>Agr. Biol. Chem.</u>, 1977, <u>41</u>, 1075;
  J. MacMillan, C.L. Willis, <u>J. Chem. Soc. Perkin Trans. 1</u>, 1984, 351.
- Kauran 16α,17-epoxide has been used as an intermediate in the formation of a 14,17-ether by its conversion to the 16α-CH<sub>2</sub>OH followed by oxidation with Pb(OAe)<sub>4</sub>. M. Node, T. Koyimoto, K. Nishida, E. Fugita. <u>Tetrahedron Letters</u>, 1984, 25, 219.
- A literature survey revealed only one other reported oxidation of epoxides, namely the oxidation with DMSO/BF<sub>3</sub>.Et<sub>2</sub>0 to give α-hydroxy ketones or aldehydes: T. Cohen, T. Tsujii <u>J. Org.</u> Chem., 1961, <u>26</u>, 1681; T. Santosusso, D. Swern. <u>J. Org. Chem.</u>, 1975, <u>40</u>, 2764.
- 5. Typical procedure: To a solution of the epoxide (0.25 mmol) in dry CH<sub>2</sub>Cl<sub>2</sub> (25 ml) was added SO<sub>2</sub>Cl<sub>2</sub> (0.25 mmol, freshly distilled) under nitrogen. The reaction mixture was heated to reflux for 6h then washed with water and concentrated under reduced pressure. The crude products were purified by flash chromatography.

- For example: M.F. Grenier-Loustalot, P. Iratcabal, F. Métras. J. Pétrissans. <u>Synthesis</u>, 1976, 33;
  M.S. Kharasch, H.C. Brown. <u>J. Am. Chem. Soc.</u>, 1939, <u>61</u>, 3432.
- An analogous Wagner-Meerwein type rearrangement of GA<sub>3</sub>-16,17-epoxide under acid conditions has been reported: K. Schreiber, G. Sneider, G. Sembdner. <u>Tetrahedron</u>, 1968, <u>24</u>, 73; M.F. Barnes, R.C. Durley, J. MacMillan <u>J. Chem. Soc. (c)</u>, 1970, 1341.
- 8. J.R. Campbell, J.K.N. Jones, S. Wolfe. Can. J. Chem., 1966, 44, 2339.
- 9. All compounds gave <sup>1</sup>H-nmr (270MHz) and mass spectra consistent with their assigned structures: (4) and (5) gave satisfactory microanalytical data; other products, which were gums, gave satisfactory high resolution mass spectra and/or <sup>13</sup>C-nmr spectra e.g. (3)  $\delta$  1.18 (s, 18-H<sub>3</sub>), 2.70 (d, J = 10Hz, 6-H), 3.26 (d, J = 10Hz, 5-H), 3.71 (s, -OMe), 3.81 (br.s, 3-H), 6.89 (s, 15-H), 9.65 (s-CHO); m/z 360 (M<sup>+</sup>, 23%), 342 (3), 298 (44) 239 (32), 215 (79), 183 (29), 115 (34), 105 (26) and 91 (65); Found: M<sup>+</sup>, 360.1545 C<sub>20</sub>H<sub>24</sub>O<sub>6</sub> requires M, 360.1573. (4)  $\delta$ [(CD<sub>3</sub>)<sub>2</sub>CO] 1.16 (s, 18-H<sub>3</sub>), 2.17 (d, J = 18.5Hz, 15-H) 2.73 (d, J = 6.5Hz, 6-H), 2.82 (d,d, J = 4, 18.5Hz, 15-H), 3.28 (d, J = 6.5Hz, 5-H), 3.41 and 3.69 (q, J<sub>AB</sub> = 11Hz, <u>CH<sub>2</sub>OH</u>), 3.72 (s, -OMe), 3.78 (m, 3-H); m/z. 378 (M<sup>+</sup>, 78%), 360 (81), 346 (85), 332 (46), 318 (100), 300 (52), 256 (64) and 91 (65).

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