

SYNTHESIS OF α, β -UNSATURATED BUTENOLIDES FROM ALLENIC ACIDS

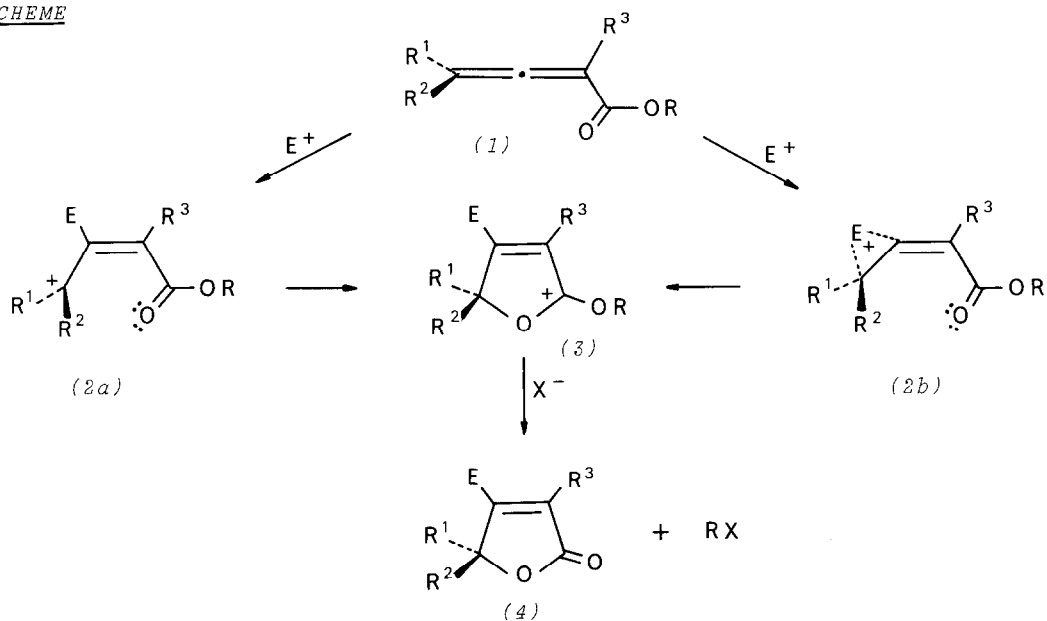
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The electrophile-initiated cyclisation of allenic acids and esters provides a general route for the synthesis of β -substituted α, β -unsaturated butenolides.

The γ -lactone ring system is a common feature in a wide variety of natural products, and a number of methods are available for its construction.¹ We were intrigued by the synthetic potential of the rather direct approach shown in the *Scheme*, especially since the strategy is open to a potentially wide variety of initiating electrophiles E^+ , and includes the possibility of transfer of axial chirality in the allene (1) into central chirality in the butenolide (4). If cyclisation is to be feasible, then E^+ must attack the central C atom of the allene *anti* to the carboxyl group. This may be especially favourable because of nucleophilic assistance from one of the lone pairs of the carbonyl oxygen atom. In the *s-cis* conformations shown

Scheme



for the intermediate ions (2a) and (2b), the lone pair in the p-orbital of oxygen is close to, and in the same plane as the p-orbital of the electron-deficient non-vinyl C atom. Thus, stereoselectivity could accrue from reaction through the perpendicular allyl cation (2a), as well as *via* the onium ion (2b).

These synthetic possibilities, including the transfer of chirality, have been partially realised already, but only for the electronically favourable cases where R¹ and/or R² is aryl, and then only for protonation (E⁺ = H⁺; R = H, Me, or Et)² and bromination (E⁺ = Br⁺; R = H).³ We have conducted a short feasibility study of the more general application of the above strategy for butenolide synthesis, concentrating mainly on simple allenic acids and esters (1) in which R¹, R², and R³ are H or alkyl, and present typical results here. Product yields and reaction conditions have not been optimised at this time.⁴

Reaction of the esters (1a) and (1c)⁵ with 1 equivalent of bromine in carbon tetrachloride solution at 20° C for 12 h afforded, respectively, the bromolactones (4a; 56%, m.p. 106-108° C) and (4e; 58%, m.p. 96-98° C). Iodolactonisation of the acid (1b)⁶ with 1 equivalent of iodine in acetonitrile solution, under similar conditions, gave 4-iodo-3,5,5-trimethyl-2(5H)-furanone (4d), m.p. 140-141° C, in 75% yield. Treatment of the racemic acids (1d) and (1e)⁷ with 2 equivalents of iodine and 5-6 equivalents of potassium iodide in 0.5M sodium hydrogen carbonate at 20° C for 24-48 h afforded, respectively, the iodolactones (4e; 57%, m.p. 58-59° C) and (4k; 55%, m.p. 154-156° C).

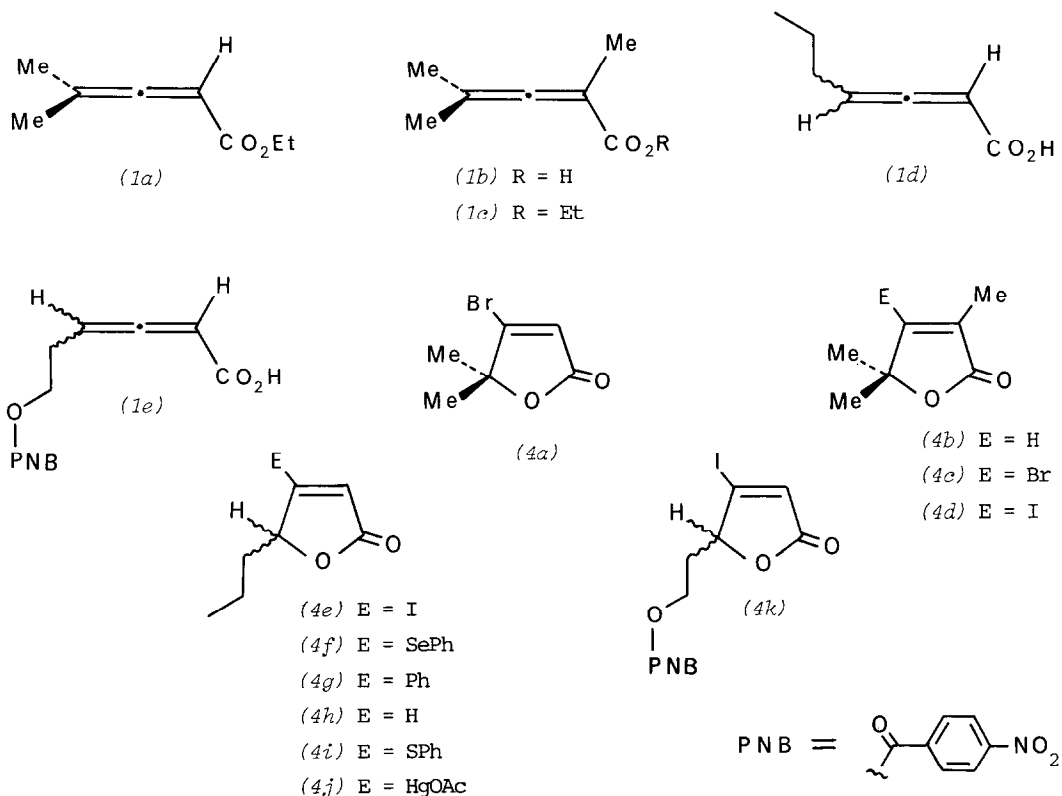
Proton-initiated cyclisation also proceeds readily; for example, reaction of the acid (1b) with aqueous ethanolic sulphuric acid at reflux for 12 h gave lactone (4b), m.p. 56-57° C, in 52% yield. Acetoxymercuration may also be of general synthetic value for treatment of the acid (1d) with 1 equivalent of mercuric acetate in methanol at 20° C for 48 h gave lactone (4j) in 70% yield.

The preliminary results obtained with electrophilic sulphur or selenium were somewhat disappointing. Thus, reaction of the acid (1d) with phenylselenenyl chloride (1.1 equivalents) in dichloromethane containing triethylamine (1 equivalent) at -78° C for 6 h, and then 20° C for 12 h, gave the lactone (4f), an oil, in 34% yield. The similar reaction of (1d)

with phenylsulphenyl chloride gave lactone (4i), also an oil, in only 12% yield. However, optimisation of the reaction conditions may well greatly improve the efficiencies of these processes.

De-selenization of (4f) with W-2 Raney nickel in acetone at reflux for 7 h followed an interesting pathway for it afforded a 4:7 mixture of the lactones (4g) and (4h), respectively, in almost quantitative yield. These compounds were separable by column chromatography over silica gel.

The application of the above strategy to the direct introduction of oxygen functionality (*e.g.* $E^+ = ^+OH$) would clearly be of considerable value, for it would give simple access to the tetric acids. Furthermore, the indirect introduction of other types of E group, *e.g.* by a nucleophilic 1,4-addition/elimination sequence (with expulsion of halide ion), for which there is adequate precedent,⁹ would appreciably diversify the general synthetic method. The various ramifications of the conversion of allenic acids and esters into butenolides, including stereospecificity, form part of our continuing interest in this area.



Acknowledgements: M. S. I. thanks the Universiti Teknologi Malaysia for financial support. We are happy to acknowledge the contributions of Janet Liston and Brian J. Veitch to this study *via* undergraduate project work. We are indebted to Mr. R.A. Fleming for n.m.r. services.

REFERENCES

- ¹ (a) F.M. Dean, 'Naturally Occurring Oxygen Ring Compounds', Butterworths, London, 1963.
(b) G. Pattenden, *Fortschr. Chem. org. Naturstoffe*, 1978, **35**, 133.
(c) Y.S. Rao, *Chem. Rev.*, 1976, **76**, 625.
- ² E.P. Kohler and W.J. Whitcher, *J. Am. Chem. Soc.*, 1940, **62**, 1489; G. Asknes and P. Frøyen, *Acta Chem. Scand.*, 1968, **22**, 2347; G. Kresze, W. Runge, and E. Ruch, *Annalen*, 1972, **756**, 112; S. Musierowicz and A. Wróblewski, *Zesz. Nauk. Politech. Lodz, Chem.*, 1973, 165 (*Chem. Abstr.*, 1974, **80**, 108128p); S. Musierowicz, A. Wróblewski, and H. Krawczyk, *Tetrahedron Lett.*, 1975, 437; G. Kresze, L. Kloimstein, and W. Runge, *Annalen*, 1976, 979.
- ³ K. Shingu, S. Hagishita, and M. Nakagawa, *Tetrahedron Lett.*, 1967, 4371.
- ⁴ Satisfactory spectroscopic, mass spectral, and micro-analytical data were obtained for all new compounds.
- ⁵ R.W. Lang and H.-J. Hansen, *Helv. Chim. Acta*, 1980, **63**, 438.
- ⁶ Prepared by hydrolysis of the ester (1c) with 2M aqueous sodium hydroxide in methanol (3:2 v/v) at 20° C for 12 h.
- ⁷ The carboxyl groups of the acids (1d) and (1e) were introduced by the ene addition of the 1-alkyne [*i.e.* 1-hexyne for (1d)] to indane-1,2,3-trione, followed by oxidative cleavage of the ene adduct with periodic acid:
G.B. Gill and K.S. Kirollos, *Tetrahedron Lett.*, 1982, **23**, 1399.
- ⁸ For example, see: D. Caine, A.S. Frobese, and V.C. Ukachukwu, *J. Org. Chem.*, 1983, **48**, 740.

(Received in UK 17 July 1985)