

Novel Oxidative Conversion of β,γ -Unsaturated Acids into Butenolides: Synthesis of Heritonin and Heritolt

Subhash P. Chavan,* P. K. Zubaidha, Chitra A. Govande and Y. Tripura Subba Rao

National Chemical Laboratory, Pune 411 008, India

A novel strategy of converting β,γ -unsaturated esters to butenolides involving oxidative cyclisation with ceric ammonium nitrate at room temperature is described.

Interest in the synthesis of butenolides, as a consequence of their natural abundance in a variety of natural products including biologically active molecules, has been the focus of current interest and continues to stimulate development of new strategies.^{1,2}

In continuation of our work in the synthesis of biologically active molecules *viz.* heritol **1a**,^{3,4a} heritonin **1b**,^{3,4b} heritanin **3b**, vallipin **2**,^{4b} vallapianin **3a**^{4b} and related compounds isolated recently from the mangrove plant *Heritiera littoralis* by Miles and coworkers, we became interested in the development of methodologies to generate these unusual skeletons. We have recently reported² an efficient entry into butenolides from β,γ -unsaturated esters *via* diols involving transesterification with concomitant dehydration. Although palladium mediated direct conversion of β,γ -unsaturated acids to butenolides has been reported to proceed in poor to moderate yields,⁵ a recent publication reports that these results could not be duplicated.⁶

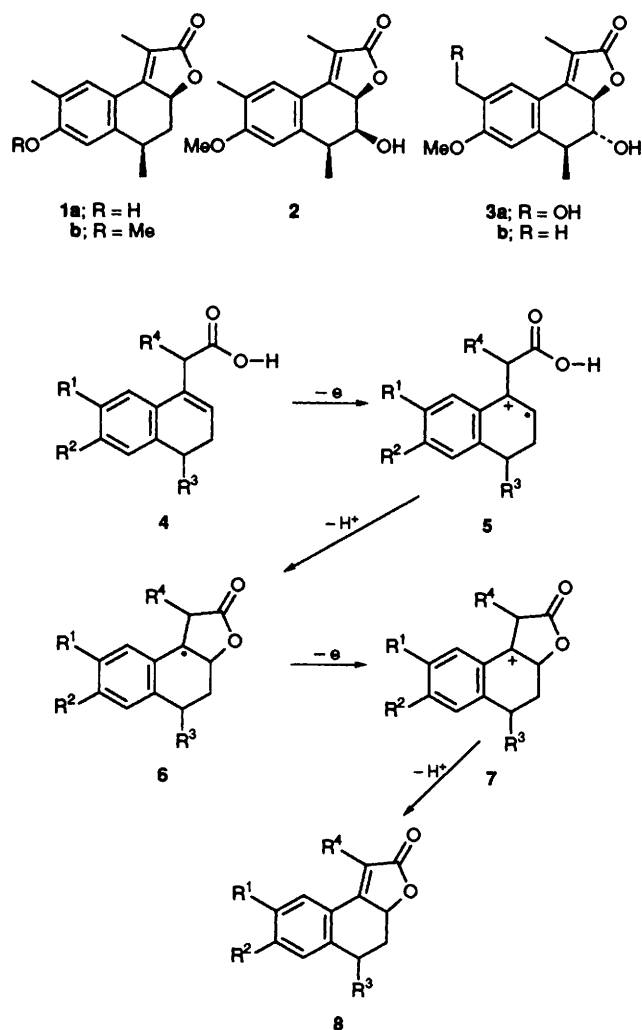
We reasoned that it should be possible to directly convert β,γ -unsaturated acid **4** to butenolide **8** if one can selectively

and effectively generate the cation radical **5**. Intramolecular trapping of the cation radical would generate the butyrolactone **6** which on further oxidation and loss of proton would generate butenolide **8**.

The concept of atom economy as a strategy for synthetic efficiency has been of recent interest and is practised and described by Trost.⁷ This paper describes our contribution of atom economy as a strategy to construct butenolides efficiently.

We describe a novel, mild and efficient methodology based on the above mentioned strategy to convert β,γ -unsaturated acids to butenolides. The propensity of ceric ammonium nitrate (CAN) to act as a single electron oxidant is well documented in literature.⁸ Thus, when acid of general formula **4** was subjected to treatment with CAN, butenolides **8** were obtained in good to excellent yields (Table 1).[‡]

The β,γ -unsaturated acids **4** were prepared easily by the saponification of the corresponding esters **10** which in turn were prepared from corresponding ketones in high yields. Typical procedure is as follows: To a mixture of CAN (0.2 mmol) and NaHCO₃ (0.2 mmol) in 20 ml of dry acetonitrile was added the acid **4** (0.1 mmol) during a period of 5 min. After completion of the reaction, monitored by TLC, the reaction mixture was filtered through celite and concentrated to a residue which was chromatographed on silica gel with (9 : 1) petroleum : ethyl acetate as eluent.



Scheme 1

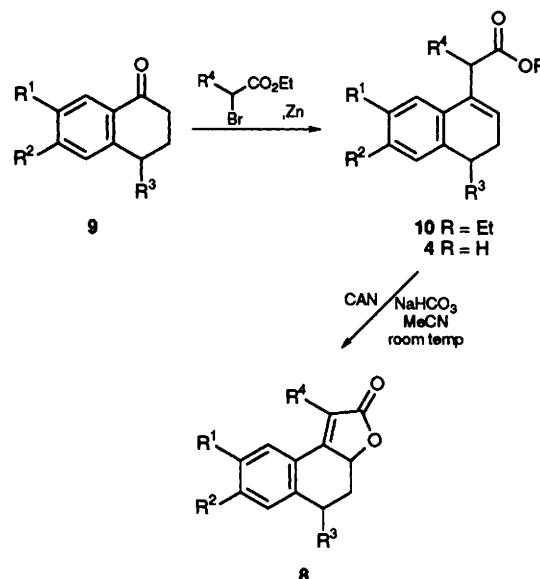


Table 1

Entry	R ¹	R ²	R ³	R ⁴	10 yield (%)	4 yield (%)	8 yield (%)
1	H	H	H	H	87	82	67
2	H	H	H	Me	90	86	72
3	H	H	H	Et	92	84	87
4	H	H	H	Pr ⁱ	89	89	92
5	Me	H	Me	Me	80	78	74
6	OMe	Me	H	Me	90	81	70
7	Me	OMe	Me	Me	85	89	36

To delineate the generality and efficacy of our methodology, we chose to incorporate bulky groups on the butenolide moiety. A noteworthy feature of this transformation is obvious from Table 1 in that on progressing from R = H to Pri (entries 1–4), there is a steady increase in the bulk of R and there is a corresponding steady increase in the yield of formation of butenolides.

This trend although surprising from the point of view of *peri* interactions may help the approach of the carboxylic acid to the double bond. This effect also may be attributed to the 'Thorpe-Ingold' effect which helps the cyclisation to proceed in high efficiency. This observation is in stark contrast to the poor yields obtained in intramolecular Wittig-Horner-reactions ascribed to *peri* interactions.⁹

To extend the scope of the methodology we have synthesized a variety of butenolides using the above protocol (see Table 1). We have successfully employed the above concept towards the synthesis of natural products heritonin **1a** (entry 7). Since the conversion of heritonin to heritol has been already reported by us earlier,³ this constitutes a total formal synthesis of heritol.

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Footnotes

† NCL Communication No. 5927.

‡ The spectral (IR, NMR ¹³C, mass) properties of the compounds were consistent with the assigned structures. All new compounds were characterised by elemental analyses as well.

References

- 1 (a) T. H. Black and T. S. McDermott, *J. Chem. Soc., Chem. Commun.*, 1991, 184; (b) R. B. Cory, B. M. Ritchie and A. Shrier, *Tetrahedron Lett.*, 1990, **31**, 6789 and references therein.
- 2 S. P. Chavan, P. K. Zubaidha and N. R. Ayyangar, *Tetrahedron Lett.*, 1992, **33**, 4605.
- 3 P. K. Zubaidha, S. P. Chavan, U. S. Racherla and N. R. Ayyangar, *Tetrahedron*, 1991, **47**, 5759.
- 4 (a) D. H. Miles, D. S. Lho, A. A. de la Cruz, E. D. Gomez, J. A. Weeks and J. L. Atwood, *J. Org. Chem.*, 1987, **52**, 2930; (b) D. H. Miles, A. Ly, V. Chittawong, A. A. de la Cruz and E. D. Gomez, *J. Nat. Prod.*, 1989, **52**, 896.
- 5 A. Kasahara, T. Izumi, K. Sato, M. Maemura and T. Hayasaka, *Bull. Chem. Soc. Jpn.*, 1977, **50**, 1899.
- 6 R. C. Larock and T. R. Hightower, *J. Org. Chem.*, 1993, **58**, 5298.
- 7 B. M. Trost, *Science*, 1991, 1471 and references therein.
- 8 G. A. Molander, *Chem. Rev.*, 1992, **92**, 29 and references therein.
- 9 H. Irie, R. Matsumoto, M. Nishimura and Y. Zang, *Chem. Pharm. Bull.*, 1990, **38**, 1852.