

Preliminary communication

NATURAL PRODUCT SYNTHESIS USING π -ALLYLTRICARBONYLIRON LACTONE COMPLEXES: SYNTHESIS OF PARASORBIC ACID, THE CARPENTER BEE PHEROMONE AND MALYNGOLIDE

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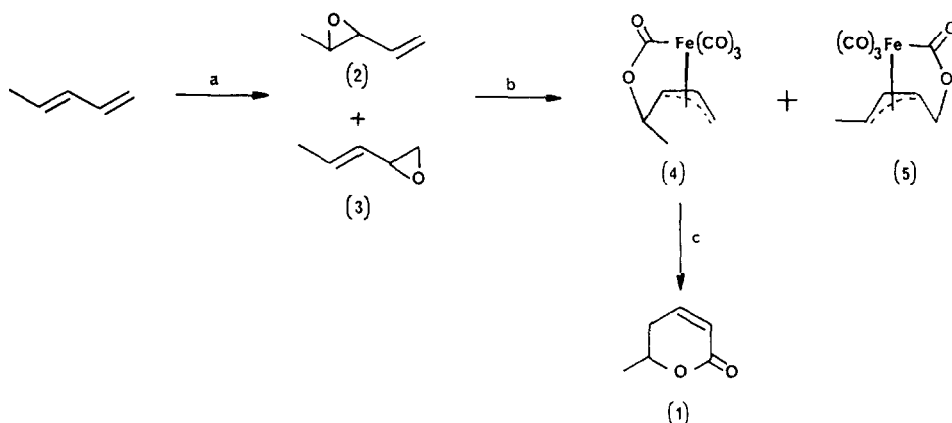
Summary

Preparation of three δ -lactonic natural products, parasorbic acid, the carpenter bee pheromone and malyngolide has been achieved from π -allyltricarbonyliron lactone complexes as the key synthetic intermediates.

π -Allyltricarbonyliron lactone complexes have been used as novel precursors for the preparation of both β -lactones [1] and lactams [2]. We [3] and others [4] have also shown, in a limited number of examples, that these complexes may be exhaustively carbonylated to the δ -lactones. Since these iron complexes can now be conveniently prepared from vinyl epoxides using either $\text{Fe}_2(\text{CO})_9$ in benzene under ultrasonic conditions or from $\text{Fe}_2(\text{CO})_9$ in tetrahydrofuran solution [5], it was attractive to extend the method to δ -lactone natural product synthesis. Here we describe routes to three such compounds.

The first of these was parasorbic acid (1) a natural δ -lactone isolated from the tree *Sorbus acucuparia* [6]. This was achieved by epoxidation of penta-1,3-diene with peracetic acid which gave an inseparable mixture of epoxides 2 and 3 in a 3/1 ratio. Attempts to improve this ratio by using other peracids showed no noticeable advantage. Reaction of the crude epoxides with $\text{Fe}_2(\text{CO})_9$ in THF gave a mixture of π -allyltricarbonyliron lactone complexes, 4 and 5, in 32 and 10% overall yield respectively, which were separable by silica gel chromatography. The structural assignment for these complexes follows from their high field ^1H NMR spectra which are fully in accord with similar compounds [1]. Carbonylation of the complex 4 gave directly parasorbic acid 1 in 73% isolated yield (Scheme 1).

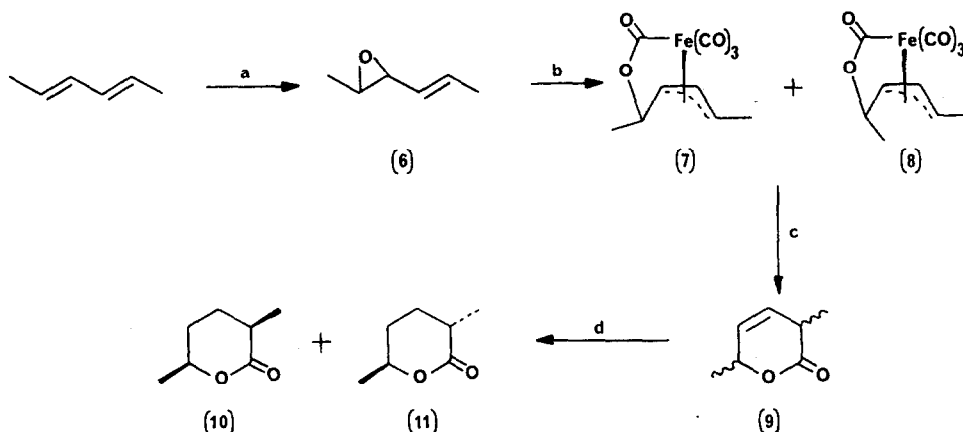
Similarly, epoxidation of hexa-2,4-diene with buffered peracetic acid gave the vinyl epoxide 6. Reaction of 6 with $\text{Fe}_2(\text{CO})_9$ under ultrasonic conditions gave a separable 4/1 mixture of the two π -allyltricarbonyliron complexes 7 and 8 in



SCHEME 1. (a) MeCO_3H , Na_2CO_3 , CH_2Cl_2 , -5°C ; (b) $\text{Fe}_2(\text{CO})_9$, THF; (c) CO, 60 atm, 195°C , 4 h, benzene.

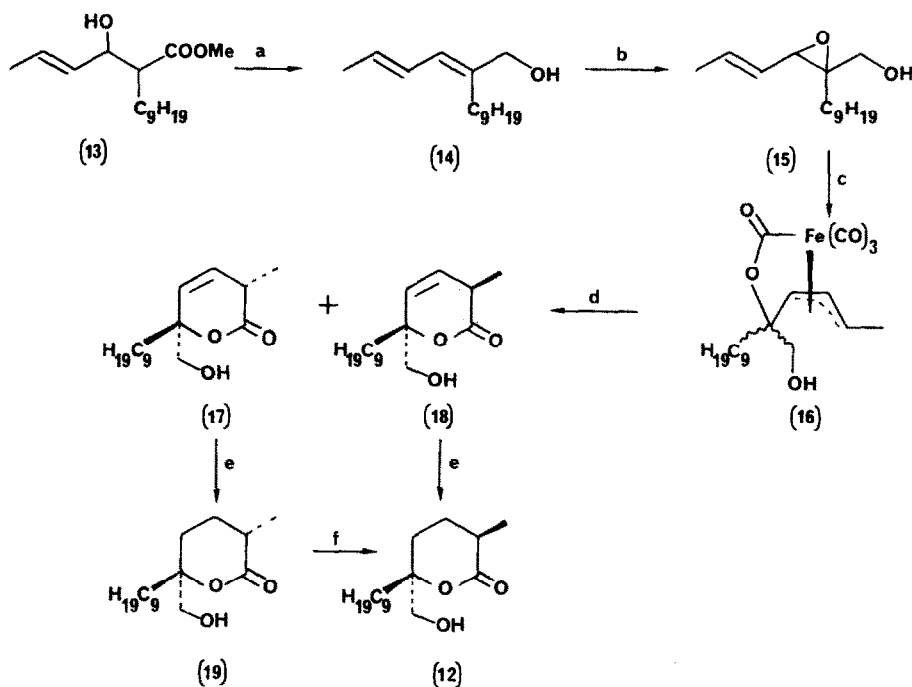
55% combined yield. The structural assignments of 7 and 8 again follow both from careful analysis of their high field ^1H NMR spectra and independent single crystal X-ray structure determinations*. Treatment of 7 or 8 individually or as a mixture, with carbon monoxide gave an identical 1/1 diastereoisomeric mixture of unsaturated δ -lactones 9 (89%). This observation indicates that the lactone complexes undergo isomerisation under the reaction conditions. Hydrogenation of 9 using a Pd/C catalyst gave a 1/1 mixture of the carpenter bee pheromone (10) and the *trans*-isomer 11 in 92% combined yield (Scheme 2). These two δ -lactones are separable by preparative GLC methods. The spectroscopic data for 10 are entirely consistent with previously reported data for the natural products isolated from the mandibular glands of the male bee *Xylocopa hirsutissima* [7].

Finally, synthesis of the unusual δ -lactone antibacterial agent malyngolide (12) was investigated. Malyngolide was first isolated from methanol extracts of an Hawaiian marine blue-green algae *Lyngbya majuscula* [8] and has been the subject of several synthetic studies [9]. Condensation of the anion derived from



SCHEME 2. (a) MeCO_3H , Na_2CO_3 , CH_2Cl_2 , 0°C ; (b) $\text{Fe}_2(\text{CO})_9$, benzene, 1 h ; (c) CO, 300 atm, 90°C , 24 h, (d) H_2 , Pd/C, EtOAc.

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SCHEME 3. (a) KHSO₄, toluene, Δ, 48 h; then DBU, RT, 24 h, then LiAlH₄ in ether added at 0°C; (b) BuOOH, VO(acac)₂, benzene, Δ, 10 min; (c) Fe₂(CO)₉, THF; (d) CO, 300 atm, 90°C, 24 h; (e) PtO₂/H₂, MeOH; (f) LDA, -78°C H⁺ work-up [9d] affords a 9/4 ratio 12/19.

methylundecanoate with crotonaldehyde gave a diastereoisomeric mixture of alcohols 13 in 88% yield. Dehydration of the alcohols 13 was not straightforward and required a one-pot sequence involving initial warming in toluene with potassium bisulphate followed by isomerisation with DBU at room temperature and reductive work-up with ethereal lithium aluminium hydride to give the alcohol 14 in 71% overall yield. Directed epoxidation of the proximal double bond in 14 was achieved using *t*BuOOH/VO(acac)₂ in 88% yield to give (15). Reaction with Fe₂(CO)₉ in THF gave a mixture of tricarbonyliron lactone complexes 16 (71%). Separation of these complexes was possible but was unnecessary in the light of the previously noted isomerisation which occurred on carbonylation. It should also be noted that protection of the primary alcohol during the formation of the iron complexes was not necessary. Carbonylation of 16 using carbon monoxide at 90°C gave a separable mixture of diastereoisomeric δ-lactones 17 and 18 in 74% combined yield. Hydrogenation of 18 using Adams' catalyst gave a 79% yield of malynolide 12 which was identical in all respects to the previously synthesised material [9]. Similarly reduction of 17 gave the alternative isomer 19 (80%) which had previously been shown to be partially convertible to malynolide on treatment with LDA [9d] (Scheme 3). The overall yield of malynolide by this route from methylundecanoate is 11%.

The above syntheses demonstrate that π-allyltricarbonyliron lactone complexes can be used as viable intermediates for natural product synthesis.

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References

- 1 G.D. Annis, S.V. Ley, C.R. Self and R. Sivaramakrishnan, *J. Chem. Soc., Perkin Trans. I*, (1981) 270; G.D. Annis, S.V. Ley, R. Sivaramakrishnan, A.M. Atkinson, D. Rogers and D.J. Williams, *J. Organomet. Chem.*, 182 (1979) C11.
- 2 (a) G.D. Annis, E.M. Hebblethwaite, S.T. Hodgson, D.M. Hollinshead and S.V. Ley, *J. Chem. Soc., Perkin Trans. I*, 1983, 2851; (b) S.T. Hodgson, D.M. Hollinshead, S.V. Ley, *J. Chem. Soc., Chem. Commun.*, 1984, 494.
- 3 G.D. Annis, S.V. Ley, C.R. Self, R. Sivaramakrishnan and D.J. Williams, *J. Chem. Soc., Perkin Trans. I*, (1982) 1355.
- 4 R. Aumann, H. Ring, C. Kruger and R. Goddard, *Chem. Ber.*, 112 (1979) 3644.
- 5 A.M. Horton, D.M. Hollinshead and S.V. Ley, *Tetrahedron*, (1984) 1737.
- 6 F. Dean, *Naturally Occurring Oxygen Ring Compounds*, Butterworths, London, 1963, p. 102; L.J. Haynes in *Modern Methods of Plant Analysis*, K. Paech (Ed.), Vol. II, Springer Verlag, Berlin, 1955, p. 583.
- 7 H.H.W. Velthuis and J.F. De Camargo, *Neth. J. Zoology*, 25 (1975) 516.
- 8 J.H. Cardllina II, R.E. Moore, E.V. Arnold and J. Clardy, *J. Org. Chem.*, 44 (1979) 4039.
- 9 (a) Y. Sakito, S. Tanaka, M. Asami and T. Mukaiyama, *Chem. Lett.*, (1980) 1223; (b) J.H. Babler, B.J. Invergo and S.J. Sarussi, *J. Org. Chem.*, 45 (1980) 4241; (c) G. Cardillo, M. Orena, G. Porzi and S. Sandri, *J. Org. Chem.*, 46 (1981) 2439; (d) K. Matsuo, T. Kinuta and K. Tanaka, *Chem. Pharm. Bull.*, 29 (1981) 3047; K. Matsuo and K. Tanaka, *Chem. Pharm. Bull.*, 29 (1981) 3070; (e) S. Torii, T. Inokuchi and K. Yoritaka, *J. Org. Chem.*, 46 (1981) 5030; (f) T. Kogure and E.L. Eliel, *J. Org. Chem.*, 49 (1984) 576.