Tetrahedron Letters,Vol.24,No.52,pp 5827-5830,1983 0040-4039/83 $3.00 + .00
Printed in Great Britain

CONJUGATE PHENYLSELENOLACTONIZATION COUPLED WITH ALLYLIC SELENOXIDE REARRANGEMENT FOR FUNCTIONALIZING DIENYLACETIC ACIDS

ANTHONY J. PEARSON,*[1a] TAPAN RAY,[1a] IAN C. RICHARDS,[1a]
JON CLARDY[1b] and LINDA SILVEIRA[1b]

Department of Chemistry, Case Western Reserve University, Cleveland, Ohio 44106
Department of Chemistry, Baker Laboratory, Cornell University, Ithaca, New York 14853 (U.S.A.)

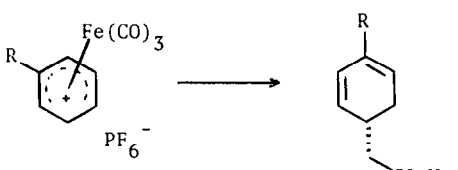
Abstract - Use of the title reactions for the regioselective, and stereoselective functionalization of a range of dienylacetic acids, available from simple organoiron chemistry, is presented.

In order to be useful for organic synthesis, nucleophile addition to tricarbonyldienyliron cations,[2] followed by demetallation, must result in substituted dienes (a) which are not readily available by standard organic synthesis methodology and (b) which can be further functionalized in a selective manner. We report herein a sequence of diene functionalization using organoiron and organoselenium chemistry which meets these requirements and which capitalizes on diene selenolactonization coupled with allylic selenoxide [2,3]sigmatropic rearrangement[3] to provide a potentially useful approach to intermediates of defined regio- and stereochemistry. While selenolactonization of monoolefinic acids is a well-established procedure,[4] the potential for carrying out the reaction in a conjugate manner does not appear to have been widely investigated.[5]

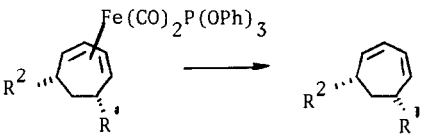
A number of cyclic and acyclic dienylacetic acids were prepared as outlined in Scheme 1, and a typical procedure is described for the cyclohexadiene derivative 1a, not available by standard procedures, but readily prepared in good overall yield from tricarbonylcyclohexadienyliron hexafluorophosphate using a four-step sequence:(i) $NaCH(CO_2Me)_2$, THF, 0°C, 10 min; (ii) Me_3NO, benzene, 30°C, 24 h;[3](iii) NaCN, wet DMSO, 110°C, 24 h; (iv) KOH, H_2O, MeOH, 20°C, 4 h. The cycloheptadiene derivatives 4a and 4b were prepared by demetallation of the previously reported complexes[7] 2a and 2b, followed by decarboxylation, but some diene rearrangement was observed at temperatures above 90°C so this conversion was performed at lower temperatures for prolonged reaction time (NaCN, wet DMSO, 70°C, 36 h). Alternatively, the acids could be produced in higher yield by desulfurization[8] of the phenylsulfonylacetic ester derivatives 3c and 3d (6% Na-Hg amalgam, MeOH, Na_2HPO_4, 0°C, 1 h, then 23 °C, 1 h, 75% yield), themselves readily available by oxidative demetallation of the complexes 2c and 2d. The preparation of the acyclic dienylacetic ester 5 illustrates the potential usefulness of organoiron chemistry for functionalizing readily available acyclic dienes,[9] (see Scheme 1).

With appropriate diene derivatives now in hand we turned our attention to their selenolactonization reactions, summarized in Scheme 2. The cyclohexadienes 1a and 1b underwent very clean reactions (PhSeCl, Et_3N, CH_2Cl_2, 23°C, 2.5 h) to give single crystalline γ lac-

tones (ν_{max} 1775 cm^{-1}) in yields greater than 90%, readily assigned the gross structures 6a (m.p. 80°C) and 6b (m.p. 74°C), respectively, on the basis of ^1H NMR decoupling experiments. However, the stereochemistry of these selenolactones could only be resolved by single crystal X-ray analysis[11] of 6a (see Figure).[12] Treatment of 6a with hydrogen peroxide (5% aq. H_2O_2, pyridine, aqueous work-up) afforded the hydroxy lactone 7a via [2,3]sigmatropic rearrangement of an intermediate allylic selenoxide.[3] Conversion of 7a to the acetate 7b (Ac_2O, py., 0°C, o/night) followed by ozonolysis (O_3, CH_2Cl_2-MeOH, -78°C; Me_2S work-up) afforded the dialdehyde 8, which has relative stereochemistry corresponding to C(4), C(5) and C(6) of the macrolide antibiotic magnamycin B (9). Thus, the sequence: conjugate selenolactonization/selenoxide rearrangement provides an excellent method equivalent to regiospecific and stereospecific bis-hydroxylation of 2,4-cyclohexadienylacetic acids.

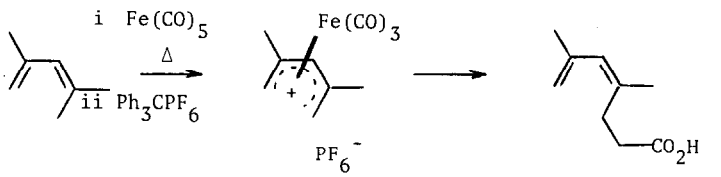


1a R = H
1b R = Me



2a R' = H, R^2 = $CH(CO_2Me)_2$ 3a
2b R' = Me, R^2 = $CH(CO_2Me)_2$ 3b
2c R' = H, R^2 = $CH(SO_2Ph)CO_2Me$ 3c
2d R' = Me, R^2 = $CH(SO_2Ph)CO_2Me$ 3d

4a R' = H, R^2 = CH_2CO_2H
4b R' = Me, R^2 = CH_2CO_2H



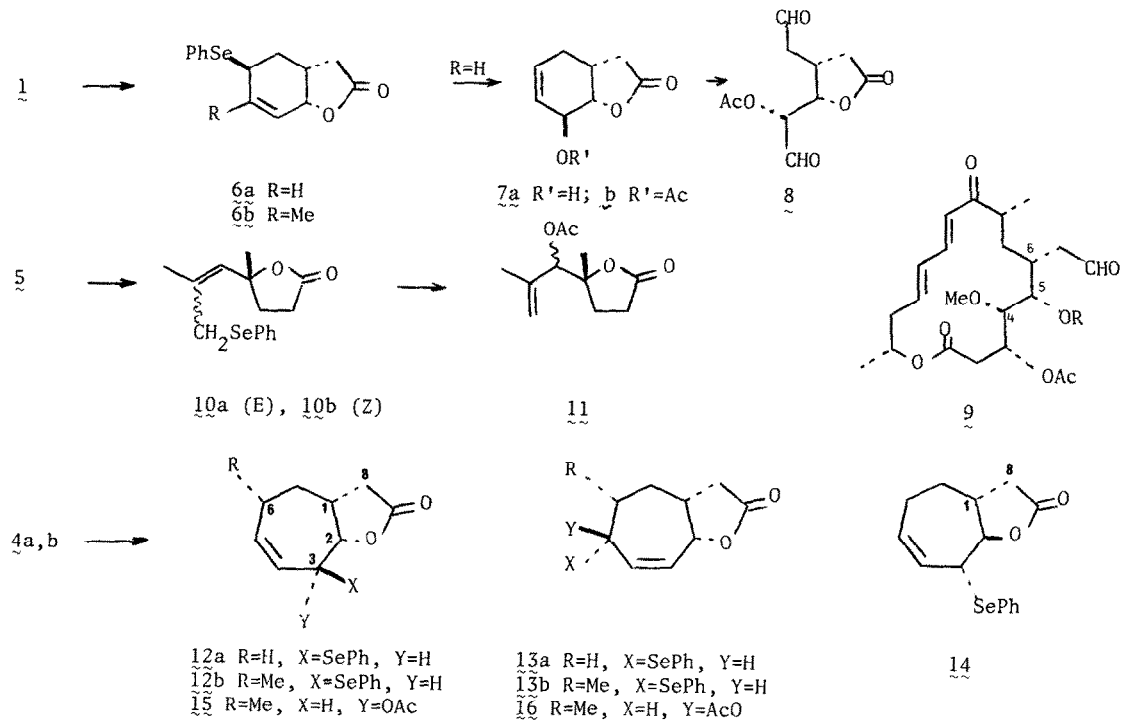
SCHEME 1

5

The acyclic dienylacetic acid 5 was subjected to similar lactonization conditions (PhSeCl, Et_3N, CH_2Cl_2, 20°C, 24 h) to give a 4:1 mixture (NMR) of E and Z unsaturated lactones 10a and 10b inseparable on TLC. Assignment of double bond geometry of the major isomer was accomplished using n.O.e. difference spectroscopy: irradiation at the vinyl proton singlet (δ 5.13) caused pronounced enhancement of the CH_2SePh singlet (δ 3.42), but no effect on the vinyl-Me singlet. Subjection of the mixture of lactones to selenoxide formation/rearrangement conditions (3% aq. H_2O_2, THF, 20°C, 2 h; addition of Et_3N and aqueous work-up), followed by acetylation (Ac_2O, py., 23°C, 24 h) gave a 3:2 mixture of two stereoisomeric acetates 11 in 60% yield (200 MHz ^1H NMR: AcO singlets at δ 2.098, major, and δ 2.081, minor isomer).

The cycloheptadiene derivatives 4a and 4b furnished some very interesting results of selenolactonization, best results being obtained using the more reactive PhSeBr. Lactonization of the monosubstituted diene 4a (1.0 equiv PhSeBr, Et_3N, CH_2Cl_2, -72°C then -20°C, 2 h) gave

85-90% yield of a mixture of three products 12a, 13a and 14 in ratio 15:5:1, separated by preparative HPLC.[10] The structure and stereochemistry of the major and minor products (12a and 14) were readily assigned using 200 MHz ^{1}H NMR shieldings and coupling constant data, from extensive spin decoupling experiments, but the stereochemistry of 13a was assigned only after comparison with products from the disubstituted cycloheptadiene 4b. Clearly, formation of 12a (m.p. 95°C) as the major product indicates that the cycloheptadiene 4a behaves predominantly as though it were a monoalkene, strongly suggesting that the diene in this compound adopts a twisted conformation in which there is very little conjugation.[13] Dreiding models indicate that the planar diene conformation has considerable angle strain.



SCHEME 2

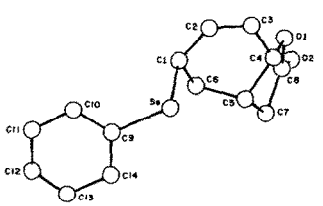


FIGURE. Computer plot of X-ray structure of lactone 6a.

The methyl-substituted cycloheptadienylacetic acid 4b underwent selenolactonization (1 equiv PhSeBr, Et_3N, CH_2Cl_2, -72°C to -20°C, 2 h) to give an equimolar mixture of lactones 12b, m.p. 96°C, and 13b (oil) separated by HPLC. In fact, the ratio of lactones obtained from 4b is more variable and is strongly dependent on quality of the PhSeBr and reaction conditions. For example, performing the reaction at -20°C for 1 h (instead of starting at -72°C) resulted in a 1:4 mixture of 12b and 13b.

The stereochemistry of the conjugate lactonization product 13b was arrived at as follows. Oxidation of 12b and 13b (8% H_2O_2, THF, -20°C, 3 h; addition of Et_3N, followed by aqueous work-up) and acetylation (Ac_2O, py., 20°C, 16 h) gave acetates 16 and 15, respectively, which differed in their ^1H NMR coupling constant data from the selenolactones of related structure. For example, 15 gave $J_{1,2}$ = 8.9 Hz, and $J_{2,3}$ = 2.2 Hz, compared to 12b, which gave $J_{1,2}$ = 6.6 Hz, and $J_{2,3}$ = 8.9 Hz. The data is consistent with the stereochemical assignment shown, assuming a chair-like conformation with Me and lactone groupings equatorial, and OAc axial. An alternative trans-lactone structure for 15, with OAc and lactone oxygen substituents cis, also fits the NMR data, but careful analysis of Dreiding models for the corresponding selenolactone is strongly indicative that [2,3]-sigmatropic rearrangement of a derived selenoxide would be a very high energy, and highly unlikely, process.

Acknowledgements We are extremely grateful to the National Institutes of Health, General Medical Sciences, for financial support of our programs, the National Science Foundation for a grant (CHE 80-24633) towards the purchase of a Varian XL-200 NMR machine, and to Dr. E. Constable, Cambridge University, England, for the n.O.e. difference spectra (on Bruker WH400).

References

1) (a) Case Western Reserve University, (b) Cornell University.
2) Reviews: A. J. Pearson, Acc. Chem. Res., 1980, 13, 463; Comprehensive Organometallic Chemistry, Ed. G. Wilkinson, F. G. A. Stone, E. W. Abel, Pergamon Press, 1982, Chapter 58; Transition Met. Chem., 1981, 6, 67.
3) K. B. Sharpless and R. F. Lauer, J. Am. Chem. Soc., 1972, 94, 7154; 1973, 95, 2697; H. J. Reich, J. Org. Chem., 1975, 40, 2570.
4) M. de M. Campos and N. Petragnani, Tetrahedron Lett., 1959, 6, 11; Chem. Ber., 1960, 93, 317; K. C. Nicolaou, S. P. Seitz, W. J. Sipio and J. F. Blount, J. Am. Chem. Soc., 1979, 101, 3884; D. L. J. Clive, V. Farina, A. Singh, C. K. Wong, W. A. Kiel and S. M. Menchen, J. Org. Chem., 1980, 45, 2120; K. C. Nicolaou, Tetrahedron, 1981, 37, 4097.
5) We are aware of only one previous example of conjugate cyclofunctionalization: T. R. Hoye and A. J. Caruso, J. Org. Chem., 1981, 46, 1198.
6) Y. Shvo and E. Hazum, J. Chem. Soc. Chem. Commun., 1974, 336.
7) A. J. Pearson, S. L. Kole and B. Chen, J. Am. Chem. Soc., 1983, 105, 4483.
8) For typical procedure, see: B. M. Trost, H. C. Arndt, P. E. Strege and T. R. Verhoeven, Tetrahedron Lett., 1976, 3477.
9) For other acyclic diene-$Fe(CO)_3$ complexes see: H. Reihlen, A. Gruhl, G. von Hessling and O. Pfrengle, Liebigs Ann. Chem., 1930, 482, 161; J. E. Mahler and R. Pettit, J. Am. Chem. Soc., 1963, 85, 3955;G. F. Emerson and R. Pettit, ibid., 1962, 84, 4591; R. Pettit, J. C. Barborak and L. Watts, ibid., 1966, 88, 1328; C. P. Lillya and R. A. Sahatjian, J. Organomet. Chem., 1971, 32, 371; R. E. Graf and C. P. Lillya, Chem. Comm., 1973, 271; T. H. Whitesides and R. W. Arhart, J. Am. Chem. Soc., 1971, 93, 5296; T. H. Whitesides, R. W. Arhart and R. W. Slaven, ibid., 1973, 95, 5792; T. H. Whitesides and J. P. Neilan, ibid., 1973, 95, 5811; T. H. Whitesides and R. W. Slaven, J. Organomet. Chem., 1974, 67, 99.
10) All compounds were obtained as racemic mixtures and were fully characterized using 200 MHz ^1H NMR and IR spectroscopy, and high resolution mass spectroscopy and/or combustion analysis. NMR assignments in most cases were made by spin decoupling experiments, and details will be reported in a full paper.
11) Full details will be given elsewhere. Refined coordinates are deposited at the Cambridge Crystallographic Data Centre.
12) The stereochemistry of conjugate lactonization is mechanistically interesting and will be discussed in a forthcoming full paper.
13) See also: P. Crews, Chem. Comm., 1971, 583; B. Schrader and A. Ansmann, Angew. Chem. Int. Ed. Engl., 1975, 14, 364; J. F. Chiang and S. H. Bauer, J. Am. Chem. Soc., 1966, 88, 420; K. Hagen and M. Traetteberg, Acta Chem. Scand., 1972, 26, 3643.

(Received in USA 5 August 1983)